

# Treatment delays of cervical cancer with or without Human Immunodeficiency Virus infection in Botswana 2013-2020

Jane Muni<sup>1</sup>, Jessica George<sup>2</sup>, Shawna Tuli<sup>2</sup>, Surbhi Grover MD<sup>3</sup>

School of Nursing, University of Pennsylvania, Philadelphia, PA<sup>1</sup>, Donald Bren School of Information and Computer Sciences, University of California, Irvine, Irvine, CA<sup>2</sup>, Perelman School of Medicine.

## Introduction/Objectives

- Cervical cancer (CC) is the second most common cancer in low and middle income countries,
- In 2020, 84-90% of the 604,000 new cases of cervical cancer and 342,000 deaths from the disease occurred in LMICs [1].
- Cervical cancer is the most common cancer and leading cause of cancer death in Botswana, a LMIC in Sub-Saharan Africa where 25.1% of women aged 15-49 were living with HIV as of 2019 [2].
- Cervical cancer is generally caused by chronic human papillomavirus (HPV) infection.
- Women with human immunodeficiency virus (HIV) are more likely to exhibit chronic HPV infection, placing them at a greater risk of developing cervical cancer.
- Despite its high mortality, cervical cancer is one of the most treatable cancers when detected early.
- Reducing the mortality of cervical cancer remains a challenge in LMICs due to barriers to accessing cervical cancer screening and longer delays to treatment initiation [3].
- More advanced stages at presentation are associated with poor survival outcomes, therefore, it is important that treatment delays are minimized to optimize survival for cervical cancer patients in Botswana [6].
- This study presents treatment delays for cervical cancer patients who initiated radiation therapy (RT) or chemoradiation therapy (CRT) in Botswana with or without HIV as well as factors associated with delays.

## Methods

- Between 2013-2019, women with cervical cancer (Stages IB2-IVB), with/without HIV, initiating RT/CRT in Botswana were prospectively enrolled in an observational cohort study.
- A treatment delay was defined as the number of days elapsed from the date of pathology review to the date of treatment start.

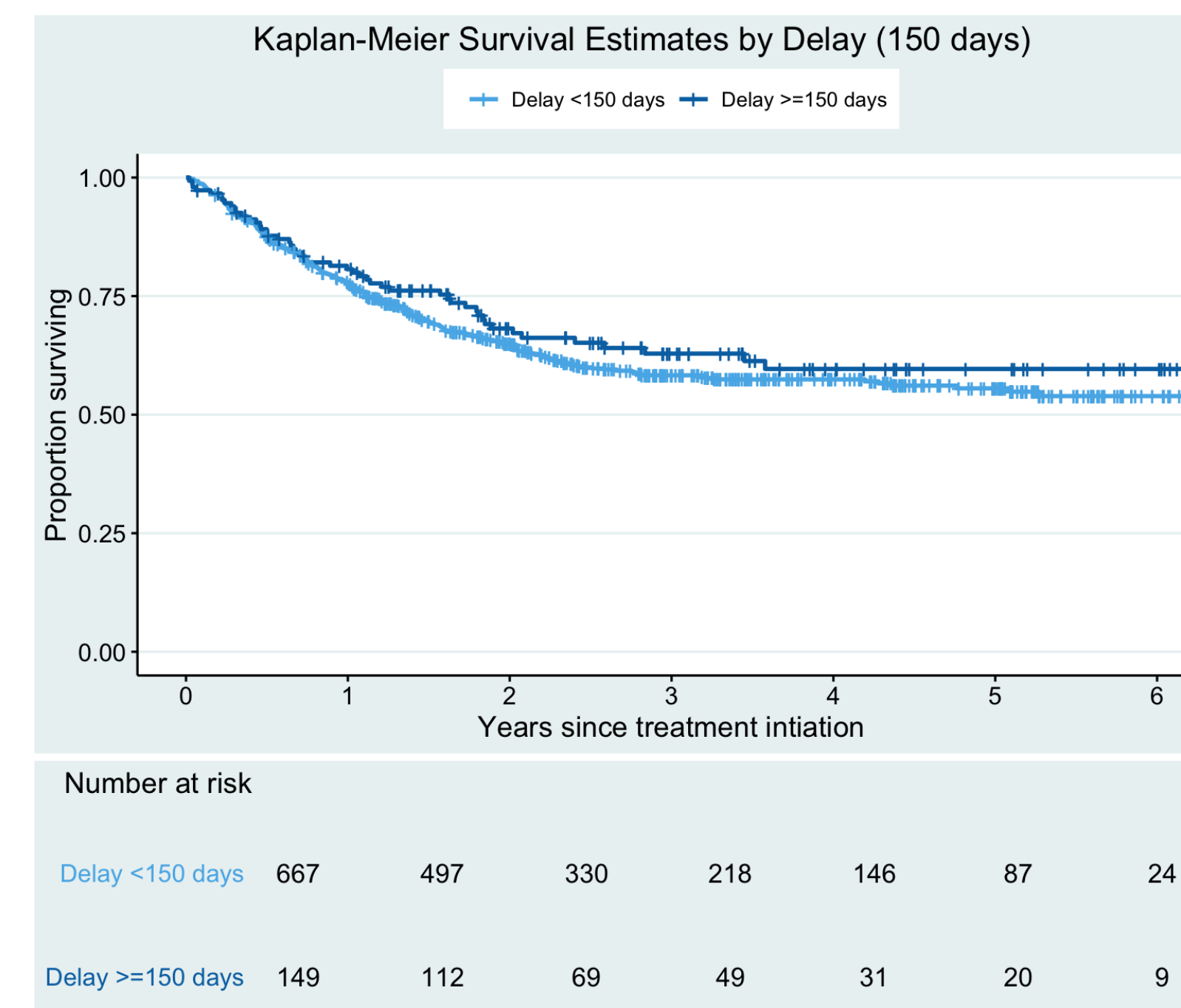
Table 1: Baseline demographic and treatment characteristics by HIV status of female cervical cancer patients in Botswana

