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Prioritizing cervical cancer screening services during the COVID-19 pandemic: Response of an academic medical center and a public safety net hospital in California

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ABSTRACT

The expeditious diagnosis and treatment of high-grade cervical precancers are fundamental to cervical cancer prevention. However, during the COVID-19 pandemic healthcare systems have at times restricted in-person visits to those deemed urgent. Professional societies provided some guidance to clinicians regarding ways in which traditional cervical cancer screening might be modified, but many gaps remained. To address these gaps, leaders of screening programs at an academic medical center and an urban safety net hospital in California formed a rapid-action committee to provide guidance to its practitioners. Patients were divided into 6 categories corresponding to various stages in the screening process and ranked by risk of underlying high-grade cervical precancer and cancer. Tiers corresponding to the intensity of the local pandemic were constructed, and clinical delays were lengthened for the lowest-risk patients as tiers escalated. The final product was a management grid designed to escalate and de-escalate with changes in the local epidemiology of the COVID-19 pandemic. While this effort resulted in substantial delays in clinical screening services as mandated by the healthcare systems, the population effects of delaying on both cervical cancer outcomes as well as the beneficial effects related to decreasing transmission of severe acute respiratory coronavirus 2 have yet to be elucidated.

1. Introduction

The expeditious diagnosis and treatment of high-grade cervical precancers are fundamental to cervical cancer prevention. During the COVID-19 pandemic, healthcare systems have at times required delay of elective surgical procedures, and restriction of in-person visits to those deemed urgent. To assist in guiding practitioners, the ASCCP endorsed postponement of diagnostic evaluation of patients with minimally abnormal cervical cancer screening test results (ASCCP, 2020). Specifically, the ASCCP stated that individuals with low-grade cervical cancer screening tests may postpone diagnostic evaluations up to 6 to 12 months, but that those with high-grade test results should have a diagnostic evaluation scheduled within 3 months. Individuals with high-grade cervical disease without suspected invasive disease should have procedures within 3 months, but if invasive disease is suspected evaluation should be within 4 weeks. The American College of Obstetricians and Gynecologists (ACOG) stated that screening average-risk patients could potentially be deferred until after the pandemic had ended (American College of Obstetricians and Gynecologists, 2020). These organizations did not address how to modify care for individuals under surveillance for prior test abnormalities or after cervical treatments for high-grade precancerous cervical lesions.

At the beginning of the pandemic, clinicians at the University of California San Francisco (UCSF) Medical Center and Zuckerberg San Francisco General Hospital and Trauma Center (ZSFG) were asked to review histories of all scheduled patients in an effort to distinguish essential visits from those that may be safely delayed for 6 weeks, yet there was no consensus as to how this determination was to be made; in pragmatic terms, front-line clinicians were faced with making such determinations using their own best judgment. To address these gaps in

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guidelines, leaders of the cervical cancer screening programs at both UCSF and ZSFG formed a committee to provide guidance for its practitioners. UCSF is an academic medical center providing quaternary care to approximately 250,000 patients per year; the UCSF Dysplasia Clinic provides consultation and treatment of complex patients with dysplastic lesions of the lower genital tract who live in the San Francisco Bay Area as well as in greater Northern and Central California. ZSFG is an urban safety net hospital that provides about 310,000 primary care visits per year to underserved residents of San Francisco; the ZSFG Dysplasia Clinic provides comprehensive screening, diagnosis and treatment of dysplastic lesions of the lower genital tract. Leaders from both clinical sites were charged with producing clinical guidance designed to escalate and deescalate with changes in the local epidemiology of the COVID-19 pandemic. One major goal of having a single source of guidance for both institutions was to strive for equitable treatment of patients regardless of specific healthcare setting.

The objectives of this report are to describe the process by which we crafted rapid-action evidence-based clinical guidelines for cervical cancer screening during the COVID-19 pandemic and to share our guidelines with others facing similar challenges.

2. Methods

All authors of this work were committee members; four are obstetrician-gynecologists (GFS, RL, MPB, KSM) with a long history of collaboration, and one is a family medicine physician (HH). All team members have collaborated in both clinical care and scholarly work. Most work was completed by electronic mail over a period of 2 weeks. Disagreements were managed through on-line discussion, and final recommendations were agreed upon by all.

