

Article

High burden of abnormal cervical smears in South African primary health care: health programmes implications

Olufemi B. Omole^{1,*}, Joel M. Francis¹, John M. Musonda¹, Pumla P. Sodo¹, Elizabeth Reji², Nyundu S. J. Phukuta³, Honey L. M. Mabuza⁴, Joyce S. Musonda⁵, Jimmy Akii¹, John V. Ndimande³ and Olalekan A. Ayo-Yusuf⁶

¹Department of Family Medicine and Primary Care, University of the Witwatersrand, 4th Floor, Phillip Tobias Building, 29 Princess of Wales Street, Parktown, Johannesburg 2193, South Africa

²Department of Family Medicine, University of Free State, Universitas Academic Hospital, 1 Logeman Street, Bloemfontein 9301, South Africa

³Department of Family Medicine and Primary Care, Sefako Makgatho Health Sciences University, Molotlegi Street, Ga-Rankuwa, Pretoria, Medunsa 0204, South Africa

⁴Deans Office, Faculty of Health Sciences, Sefako Makgatho Health Sciences University, Molotlegi Street, Ga-Rankuwa, Pretoria 0204, South Africa

⁵Department of Family Medicine, University of Pretoria, Bophelo Road, Prinshof 349-Jr, Pretoria 0084, South Africa

⁶School of Health Systems and Public Health, University of Pretoria, HW Snyman Building, Bophelo Road, Pretoria 0084, South Africa

*Corresponding author. E-mail: Olufemi.Omole@wits.ac.za

Abstract

Cervical cancer is the second most common malignancy among South African women and the load of abnormal cervical smears has clinical, programmatic and policy implications. This cross-sectional study of women who presented for cervical cancer screening aimed to determine the prevalence of abnormal cervical smears and associated factors in primary health care (PHC) facilities in Gauteng—the most densely populated province in South Africa. A questionnaire collected data on socio-demography, tobacco use, sexual behaviours, HIV status, past treatment for sexually transmitted infections (STI) and cervical cancer screening in the past 10 years. Cytology reports were extracted from the laboratory reports. Of 749 participants, most were black (89.7%), aged 30–49 years (62.2%), single (57.5%) and attained high school education (76.8%). About 43.9% were HIV positive with almost all (97.2%) on antiretroviral therapy. Cytology results were available for 612 (81.9%) participants. Of these, 25.8% (159) were abnormal: 13.2% low-grade squamous intraepithelial lesion; 5.7% atypical squamous cells of undetermined significance and 4.9% high-grade squamous intraepithelial lesion. In bivariate and multivariable analysis, abnormal cervical cytology was not associated with any sociodemographic characteristics, HIV status, tobacco use status, sexual behaviours or past treatment for STI. In conclusion, the prevalence of abnormal cervical smears is high across all demographic groups and irrespective of HIV status and highlights the need to increase screening uptake, including advocacy for self-sampling. It also calls for capacity building to allow for the devolution of some downstream clinical care from specialist to district hospitals and large PHC facilities.

Keywords: cervical smear, cytology, primary health care, load/burden, implications, treatment

Contribution to Health Promotion

- Highlights the programmatic implications of high load of abnormal cytology.
- Highlights the need for intensified awareness campaign and uptake of HPV self-sampling, and
- The need to build the capacity of the South African primary health care to effectively respond to potential increased load of abnormal cytology.

BACKGROUND

Cervical cancer is the second most common cancer among women and accounts for 3.1% of all cancers worldwide ([Sung et al., 2021](#)). An estimated 570 000 new cases and 311 000 deaths were reported worldwide in 2018. Of these, 85% occurred in low- and middle-income countries (LMICs), with

sub-Saharan African countries bearing the biggest burden with an age-standardized incidence of 38.2 per 100 000 compared to 10.4 per 100 000 in high-income countries (HICs). Similarly, an age-standardized mortality of 30 per 100 000 in sub-Saharan Africa compared to 1.9 per 100 000 in North America ([Arbyn et al., 2020](#)).

The risk factors for cervical cancer include infection with high-risk strains of the human papillomavirus (HPV), early coitarche, multiple sexual partners, late menopause and history of sexually transmitted infections (STI). HIV co-infection and cigarette smoking are also risk factors (Katumba *et al.*, 2016; Nagelhout *et al.*, 2021). Of these risk factors, HPV infection is the strongest (Gray and Vawda, 2017).

In South Africa, cervical cancer is also the second most common cancer among women representing 15% of all cancer diagnoses in this population, and accounting for over 3000 deaths every year and about 50 027 years of life lost (Hank *et al.*, 2013; Hoque and van Hal, 2014). Most of the cervical cancer diagnosed in South Africa is in black women (82.7%) and only 9% in white women, indicating epidemiological disparities, which have been suggested to be a result of socioeconomic rather than racial differences (Gray and Vawda, 2017). The same socioeconomic disparities explain the disproportionately high age-standardized incidence and mortality rate in LMICs, such as South Africa, where a case fatality rate of over 50% was reported in a recent policy report (National Department of Health, South Africa, 2017), which is much higher than estimates from HICs (Canfell *et al.*, 2020). In particular, an age-standardized mortality rate of 18 per 100 000 women was reported in South Africa in 2012, compared to 6.8 per 100 000 in HICs in the same period (Gray and Vawda, 2017). The high mortality rate in LMICs including SA, is preventable and relates to late diagnosis and presentation from low screening coverage, poor access and backlogs in treatments, ill-equipped and poorly responsive health system and logistical and cultural issues. (Hull *et al.*, 2020).