Characteristic	Delay <150 days (N = 667)	Delay >=150 days (N = 149)	All (N = 815)	P
Age (y)	47 (40-58)	49 (42-60)	47 (41-59)	0.171
21-39	154 (%)	26 (%)	180 (%)	
40-59	363 (%)	81 (%)	444 (%)	
>60	149 (%)	42 (%)	191 (%)	
Marital status				0.838
Single	426 (%)	93 (%)	519 (%)	
Married/partnered	158 (%)	35 (%)	193 (%)	
Divorced/widowed	82 (%)	21 (%)	103 (%)	
Previously screened for cervical cancer	377 (%)	80 (%)	457 (%)	0.547
Distance from treatment facility (km)				0.156
<100 km (South-east, Kweneng, Southern)	298 (%)	54 (%)	352 (%)	
100-500 km (Central or Boteti, Kgatleng, North-east)	312 (%)	72 (%)	384 (%)	
>500 km (Kgalegadi, Ghanzi, Ngamiland, None above)	53 (%)	17 (%)	70 (%)	
Disease stage				
I (IB2, IB3)	43 (%)	9 (%)	52 (%)	
II (IIA, IIB)	298 (%)	77 (%)	375 (%)	
III (IIIA, IIIB, IIIC)	268 (%)	46 (%)	314 (%)	
IV (IVA, IVB)	58 (%)	17 (%)	75 (%)	
Baseline laboratory values				0.986
Creatinine (µmol/L)	60.0 (-)	59.5 (-)	60.0 (-)	
Hemoglobin (g/dL)	11.0 (9.5-12.4)	11.5 (9.8-12.8)	11.1 (9.5-12.4)	0.399
ANC (x10 <sup>9</sup> /L)	4.1 (-)	3.5 (-)	3.9 (-)	0.122
WBC (x10 <sup>9</sup> /L)	6.6 (4.9-8.8)	5.5 (4.0-7.8)	6.4 (4.7-8.6)	0.537
Albumin (g/L)	38.6 (-)	40.0 (-)	39.0 (-)	0.011
Baseline performance status (KPS)				0.983
>=90	480 (%)	107 (%)	587 (%)	
<90	166 (%)	38 (%)	204 (%)	
HIV characteristics				0.918
HIV status				
Seronegative	200 (%)	46 (%)	246 (%)	
Seropositive	457 (%)	101 (%)	558 (%)	
CD4 (cells/µL)				0.715
Median (Q1-Q3)	404.0 (227.0-590.0)	418.5 (260.3-634.0)	410.0 (230.0-594.0)	
CD4 category				0.558
<200	73 (%)	10 (%)	83 (%)	
>=200-<350	81 (%)	22 (%)	103 (%)	
>=350-<500	66 (%)	13 (%)	79 (%)	
>=500	131 (%)	29 (%)	160 (%)	
Viral Load				0.789
<400 (Undetectable)	258 (%)	52 (%)	310 (%)	
>=400 (Detectable)	60 (%)	14 (%)	74 (%)	
On ARV	436 (%)	94 (%)	530 (%)	0.353
Treatment				
Surgery	1 (%)	0 (0.0%)	1 (%)	0.999
RT	254 (%)	58 (%)	312 (%)	0.999
Chemo	6 (%)	1 (%)	7 (%)	0.999
CRT	397 (%)	87 (%)	484 (%)	0.934
Surgery + Chemo	2 (%)	1 (%)	3 (%)	0.999
Surgery + RT	2 (%)	0 (0.0%)	2 (%)	0.999