We first set forth guiding principles for the process, defining the stakeholders and acknowledging the dynamic nature of the response to the pandemic (Table 1). Guidance from ASCCP and ACOG was reviewed periodically to better understand gaps in clinical advice that needed to be provided to local clinics. We then defined 6 clinical scenarios applicable to all patients with abnormal cervical cancer screening test results within the prior 3 years, and we ranked them in order of risk of underlying cervical intraepithelial neoplasia (CIN) grade 3 and early asymptomatic cancers (collectively known as CIN3+). Recent published estimates were used to guide this determination (Demarco et al., 2020; Egemen et al., 2020; Perkins et al., 2020). These estimates provide the evidence upon which current management guidelines are based and to which both clinics adhere.

We did not offer specific advice to clinicians regarding primary screening, as most clinic visits exclusively for preventive care were postponed. Instead, we focused on individuals with new cervical cancer screening test abnormalities and those under active surveillance for a prior abnormality or a recent cervical treatment. Because recent guidelines do not recommend different management for individuals at potentially higher-than-average risk of CIN3+ (e.g., those living with HIV), we did not make separate recommendations for this group. The target groups for guidance were a wide variety of clinicians in primary care and specialty settings engaged in cervical cancer screening throughout San Francisco. Dissemination was through electronic messaging as well as shared intranet folders.

Because recommendations were designed to anticipate changes in the balance of benefits and harms of a clinic visit during the pandemic, we developed a consensus-based system of tiers escalating from 1 to 4, reflecting the medical centers' ability to conduct non-urgent visits during the pandemic. As tiers increase, clinic visits are delayed, and thresholds for colposcopy and treatment increase accordingly. The length of the delays ranged from 6 weeks to one year and were based largely on the reasoned judgment of the committee. Various factors could drive tier escalation including local, state and federal mandates; stress on the hospital system due to COVID-19; and emergency redeployment of healthcare workers by the healthcare system away from outpatient clinics to acute care areas. Tier de-escalation was based on guidance from the healthcare system regarding the improved availability to schedule elective surgeries and schedule non-urgent in-person visits. Because shelter-in-place orders were imminent at the beginning of the process, we also considered the content of clinical visits to minimize patient returns among those venturing out for clinic appointments during the pandemic to receive recommended care. Although our guidance focused on cervical cancer screening, we also provided advice about treatment of vulvar and vaginal dysplasia, largely based on ACOG recommendations and clinical judgment (Committee Opinion No.675: Management of Vulvar Intraepithelial Neoplasia, 2016).

Table 1
Guiding principles for prioritizing cervical cancer screening services during the COVID-19 pandemic.

- The balance of benefits and harms of a dysplasia clinic visit during the COVID-19 pandemic is dynamic.
- The benefits are incurred predominately at the level of the individual patient.
- The harms are incurred not only by the individual patient, but also the healthcare providers and staff and those in the community with whom they may be in close contact after the visit.
- On the basis of underlying risk of high-grade precancerous lesions and early asymptomatic cancers, some patients should be encouraged to keep appointments and others should delay appointments.
- Because the course of the pandemic is unknown, delaying patients may push their visit into a time frame in which the pandemic is substantially worse.
- Some patients may be at risk of both adverse consequences of exposure to severe acute respiratory coronavirus and the progression of cervical precancerous to cancers (e.g., immunocompromised after lung transplantation).
- Guidelines were not meant to be an absolute substitution for clinical judgment.

3. Results

Table 2 shows our rank ordering of clinical scenarios based on underlying risk of CIN3+ (Demarco et al., 2020; Egemen et al., 2020; Perkins et al., 2020). The lowest risk group was composed of patients with a colposcopy 12 months prior showing no evidence of CIN2+, and the highest risk patients were those with untreated, biopsy-proven CIN3 and/or adenocarcinoma in situ lesions. For the lowest-risk group, we recommended delays in diagnostic evaluations (6 weeks, then 6 weeks to 6 months, then 6 months). For the highest-risk group, we recommended no delay in treatments from tiers 1 to 3; treatments were delayed up to 6 months after diagnosis in tier 4.

We reviewed the content of clinic visits with a goal of minimizing return visits, and we made changes to recommendations in two clinical scenarios (Table 3). For patients with CIN2 or CIN3 treated with an excisional procedure and found to have negative surgical margins, we recommended that clinicians perform a colposcopy 6 months after treatment instead of cytology plus HPV testing. We based this recommendation on the relatively high likelihood of a positive HPV test [at least 30% (Chan et al., 2009)] and a modeling study showing that this strategy is cost-effective compared with either cytology or HPV testing at the 6-month visit (Melnikow et al., 2010). We also recommended that clinicians strongly consider performing an excisional procedure as opposed to colposcopy with biopsy for patients with a cytologic diagnosis of high-grade squamous intraepithelial lesion (HSIL).