South Africa adopted the WHO global strategy to eliminate cervical cancer with three main pillars implemented collectively and at scale: 90% of girls should be fully vaccinated with the HPV vaccine by the age of 15 years; 70% of eligible women must be screened and 90% of women identified with pre-cancer and invasive cancer managed. (Bruni *et al.*, 2022) The National Department of Health makes provision for all women older than 30 years to undergo three free cervical cancer screening tests at 10-year intervals in the public health sector (Massyn *et al.*, 2020). In line with the WHO goals, SA sets its national screening coverage target at 70%, but most provinces are far from achieving this, with Gauteng province—the most densely populated province in South Africa, reporting a coverage of only 47.7% in 2017/2018 (Phaswana-Mafuya *et al.*, 2018; Massyn *et al.*, 2019; Akokuwebe *et al.*, 2021; Hopkins *et al.*, 2021; Mabotja *et al.*, 2021; Tafadzwa *et al.*, 2021). However, despite this low screening coverage, there is a significant bottleneck in access to further care and service backlog for women with abnormal cervical cytology on screening (Mabotja *et al.*, 2021). In South Africa, these downstream services are currently based in specialist hospitals. The lack of downstream services for those who need care post-screening may also discourage others from taking up cervical screening.

In South Africa, the yearly incidence of abnormal cervical smears cytology varies from 6.48% among HIV-negative women to 11.71% among those with previously inadequate smears (Adam *et al.*, 2012). In settings where screening rates are high, such as the USA, the incidence rate may be up to 20% (Sirovich and Welch, 2004). So, the campaign for improved screening coverage in South Africa is expected to yield more abnormal cytological abnormalities, which in turn increases demands for treatment services such as colposcopy, large

loop electrosurgical excision procedure (LLETZ) or cryotherapy and treatments at advanced cancer centres and follow-up strategies. The increased need for these downstream services can aggravate the existing bottlenecks and limited access and backlogs (Maimela *et al.*, 2019) and worsen treatment outcomes unless there is adequate information on potential service need and novel health system interventions are planned well ahead to meet the potential need and are effectively implemented. This is particularly so, that these downstream processes of care are hospital-based in South Africa.

Very few studies have quantified the load of abnormal cervical cytology in South African primary health care (PHC), particularly in the context of a low cervical screening uptake and a renewed campaign for improved screening. This is a knowledge gap may limit the health system's response to this compelling cause of premature mortality among women in South Africa. In this study, we determined the prevalence and distribution of cervical cytology abnormalities based on the Bethesda grading system and explored the programmatic and policy implications for the South African health system.

METHODS

The methods used in this study have been previously published in detail (Musonda *et al.*, 2022), but a summary is described below:

Design

This study was a descriptive cross-sectional design.

Study setting

The study was conducted in PHC facilities in the five health districts of Gauteng province, South Africa. In 2017, the province was home to over 14.3 million residents of whom about 4.44 million were females between 15 and 55 years of age. In the same year, an estimated 21.2% of women between 15 and 49 years were HIV positive in South Africa. (Statistics South Africa, 2017).

Recruitment and sampling

All women, 18 years and older, who presented to the cervical cancer screening services in the 296 PHC clinics in Gauteng province between March 2017 and March 2020 were eligible to participate. We estimated from the 2013/2014 Gauteng cervical screening programme report that about 172 000 women would present for cervical cancer screening in 2017 (Gauteng Department of Health, South Africa, 2014). We determined the sample size to be 1032, assuming a 6.5% incidence rate of abnormal Pap smears (Adam *et al.*, 2012), a 95% confidence level and 80% power. This was adjusted upward by 10% to 1135 to accommodate inadequate smears and/or incomplete or lost data. To attenuate intra and inter-cluster correlations (ICC), we applied the formula $ESS = mk / [1 + p(m - 1)]$ (Killip *et al.*, 2004), where ESS is the 'Effective sample size', $1 + p(m - 1)$ equals the design effect, K equals the number of clinic cluster, ESS equals the effective sample size, m equals the number of participants per cluster/clinic and p equals the ICC coefficient. Assuming an ICC coefficient of 0.01, we calculated that we needed 1600 participants in 40 clinics (k) and 40 participants per clinic (m). These clinics were randomly selected from their district clusters, with the number of clinics per district proportional to the district's contribution to the Gauteng Pap smear count in 2013/2014.

