

# Cervical Cancer Burden and Opportunities for Prevention in a Safety-Net Healthcare System

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## Abstract

**Background:** The high prevalence of cervical cancer at safety-net health systems requires careful analysis to best inform prevention and quality improvement efforts. We characterized cervical cancer burden and identified opportunities for prevention in a U.S. safety-net system.

**Methods:** We reviewed tumor registry and electronic health record (EHR) data of women with invasive cervical cancer with ages 18+, diagnosed between 2010 and 2015, in a large, integrated urban safety-net. We developed an algorithm to: (i) classify whether women had been engaged in care ( $\geq 1$  clinical encounter between 6 months and 5 years before cancer diagnosis); and (ii) identify missed opportunities (no screening, no follow-up, failure of a test to detect cancer, and treatment failure) and associated factors among engaged patients.

**Results:** Of 419 women with cervical cancer, more than half (58%) were stage 2B or higher at diagnosis and 40%

were uninsured. Most (69%) had no prior healthcare system contact; 47% were diagnosed elsewhere. Among 122 engaged in care prior to diagnosis, failure to screen was most common (63%), followed by lack of follow-up (21%), and failure of test to detect cancer (16%). Tumor stage, patient characteristics, and healthcare utilization differed across groups.

**Conclusions:** Safety-net healthcare systems face a high cervical cancer burden, mainly from women with no prior contact with the system. To prevent or detect cancer early, community-based efforts should encourage uninsured women to use safety-nets for primary care and preventive services.

**Impact:** Among engaged patients, strategies to increase screening and follow-up of abnormal screening tests could prevent over 80% of cervical cancer cases. *Cancer Epidemiol Biomarkers Prev*; 27(12); 1398–406. ©2018 AACR.

## Introduction

In the United States, cervical cancer is preventable because precursor lesions can be identified through screening, additional diagnostic testing, and treated or monitored as indicated (1). Screening programs have made cervical cancer an uncommon disease with diminishing incidence and mortality (2, 3). However, significant disparities in screening exist for women who are racial/ethnic minorities, live in poverty, and have limited education and access to care (4, 5). Understanding

whether these groups are also less likely to have diagnostic follow-up after an abnormal screen result and receive treatment is limited by a lack of data. Most observational studies of follow-up are from privately insured populations receiving care from integrated healthcare systems (6, 7). Less is known about follow-up among racial/ethnic minorities and within safety-net health systems that disproportionately care for disadvantaged women (8, 9).

Studies from developed countries characterizing screening programs and contributors to cervical cancer occurrence are inadequate to inform quality improvement (QI) in safety-net systems for four key reasons: (i) most were published before introduction of high-risk human papillomavirus (hrHPV) testing, which gave rise to multiple changes in screening and management guidelines since 2001 (10); (ii) many studies either predate adoption of electronic health records (EHR) or rely on registry or claims data (7, 11–17); (iii) only a few studies reviewed opportunities for improvement beyond initial Pap screening (12, 18–20); most ignore the subsequent steps in the screening process (diagnostic follow-up, treatment, and surveillance); and (iv) the majority of studies are conducted among white women and those with commercial insurance, particularly those in health maintenance organizations (HMO) with organized screening programs (16, 17, 21). To our knowledge, like the majority of all U.S. settings (22, 23), most safety-net systems and clinics still deliver screening opportunistically. Thus, case reviews have significant potential

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**Note:** Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (<http://cebp.aacrjournals.org/>).

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to inform QI and improve delivery of the screening process in safety-net settings. We conducted this retrospective case series to:

- (i) Characterize women diagnosed with cervical cancer and their processes of care, including varied pathways into a large, urban, safety-net healthcare system; for example, whether they had been previously engaged in care in the system at the time of cancer diagnosis; and
- (ii) Identify healthcare system opportunities to improve the screening process through a correlated analysis of lack of screening and follow-up among the women engaged in care.

## Materials and Methods

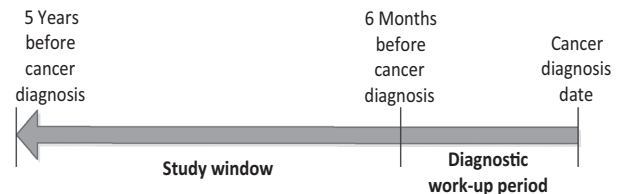
### Study setting and screening policies

This study was conducted at the Parkland Health and Hospital System (Parkland), a publicly funded safety-net healthcare system in Dallas, TX. Parkland includes a 862-bed hospital, 12 community-based adult primary care clinics, 11 women's health clinics, and other specialty clinics, all connected by a single comprehensive EHR. Each year, Parkland provides care and offers cervical cancer screening to approximately 84,000 women through its primary care and women's health clinics. Parkland accepts commercial insurance plans, participates in federal-state programs [e.g., National Breast and Cervical Cancer Early Detection Program (NBCCEDP)] that pay for screening and diagnostic services, and administers a county-funded sliding fee scale medical assistance program for uninsured and underinsured Dallas County residents.

