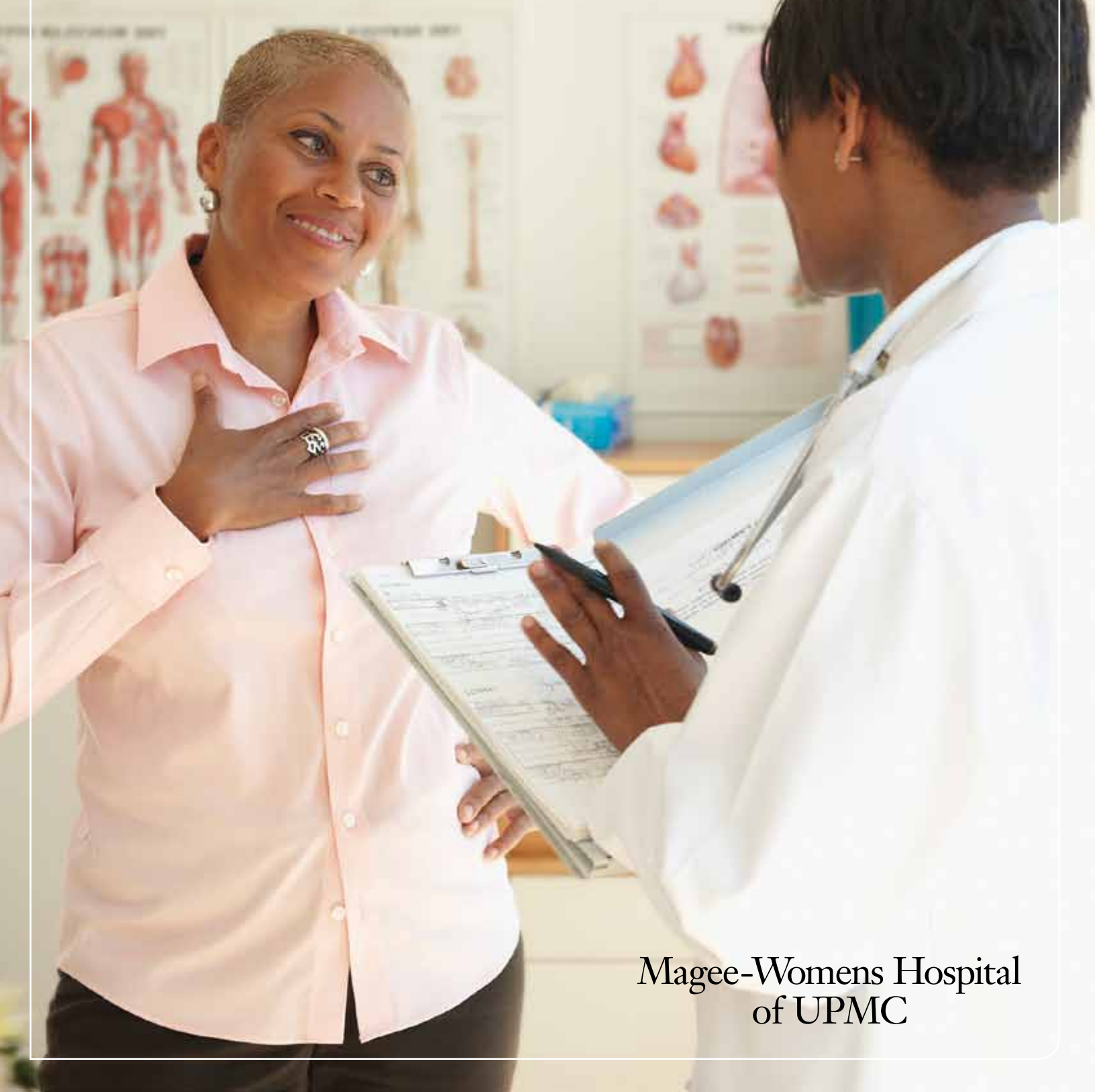


Magee 2010-2011 Cancer Program Annual Report

FOCUS ON CERVICAL CANCER



Magee-Womens Hospital
of UPMC

INTRODUCTION FROM THE CHAIRMAN

Magee-Womens Cancer Program of UPMC Cancer Centers continues its commitment to provide comprehensive cancer care for its patients through a multidisciplinary approach. State-of-the-art services provide the highest level in prevention, diagnosis, treatment, and survivorship. The physicians and associated health care members work with patients and their families to develop personal treatment plans to customize care.



Physician specialists include breast and gynecologic oncologists, urologists, gastroenterologists, surgical and medical oncologists, radiation oncologists, behavioral health professionals, plastic and reconstructive surgeons, pathologists, geneticists, radiologists, palliative care specialists, and melanoma specialists. Other health care professional members include nurses, pharmacists, dietitians, social workers, sonographers, and technologists specializing in women's cancers.

Support groups, a variety of educational activities, a patient resource room, and Internet access to the Magee-Womens Hospital of UPMC website are available. Magee-Womens Hospital, Magee-Womens Research Institute, and the University of Pittsburgh Cancer Institute, a National Cancer Institute-designated Comprehensive Cancer Center, offer the most current therapies and clinical trials. The Magee-Womens High Risk Breast Cancer and Ovarian Cancer programs provide women with a thorough assessment of their individual risks, along with risk-reduction and surveillance

strategies. A multidisciplinary team of the medical staff and allied health professionals meets weekly for a breast cancer conference and a separate gynecologic oncology tumor board conference. The team discusses patient evaluations, for both prospective and continuing care, and plans for future care of selected patients with malignancies.

The Cancer Committee provides leadership and guidance to the cancer program, ensuring that the highest quality of health care continues to be provided for its patients. The committee also monitors and coordinates all cancer-related activities. The committee meets bimonthly, and comprises representatives from each department involved in cancer management and care. The Magee 2010-2011 Cancer Program Annual Report will summarize the accomplishments and commitment to excellence that the Cancer Program maintains at Magee.

This year, the annual report focuses on cervical cancer, and highlights key programmatic accomplishments that support cervical cancer patients.

Paniti Sukumvanich, MD

Chairman, Cancer Committee

PROGRAM INNOVATIONS

Magee-Womens Cancer Program of UPMC Cancer Centers remains at the forefront of patient care and state-of-the-art technology and treatment. Through its commitment to clinical innovations and quality initiatives, Magee's Cancer Program continues to expand its capabilities in diagnosing and treating cervical cancer and managing patient survival.

Advances in Surgery for Cervical Cancer

Cervical cancer accounts for 17 percent of all deaths due to gynecologic malignancies. According to the National Cancer Institute, there were approximately 12,710 new cases of cervical cancer in 2011, with an expected 4,290 deaths from this disease. There are multiple options for treatment of early stage cervical cancer. Patients have the option of either a radical hysterectomy with pelvic node dissection or concurrent chemotherapy with radiation therapy. Surgical treatment has the advantage of allowing a patient to preserve her ovaries. Such surgery traditionally has been performed through a large abdominal incision, which can result in at least a three-to-five day stay in the hospital postoperatively.

Laparoscopic Surgery

In recent years, advances in surgical techniques, such as robotic surgery and laparoscopic surgery, have been applied to patients with cervical cancer. Patients have access to advanced laparoscopists at Magee, who are able to perform radical hysterectomies, as well as node dissection. Such surgeries have the advantage of smaller scars and faster recovery from surgery. Patients undergoing laparoscopic radical hysterectomy usually can go home the next day, and the typical four weeks of recovery time may be cut in half.