Consecutive women who presented to the cervical cancer screening programmes at each clinic were approached by trained research assistants at the vital signs station, where each patient was given a participant information leaflet and the nature and objective of the study explained. Those who showed interest were directed to a room where written consent was obtained, and the questionnaire was administered thereafter. Afterwards, participants were directed to the nurse who performed the cervical smear according to usual care or, if not yet their time, back to their positions in the queue. Women who were very ill or pregnant were excluded. Recruitment continued in consecutive selected clinics but was stopped with the coronavirus disease 2019 (COVID-19) pandemic restrictions in March 2020. A total of 749 participants were recruited in only 20 clinics across the five districts—Johannesburg ($n = 315$), Ekurhuleni ($n = 170$), Tshwane ($n = 79$), West Rand ($n = 105$) and Sedibeng district ($n = 80$). No information was collected from patients who declined to participate.

Tool and data collection

An interviewer-administered questionnaire collected information on socio-demographics, tobacco use, HIV and treatment status, sexual behaviours and history of past screening and history of treatment for STI from participants. After completing the cervical smear procedure, each completed questionnaire was affixed with a laboratory form code sticker that allowed tracking of the result by healthcare professionals to extract them onto the study data set by a research team member, matched to each participant's questionnaire code. All patients with abnormal smears were further managed according to local care standards.

Analysis

The data was captured and analysed using Stata version 18. Of the 749 participants enrolled, only 612 had cervical smear cytology results and were included in this analysis. Descriptive statistics were used to describe the distributions of participants' characteristics, sexual behaviours, HIV status, tobacco use, past treatment for STI and the Bethesda grades of the cytology results (Apgar *et al.*, 2003). The cytological grades were reported as one of normal/no intraepithelial lesions, atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells, cannot exclude high-grade lesion (ASC-H), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), squamous cell carcinoma (SCC) and adenocarcinoma (ADC).

Cytology results were then grouped into normal and abnormal categories (ASC-US, ASC-H, LSIL, HSIL SCC, ADC and the 'indeterminate'). Bivariate analysis used Chi-squared test to explore associations between the cytological results (normal or abnormal) and sociodemographic characteristics, sexual behaviours, HIV status, tobacco use status and history of STI treatment. Age, age at coitarche, HIV status, tobacco use, number of lifetime sex partners and ever treated for STI were a priori decided as potential confounders and therefore entered in the multivariable model regardless of the p -value at the bivariate analysis. Other factors were entered if they had a p -value < 0.20 in the bivariate analysis. We used the logistic regression to examine factors that are independently associated with abnormal cervical smear cytology and the measure of association was expressed as adjusted odds ratio (aOR). Statistical significance was set at a p -value < 0.05 .

Ethical considerations

Ethical clearance and permissions were obtained from the Human Research Ethics Committee of the University of Witwatersrand (Certificate number M160209) and the district management teams. Participants signed written consent and those who reported any risky health behaviours such as engaging in unprotected sex or having multiple sexual partners or HIV positive but not on treatment, were briefly counselled and directed to access the required services. Data were coded and anonymized in analysis. All data were kept confidential, archived and accessible only to the research team.

RESULTS

A total of 749 participants were recruited in the study and their characteristics are shown in Table 1. The median age was 38 years, with most aged 30–49 years (62.2%), had attained at least a high school education (76.8%), were unemployed (62.4%), single (57.5%) and self-identified as being of Black African ethnicity (89.7%). Almost half (43.9%) were HIV positive with most (97.2%) on antiretroviral therapy (ART).

Of the 749 participants, only 612 (81.7%) had cervical cytology results and constituted samples for further analysis (Table 2). Using the Bethesda grading system (Apgar *et al.*, 2003), most results were normal (74.2%) and just over a quarter (25.8%) were abnormal. The proportions of all results that constituted LSIL was 13.24%, ASC-US was 5.7% and HSIL was 4.9%.

Table 1: Characteristics of women ($N = 749$) attending Pap Smears at Primary Health Care Clinics in Gauteng Province, South Africa 2017–2020

Characteristic	Categories	N (%)
Age (years)	Median [IQR]	38 [31–38]
Age categories (years)	18–29	129 (17.4)
	30–49	461 (62.2)
	Above 50	151 (20.4)
Education	Less than high school	109 (14.7)
	High school	570 (76.8)
	Post-high school	63 (8.5)
Occupational status	Unemployed	465 (62.4)
	Employed	246 (33.0)
	Student	26 (3.5)
	Others	8 (1.1)
Ethnic group	Black	672 (89.7)
	Coloured	68 (9.1)
	Others (Whites & Indians)	9 (1.2)
Marital status	Single	431 (57.5)
	Married	188 (25.1)
	Previously married	130 (17.3)
HIV status	Positive	328 (43.9)
	Negative	377 (50.4)
	Unknown	43 (5.8)
On antiretroviral therapy	Yes	316 (97.2)
	No	9 (2.8)
CD4 count (cells/ μ l)	≤ 200	32 (16.5)
	> 200	162 (83.5)

Table 2: Pattern of cervical smear abnormalities women attending Pap Smears at Primary Health Care Clinics in Gauteng Province, South Africa 2017–2020

Bethesda cervical smear stage	N	%
Normal	453	74.2
Abnormal	159	25.8
• ASC-US	35	5.7
• ASC-HG	12	2.0
• LSIL	81	13.2
• HSIL	30	4.9
• SCC	—	—
• ADC	1	0.2
Total	612	100

In both the bivariate and multivariable regression analyses, cytological abnormality was not associated with any socio-demographic, gynaecological or sexual behaviour variables—Tables 3 and 4. Although not reaching statistical significance, the odds of an abnormal cytology result tended to be highest among those age > 50 years (compared with those younger), previously married (compared to being single), and lowest among those reporting post-high school education (compared to less than high school). In contrast, the odds of an abnormal cytology result tended to be lower with reporting tobacco use (compared to no tobacco use) and with a history of ever-treatment for STI (compared with never).

