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Early Detection of Cancer and Precancerous Lesions in Persons With HIV Through a Comprehensive Cancer Screening Protocol

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Background. Non-AIDS defining malignancies present a growing challenge for persons with human immunodeficiency virus (HIV, PWH), yet tailored interventions for timely cancer diagnosis are lacking. The Spanish IMPAC-Neo protocol was designed to compare two comprehensive cancer screening strategies integrated into routine HIV care. This study reports baseline data on the prevalence and types of precancerous lesions and early-stage cancer among participants at enrolment. Acceptability of the procedure was additionally assessed.

Methods. Cross-sectional analysis of a comprehensive screening protocol to detect precancer and cancer. The readiness of healthcare providers to implement the protocol was evaluated using a validated 4-item survey.

Results. Among the 1430 enrolled PWH, 1172 underwent 3181 screening tests, with positive findings in 29.4% of cases, leading to further investigation in 20.7%. Adherence to the protocol was 84%, with HIV providers expressing high acceptability (97.1%), appropriateness (91.4%), and feasibility (77.1%). A total of 145 lesions were identified in 109 participants, including 60 precancerous lesions in 35 patients (3.0%), 9 early-stage cancers in 9 patients (0.8%), and 76 low-risk lesions in 65 subjects (5.5%). Adverse events related to screening occurred in 0.8% of participants, all mild. The overall prevalence of cancer precursors or early-stage cancer was 3.8% (95% confidence interval [CI], 2.74%–5.01%), with highest rates observed in individuals screened for anal and colorectal cancers.

Conclusions. The baseline comprehensive cancer screening protocol of the IMPAC-Neo study successfully identified a significant proportion of PWH with precancerous lesions and early-stage cancer. High adherence rates and positive feedback from providers suggest effective implementation potential in real-world healthcare settings.

Keywords. HIV; cancer; screening; surveillance; early diagnosis.

Cancer has emerged as a significant comorbidity among persons with human immunodeficiency virus (HIV, PWH), and its prevalence in this population is expected to rise with aging [1–3]. Notably, non-AIDS defining malignancies now constitute a considerable proportion of cancers and represent a leading cause of mortality in PWH receiving antiretroviral therapy

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(ART) [4–8]. This phenomenon is partly attributed to premature aging, compromised immune function, higher rates of coinfection with oncogenic viruses and a high prevalence of traditional cancer risk factors such as smoking [9, 10]. Cancer impacts PWH more acutely due to occurrences at younger ages, late-stage diagnoses, and elevated mortality rates [2, 11–13].

Despite the escalating burden of non-AIDS defining malignancies and suboptimal outcomes, research on tailored interventions for timely cancer diagnosis in the HIV population is lacking. Although screening for certain cancers in the general population has proven effective in detecting precursor lesions and early-stage cancer, data suggest that PWH may exhibit poorer adherence to population-based screening programs compared to their HIV-negative counterparts [14–17]. Moreover, it remains uncertain whether screening guidelines intended for the general population are also suitable for PWH or if an alternative approach, such as earlier or enhanced screening, would be needed to achieve clinically impactful results in this unique population [18].

The IMPAC-Neo study is an innovative randomized trial comparing an enhanced cancer screening program with standard-of-care practice for diagnosing early-stage cancer in PWH. Leveraging baseline data from the IMPAC-Neo protocol, this report outlines the prevalence and spectrum of precancerous and early-stage cancer and associated factors among study participants in the overall enrolled group, along with the readiness of healthcare providers to implement the protocol in clinical practice.

METHODS

Study Participants

This cross-sectional analysis used baseline data from the IMPAC-Neo protocol, a cancer screening intervention study conducted in medical centers providing healthcare to PWH in Spain within the National Health Service [19]. In brief, this is a multicenter, pragmatic, randomized protocol comparing a comprehensive enhanced screening program for the early diagnosis of cancer in PWH with the standard-of-care practice recommended by the European AIDS Clinical Society (EACS) [20].

The IMPAC-Neo study received approval from the Institutional Review Board of each research site and was registered on ClinicalTrials.gov (NCT04735445). Women aged ≥18 and men aged ≥40 years with confirmed HIV infection on ART, without AIDS and without non-AIDS-defining diseases, receiving medical care in any of the participating centers were eligible for enrollment, including those participating in any of the Spanish population-based cancer screening programmes during the recruiting period (breast, colorectal, and cervical cancers). Written informed consent was obtained prior to participation. Study data were collected and managed using REDCap® electronic data capture tools.