The delivery of the cervical screening process in all health systems is shaped by organizational factors and systems, funding sources, and resource constraints. Parkland is disproportionately dependent on government payers, which impacts delivery of care in multiple ways. For example, at the time this study was conducted, the NBCCEDP in Texas did not reimburse for genotyping or for cotests. Parkland, like all health systems, implements changes to the screening process in response to evolving guidelines. From 2010 to 2015 (study period), Pap alone every 2 to 3 years was the predominant screening strategy. However, providers were free to choose between Pap and cotesting (Pap plus hrHPV). Abnormal results were sent to performing providers' EHR inbaskets; providers electronically referred those needing follow-up to a gynecology dysplasia clinic. The EHR health maintenance section alerted providers when cervical cancer screening was due for patients. In addition, cervical cancer screening is a clinical quality metric and providers were given monthly reports on screening rates for established patients seen that month.

### Data collection and study population

Data were obtained from the Parkland tumor registry and EHR. We used the registry to identify adult (ages 18 and older) women diagnosed with primary cervical cancer from 2010 to 2015. A board-certified gynecologist (C.L. Werner) reviewed patients' EHRs to verify primary cervical (i.e., not endometrial) origin. The EHR was then searched for outcome variables and covariates occurring between 6 months and 5 years prior to cervical cancer diagnosis date (hereafter the study window; Fig. 1). Data collection focused on the screening process; thus, we excluded tests and procedures during the diagnostic workup



**Figure 1.**

Timeline of retrospective data collection. Figure 1 includes 6-month diagnostic work-up period and overall 5-year study window in relation to the date of cancer diagnosis.

period, defined as the 6 months prior to diagnosis (12, 13, 19, 21, 24). Diagnostic procedures and results occurring prior to this time were abstracted.

### Outcome: Identifying prevention opportunities

Using an iterative approach, we developed an algorithm applied to EHR data to classify two outcomes reflecting opportunity to prevent cervical cancer (Supplementary Fig. S1 online supplement). First, we classified engagement in care. A woman was defined as engaged in care if she had  $\geq 1$  inpatient, outpatient, or emergency department (ED) encounter between 6 months and 5 years before cancer diagnosis. We defined women as engaged in care, regardless of the type or location (e.g., ED) of care they had previously received, because for all these women, Parkland had some opportunity either to provide screening or to refer the patient to primary care, the primary setting in which screening is delivered. In contrast, new patients presented to Parkland  $< 6$  months before diagnosis with a preexistent cervical cancer. Second, among engaged patients who were screening-age eligible ( $< 70$  years at diagnosis, thus  $< 65$  years at some time during the study period), we categorized efforts to deliver the screening process and results of those tests/procedures into one of four mutually-exclusive categories in this order (see Table 1 for definitions):

- (i) did not receive screening;
- (ii) did not receive follow-up after an abnormal screening test;
- (iii) developed cervical cancer subsequent to a negative screening or diagnostic test (failure to detect); or
- (iv) developed cervical cancer after excisional or ablative treatment (treatment failure).

### Covariates

We measured patient, tumor, and process-of-care characteristics. Patient characteristics included age, race/ethnicity, county of residence (Dallas or elsewhere), and year of diagnosis. Charlson comorbidity index (ref. 25; excluding tumors) was assessed at cancer diagnosis for patients engaged in care. Insurance was classified as uninsured (including self-pay and charity care), Medicaid, Medicare, other government payer, or commercial. Tumor characteristics were gathered from the tumor registry and included stage, histology, and tumor differentiation. Using International Federation of Gynecology and Obstetrics (FIGO) staging, we categorized clinical stage as local ( $\leq 2A$ ) or advanced ( $\geq 2B$ ); if missing, we used pathologic stage. If both were missing, stage was determined via manual review (C.L. Werner). We categorized histology as adenocarcinoma, adenosquamous, squamous, or other/unknown. For process-of-care characteristics, we used the registry to determine whether the diagnosis occurred

**Table 1.** Definitions of opportunities to prevent cervical cancer

Missed opportunity	Definition
Did not receive screening	(i) Did not have a screening Pap or cotest within the study window or (ii) did not have a screening Pap or cotest 3.5 years after a NILM Pap or ASC-US/HPV – result within the 5-year study window (if time permitted) given current recommendations for 3-year screening intervals.
Did not receive follow-up after an abnormal screening or diagnostic test	Had 1 or more Pap or cotest with an abnormal result (ASC-US/HPV+ or worse) and (i) did not have a colposcopy within 1 year after the first abnormal screening test in the study window, or (ii) did not have a treatment procedure within 6 months after a colposcopy result of CIN 2/3 or greater, or (iii) did not have a colposcopy within 1 to 1.5 years after a treatment during the study window (if time permitted).
Test(s) failure to detect a cervical abnormality (CIN 2/3 or cancer)	Developed cervical cancer subsequent to: (i) NILM Pap or negative cotests during the study window, or (ii) received a colposcopy/biopsy result less than CIN 2/3 within 1 year after first abnormal screening test in the study window.
Treatment failure	Developed cervical cancer within 1.5 years after receiving excisional or ablative treatment and surveillance as indicated.

