Screening of HPV-related Anogenital Cancers in Immunocompromised Women: A Systematic Review of Clinical Practice Guidelines

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Introduction

- The main aetiologic agent for anogenital squamous cell carcinomas in women is persistent oncogenic human papillomavirus (HPV) infection.
- Immunosuppressed patients* are disproportionately affected by anogenital cancers due to poorer HPV clearance and faster progression of dysplastic cells.
  - * Includes patients living with HIV (PLHIV), patients taking regular immunosuppressants for autoimmune diseases or as organ transplant recipients
- Currently, there is little consensus on how to conduct enhanced screening due to a lack of robust evidence

Objectives

- To review existing clinical practice guidelines (CPGs) pertaining to anogenital cancer screening among immunosuppressed female patients.

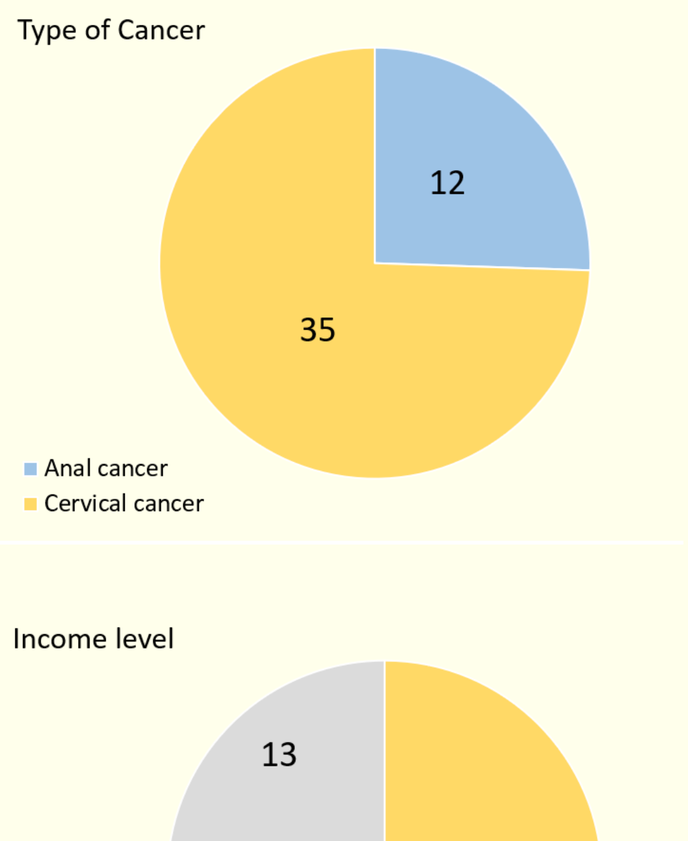
Methods

- Systematic review using PRISMA guidelines of major CPG databases
  - PROSPERO ID: CRD42022341484
- Time frame: from January 2004 to October 2023

Results

- A total of 2933 articles screened, 305 full-text articles reviewed, and 47 population-specific guidelines across 36 CPG articles included in systematic review
  - Most guidelines were focused on PLHIV, and most guidelines were focused on cervical cancer
  - No guidelines were found for vulva/ vaginal cancer screening in the immunocompromised population
- Majority of guidelines recommended initiation of screening at or within the first year of sexual debut, or at the point of diagnosis of an immunocompromised state.
- Co-testing was more frequently recommended for cervical screening in the transplant and autoimmune sub-populations on immunosuppressant medication, compared to the other sub-populations included.
- Most guidelines were from organisations based in high income countries.