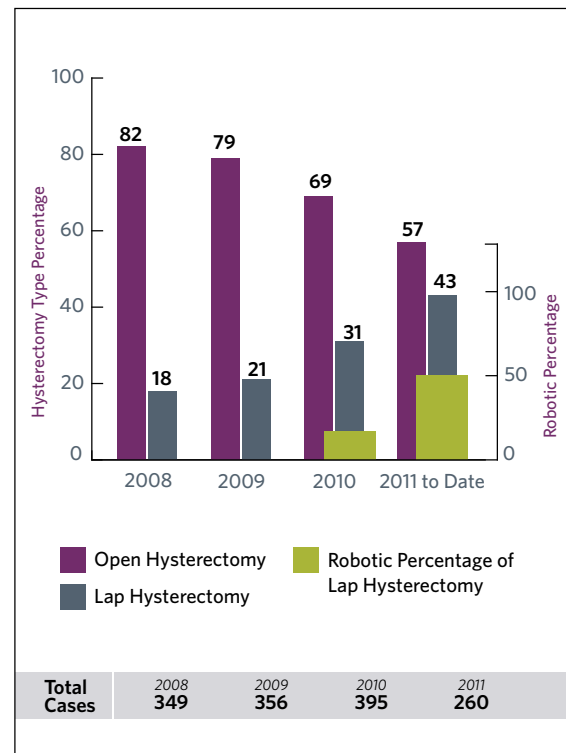
Robotic Surgery

In the past two years, Magee has invested heavily in robotic surgery, and the current robot available at Magee is the latest model available. Surgeons at Magee are highly trained in robotic surgery, and performed more such surgeries in the past year than at any other hospital in the UPMC system. Like laparoscopic surgery, patients undergoing robotic surgery may recover faster, with less pain, than patients undergoing traditional open surgery. Overall outcomes for both laparoscopic and robot-assisted radical hysterectomies appear to

be equivalent, with greater than 90 percent survival in patients with early stage cervical cancer.

Laparoscopic and robotic surgery allows patients to have their staging survey completed in a more minimally invasive manner than patients who have hysterectomies elsewhere that are not completely staged. Lymph node dissections can be done laparoscopically or robotically. These patients may have less pain than patients undergoing open laparotomy for lymph node dissection. Patients often can go home the same day after surgery, unlike patients treated with older techniques, who typically have to be admitted to the hospital for three to five days.

Growth of laparoscopy and robotic surgery for hysterectomy procedures:



Other Surgical Innovations

Another advanced surgical innovation available at Magee is the radical trachelectomy. Radical trachelectomy involves the removal of the cervix while leaving the uterus in place. In highly selected patients, this surgery allows for treatment of cervical cancer while preserving the patients' fertility. A review of the current literature on pregnancies after trachelectomies found that, while there was an increase in preterm labor, more than half of the pregnancies resulted in term or near-term deliveries. The overall rate of cervical cancer recurrence was less than five percent, and mortality was two to three percent in more than 550 cases of patients undergoing this procedure.

Radiation Oncology

UPMC Cancer Center at Magee-Womens Hospital of UPMC offers advanced radiation therapy for cervical cancer. It offers PET-CT-based simulation with IMRT and IGRT for external beam radiation therapy, which helps in conforming dose to tumor and reducing side effects. It is one of the few centers in the country to offer MRI-based intracavitary brachytherapy for cervical cancer, which helps in conforming dose to tumor and reducing the dose to critical organs. Magee also offers image-based interstitial brachytherapy, which is sometimes required for advanced cervical cancer. The program is at the forefront of using and evaluating these advanced technologies for improving cancer outcomes, and is a recognized leader in the field of radiation oncology for gynecologic cancers.

Pathology — Where the Final Diagnosis Is Made

Much of the progress in the past seven decades in converting cervical cancer from the No. 1 killer of women in the United States to representing less than two percent of cancer deaths in women can be attributed to the widespread use of a screening test known as the Pap smear, pioneered by and named after a Greek-American immigrant, George Papanicolaou, MD. The Pap smear is widely recognized as the most successful and cost-effective cancer screening test in the history of medicine. Since 1996, the conventional Pap smear has been enhanced by an FDA-approved method of liquid-based cytology, in which almost all cells retrieved on the Pap collection device are placed into a preservative fluid vial and prepared into monolayer slides, which removes background obscuring inflammation and blood. More recently, over the last 10 years, FDA-approved adjunctive

HPV DNA molecular testing, along with the Pap smear, has increased the sensitivity of cervical screening to detect the highest-risk cervical lesions. Magee has been a leader in introducing these new screening technologies for the benefit of Pittsburgh-area women.

Analysis of Pap tests is performed by cytotechnologists — highly trained professionals who have a college degree and a year or more of specialized training, and certification by a rigorous national examination. The Anisa Kanbour School of Cytotechnology, named after a veteran Magee pathologist and benefactor, is now the second-oldest training school in the country. For decades, it has trained cytotechnologists who have served throughout western Pennsylvania, Ohio, and West Virginia.

Final diagnoses of abnormal tests are rendered by pathologists, who typically have at least four years of postgraduate medical training, medical licensure, and board certification. More recently, subspecialty fellowship training in cytopathology has been commonplace. The University of Pittsburgh School of Medicine has been a leader in all levels of specialized pathology training. Together, they perform the critical phases of the Pap smear: the cytologic screening and interpretation. While the Pap smear is an effective screening test, confirmation of a diagnosis of cervical cancer or precancerous dysplasia requires a biopsy of the cervix. This is examined and interpreted by a specialized pathologist. The results of the Pap smear, HPV DNA test, and cervical biopsy serve as an essential guide for further clinical management and treatment of patients. The professional team in the Pathology Department plays an important role in the prevention, diagnosis, and management of cervical cancer.

Recently, research on cervical screening at Magee has focused on risk stratification of screened patients, evaluating the contributions of both Pap and HPV tests and incorporating the data into a unique Pittsburgh Cervical Cancer Screening Model. The Bayesian, network-driven Pittsburgh Cervical Screening model was developed in collaboration with computer scientists at the University of Pittsburgh School of Information Science and international experts in the field. By combining state-of-the-art liquid-based cytology, adjunctive HPV testing, and risk stratification, the highest levels of protection possible are provided to screened women in the community.

PATIENT- AND FAMILY-CENTERED CARE (PFCC)

Oncology-Focused Patient Experience Initiatives

The focus of the women's oncology PFCC work was gynecologic cancer patients in 2010-11, with expansion to other women's cancer patient populations and service areas as appropriate. Specific PFCC initiatives included:

- Enhancing the discharge process, including improving timeliness of discharge, discharge education, and transitioning of care to home and home care agencies.
- Improving patient and caregiver communication, including restructuring of after-hours phone services and improving patient education materials.
- Improving the functionality of patient educational materials by utilizing access to instructional videos on the website dealing with chemotherapy and doctor-to-patient communication.

LiveWell Survivorship Program

As part of the patient- and family-centered care initiative, patient advisers, along with a multidisciplinary team of physicians, nurses, social workers, navigators, and educators, assisted the Magee-Womens Cancer Program in developing the "LiveWell" Cancer Survivorship Program in 2009. The program has been introduced to cancer survivors at Magee-Womens Hospital of UPMC through a few key initiatives:

Cancer Survivorship Workshop

Between 150 and 200 cancer survivors and family attend four-hour workshops in May and September that focus on issues relevant to survivorship, including genetics, sexuality and intimacy, changing relationships, menopause, nutrition, surveillance, recurrence, and research. The workshops also include a panel of breast and gynecologic cancer survivors who share personal survival stories.

Survivorship Education Series

Held every other month, the Survivorship Education Series, initiated in 2010, brings together cancer survivors and experts in the field of survivorship, focusing on areas of fitness and nutrition, communication, community resources, and living with uncertainty.

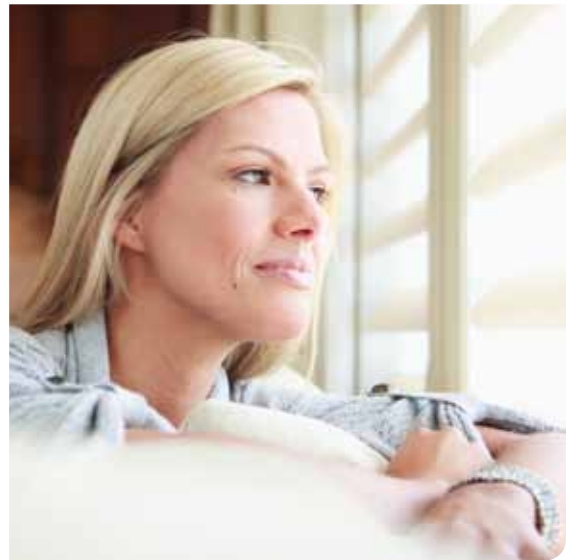


ADVOCACY, COMMUNITY OUTREACH, AND EDUCATION

Part of the mission of Magee-Womens Hospital of UPMC is to raise awareness and offer support to cancer patients, their families, and friends through advocacy, education, and community events. The 2010-2011 cervical cancer awareness efforts included:

“Pride, Polish, and Protect” — Taking Education, Prevention, and Early Detection to the Community

In 2009, the Wilkinsburg Neighborhood WomanCare Center of Magee-Womens Hospital implemented a program of community education for STD, HPV, and preventive/early detection women’s health services, including HVP testing and Pap smears for cervical cancer. The program is called, “Pride, Polish, and Protect,” and staff from the Wilkinsburg Neighborhood WomanCare Center partner with local nail salons and community organizations for education and awareness programs. Their efforts include getting local women to sign up for health exams and screenings, as well as creative educational programming. The program continues today with expanded community partnership.



