"NONSPECIFIC DIAGNOSES" IN ONCOLOGIC PATHOLOGY: ASSOCIATION WITH CANCER CENTER VOLUME AND FACILITY TYPE AND PATIENT CHARACTERISTICS

BY

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"NONSPECIFIC DIAGNOSES" IN ONCOLOGIC PATHOLOGY:
ASSOCIATION WITH CANCER CENTER VOLUME AND FACILITY TYPE AND PATIENT CHARACTERISTICS

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ABSTRACT

Purpose: Precise characterization of cancers is essential for clinical management and research. Prior studies of cancer care reported associations of process measures and outcomes with cancer center facility type and case volume. However, it is not known whether these facility characteristics are associated with use of nonspecific cancer diagnoses.
Methods: This exploratory study of records in the National Cancer Database (NCDB) for patients diagnosed from 1998-2008 used bivariate analyses to identify diagnoses with the greatest variation among cancer center types (Community Center, Comprehensive Community Center, Community Network, Teaching/Research Center, and National Cancer Institute (NCI)-designated Comprehensive Program). Diagnoses from this list that were likely to compromise clinical management were selected for study of the influence of facility characteristics on trends in prevalence over time. Logistic regression was used to determine whether the association of facility type with nonspecific diagnoses was independent of center case volume and patient characteristics.
Results: Exploratory review of 14 highest incidence cancer sites identified 10 nonspecific diagnoses from 5 sites were identified as likely to adversely affect patient care and/or research and which were used more often at Community Centers than at NCI-designated Comprehensive Programs. Diagnoses with the greatest prevalence differences included “adenocarcinoma, not otherwise specified (NOS)” of the uterinus (20.4%); “renal cell carcinoma, NOS” (15.0%); “adenocarcinoma, NOS of the ovary (8.2%)”, and “malignant non-Hodgkin’s lymphoma, NOS (4.9%)”. From 1998-2008, the nonspecific diagnosis prevalence gap between Community Centers and NCI-designated Programs decreased for ovarian “papillary adenocarcinoma, NOS”; and uterine “adenocarcinoma, NOS”, increased for “renal cell carcinoma, NOS”; “malignant lymphoma, NOS”; and pancreatic “malignant neoplasm, NOS”, and remained relatively stable for “non-Hodgkin’s lymphoma, NOS”; ovarian “adenocarcinoma, NOS”; ovarian “carcinoma, NOS”; and pancreatic “carcinoma, NOS”. Facility type remained significantly associated with nonspecific diagnoses in logistic regression models including facility case volume and regional location, and several patient-level variables.
Conclusion: Prevalence of nonspecific cancer diagnoses varies substantially and independently by facility type and may adversely influence patient care and research.

CHAPTER I – INTRODUCTION

Introduction and rationale

Cancer is the second most common cause of death in the United States and worldwide.[1,2] The prognosis for people diagnosed with cancer has improved substantially; 5-year survival has increased from 50% between 1975 and 1977 to 68% between 1999 and 2005.[3] However, cancer is not a single disease; it is a family of hundreds of related diseases, each of which has a unique profile of epidemiologic, clinical, and molecular characteristics. Clinical and public health interventions to reduce the burden of cancer therefore require accurate characterization of the type(s) of cancer present in individuals and populations. Although clinical symptoms, physical examination, and diagnostic imaging tests can suggest a diagnosis of malignancy, definitive diagnosis and classification of cancer is almost always based on examination of tissue samples by a pathologist. Classification of neoplastic disease is increasingly supplemented by molecular diagnostic testing, but still remains largely dependent on interpretation of light microscopic observations. High quality of testing in oncologic surgical pathology is therefore the cornerstone of clinical oncology and cancer surveillance.

The main goal of oncologic surgical pathology is to accurately classify the tumor or, in other words, assign a name that conveys useful information to clinicians reading the pathology report that will help them make decisions concerning the most appropriate treatment options for a patient. Other goals include providing information regarding the extent to which the tissue samples are affected by cancer (this information is used in determining the cancer's stage) and regarding morphological and molecular

characteristics of the cancer that may help assess the patient's regarding prognosis and likely response to various treatments.

Any system of classification and any users of such systems can be placed at some point along a spectrum of "lumping" (use of a relatively small number of broad categories) versus "splitting" (use of a larger number of narrower categories). Although these terms may sound somewhat colloquial, they are widely used and recognized in pathology practice and academic literature (and other fields involving classification of medical diagnoses) .[4-8] A diagnosis of "malignant neoplasm, not otherwise specified (NOS)" represents the "lumpiest" of cancer diagnoses. A diagnosis any broader would express uncertainty as to whether a neoplasm is benign or malignant. Moving along this spectrum, slightly narrower diagnoses would include "carcinoma, NOS", "sarcoma, NOS", "lymphoma, NOS", etc. A broad or low resolution diagnosis may be appropriate in some clinical situations but in other situations may not provide sufficient information for guiding therapeutic decisions (or for use in cancer surveillance systems or in analytic epidemiologic investigations of cancer etiology). For example, "lymphoma, NOS" would not be sufficiently detailed to guide a medical oncologist's selection of chemotherapy or immunotherapy regimens. Thus, in some situations, a splitter's highly granular or high-resolution diagnosis might indicate higher quality of pathology services than an excessively broad diagnosis.

Although there are a number of approaches utilized by diverse organizations to assess and improve quality of oncologic surgical pathology, this endeavor faces some unique challenges.[9] Data from registries, from the administrative records of healthcare transactions, and from electronic health records are increasingly applied to quality

assessment in several clinical specialties but, for a number of reasons, have not been used to a significant degree in surgical pathology.

For decades, various professional societies, governmental agencies, and other organizations have collected, analyzed and in some cases publically disclosed data regarding healthcare organizations' structure, processes, and outcomes. Associations between health outcomes and structure or processes of healthcare organizations have been studied in many contexts and provide the rationale for quality recognition and improvement programs that measure structure or processes. For example, the Commission on Cancer sets standards for cancer centers, which address structure (for example, affiliation of physicians in certain specialties with the center) and processes (such as conducting multidisciplinary conferences).[10]

Data from the cancer center-based National Cancer Database (NCDB) have been used for identifying associations between quality and certain characteristics of healthcare organizations. For example, many studies have reported associations between institutional case volume for several complex surgical procedures (such as esophagectomy, pancreatoduodenectomy, radical prostatectomy, or coronary artery bypass grafting) and outcomes including perioperative mortality or morbidity, and even long-term survival.[11,12] However, databases such as NCDB have not been used often to assess quality in oncologic surgical pathology and associations of quality with center characteristics.

Problem statement

Reasons for the recent progress in using registry data for research into relationships between characteristics of healthcare organizations and quality of care include the following:

- Registry data are more available to researchers than results of most quality improvement programs and are collected long term and nationwide
- A 2000 Institute of Medicine (IOM) report on use of cancer data systems for quality improvement [13] and a 2005 IOM report on measuring quality of cancer care [14] have provided guidance for improving such systems and greater awareness of opportunities and benefits.

Application of these approaches to quality assessment and improvement in diagnostic oncologic pathology can be particularly challenging, however. One reason is that the output of surgical pathology is a diagnosis, which is not a "health outcome." Although it is clear that accurate diagnosis is a prerequisite to appropriate treatment, the process/outcome and structure/outcome relationships are difficult to study, because the relationships between health outcomes and the outputs of pathology services (diagnoses) are so strongly influenced by treatment decisions.

Some pathology processes, such as the number of lymph nodes dissected from bowel resection specimens, or reporting of data elements needed to determine pathologic stage, have been associated with institutional volume or teaching/academic status in registry-based studies.[15,16] On the other hand, the primary measure of pathology quality – a correct diagnosis – has not been addressed in these studies.

The "gold standard" for quality assessment in anatomic pathology is concordance with the diagnosis rendered by a recognized expert or by the consensus of qualified

colleagues. This approach is the basis of quality measurement and quality improvement programs provided by organizations such as the College of American Pathologists and the American Society for Clinical Pathology.[9,17] Histologic preparations of tumors on glass microscopic slides (or images of such preparations) are provided to participating laboratories. Each laboratory's diagnosis is submitted and the organization administering the quality assessment program returns information on distributions of diagnoses submitted by other participating laboratories. In other quality assessment and improvement programs, laboratories are instructed to compare their diagnoses to the diagnoses of other laboratories from institutions to which patients have been referred (that is, the patient seeks a second opinion or treatment at a different institution, and that institution's laboratory provides and independent diagnostic opinion on the original specimen) or to diagnoses of expert consultants (for cases with uncertain diagnoses, or upon request of a clinician or patient, the laboratory will send the sample for consultation by a recognized expert at another institution).

Despite their obvious value, limitations of these approaches are that (1) these programs include a minority of patient samples, (2) data from interlaboratory second opinions reside within laboratory information systems and are not readily linked with laboratory structural features and processes, or with patient outcomes, (3) data from consensus surveys of test cases are not linked to databases that include information on health outcomes.

Thus, the problem to be addressed by this project is to determine whether data from registries such as the NCDB can be used to study associations between a quality indicator related to the actual diagnosis in oncologic pathology services (broadness vs. focus of the

diagnosis) and cancer center characteristics such as academic and teaching status or case volume.

Purpose statement

The purpose of this project is, using records in the NCDB for patients diagnosed with cancer from 1998 through 2008, to evaluate the potential relevance of the proportion of low resolution or broad diagnoses to assessment of the quality of diagnostic oncologic pathology services, and explore associations of low resolution diagnoses with cancer center facility type (Community, Community Network, Comprehensive Community, Teaching and Research, and Nation Cancer Institute-designated Comprehensive) and other center-level and patient-level characteristics.

Research questions

This purpose statement is addressed by the following research questions:

1. What is the proportion of broad or nonspecific diagnoses in the NCDB for patients diagnosed with cancer from 1998 through 2008, and treated at cancer centers with varying characteristics (specifically, varying facility type and volume)?

2. For which cancer sites (for example, breast, colorectal, lung, etc.) and for which broad or nonspecific diagnoses are differences in diagnosis prevalence between center types (Community Cancer Center, Community Cancer Network, Comprehensive Community Cancer Center, Teaching and Research Cancer Center, or National Cancer Institute-designated Comprehensive Cancer Program) and case volume categories greatest and, more importantly, likely to be clinically relevant for a substantial number of patients?

3. In multivariable analyses, does the association between the prevalence of nonspecific diagnoses and facility type (Community Cancer Center, Community Cancer Network,

Comprehensive Community Cancer Center, Teaching and Research Cancer Center, or National Cancer Institute-designated Comprehensive Cancer Center) remain statistically significant in models that also include facility case volume by cancer site, as well as patient-level characteristics such as demographics and insurance status.

Significance statement

As noted in the Institute of Medicine (IOM) report on "Interpreting the Volume-Outcome Relationship in the Context of Health Care Quality" [11], associations between facility characteristics and quality of care are important to health insurance purchasers and health plans, consumers (patients), insurers, hospital administrators, regulators, accrediting organizations, professional organizations, and medical educators. Although this IOM report focuses on volume-quality relationships, the same principles apply equally to associations among quality and other facility characteristics such as teaching, research, and academic status. All of these healthcare stakeholders have reasons to be interested in identifying clinical situations in which patients might be better served by having their specimens examined at high volume centers or in those with strong academic affiliations (if our analyses indicate a lower prevalence of clinically-relevant nonspecific diagnoses provided by such facilities).

Thus, this research could serve as a proof of concept regarding a quality assessment and improvement approach that could improve cancer outcomes.

Definition of terms

(Unless otherwise noted by a *, these definitions are based largely on the American Cancer Society online cancer glossary, which as part of my work as ACS Director of Medical Content, I helped write 15 years ago.) [18]

Carcinoma: a cancer that begins in the lining layer (epithelial cells) of organs. At least 80% of all cancers are carcinomas.

ICDO-3*: The third edition of the World Health Organization International Classification of Disease for Oncology. This is the glossary or menu of diagnoses and corresponding codes used by cancer registries and in this study.

Lumping*: Combination of two or more narrow categories into a single broader taxonomic category. In oncologic surgical pathology, "malignant lymphoma, not otherwise specified" and "sarcoma, not otherwise specified" are examples of rather broad or nonspecific diagnoses. Also see splitting.

Lymphoma: a cancer of the lymphatic system, a network of thin vessels and nodes throughout the body that helps to fight infection. The 2 main types of lymphoma are Hodgkin's disease and non-Hodgkin's lymphoma. The treatments for these 2 types of lymphomas are very different.

Non-Hodgkin's lymphoma: a type of cancer of the lymphatic system. The lymphatic system is a network of thin vessels and nodes throughout the body that helps to fight infection. There are many subtypes of non-Hodgkin's lymphoma.

Melanoma: a cancerous (malignant) tumor that begins in the cells that make the skin coloring (melanocytes). Melanoma is almost always curable in its early stages. But it is likely to spread, and once it has spread to other parts of the body the chances for a cure are much lower.

National Cancer Database*: A national hospital-based cancer registry. Data are collected from more than 1,450 hospitals, regarding more than 1 million newly diagnosed patients each year, representing approximately 70% of cancer incidence in the United States

Outcome *: "Health outcomes are the direct result of a patient's health status as a consequence of contact with the health care system. In the above example, the patient's receiving the preventive medications mentioned above could decrease the chance of dying from a heart attack." [19]

Process *: "Process of care denotes what is actually done to the patient in the giving and receiving of care. Building on the example above, the provider could review whether an eligible patient has been placed on an angiotensin-converting enzyme inhibitor to help prevent future heart attacks." [19]

Sarcoma: a malignant tumor growing from connective tissues, such as cartilage, fat, muscle, or bone.

Splitting*: Use of several narrow taxonomic categories rather than a smaller number of broader ones. In oncologic surgical pathology, "follicular lymphoma, grade 1" and "embryonal rhabdomyosarcoma" are examples of rather narrow or specific diagnoses. Also see lumping.

Stage (of cancer): the process of staging determines whether cancer has spread and if so, how far; that is, to learn the stage of the cancer. There is more than one system for staging different types of cancer. The TNM staging system, which is used most often in clinical practice, gives 3 key pieces of information: • T refers to the size of the tumor • N describes whether the cancer has spread to nearby lymph nodes, and if so, how many • M shows whether the cancer has spread (metastasized) to other organs of the body Letters or numbers after the T, N, and M give more details about each of these factors. To summarize this information, the TNM descriptions can be grouped together into a simpler

set of stages, labeled with Roman numerals (usually from I to IV). The lower the number, the less the cancer has spread. A higher number means a more serious cancer.

Structure *: “Structure refers to the attributes of the settings in which providers deliver health care, including material resources (e.g., electronic health records), human resources (e.g., staff expertise), and organizational structure (e.g., hospitals vs. clinics). For example, a cardiologist may use a disease registry to track whether a patient with cardiovascular disease is receiving drugs for lowering cholesterol.” [19]

CHAPTER II – REVIEW OF THE LITERATURE

Introduction

This section reviews literature relevant to the following topics:

- *Cancer as a public health problem*
- *The National Cancer Database (NCDB)*
- *Facility characteristics and healthcare quality*
- *Patient characteristics and cancer disparities*
- *Quality assessment and improvement in oncologic surgical pathology*
- *Relevance of registries such as the NCDB to quality assessment and improvement in oncologic surgical pathology and associations of quality and hospital or laboratory characteristics*
- *Gaps in the published literature*
- *Summary of the literature and its gaps*

Cancer as a public health problem

Cancer is the second most common cause of death in the United States and worldwide, exceeded only by cardiovascular diseases.[1,2] The American Cancer Society estimated that approximately 569,490 people would be diagnosed with cancer and 1,529,560 would die from cancer during 2010.[1]

Cancer is not a single disease. Rather, cancer includes many hundreds of related diseases that share some common characteristics, such as the potential for invasion and metastasis, but which differ substantially regarding epidemiologic, clinical, and molecular characteristics. Although cancer is often classified according to site of origin (for

example, breast cancer, colorectal cancer, lung cancer), cases within each site are further subdivided according to histology (light microscopic appearance) and in some cases, according to results of ancillary molecular tests. Recognition of this diversity is essential to understanding cancer biology and epidemiology, and to clinical management of patients with cancer.[20]

The prognosis for people diagnosed with cancer has improved substantially during the past few decades; 5-year survival has increased from 50% between 1975 and 1977 to 68% between 1999 and 2005. This improvement reflects progress in screening (with detection of less advanced cancers that are more successfully treated) as well as development and use of more effective treatments.[3]

The National Cancer Database

The National Cancer Database (NCDB) is a collaboration of the American College of Surgeons and the American Cancer Society. Data are collected from more than 1,450 hospitals, regarding more than 1 million newly diagnosed patients each year, representing approximately 70% of cancer incidence in the United States.[21] Information from hospital cancer registries is submitted to the NCDB in a standardized electronic format, and includes information on patient characteristics, cancer type and stage, treatment received by the patient, and treatment outcomes. Research involving the NCDB has included studies of patterns of care and health outcomes. Collaborative projects including American Cancer Society researchers have recently focused on racial and socioeconomic (especially related to insurance status) disparities in cancer outcomes.[22-28] In addition to these research applications, cancer centers can obtain from NCDB a variety of benchmarking reports that facilitate quality improvement programs.[21]

Facility characteristics and healthcare quality

Several systematic reviews and meta-analyses have found convincing evidence of positive volume-quality associations for a number of conditions. Updating these reviews systematically and comprehensively regarding all aspects of healthcare is outside the scope of this project. Rather, it seems sufficient to discuss the most comprehensive of these reviews and the most relevant studies that were published after those reviews were undertaken, and to note that the strength and consistency of these relationships are sufficient to justify hypothesizing an association between hospital volume (and other characteristics) and quality of oncologic pathology services.

An IOM report published in 2000 included a systematic review of volume-quality studies of coronary artery bypass graft surgery, pediatric cardiac surgery, carotid endarterectomy, abdominal aortic aneurysm repair, cancer surgery, percutaneous transluminal coronary angioplasty, and management of acute myocardial infarction or acquired immunodeficiency syndrome.[11] The report noted statistically significant associations of better outcomes and hospital volume (in 79% of studies) and physician volume (in 77% of studies). No studies reported inverse relationships, and all of the highest quality studies reported a positive relationship.

A systematic review and meta-analysis published in 2009 identified significant positive volume-outcome associations for surgical treatment of most digestive system cancers, but noted that it was difficult to separate the contributions of hospital and provider volume. One gap identified by this review is that the most frequently studied outcome was perioperative mortality, and that much less is known regarding long term morbidity and mortality.[29]

The conclusions of these two systematic reviews are generally supported, despite some noteworthy exceptions, by recent studies not included in either of the reviews, several of which are summarized below:

- Patients with soft tissue sarcomas treated in Florida from 1981 through 2001 had longer survival and lower likelihood of undergoing limb amputation, according to univariate analyses, when treated at a higher volume center. Multivariate analyses confirmed center volume as an independent predictor or survival.[30]
- For women with infiltrating ductal carcinoma of the breast treated in Florida from 1994 through 2000, a multivariate model including patient and hospital factors indicated greater use of multimodality therapy and a significant survival benefit associated with treatment at teaching hospitals, in comparison with community hospitals.[31]
- High surgeon volume and high hospital volume independently predicted longer survival for women with breast cancer treated in Taiwan between 1997 and 1999.[23]
- Treatment at a teaching hospital or high volume center independently predicted longer survival among lung cancer patients treated in Florida between 1998 and 2002.[32]
- Analysis of NCDB records from 1996-1998 for patients with early stage laryngeal cancer concluded that treatment at a low-volume center independently predicted shorter survival.[24]
- In a study of NCDB records from 1996-2005 for women with stage IIIc and IV ovarian cancer, high hospital ovarian cancer surgical volume predicted adherence

to recommended multimodality treatment, and independently predicted longer survival.[33]

- Analysis of NCDB records from 1996-2002 for patients with advanced stage laryngeal cancer concluded that treatment at a high-volume teaching facility independently predicted improved survival.[25]

In general, volume-outcome associations and facility type-outcome associations appear strongest and most consistent for technically difficult procedures. It is generally recognized that, independent of other factors, volume and facility type do not directly influence healthcare quality. Rather, the assumption is that volume and facility type are associated with human and material resources and with policies and procedures that optimize processes of care administered by an institution and its providers. As noted previously, it is difficult to disentangle the effects of institutional volume and experience of individual providers, although this has been done in some studies. It is also recognized that volume-quality associations can be altered by:

1. Differences in other institutional characteristics: For example, low volume institutions tend to be community hospitals whereas most academic comprehensive cancer centers are high volume institutions.