Abbreviations: ASC-US, atypical squamous cells of undetermined significance; CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; NILM, negative for intraepithelial lesion and malignancy.

elsewhere prior to presentation at Parkland and where women received subsequent cancer treatments. Using EHR data, we defined location of the women's first Parkland visit (within the 6-month diagnostic window) as: ED, gynecology dysplasia clinic, or a primary care/women's health/specialty clinic. The study was approved by the Institutional Review Board at UT Southwestern Medical Center (Dallas, TX; STU 042014-045).

### Statistical analysis

We compared new versus engaged patients across covariates using descriptive statistics and univariate logistic regression models. We compared characteristics of unscreened women to those lacking follow-up using  $\chi^2$  and Fisher exact tests due to small cell sizes to identify statistically significant differences between women in these groups. For women whose screening or diagnostic tests did not detect cancer, we did not compare their demographics to other groups as such factors are unlikely to drive test failure (prior data indicate test failures are related to tumor characteristics, such as histology; ref. 26). Statistical significance was defined as  $P \leq 0.05$ . Statistical analysis was conducted using SAS 9.4. Study authors selected case studies that illustrated and exemplified why engaged patients failed to receive screening or follow-up. Case descriptions were drafted by A.C. Betts and reviewed for accuracy by C.L. Werner.

## Results

### Characteristics of women diagnosed with cervical cancer and their processes of care

After review of 430 women in the registry, 11 (2.6%) were excluded because their cancer was not invasive or of cervical origin. Table 2 shows characteristics of the 419 eligible women. The majority were Dallas County residents at diagnosis (85.7%). Median age was 46 (range 20–89) with only 36 women (8.6%) over age 65. Nearly half were Hispanic (48.7%); the distribution of non-Hispanic white (23.9%) and black (23.2%) women was about equal. Forty percent were uninsured/receiving charity care. The majority of tumors (58.2%) were advanced stage ( $\geq 2B$ ). Histology was mostly squamous cell carcinoma (76.6%). More than a third (35.6%) had cancer diagnosed at another facility before coming to Parkland. Because of small cell sizes, we did not include pregnancy ( $n = 5$ ) or HIV status ( $n = 4$ ) in the tables. Figure 2 illustrates the distribution across the two primary outcomes.

### Contact with the safety-net system: New versus engaged patients

The majority of cases (69.1%,  $n = 289$ ) were new patients with no history of care at Parkland prior to the 6-month diagnostic workup period. Compared with engaged patients, new patients were more likely to be non-Hispanic white (vs. Hispanic), to have commercial/other insurance (vs. uninsured), and to live outside of Dallas County (Table 2). New patients were more likely to be diagnosed with advanced tumors (63.3%) compared with engaged patients (46.9%).

As expected, new patients were more likely to have had their cancer diagnosed elsewhere; they were more likely to visit the ED or the gynecology dysplasia clinic (usually by referral), than primary care/women's health/specialty clinics. After diagnosis, new patients were more likely to receive cancer treatment outside of Parkland.

Among engaged patients, the extent of prior contact with Parkland varied: 25% had one primary care or women's health visit during the study window; 38% had 2+ visits; 36% had one visit to the ED whereas 27% had 2+ ED visits. About 25% of the engaged patients had a Charlson comorbidity score of  $\geq 1$  at cancer diagnosis (Table 2). Ten percent of engaged patients received their cancer diagnosis outside of Parkland and, for 40%, first visit in the diagnostic work-up period was at the ED.

### Opportunities for prevention among engaged patients

Among engaged patients, 8 (6.2%) were age  $\geq 70$  years at diagnosis and were excluded. Of the remaining 122 (Fig. 2), 63.1% were not screened, 20.5% did not receive follow-up, and 16.4% had a screening or diagnostic test that did not detect their cancer. There were no excisional or ablative treatment failures. Table 3 presents characteristics of engaged patients by opportunity to prevent cervical cancer. Table 4 provides case summaries that illustrate some of the challenges to delivering the screening process to safety-net populations.

Unscreened women were more likely to be diagnosed with advanced stage disease (62.3%) than those screened but not followed up (24%). Many had opportunities for screening: 22% had one primary care or women's health visit during the study period and 32% had 2+ visits, whereas 45% visited the ED or a specialty clinic. Unscreened women had similar Charlson comorbidity scores when compared with women who did not receive follow-up; over one quarter (27.3%) had a score of  $\geq 1$  at the time of cancer diagnosis (excluding tumors;

**Table 2.** Characteristics of women with cervical cancer and comparison of new patients versus engaged patients in an urban safety-net system, *N* = 419