Recruitment across 23 HIV/AIDS units commenced on 25 June 2019 but was temporarily halted due to the coronavirus disease 2019 (COVID-19) pandemic. It gradually resumed during the second term of 2021 based on the pandemic situation at each participating institution. The protocol was amended to extend the enrollment and follow-up periods according to interim data analysis. The last patient was enrolled on 31 December 2023, with planned follow-up through 2028. For this cross-sectional study, we included all enrolled patients who had completed the baseline screening cascade as of 30 November 2023.

Assessment of Baseline Characteristics and Interventions

Participants were randomized 1:1 to either standard or enhanced surveillance for early detection of lung, liver, anal, cervical, breast, prostate, colorectal, and skin cancer (Supplementary Table 1). Detailed interventions for each arm have been previously published [19].

Irrespective of the randomization group, at baseline, all sexually active women had cervical cytology, and all men who have sex with men (MSM) aged ≥40 years had anal cytology, to screen for cervical and anal precancer and cancer. Fecal occult blood tests (FOBT) were conducted for colorectal cancer (CRC) screening in all individuals aged 50 to 75 (>40 years in those randomized to the enhanced arm). Liver ultrasound and alpha-fetoprotein tests were performed for hepatocellular carcinoma screening in all individuals with cirrhosis (fibrosis ≥F3 in those randomized to enhanced arm) and in hepatitis B virus (HBV) positive non-cirrhotic individuals with risk factors for hepatocellular carcinoma (all in those randomized to enhanced arm), regardless of the presence of fibrosis. Mammograms for breast cancer screening were conducted in females aged 50–70 (≥45 years in those randomized to enhanced arm), and males aged ≥50 underwent prostate-specific antigen (PSA) testing for prostate cancer screening. Additionally, individuals randomized to the enhanced arm underwent general inspection for skin lesions and lung cancer screening with low-dose computed tomography (LDCT) for those aged >40 years, active smokers or those who quit in the last 3 years, with an accumulated index ≥20 pack-years, and without contraindications for thoracic surgery, and with no lung infections in the last 2 months.

Statistical Analysis

The prevalence of precancer and cancer at baseline was stratified by patient characteristics at enrollment. Associations of covariates with outcomes of the screening cascade were explored using univariable logistic regression analysis. Covariates with $P < .10$ from the univariable analysis were included in a multivariable logistic regression. In both univariable and

multivariate analyses, associations were expressed as odds ratios (OR) and adjusted OR (AOR).

To assess readiness for implementation of the screening protocol from the perspective of HIV providers of the participating centres, we used a validated 4-item measures: acceptability of intervention measure (AIM), intervention appropriateness measure (IAM), and feasibility of intervention measure (FIM) [21]. The responses on the scale for each of the 4 items range from "completely disagree" to "completely agree," respectively. The level of agreement of the scales was quantified by the Cronbach's alpha as a measure of internal consistency. Statistical analyses were performed using R software (R-Core Team 2020, R-4.1.2.1).

RESULTS

Baseline Characteristics of Study Participants

A total of 1172 of the 1430 PWH enrolled in the IMPAC-Neo trial from 23 Spanish medical centers, were included in this cross-sectional study (Supplementary Figure 1). Table 1 shows baseline characteristics of the study participants. Median age was 54 years, with 79% identified as male at birth. The most common transmission route was MSM in 566 (40%) of participants, 43% were current or former smokers and 24% were co-infected with chronic hepatitis viruses (19% HCV, 4.5% HBV). Median CD4 cell count was 720 cells/uL, and 98% had human immunodeficiency virus type 1 (HIV-1) RNA levels below 200 copies/mL.

Screening Outcomes

The distribution of study participants undergoing different cancer screenings at baseline is illustrated in Supplementary Figure 1, and screening outcomes are detailed in Table 2 and Supplementary Table 2. Overall, adherence to the protocol was 83.8%, with no significant differences between those who adhered to it and those who did not (Supplementary Table 3). A total of 3181 screening tests were conducted in 1172 participants, yielding positive results in 344 (29.4%) subjects, and prompting further investigations in 248 (20.7%). A total of 145 lesions were identified among 109 participants, constituting 9.3% of the total cohort. Specifically, 75 lesions were detected in patients assigned to the standard of care group, whereas 70 lesions were found in those undergoing enhanced screening. Supplementary Table 2 shows the lesions diagnosed by study group. The lesion distribution was categorized as follows: 60 precancerous lesions affecting 35 patients (3.0%; 95% CI, 2.09%–4.13%), 9 early-stage cancers detected in 9 patients (0.8%; 95% CI, .35%–1.45%), and 76 lesions classified as low-risk for malignant transformation, identified in 65 subjects (5.5%; 95% CI, 4.31%–7.01%). Adverse events associated with the screening strategies were recorded in 9 participants, comprising 0.8% of the sample (95% CI, .35%–1.45%). These events included hemorrhage in 7 cases, localized infection in 2 cases, and local pain in 2 cases, all of mild severity. The overall prevalence of cancer precursors or early-stage cancer among participants was 3.8% (95% CI, 2.74%–5.01%) and tended to occur more frequently in subjects >70 years (AOR 2.75; 95%CI, .71–9.06; $P = .110$) (Supplementary Table 4).