Healthy Woman Project

Magee and medical staff participate in the Healthy Woman Project. Funded by the National Breast and Cervical Cancer Early Detection Program of the Centers for Disease Control and Prevention, the Healthy Woman Project provides screening services, including clinical breast examinations, mammograms, pelvic examinations, and Pap tests to low-income women. The program also provides post screening diagnostic services, such as surgical consultations and biopsies, to ensure that all women with abnormal results receive timely and adequate referrals, as well as coverage of treatment and follow-up services.

Cancer Survivors Day

Planned by a multidisciplinary committee, this program is a tradition at Magee. The celebration of survivorship includes an uplifting program with a welcome from oncology physicians, along with music and food. More than 250 survivors and their families, physicians, and other care providers from Magee attend each year.

Support Programs

The Patient Navigator Program, established in January 2008, consists of patient navigators who provide individualized assistance to patients, family, and caregivers throughout their health care experience. The patient navigator’s mission is to help guide the patient through her cancer diagnosis and treatment by answering questions and providing information about available resources to ensure a comfortable experience.

Oncology social workers provide counseling and support to patients and their families, and facilitate group support meetings and peer support programs focused on gynecologic cancer patients.

Holistic Care Services

In 2010, the Holistic Care Center was transformed into an individual patient need process whereby individual meditation, guided imagery, and relaxation tapes were distributed to patients on an as-needed basis in clinical service areas such as breast biopsy, surgery, chemotherapy, radiation therapy, and palliative care.

Community Education

Magee experts presented a variety of community programs throughout 2010-2011. Topics included:

- Prevention and early detection
- Living with cancer
- Clinical innovations
- Research updates
- Cancer risk assessment

Continuing Medical Education

Magee specialists presented at a variety of professional education venues regionally, nationally, and internationally in 2010-2011. Our experts continue to publish research and clinical care/outcome articles, and abstracts in national and international peer-reviewed journals. Below is a list of publications related to cervical cancer from the cancer care team at Magee:

Publications for 2010-2011

"Consensus Guidelines for Delineation of Clinical Target Volume for Intensity-Modulated Pelvic Radiotherapy for the Definitive Treatment of Cervix Cancer." Lim K, Small W Jr, Portelance L, Creutzberg C, Jurgenliemk-Schulz IM, Mundt A, Mell LK, Mayr N, Viswanathan A, Jhingran A, Erickson B, De Los Santos J, Gaffney D, Yashar C, Beriwal S, Wolfson A, Taylor A, Bosch W, El Naqa I, Fyles, A Gyn IMRT Consortium. *Int J Radiat Oncol Biol Phys* 2010; May 14. [Epub ahead of print]. PMID: 20472347

"Clinical Utility of Adjunctive High Risk HPV DNA Testing in Women with Pap Test findings of Atypical Glandular Cells." Zhao C, Florea A, Austin RM. *Archives of Pathology and Laboratory Medicine* 2010; 134: 103-108.

"Computer-Assisted Pap Imaging: Another Valuable Tool in the Challenge of Pap Test Screening for Glandular Neoplasia." Austin RM. *Cancer Cytopathology* 2010; 118: 1-3.

"Cytological Results and Clinical Findings Associated with 265 Histopathological Diagnoses of Cervical Glandular Neoplasia: Results of 10 Years." Zhao C, Austin RM. *Modern Pathology* 2010; 23S: 271A.

"Dosimetric Analysis of 3d Image-Guided HDR Brachytherapy Planning for the Treatment of Cervical Cancer: Is Point A-based Dose Prescription Still Valid in Image-Guided Brachytherapy?" Kim H, Beriwal S, Houser C, Huq MS. *Med Dos* 2011; Jan. [Epub ahead of print]. PMID: 20488690.

"MicroRNA Analysis in Human Papillomavirus (HPV)-Associated Cervical Neoplasia and Cancer." McBee WC, Gardiner AS, Edwards RP, Lesnock JL, Bhargava R, Austin M, Guido RS, Khan SA. *Journal of Carcinogene Mutagene* 2011; vol. 2, no. 1, 1000114, ISSN:2157-2158.

"Oral HPV Infection and Sexuality: A Cross-Sectional Study in Women." Ragin C, Edwards R, Larkins-Pettigrew M, Taioli, Eckstein S, Thurman N, Bloome J, Markovic N. *Int. J Mol. Sci.* 2011; June, 12, 3928-3940; doi:10.3390ijms12063928 (ISSN1422-0067).

"Surgery Versus Radiation Therapy for Stage IB2 Cervical Carcinoma: A Population-based Analysis." Rungruang B, Courtney-Brooks M, Beriwal S, Zorn K, Richard S, Olawaiye A, Krivak T, Sukumvanich, P. *International Journal of Gynecological Cancer* Nov 2011.

"Three-Dimensional High Dose Rate Intracavitary Image-Guided Brachytherapy for the Treatment of Cervical Cancer Using a Hybrid Magnetic Resonance Imaging/Computed Tomography Approach: Feasibility and Early Results." Beriwal S, Kannan N, Kim H, Houser C, Mogus R, Sukumvanich P, Olawaiye A, Richard S, Kelley JL, Edwards RP. *Clinical Oncology (Royal College of Radiologists)*. 2011 Dec; 23(10):685-90.

Gynecologic Tumor Board Conference

The Magee-Womens Gynecologic Tumor Board is a weekly multidisciplinary conference that focuses on patient-management issues and current trends in gynecologic cancer care. It is attended by individuals within the subspecialties of gynecologic oncology, radiation oncology, radiology, pathology, genetics, patient care services, and social work.

Clinical dilemmas and controversial and unusual patient cases are selected by the attending staff, presented, and discussed by the participants. Radiographic and pathologic findings are correlated with the clinical findings. Rationale for an approach to the clinical problem is discussed by the attendees. This conference allows discussion of different approaches to the problems encountered in gynecologic cancer care. The opportunity for possible recruitment of patients within research protocols also occurs during this meeting.

RESEARCH

Advances in Chemotherapy for Cervical Cancer: GOG 240

Cervical cancer accounts for 17 percent of all deaths due to gynecologic malignancies. According to the National Cancer Institute, there were approximately 12,710 new cases of cervical cancer in 2011, with an expected 4,290 deaths from this disease. For many years, the cornerstone of treatment of locally advanced cervical cancer has been radiation therapy. Recent advances in the past decade have now made concomitant cisplatin with radiation the new standard of care, with a 50 percent decrease in the risk of dying from cervical cancer.

Multiple chemotherapies have been tried in patients with recurrent or metastatic cervical cancer. A recent trial from the Gynecologic Oncology Group has shown that various chemotherapy combinations with cisplatin are all equivalent in efficacy. Thus, at the present

time cisplatin with paclitaxel (Taxol®) is considered standard treatment for these patients. Unfortunately, despite these trials, outcomes are still extremely poor. At the present time, there is a search for newer and better regimens. Since the majority of patients have already been treated with cisplatin in the past, one strategy to find a better regimen is to include regimens that do not contain cisplatin.

Other newer chemotherapy agents, such as bevacizumab (Avastin®), also have shown to be effective in small studies. Therefore, the Gynecologic Oncology Group is now comparing cisplatin/paclitaxel with and without bevacizumab versus topotecan/paclitaxel with and without bevacizumab (GOG 240). In the last year, patients at Magee have been enrolled in this trial.