Shortly after our guidance was disseminated, ASCCP updated its management guidelines stating that the "preferred" management of patients who have undergone a treatment for CIN2 or CIN3 is an HPV-based test 6 months after the procedure. An alternative management plan deemed "acceptable" by ASCCP is to perform a colposcopy and endocervical curettage at the 6-month visit. The new ASCCP guidelines also deemed both colposcopy and treatment to be "acceptable" first-line approaches for patients with a predicted underlying risk of CIN3+ of 25–59% (e.g., patients with a cytology test interpreted as HSIL). Thus, our recommendations were generally in agreement with these new guidelines. To be more fully concordant with these guidelines, we made

Table 2
Guidelines for management of individuals with abnormal cervical cancer screening test results during the COVID-19 pandemic.

Tier	Delay/Action	Step in the cervical cancer screening process approximating <- lowest to highest -> risk of CIN3+					
		Surveillance: 12-month return (e.g., prior colposcopy with no CIN2+ found)	Screening: Abnormal test results[a]	Surveillance: 6-month return (e.g., CIN2 with adequate colposcopy, ages 21–24)	Post-treatment: 6-month return	Diagnostic excisional procedures (e.g., HSIL with inadequate colposcopy)	Treatment (biopsy-proven CIN2, CIN3, AIS)
1	6-week delay	Delay HPV-based testing from 12 to 13.5 months	Do not delay colposcopy for high-grade test results.[c] Delay colposcopy 1.5 months for low-grade test results.[d]	Delay follow-up from 6 to 7.5 months	Do not delay.		
2	6-week to 6-month delay; revised treatment threshold	Delay HPV-based testing from 12 to 16 months	Do not delay colposcopy for high-grade test results.[c] Delay colposcopy 6 months for low-grade test results.[d]	Delay follow-up from 6 to 10 months	Delay from 6 to 7.5 months	Delay those with ASC-H/HPV negative from 'next available' to 4 months after diagnosis.[b] Do not delay others.	Do not delay for CIN3, AIS For CIN2, do colposcopy 6 months after diagnosis if criteria for surveillance met.
3	4- to 6-month delay; raised colposcopy threshold	Delay HPV-based testing from 12 to 18 months	Do not delay colposcopy for high-grade test results.[c] Delay colposcopy 12 months for low-grade test results.[d]	Delay follow-up from 6 to 12 months	Delay from 6 to 10 months		
4	6-month delay; further raised colposcopy and treatment threshold		Delay colposcopy 6 months for high-grade test results.[c] Delay colposcopy 12 months for low-grade test results.[d]		Delay from 6 to 12 months	Delay from 'next available' to 6 months after diagnosis.[b]	Delay all from 'next available' to 6 months after diagnosis.[b]

Abbreviations: CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; AIS, adenocarcinoma in situ; HSIL, high grade squamous intraepithelial lesion ASC—H, atypical squamous cells, cannot exclude HSIL; CIN3+, CIN3, AIS and/or cancer; CIN2+, CIN2, CIN3+.
[a] excisional procedures for patients with inadequate colposcopy and ASC-H/HPV+ or HSIL cytology recommended to minimize returns.
[b] unless cancer suspected.
[c] HSIL, ASC—H, atypical glandular cells; AIS and/or cancer.
[d] normal cytology with an HPV-positive test; atypical squamous cells of undetermined significance; low-grade squamous intraepithelial lesion.

Table 3
Recommended clinical actions before and during the COVID-19 pandemic to minimize patient return visits.

Clinical scenario	Clinical action before the pandemic	Clinical action during the pandemic
Initial post-treatment follow-up visit in patients with negative margins on excisional specimens	Cytology plus HPV testing[a]	Colposcopy[a]
Cytology interpreted as high-grade squamous intraepithelial lesion	Colposcopy or treatment	Treatment

Abbreviations: HPV, human papillomavirus; CIN, cervical intraepithelial neoplasia; CIN3+, CIN3, adenocarcinoma in situ and/or cancer.
[a] 2020 ASCCP management guidelines state that HPV-based testing is preferred 6 months after treatment and that colposcopy with endocervical curettage is acceptable. (Perkins et al., 2020).

minor adjustments to our guidance that are reflected in Table 2 (e.g., updating the post-treatment follow-up interval from 12 months to 6 months).