DISCUSSION

This study found that a substantial proportion (25.8%) of the cervical smear cytology was abnormal with just a little over half of these being LSIL (13.2%), followed by ASC-US (5.7%) and HSIL (4.9%). Although not statistically significant, the odds of abnormal cytology tended to increase with age and were highest among those previously married and with less than high school education. These study findings have implications for health promotion programming and policy intervention for South African PHC system.

The proportion of abnormal cervical cytology in this study is higher than previously reported in similar settings—2.2% in Saudi Arabia (AlBabtain *et al.*, 2020), and 6.5% and 11.7% in South Africa, among HIV-negative patients and those with previously inadequate smears, respectively (Adam *et al.*, 2012; Gauteng Department of Health, South Africa, 2014). However, proportions up to 20% have been reported in the USA where screening coverage is much higher than in South Africa (Sirovich and Welch, 2004). The high prevalence of abnormal cytology found in this study has health system implications in that the 25.8% abnormal cytology constitutes a substantial number at the population level at the current 42.7% screening coverage (Musonda *et al.*, 2022), and these would require further treatments. Furthermore, these findings suggest a large proportion of the general adult women population who do not present to the health facilities for cervical cancer screening might be sitting with cervical lesions that would require further clinical care and would possibly be presenting too late in the future. This calls for awareness-raising campaigns and the need to introduce self-sampling HPV testing, particularly that self-sampling has been found to be more

acceptable than clinician-sampling in settings similar to South Africa (Behnke *et al.*, 2020).

From the programmatic perspective, it is likely that the number of those with abnormal cytology will increase significantly as campaigns for increased screening coverage are intensified and the PHC services transit to the better-yield HPV screening test. However, a Korean study suggested that Pap smear is both a screening and diagnostic tool, and useful for the detection of HSIL, SCC and glandular lesions (Kang *et al.*, 2020). Either way, the potential increase in load may aggravate the current long waiting times for colposcopy and LLETZ services, which in many public specialized hospitals in Gauteng province is currently greater than 6 months (Maimela *et al.*, 2019). This is not only psychosocially distressful (Jentschke *et al.*, 2020) but may dissuade other women from screening.

The distribution of cytological abnormalities found in this study (Table 2) shows a pattern similar to the findings of previous studies conducted in South Africa (Gray and Vawda, 2017) and has clinical and programmatic implications. Although most LSIL will regress on their own and so may only need follow-up under close observation, it is more expedient to perform colposcopy and treat suspicious lesions with LLETZ/ Laser or cryotherapy in poorly resourced settings like South Africa, since follow-up may be challenging, and many patients, for several reasons, are lost to follow-up (Botha and Dreyer 2017; National Department of Health, South Africa, 2017). Patients with higher Bethesda grades like ASC-US/HG and HSIL (together constituting almost half of those with abnormal cytology) require colposcopy, biopsy with/without LLETZ/ laser, cryotherapy or hysterectomy (where there is no desire for further children), and where indicated, more advanced oncological treatment (National Department of Health, South Africa, 2017). Put together, all the women with grades higher than LSIL require at least colposcopy, and the high load of such patients, the shortage of specialist gynaecologists, competing obstetrical and gynaecological emergency procedures and the current limited number of sites for colposcopy, all underscore the need for policy change to devolve the colposcopy and LLETZ services to the district hospitals and larger community health centres (CHC) across Gauteng province. This has the potential to relieve the current bottlenecks to access and address the anticipated increased load of abnormal cervical cytology that will accompany increased screening coverage and better yield of the HPV antigen test in South African PHC. Indeed, Maimela *et al.* (Maimela *et al.*, 2019) reported a three-fold increase in uptake in colposcopy and LLETZ services in the Johannesburg district with decentralization from the tertiary hospital to a nearby CHC (Maimela *et al.*, 2019). To maximize the public health benefit, follow-up care to women with HSIL or higher grades should take priority over providing follow-up care to women with lower grade abnormalities and should preferably be a single-visit of point-of-care screening with HPV antigen test followed by immediate excisional treatment if indicated.