2. Differences in severity or stage of disease: In the case of cancer care, high volume centers may tend to treat patients with more aggressive or more advanced disease.

3. Differences in comorbidity: High volume centers may attract patients with greater severity and number of cormorbid conditions, with greater risk of treatment complications.

4. Other differences in patient population: Some high volume centers may treat large numbers of uninsured or Medicaid patients, who are more likely to face health literacy issues and whose financial resource limitations might adversely affect adherence to treatment plans. Other high volume centers might attract a medically-sophisticated and relatively affluent population that is better able to adhere to treatment protocols.

Patient characteristics and cancer disparities

Numerous studies and reviews have documented racial, ethnic, and socioeconomic (including health insurance status) disparities in health outcomes, including cancer-related outcomes.[22,34-36] Although there are many factors, unequal access to high quality care contributes substantially to many of these inequities. Recent reports indicate that medically underserved racial groups and the uninsured are less likely to receive care from high-volume providers and high-volume centers.[37-40]

Quality assessment and improvement in oncologic surgical pathology

Accurate and precise diagnosis of neoplastic diseases is essential for assessment of patient prognosis and selection of appropriate treatment. However, variations in therapy can obscure associations between quality of diagnostic services and far-downstream health outcomes.

For these reasons, the surgical pathology quality measurement and quality improvement programs are based on a combination of structural criteria, processes, and upstream/proximal outcomes.[17,41] The "gold standard" for quality assessment in surgical pathology is concordance with the diagnosis rendered by a recognized expert or by the consensus of qualified colleagues. This approach is the basis of some quality measurement and quality improvement programs provided by organizations such as the

College of American Pathologists and the American Society of Clinical Pathologists. In these programs, histologic preparations of tumors on glass microscopic slides or images of such slides are provided to participating laboratories. Each laboratory's diagnosis is submitted and the program staff return information on distributions of diagnoses submitted by other participating laboratories. In other quality assessment and improvement programs, laboratories are instructed to compare their diagnoses to the diagnoses of other laboratories from institutions to which patients have been referred (that is, the patient seeks a second opinion or treatment at a different institution, and that institution's laboratory provides and independent diagnostic opinion on the original specimen) or to diagnoses of expert consultants (for cases with uncertain diagnoses, or upon request of a clinician or patient, the laboratory will send the sample for consultation by a recognized expert at another institution).

Despite their obvious value, limitations of these approaches include the following:

- these programs include a small percentage of patient samples
- data from interlaboratory second opinions reside with laboratory information systems and are not readily linked with structural features, processes, and outcomes of patients and the rest of the healthcare institution's data set
- data from consensus surveys are not linked to actual patients in healthcare information systems or even in laboratory information systems

Measures for tracking the quality of cancer diagnosis of cancer centers have been proposed in an Institute of Medicine report. These measures focus largely on the inclusion of key data elements in pathology reports.[14] The fact that none of the 14

measures address accuracy or precision of the actual diagnosis highlights the challenge in obtaining this information and the unmet need for innovative approaches.

Use of registries in quality assessment and improvement in oncologic surgical pathology, and associations of quality with hospital or laboratory characteristics

Several literature searches identified no published studies that used registries such as the NCDB for quality assessment of surgical pathology. And, in particular, no publications were identified that appeared relevant to association of diagnostic accuracy in cancer classification and laboratory or hospital volume, or other laboratory characteristics (such as academic affiliation).

1. A PubMed search of (laboratory workload OR laboratory volume OR laboratory caseload) AND (Outcome and Process Assessment (Health Care) OR Quality of Health Care OR pathology review) yielded no relevant publications.

2. Examination of references from and citations of more than 25 review articles and primary research papers describing associations of hospital volume or hospital type with quality of surgical care or cancer outcomes did not yield any relevant publications.

Two studies were identified that addressed an association of hospital characteristics with other aspects of quality in oncologic surgical pathology:

- In comparison with high-volume hospitals, low- volume hospitals were more likely to recover fewer than 7 lymph nodes from colon cancer resection specimens. Prior studies have suggested that examination of an insufficient number of lymph nodes diminishes the accuracy of staging and that under-staged patients may not receive appropriate therapy and, therefore, have poorer outcomes.[15]

- The Association of Directors of Anatomic and Surgical Pathology issued recommendations for data elements to be routinely included in pathology reports for colon cancer resection specimens. As compared with teaching hospital pathology laboratories and contract pathology laboratories, community hospital pathology laboratories less consistently included several of these data elements in their pathology reports.[16]

Perhaps the closest approximation to the issue of volume and pathology quality can be found in the radiology literature. There have been several studies indicating an association between radiologist experience with interpreting mammograms and quality of their reports.[42,43]

Gaps in the published literature

As previously noted, more remains to be learned about factors that confound associations between treatment center characteristics and measures (process measures and outcome measures) of the quality of care. These confounding variables include physician factors and patient factors. In addition, modeling these associations is likely to be complicated by correlations among various center characteristics such as center type (community vs. teaching) and case volume. With few exceptions, teaching hospitals and NCI-designated comprehensive cancer centers have higher case volume than community hospitals.

A second gap is that most studies have measured outcomes that are the most easily measurable. Consequently, much more is known about perioperative mortality than about long term survival or quality of life.

Perhaps the widest gap in the literature is that much more is known about relationships between facility or clinician characteristics and outcomes of surgical procedures, than

about corresponding associations for non-surgical care. And, with regard to the possible association of facility characteristics and accuracy or precision of diagnoses in oncologic surgical pathology, no relevant publications were identified.

Summary of the literature and its gaps

Research during the past decade offers some guidance regarding referral of patients for complex cancer surgery. For a number of complex procedures, it seems prudent to seek care from a highly experienced surgeon in a high volume center and for some procedures, at a center with academic affiliation, unless this advice is contraindicated by other clinical considerations or access limitations.[11,23,25,29,30,32,33] In fact, several studies suggest that a greater proportion of these complex surgical procedures are now being done by high volume providers in high volume centers.[38,40]

But, the literature offers essentially no evidence regarding whether the precision of surgical pathology diagnoses differ between high and low volume providers or between high and low volume centers, or between community centers and academic centers. This information has great relevance to continuing professional education, quality improvement, and consultation decisions. By analogy with the surgical literature, and as a matter of face validity, it seems reasonable to hypothesize that for rare, complex, subtle, or otherwise difficult diagnoses, subspecialist pathologists practicing in high volume centers and/or academic cancer centers will provide more accurate and more narrowly focused diagnoses. Accuracy of diagnoses is best determined, as noted previously, by expert review or consensus review, and cannot be readily addressed in registry data. But, broad or vague diagnoses can be distinguished from narrowly focused ones in registry data.

For this reason, the primary goal of this study is to determine whether cancer center type and volume are significantly associated with the prevalence of less precise or lower resolution diagnoses such as “lymphoma, not otherwise specified” or “carcinoma , not otherwise specified” and whether this association persists with multivariable modeling that includes patient-level variables (demographic characteristics and insurance status). Considering broadness versus narrowness of cancer diagnoses as a quality measure need not imply that maximally narrow diagnoses are clinically necessary in all cases or that less focused diagnoses are not adequate for clinical management of some patients. Thus, prevalence of such diagnoses is not expected to be zero. In fact, their appropriate prevalence need not be known. But, observing large differences in prevalence of these diagnoses among centers of different types or between low and high volume centers could suggest differences in quality. By analogy, variations in treatment may be the consequence of factors not recorded in registry data (for example, personal preference or availability of transportation to a radiotherapy center could legitimately affect the choice between mastectomy and breast conserving therapy), yet large differences in utilization of these treatments associated with facility types with similar patient populations would raise concerns.

CHAPTER III -- METHODOLOGY

Introduction

The goal of this project was to explore the relevance of the prevalence of vague, nonspecific, or broad diagnoses to evaluating the quality of diagnostic oncologic pathology services, and to explore associations of broad diagnoses with cancer center-level (especially facility type and case volume) and patient-level characteristics. This cross sectional exploratory study of records in the National Cancer Database (NCDB) for patients diagnosed between 1998 and 2008 used bivariate analyses and multivariable logistic regression models to evaluate these associations.

Population, sample, and variables

The study population included patients diagnosed and treated at facilities that participate in the National Cancer Database (NCDB) between 1998 and 2008. The NCDB represents a collaboration of the American College of Surgeons and the American Cancer Society. More than 1,450 hospitals collectively submit records from more than 1 million newly diagnosed patients each year in the United States.[21] Unlike the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) program, the NCDB is not population-based. The NCDB is a hospital-based registry and therefore may not be ideally representative of cancers that are frequently diagnosed and treated entirely in office-based practices. However, because of its broad population coverage (approximately 70% of all cases of cancers), and because it contains information concerning treatment facility characteristics not available in other databases, it is an excellent sample for this study.

These are the main variables in the NCDB dataset that were used with all cancer sites for this study. Additional variables were created for ICDO3 codes of interest for each cancer site or type (see section on nonspecific diagnosis codes).

Patient variables	**Values**	**Comments**
AGE	Integers	
SEX	1 'Male'	
	2 'Female'	
Race	0'0-Non-Hispanic, White'	
	1'1-Hispanic'	
	2'2-Black'	
	3'3-Asian & PI'	
	4'4-Other'	
	9'9-Missing'	
PRIMPAY (primary payer)#	1 '1-Uninsured'	
	2'2-Medicaid'	
	3'3-Medicare'	including Medicare alone and Medicare with supplement
	4'4-Younger Medicare'	Age 18-64
	5'5-Older Medicare'	Age 65+
	6'6-Government'	Veterans Administration, Indian Health Service, Public Health Service, welfare, state funded NOS, and federally funded NOS
	7'7-Private'	
inc_400 (median income in patient's ZIP code)*	1 '1-<$30,000'	This variable relies on 2000 census data
	2 '2-$30,000-$34,999'	
	3 '3-$35,000-$45,999'	
	4 '4-$46,000+'	
	9'Missing'.	
nhs_400 (% in patient's ZIP code without high diploma)*	1'1-29%+'	This variable relies on 2000 census data
	2'2-20-28.9%'	
	3'3-14-19.9%'	
	4'4-<14%'	
	9'Missing'	

* based on 2000 census.

Tumor variables	Values	Comments
DXCONF (diagnostic confirmation)	1 'Positive histology'	
	2 'Positive cytology'	Not included in this study
	4 'Positive microscopic confirmation, NOS'	Not included in this study
	5 'Positive laboratory test/marker study'	Not included in this study
	6 'Direct visualization without microscopic confirmation'	Not included in this study
	7 'Radiography/Imaging without microscopic confirmation'	Not included in this study
	8 'Clinical diagnosis only'	Not included in this study
	9 'Unknown whether or not microscopically confirmed'	Not included in this study
BM_HIST (Histology best morphology)	ICDO-3 codes	
BEH3 (Tumor behavior)	0 'Benign'	Not included in this study
	1 'Borderline'	Not included in this study
	2 'In situ'	Not included in this study except for bladder carcinoma in situ
	3 'Invasive'	

Facility variables	Values	Comments
volume_grp	0 'Low Volume'	Pre-exclusion site specific volume was calculated by counting the number of patients treated by each institution over the study period and dividing the distribution into equal-sized tertiles of facilities.
	1 'Medium Volume'	
	2 'High Volume'	
Category (facility category)	1 '1-Community Cancer Program'	treat at least 300 cancer cases each year and have a full range of services for cancer care, but patients need referral for portions of their treatment
	2 '2-Comprehensive Community Cancer Program'	offer the same range of services as the community hospitals but have at least 750 annual cancer cases and conduct weekly cancer conferences
	3 '3-Teach/Rsch'	have residency programs and ongoing cancer research
	4 '4-NCI Program/Network'	National Cancer Institute-designated Comprehensive Cancer Programs
	5 '5-Community Networked Programs'	The organization owns multiple facilities providing integrated cancer care and offers comprehensive services. Generally, networks are characterized by a network-wide cancer committee leadership body or functional equivalent, standardized registry operations with a uniform data repository, and coordinated service locations and practitioners. The network participates in clinical research.
	6 '6-Pediatric Programs'	Not included in this study
	7 '7-Other'	Not included in this study
REGION	1'Northeast'	Based on Census
	2'Atlantic'	
	3'Southeast'	
	4'Great Lakes'	
	5'South'	
	6'Midwest'	
	7'West'	
	8'Mountain'	
	9'Pacific'	

Research design

This was a cross sectional exploratory study of adult patients in the National Cancer Database (NCDB) who were diagnosed with their first primary invasive (with the exception of bladder, for which in situ disease is also included) cancer between 1998 and 2008 (n=8,575,431). Patients who were not diagnosed by positive histology (n=859,205) were excluded. Due to small numbers, patients with government insurance (Indian Bureau of Affairs, Public Health Service) (n=246,679) and patients reported from pediatric facilities were also excluded (n=820). The analytic study population contained 7,690,727 patients. Independent variables included facility type and case volume, as well as patient demographic characteristics and insurance status. Associations of these independent and dependent variables were evaluated by bivariate analyses and multivariable logistic regression models.

Procedures

Identification of nonspecific codes and selection of cancer sites for more detailed analysis

One approach that was initially considered for identifying nonspecific diagnoses and corresponding ICD-O3 codes was to review the entire ICDO-3 dictionary and select all codes representing diagnoses that were not as narrowly focused as might be expected in ordinary clinical practice of surgical pathology. In beginning this task, it was noticed that many of the diagnoses selected were extremely rare, and therefore of minimal, if any, relevance to most anatomic sites.

An alternative approach, which was the one applied to this research, was to choose the nonspecific diagnoses of greatest relevance to one or more reasonably common cancer

sites. I plan to undertake subsequent studies that will take a more detailed look at individual cancer sites, considering even relatively rare diagnoses. On the other hand, this initial overview study is more concerned with common nonspecific diagnoses for cancers of common sites, which are expected to have the most substantial clinical impact on the overall patient population.

These decisions involved several steps:

1. The NCDB cases of invasive cancer (and in situ bladder cancer) were separated into the 10 highest incidence sites for males and females based on 2010 ACS Facts and Figures estimates, for a total of 14 sites.[3] The 14 sites are listed below in alphabetical order, with the letters in parentheses indicating whether they are among to top 10 incidence list for males, females, or both sexes:

- Breast (F)
- Colon & rectum (M, F)
- Kidney & renal pelvis (M, F)
- Leukemia (M)
- Lung & bronchus (M, F)
- Melanoma (M, F)
- Non-Hodgkin lymphoma (M, F)
- Oral cavity and pharynx (M)
- Ovary (F)
- Prostate (M)
- Pancreas (M, F)
- Thyroid (F)

- Urinary bladder (M)
- Uterine corpus (F)

Although some of these sites are in the top 10 incidence list for only males or females, in this study cases in both sexes were included (with the obvious exception of sex-specific sites such as ovary or prostate). Thus, we included thyroid cancer in males, even though this disease was among the 10 highest incidence sites only for females.

2. For each of these sites, the percentages of cases corresponding to each code were compared for Community Cancer Centers and NCI-designated Comprehensive Cancer Programs (the 2 extremes of the facility spectrum). Diagnoses were ranked according to the absolute value of the difference in prevalence at these 2 types of facilities. The goal of this procedure was to identify diagnoses that were common for a particular anatomic site, and which are assigned with substantially different frequency based on facility type. It is based on the hypothesis that comparing the 2 extremes of the facility spectrum in an exploratory analysis of diagnosis frequency for each cancer site (breast, colon and rectum, etc.) would be a useful first step in identifying clinically-relevant variations in oncologic pathology practice. Absolute values of differences in the prevalence of diagnoses were ranked to juxtapose nonspecific diagnoses (which were generally more common for Community Centers) and the most common alternative specific diagnoses (which tended to be more common for NCI-designated Comprehensive Programs). This juxtaposition facilitated consideration of the clinical relevance of a pathologist assigning a relatively nonspecific diagnosis to a patient's cancer.

3. The 10 diagnoses with the greatest prevalence difference were listed and more diagnoses were added until all diagnoses with an absolute prevalence difference of 1%

had been included. For some of the cancer sites, nearly all of the cumulative difference between Community Cancer Centers and NCI-designated Comprehensive Cancer Programs was due to a small number of diagnoses. In these situations, any diagnosis beyond the tenth diagnosis would have a very small absolute difference in prevalence, and that diagnostic distinction would therefore be unlikely to have a large impact on the patient population (although the impact could still be substantial for individual patients with rare cancer types). Even though the eighth, ninth, or tenth items for these sites were relatively uncommon diagnoses (and therefore not likely to have substantial clinical impact on the overall patient population), it was felt that they were worth listing because they indicate variation in pathology practice worth considering in more detailed analysis of future studies of individual cancer sites. For other cancer sites, the cumulative diagnostic variation was more evenly distributed among a greater number of diagnoses. For these sites, additional diagnoses were listed in order to present all diagnoses with a prevalence difference of 1% or greater, which was (subjectively) considered to be a reasonable cutoff for differences with substantial impact on the patient population. Thus, the lists (results shown in Tables 1-14) contained at least 10 diagnoses for some sites and a few more diagnoses for other sites.

4. Nonspecific diagnoses for which prevalence differences were likely to have arisen from differences in patient populations were excluded.

5. Nonspecific diagnoses that seemed unlikely to have a significant clinical impact were excluded. Assessment of likely clinical impact was based largely on clinical practice guidelines of the National Comprehensive Cancer Network (NCCN, a consortium of NCI-designated Comprehensive Cancer Programs). In addition to NCCN guidelines,

individual studies and reviews from the oncology and pathology literature were also considered in assessing the clinical relevance of variations in use of nonspecific diagnoses.

6. Cancer sites were included or excluded based on the combined magnitude of variation of clinically-relevant nonspecific diagnoses as well as the combined magnitude of variation of clinically-relevant alternate diagnoses that are more specific. For example, a particular nonspecific diagnosis might be 10% more common for Community Centers than for NCI-designated Comprehensive Programs, and this difference might be largely balanced by an excess of 5 more specific diagnoses at the latter category of facilities. Although the magnitude in difference of in the nonspecific diagnosis is large, this cancer site would be excluded from time trend analysis and logistic regression analysis in this study if the distinction with only one among the 5 alternative diagnoses was clinically relevant and if the magnitude of that difference for the specific diagnosis was small.

In another example, there may be several pairs of clinically relevant nonspecific diagnoses and alternate specific diagnoses. Even though the magnitude of differences among facility types for each pair might not be very large, the site would receive a high priority if the sum of differences for all pairs was large.

Because these decisions are based on results of the initial exploratory analysis of diagnosis frequencies by site and by facility type, and because these decisions could not be made before that analysis, the specific clinical reasons for these choices are explained in the results section under "*Differences in prevalence of diagnoses by facility type*".

The following list summarizes the cancer sites and the diagnoses (codes) that were chosen for graphical analysis of time trends and for logistic regression analysis.