CLINICAL TRIALS SPECIFIC TO GYNECOLOGIC CANCER AT MAGEE-WOMENS HOSPITAL OF UPMC

Active Gynecologic Cancer Studies

PHASE	PRINCIPAL INVESTIGATOR	SPONSOR	TITLE
III	Robert Edwards, MD Kristin Zorn, MD	Sponsored by the Gynecologic Oncology Group (GOG) a National Cooperative Group funded by the National Cancer Institute	(UPCI 10-106) GOG 262: A Randomized Phase III trial of Every-3-Weeks Paclitaxel Combined with Carboplatin versus Dose Dense Weekly Paclitaxel Combined with Carboplatin with or without Concurrent and Consolidation Bevacizumab (NSC #704865, IND #7921) in the Treatment of Primary Stage III or IV Epithelial Ovarian, Peritoneal or Fallopian Tube Cancer
III	Robert Edwards, MD Kristin Zorn, MD	Sponsored by the Gynecologic Oncology Group (GOG) a National Cooperative Group funded by the National Cancer Institute	(UPCI 05-068) GOG 212: A Randomized Phase III Trial of Maintenance Chemotherapy Comparing 12 Monthly Cycles of Single Agent Paclitaxel Or XYOTAX™ (CT-2103) (IND# 70177), Versus No Treatment Until Documented Relapse In Women With Advanced Ovarian or Primary Peritoneal Cancer Who Achieved a Complete Clinical Response to Primary Platinum/Taxane Chemotherapy
I	Kristin Zorn, MD	Sanofi-Aventis	(UPCI 07-045) OX-06-009 Phase I Phase I Dose-Escalation Parallel Studies of Intraperitoneal Oxaliplatin (Eloxatin®) with Intravenous Docetaxel (Taxotere®) and Intravenous Oxaliplatin with Intraperitoneal Docetaxel In Platinum-Sensitive or Platinum-Resistant Recurrent Ovarian, Primary Peritoneal, and Fallopian Tube Cancer
II	Kristin Zorn, MD	Novartis Pharmaceuticals, Inc.	(UPCI 09-033) Phase II Study of RAD001 and Bevacizumab in Recurrent ovarian, peritoneal, and Fallopian Tube Cancer: An Investigator-Initiated, Single-Institution Trial at Magee-Womens Hospital (Support: Novartis/Genentech)

PHASE	PRINCIPAL INVESTIGATOR	SPONSOR	TITLE
III	Robert Edwards, MD Kristin Zorn, MD	Sponsored by the Gynecologic Oncology Group (GOG) a National Cooperative Group funded by the National Cancer Institute	(UPCI 09-055) GOG 249: A Phase III Trial of Pelvic Radiation Therapy Versus Vaginal Cuff Brachytherapy Followed by Paclitaxel/Carboplatin Chemotherapy in Patients with High Risk, Early Stage Endometrial Carcinoma
III	Robert Edwards, MD Kristin Zorn, MD	Sponsored by the Gynecologic Oncology Group (GOG) a National Cooperative Group funded by the National Cancer Institute	(UPCI 09-054) GOG 258: A Randomized Phase III Trial of Cisplatin and Tumor Volume Directed Irradiation Followed by Carboplatin and Paclitaxel vs. Carboplatin and Paclitaxel for Optimally Debulked, Advanced Endometrial Carcinoma
III		Sponsored by the Gynecologic Oncology Group (GOG) a National Cooperative Group funded by the National Cancer Institute	"(UPCI 10-26) GOG 259 Non-treatment Write Study Phase III Quality of Life Assessment in Recurrent Ovarian Cancer"
Surgical/ Tissue Trials	Robert Edwards, MD		(UPCI 07-058) Prognostic Marker: Acquisition of Blood Samples and Tissue for Research Purposes (All Gynecologic Diseases)
Surgical/ Tissue Trials	Kristin Zorn, MD		(09-046) UPCI High Risk: Cancer Family Registry for Research and Surveillance (Ovarian) (High Risk Program)

2010 SITE-SPECIFIC ANALYSIS FOR MAGEE-WOMENS HOSPITAL OF UPMC

Invasive Cervical Cancer

Incidence

In the United States, an estimated 12,200 cases of invasive cervical cancer are expected to be diagnosed in 2010. In Pennsylvania the projected number of invasive cervical cancer cases expected to be diagnosed in 2010 is 585. Magee-Womens Hospital of UPMC total number of new invasive cervical cancer cases in 2010 is 82. Incidence rates continue to increase at Magee-Womens Hospital for invasive cervical cancer, along with all other primary site gynecologic cancers, as it is a large research and referral center for the diagnosis and treatment of women's cancers. (Figure 1).

Although cervical cancer is decreasing in the United States because of the routine use of Pap smears it remains a major health problem for women. The global yearly incidence of cervical

cancer for 2002 was 493,200. It is the third most common cancer in women worldwide. Cervical cancer was once one of the most common cancers affecting U.S. women, but now ranks 14th in frequency. In gynecological cancers it ranks behind endometrial cancer and ovarian cancer in the United States and at Magee. At Magee-Womens Hospital in 2010 invasive cervical cancer is the fifth major cancer site. (Figure 2) (Table 1). Persistent human papillomavirus (HPV) infection is regarded as the most important factor contributing to the development of cervical cancer.

