

the Gleason score with 10 discreet levels than by the 3 discreet categories of differentiation. In our data, degree of differentiation distinguishes groups with an almost 50-fold difference in risk of death from prostate cancer.¹

Second, with respect to the appropriateness of generalizing our results to tumors detected with prostate-specific antigen testing, we noted in our article that this should not be done. We stated for example that “the results are directly relevant for patients with clinical disease diagnosed before the PSA era and also to preclinical disease detected at transurethral resection for presumed benign prostatic hyperplasia.” We also wrote that counselling is “complicated by the fact that a lead time that cannot be individually determined has to be added to the approximately 15 years that may precede more rapid tumor progression” in patients with cancer detected by prostate-specific antigen testing. We contend, however, that our data strengthen indications for early radical treatment of patients diagnosed as having early clinical disease if they have a long life expectancy.

We agree with Dr Oláno that watchful waiting can be an alternative for many patients with newly diagnosed localized prostate cancer because overtreatment is a major problem with routinely performed radical prostatectomies. In 1989, we started the first large randomized trial comparing watchful waiting with radical surgery.²

Jan-Erik Johansson, MD, PhD
jan-erik.johansson@orebroll.se

Ove Andréén, MD

Swen-Olof Andersson, MD, PhD

Anders Magnusson, BSc

Örebro University Hospital and
Center for Assessment of Medical Technology
Örebro, Sweden

Paul W. Dickman, PhD

Karolinska Institute

Stockholm, Sweden

Lars Holmberg, MD, PhD

Regional Oncologic Center

University Hospital

Uppsala, Sweden

Hans-Olov Adami, MD, PhD

Karolinska Institute

Stockholm, Sweden

Harvard School of Public Health

Boston, Mass

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Cervical Cancer Screening Among Women Without a Cervix

To the Editor: Self-reporting of Papanicolaou (Pap) smears by patients, which was used in the study by Drs Sirovich and Welch,¹ may be subject to overreporting, as patients tend

to associate Pap smears with any speculum examination. A better estimate may come from commercial laboratories that also tend to collect information on patient characteristics such as hysterectomy status. Insinga et al² reported lower Pap smear utilization using data from the Kaiser Permanente Northwest Health Plan compared with national surveys based on patient self report.

One reason for the tendency of physicians to perform Pap smears in patients who have undergone hysterectomy may be lack of knowledge of the indication for the hysterectomy. A Pap smear is still recommended after a hysterectomy for women with a history of cervical dysplasia or cancer, or of in utero exposure to diethylstilbesterol. The Pap smear may also serve as an important way of bringing patients back for other preventive health services, such as screening for other cancers, hypertension, and hypercholesterolemia. Given these issues, it seems unlikely that a recommendation to not perform Pap smears for women after hysterectomy will be followed universally or consistently.

Vani Dandolu, MD

dandolu@tuhs.temple.edu

Department of Obstetrics and Gynecology

Oz Harmanli, MD

Division of Urogynecology

Temple University Hospital

Philadelphia, Pa

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To the Editor: Drs Sirovich and Welch¹ report that approximately 10 million US women, or almost half of those who have undergone a hysterectomy and therefore have no cervix, are undergoing Pap smear screening for cancer of the cervix. They have brought attention to a procedure that is unnecessary in women who are no longer at risk of cervical cancer. Vaginal cancer is so rare that there is virtually no secondary benefit of cytologic screening in these women. Thus, either patients or the US health care system incurs costs for unnecessary screening: conventional Pap smears cost \$15 and new, more sensitive screening methods such as liquid-based cytology (\$28 per test) and human papillomavirus (HPV) testing (\$48.50 per test) are even more expensive.² Eliminating Pap smear screening in these women would be cost-effective.