The high HIV prevalence in the study population (43.9%) may partly explain the high proportion of abnormal cytology since HIV increases the risk of cervical dysplasia and cancer by delaying HPV clearance and/ or by its own oncogenic properties (Stelzle *et al.*, 2021). However, abnormal cytology did not differ by HIV status, possibly due to a high ART uptake among our participants (92.7%)—an intervention that significantly reduces the risk of cervical cancer in

Table 3: Bivariate analysis findings of factors associated with cervical dysplasia among women attending Pap Smears at Primary Health Care Clinics in Gauteng Province, South Africa 2017–2020

Characteristic	Categories ^a	Cytology results				Total ^a	p-Values
		Normal		Abnormal			
		n	%	n	%		
Age (years)	18–29	64	75.3	21	24.7	85	0.181
	30–49	296	75.7	95	24.3	391	
	>50	90	67.7	43	32.3	133	
	Total	450	73.9	159	26.1	609	
Education status	Less than high school	64	66.7	32	33.3	96	0.073
	High school	340	74.1	119	25.9	459	
	Post-high school	42	84.0	8	16.0	50	
	Total	446	73.7	159	26.3	605	
Occupation status	Unemployed	287	72.3	110	27.7	397	0.219
	Employed	163	76.9	49	23.1	212	
	Total	450	73.9	159	26.1	609	
Marital status	Single	267	76.7	81	23.3	348	0.098
	Married	115	73.2	42	26.8	157	
	Previously married	71	66.4	36	33.6	107	
	Total	453	74.0	159	26.0	612	
Age at menarche (years)	9–15	275	74.3	95	25.7	370	0.947
	16–25	173	74.6	59	25.4	232	
	Total	448	74.4	154	25.6	602	
Stopped menstruation	No	331	74.5	113	25.5	444	0.518
	Yes	118	72.0	46	28.0	164	
	Total	449	73.8	159	26.2	608	
HIV status	Negative	237	75.7	76	24.3	313	0.257
	Positive	186	71.5	74	28.5	260	
	Total	423	73.8	150	26.2	573	
Age at coitarche (years)	10–12	9	75.0	3	25.0	12	0.877
	13–19	317	74.1	111	25.9	428	
	20–29	112	76.2	35	23.8	147	
	Total	438	74.6	149	25.4	587	
Have sex partners	Yes	340	73.9	120	26.1	460	0.793
	Not now	111	75.0	37	25.0	148	
	Total	451	74.2	157	25.8	608	
Number of lifetime sex partners	One or less	51	78.5	14	21.5	65	0.388
	Two or more	388	73.5	140	26.5	528	
	Total	439	74.0	154	26.0	593	
Number of sex partners in last 12 months	0	76	71.0	31	29.0	107	0.680
	1	340	75.1	113	24.9	453	
	Two or more	28	75.7	9	24.3	37	
	Total	444	74.4	153	25.6	597	
Ever treated for STI	No	327	73.6	117	26.4	444	0.741
	Yes	117	75.0	39	25.0	156	
	Total	444	74.0	156	26.0	600	
Treated for STI in last 12 months	No	57	73.1	21	26.9	78	0.542
	Yes	58	77.3	17	22.7	75	
	Total	115	75.2	38	24.8	153	
Tobacco use	No	246	72.8	92	27.2	338	0.843
	Yes	109	73.6	39	26.4	148	
	Total	355	73.0	131	27.0	486	
Current smoke cigarette	No	308	73.3	112	26.7	420	0.862
	Yes	39	72.2	15	27.8	54	
	Total	347	73.2	127	26.8	474	

Table 3. Continued

Characteristic	Categories ^a	Cytology results				Total ^a	<i>p</i> -Values
		Normal		Abnormal			
		<i>n</i>	%	<i>n</i>	%		
Current snuff use	No	303	72.8	113	27.2	416	0.626
	Yes	44	75.9	14	24.1	58	
	Total	347	73.2	127	26.8	474	

^aVarying totals because of missing values due to participants declining to respond, STD = sexually transmitted diseases.

Table 4: Multivariable analysis findings of factors associated with cervical dysplasia among women attending Pap Smears at Primary Health Care Clinics in Gauteng Province, South Africa 2017–2020

Characteristic	Categories	Abnormal cytology		aOR	95% CI
		n	%		
Age categories (Years)	18–29	21	24.7	1	
	30–49	95	24.3	0.83	0.44–1.57
	>50	43	32.3	1.47	0.66–3.30
Education	Less than high school	32	33.3	1	
	High school	119	25.9	1.10	0.57–2.10
	Post-high school	8	16.0	0.42	0.15–1.21
Marital status	Single	81	23.3	1	
	Married	42	26.8	1.65	0.95–2.88
	Previously married	36	33.6	1.77	0.97–3.23
HIV status	Negative	76	24.3	1	
	Positive	74	28.5	1.10	0.69–1.75
Age at coitarche (years)	10–12	3	25.0	1	
	13–19	111	25.9	1.79	0.42–7.53
	20–29	35	23.8	1.34	0.30–5.98
Number of lifetime sex partners	One or less	14	21.5	1	
	Two or more	140	26.5	1.12	0.52–2.43
Ever treated for STI	No	117	26.4	1	
	Yes	39	25.0	0.96	0.57–1.62
Tobacco use	No	92	27.2	1	
	Yes	39	26.4	0.81	0.49–1.34

HIV-positive women (de Vries and Steenberg, 2018). This suggests that the prevalence of abnormal cytology could have been higher with lower ART uptake (Katumba *et al.*, 2016) and explains why the high uptake might explain the lack of statistically significant differences by HIV status in the current study. Of importance is that cervical cancer screening is free in South Africa for all women and the requirement for HIV-positive women to screen at shorter intervals may be a source of pressure on both the cervical cancer screening services and patient.