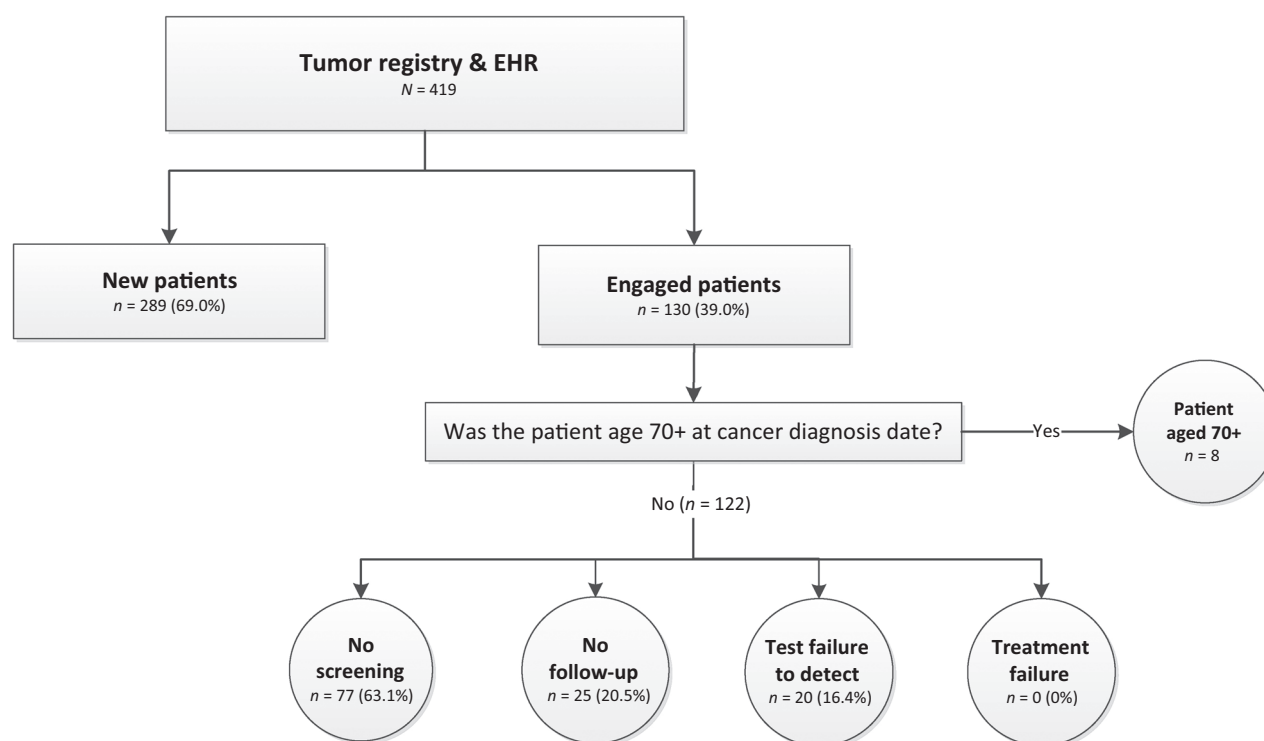
	Total <i>N</i> = 419 (%)	New patients <i>n</i> = 289 (69.1%)	Engaged patients <i>n</i> = 130 (30.9%)	Unadjusted OR <sup>a</sup> (95% CI)
Age at cancer diagnosis				
18–29	25 (6.0)	20 (6.9)	5 (3.8)	1.89 (0.68–5.25)
30–49	221 (52.7)	150 (51.9)	71 (54.6)	Reference
50–64	137 (32.7)	94 (32.5)	43 (33.1)	1.04 (0.65–1.64)
65–Older	36 (8.6)	25 (8.7)	11 (8.5)	1.08 (0.50–2.31)
Race-ethnicity				
Hispanic	204 (48.7)	138 (47.8)	66 (50.8)	Reference
Black	97 (23.2)	55 (19.0)	42 (32.3)	0.63 (0.38–1.03)
White	100 (23.9)	84 (29.1)	16 (12.3)	2.51 (1.37–4.62)
Other	18 (4.3)	12 (4.2)	6 (4.6)	0.96 (0.34–2.66)
Payer at cancer diagnosis				
Uninsured (charity)	241 (57.5)	156 (54.0)	85 (65.4)	Reference
Commercial/other <sup>b</sup>	83 (19.8)	79 (27.3)	4 (3.1)	10.76 (3.81–30.38)
Medicaid	47 (11.2)	29 (10.0)	18 (13.8)	0.88 (0.46–1.67)
Other government	34 (8.1)	15 (5.2)	19 (14.6)	0.43 (0.21–0.89)
Medicare	14 (3.3)	10 (3.5)	4 (3.1)	1.36 (0.42–4.47)
Charlson comorbidity score (no tumor)				
0			17 (13.1)	
≥1			32 (24.6)	
Unknown			81 (62.3)	
Dallas County resident at cancer diagnosis				
Yes	359 (85.7)	236 (81.7)	123 (94.6)	Reference
No/unknown <sup>c</sup>	60 (14.3)	53 (18.3)	7 (5.4)	3.94 (1.74–8.94)
Cancer diagnosis year				
2010–2011	148 (35.3)	105 (36.3)	43 (33.1)	Reference
2012–2013	150 (35.8)	103 (35.6)	47 (36.2)	0.90 (0.55–1.47)
2014–2015	121 (28.9)	81 (28.0)	40 (30.8)	0.83 (0.49–1.39)
Cancer stage				
Local	167 (39.9)	101 (34.9)	66 (50.8)	Reference
Advanced	244 (58.2)	183 (63.3)	61 (46.9)	1.96 (1.28–3.00)
Not assigned	8 (1.9)	5 (1.7)	3 (2.3)	1.09 (0.25–4.71)
Histology				
Squamous	321 (76.6)	220 (76.1)	101 (77.7)	Reference
Adenocarcinoma	63 (15.0)	39 (13.5)	24 (18.5)	0.75 (0.43–1.31)
Adenosquamous	20 (4.8)	17 (5.9)	3 (2.3)	2.60 (0.75–9.08)
Carcinoma NOS/other	15 (3.6)	13 (4.5)	2 (1.5)	2.98 (0.66–13.47)
Tumor differentiation				
Low	210 (50.1)	141 (48.8)	69 (53.1)	Reference
High	143 (34.1)	97 (33.6)	46 (35.4)	1.03 (0.66–1.63)
Unknown	66 (15.8)	51 (17.6)	15 (11.5)	1.66 (0.87–3.17)
Location of first visit during 6-month diagnostic work-up period				
Primary care/women's/specialty	95 (22.7)	29 (10.0)	66 (50.8)	Reference
Gynecology dysplasia	78 (18.6)	66 (22.8)	12 (9.2)	12.5 (5.89–26.61)
Emergency department	246 (58.7)	194 (67.1)	52 (40.0)	8.49 (4.98–14.47)
Initial cancer diagnosis location				
Parkland/affiliated	270 (64.4)	153 (52.9)	117 (90.0)	Reference
Elsewhere	149 (35.6)	136 (47.1)	13 (10.0)	8.0 (4.31–14.84)
Cancer treatment location				
All Parkland	163 (38.9)	103 (35.6)	60 (46.2)	Reference
Some Parkland	206 (49.2)	146 (50.5)	60 (46.2)	1.42 (0.92–2.20)
All elsewhere	50 (11.9)	40 (13.8)	10 (7.7)	2.33 (1.09–5.00)