## Results

- 768 patients were prescribed RT/CRT: 57.4% (441/768) CRT, 35.7% (274/768) RT alone, and 6.9% (53/768) no treatment. 68% (520/768) were HIV-positive: median CD4 count at cancer diagnosis of 423 cells/mm<sup>3</sup> and 13.5% (70/520) with a detectable viral load.
- Median age was 47 years. Most patients presented with Stage II (42%) or Stage III (38%) disease.
- 80% of the patients had treatment delays <150 days and 20% had delays >150 days.
- Delays were significantly reduced over time ranging from median 93 days for patients diagnosed before 2016 vs. 49 days for patients diagnosed in 2019.
- For patients delayed >150 days, 22% were upstaged between initial consultation and start of RT.
- On univariate logistic regression analysis, patients less likely to experience delays were those who received curative vs. palliative treatment (OR=0.58 p=0.009); patients more likely to experience delays were those with Stage II/III/IV vs. Stage I (Stage II OR=2.72 p=0.06, III OR=2.62 p=0.08, IV OR=2.76 p=0.09) and those diagnosed in years <2015 vs. 2018-2019 (2018 OR=0.45 p=0.007, 2019 OR=0.31 p=0.001).

Figure 1: Survival Outcomes by stage



## Conclusion

- In this cohort of women with cervical cancer in Botswana, treatment was delayed >150 days for 20% of patients.
- Over time, treatment delays have decreased between 2015-2019 due to several interventions for managing cervical cancer patients in Botswana.
- Patients with higher stages of cervical cancer experienced longer delays and future interventions should focus on higher stage patients.

## References/Acknowledgements

- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021; 71: 209- 249. <https://doi.org/10.3322/caac.21660>
- Country Factsheets: Botswana 2019. Vol. 2021 (UNAIDS, 2019).
- Cubie HA, Campbell C. Cervical cancer screening - The challenges of complete pathways of care in low-income countries: Focus on Malawi. *Womens Health (Lond).* 2020;16:1745506520914804. doi:10.1177/1745506520914804
- Hung P, Zahnd WE, Brandt HM, Adams SA, Wang S, Eberth JM. Cervical cancer treatment initiation and survival: The role of residential proximity to cancer care. *Gynecol Oncol.* 2021;160(1):219-226. doi:10.1016/j.ygyno.2020.10.006
- Ferreira da Silva I, Ferreira da Silva I, Koifman RJ. Cervical Cancer Treatment Delays and Associated Factors in a Cohort of Women From a Developing Country. *J Glob Oncol.* 2019;5:1-11. doi:10.1200/JGO.18.00199.
- Article 1 or other study
- Ouasmani F, Hanchi Z, Haddou Rahou B, Bekkali R, Ahid S, Mesfioui A. Determinants of Patient Delay in Seeking Diagnosis and Treatment among Moroccan Women with Cervical Cancer. *Obstet Gynecol Int.* 2016;2016:4840762. doi:10.1155/2016/4840762

I am extremely grateful to Surbhi Grover, Jessica George and Shawna Tuli for guiding me through my research project. I am also grateful to CURF and PURM for providing me with this opportunity.