The highest proportion of positive results was observed in persons undergoing screening for anal and colorectal cancers. Among the 445 PWH participating in anal cancer screening, representing 72.3% of those eligible according to the study protocol (median age [interquartile range {IQR}], 52 [46–58] years; sex at birth, 83.6% males; median CD4+ cell count [IQR], 708 [526–949] cells/μL), anal cytology was abnormal in 175 individuals (39.3%; 95% CI [34.76%–44.04%]). Low-grade anal squamous intraepithelial lesion (LSIL) was identified in 62 (13.9%, 95% CI, 10.85–17.50) participants; 51 histologically confirmed results and 11 with cytological lesions, whereas high-grade anal squamous intraepithelial lesion (HSIL) was found in 22 (4.9%, 95% CI, 3.12%–7.39%); 20 histologically confirmed results and 2 cytological lesions. Of the 108 high-resolution anoscopy (HRA) procedures conducted, biopsy-proven LSIL was identified in 47.2%, and HSIL in 18.5% (Figure 1*A*). The presence of either anal HSIL or LSIL following completion of the screening cascade was associated with male gender (AOR, 3.37; 95% CI, 1.2711.77; $P = .029$), CD4+ cell count <350 cells/uL (AOR, 2.95; 95% CI, 1.09–7.81; $P = .028$) and CD4/CD8 ratio <1 (AOR, 2.09; 95% CI, 1.13–4.05; $P = .021$) in multivariable logistic regression analysis (Table 3).

Among the 894 PWH participating in CRC screening, representing 88% of those eligible per study protocol (median age [IQR], 56 [51–06] years; sex at birth, 82% males; median CD4+ cell count [IQR], 713 [514–949] cells/μL), 81 (9.1%; 95% CI [7.26%–11.15%]) had a positive FOBT result. 69 participants underwent colonoscopy, identifying 35 colorectal lesions (33 adenomas, 2 carcinomas) in 14 (20%) patients (Figure 1*B*). Positive FOBT results were numerically more common in individuals aged 50 years and older, and in former or current smokers, but the associations were not statistically significant (Supplementary Table 5).

Among the 197 subjects participating in lung cancer screening (median age [IQR], 56 [51–56] years; sex at birth, 81.2% males; median CD4+ cell count [IQR], 752 [560–977 cells/μL), 27 (13.7%) individuals exhibited abnormalities in the LDCT (Table 2). The most common finding was noncalcified nodules in 11 cases. Fourteen participants required additional investigations, in most cases follow-up scans. Only one instance warranted a prompt invasive procedure, as determined by the attending clinicians and radiologists. Subsequent confirmation through lung biopsy in that particular patient unveiled the existence of early-stage adenocarcinoma, facilitating the immediate commencement of therapy.

Table 1. Demographic and Selected Characteristics of the Study Participants[a]