Abbreviation: CI, confidence interval.

<sup>a</sup>Univariate logistic regression models in which engaged patients are the referent group.<sup>b</sup>Other types of payers included veterans' benefits and workman's compensation.<sup>c</sup>46 patients had an unknown county of residence (*N* = 42 new patients and *N* = 4 engaged patients).

Table 3). Case summaries (Table 4) revealed that women who did not receive screening despite significant Parkland inpatient and outpatient utilization often were undergoing management of one or multiple comorbid conditions, including diabetes, hypertension, and HIV. Some had cancelled or did not show for scheduled Pap appointments. Across the study window, 10.4% of unscreened women had a missed clinic appointment and 33.8% missed 2+ appointments (Table 3).

Among the 25 women who did not receive follow-up, the reference test was either a Pap/cotest (*n* = 20) or a colposcopy/biopsy (*n* = 5). About half (52%) had completed at least one primary care or outpatient clinic visit (median = 1, range 0–33) after the abnormal result (i.e., there were opportunities to stress the importance of or arrange for follow-up; see Table 4 for example case summaries). Notably, 40% (median = 1, range 0–17) missed 2+ appointments for follow-up during the study



**Figure 2.**

Study schema. Women with cervical cancer were classified using the tumor registry and electronic health record (EHR) as new patients or engaged patients; engaged patients aged <70 years were further classified by opportunity to prevent cervical cancer: no screening, no follow-up of abnormal screening, failure of a test to detect cancer, or a treatment failure.

window (Table 3). Case reviews revealed a variety of reasons for lack of follow-up with reasons documented in various EHR locations, including progress notes of patient encounters, telephone encounters, and under the "letters" tab. Reasons included competing demands such as caring for family, managing chronic and acute diseases, having limited contact with primary or gynecology clinics (vs. other sub-specialty care), or problems with results communication among providers, clinic or laboratory staff, and patients. For example, although reviews demonstrated that women were informed of their abnormal results in several ways (telephone, regular mail, or certified letter), for many cases we could not determine in the EHR whether women actually received or understood these communications. Reviews indicated multiple reasons for lack of follow-up and cannot simply be attributed to patient nonadherence or provider/system failure to inform or arrange further evaluation.

For 16.4% ( $n = 20$  cases), we identified a prior test that did not detect a presumably existent cervical cancer or precursor lesion. Tests occurred in a median of 31 months (range 7 to 45 months) prior to cancer diagnosis. Three women had a negative or CIN I colposcopy/biopsy prior to cancer diagnosis. Of these, two had squamous cancer and one had adenocarcinoma. Seventeen women had a negative screening test <3.5 years of cancer diagnosis. One of these was a negative cotest; one was an ASC-US/HPV negative cotest; the remaining 15 received cytology alone with a NILM result. Most women were previously under-screened: for 71% (12/17), the negative screening test was the first and only screen on record prior to cancer diag-

nosis. Approximately half of the 20 cancers in this group were adenocarcinomas.