Recommendation		Guidelines in agreement						
		Cervical				Anal		
		General	PLHIV	SOTR/ HSCTR	Autoimmune diseases	General	PLHIV	SOTR/ HSCTR
Initiation of screening	Within 1st year of sexual debut	Brazil (183), ASCCP (737), FOGSI (925), CDC (385)	KP (O2), CDC (385)	EGBMT,CIBMTR, ASBMT (O44), JLGTD (1031), Kaiser Permanente (O2)	JLGTD (1031), KP (O2)			
	Upon diagnosis or within 1st year of immunocompromised status / disease (e.g., HIV)	ASCO (1679u), FOGSI (925), Kenya (O48), CDC (385)	BHA (3423u), NIHCDC (3676u), Ethiopia (O47), Kenya (O48), WHO (2429), South Africa (3166u), CDC (385)	ASTID (1139), ASTCT (1028), NCCN (O42), CIBMTR/EGBMT (O41), JLGTD (1031)	JLGTD (1031)			
	Empirically at age 21	SOGC (2856u), CDC (385)	HMA-ISDA (O34), KP (O2), CDC (385)	EGBMT,CIBMTR, ASBMT (O44), KP (O2)	KP (O2)			
	Other ages or timepoints		CCA (O45), WHO (601, 602)	CCA (O45)			AJG (267)	
Screening modalities	HPV (including co-testing)	ASCO (1679u), Brazil (183), ASCCP (737), FOGSI (925), Kenya (O48), CDC (385)	CCA (O45), WHO (601, 602, 2429), HMA-ISDA (O34), NIHCDC (3676u), Kenya (O48), South Africa (3166u), KP (O2), CDC (385)	CCA (O45), ASTID (1139), ASTCT (1028), CIBMTR/EGBMT (O41), JLGTD (1031), KP (O2)	CCF (315), JLGTD (1031), KP (O2)	ASCRS (2701)	AJG (267), GeSIDA (2274u), SCRS (1669), ASCRS (2701u)	
	Cytology (including reflex cytology and co-testing)	ASCO (1679u), Brazil (183), ASCCP (737), FOGSI (925), SOGC (2856u), Kenya (O48), CDC (385)	CCA (O45), WHO (601, 602, 2429), HMA-ISDA (O34), Italy (3292), BHA (3423u), NIHCDC (3676u), Ethiopia (O47), Kenya (O48), South Africa (3166u), KP (O2), CDC (385)	CCA (O45), ASTID (1139), ASTCT (1028), NCCN (O42), EGBMT,CIBMTR, ASBMT (O44), JLGTD (1031), KP (O2)	CRA (1338u), CCF (315), JLGTD (1031), EULAR (1705), KP (O2)	ASCRS (2701), IDSA/CDC (191)	AJG (267), GeSIDA (2274u), HMA-ISDA (O34), Italy (3292), ASCRS (2701u)	ASTID (1139)
	Colposcopy/ Anoscopy	Brazil (183), ASCCP (737), CDC (385)	CCA (O45), WHO (602, 2429), HMA-ISDA (O34), Italy(3292), BHA (3423u), NIHCDC (3676u), Ethiopia (O47), KP (O2), CDC (385)	CCA (O45), ASTID (1139), CIBMTR/EGBMT (O41), KP (O2)	KP (O2)		SCRS (1669), HMA-ISDA (O34), Italy (3292), ASCRS (2701u)	ASTID (1139)
Screening interval	More frequently than annually	Brazil (183)		ASTID (1139)				
	Annually	NZSHS (O28), SOGC (2856u), ASCCP (737), Kenya (O48), CDC (385), British Columbia (O20)	BHA (3423u), NIHCDC (3676u). Kenya (O48), KP (O2), CDC (385)	ASTID (1139), ACG (1648), ASTCT (1028), NCCN (O42), CIBMTR/EGBMT (O41), EGBMT,CIBMTR, ASBMT (O44), JLGTD (1031), KP (O2)	CRA (1338u), CCF (315), JLGTD (1031), EULAR (1705), KP (O2)		AJG (267), GeSIDA (2274u)	ASTID (1139)
	Less frequently than annually or others	FOGSI (925), ASCCP (737), ASCO (1679u), Kenya (O48), CDC (385)	CCA (O45), WHO (601, 602, 2429), NIHCDC (3676u), Ethiopia (O47). Kenya (O48), South Africa (3166u), KP (O2), CDC (385)	CCA (O45), NCCN (O42), EGBMT,CIBMTR, ASBMT (O44), JLGTD (1031), KP (O2)	CCF (315), JLGTD (1031), KP (O2)		AJG (267), GeSIDA (2774u)	
Screening not recommended, or screening recommended as per general population					ECCO (3224u)		German-Austrian guidelines (2159), BHA (3423u)	



Conclusion

- There is a gap in care catered for PLHIV in low-middle income countries (LMICs)
- As treating anal HSIL reduces the risk of anal cancer (as per the 2022 ANCHOR trial), there is renewed relevance for developing robust guidelines for anal cancer screening.
- With the emergence of new pharmaceuticals and biologics to achieve immunosuppression, more evidence is needed to determine risks of HPV-related anogenital cancer and to develop dedicated CPGs for the population of patients on immunosuppressive medications.
- Coordinated multi-disciplinary efforts are key to optimise screening among immunocompromised patients.