Figure 1

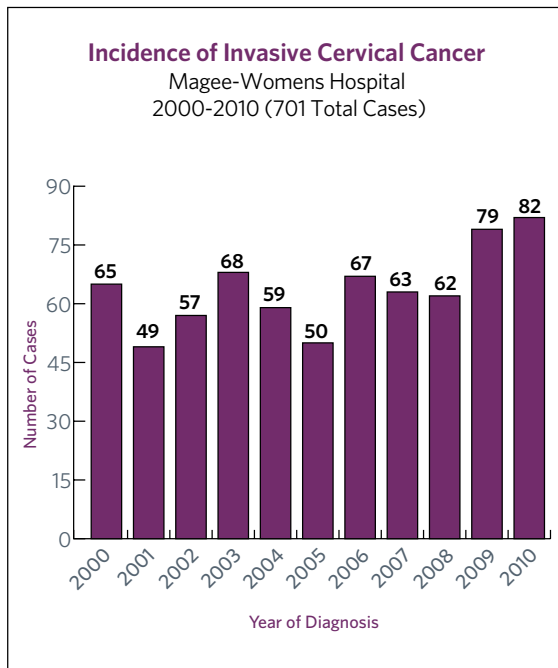


Figure 2

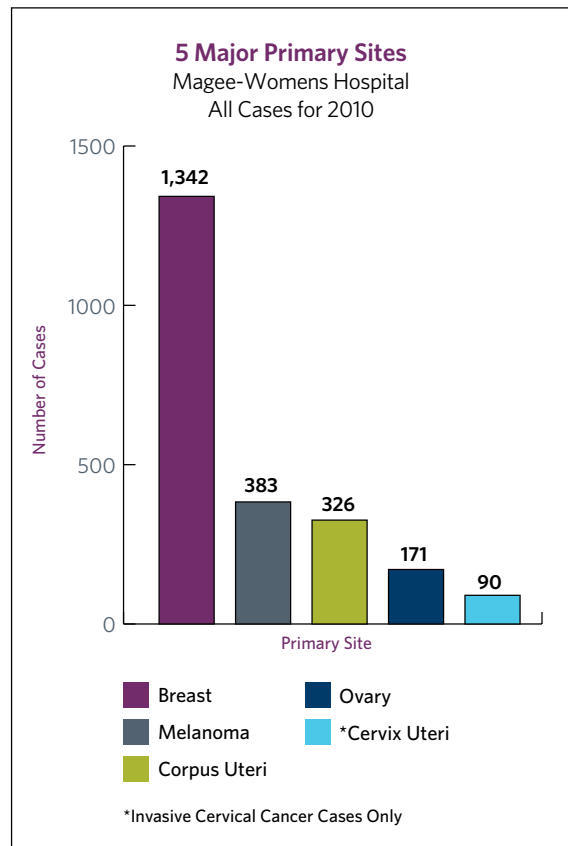


Table 1

2010 MAGEE-WOMENS HOSPITAL PRIMARY SITE DISTRIBUTION TABLE			Sex		Class of Case		Stage Distribution-Analytic Cases						
Primary Site	Total (#)	Total (%)	M	F	Analy	Non-Analy	0	I	II	III	IV	88	Unk
BREAST	1,342	48.4%	7	1,335	1,289	53	284	513	345	91	31	3	22
MELANOMA	383	13.8%	223	160	346	37	34	179	73	50	5	1	4
FEMALE GENITAL SYSTEM	731	26.4%	0	731	680	51	56	336	55	139	63	16	15
Corpus Uteri	326	11.8%	0	326	304	22	0	225	17	30	18	11	3
Ovary	171	6.2%	0	171	156	15	0	62	12	51	23	1	7
Cervix Uteri	108	3.9%	0	108	100	8	18	27	19	22	12	0	2
Vulva	71	2.6%	0	71	68	3	30	18	3	13	1	1	2
Fallopian Tube	26	0.9%	0	26	24	2	1	2	2	12	7	0	0
Vagina	19	0.7%	0	19	19	0	7	2	2	5	1	2	0
Retroperitoneum & Peritoneum	10	0.4%	0	10	9	1	0	0	0	6	1	1	1
ORAL CAVITY & PHARYNX	22	0.8%	13	9	15	7	0	2	1	6	4	1	1
Lip	1	0.0%	1	0	0	1	0	0	0	0	0	0	0
Base of Tongue	3	0.1%	2	1	2	1	0	0	0	1	1	0	0
Other Tongue	3	0.1%	1	2	1	2	0	0	0	0	1	0	0
Floor of Mouth	1	0.0%	1	0	1	0	0	0	0	0	0	0	1
Palate	1	0.0%	0	1	1	0	0	1	0	0	0	0	0
Other Major Salivary Glands	1	0.0%	0	1	0	1	0	0	0	0	0	0	0
Tonsil	5	0.2%	3	2	5	0	0	1	0	3	1	0	0
Oropharynx	2	0.1%	1	1	2	0	0	0	0	2	0	0	0
Nasopharynx	1	0.0%	1	0	1	0	0	0	0	0	1	0	0
Pyiform Sinus	2	0.1%	1	1	1	1	0	0	1	0	0	0	0
Other Lip, Oral Cavity & Pharynx	1	0.0%	1	0	0	1	0	0	0	0	0	0	0
Accessory Sinuses	1	0.0%	1	0	1	0	0	0	0	0	0	1	0
DIGESTIVE SYSTEM	67	2.4%	28	39	58	9	10	7	9	7	20	0	5
Esophagus	2	0.1%	2	0	2	0	0	1	0	1	0	0	0
Stomach	3	0.1%	1	2	2	1	0	0	0	0	1	0	1
Small Intestine	5	0.2%	1	4	4	1	0	0	0	1	3	0	0
Colon	23	0.8%	10	13	21	2	0	3	4	2	12	0	0
Rectosigmoid Junction	3	0.1%	0	3	2	1	0	0	1	1	0	0	0
Rectum	9	0.3%	4	5	8	1	1	1	2	0	1	0	3
Anus & Anal Canal	11	0.4%	7	4	11	0	9	1	1	0	0	0	0
Liver & Intrahepatic Bile Duct	1	0.0%	1	0	0	1	0	0	0	0	0	0	0
Gallbladder	1	0.0%	0	1	1	0	0	0	0	0	1	0	0
Other Parts of Biliary Tract	1	0.0%	0	1	1	0	0	0	0	1	0	0	0
Pancreas	8	0.3%	2	6	6	2	0	1	1	1	2	0	1
RESPIRATORY SYSTEM	69	2.5%	28	41	53	16	0	4	5	12	30	1	1
Larynx	4	0.1%	4	0	2	2	0	0	0	1	1	0	0
Bronchus & Lung	63	2.3%	22	41	49	14	0	4	5	10	29	0	1
Thymus	1	0.0%	1	0	1	0	0	0	0	0	0	1	0
Heart, Mediastinum & Pleura	1	0.0%	1	0	1	0	0	0	0	1	0	0	0
MALE GENITAL SYSTEM	46	1.7%	46	0	41	5	0	4	24	7	6	0	0
Prostate Gland	45	1.6%	45	0	40	5	0	4	24	6	6	0	0
Testis	1	0.0%	1	0	1	0	0	0	0	1	0	0	0
URINARY SYSTEM	51	1.8%	22	29	42	9	9	16	6	5	2	0	4
Kidney	25	0.9%	15	10	24	1	0	14	3	4	0	0	3
Ureter	4	0.1%	1	3	4	0	2	1	1	0	0	0	0
Bladder	21	0.8%	6	15	14	7	7	1	2	1	2	0	1
Other Urinary Organs	1	0.0%	0	1	0	1	0	0	0	0	0	0	0
BRAIN & OTHER NERVOUS SYSTEM	7	0.3%	3	4	4	3	0	0	0	0	0	4	0
Meninges	1	0.0%	1	0	0	1	0	0	0	0	0	0	0
Brain	6	0.2%	2	4	4	2	0	0	0	0	0	4	0
ENDOCRINE SYSTEM	6	0.2%	3	3	4	2	0	0	0	3	1	0	0
Thyroid Gland	5	0.2%	2	3	4	1	0	0	0	3	1	0	0
Other Sites	1	0.0%	1	0	0	1	0	0	0	0	0	0	0
LYMPH NODES	13	0.5%	5	8	10	3	0	0	3	3	3	0	1
UNKNOWN PRIMARY SITE	17	0.6%	6	11	15	2	0	0	0	0	0	15	0
HEMATOPOIETIC AND RETICULOENDO SYSTEM	9	0.3%	6	3	3	6	0	0	0	0	0	3	0
BONES AND CARTILAGE AND OTHER	1	0.0%	1	0	1	0	0	0	0	0	1	0	0
CONNECTIVE AND OTHER SOFT TISSUE	5	0.2%	3	2	5	0	0	1	2	2	0	0	0
EYE AND ADNEXA	1	0.0%	0	1	1	0	0	0	0	0	0	1	0
TOTAL	2,770	100.0%	394	2,376	2,567	203	393	1,062	523	325	166	45	53

Histologic Classification

About 80 percent of all cervical cancers are squamous cell carcinomas with the remaining 20 percent adenocarcinomas. Less common cervical cancers are mixed adenosquamous. Mixed non-carcinoma malignancies rarely occur in the cervix, and include melanoma and lymphoma. Due to effective screening, there has been a substantial decline in incidence and mortality of squamous cell carcinoma of the cervix. However, adenocarcinoma of the cervix has increased over the last three decades, most likely due to the fact that cervical cytologic screening methods are less effective for adenocarcinoma. Screening methods for HPV may increase detection for adenocarcinoma.

Histologic classification for invasive cervical carcinoma cases diagnosed at Magee-Womens Hospital between 2005 and 2010 appears below in Figure 3 with 66 percent of the cases squamous cell carcinoma, 20 percent adenocarcinoma, 7 percent adenosquamous, 6 percent carcinoma and 1 percent lymphoma, carcinosarcoma and malignant melanoma.

Risk Factors

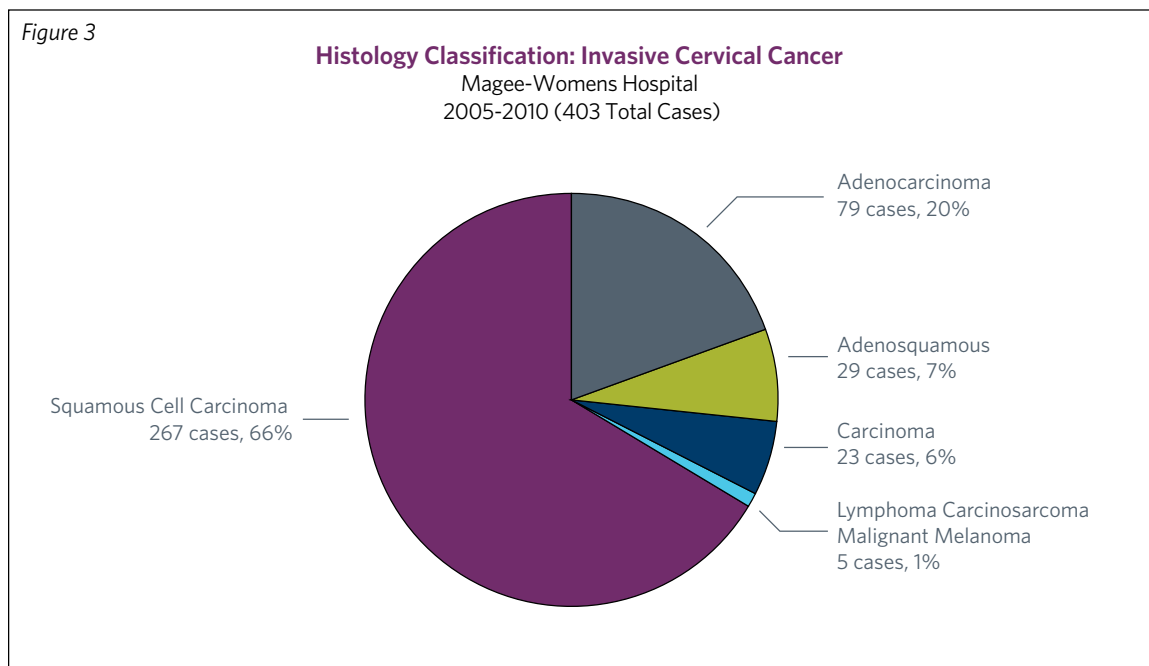
The primary cause of cervical cancer is infection with certain types of human papillomavirus (HPV). There are about 40 types of HPV that can infect the cervix and about 15 of them have been linked to cervical cancer. Two of these high-risk types, HPV-16 and HPV-18, cause about 70 percent of