Although not statistically significant, the high prevalence of abnormal cytology among participants who were previously married is counterintuitive and may support the report that though most women experience some form of support from their partners on sexual and women's health issues, a considerable number experience opposition also (Adewunmi *et al.*, 2019). In this context, this study finding may reflect a false sense of "safety" that may make women in a stable relationships perceive themselves not to be at health risk, and so, they (or their partner) may engage in risky behaviours that may

increase their risk of abnormal cervical cytology. Hence, considering the complexity of screening behaviours, further studies are required to elucidate the above finding, more so that a previous South African study (Musonda *et al.*, 2022) had reported that married women may also be less likely to screen for cervical cancer compared to their unmarried counterparts. The tendency for lower prevalence of abnormal cytology in participants with post-high school educational attainments aligns with the understanding that higher education promotes better health literacy, self-awareness and personalization of health risks, such that healthier behavioural choices are made compared to less educated women (Hamoonga *et al.*, 2017).

Summed together, to respond to the high load of abnormal cervical cytology in South African PHC, a multi-pronged approach may be needed. For primary prevention: improved HPV vaccination coverage is needed by targeting high-risk districts, out of schoolgirls, those in private schools and counteracting negative media that sustain HPV vaccine hesitancy among adolescents and their parents (Arie, 2019; Ngcobo *et al.*, 2019). Serious consideration needs to be given to HPV

home-self-testing and self-sampling for cytology with supervision by the community health care workers within the household. This has been shown to be acceptable to women and effective in scaling up screening without affecting the quality of testing (Pedersen *et al.*, 2018; Winer *et al.*, 2019; Meenan *et al.*, 2023). Lastly, community-based campaigns and counselling are directed at preventing or reducing risks exposure among young people. For secondary prevention: access to colposcopy, LLETZ and other downstream investigations and treatments need to be increased for uncomplicated patients with HSIL or higher grade, by devolving these procedures to district hospitals and large CHCs. However, the later will require carefully thought-out criteria for patient selection, needs analysis for resources (human, infrastructural and equipment), training of PHC clinicians and sustained clinical outreach support by Gynaecologists in each district. The goal should not be to create another vertical programme within the PHC stream but to integrate these services into existing women's health services and other related programmes such as the HIV treatment programme.

This study has limitations: stopping data collection prematurely with the COVID-19 restriction resulted in a smaller than required sample size and might have resulted in loss of statistical power to detect significant differences with regards to the associations between the stages of cervical dysplasia and some of the exposure variables. The consecutive sampling that was not proportionally stratified by HIV status could also have resulted in an over-representation of HIV-positive patients and therefore affected some HIV-related outcome estimates. Our study did not utilize the more sensitive high-risk HPV DNA test for screening with the potential for under-detection of women at risk for cervical dysplasia and cancer. Lastly, the self-reporting of several variables such as HIV and tobacco use status, STI and sexual behaviours, lends the study to information and social desirability biases, which could have affected outcome estimates. Notwithstanding these limitations, this study is one of few in South African PHC that provides insight into the load of abnormal cervical smear cytology and highlights the need to capacitate the PHC level of care to provide downstream services such as colposcopy and biopsy and LLETZ services to address the bottlenecks and backlogs in the cervical cancer screening and treatment programme in South Africa.

In conclusion, the burden of abnormal cervical cytology in South African PHC is high and may increase as screening coverage and detection yields increase. Devolving and integrating colposcopy and LLETZ services into existing women's health services in PHC are programmatic imperatives that address the potential aggravation of the current backlog to these services. Additionally, promoting home-based self-sampling, particularly during follow-up may increase screening coverage and detection yields, but reduce the need for clinic attendance. Given the study limitations, larger studies and implementation science projects are needed to understand how best to respond to the high load of abnormal cytology result in South African PHC and similar settings.

AUTHORS' CONTRIBUTIONS

O.B.O., E.R., N.S.J.P., H.L.M.M., J.M.M., J.S.M., J.A., J.V.N. and O.A.A.-Y. contributed to the conceptualization and protocol development. O.B.O., J.M.M., E.R., N.S.J.P., H.L.M.M., J.S.M., J.A. and J.V.N. contributed to data collection. J.M.F.

and O.A.A.-Y. contributed to data analysis. O.B.O., J.M.F., J.M.M., P.S., E.R., N.S.J.P., H.L.M.M., J.S.M., J.V.N. and O.A.A.-Y. contributed to the manuscript development and approved the final draft.

ACKNOWLEDGEMENTS

We thank all the women who volunteered their time to participate in this study and the staff of the various clinics for their cooperation. This work was supported by funds from the Project FHP 000 of the Department of Family Medicine, University of the Witwatersrand and the National Research Foundation, Grant number: 93093. The authors declare that they have no conflict of interest.