It is noteworthy that the absence of a cervix does not preclude women who have undergone hysterectomy from having HPV infections, and even oncogenic HPV infections, which cause virtually all cervical cancer worldwide.³ In a population-based study of HPV and cervical neoplasia in Guanacaste, Costa Rica, my colleagues and I recently reported that the vaginal prevalence of oncogenic HPV in women who had undergone a hysterectomy was similar to the cervical prevalence in those who had not.⁴ The vaginal prevalence of oncogenic HPV was greater in women who had under-

gone hysterectomy more than 15 years ago compared with women who had undergone the procedure within the last 5 years, suggesting that infections may “accumulate” and persist in the vagina but without any known appreciable risk for cancer. With the introduction of HPV testing into cervical cancer screening programs,³ many women who have had a hysterectomy may test positive for what is a clinically irrelevant infection.

Philip Castle, PhD, MPH
castlep@mail.nih.gov
Division of Cancer Epidemiology and Genetics
National Cancer Institute
Bethesda, Md

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To the Editor: Drs Sirovich and Welch¹ show clearly that the recommendations of the 1996 US Preventive Services Task Force are not being followed. However, I believe that patients may equate not needing a Pap smear with not needing a pelvic examination. The authors did not address the value of pelvic examinations in women who have had hysterectomies for benign reasons and are asymptomatic, and whether this would change based on their ovarian status.

Clay W. Richardson, MD
clayjoanj@hci.net
Table Rock Family Medicine
Glen Alpine, NC

1. Sirovich BE, Welch HG. Cervical cancer screening among women without a cervix. *JAMA*. 2004;291:2990-2993.

To the Editor: Drs Sirovich and Welch¹ speculate that performance measures may be one reason why women who have had a hysterectomy continue to get screened with a Pap test. One performance measure, the Health Plan Employer Data and Information Set (HEDIS), does specify 1 exclusion, albeit optional, for calculating cervical cancer screening rates. The HEDIS technical specifications state that women should be excluded if they have no residual cervix after hysterectomy.² The documentation advises managed care organizations to look for evidence of a hysterectomy as far back as possible in the patient's history, through either administrative data or a medical record review, and provides a list of current procedural terminology codes and *International Classification of Diseases, Ninth Edition* codes for hysterectomy. Although this might be burdensome for managed care organizations, making this exclusion a requirement rather than an option might ensure that the Pap test HEDIS measure is

more meaningful. Moreover, it would be reasonable for HEDIS to consider Pap tests conducted in women after hysterectomy for benign reasons a measure of poor performance.

The authors appropriately examined self-reported Pap testing before and after the release of the evidence-based US Preventive Services Task Force guidelines in 1996; however, primary care physicians often use American Cancer Society (ACS) cancer screening guidelines,³ and obstetricians and gynecologists may be more likely to use their specialty guidelines. Since late 2002, both the ACS and the American College of Obstetricians and Gynecologists (ACOG) have revised their guidelines to reflect that cervical cancer screening should be discontinued in women who have had a total hysterectomy for benign reasons.^{4,5} Continued use of the Centers for Disease Control and Prevention's Behavioral Risk Factor Surveillance System data to monitor this practice after the ACS and ACOG recommendations might show a decrease in the number of women without a cervix who get a Pap test.

Mona Saraiya, MD
yzs2@cdc.gov
Division of Cancer Prevention and Control
Centers for Disease Control and Prevention
Atlanta, Ga

George F. Sawaya, MD
Departments of Obstetrics, Gynecology and
Reproductive Sciences and Epidemiology and Biostatistics
University of California, San Francisco

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In Reply: Drs Dandolu and Harmanli are correct that the use of self-reported data are likely to have led to an overestimate of screening, a limitation that we acknowledged in our article. However, this limitation affects neither our finding that the 1996 US Preventive Services Task Force recommendation had no impact, nor our conclusion that millions of women are being screened unnecessarily. Their observation that physicians may sometimes perform a Pap smear because they are unaware of the indication for a woman's hysterectomy is probably true. However, their suggestion that the Pap smear may be a good way to bring women in for general preventive health care strikes us as poor justification for the continued use of a test without value.

We agree wholeheartedly with Dr Castle that unnecessary Pap smear screening of women who have undergone hysterectomy represents a waste of resources. We would ar-

gue that the most valuable resource being wasted is not money, but time—both for women and their clinicians. Limited time during office visits would certainly be better spent on issues more important to patients than on performing a useless test that is distinctly uncomfortable for some. The additional risk of labeling women without a cervix as HPV positive when the diagnosis is irrelevant represents yet another potential harm of continued screening.