cervical cancer worldwide. The vaccines Cervarix® and Gardasil® are available to protect against infection with HPV types 16 and 18. Highly sensitive and specific molecular tests are now available to identify DNA from high-risk HPV types in cervical specimens. HPV infection is common but only a very small number of women infected, with HPV develop cervical cancer. Persistence of HPV infection and progression to cancer may be influenced by several risk factors (Table 2). Although these risk factors increase the chances of developing cervical cancer many women with these risks do not develop the disease.

Table 2

RISK FACTORS:

- Smoking
- Chronic immunosuppression
- Age
- Race
- History of sexually transmitted disease
- Oral contraceptives
- Parity
- Low socioeconomic status
- DES
- Early age of onset of coitus/large number of sexual partners
- Family history of cervical cancer



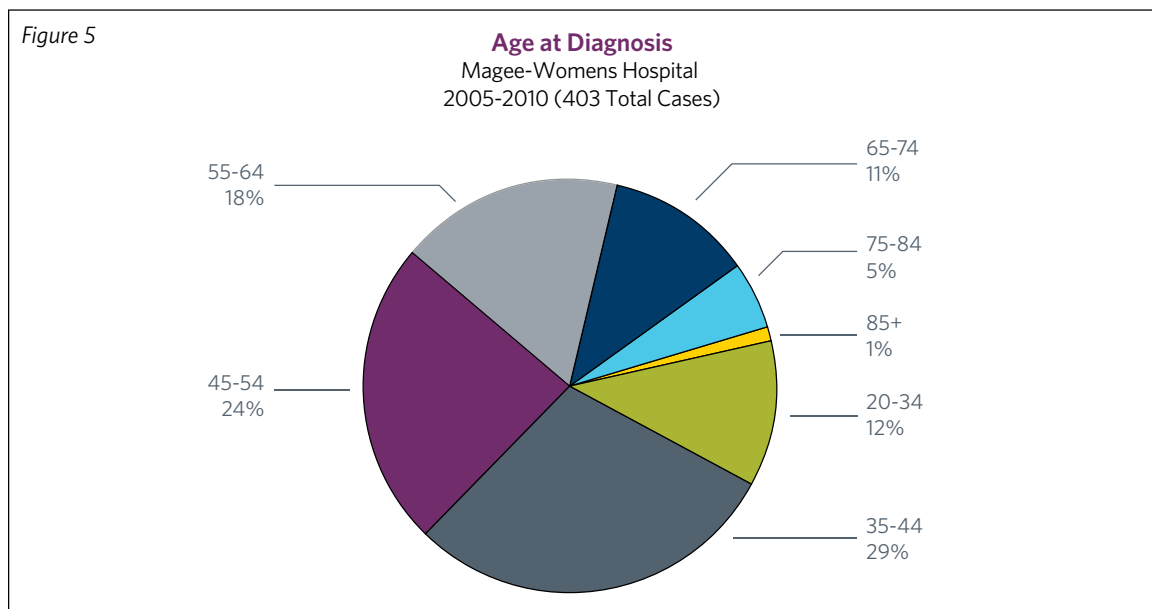
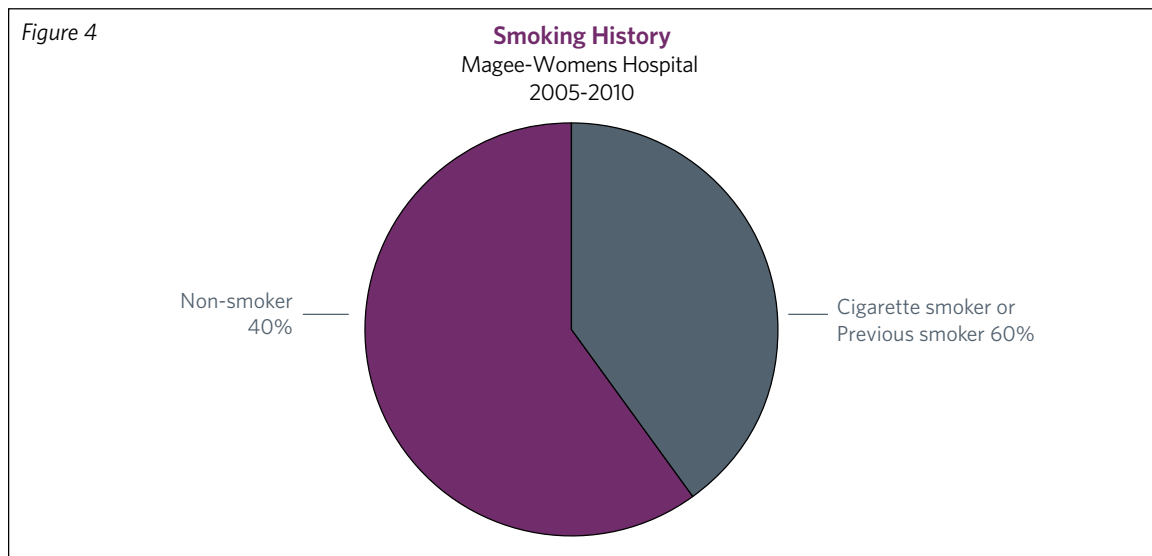
Smoking

Smoking cigarettes and breathing in secondhand smoke increase the risk of cervical cancer. Among women infected with HPV, dysplasia and invasive cancer occur two to three times more often in current and previous smokers. Secondhand smoke causes a smaller increase in risk. Figure 4 shows the smoking history for cervical cancer patients at Magee-Womens Hospital.

Age

Cancer of the cervix can occur at any age. According to the NCI's Surveillance Epidemiology and End Results (SEER), between 2004 and 2008, the median age at cervical cancer diagnosis in the United States was 48 until approximately age 55