Kidney: renal cell carcinoma, NOS (8312)

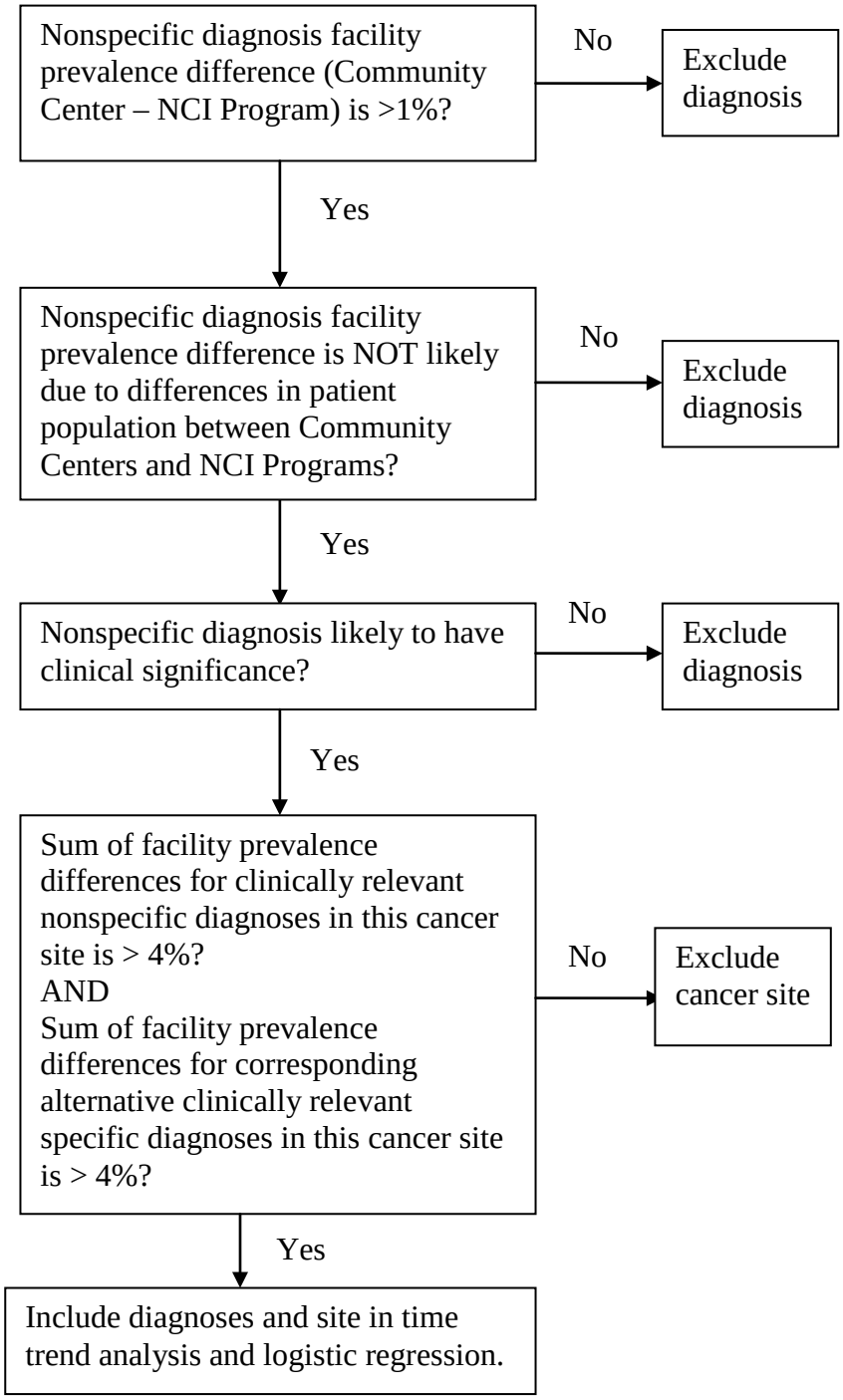
Non-Hodgkin lymphoma: malignant non-Hodgkin’s lymphoma, NOS (9591); follicular lymphoma, NOS (9690); malignant lymphoma, NOS (9590)

Ovary: adenocarcinoma, NOS (8140); carcinoma. NOS (8010); papillary adenocarcinoma, NOS (8260)

Pancreas: carcinoma NOS (8010); neoplasm NOS (8000)

Uterine corpus: adenocarcinoma, NOS (8140)

Algorithm for selection of cancer sites and nonspecific diagnoses



Data analysis

Analyses were performed with the SAS software package (version 9.1; SAS Statistical Institute, Cary, NC) and PASW Statistics (version 18.0.0, SPSS, Inc. Chicago, IL).

Trends over time in prevalence of nonspecific diagnoses, stratified by facility type and volume group

The prevalence of each of the nonspecific diagnoses chosen in the preceding section was determined for each year from 1998 through 2008, for each of the facility types and volume groups. Pediatric cancer centers and miscellaneous category of "other" facilitations, which collectively account for no greater than 2% of cases for any cancer type (and for most types represented less than 1%) were not shown on these graphs. These results were displayed graphically to assist in recognition of trends over time. The following list summarizes the cancer sites and the diagnoses (codes) that were chosen for graphical analysis of time trends and for logistic regression analysis.

Kidney: renal cell carcinoma, NOS (8312)

Non-Hodgkin lymphoma: malignant non-Hodgkin's lymphoma, NOS (9591); follicular lymphoma, NOS (9690); malignant lymphoma, NOS (9590); combination of any of these 3 diagnoses/codes

Ovary: adenocarcinoma, NOS (8140); carcinoma. NOS (8010); papillary adenocarcinoma, NOS (8260); combination of any of these 3 diagnoses/codes

Pancreas: carcinoma NOS (8010); neoplasm NOS (8000); combination of either of these 2 diagnoses/codes

Uterine corpus: adenocarcinoma, NOS (8140)

Multivariable modeling of patient factors associated with nonspecific diagnoses

Logistic regression models were used to estimate odds ratios (OR) and 95%CI confidence intervals (CI) for each cancer site, with the dichotomous outcome variable being occurrence of any of the nonspecific diagnoses selected for that site.

The following list summarizes the sites and diagnoses used in these analyses:

Kidney: renal cell carcinoma, NOS (8312) versus all other histology codes.

Non-Hodgkin lymphoma: malignant non-Hodgkin's lymphoma, NOS (9591) or follicular lymphoma, NOS (9690) or malignant lymphoma, NOS (9590) versus all other histology codes.

Ovary: adenocarcinoma, NOS (8140) or carcinoma, NOS (8010) or papillary adenocarcinoma, NOS (8260) versus all other histology codes .

Pancreas: carcinoma NOS (8010) or neoplasm NOS (8000) versus all other histology codes.

Uterine corpus: adenocarcinoma, NOS (8140) versus all other histology codes.

In addition to the aforementioned facility factors (volume and facility type), age, sex (where appropriate), race/ethnicity, insurance status, area level income, area level education, geographic region, and diagnosis year were adjusted for. Because community network programs represented a relatively small number of programs and were similar to comprehensive cancer centers in bivariate analyses, they were grouped with comprehensive community cancer centers.

Limitations and delimitations

Limitations (potential weaknesses of the project beyond the control of the investigator):

- The NCDB includes data on only 70% of cancer incidence. And, coverage is somewhat lower for cancers that can be treated by outpatient practices for which data are not captured in registries of Commission on Cancer facilities.
- The income and education level variables are based on ZIP code area (not on data from individual patients).
- NCDB does not include provider information, so it is not possible to determine whether any relationships between facilities and quality measures are due to aggregate characteristics of the institution or specifically due to skill of the institutions' pathologists.
- The diagnoses in NCDB are based on ICDO codes submitted by cancer registrars at each facility. In some cases, selecting a code for some diagnoses on a pathology report is not straightforward. Therefore, differences in ICDO codes in this database may reflect differences in the diagnosis made by the pathologist as well differences in assigning an appropriate IDCO code.

Delimitations (factors, set by the investigator, that narrow the scope of the study):

- Cases of the 10 highest incidence sites for males and females based on 2010 ACS Facts and Figures estimates, for a total of 14 sites, were included for the exploratory bivariate analyses of diagnosis prevalence and facility type. Based on these results, 5 sites (kidney and renal pelvis, non-Hodgkin's lymphoma, ovary, pancreas, and uterine corpus) were selected from examination of time trends in diagnoses, and for logistic regression modeling.
- Patients who were not diagnosed by positive histology were excluded.

- With the exception of urinary bladder cancer for which both invasive and in situ cases were included (for consistency with usual surveillance research practices), only cases of invasive cancer were studied.
- Only cases among adults were included.

CHAPTER IV – RESULTS

Introduction

There are a number of nonspecific diagnoses for which differences in prevalence among facility types and volume groups are of a magnitude likely to be clinically significant. Multivariable logistic regression models that include patient-level covariates confirmed the significance of both facility type and volume group in predicting the prevalence of broad or nonspecific diagnoses. Among several patient-level factors (including race, insurance status, area income, and area educational attainment), only education level, based on quartiles of the percent of residents in a ZIP area without a high school diploma was significantly associated with nonspecific diagnoses for all cancer sites.

Findings

Differences in prevalence of diagnoses by facility type

There were many differences between prevalence of diagnoses by facility type (Tables 1-14). These were sorted according to the absolute difference in percentage points between Community Cancer Centers and NCI-designated Comprehensive Cancer Programs. For diagnoses with substantial differences in prevalence between these 2 facility types, Teaching and Research Facilities were closer to the NCI programs and Comprehensive Community Centers and Community Networks were closer to the Community Cancer Centers. For the sake of brevity, presentation of results in this section focuses on large differences between Community Centers and NCI-designated Comprehensive Cancer Programs. This portion of the results section also includes some discussion of how these

results from the 14 sites included in the exploratory analyses were used to select the 5 cancer sites examined in greater detail by analyses of time trends and logistic modeling.

Breast cancer (Table 1). The greatest differences between Community Centers and NCI-designated Comprehensive Programs were an excess of infiltrating duct carcinoma in the former and a greater percentage of infiltrating duct and lobular carcinoma in the latter. This distinction would not, according to NCCN treatment guidelines, influence clinical management.[44] Among the 10 diagnoses with the greatest difference in prevalence between Community Centers and NCI-designated Comprehensive Programs, the only two that most pathologists would consider unusually broad are "adenocarcinoma, NOS" and "neoplasm, NOS." Both diagnoses were rarely used in any facility types and the prevalence differences were less than 1%. Although there may be some clinically important differences in prevalence of uncommon diagnoses, no substantive differences in common diagnoses were noted. For this reason, breast was not among the sites selected for more detailed analysis in this study.

Colorectal cancer (Table 2). The most prominent difference was that "adenocarcinoma, NOS" was more frequently (by 5.0%) diagnosed in Community Centers than in NCI-designated Comprehensive Programs. In contrast, Community Centers were less likely to report that adenocarcinoma had developed in an adenoma (a tubulovillous adenoma or an adenomatous polyp). This is a clinically-relevant distinction.[45] However, the incidence of these diagnoses depends on the stage distribution of cancers diagnosed at each facility. In a population with higher adherence to screening, one would expect to find cancer at an early stage, and cancer within a polyp is the earliest stage of colon cancer. In the present analysis, it is not possible to distinguish the extent to which differences in stage

distribution versus differences in precision of diagnostic interpretation account for this finding. This question could be addressed by restricting the analysis by stage, which is among the questions to address in subsequent studies of individual cancer sites. Community Centers more often diagnosed mucin-producing adenocarcinomas whereas the NCI programs reported more mucinous adenocarcinomas and signet ring cell adenocarcinoma. Accurate and complete identification of these subtypes can have implications for identification of patients with Lynch syndrome and referral for genetic counseling.[6] Because the magnitudes of these differences were relatively small (<2%) and differences in prevalence of mucinous and mucin-producing adenocarcinomas were in the opposite directions, it was concluded that these findings are best addressed in a subsequent study focused on colorectal cancer. Therefore, colon was not among the sites selected for more detailed analysis in this study.

Kidney and renal pelvis cancer (Table 3). Community Centers diagnosed lesions as "renal cell carcinoma"15% more often than did NCI-designated Comprehensive Programs. The opposite pattern occurred regarding specific renal cell carcinoma subtypes (clear cell, papillary, chromophobe, and sarcomatoid). Based on the magnitude of this difference and potential relevance of some renal cell carcinoma subtypes to prognosis and genetic counseling, this diagnosis was among those chosen for more focused analysis over time, and by multivariable logistic regression.[4,7]

Leukemias (Table 4). "B-Cell Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia" was reported 18.9% more often by Community Centers than by NCI-designated Comprehensive Programs. To the contrary, several forms of acute leukemia were more common for NCI-programs. This pattern is presumed to largely reflect

different patient populations (treatment of acute leukemia is more intensive and more complex, and therefore referral to a larger or more academic center is likely) rather than variation in diagnostic interpretation of similar cases. For this reason, leukemia was not among the sites/types selected for more detailed analysis in this study.

Lung cancer (Table 5). In comparison with NCI-designated Comprehensive Programs, Community Centers were more likely to report small cell, squamous cell, and large cell carcinomas (by 4.4, 3.7, and 2.4%, respectively) and were less likely to report adenocarcinomas, adenocarcinoma with mixed subtypes, and broncliolo-alvelolar carcinomas (by 6.1, 2.0, and 1.8%, respectively). Most of these differences are likely to be due to differences in patient populations. Differences in use of broad diagnoses (such as "neoplasm, NOS"; "non-small cell carcinoma", and "carcinoma, NOS") were all less than 1%. Therefore, lung was not among the sites selected for more detailed analysis in this study.

Melanoma (Table 6). In comparison with NCI-designated programs, "Melanoma, NOS" was 16.0 % more commonly diagnosed by Community Centers. This was mostly balanced by a 12.8% excess of superficial spreading melanoma in the NCI-designated Comprehensive Programs. However, this distinction is not noted in NCCN guidelines as one that should influence clinical management. In contrast, recognition of desmoplastic melanoma could influence decisions regarding adjuvant radiation therapy.[46] Although desmoplastic melanoma was more than twice as likely to be diagnosed at NCI-designated Comprehensive Programs than at Community Centers, the absolute difference in prevalence (1.1% higher in the former) was rather small. For this reason, and because no

other common diagnoses had substantially different prevalence among facility types, melanoma was not selected as one of the sites for more detailed analysis in this study.

Non-Hodgkins lymphoma (Table 7). In comparison with NCI-designated Programs, Community Centers were more likely to report small B lymphocytic lymphoma (by 3.3%) and less likely to report mycosis fungoides, Burkitt lymphoma, mantle cell lymphoma, cutaneous T-cell lymphoma, and mantle cell lymphoma (by 4.0, 1.9, 1.9, 1.9, and 1.4%,respectively). However, most of these differences seem likely to be due in large part to differences in patient populations, particularly for lymphoma subtypes that require complex or intensive treatment. Two nonspecific diagnoses made more often in Community Centers, "malignant lymphoma, NOS" (by 2.2%) and "malignant lymphoma, non-Hodgkin, NOS" (by 4.9%) are insufficient to guide treatment choices in most cases. A third relatively broad diagnosis, "follicular lymphoma, NOS", was 3.3% more common in Community Centers and also could be less than optimal for clinical management of some cases.[47] These three diagnoses were therefore chosen for more detailed investigation.

Oral and pharyngeal cancer (Table 8). Several squamous cell carcinoma subtypes (keratinizing, large cell nonkeratinizing, and basaloid) were diagnosed more often (by 2.8, 1.6, and 0.9%, respectively) in NCI-designated Comprehensive Programs than in Community Centers; the opposite was observed regarding diagnosis of "squamous cell carcinoma, NOS" by a margin of 7.9%. Among these, large cell nonkeratinizing squamous cell carcinoma is the only one for which potential clinical implications are noted in the NCCN guideline, and even in this case the guideline narrative notes that NCCN member institutions disagreed regarding this point.[48] Because the only clinically-

significant diagnostic distinction exhibited a prevalence difference of less than 2%, this site was not selected for more detailed analysis in this study. However, differences in subclassification of squamous cell carcinoma as well as differences in prevalence of some uncommon cancer types (such as polymorphous low grade adenocarcinoma) are potential topics for subsequent studies that focus on this site.

Ovarian cancer (Table 9). Three diagnoses ("adenocarcinoma, NOS"; "papillary adenocarcinoma, NOS"; and "carcinoma, NOS") that do not indicate a specific cell type were more common for Community Centers (by 8.2, 3.8, and 2.1%, respectively), whereas most of the subtypes of ovarian carcinoma were reported more often by NCI-designated Comprehensive Programs. Description of the cell type of ovarian cancer is common practice and may have prognostic relevance for some patients.[49] Additionally, NCCN guidelines indicate that patients with a diagnosis of mucinous ovarian carcinoma should undergo evaluation to exclude a digestive tract primary tumor (with an ovarian metastasis) and that appendectomy should be considered.[50] For these reasons and because of the large absolute difference in the prevalence of three relatively nonspecific diagnoses, this site was among those selected for further analysis in this study.

Pancreatic cancer (Table 10). Although the majority of pancreatic cancers for all center types were diagnosed as "adenocarcinoma, NOS", this diagnosis was more common for Community Centers than for NCI-designated Comprehensive Programs (by 6.2%), and the latter more often reported infiltrating duct carcinomas (by a margin of 6.9%). Because ductal carcinomas represent more than 90% of pancreatic cancer [51], some pathologists and clinicians may assume that "adenocarcinoma, NOS" refers to ductal adenocarcinoma, unless otherwise noted. Neuroendocrine/islet cell carcinomas were more often reported

by NCI-designated Comprehensive Programs, although the available data cannot determine whether this reflects patient populations and referral patters rather than diagnostic interpretations. The most notable findings are that two nonspecific diagnoses, “carcinoma, NOS” and “malignant neoplasm, NOS” do not make the clinically-essential distinction between exocrine and endocrine cancers and were more often reported by Community Centers than for NCI-designated Comprehensive Programs by margins of 3.86 and 1.87%, respectively. These diagnoses were therefore chosen for further analysis.

Prostate cancer (Table 11). The vast majority of prostate cancers (89.4 to 97.4%, depending on facility type) were classified as “adenocarcinoma, NOS”, regardless of center type. In comparison with Community Centers, NCI-designated Comprehensive Programs were more likely to report acinar cell adenocarcinoma and less likely to report “adenocarcinoma, NOS” (by margins of 8.3 and 8.0%, respectively). Although distinguishing some uncommon histological subtypes of prostate cancer (such as neuroendocrine carcinoma)can have clinical relevance, [52] with the exception of the aforementioned differences in prevalence of “adenocarcinoma, NOS” and acinar cell adenocarcinoma, there were no other diagnoses for which the absolute difference in prevalence for Community Centers and NCI-designated Comprehensive Programs exceeded 1%. Therefore, prostate was not among the sites selected for more detailed analysis in this study.

Thyroid cancer (Table 12). The most prominent differences between Community Centers and NCI-designated Comprehensive Programs were more common diagnoses of “papillary carcinoma, NOS” and follicular variant of papillary carcinoma by the former (by 10.0 and 5.8%, respectively) and “papillary adenocarcinoma, NOS” by the latter (by

14.7%). In the context of thyroid pathology, papillary carcinoma and papillary adenocarcinoma would be widely understood as synonyms for the same lesion. Interestingly, the columnar cell type of papillary carcinoma was more commonly noted (by 1.8%) by NCI Programs, as was medullary carcinoma (by 1.4%). It would be difficult to estimate the extent to which differences in patient populations or diagnostic interpretations contribute to these differences, and such analyses would be beyond the scope of this exploratory study. Thyroid was therefore not among the sites selected in this study for more detailed analysis.

Urinary bladder cancer (Table 13). The main difference for this site was a 17.3% excess of papillary transitional cell carcinoma and a 14.7% lower prevalence of "transitional cell carcinoma, NOS" for Community Centers in comparison with NCI-designated Comprehensive Programs. Because the papillary transitional cell lesions tend to be low grade and low stage, this difference in diagnostic prevalence may reflect different patient populations rather than different interpretations or different use of terminology. More detailed analysis of this site was therefore not undertaken as part of this study.

Uterine corpus cancer (Table 14). The 20.4% difference in prevalence of "adenocarcinoma, NOS" between Community Centers and NCI-designated Comprehensive Programs (with higher prevalence in the former) was greater than for any other diagnosis of any site in this study. NCI-designated Comprehensive Programs more often diagnosed several adenocarcinoma subtypes, some of which (such as papillary serous cancers) have implications for prognosis and even clinical management.[53] This diagnosis was therefore among those selected for further analysis.