## Discussion

We described the cervical cancer burden in a large, urban safety-net system, characterized clinical care pathways of engaged patients prior to their cervical cancer diagnosis, and, in doing so, identified opportunities to improve delivery of the screening process. Most women (69%) had no healthcare system contact prior to diagnostic work-up. To deliver the screening process and prevent cancer among these women, outreach to the broader community would be needed. Furthermore, of the 122 engaged in care, 63% were not screened. This suggests that, to prevent cervical cancer at Parkland, QI efforts' highest priority should be screening outreach. Comparing our data with the population-based Texas Cancer Registry (27) reveals that Parkland cared for 49% of all women with cervical cancer diagnosed in Dallas County and 10% of all cervical cancer cases in Texas. Dallas represents the ninth most populous U.S. county and Texas is the second most populous U.S. state, according to the U.S. Census Bureau 2011–2015 American Community Survey. Thus, future interventions within our system could significantly impact the population-level cervical cancer burden. The large burden observed in our study underscores the fact that cervical cancer is a disease predominantly borne by low socioeconomic status, African American, and Hispanic women—populations served by safety-net systems.

**Table 3.** Characteristics of engaged patients by opportunity to prevent cervical cancer among women aged <70 years at diagnosis in an urban safety-net system, *N* = 122

	Total <i>N</i> = 122 (%)	Test did not detect cancer <i>n</i> = 20 (16.4%)	No screening <i>n</i> = 77 (63.1%)	No follow-up for abnormal test <i>n</i> = 25 (20.5%)	<i>P</i> <sup>a</sup>
Age at cancer diagnosis					0.180
18–29	5 (4.1)	0 (0.0)	3 (3.9)	2 (8.0)	
30–49	71 (58.2)	16 (80.0)	38 (49.4)	17 (68.0)	
50–64	43 (35.2)	4 (20.0)	33 (42.9)	6 (24.0)	
65–Older	3 (2.5)	0 (0.0)	3 (3.9)	0 (0.0)	
Race-ethnicity					0.421
Hispanic	63 (51.6)	14 (70.0)	37 (48.1)	12 (48.0)	
Black	37 (30.3)	6 (30.0)	21 (27.3)	10 (40.0)	
White	16 (13.1)	0 (0.0)	13 (16.9)	3 (12.0)	
Other	6 (4.9)	0 (0.0)	6 (7.8)	0 (0.0)	
Payer at cancer diagnosis					0.152
Uninsured (charity)	79 (64.8)	7 (35.0)	58 (75.3)	14 (56.0)	
Commercial	4 (3.3)	1 (5.0)	2 (2.6)	1 (4.0)	
Medicaid	17 (13.9)	3 (15.0)	10 (13.0)	4 (16.0)	
Other government	19 (15.6)	7 (35.0)	6 (7.8)	6 (24.0)	
Medicare	3 (2.5)	2 (10.0)	1 (1.3)	0 (0.0)	
Charlson comorbidity score (no tumor)					0.822
0	17 (13.9)	8 (40.0)	6 (7.8)	3 (12.0)	
≥1	32 (26.2)	4 (20.0)	21 (27.3)	7 (28.0)	
Unknown	73 (59.8)	8 (40.0)	50 (64.9)	15 (60.0)	
Dallas County at cancer diagnosis					0.549
Yes	115 (94.3)	20 (100)	72 (93.5)	23 (92.0)	
No/Unknown <sup>b</sup>	7 (5.7)	0 (0.0)	5 (6.5)	2 (8.0)	
Cancer diagnosis year					0.032
2010–2011	42 (34.4)	10 (50.0)	23 (29.9)	9 (36.0)	
2012–2013	44 (36.1)	5 (25.0)	31 (40.3)	8 (32.0)	
2014–2015	36 (29.5)	5 (25.0)	23 (29.9)	8 (32.0)	
Cancer stage					0.002
Local	62 (50.8)	16 (80.0)	28 (36.4)	18 (72.0)	
Advanced	58 (47.5)	4 (20.0)	48 (62.3)	6 (24.0)	
Not assigned	2 (1.6)	0 (0.0)	1 (1.3)	1 (4.0)	
Histology					0.096
Squamous	96 (78.7)	10 (50.0)	65 (84.4)	21 (84.0)	
Adenocarcinoma	21 (17.2)	8 (40.0)	9 (11.7)	4 (16.0)	
Adenosquamous	3 (2.5)	2 (10.0)	1 (1.3)	0 (0.0)	
Carcinoma NOS/other	2 (1.6)	0 (0.0)	2 (2.6)	0 (0.0)	
Tumor differentiation					0.010
Low	64 (52.5)	14 (70.0)	34 (44.2)	16 (64.0)	
High	44 (36.1)	4 (20.0)	34 (44.2)	6 (24.0)	
Unknown	14 (11.5)	2 (10.0)	9 (11.7)	3 (12.0)	
Initial cancer diagnosis location					0.30
Parkland	110 (90.2)	17 (85.0)	69 (89.6)	24 (96.0)	
Elsewhere	12 (9.8)	3 (15.0)	8 (10.4)	1 (4.0)	
Cancer treatment location					0.045
All Parkland	57 (46.7)	12 (60.0)	32 (41.6)	13 (52.0)	
Some Parkland	57 (46.7)	7 (35.0)	39 (50.6)	11 (44.0)	
All elsewhere	8 (6.6)	1 (5.0)	6 (7.8)	1 (4.0)	
Location of first visit during 6 month diagnostic work-up period					0.066
Primary care/women's/specialty	60 (49.2)	13 (65.0)	37 (48.1)	10 (40.0)	
Gynecology dysplasia	12 (9.8)	1 (5.0)	5 (6.5)	6 (24.0)	
Emergency department	50 (41.0)	6 (30.0)	35 (45.5)	9 (36.0)	
Number of missed appointments during study window					0.26
0	66 (54.1)	13 (65.0)	43 (55.9)	10 (40.0)	
1	15 (12.3)	2 (10.0)	8 (10.4)	5 (20.0)	
≥2	41 (33.6)	5 (25.0)	26 (33.8)	10 (40.0)	