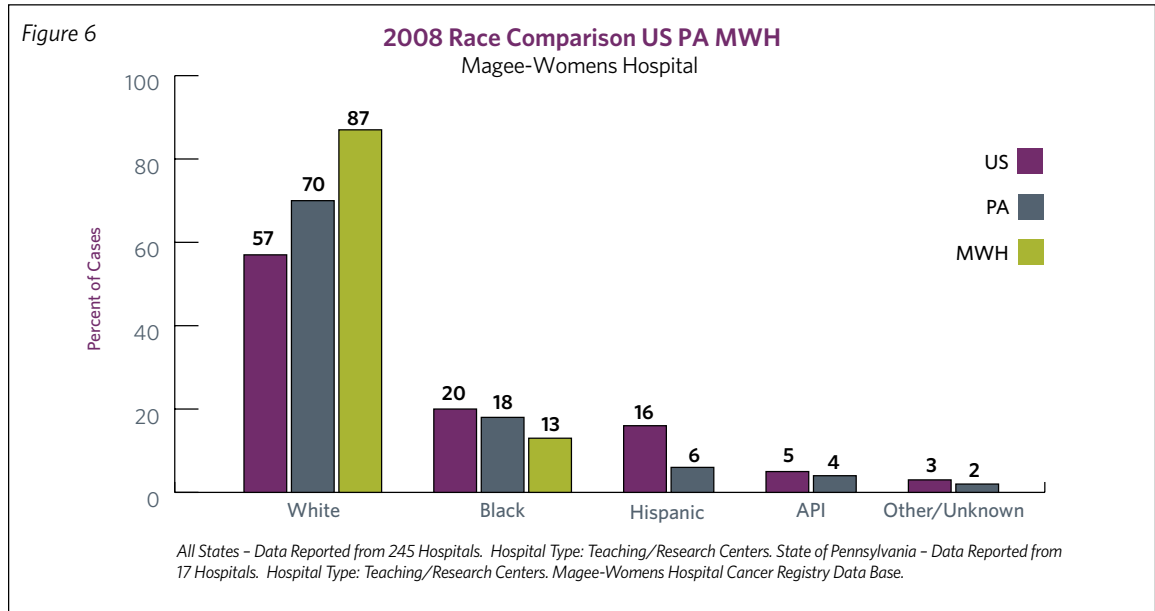
when it drops off again. Approximately half of the cervical cancer cases are diagnosed in women between the ages of 35 and 54. Less than 15 percent of the cases were among women under age 35. Cervical cancer is extremely rare in women younger than age 20. However, many young women become infected with multiple types of HPV, which can increase their risk of getting cervical cancer in the future. Young women with early abnormal changes who do not have regular examinations are at high risk for localized cancer by the time they are age 40, and for invasive cancer by age 50. These age patterns also are shown using Magee-Womens Hospital data below in Figure 5.



Race

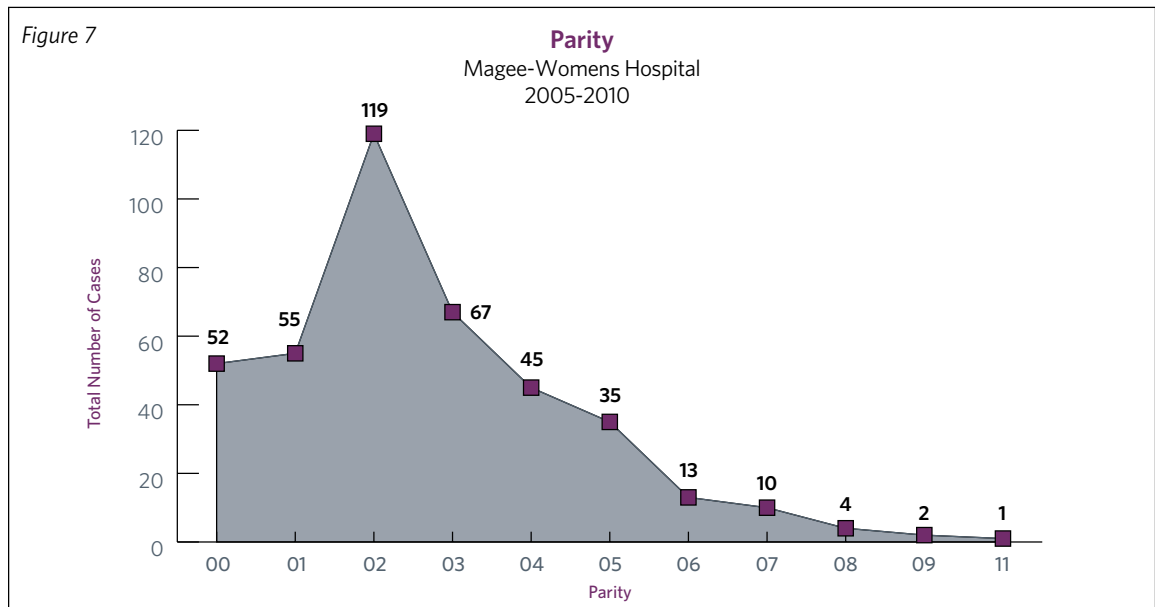
Although the rate of cervical cancer has declined among both Caucasian and African-American women over the past decades, it remains much more prevalent in African-American women. Hispanic-American women have the highest cervical cancer incidence rate. White women living in Appalachia suffer a disproportionately higher risk for developing cervical cancer than other white women. The highest death rate from

cervical cancer is among African-American/Black women. Cervical cancer is usually diagnosed at an early stage more often in whites than in African Americans. 2008 race incidence comparison for U.S., Pennsylvania and Magee-Womens Hospital (MWH) using the 2008 data from the National Cancer Data Base Benchmark Reports and the Magee-Womens Hospital Cancer Registry Data Base is displayed below in Figure 6.



Parity

Women who have had multiple full-term pregnancies have an increased risk of developing cervical cancer.



Geographic Patterns for Cervical Cancer

Despite advances in early detection and prevention of cervical cancer, a consistent pattern of high cervical incidence has existed for decades in specific geographic areas and populations. In countries where women cannot get routine Pap tests, cervical cancer is usually diagnosed at a late (invasive) stage resulting in increased mortality. Cervical cancer is an indicator of larger health system concerns, including medical care access, lack of insurance, cultural issues, and health communication and education. Magee-Womens Hospital provides multiple services for screening, HPV testing and vaccinations, and education in its clinic and doctors offices. There also are patient navigators in the hospital setting to offer assistance with coordination of care for treatment and follow-up. Tests for cervical cancer are now more

available to medically underserved women through the National Breast and Cervical Cancer Early Detection Program (NBCCEDP). This program offers cervical cancer early detection testing to women without health insurance for free or at very little cost. The NBCCEDP tries to reach as many women in medically underserved communities as possible, including older women, women without health insurance, women of racial and ethnic minority groups.

Table 2 displays the geographic distribution of invasive cervical cancer cases diagnosed and/or treated at Magee-Womens Hospital between 2005 and 2010 by county. Table 3 displays the geographic distribution of invasive cervical cancer cases diagnosed and/or treated at Magee-Womens Hospital between 2005 and 2010 by state.

Table 2

2005-2010 MAGEE-WOMENS HOSPITAL INVASIVE CERVICAL CANCER BY COUNTY	
COUNTIES WITHIN PENNSYLVANIA	
Allegheny County	143
Erie County	32
Westmoreland County	31
Butler County	18
Fayette County	17
Washington County	17
Mercer County	16
Beaver County	13
Crawford County	12
Lawrence County	12
Cambria County	11
Blair County	8
Somerset County	8
Clearfield County	7
Indiana County	5
Greene County	4
Venango County	4
Armstrong County	3
Bedford County	3
Clarion County	3
Elk County	3
Huntingdon County	2
Centre County	1
Jefferson County	1
Bradford County	1
Lycoming County	1
McKean County	1
Potter County	1
Warren County	1
Total	379

Table 3

2005-2010 MAGEE-WOMENS HOSPITAL INVASIVE CERVICAL CANCER BY STATE	
New York	1
Ohio	12
South Carolina	1
West Virginia	10
Total	24

AJCC Staging and Treatment

Clinical staging is the preferred method of staging for cervical cancer since many patients are treated by concurrent radiation and chemotherapy or radiation alone and never undergo surgical-pathologic staging. Clinical staging therefore provides uniformity for the staging of cervical cancers and is determined prior to the start of definitive treatment. The 2008 Federation Internationale de Gynecologie et d' Obstetrique (FIGO) "T" staging has been adopted and is based on clinical staging.

Surgery is typically reserved for early stage cervical cancer and smaller lesions such as stage IA, IB1, and selected IIA1. For patients with stage IA2, IB1, or IIA1 disease who have negative lymph nodes after surgery, but have large primary tumor size, deep stromal invasion, and /or LVSI, pelvic radiation is recommended. When surgery is the primary treatment, the histologic findings permit the case to have pathologic staging. Concurrent

chemoradiation is the primary treatment for stages IB2-IVA disease. Chemoradiation also can be used for patients who are not surgical candidates. Single agent cisplatin is typically administered at the time of external beam pelvic radiation with or without vaginal brachytherapy. For patients with distant metastatic disease stage IVB, primary treatment is chemotherapy and individualized radiation may be considered for control of other disease and symptoms.

Cervical cancer is one of the most common cancers diagnosed during pregnancy. Treatment depends on the stage of the disease and in part whether a patient wishes to continue the pregnancy and her desire for future fertility.