Time trends in prevalence of diagnoses by facility type and volume group

Figures 1-5 illustrate changes from 1998 to 2008 in the prevalence (separated by facility type and volume group) of selected nonspecific diagnoses. As expected from the comparisons of overall data from the entire ten year period shown in Tables 1-14, there were substantial differences. However, the graphs also illustrated that, for some diagnoses, differences among facilities remained relatively constant over time whereas but for others they increased or decreased over time.

Kidney and renal pelvis cancer (Figure 1). In 1998, the majority of cancers for this site were diagnosed as "renal cell carcinoma", regardless of facility type or volume. Over the subsequent decade, prevalence of this diagnosis declined to a substantially greater degree at NCI-designated Comprehensive Programs and at high volume facilities.

Non-Hodgkin lymphoma (Figure 2). Differences by facility type and volume group in the prevalence of "non-Hodgkin lymphoma, NOS" changed little during this period. Throughout this period, this diagnosis was most common at Community Centers and low volume facilities, and least common at NCI-designated Comprehensive Programs and at high volume facilities. In contrast, prevalence of "follicular lymphoma, NOS" was initially similar for all facility types and volume groups, increased over time for all facility types and volume groups, but leveled off sooner and at a lower level for more academic facility types (Teaching and Research Centers and NCI-designated Comprehensive Programs) and high volume facilities. Prevalence of "malignant lymphoma, NOS" decreased over time for all facility types and volume groups, but the decline was more prominent for NCI-designated Comprehensive Programs and high volume facilities. Prevalence of the combination of these 3 diagnoses increased for

Community Centers, decreased for NCI-designated Comprehensive Programs, and remained relatively stable for other facility types. This combination of diagnoses started and remained highest among Community Centers and lowest at NCI-designated Comprehensive Programs.

Ovarian cancer (Figure 3). Prevalence of “adenocarcinoma, NOS” was initially lowest in NCI-designated Comprehensive Programs and high volume facilities, and was highest for Community centers and low volume facilities. These differences became even more prominent over time. Prevalence of “carcinoma, NOS” was initially lower for more academic and higher volume facilities; these differences difference did not change substantially over time. Prevalence of “papillary adenocarcinoma, NOS” was initially highest for Community Centers and for low and medium volume facilities, and was lowest for NCI-designated Comprehensive Programs and high volume facilities. Use of this diagnosis declined for all type and volume categories but the gap among facility types and volume groups narrowed somewhat over time. The combined prevalence of these 3 diagnoses declined over time for all facility types and volume groups, but started and remained highest for Community Centers and low volume facilities and lowest for NCI-designated Comprehensive Programs and high volume facilities.

Pancreatic cancer (Figure 4). Prevalence of “carcinoma, NOS” was initially highest among Community Centers and among low and medium volume facilities, and there was little change for these facilities over time. Use of this diagnosis by Community Networks and Teaching and Research Centers declined substantially. NCI-designated Comprehensive Programs and high volume facilities used this diagnosis least throughout the entire time period. Prevalence of “malignant neoplasm, NOS” was initially very low

at NCI-designated Comprehensive Programs, Teaching and Research Centers, and high volume facilities, and remained so throughout the period of observation. Prevalence of this diagnosis, in contrast, increased substantially over time for Community Centers, low volume facilities, and medium volume facilities. The combined prevalence of these 2 diagnoses was relatively stable over time, beginning and ending at highest levels for Community Centers, low volume facilities, and medium volume facilities, and at lowest levels for Teaching and Research Centers, NCI-designated Comprehensive Programs, and high volume facilities.

Uterine corpus cancer (Figure 5). Prevalence of “adenocarcinoma, NOS” began and ended lowest among NCI-designated Comprehensive Programs and high volume facilities, and highest among Community Centers, Comprehensive Community Centers, low volume facilities, and medium volume facilities. NCI-designated Comprehensive Programs started with far lower use of this diagnosis, and other facility types narrowed this gap somewhat over time.

Multivariable logistic regression models

Facility type and volume group remained highly significant as predictors of the level of diagnostic detail (as measured by the combined prevalence of nonspecific diagnoses for each site), even after inclusion of additional patient-level (sex, age, race, insurance status or type, ZIP code area income, ZIP code area education level) and facility-level (regional location) variables (Table 15).

In comparison with Community Centers, the prevalence of nonspecific diagnoses was significantly lower at NCI-designated Comprehensive Programs for each of the 5 sites in this analysis (kidney and renal pelvis, non-Hodgkin’s lymphoma, ovary, pancreas, and

uterine corpus). Odds ratios varied from 0.36 (95% CI 0.34-0.39) for uterine corpus to 0.69 (0.66-0.72) for kidney and renal pelvis. In comparison with Community Centers, the prevalence of nonspecific diagnoses in Teaching and Research facilities was significantly lower for 4 sites (kidney, ovary, pancreas, and uterine corpus) and was significantly lower in Comprehensive Community and Community Network facilities (combined) for 2 sites (kidney and ovary). In comparison with low volume facilities, the prevalence of nonspecific diagnoses was significantly lower at high volume facilities for all 5 sites, and was lower at medium volume facilities for 1 site (non-Hodgkin’s lymphoma).

One other variable showing a consistent pattern of association with prevalence of nonspecific diagnoses is area education level, based on quartiles of the percent of residents in a ZIP area without a high school diploma. Compared with patients who live in areas with the highest quartile of high school graduation, those in the lowest quartile were significantly more likely to receive nonspecific diagnoses for cancers of each of the 5 sites studied by multivariate analyses.

The only other demographic variable with a somewhat consistent pattern of association with nonspecific diagnoses is age. In comparison with patients younger than 50 years, those aged 85 years or older were more likely to receive nonspecific diagnoses for non-Hodgkin’s lymphoma and for cancers of the ovary, pancreas, and uterine corpus. But, for unclear reasons, they were significantly less likely to have a nonspecific diagnosis for kidney and renal pelvis cancers.

Uninsured patient were significantly less likely than those with private insurance to receive nonspecific diagnoses for 2 cancer sites (kidney and ovary) but were not any less likely to receive such diagnoses for the remaining 3 sites.

There were several significant associations between race and prevalence of nonspecific diagnoses, but none appeared in any consistent pattern. For example, as compared to Whites, Blacks were significantly more likely to received nonspecific diagnoses non-Hodgkin's lymphoma and cancer of the ovary, but were less likely to receive such diagnoses for cancer of the uterine corpus.

As compared to patients diagnosed in the Northeast, those diagnosed in other regions had greater likelihood of receiving a nonspecific diagnosis for some sites and a lower likelihood for other sites. Only the South had a greater prevalence of nonspecific diagnoses for all 5 sites studied. The prevalence of nonspecific diagnoses declined significantly over time (in comparison with the initial year, 1998) for four cancer sites (kidney, non-Hodgkin lymphoma, ovary, and uterus) but not for pancreas.

Summary

Bivariate and multivariable analyses demonstrated statistically significant relationships between the prevalence of nonspecific diagnoses and two facility characteristics – facility type and facility volume. In models including several patient-level covariates, nonspecific diagnoses were least likely to be used by NCI-designated Comprehensive Programs and by high volume facilities and were most common for Community Centers and low volume facilities. Consistent positive associations with nonspecific diagnoses were noted with age of at least 85 years, and with residing in ZIP code areas with the lowest quartile for high school graduation. Use of nonspecific diagnoses for 4 of the 5 sites declined from 1998 to 2008.

CHAPTER V – DISCUSSION

Introduction

This study used the National Cancer Database to examine associations between cancer treatment facility characteristics (facility type and volume) and the level of detail in the diagnoses made by pathologists at these centers. Patient-level demographic characteristics were also included in multivariable analyses.

Summary of study

Differences in prevalence of diagnoses by facility type in exploratory analyses of 14 cancer sites are shown in detail in Tables 1-14 and are also described in the Results section. This discussion will therefore focus only on the 5 sites and 13 diagnoses selected for more detailed analysis, based on the magnitude of differences by facility type and potential for relevance to prognosis, therapeutic decisions, or genetic counseling.

Kidney and renal pelvis

Although treatment of renal cell carcinoma historically has not varied by histological subtype, subtyping of these cancers has become more common over time, especially for more academic facilities (NCI-designated Comprehensive Programs and Teaching and Research Centers) and for higher volume facilities. For some patients, identification of clear cell or papillary subtypes can have prognostic and genetic counseling implications. Recent studies have also revealed that the histological heterogeneity among renal cell carcinomas reflects similar heterogeneity on a molecular level. For this reason, subclassification of renal cell carcinoma may become increasingly important in selection of molecularly targeted therapies; recently, eligibility for some clinical trials of such

agents has been restricted to certain renal cell carcinoma subtypes.[4,7] In summary, subclassification of renal cell carcinoma is becoming more common and more clinically relevant. From 1998-2008, the decline in prevalence of "renal cell carcinoma" as a diagnosis was most substantial in more academic and higher volume centers.

Non-Hodgkin lymphoma

Non-Hodgkin lymphomas are an extremely heterogeneous group of diseases. With the exception of patients whose comorbidities preclude cancer-directed drug therapy, diagnoses such as "malignant lymphoma" or "non-Hodgkin's lymphoma" clearly lack sufficient detail upon which to base clinical management decisions.[47] Use of these two diagnoses is, by a substantial amount, lowest for NCI-designated Comprehensive Programs and high volume facilities. In addition, diagnosis of "follicular lymphoma, NOS" was most common among Community Centers and low volume facilities. Use of this diagnosis increased during the late 1990s and early 2000s, perhaps related to recognition of this entity in the Revised European American Lymphoma classification and the subsequent World Health Organization (WHO) classification.[54,55] However, the WHO classification recommends grading of follicular lymphomas, and the ICDO-3 includes separate diagnoses and codes for low, intermediate, and high grade types. Unlike the situation for most other cancers, grade is not only reflected in the grade field of the NCDB (or of pathology reports), but also as distinct diagnoses. This distinction has prognostic relevance and, the NCCN recommends different regimens for low grade (1 or 2) and high grade (3) follicular lymphoma.[47]

Ovarian cancer

Epithelial ovarian carcinoma is typically subclassified according to cell type (serous, mucinous, endometrioid, etc.). Diagnoses that do not make this distinction were made most often by Community Centers and low volume centers. Although this distinction rarely affects treatment, it may have prognostic implications.[49]

Pancreatic cancer

A diagnosis of pancreatic malignancy should clearly distinguish between exocrine and endocrine carcinomas. Although most clinicians would assume that by default, "pancreatic carcinoma" or even more vaguely, "malignant neoplasm" refers to the far more common exocrine cancers, such assumptions should not be required in interpreting a pathology report, a situation which appears to occur least often at more academic and higher volume facilities.

Uterine corpus cancer

A diagnosis of "adenocarcinoma, NOS", which is made least often by more academic and higher volume centers does not distinguish between the usual endometrioid subtypes and less common clear cell and papillary serous subtypes. This distinction has prognostic and therapeutic implications.[53]

Multivariable models

Even with inclusion of patient-level demographic and socioeconomic covariates, facility type and volume group remain very strongly associated with the proportion of relatively nonspecific diagnoses assigned to patients at these institutions. Some patient-level factors (residing in ZIP code areas in the lowest quartile for high school graduation, or age of at least 85 years) were also significantly associated with nonspecific diagnoses for most cancer sites, but there were no consistent patterns that indicate a disparity in quality of

pathology services based independently on race, area income, or insurance status. Although previous research has shown that medically-underserved population groups are less likely to receive care from high volume centers,[37-40] the socioeconomic variables in this model do not appear to be independently associates with quality of diagnostic pathology services. This finding is expected, as it seems unlikely that pathologists consider, or are even aware of, these demographic factors when making decisions regarding specimen analysis and selection of diagnoses.

Limitations

The main limitation of this study is that the NCDB includes approximately 70% of cancer cases. These cases are submitted by participating facilities, and it is possible that cases from participating and non-participating facilities differ in ways that are relevant to this study. However, these differences do not seem likely to substantially attenuate the relationships observed in these analyses between diagnostic detail and facility type and volume. The non-participating facilities tend to be at both extremes of the volume and academic spectrum. Small community hospitals that treat few patients with cancer often do not participate in the Commission on Cancer Approval program and do not submit cases to the NCDB. At the other extreme, a few of the largest NCI-designated Comprehensive Cancer Centers do not contribute their data to the NCDB. Therefore, it is possible that this limitation could result in our analyses underestimating, rather than overestimating, the magnitude of the associations we have reported, but the actual direction is speculative.

The NCDB also does not include data from cases treated entirely in outpatient facilities not associated with hospitals or cancer centers. This is most relevant to early stage

cutaneous melanoma, but may also have some impact on some other cancer sites and types.

NCDB does not include data regarding healthcare provider characteristics, so it is not possible to determine whether any relationships between facilities and quality measures are due to aggregate characteristics of the institution or specifically due to skill of the institutions’ pathologists. It is likely that the observed relationships between diagnostic detail and both center type and volume are mediated by institutional characteristics (facility credentialing policies that limit providers’ scope of practice, strength of quality improvement programs, promotion of internal and external consultation for difficult cases, quality of communication between pathologists and clinicians, etc.) and also by characteristics of individual pathologists (experience with specimens from particular sites, familiarity with current classification systems, specialty and subspecialty training including fellowship training, continuing professional education, etc.). More highly academic centers and higher volume centers tend to employ greater numbers of pathologists, many of whom have subspecialty training and experience with particular types of cancer and cancer sites. In some of these centers, the specimens from certain sites may be routinely assigned to subspecialists. For example, in academic centers, virtually all lymphomas are examined by pathologists with subspecialty certification in hematopathology. Other surgical pathologists may have expertise in areas such as gastrointestinal disease, respiratory disease, etc., that may have been acquired by fellowship training and/or other experiences or training, but are not reflected by subspecialty certification. One notable aspect of pathology practice is the relative ease of consultation, especially in large cancer centers. In contrast to surgical practice, in which

seeking some types of assistance might require a consultant to be present at the time the operation is in progress, timing of pathology consultation is more flexible. Difficult or complex cases are often set aside for daily or weekly conference, during which subspecialists gather around a multi-headed microscope (or view digital images) to provide advice within their area of expertise. Thus, for some specialties, quality is largely dependent on the individual provider caring for a patient. For pathology, assuming an appropriate level of cooperation and collegiality within the department, quality might be more substantially influenced by the collective knowledge and experience of the pathology staff.

Another potential limitation reflects the exploratory nature of these analyses and the decision to select only the diagnostic groups with prevalence differences greater than 1%. Although it unclear how this affects results, if at all, this part of the design will be modified for subsequent, more analytic approaches in future studies.

A final limitation is that socioeconomic (education and income) variables are based on ZIP code area aggregate data rather than individual data, and therefore are expected to be less useful in detecting associations with the prevalence of nonspecific diagnoses.

Conclusion

An exploratory inventory of the level of diagnostic detail for cases in the National Cancer Database identified several substantial differences among facilities of different types and volume groups that were interpreted as likely to be clinically relevant. These observations are consistent with a growing body of literature on facility-level differences in health outcomes and process-related measures of treatment quality. However, to our knowledge, this is the first report describing use of registry data to investigate such differences in

quality of oncologic pathology services, or to explore nonspecific diagnoses in surgical pathology as a quality measure.

The associations and time trends described in this report are intended as an exploratory overview of this approach. The opportunities for speculation regarding the time trends in prevalence of various diagnoses provided in different categories of facilities are beyond the scope of this initial study and can be better addressed in a series of follow-up studies, each of which is focused on a broader list of diagnoses (including some uncommon conditions) for individual sites. Some of these opportunities have also been alluded to earlier in this document. Further research in this field could also explore potential interactions between facility type and volume that might influence the prevalence of nonspecific diagnoses. Future studies could also use databases that include provider (in this case, regarding the pathologist) characteristics to examine associations with diagnostic precision and interactions with facility characteristics.

One notable and noteworthy trend is that for most sites, the prevalence of most of the clinically-relevant nonspecific diagnoses we studied has been declining. One explanation is the growing use of College of American Pathologists' cancer protocols (although this hypothesis cannot be proven by data available to us). These structured templates can be used as part of the pathology report not only to assure inclusion of data elements commonly required for clinical decisions, but also to provide a list of cancer types from which the pathologist may choose a diagnosis, thereby increasing adherence to standardized nomenclature.

Implications

These results have implications for consultation and second opinion practices in pathology, and for design and implementation of quality assessment and quality improvement programs. Upon receiving one of the relatively nonspecific diagnoses identified in this study as being associated with less academic facility types and lower volume facilities, patients receiving care from such institutions (or their physicians) may wish to seek consultation from subspecialty pathologists practicing at a high volume or more academic facility.

Pathologists practicing in Community Centers and low volume facilities may use the results of this study to help guide their policies regarding routine second opinions of certain categories of cases. They could use these results to prioritize their continuing medical education activities, based on patterns associated with their practice settings. Even better, comparison of institutional data on prevalence of nonspecific diagnoses with national benchmarks could be used in quality assessment and quality improvement programs. In addition to potential adverse clinical outcomes resulting from nonspecific diagnoses, such diagnoses might also be considered as a sentinel event. Pathologists or pathology departments with higher prevalence of nonspecific diagnoses for a particular site might also be likely to provide poorer quality care in other areas (incorrect diagnoses, or absence of some data elements needed for clinical management). Thus, identifying a high level of nonspecific diagnoses might trigger focused retrospective review of a sample of similar cases and could provide an opportunity for quality improvement.

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APPENDIX A – TABLES

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
8522 Infiltrating Duct and Lobular Carcinoma	9740 (4.68)	5153 (6.12)	37700 (5.95)	22173 (7.04)	9344 (10.32)	-5.64
8500 Infiltrating Duct Carcinoma	152973 (73.43)	62037 (73.68)	462464 (73.01)	225795 (71.72)	62603 (69.14)	4.29
8480 Mucinous Adencarcinoma	5020 (2.41)	1703 (2.02)	13784 (2.18)	6017 (1.91)	1351 (1.49)	0.92
8140 Adenocarcinoma, NOS	3137 (1.51)	693 (0.82)	6655 (1.05)	3711 (1.18)	949 (1.05)	0.46
8523 Infiltrating Duct Mixed with Other Types of Carcinoma	4682 (2.25)	1946 (2.31)	15486 (2.44)	7724 (2.45)	2441 (2.70)	-0.45
8510 Medullary Carcinoma, NOS	1602 (0.77)	426 (0.51)	3047 (0.48)	1651 (0.52)	347 (0.38)	0.39
8521 Infiltrating Ductular Carcinoma	1096 (0.53)	121 (0.14)	1919 (0.30)	938 (0.30)	212 (0.23)	0.29
8501 Comedocarcinoma, NOS	910 (0.44)	290 (0.34)	1833 (0.29)	1115 (0.35)	133 (0.15)	0.29
8530 Inflammatory Carcinoma	1647 (0.79)	664 (0.79)	5033 (0.79)	2496 (0.79)	912 (1.01)	-0.22
8000 Neoplasm, NOS	376 (0.18)	109 (0.13)	857 (0.14)	635 (0.20)	72 (0.08)	0.10
TOTAL	208329	84199	633452	314830	90546	
% total for all facilities	15.50	6.27	47.14	23.43	6.74	

Table 1. Breast cancer diagnoses by facility type.