<sup>a</sup>*P* for comparison of screen and follow-up columns.<sup>b</sup>Four patients had unknown county of residence (*N* = 2 no screening and *N* = 2 no follow-up).

We identified multiple opportunities to improve cervical cancer prevention efforts. Consistent with prior findings, lack of screening was the leading driver of cervical cancer (16, 17, 21) occurring in 63% of our engaged patients. For the 16% whose test failed to detect cancer, the over representation of

nonsquamous histologies is somewhat expected because Pap tests are more sensitive for detecting squamous cell carcinomas than adenocarcinomas (26, 28, 29). The patterns of care before cervical cancer and potential opportunities for prevention identified in our system, differed somewhat from prior reviews.

**Table 4.** Illustrative case summaries of engaged women with cervical cancer

<b>Failure to screen</b>
<p>Case 1: Age mid-thirties</p> <ul style="list-style-type: none"> <li>• Did not attend 16 scheduled Pap appointments in the HIV OB/GYN clinic in the 5 years prior to the abnormal Pap that led to cervical cancer diagnosis.</li> <li>• Routinely seen in the HIV clinics during the study period.</li> <li>• Poorly controlled HIV infection with increased viral load at multiple time points and self-reported nonadherence to medications.</li> <li>• During HIV visits, providers stressed the importance of medication adherence so that she would be well enough to care for her family, as well as the importance of keeping gynecology appointments.</li> <li>• <b>Reported stress and competing demands, including caring for ill family members that involved travel.</b></li> </ul>
<p>Case 2: Age late fifties</p> <ul style="list-style-type: none"> <li>• Postmenopausal with multiple comorbidities including tobacco use, hepatitis C, hypertension, dyslipidemia, multiple gastrointestinal conditions, and chronic abdominal pain.</li> <li>• Nine emergency department visits in first 2 years of study for severe abdominal pain and GI symptoms. Seen frequently in GI-Liver Clinic and received multiple GI diagnostic evaluations. Seen at least annually in the same primary care clinic for 4 of 5 study years. Treatment through both primary care and specialty clinics focused on extreme hyperlipidemia and control of chronic GI symptoms.</li> <li>• No Pap until seen for the first time at a women's clinic at which time the patient was symptomatic (abnormal vaginal bleeding) and had a Pap performed indicative of cervical cancer.</li> </ul>
<p>Case 3: Age early sixties</p> <ul style="list-style-type: none"> <li>• Postmenopausal with poorly controlled type II diabetes, hypertension, hyperlipidemia, congestive heart failure, and depression/anxiety.</li> <li>• Seen regularly in primary care for 2.5 years before cancer diagnosis, with focus on control of diabetes and hypertension. Hospitalized for hypertensive crisis approximately 1 year prior to cervical cancer diagnosis; thereafter, attended cardiology clinic in addition to primary care clinic.</li> <li>• CT angiography incidentally showed adnexal masses, confirmed by pelvic sonogram. The patient was seen in gynecology clinic 4 months later for further evaluation, which included her initial Pap within the system. Cervical cancer was subsequently diagnosed because of this Pap being abnormal.</li> </ul>
<b>Failure to follow-up abnormal test</b>
<p>Case 4: Age late thirties</p> <ul style="list-style-type: none"> <li>• Reproductive-aged patient with history of diabetes mellitus and new diagnosis of advanced invasive breast cancer during the study period. Underwent mastectomy followed by neoadjuvant chemotherapy for over 1 year.</li> <li>• Screened for cervical cancer with cotests one year apart in primary care clinic; both showed a negative Pap with positive high-risk HPV testing. However, the patient was not referred for colposcopy as per management guidelines following the second such result.</li> <li>• Thereafter, patient attended oncology the follow-ups and infrequent primary care encounters that focused on her diabetes.</li> <li>• Cholecystectomy performed after positive evaluation for gall bladder disease.</li> <li>• Received a third Pap test approximately 2 years after the last cotest, with a negative result.</li> <li>• Patient presented to gynecology clinic with symptoms of cervical cancer approximately 1 year after the third negative Pap. A cervical mass was identified upon presentation to gynecology clinic.</li> </ul>

For example, studies conducted in non-safety-net settings demonstrated a higher rate of screening test failures and treatment failures; we found none of the latter (16, 17). These differences highlight the importance of healthcare systems conducting their own reviews to select interventions and deploy resources that will have the greatest impact for their patients. Our findings suggest that increasing screening and follow-up may potentially decrease cancer incidence irrespective of a system's policies on screening test modality or interval.