A comparison of AJCC Staging and First Course of Treatment using the 2008 data from the National Cancer Data Base Benchmark Reports and the Magee-Womens Hospital Cancer Registry Data Base is displayed below in Figure 8 and Figure 9.

Figure 8

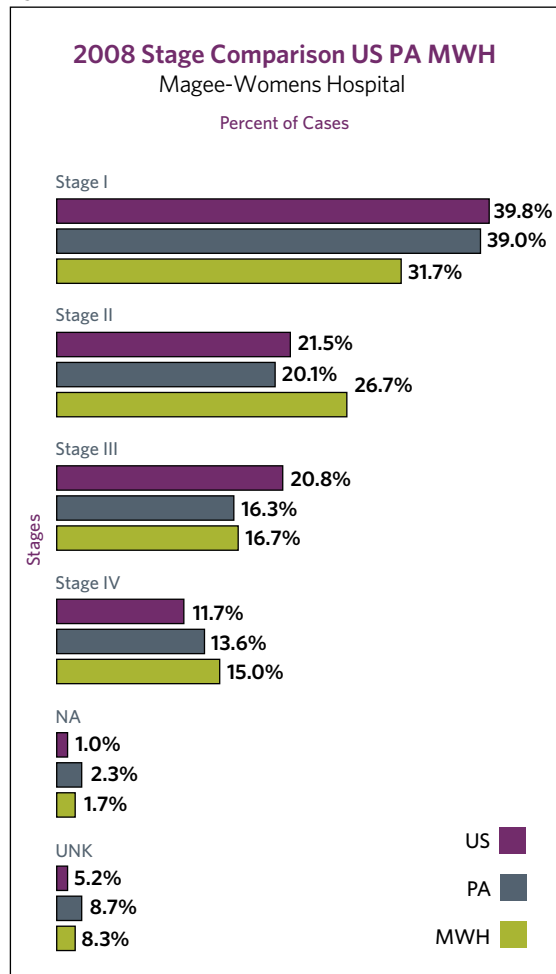
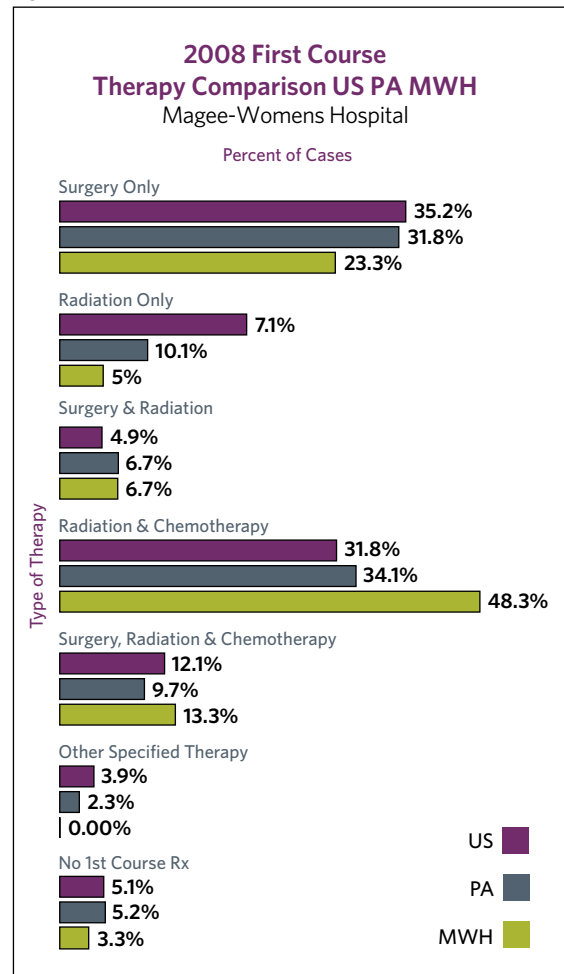


Figure 9



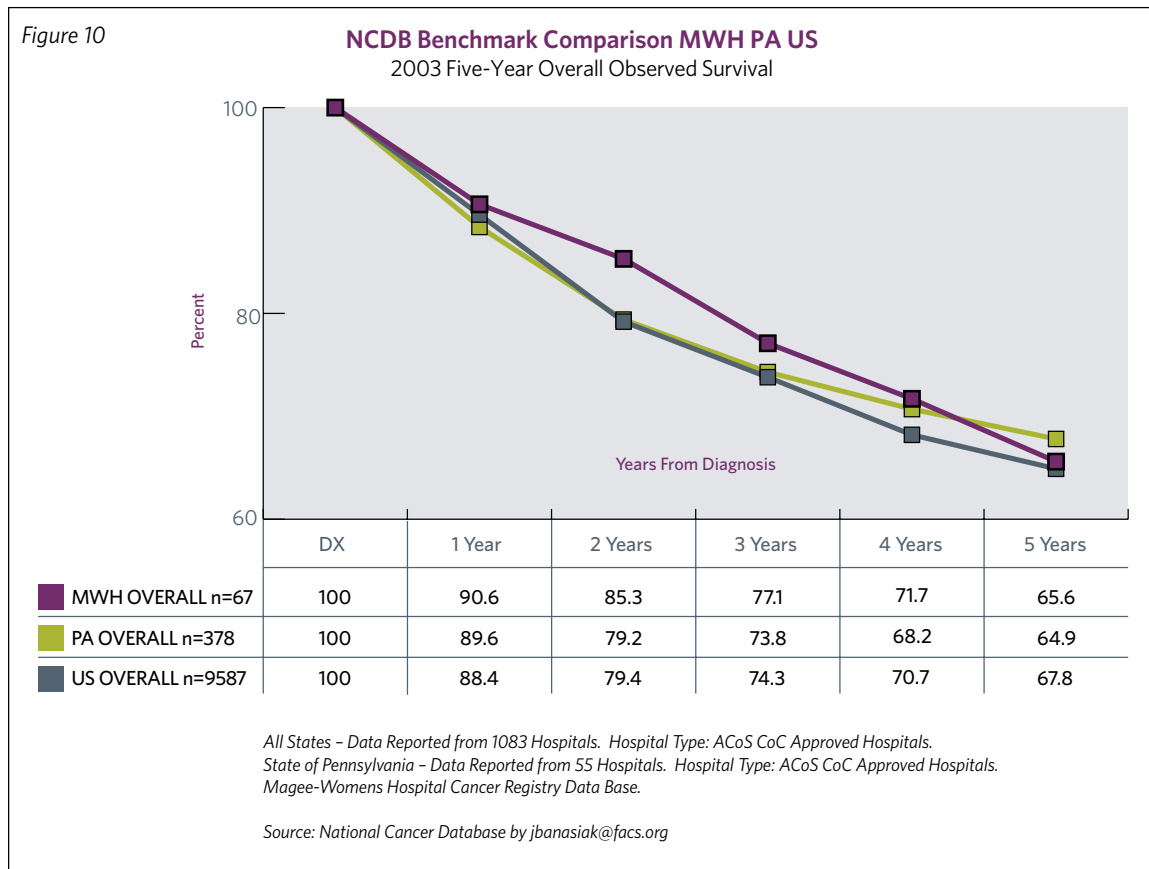
©2011 National Cancer Data Base (NCDB) / Commission on Cancer (CoC) / Developer: Florin Petrescu

Survival

The prognosis for patients with cervical cancer is markedly affected by the extent of disease at the time of diagnosis. Clinical stage along with volume and grade of tumor, histologic type, lymphatic spread, and vascular invasion are all factors affecting the patients outcome. Cervical cancer is the second most common cause of death for women in developing nations. Mortality rates have declined steadily over the past several decades due to prevention and detection as a result of screening, although this trend has slowed since 2003. A vast majority (90%) of these cases can and should be detected early through the use of Pap tests and

HPV testing, however the current death rate is far higher than it should be, which reflects that even today the Pap test and HPV testing are not done on approximately 33% of eligible women. An estimated 4,210 cervical cancer deaths are expected in the U.S. for 2010. Projected for Pennsylvania for 2010 are 170 cervical cancer deaths.

The following five-year overall observed survival graph (Figure 10) was generated using the American College of Surgeons Commission on Cancer (ACOS CoC) National Cancer Data Base (NCDB) Hospital Benchmark Survival Comparison Reports and the Magee-Womens Hospital Cancer Registry. Cases were collected with a diagnosis year of 2003.



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