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
8140 Adenocarcinoma, NOS	121103 (74.04)	35613 (72.03)	291491 (72.46)	136494 (72.03)	32846 (69.06)	4.98
8263 Adenocarcinoma in Tubulovillous Adenoma	7865 (4.81)	3125 (6.32)	23305 (5.79)	10253 (5.41)	3343 (7.03)	-2.22
8480 Mucinous Adencarcinoma	11116 (6.80)	3867 (7.82)	29050 (7.22)	13804 (7.28)	4055 (8.53)	-1.73
8481 Mucin-Producing Adenocarcinoma	3900 (2.38)	757 (1.53)	8477 (2.11)	3877 (2.05)	594 (1.25)	1.14
8210 Adenocarcinoma in Adenomatous Polyp	6836 (4.18)	1874 (3.79)	16637 (4.14)	7784 (4.11)	2415 (5.08)	-0.90
8490 Signet Ring Cell Carcinoma	1492 (0.91)	557 (1.13)	4283 (1.06)	2334 (1.23)	780 (1.64)	-0.73
8261 Adenocarcinoma in Villous Adenoma	4001 (2.45)	1156 (2.34)	10813 (2.69)	4609 (2.43)	930 (1.96)	0.49
8246 Neuroendocrine Carcinoma	386 (0.24)	178 (0.36)	1078 (0.27)	612 (0.32)	252 (0.53)	-0.29
8240 Carcinoid Tumor, NOS	2487 (1.52)	852 (1.72)	6377 (1.59)	3752 (1.98)	861 (1.81)	-0.29
8000 Neoplasm, NOS	312 (0.19)	96 (0.19)	643 (0.16)	404 (0.21)	83 (0.17)	0.02
TOTAL	163572	49444	402285	189509	47564	
% total for all facilities	18.98	5.74	46.69	21.99	5.52	

Table 2. Colorectal cancer diagnoses by facility type.

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
8312 Renal Cell Carcinoma	16705 (55.93)	6964 (48.83)	47313 (49.80)	29257 (47.96)	11168 (40.91)	15.02
8310 Clear Cell Adenocarcinoma, NOS	6707 (22.45)	3853 (27.02)	25784 (27.14)	16657 (27.30)	8709 (31.90)	-9.45
8260 Papillary Adenocarcinoma, NOS	1452 (4.86)	1060 (7.43)	5770 (6.07)	4843 (7.94)	2700 (9.89)	-5.03
8317 Renal Cell Carcinoma,Chromophobe Type	652 (2.18)	454 (3.18)	2707 (2.85)	2124 (3.48)	1321 (4.84)	-2.66
8130 Papillary Transitional Cell Carcinoma	1126 (3.77)	449 (3.15)	3462 (3.64)	1747 (2.86)	674 (2.47)	1.30
8120 Transitional Cell Carcinoma, NOS	1214 (4.06)	454 (3.18)	3414 (3.59)	1823 (2.99)	767 (2.81)	1.25
8318 Renal Cell Carcinoma,Sarcomatoid	391 (1.31)	180 (1.26)	1243 (1.31)	978 (1.60)	554 (2.03)	-0.72
8140 Adenocarcinoma, NOS	232 (0.78)	86 (0.60)	560 (0.59)	267 (0.44)	71 (0.26)	0.52
8010 Carcinoma, NOS	200 (0.67)	69 (0.48)	550 (0.58)	335 (0.55)	106 (0.39)	0.28
8000 Neoplasm, NOS	35 (0.12)	26 (0.18)	143 (0.15)	88 (0.14)	20 (0.07)	0.04
TOTAL	29869	14261	95001	61009	27299	
% total for all facilities	13.05	6.23	41.52	26.66	11.93	

Table 3. Kidney and renal pelvis cancer diagnoses by facility type.

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
9823 B-Cell Chronic Lymphocytic Luekemia/Small Lymphocytic Leukemia	5265 (33.10)	1579 (22.33)	14002 (27.07)	7881 (19.88)	2764 (14.19)	18.92
9836 Precursor B-Cell Lymphoblastic Leukemia	177 (1.11)	143 (2.02)	899 (1.74)	1169 (2.95)	921 (4.73)	-3.61
9874 Acute Myeloid Leukemia with Maturation	217 (1.36)	161 (2.28)	1144 (2.21)	924 (2.33)	857 (4.40)	-3.03
9835 Precursor Cell Lymphoblastic Leukemia, NOS	609 (3.83)	426 (6.02)	2449 (4.73)	2729 (6.88)	1297 (6.66)	-2.83
9861 Acute Myloid Leukemia,NOS	3331 (20.94)	1781 (25.18)	11999 (23.20)	10474 (26.42)	4606 (23.64)	-2.70
9866 Acute Promyelocytic Leukemia, t(15;17)(q22;q11-12)	321 (2.02)	267 (3.78)	1537 (2.97)	1613 (4.07)	858 (4.40)	-2.39
9873 Acute Myeloid Leukemia without Maturation	165 (1.04)	140 (1.98)	1047 (2.02)	745 (1.88)	630 (3.23)	-2.20
9895 Acute Myeloid Leukemia with Multilineage Dysplasia	213 (1.34)	91 (1.29)	792 (1.53)	783 (1.98)	621 (3.19)	-1.85
9940 Hairy Cell Leukemia	597 (3.75)	239 (3.38)	1952 (3.77)	1106 (2.79)	390 (2.00)	1.75
9801 Acute Leukemia, NOS	353 (2.22)	112 (1.58)	941 (1.82)	557 (1.40)	138 (0.71)	1.51
9945 Chronic Myelomonocytic Leukemia, NOS	664 (4.18)	246 (3.48)	1670 (3.23)	1042 (2.63)	558 (2.86)	1.31
9891 Acute Monocytic Leukemia	334 (2.10)	227 (3.21)	1435 (2.77)	1072 (2.70)	656 (3.37)	-1.27
TOTAL	15904	7072	51722	39645	19483	
% total for all facilities	11.81	5.25	38.41	29.44	14.47	

Table 4. Leukemia diagnoses by facility type.

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
8041 Small Cell Carcinoma, NOS	25812 (16.71)	6967 (14.43)	62359 (14.90)	25256 (12.77)	5664 (9.33)	7.38
8140 Adenocarcinoma, NOS	39427 (25.53)	14499 (30.04)	119283 (28.49)	58723 (29.70)	19196 (31.63)	-6.11
8070 Squamous Cell Carcinoma, NOS	33746 (21.85)	9423 (19.52)	85611 (20.45)	40659 (20.56)	10999 (18.13)	3.72
8012 Large Cell Carcinoma	7021 (4.55)	2158 (4.47)	18839 (4.50)	7828 (3.96)	1297 (2.14)	2.41
8255 Adenocarcinoma with Mixed Subtypes	160 (0.10)	103 (0.21)	745 (0.18)	635 (0.32)	1259 (2.07)	-1.97
8250 Bronchiolo-Alveolar Adenocarcinoma	3498 (2.26)	1239 (2.57)	11361 (2.71)	6278 (3.17)	2451 (4.04)	-1.77
8240 Carcinoid Tumor, NOS	1189 (0.77)	753 (1.56)	4967 (1.19)	3167 (1.60)	1502 (2.48)	-1.71
8042 Oat Cell Carcinoma	2056 (1.33)	298 (0.62)	4460 (1.07)	1063 (0.54)	91 (0.15)	1.18
8010 Carcinoma, NOS	7434 (4.81)	2291 (4.75)	18731 (4.47)	9247 (4.68)	2458 (4.05)	0.76
8046 Non-Small Cell Carcinoma	20086 (13.00)	5874 (12.17)	51834 (12.38)	24101 (12.19)	8348 (13.76)	-0.75
8000 Neoplasm, NOS	781 (0.51)	181 (0.37)	1559 (0.37)	820 (0.41)	95 (0.16)	0.35
TOTAL	154460	48270	418650	197741	60680	
% total for all facilities	17.39	5.44	47.15	22.27	6.83	

Table 5. Lung cancer diagnoses by facility type.

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
8720 Melanoma, NOS	15199 (57.87)	7548 (56.25)	52406 (58.32)	35615 (57.24)	17743 (41.84)	16.03
8743 Superficial Spreading Melanoma	6406 (24.39)	3497 (26.06)	21844 (24.31)	15007 (24.12)	15773 (37.20)	-12.81
8745 Desmoplastic Melanoma	215 (0.82)	152 (1.13)	1028 (1.14)	775 (1.25)	792 (1.87)	-1.05
8744 Acral Lentiginous Melanoma	232 (0.88)	167 (1.24)	950 (1.06)	790 (1.27)	765 (1.80)	-0.92
8771 Epithelioid Cell Melanoma	71 (0.27)	40 (0.30)	310 (0.34)	165 (0.27)	385 (0.91)	-0.64
8723 Regressing Melanoma	99 (0.38)	41 (0.31)	356 (0.40)	446 (0.72)	337 (0.79)	-0.42
8721 Nodular Melanoma	2406 (9.16)	1100 (8.20)	7454 (8.29)	5083 (8.17)	4045 (9.54)	-0.38
8730 Amelanotic Melanoma	123 (0.47)	58 (0.43)	443 (0.49)	277 (0.45)	86 (0.20)	0.27
8772 Spindle Cell Melanoma, NOS	320 (1.22)	195 (1.45)	1105 (1.23)	767 (1.23)	593 (1.40)	-0.18
8761 Melanoma in Giant Pigmented Nevus	101 (0.38)	43 (0.32)	219 (0.24)	151 (0.24)	96 (0.23)	0.16
TOTAL	26262	13419	89866	62225	42402	
% total for all facilities	11.16	5.70	38.18	26.44	18.02	

Table 6. Melanoma diagnoses by facility type.

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
9591 Malignant Lymphoma, Non-Hodgkin, NOS	4262 (9.31)	1315 (7.61)	10424 (7.93)	6001 (7.96)	1358 (4.41)	4.90
9700 Mycosis Fungoides	146 (0.32)	60 (0.35)	470 (0.36)	1238 (1.64)	1332 (4.33)	-4.01
9670 Small B Lymphocytic Lymphoma, NOS	3228 (7.05)	891 (5.16)	8050 (6.12)	3669 (4.87)	1148 (3.73)	3.32
9690 Follicular Lymphoma, NOS	3630 (7.93)	1191 (6.90)	9642 (7.33)	4555 (6.04)	1442 (4.68)	3.25
9590 Malignant Lymphoma, NOS	2486 (5.43)	845 (4.89)	6501 (4.94)	3977 (5.28)	1008 (3.27)	2.16
9687 Burkitt Lymphoma, NOS	465 (1.02)	399 (2.31)	1853 (1.41)	1849 (2.45)	901 (2.93)	-1.91
9673 Mantle Cell Lymphoma	1570 (3.43)	591 (3.42)	4778 (3.63)	2594 (3.44)	1643 (5.34)	-1.91
9709 Cutaneous T-Cell Lymphoma	262 (0.57)	97 (0.56)	827 (0.63)	1113 (1.48)	754 (2.45)	-1.88
9699 Marginal Zone B-Cell Lymphoma	2876 (6.28)	1375 (7.96)	9202 (7.00)	5288 (7.02)	2378 (7.73)	-1.44
9702 Mature T-Cell Lymphoma, NOS	692 (1.51)	322 (1.86)	2074 (1.58)	14461.92v	687 (2.23)	-0.72
TOTAL	45761	17272	131511	75365	30781	
% total for all facilities	15.09	5.69	43.36	24.85	10.15	

Table 7. Non-Hodgkin lymphoma diagnoses by facility type.

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
8070 Squamous Cell Carcinoma, NOS	17079 (69.32)	7338 (63.50)	48642 (68.01)	38566 (66.71)	15802 (61.43)	7.89
8071 Keratinizing Squamous Cell Carcinoma, NOS	2243 (9.10)	1332 (11.53)	6925 (9.68)	6150 (10.64)	3056 (11.88)	-2.78
8072 Large Cell, Nonkeratinizing Squamous Cell Carcinoma	576 (2.34)	375 (3.25)	1960 (2.74)	1607 (2.78)	1001 (3.89)	-1.55
8200 Adenoid Cystic Carcinoma	521 (2.11)	321 (2.78)	1488 (2.08)	1273 (2.20)	878 (3.41)	-1.30
8083 Basaloid Squamous Cell Carcinoma	240 (0.97)	123 (1.06)	827 (1.16)	689 (1.19)	482 (1.87)	-0.90
8430 Mucepidermoid Carcinoma	854 (3.47)	543 (4.70)	2659 (3.72)	2244 (3.88)	1019 (3.96)	-0.50
8010 Carcinoma, NOS	608 (2.47)	244 (2.11)	1591 (2.22)	1414 (2.45)	531 (2.06)	0.40
8525 Polymorphous Low Grade Adenocarcinoma	54 (0.22)	50 (0.43)	180 (0.25)	236 (0.41)	148 (0.58)	-0.36
8090 Basal Cell Carcinoma, NOS	68 (0.28)	23 (0.20)	182 (0.25)	86 (0.15)	19 (0.07)	0.20
8000 Neoplasm, NOS	59 (0.24)	23 (0.20)	126 (0.18)	90 (0.16)	26 (0.10)	0.14
TOTAL	24637	11555	71519	57808	25723	
% total for all facilities	12.77	5.99	37.07	29.96	13.33	

Table 8. Oral and pharyngeal cancer diagnoses by facility type.

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
8140 Adenocarcinoma, NOS	2012 (15.04)	700 (8.40)	5797 (11.30)	3367 (8.51)	920 (6.89)	8.15
8441 Serous Cystadenocarcinoma, NOS	1416 (10.58)	1166 (13.99)	6087 (11.86)	5486 (13.86)	2388 (17.87)	-7.29
8260 Papillary Adenocarcinoma, NOS	603 (4.51)	168 (2.02)	1348 (2.63)	683 (1.73)	97 (0.73)	3.78
8461 Serous Surface Papillary Carcinoma	821 (6.14)	794 (9.53)	4284 (8.35)	3398 (8.59)	1316 (9.85)	-3.71
8460 Papillary Serous Cystadenocarcinoma	2820 (21.07)	2147 (25.77)	12937 (25.22)	10023 (25.33)	3271 (24.48)	-3.41
8323 Mixed Cell Adenocarcinoma	79 (0.59)	132 (1.58)	788 (1.54)	828 (2.09)	487 (3.64)	-3.05
8010 Carcinoma, NOS	588 (4.39)	229 (2.75)	1865 (3.64)	1071 (2.71)	308 (2.31)	2.09
8470 Mucinous Cystadenocarcinoma, NOS	456 (3.41)	191 (2.29)	1288 (2.51)	968 (2.45)	237 (1.77)	1.63
8310 Clear Cell Adenocarcinoma, NOS	584 (4.36)	456 (5.47)	2546 (4.96)	2400 (6.07)	766 (5.73)	-1.37
8000 Neoplasm, NOS	94 (0.70)	32 (0.38)	240 (0.47)	132 (0.33)	29 (0.22)	0.49
8380 Endometrioid Adenocarcinoma	1478 (11.04)	976 (11.71)	5869 (11.44)	4598 (11.62)	1478 (11.06)	-0.02
TOTAL	13382	8332	51304	39570	13361	
% total for all facilities	10.54	6.56	40.42	31.18	10.53	

Table 9. Ovarian cancer diagnoses by facility type.

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
8140 Adenocarcinoma, NOS	11740 (73.74)	5418 (69.75)	36439 (73.42)	23917 (69.40)	12262 (66.80)	6.94
8500 Infiltrating Duct Carcinoma	936 (5.88)	784 (10.09)	3441 (6.93)	3296 (9.56)	2216 (12.07)	-6.19
8246 Neuroendocrine Carcinoma	302 (1.90)	239 (3.08)	1171 (2.36)	1164 (3.38)	1101 (6.00)	-4.10
8010 Carcinoma, NOS	978 (6.14)	377 (4.85)	2534 (5.11)	1438 (4.17)	420 (2.29)	3.86
8150 Islet Cell Carcinoma	99 (0.62)	84 (1.08)	491 (0.99)	416 (1.21)	458 (2.50)	-1.87
8481 Mucin-Producing Adenocarcinoma	392 (2.46)	131 (1.69)	934 (1.88)	703 (2.04)	212 (1.15)	1.31
8000 Neoplasm, NOS	249 (1.56)	65 (0.84)	542 (1.09)	273 (0.79)	102 (0.56)	1.01
8453 Intraductal Papillary-Mucinous Carcinoma	15 (0.09)	15 (0.19)	83 (0.17)	108 (0.31)	94 (0.51)	-0.42
8041 Small Cell Carcinoma, NOS	78 (0.49)	20 (0.26)	162 (0.33)	64 (0.19)	21 (0.11)	0.38
8480 Mucinous Adencarcinoma	407 (2.56)	250 (3.22)	1393 (2.81)	1184 (3.44)	501 (2.73)	-0.17
TOTAL	15920	7768	49634	34464	18356	
% total for all facilities	12.53	6.11	39.06	27.12	14.45	

Table 10. Pancreatic cancer diagnoses by facility type.

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
8550 Acinar Cell Carcinoma	2383 (1.46)	1236 (1.84)	10827 (2.01)	4560 (1.59)	11683 (9.74)	-8.28
8140 Adenocarcinoma, NOS	158676 (97.43)	65254 (97.28)	522778 (97.13)	279996 (97.45)	107263 (89.41)	8.02
8010 Carcinoma, NOS	901 (0.55)	214 (0.32)	2098 (0.39)	1339 (0.47)	175 (0.15)	0.41
8500 Infiltrating Duct Carcinoma	107 (0.07)	46 (0.07)	333 (0.06)	206 (0.07)	253 (0.21)	-0.15
8000 Neoplasm, NOS	314 (0.19)	125 (0.19)	762 (0.14)	390 (0.14)	77 (0.06)	0.13
8480 Mucinous Adencarcinoma	81 (0.05)	48 (0.07)	268 (0.05)	177 (0.06)	179 (0.15)	-0.10
8255 Adenocarcinoma with Mixed Subtypes	30 (0.02)	17 (0.03)	116 (0.02)	59 (0.02)	58 (0.05)	-0.03
8120 Transitional Cell Carcinoma, NOS	47 (0.03)	16 (0.02)	89 (0.02)	61 (0.02)	9 (0.01)	0.02
8490 Signet Ring Cell Carcinoma	13 (0.01)	10 (0.01)	38 (0.01)	53 (0.02)	33 (0.03)	-0.02
8323 Mixed Cell Adenocarcinoma	3 (0.00)	0 (0.00)	8 (0.00)	11 (0.00)	15 (0.01)	-0.01
TOTAL	162862	67081	538225	287332	119962	
% total for all facilities	13.74	5.66	45.41	24.24	10.12	

Table 11. Prostate cancer diagnoses by facility type.

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
8260 Papillary Adenocarcinoma, NOS	4459 (21.54)	3793 (29.94)	23271 (28.46)	14737 (26.68)	7723 (36.24)	-14.70
8050 Papillary Carcinoma, NOS	6043 (29.19)	3203 (25.28)	21148 (25.87)	15321 (27.74)	4082 (19.16)	10.03
8340 Follicular Variant Papillary Carcinoma	5742 (27.74)	3368 (26.59)	21624 (26.45)	14401 (26.07)	4685 (21.99)	5.75
8344 Papillary Carcinoma, Columnar Cell	122 (0.59)	87 (0.69)	535 (0.65)	398 (0.72)	517 (2.43)	-1.84
8330 Follicular Adenocarcinoma, NOS	1199 (5.79)	589 (4.65)	4247 (5.19)	2894 (5.24)	897 (4.21)	1.58
8510 Medullary Carcinoma, NOS	287 (1.39)	196 (1.55)	945 (1.16)	859 (1.56)	583 (2.74)	-1.35
8341 Papillary Microcarcinoma	806 (3.89)	420 (3.32)	2665 (3.26)	1995 (3.61)	989 (4.64)	-0.75
8335 Follicular Carcinoma, Minimally Invasive	310 (1.50)	141 (1.11)	1046 (1.28)	671 (1.21)	182 (0.85)	0.64
8010 Carcinoma, NOS	185 (0.89)	80 (0.63)	810 (0.99)	348 (0.63)	90 (0.42)	0.47
8000 Neoplasm, NOS	44 (0.21)	16 (0.13)	184 (0.23)	89 (0.16)	23 (0.11)	0.10
TOTAL	20703	12668	81754	55232	21309	
% total for all facilities	10.74	6.57	42.41	28.65	11.05	

Table 12. Thyroid cancer diagnoses by facility type.