With regard to treatment of vulvar and vaginal dysplasia, our recommendations were largely based on those of ACOG but tailored to clinical circumstance. We recommended that patients with vulvar intraepithelial neoplasia (VIN) grade 3 be treated without delay; medical management with topical therapies based on documented clinical examination were encouraged along with video visits to discuss how to use these therapies properly and safely. For patients with vaginal intraepithelial neoplasia (VAIN) grade 3, we also recommended treatment without delay. For patients with asymptomatic VIN1 or 2 or with VAIN1 or 2, delays for up to 6 months were advised.

We began at tier 1 on March 1, 2020 but escalated to tier 2 shortly after shelter-in-place orders were instituted in San Francisco on March 17, 2020. The Fig. 1 shows temporal changes in the overall number of cervical cytology tests performed for both screening and surveillance at UCSF and ZSFG in 2020 compared with 2019; the testing nadir occurred in April 2020 and recovered at both sites by October 2020. Similarly, the number of colposcopies performed dropped in April 2020 at UCSF and recovered by June 2020; comparable data from ZSFG were not available. In our experience, most patients were relieved to know that they could safely delay a clinic visit. A small minority of patients, however, expressed concern about delay and were allowed to keep scheduled appointments after being counselled about risks associated with traveling to a medical center. We did not recommend a second delay of any appointments but reserved the option of doing so on a case-by-case basis in the event that the pandemic escalated to a higher level. While we have toggled between tiers 1 and 2 since the pandemic began, we have not needed to escalate to tier 3 or beyond.

4. Discussion

Our consensus process produced actionable guidelines that were rapidly adopted and led to clinic visit delays at both sites. Although we believed that our efforts to keep patients at home during the pandemic contributed to "flattening the curve" and avoidance of overburdening

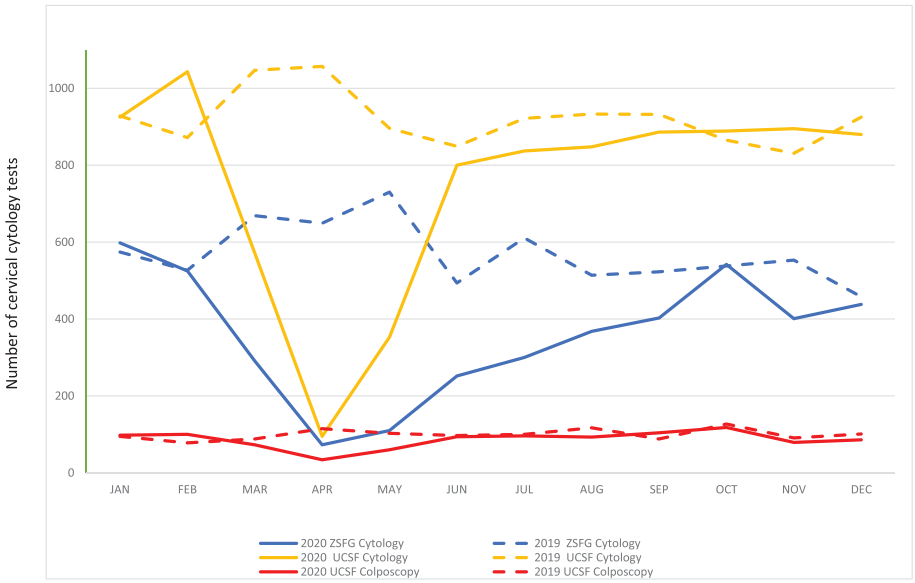

Fig. 1. Temporal changes in cervical cytology and colposcopies tests performed at the University of California San Francisco (UCSF) and cervical cytology performed at Zuckerberg San Francisco General Hospital (ZSFG) before and during the COVID-19 pandemic, January 2019 to December 2020.

our local healthcare system, we were well aware that delays in diagnostic evaluations and treatments can be expected to increase cervical cancer incidence and mortality (Epic Health Research Network, 2020a; Cancino et al., 2020; Castanon et al., 2020; Printz, 2020; Tan and Lau, 2020).

Emerging studies estimate that up to 67% of expected cervical cancer screenings were missed in 2020 in the United States due to COVID-19 (Epic Health Research Network, 2020a, 2020b). To prevent delays and missed screenings, future efforts may well focus on providing screening services that obviate the need for a clinic visit such as self-sampling for HPV testing (Ajenifuja et al., 2020; Feldman and Haas, 2020; Gorin et al., 2021; Steben et al., 2020). While we have been successful in delaying patient visits during the pandemic, the potential adverse effects of this delay on cervical cancer incidence and mortality and the beneficial effects related to decreasing transmission of severe acute respiratory coronavirus 2 remain to be elucidated.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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