DATA AVAILABILITY

The data underlying this article is in repository at the Division of Family Medicine, Department of Family Medicine and Primary Care, the University of the Witwatersrand, Johannesburg, South Africa and is available on reasonable request to JM Francis @Joel.Francis@wits.ac.za.

REFERENCES

- Adam, Y., McIntyre, J. A. and De Bruyn, G. (2012) Incidence of cytological abnormalities within 24 months of a normal cervical smear in Soweto, South Africa. *South African Medical Journal*, 103, 34–39.
- Adewunmi, K., Oketch, S. Y., Choi, Y. and Huchko, J. (2019) Female perspectives on male involvement in a human-papillomavirus-based cervical cancer-screening program in western Kenya. *BMC Women's Health*, 19, 107.
- Akokuwebe, M. E., Idemudia, E. S., Lekulo, A. M. and Motlogeloa, O. W. (2021) Determinants and levels of cervical cancer screening uptake among women of reproductive age in South Africa: evidence from South Africa Demographic and health survey data, 2016. *BMC Public Health*, 21, 2013.
- AlBabtain, F. A., Hussain, A. N., Alsoghayer, S. A., Alwahbi, O. A., Almohaisen, N. and Alkhenizan, A. H. (2020) The yield of pap smears and its characteristics in a community-based setting in Saudi Arabia. *Saudi Medical Journal*, 41, 661–665.
- Apgar, B. S., Zoschnick, L. and Wright, T. C. (2003) The 2001 Bethesda system terminology. *American Family Physician*, 68, 1992–1998.
- Arbyn, M., Weiderpass, E., Bruni, L., de Sanjosé, S., Saraiya, M., Ferlay, J. et al. (2020) Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *Lancet Global Health*, 8, e191–e203.
- Arie, S. (2019) HPV: WHO calls for countries to suspend vaccination of boys. *British Medical Journal*, 367, l6765.
- Behnke, A., Krings, A., Wormenor, C. M., Dunyo, P., Kaufmann, A. M. and Amuah, J. E. (2020) Female health-care providers' advocacy of self-sampling after participating in a workplace program for cervical cancer screening in Ghana: a mixed-methods study. *Global Health Action*, 13, 1838240.
- Botha, M. H. and Dreyer, G. (2017) Guidelines for cervical cancer screening in South Africa. *Southern African Journal of Gynaecological Oncology*, 9, 8–12.
- Bruni, L., Serrano, B., Roura, E., Alemany, L., Cowan, M., Herrero, R. et al. (2022) Cervical cancer screening programmes and age-specific coverage estimates for 202 countries and territories worldwide: a review and synthetic analysis. *Lancet Global Health*, 10, e1115–e1127.
- Canfell, K., Kim, J. J., Brisson, M., Keane, A., Simms, K. T., Caruana, M. et al. (2020) Mortality impact of achieving WHO cervical cancer elimination targets: a comparative modelling analysis in 78 low-income and lower-middle-income countries. *Lancet*, 395, 591–603.