Dr Richardson raises an even broader question—whether there is value in the pelvic examination apart from Pap smear screening. Evidence to help answer this question is scant, and guidelines are somewhat mixed. Screening for sexually transmitted diseases is recommended in all high-risk women,¹ although this can often now be accomplished with urine-based tests. The US Preventive Services Task Force recommended against routine pelvic examination as a screening test for ovarian cancer in 1996,² a recommendation that was not readdressed in the most recent update.³ Although the American Cancer Society had, until 2002, recommended annual pelvic examinations for all women aged 18 years and older,⁴ its most recent guidelines advise women to “discuss the need for these [pelvic] exams with their provider.”⁵ Thus, the decision about routine pelvic examinations is left—with little guidance—to the discretion of clinicians.

Finally, we applaud the suggestion of Drs Saraiya and Sawaya to require the exclusion of women who have undergone hysterectomy in the calculation of the HEDIS Pap smear performance measure. Unless the measure can be modified to exclude women in whom Pap smear screening is not indicated, it should be dropped as an indicator of health care quality.

Brenda Sirovich, MD, MS
brenda.sirovich@dartmouth.edu
H. Gilbert Welch, MD, MPH
VA Outcomes Group
Department of Veterans Affairs Medical Center
White River Junction, Vt

1. US Preventive Services Task Force. Screening for chlamydial infection: recommendations and rationale. *Am J Prev Med.* 2001;20(suppl 3):90-94.
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Fetal Microchimeric Cells and Breast Cancer

To the Editor: Multiple reproductive factors affect a woman's lifetime risk of developing breast cancer. Nulliparity confers an increased risk, whereas the total number of births is inversely correlated with cancer risk. The biological mecha-

nisms underlying these relationships have not been fully clarified, although both hormonal and cellular changes are implicated.¹

The study by Dr Khosrotehrani and colleagues,² which demonstrates the presence of fetal microchimeric cells in multiple maternal tissues (breast not included in analysis), suggests a novel mechanism by which parity may lower breast cancer risk: that pregnancy-associated progenitor cells provide a protective effect against the development of breast cancer. Whether as part of the glandular elements or microenvironment of the breast, fetal derived cells might communicate signals that inhibit malignant transformation, tumor angiogenesis, or both.^{3,4}

I am interested to know if Khosrotehrani et al have analyzed maternal breast tissue and cancer specimens for fetal microchimerism. Also, is there evidence for a relationship between the number of births and the percentages of breast-localized fetal microchimeric cells or their specific immunophenotypes (CD45⁺ vs cytokeratin⁺)?

Richard C. Frank, MD
richard.frank@norwalkhealth.org
Whittingham Cancer Center at Norwalk Hospital
Norwalk, Conn

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In Reply: Dr Frank describes reproductive factors and their association with lifetime risk of developing breast cancer in women, such as nulliparity conferring an increased risk and increasing parity being inversely correlated with risk. These associations suggest a protective effect of pregnancy, with hormonal and cellular changes being implicated,¹ although we agree with Frank that this effect could also be due to a novel mechanism involving the acquisition of fetal cells during pregnancy. The results of a study by Artlett et al² suggest a similarly protective effect of pregnancy on disease course and cause of death in systemic sclerosis, as they reported earlier onset of disease, more severe lung involvement, and higher rate of death in women who had never been pregnant compared with those who had had prior pregnancies.

Our group to date has not investigated whether fetal cell microchimerism is associated with breast cancer. However, we have reported on the presence of fetal cells, both CD45⁺ (ie, leukocyte) and cytokeratin⁺ (ie, epithelial), in cervical tissue from women with adenocarcinoma and squamous cell carcinoma of the cervix.³ The results of this study, along with results demonstrating the presence of fetal cells in infectious hepatitis⁴ and thyroid adenoma,⁵ has led our group to hypothesize that fetal progenitor cells acquired dur-