Consistent with our findings, prior research underscores the importance of encouraging women to obtain primary care as a key strategy for cervical cancer prevention (30). Most new patients (67%) and even many engaged patients (40%) started their cervical cancer diagnostic process in the ED presenting with symptoms such as vaginal bleeding or pain. We could not determine whether and how long these new patients had delayed seeking care or their patterns of primary care contact with other healthcare systems (31, 32). Notably, new patients were diagnosed at a later stage than engaged patients. Among engaged patients, primary care contact varied, ranging from dozens of visits over several years to a single visit or sporadic visits over a shorter time period. Furthermore, case reviews uncovered multifactorial reasons for lack of screening and follow-up in engaged patients. These included ongoing management of comorbidities and problems with results reporting and communication, in addition to limited primary care contact or coordination with specialists.

We identified several factors associated with being a new patient, which reflect Parkland's role as a regional provider of

heavily subsidized care. First, we observed that many new patients did not live within Dallas County; these noncounty residents are ineligible for subsidized primary care, but they are eligible for subsidized cervical diagnostic services through Parkland's participation in the NBCCEDP. We also observed that those with commercial insurance (vs. uninsured/charity care) were more likely to be new patients. Although counterintuitive, this finding may reflect issues of being under-insured with high deductibles. Other health systems may refer these patients because Parkland will subsidize diagnosis and treatment via county and federally supported programs, minimizing or eliminating out-of-pocket costs. We cannot assess specifics of individual patients' insurance products to test this assumption.

To put our study population in context, we compared race/ethnicity and insurance status of the women in the present study with our observational cohort of 191,185 screening-eligible women who are engaged in primary care at Parkland. Overall, white race was more common among women with cervical cancer and Hispanic ethnicity was more common in the overall cohort. Although uninsured/charity and commercial insurance was more common among women with cervical cancer, Medicaid and other government payers were more common among the overall cohort. These differences may reflect differing age distributions of cervical cancer cases versus all primary care patients, demographics of out-of-county residents referred to Parkland for cancer care, or other factors. Notably, insurance status can change over time and the insurance status of a cancer patient at time of diagnosis may not be directly comparable to insurance status of

our comparison population, which was defined at the time of a primary care visit.

Our study faces several limitations. Our algorithm assigned women into mutually exclusive categories. However, case reviews demonstrated that women could experience more than one missed opportunity for cervical cancer prevention. Realistically, health systems will never be able to fully eradicate cervical cancer due to patient noncompliance. Among women classified as "failure to detect," we cannot rule out the interval cancers arising quickly within the guideline-recommended intervals. We identified no treatment failures, which could be a result of our limited timeframe for posttreatment surveillance.

Our study has several key advantages. First, we evaluated the entire screening process, going beyond studies only focused on Pap screening (12, 18–20). Second, we analyzed an array of patients, tumors, and process-of-care covariates and presented case summaries to further contextualize findings. Third, while conducted in a single healthcare system, our study sample represents half of the overall cervical cancer burden in one of the most populous U.S. counties, and is one of the few and largest cervical cancer case reviews conducted in a U.S. safety-net system without an organized screening program. Thus, it fills a significant gap in the literature. Moreover, given the increasing trend toward formation of integrated safety-net systems (33, 34) and the fact that many patients are referred to Parkland from federally qualified health centers and other stand-alone, smaller safety-net clinics, our study has relevance in other safety-net settings.

### Implications

Our findings provide an initial evidence base to shape QI initiatives in safety-net systems and to encourage community-based interventions outside of safety-net walls. QI efforts should focus first on initial screening but also attend to increasing guideline-concordant follow-up. In our system, such strategies could potentially prevent over 80% of cervical cancers among engaged patients.

Our algorithm-driven approach, applied to longitudinal EHR data from a large, urban safety-net system, provides a starting point for other systems to conduct their own system audits. Case reviews/audits of cervical cancer patients are needed across diverse settings to identify targets for QI initiatives. We believe our framework for identifying missed opportunities can be applied, or adapted, successfully in other settings with EHRs, even in nonintegrated and primary care safety-net systems with fewer resources. Sasieni and Cuzik encourage routine audits as an ethical requirement of large-scale screening programs (35, 36). Our algorithm can be adapted for other health systems to char-

acterize how cervical cancer occurs among engaged patients and prioritize interventions to improve prevention efforts. These efforts should be used to guide development, implementation, and dissemination of multilevel strategies to prevent cervical cancer.

### Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

### Disclaimer

The content is solely the responsibility of the authors and does not necessarily represent the official views of the NCI or the NIH.

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