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
8130 Papillary Transitional Cell Carcinoma	44394 (67.89)	13248 (69.51)	111847 (69.50)	44626 (63.46)	9473 (50.61)	17.28
8120 Transitional Cell Carcinoma, NOS	17313 (26.48)	4684 (24.58)	40257 (25.01)	20874 (29.68)	7715 (41.21)	-14.74
8050 Papillary Carcinoma, NOS	943 (1.44)	232 (1.22)	1831 (1.14)	793 (1.13)	104 (0.56)	0.89
8070 Squamous Cell Carcinoma, NOS	580 (0.89)	174 (0.91)	1439 (0.89)	918 (1.31)	273 (1.46)	-0.57
8490 Signet Ring Cell Carcinoma	55 (0.08)	25 (0.13)	209 (0.13)	145 (0.21)	111 (0.59)	-0.51
8131 Transitional Cell Carcinoma, Micropapillary	29 (0.04)	17 (0.09)	138 (0.09)	78 (0.11)	81 (0.43)	-0.39
8140 Adenocarcinoma, NOS	341 (0.52)	120 (0.63)	873 (0.54)	505 (0.72)	165 (0.88)	-0.36
8041 Small Cell Carcinoma, NOS	221 (0.34)	85 (0.45)	635 (0.39)	313 (0.45)	126 (0.67)	-0.34
8071 Keratinizing Squamous Cell Carcinoma, NOS	152 (0.23)	53 (0.28)	368 (0.23)	234 (0.33)	102 (0.54)	-0.31
8010 Carcinoma, NOS	586 (0.90)	167 (0.88)	1375 (0.85)	700 (1.00)	137 (0.73)	0.16
TOTAL	65390	19059	160934	70325	18719	
% total for all facilities	19.36	5.64	47.66	20.83	5.54	

Table 13. Urinary bladder cancer diagnoses by facility type.

ICDO3	Community	Community Network	Comp Community	Teaching Research	NCI Program	Community% - NCI%
8140 Adenocarcinoma, NOS	9250 (29.94)	3244 (18.23)	28436 (25.51)	15333 (17.71)	2311 (9.59)	20.35
8380 Endometrioid Adenocarcinoma	15264 (49.41)	10357 (58.21)	59396 (53.28)	49843 (57.57)	14504 (60.19)	-10.77
8323 Mixed Cell Adenocarcinoma	241 (0.78)	307 (1.73)	1482 (1.33)	1845 (2.13)	1085 (4.50)	-3.72
8460 Papillary Serous Cystadenocarcinoma	527 (1.71)	489 (2.75)	2468 (2.21)	2369 (2.74)	825 (3.42)	-1.72
8441 Serous Cystadenocarcinoma, NOS	235 (0.76)	273 (1.53)	1161 (1.04)	1430 (1.65)	583 (2.42)	-1.66
8950 Mullerian Mixed Tumor	610 (1.97)	447 (2.51)	2457 (2.20)	2316 (2.67)	861 (3.57)	-1.60
8260 Papillary Adenocarcinoma, NOS	309 (1.00)	73 (0.41)	654 (0.59)	422 (0.49)	44 (0.18)	0.82
8890 Leiomyosarcoma	638 (2.07)	335 (1.88)	2090 (1.87)	1774 (2.05)	651 (2.70)	-0.64
8461 Serous Surface Papillary Carcinoma	93 (0.30)	98 (0.55)	482 (0.43)	481 (0.56)	206 (0.85)	-0.55
8010 Carcinoma, NOS	350 (1.13)	159 (0.89)	1070 (0.96)	788 (0.91)	169 (0.70)	0.43
TOTAL	30892	17792	111472	86584	24099	
% total for all facilities	11.32	6.52	40.86	31.74	8.83	

Table 14. Uterine corpus cancer diagnoses by facility type.

	Kidney		**N-H lymphoma**		**Ovary**		**Pancreas**		**Uterine corp.**	
Variable	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Sex (compared to male)										
female	1.01	0.99-1.03	1.1	1.08-1.12	NA	NA	0.91	0.87-0.96	NA	NA
Age (compared to <50)										
age50-59	1.06	1.03-1.08	1.05	1.03-1.08	1.08	1.03-1.14	0.89	0.82-0.97	1.05	1.02-1.08
age60-69	1.04	1.01-1.06	1.05	1.03-1.08	1.21	1.15-1.26	0.83	0.77-0.89	1.03	1-1.06
age70-79	0.98	0.95-1.01	1.06	1.03-1.09	1.3	1.23-1.36	0.86	0.8-0.93	1.04	1-1.07
age85+	0.69	0.65-0.73	1.16	1.12-1.21	2.17	2-2.34	1.65	1.48-1.83	1.1	1.04-1.16
Insurance (compared to private)										
uninsured	1.08	1.03-1.14	1.02	0.97-1.07	1.18	1.08-1.28	1.09	0.95-1.24	0.99	0.94-1.05
Medicaid	1.06	1.01-1.11	0.97	0.93-1.02	1.29	1.19-1.39	1.02	0.9-1.15	0.94	0.9-0.99
Medicare18-64	1.03	0.98-1.07	1.06	1.01-1.12	1.28	1.17-1.41	1.09	0.95-1.24	1	0.95-1.05
Medicare65+	0.91	0.89-0.94	1.03	1.01-1.06	1.69	1.61-1.76	1.1	1.03-1.18	0.97	0.94-0.99
INS_MISSING	1.47	1.4-1.55	1.17	1.12-1.23	1.44	1.32-1.57	1.02	0.89-1.18	1.16	1.1-1.22
Race (compared to non-Hispanic White)										
Hispanic	1.02	0.98-1.06	0.98	0.94-1.03	1.13	1.04-1.22	1.24	1.11-1.38	0.95	0.9-1
Black	0.97	0.94-1	0.92	0.88-0.95	1.29	1.22-1.37	1.05	0.97-1.14	0.79	0.76-0.82
Asian	0.95	0.88-1.02	0.87	0.81-0.93	0.96	0.86-1.07	1.03	0.88-1.21	0.97	0.91-1.05
other	1.06	0.97-1.16	1.11	1-1.23	1	0.83-1.2	1.03	0.78-1.36	1.04	0.93-1.16
RACE_MISSING	1.09	1.05-1.12	1.03	1-1.07	0.94	0.89-1	0.94	0.85-1.03	0.97	0.94-1
ZIP income quartile (compared to 4th)										
incq1	0.96	0.92-0.99	1.01	0.97-1.05	0.99	0.93-1.06	1.03	0.93-1.14	1.03	0.98-1.07
incq2	0.98	0.95-1.01	1	0.97-1.03	0.98	0.93-1.04	1.02	0.93-1.11	1.05	1.02-1.09

incq3	1	0.97-1.03	1	0.97-1.02	0.98	0.94-1.03	1.02	0.95-1.1	1.03	1-1.06
ZIP no HS diploma quartile(compared to 4th)										
nhsq1	1.1	1.06-1.14	1.09	1.05-1.13	1.14	1.07-1.21	1.15	1.04-1.27	1.07	1.03-1.12
nhsq2	1.08	1.05-1.11	1.01	0.98-1.04	1.06	1-1.11	0.97	0.89-1.05	1.02	0.99-1.05
nhsq3	1.06	1.03-1.08	1.02	0.99-1.05	1.03	0.99-1.08	0.98	0.91-1.06	1	0.97-1.03
Facility type (compared to community center)										
Teaching & research	0.92	0.88-0.95	1	0.97-1.04	0.78	0.73-0.83	0.79	0.72-0.87	0.76	0.73-0.79
Comp. community	0.91	0.88-0.94	1.02	0.99-1.05	0.94	0.89-0.99	0.94	0.86-1.02	0.99	0.96-1.02
NCI program	0.69	0.66-0.72	0.61	0.58-0.64	0.61	0.56-0.66	0.46	0.41-0.52	0.36	0.34-0.39
MISSING_Other	0.9	0.8-1.01	0.89	0.81-0.99	1.13	0.96-1.32	0.97	0.75-1.24	0.95	0.85-1.05
Volume group (compared to low)										
volume_med	0.96	0.92-1.01	0.9	0.87-0.94	0.98	0.91-1.05	0.96	0.87-1.06	0.99	0.95-1.04
volume_high	0.79	0.75-0.82	0.75	0.72-0.78	0.57	0.53-0.62	0.74	0.66-0.82	0.68	0.65-0.71

Region (compared to Northeast)										
Atlantic	0.8	0.77-0.84	0.95	0.91-0.99	1.09	1.01-1.18	1.23	1.1-1.38	1.83	1.74-1.92
Southeast	1.14	1.1-1.19	0.99	0.96-1.04	1.03	0.95-1.11	0.9	0.81-1.01	1.76	1.67-1.84
Great Lakes	0.97	0.92-1.02	0.72	0.69-0.76	0.82	0.75-0.91	0.8	0.7-0.93	2.33	2.21-2.47
South	1.38	1.33-1.44	1.12	1.08-1.17	1.16	1.08-1.25	1.16	1.03-1.29	2.17	2.07-2.28
Midwest	1.57	1.49-1.65	1.07	1.02-1.13	1.29	1.18-1.41	0.88	0.76-1.01	3.05	2.88-3.24
West	1.39	1.32-1.45	1.03	0.99-1.08	1.07	0.98-1.16	0.92	0.81-1.05	1.97	1.86-2.09
Mountain	0.83	0.78-0.87	0.81	0.76-0.85	0.85	0.77-0.94	0.9	0.77-1.05	1.71	1.61-1.83
Pacific	0.54	0.51-0.56	0.73	0.7-0.77	0.94	0.87-1.02	1.1	0.98-1.24	1.53	1.45-1.61
Year of diagnosis (compared to 1998)										
1999	0.99	0.94-1.04	1.06	1.01-1.1	0.96	0.9-1.03	0.98	0.87-1.11	0.83	0.8-0.87
2000	0.94	0.89-0.99	1.15	1.1-1.2	0.9	0.84-0.97	1.11	0.98-1.25	0.69	0.66-0.72
2001	0.49	0.47-0.52	0.94	0.9-0.98	0.83	0.77-0.89	0.99	0.88-1.11	0.44	0.42-0.46
2002	0.39	0.37-0.41	0.96	0.92-1	0.81	0.75-0.87	0.97	0.86-1.09	0.38	0.37-0.4
2003	0.34	0.33-0.36	0.98	0.94-1.02	0.75	0.7-0.81	0.94	0.84-1.06	0.3	0.29-0.32
2004	0.29	0.28-0.31	1.01	0.97-1.06	0.74	0.69-0.79	1	0.89-1.12	0.24	0.23-0.25
2005	0.26	0.25-0.27	0.95	0.91-0.99	0.68	0.63-0.73	0.94	0.84-1.06	0.21	0.2-0.22
2006	0.2	0.2-0.21	0.93	0.89-0.97	0.67	0.63-0.73	0.96	0.85-1.08	0.18	0.17-0.19
2007	0.14	0.14-0.15	0.93	0.89-0.97	0.61	0.56-0.65	0.89	0.79-1	0.15	0.15-0.16
2008	0.13	0.13-0.14	0.88	0.84-0.92	0.6	0.55-0.64	0.93	0.83-1.04	0.13	0.13-0.14

Table 15. Multivariable logistic regression of nonspecific diagnoses of 5 cancer sites. The dependent variable is occurrence of the following diagnoses/codes:
Kidney: renal cell carcinoma, NOS (8312) versus all other histology codes
Non-Hodgkin lymphoma: malignant Non-Hodgkin's lymphoma, NOS (9591) or follicular lymphoma, NOS (9690) or malignant lymphoma, NOS (9590) versus all other histology codes

Ovary: adenocarcinoma, NOS (8140) or carcinoma, NOS(8010) or papillary adenocarcinoma, NOS (8260) versus all other histology codes ,
Pancreas: carcinoma NOS (8010) or neoplasm NOS (8000) versus all other histology codes
Uterine corpus: adenocarcinoma, NOS (8140) versus all other histology codes

APPENDIX A -- FIGURES

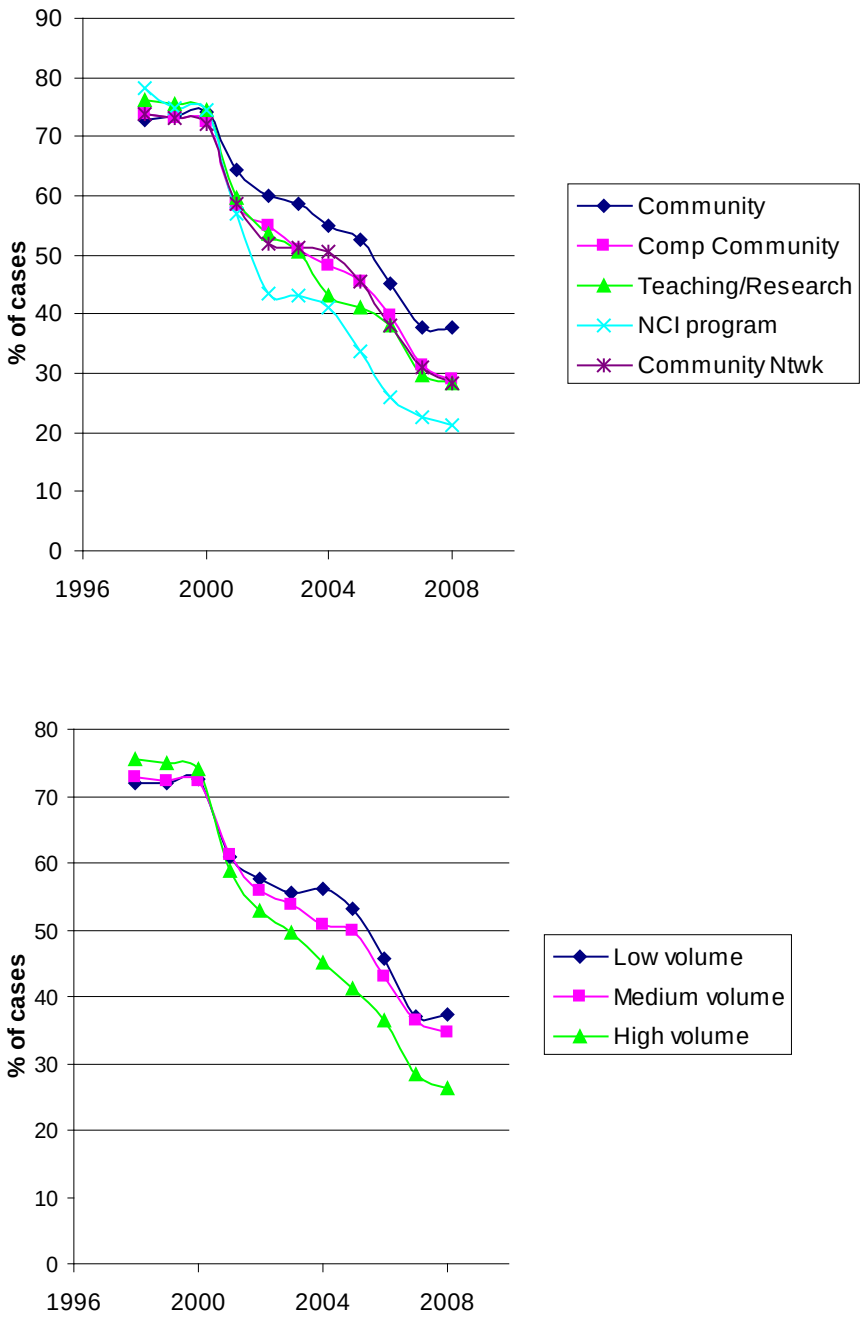

Figure 1. Site: kidney and renal pelvis. Prevalence of "renal cell carcinoma" (8312) by facility type and volume group.

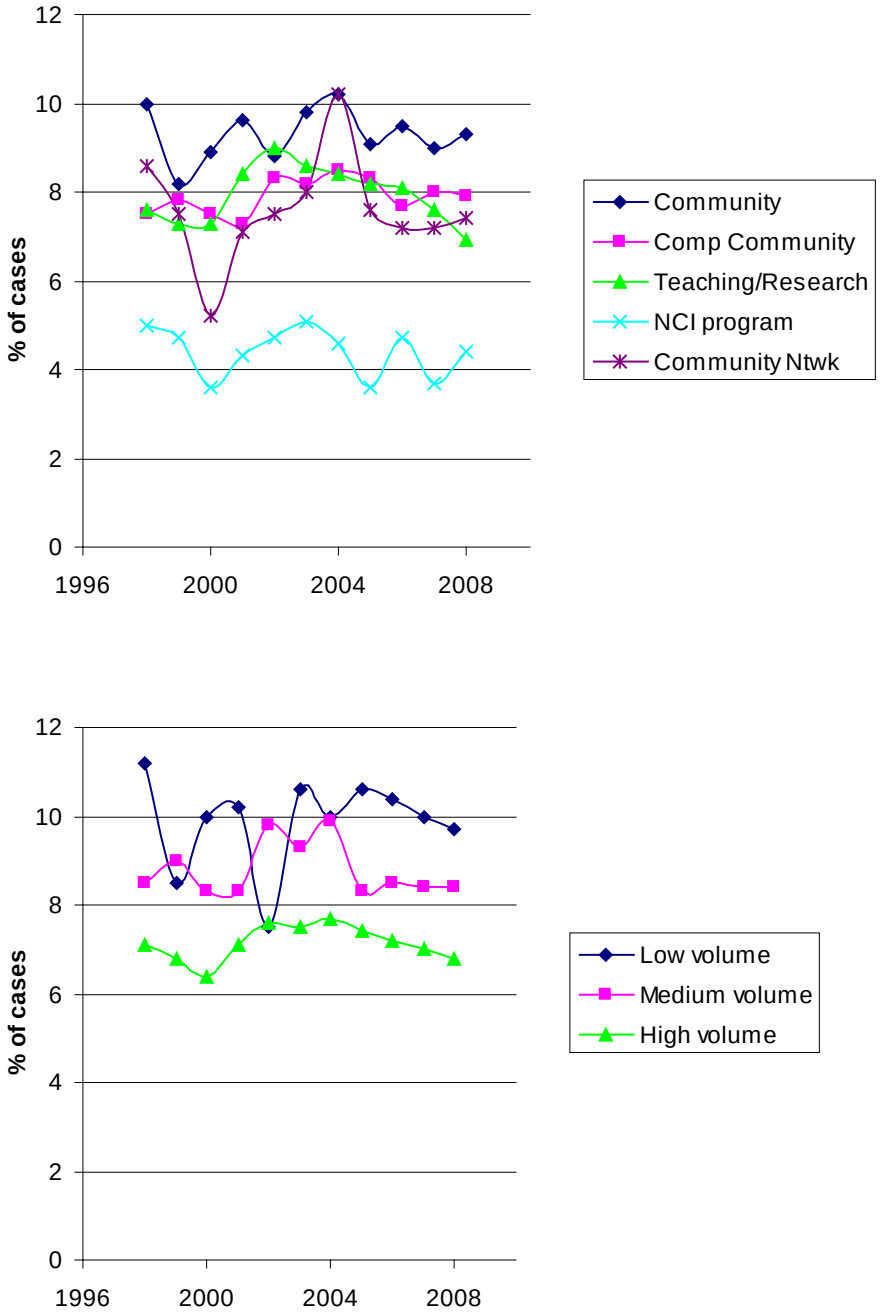

Figure 2A. Site/type: non-Hodgkin lymphoma. Prevalence of “non-Hodgkin lymphoma, NOS” (9591) by facility type and volume group.