- de Vries, H. J. C. and Steenberg, R. D. M. (2018) The effect of ART on cervical cancer precursor lesions. *The Lancet*, **5**, e6–e8.
- Gauteng Department of Health, South Africa. (2014) *2014 Gauteng Health Annual Report*. <https://provinciagovernment.co.za/department-annual/162/2014-gauteng-health-annual-report.pdf> (last accessed 20 September 2014).
- Gray, A. and Vawda, Y. (2017) Health policy and legislation. In Padarath, A. and Barron, P. (eds), *South African Health Review 2017*. Health System Trust, Durban. <http://www.hst.org.za/publications/south-african-health-review-2017>
- Hamoonga, T. E., Likwa, R. N., Musonda, P. and Michelo, C. (2017) Higher educational attainment associated with reduced likelihood of abnormal cervical lesions among Zambian women - a cross sectional study. *BMC Cancer*, **17**, 681.
- Hank, E., Hoque, M. E. and Zungu, L. (2013) Cervical precancerous lesions and cancer among patients in the gynaecology outpatient department at a tertiary hospital in South Africa. *Asian Pacific Journal of Cancer Prevention*, **14**, 4903–4906.
- Hopkins, K. L., Jaffer, M., Hlongwane, K. E., Otjombe, K., Dietrich, J., Cheyip, M. et al. (2021) Assessing national cervical cancer screening guidelines: results from an HIV testing clinic also screening for cervical cancer and HPV in Soweto, South Africa. *PLoS One*, **16**, e0255124.
- Hoque, M. E. and van Hal, G. (2014) Acceptability of human papilloma virus vaccine: a survey among Master of Business Administration Students in South Africa. *Biomed Research International*, **2014**, 257807.
- Hull, R., Mbele, M., Makhaola, T., Hicks, C., Wang, S., Manuel, R. et al. (2020) Cervical cancer in low and middle-income countries (Review). *Oncology Letters*, **20**, 2058–2074.
- Jentschke, M., Lehmann, R., Drews, N., Hansel, A., Schmitz, M. and Hillemanns, P. (2020) Psychological distress in cervical cancer screening: results from a German online survey. *Archives of Gynecology and Obstetrics*, **302**, 699–705.
- Kang, M., Ha, S. Y., Cho, H. Y., Chung, D. H., Kim, N. R., An, J. et al. (2020) Comparison of Papanicolaou smear and human papilloma-virus (HPV) test as cervical screening tools: can we rely on HPV test alone as a screening method? An 11-year retrospective experience at a single institution. *Journal of Pathology and Translational Medicine*, **54**, 112–118.
- Katumba, A. C., Reji, E., Gitau, T. and Firnhaber, C. (2016) World Health Organisation staging, adherence to HAART and abnormal cervical smears amongst HIV-infected women attending a government hospital in Johannesburg, South Africa. *Southern African Journal of Infectious Diseases*, **31**, 112–1118.
- Killip, S., Mahfoud, Z. and Pearce, K. (2004) What IS an intracluster correlation coefficient? Crucial concepts for primary care researchers. *Annals of Family Medicine*, **2**, 204–208.
- Mabotja, M. C., Levin, J. and Kawonga, M. (2021) Beliefs and perceptions regarding cervical cancer and screening associated with Pap smear uptake in Johannesburg: a cross-sectional study. *PLoS One*, **16**, e0246574.
- Maimela, G., Nene, X., Mvundla, N., Sawry, S., Smith, T., Rees, H. et al. (2019) The impact of decentralising colposcopy services from tertiary-level to primary level care in inner-city Johannesburg, South Africa: a before and after study. *BMJ Open*, **9**, e024726.
- Massyn N., Day, C., Ndlovu, N. and Padayachee, T. (eds) (2020) *District Health Barometer 2019/20*. Health Systems Trust, Durban.
- Massyn, N., Pillay, Y. and Padarath, A. (eds) (2019) *District Health Barometer 2017/18*. Health Systems Trust, Durban.
- Meenan, R. T., Troja, C., Buist, D. S. M., Tiro, J. A., Lin, J., Anderson, M. L. et al. (2023) Economic evaluation of mailed home-based Human Papillomavirus self-sampling kits for cervical cancer screening. *JAMA Network Open.*, **6**, e234052.
- Musonda, J. S., Sodo, P. P., Ayo-Yusuf, O. A., Reji, E., Musonda, J., Mabuza, L. H. et al. (2022) Cervical cancer screening in a population of black South African women with high HIV prevalence: a cross-sectional study. *PLOS Global Public Health*, **2**, e0001249.
- Nagelhout, G., Ebisch, R. M., Van Der Hele, O., Meerkerk, G., Magneé, T., De Bruijn, T. et al. (2021) Is smoking an independent risk factor for developing cervical intra-epithelial neoplasia and cervical cancer? A systematic review and meta-analysis. *Expert Review of Anticancer Therapy*, **21**, 781–794.
- National Department of Health, South Africa. (2017). *Cervical Cancer Prevention and Control Policy*. NDOH, Pretoria.
- Ngcobo, N. J., Burnett, R. J., Cooper, S. and Wiysonge, C. S. (2019) Human papillomavirus vaccination acceptance and hesitancy in South Africa: Research and policy agenda. *South African Medical Journal*, **109**, 13–15.
- Pedersen, H. N., Smith, L. W., Racey, C. S., Cook, D., Krajden, M., van Niekerk, D. et al. (2018) Implementation considerations using HPV self-collection to reach women under-screened for cervical cancer in high-income settings. *Current Oncology*, **25**, e4–e7. Epub 2018/03/07
- Phaswana-Mafuya, N. and Peltzer, K. (2018) Breast and cervical cancer screening prevalence and associated factors among women in the South African General Population. *Asian Pacific Journal of Cancer Prevention*, **19**, 1465–1470.
- Sirovich, B. E. and Welch, H. G. (2004) The frequency of Pap smear screening in the United States. *Journal of General Internal Medicine*, **19**, 243–250.
- Statistics South Africa. (2017) Mid-year population estimates 2017. <https://www.statssa.gov.za/publications/P0302/P03022017.pdf> (last accessed 08 November 2023).
- Stelzle, D., Tanaka, L. F., Lee, K. K., Khalil, A. I., Baussano, I., Shah, A. S. V. et al. (2021) Estimates of the global burden of cervical cancer associated with HIV. *Lancet Global Health*, **9**, e161–e169.
- Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, J., Jemal, A. et al. (2021) Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal For Clinicians*, **71**, 209–249.
- Tafadzwa, D., Julien, R., Lina, B., Eliane, R., Frederique, C., Leighet, J. et al. (2021) Spatiotemporal modelling and mapping of cervical cancer incidence among HIV positive women in South Africa: a nationwide study. *International Journal of Health Geographics*, **20**, 30.
- Winer, R. L., Lin, J., Tiro, J. A., Miglioretti, D. L., Beatty, T., Gao, H. et al. (2019) Effect of mailed Human Papillomavirus Test kits vs usual care reminders on cervical cancer screening uptake, precancer detection, and treatment. A randomized clinical trial. *JAMA Network Open.*, **2**, e1914729.