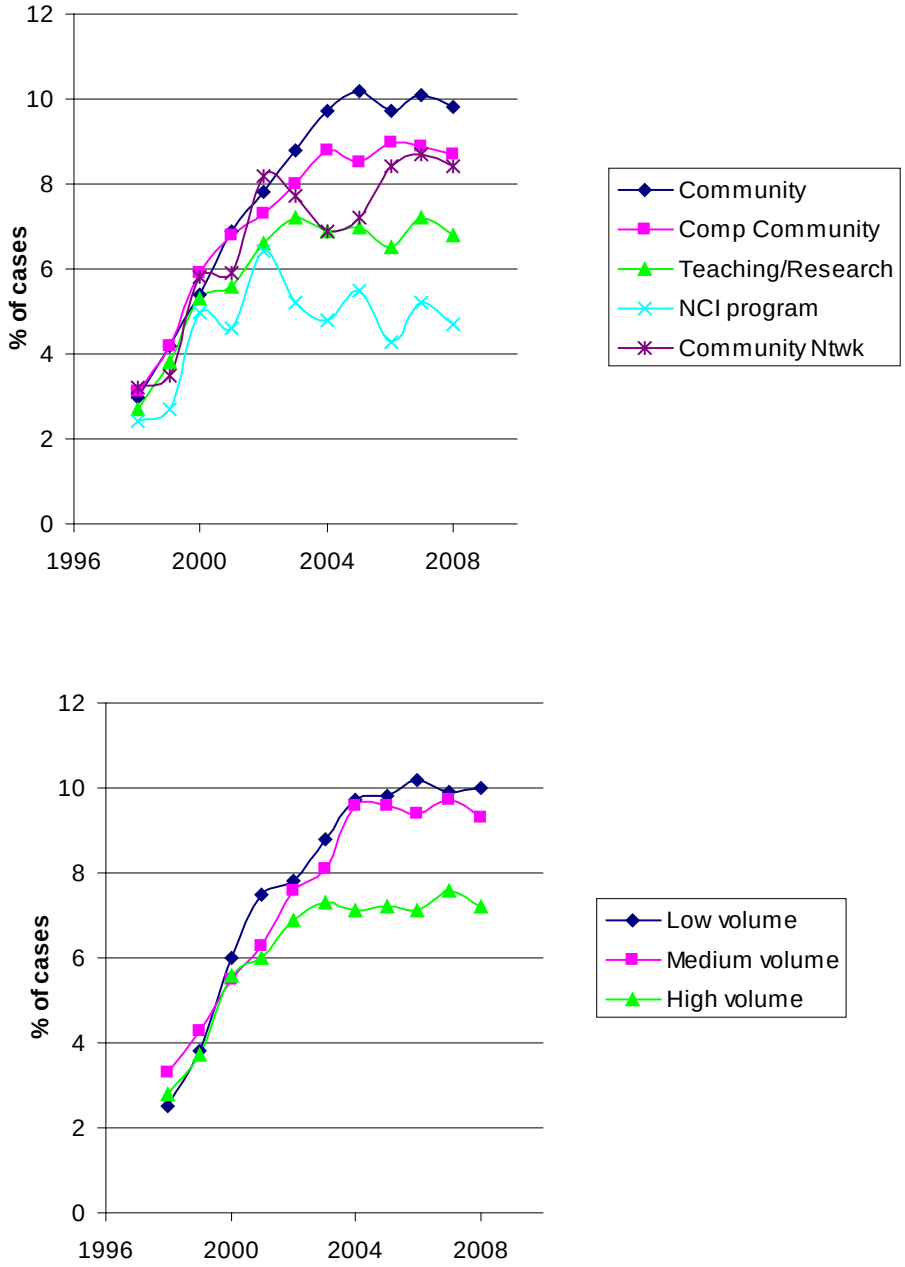

Figure 2B. Site/type: non-Hodgkin lymphoma. Prevalence of “follicular lymphoma, NOS” (9690) by facility type and volume group.

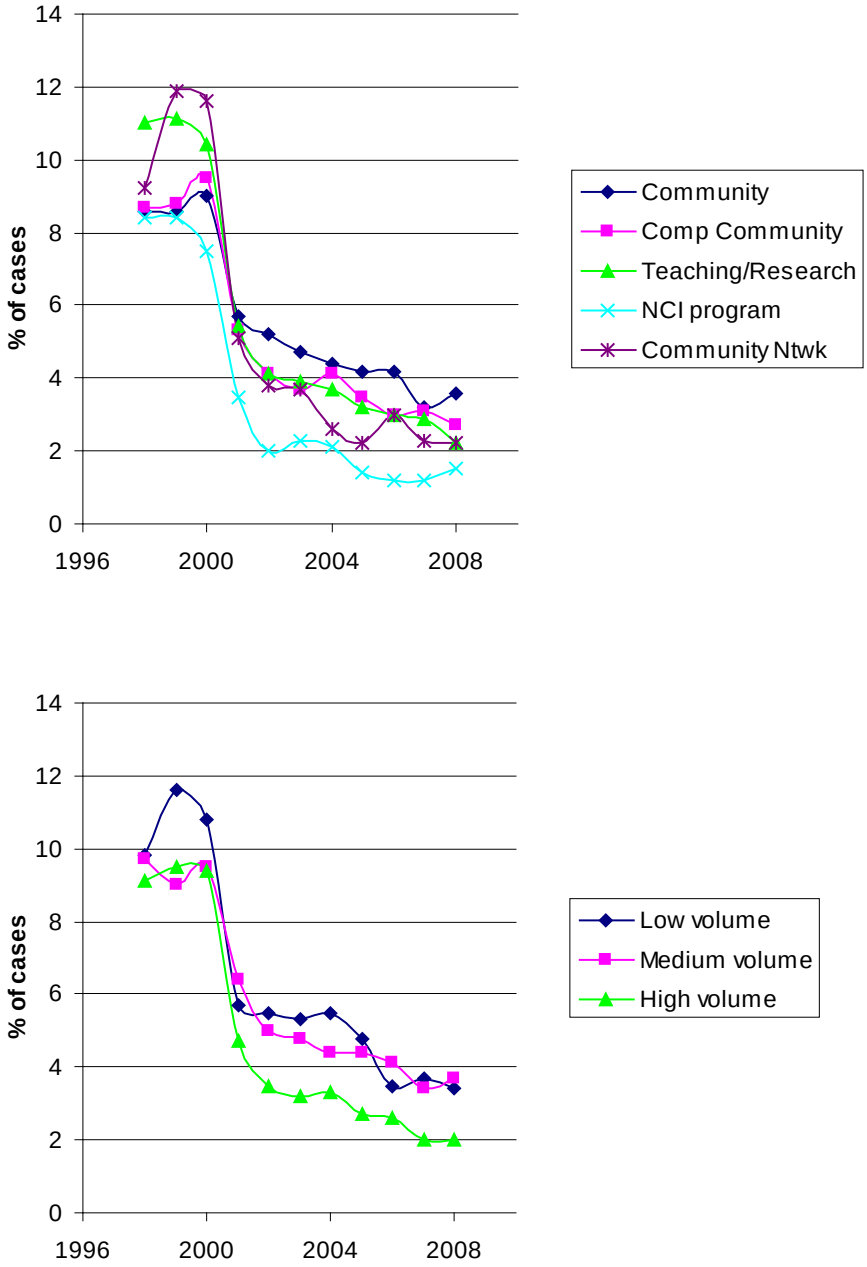

Figure 2C. Site/type: non-Hodgkin lymphoma. Prevalence of “malignant lymphoma, NOS” (9590) by facility type and volume group.

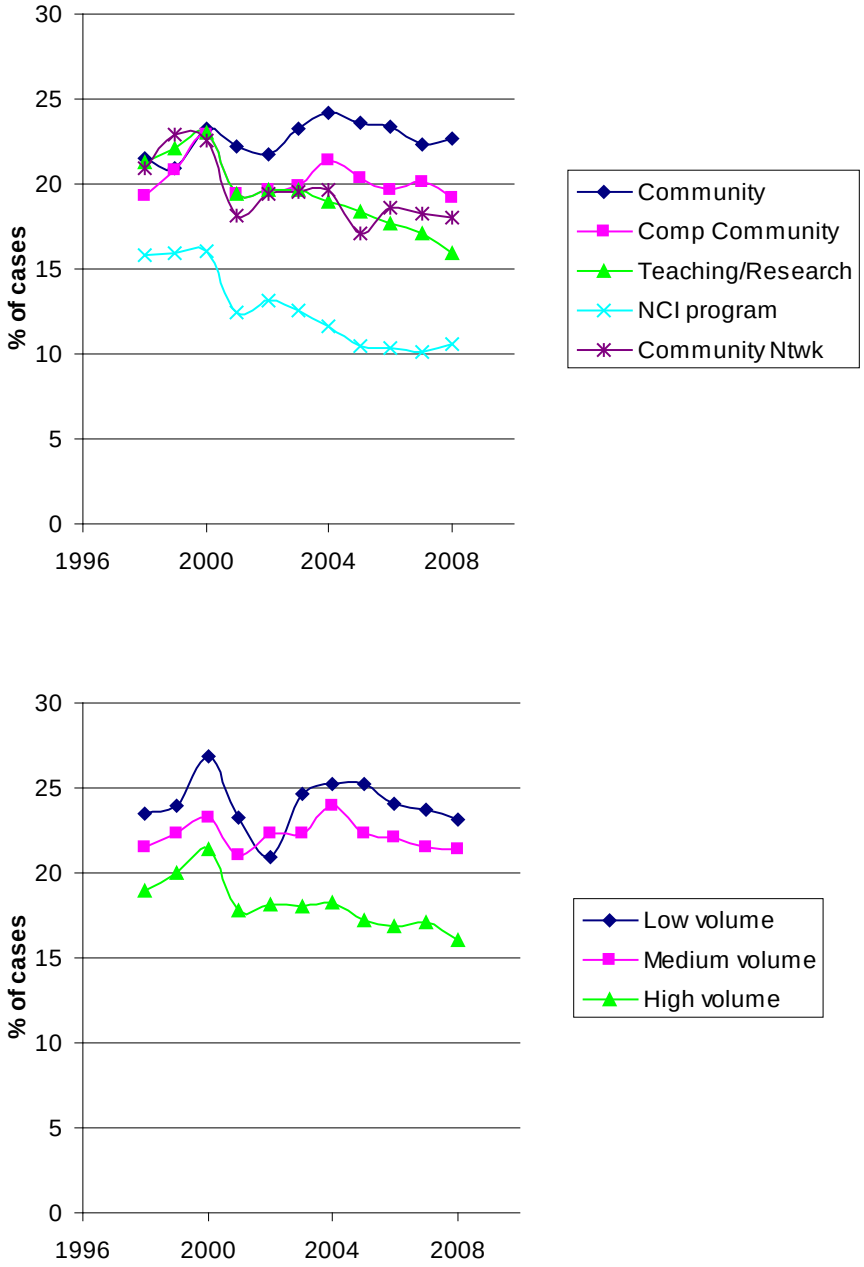

Figure 2D. Site/type: non-Hodgkin lymphoma. Prevalence of “3 nonspecific diagnoses” (9590, 9591, 9690) by facility type and volume group.

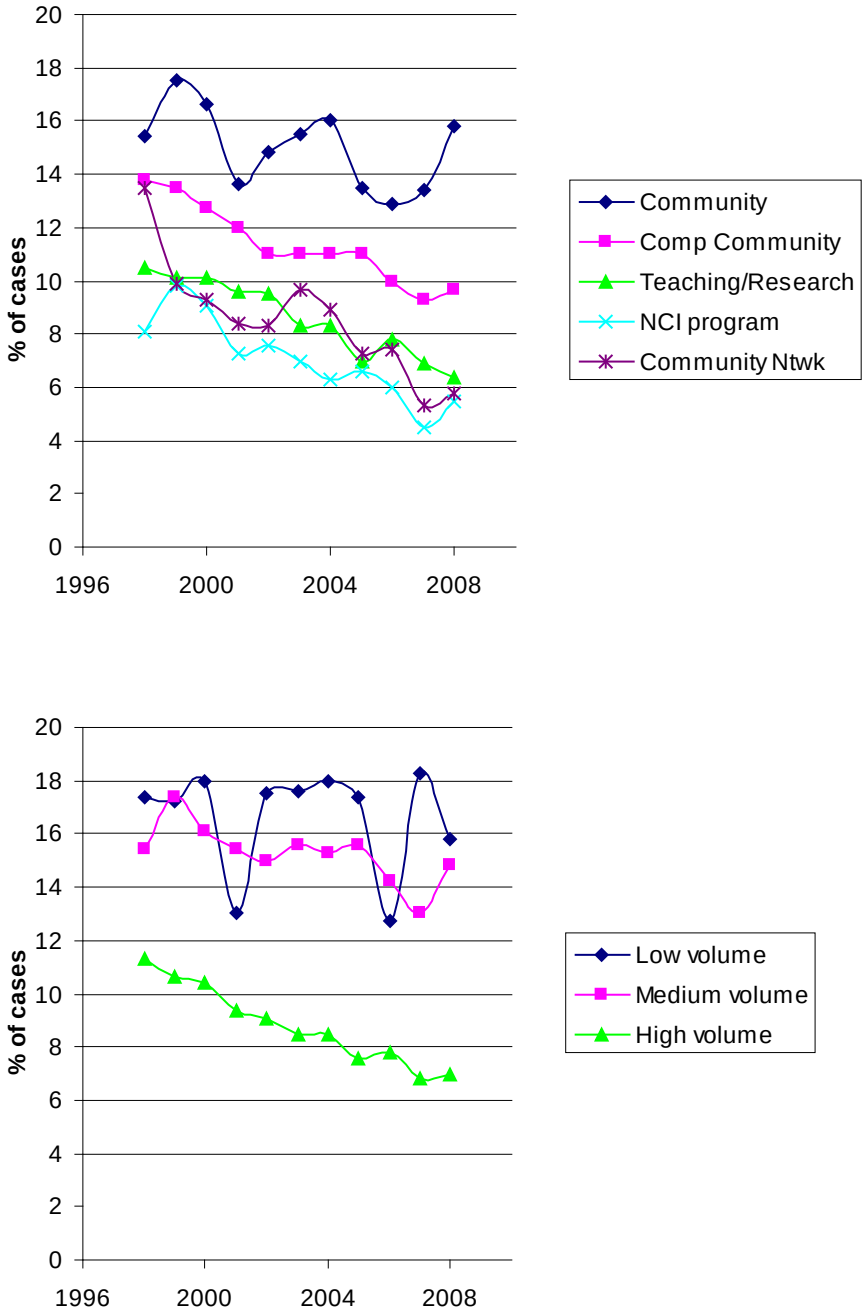

Figure 3A. Site/type: ovary. Prevalence of “adenocarcinoma, NOS” (8140) by facility type and volume group.

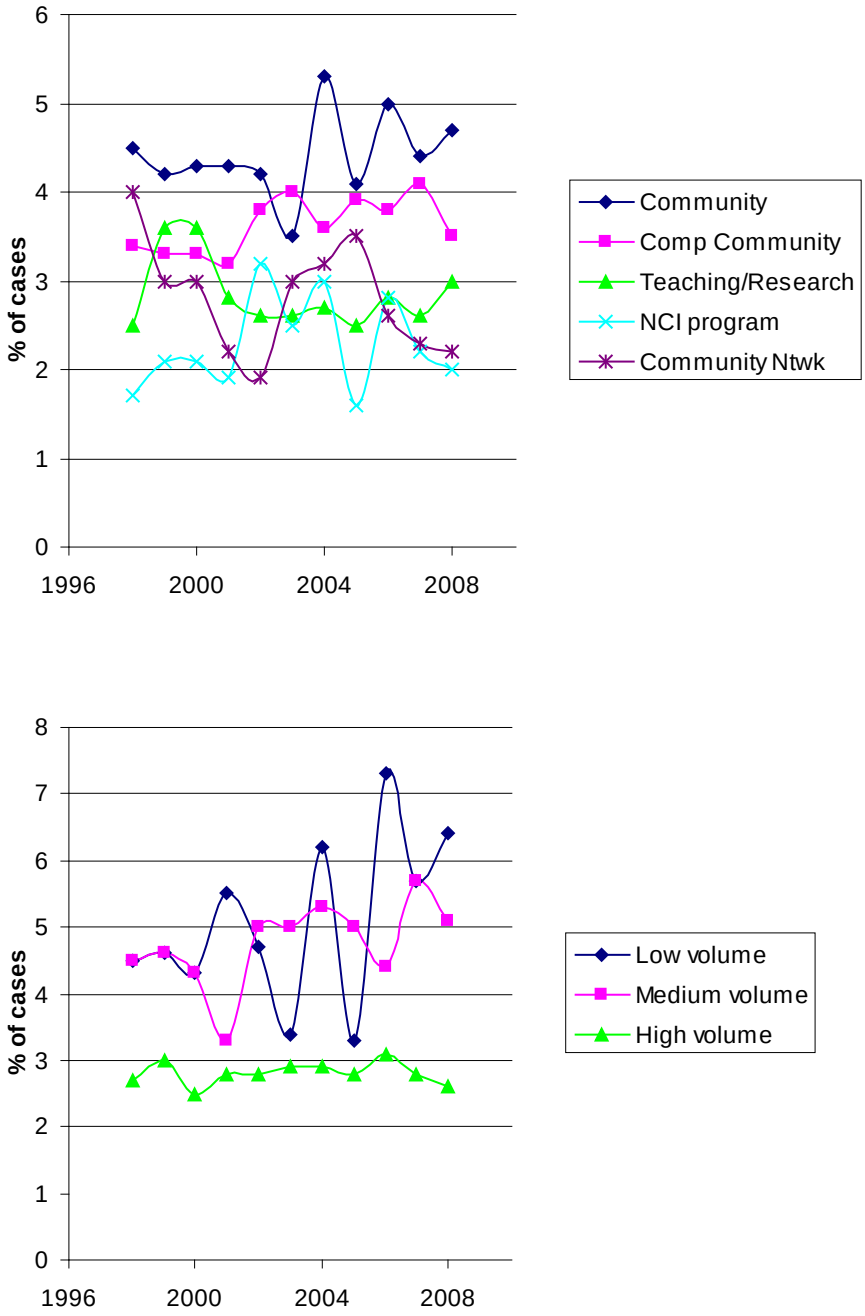

Figure 3B. Site/type: ovary. Prevalence of “carcinoma, NOS” (8010) by facility type and volume group.

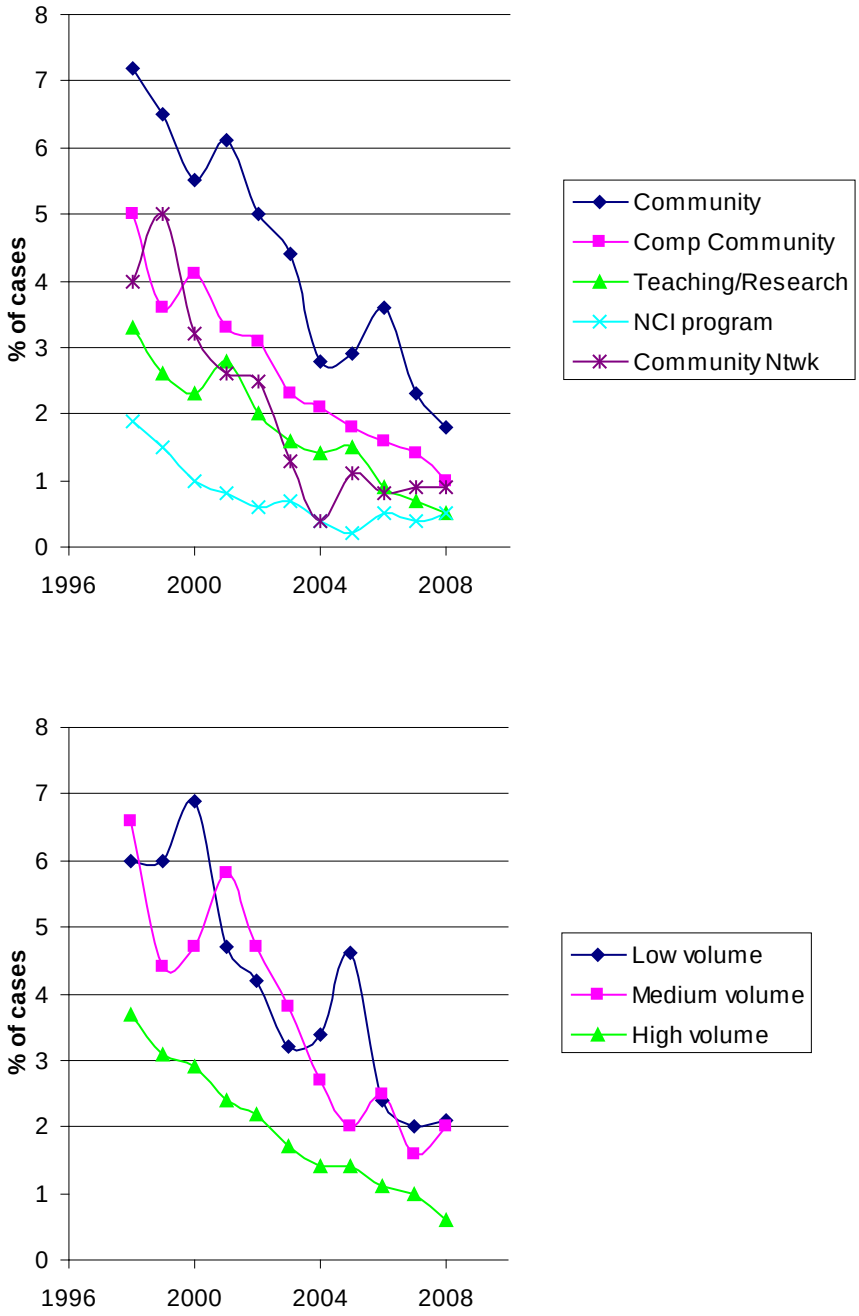

Figure 3C. Site/type: ovary. Prevalence of “papillary adenocarcinoma, NOS” (8260) by facility type and volume group.

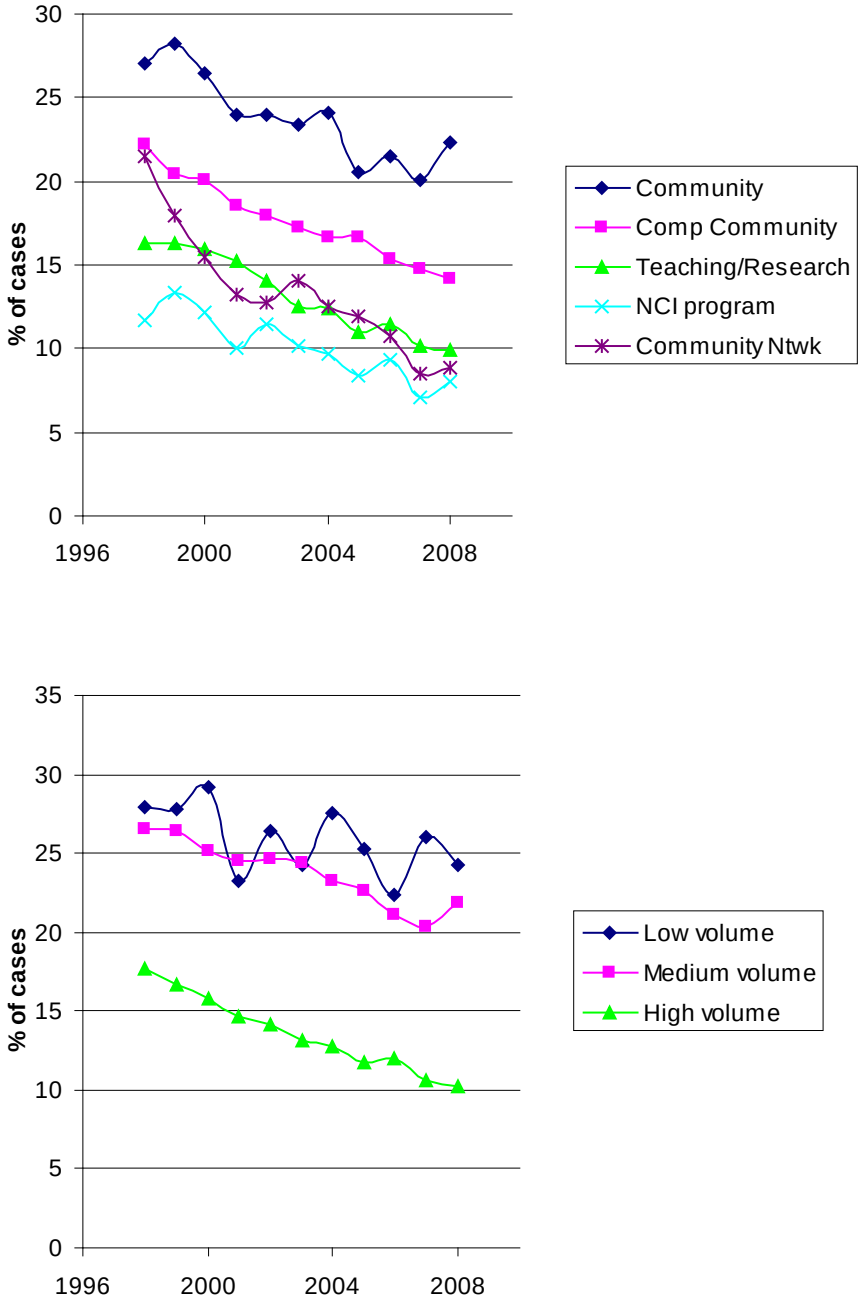

Figure 3D. Site/type: ovary. Prevalence of “3 nonspecific diagnoses” (8140, 8010, 8260) by facility type and volume group.

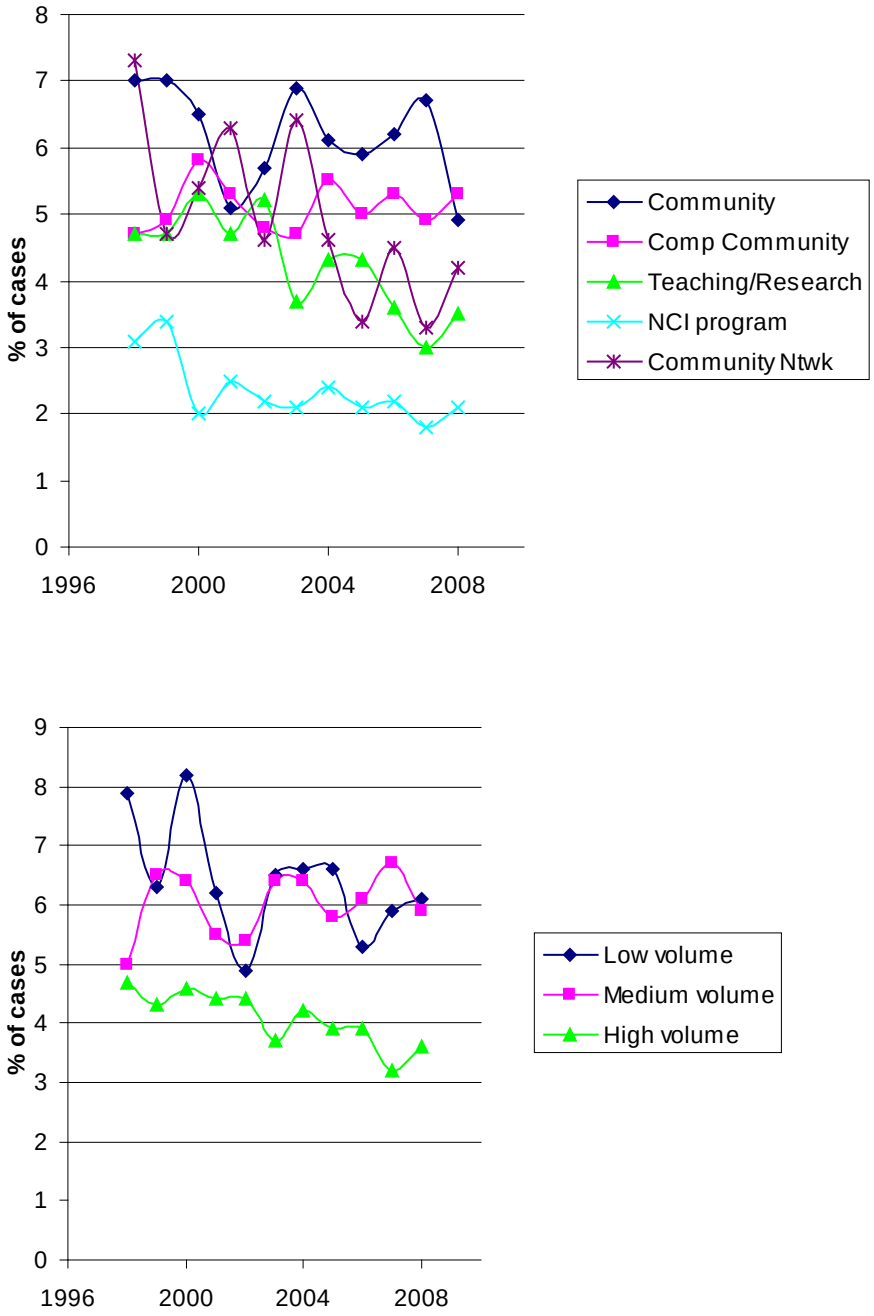

Figure 4A. Site/type: pancreas. Prevalence of “carcinoma, NOS” (8010) by facility type and volume group.

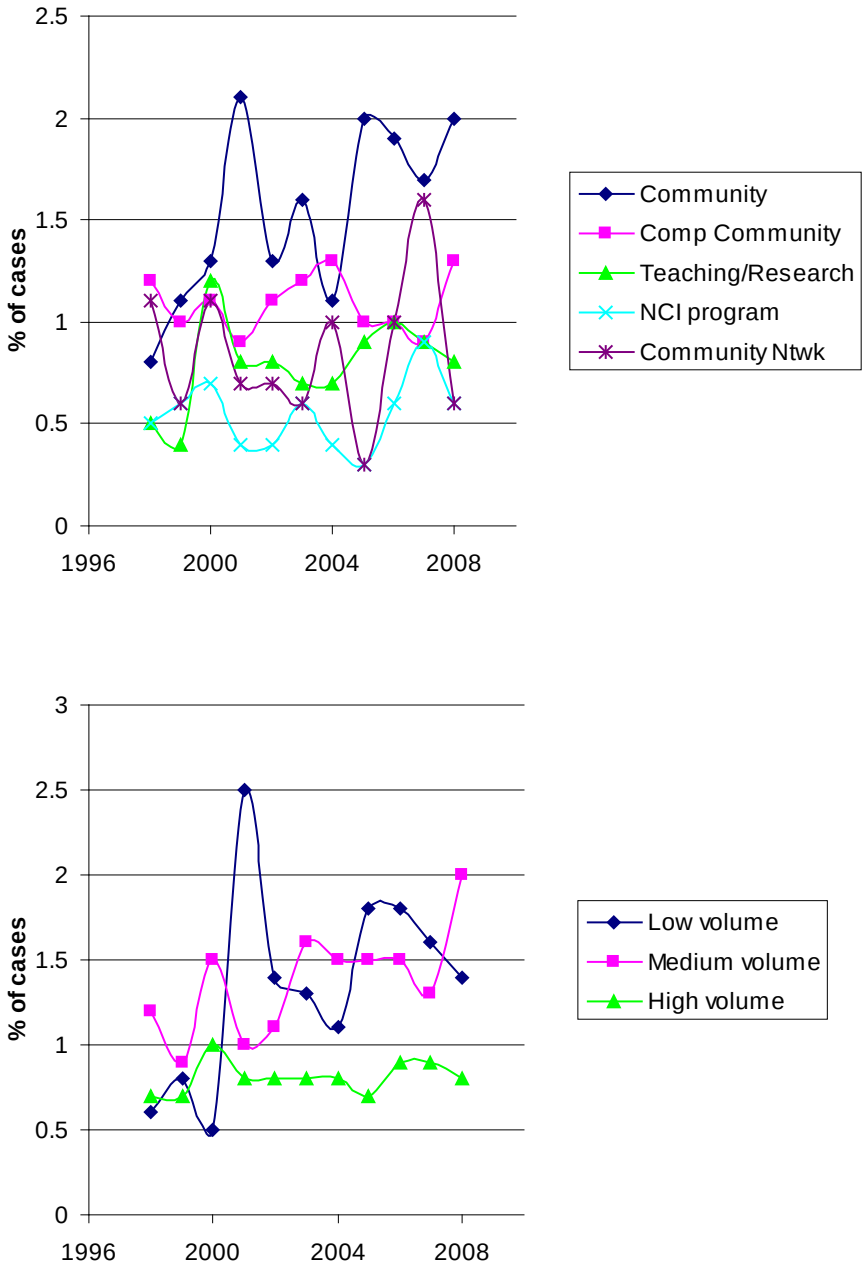

Figure 4B. Site/type: pancreas. Prevalence of “malignant neoplasm, NOS” (8000) by facility type and volume group.

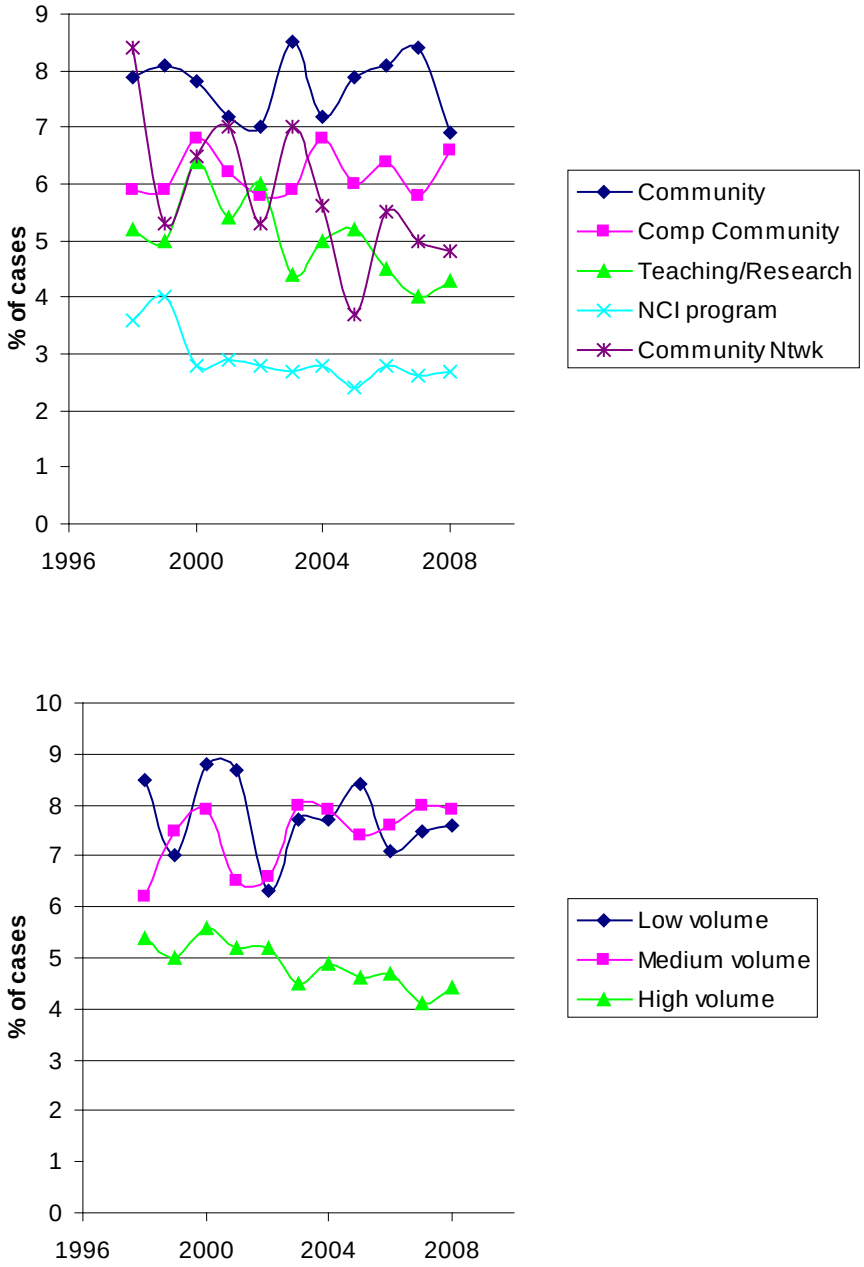

Figure 4C. Site/type: pancreas. Prevalence of “2 nonspecific diagnoses” (8010, 8000) by facility type and volume group.

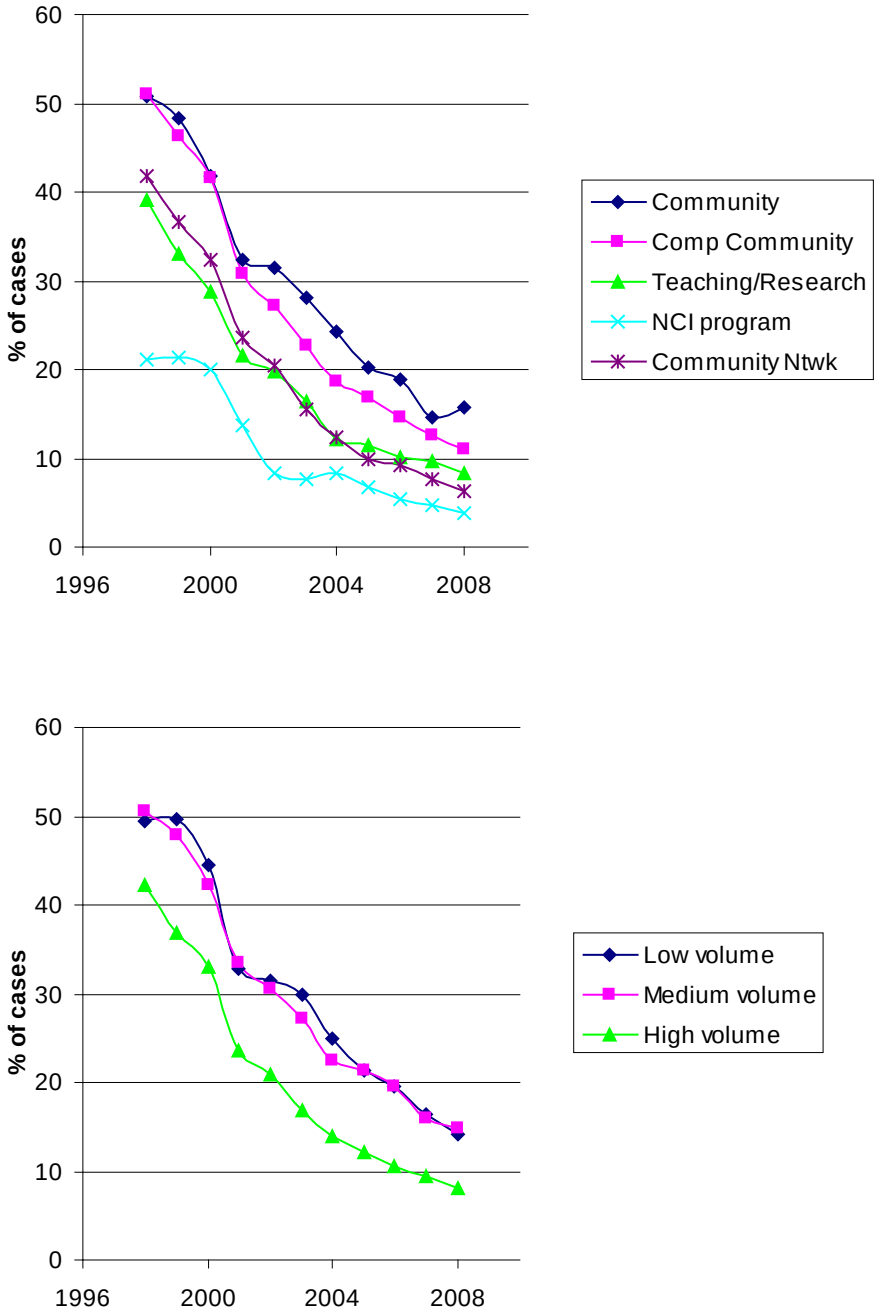

Figure 5. Site/type: uterine corpus. Prevalence of “adenocarcinoma, NOS” (8140) by facility type and volume group.