Characteristic	Total	Standard-of-care Screening	Enhanced Screening
Participants, n (%)	1430	721 (50.4)	709 (49.6)
Age, median (IQR), years	54 (49–55)	54 (49–55)	54 (48–55)
<50	423 (29.6)	213 (29.6)	210 (29.6)
50–70	959 (67.1)	481 (66.7)	478 (67.5)
>70	48 (3.3)	27 (3.7)	21 (2.9)
Sex at birth, n (%)			
Male	1133 (79.2)	572 (79.3)	561 (79.1)
Female	297 (20.8)	149 (20.7)	148 (20.9)
Race, n (%)			
White, non Hispanic	1209 (93.9)	612 (94.2)	597 (93.6)
Other	79 (6.1)	38 (5.8)	41 (6.4)
Country of origin, n (%)			
Spain	1091 (76.3)	547 (75.9)	544 (76.7)
Latin American countries	131 (9.2)	69 (9.6)	62 (8.8)
Others	40 (2.8)	18 (2.5)	22 (3.1)
Unknown	168 (11.7)	87 (12.0)	81 (11.4)
Transmission route, n (%)			
Men having sex with men	566 (39.6)	294 (40.8)	272 (38.4)
Heterosexual	342 (23.9)	167 (23.2)	175 (24.7)
Injection drug use	276 (19.3)	134 (18.6)	142 (20.0)
Other	246 (17.2)	126 (17.4)	120 (16.9)
Smoking status, n (%)			
Former/Current	616 (43.1)	290 (40.2)	326 (45.9)
Never	659 (46.1)	350 (48.9)	309 (43.5)
Unknown	155 (10.8)	81 (11.2)	74 (10.6)
Current ART user, n (%)	1302 (91)	653 (90.6)	649 (91.5)
ART regimen at entry, n (%)			
2 NRTI + 1 NNRTI	116 (8.9)	57 (8.7)	59 (9.1)
2 NRTI + 1PI	83 (6.4)	34 (5.2)	49 (7.6)
2 NRTI + 1 INSTI	353 (27.1)	171 (26.2)	182 (28.0)
Other	750 (57.6)	391 (59.9)	359 (55.3)
HIV-1 viral load, n (%)			
Supressed (≤200 copies/mL)	1095 (98.2)	544 (98.2)	551 (98.8)
Unsuppressed (>200 copies/mL)	20 (1.8)	10 (1.8)	10 (1.8)
CD4 cell count, median (IQR), cells/uL	720 (520–973)	729 (536–984)	716 (510–957)
CD4 cell count, n (%)			
<350 cells/uL	104 (8.5)	45 (7.3)	59 (9.6)
350–500 cells/uL	175 (14.2)	90 (14.6)	85 (13.9)
>500 cells/uL	951 (77.3)	483 (78.1)	468 (76.5)
CD8 cell count, median (IQR), cells/uL	821 (584–1150)	814 (576–1124)	831 (590–1179)
CD4/CD8 ratio	0.91 (0.65–1.28)	0.93 (0.68–1.28)	0.89 (0.62–1.27)
Nadir CD4 cell count, n (%)			
<200 cells/uL	359 (42.4)	178 (41.4)	181 (43.5)
200–350 cells/uL	236 (27.9)	116 (26.9)	120 (28.9)
>350 cells/uL	251 (29.7)	136 (31.6)	115 (27.6)
Hepatitis C virus antibodies, n (%)			
Negative	970 (67.8)	502 (69.6)	468 (66.0)
Positive	273 (19.1)	129 (17.9)	144 (20.3)
Unknown	187 (13.1)	90 (12.5)	97 (13.7)
Hepatitis B virus surface antigen, n (%)			
Negative	970 (67.8)	502 (69.6)	468 (66.0)
Positive	65 (4.5)	26 (3.6)	39 (5.5)
Unknown	395 (27.6)	193 (26.8)	202 (28.5)

Abbreviations: ART, antiretroviral therapy; BMI, body mass index; HIV-1, human immunodeficiency virus type 1; IQR, interquartile range; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse-transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse-transcriptase inhibitor; PI, protease inhibitor.

[a]All statistics are calculated based on participants with data collected.

Table 2. Participants Undergoing Various Cancer Screenings and the Outcomes of the Screening Cascade at Baseline

	n/N (%)[a]	Positive n (%)[b]	Additional Investigations n (%)[b]	Pre-cancer or Early-stage Cancer n (%)[b]	Other Lesions n (%)[b]
Anal	445/610 (72.3)	175[c] (39.3)	Anoscopy, 108 (24.3)	HSIL, 22 (4.9)	LSIL, 62 (13.9)
Breast	149/174 (85.6)	6 (4.0)	Follow-up scans, 2 (1.3) Breast biopsy, 2 (1.3)	Breast cancer, 1 (0.7)	
Cervix	181/227 (79.7)	17[d] (9.4)	Colposcopy, 8 (4.4)		LSIL, 6 (3.3)
Colorectal	894/1011 (88.4)	81 (9.1)	Colonoscopy, 69 (7.7)	Adenoma, 33; CRC, 2 [14 patients] (1.6)	
Liver	124/149 (81.5)	5 (4.0)	CT, 1 (0.8) MRI, 4 (3.2)	Liver cancer, 1 (0.8)	
Lung	197/241 (81.7)	27 (13.7)	Follow-up scans, 14 (7.1) Lung biopsy, 1 (0.5)	Lung cancer, 1 (0.5)	Noncalcified nodules, 11; enlarged lymph nodes, 7; emphysema, 6; other, 7[e]
Prostate	692/754 (91.8)	16 (2.3)	Prostate biopsy, 9 (1.3)	Prostate cancer, 1 (0.1)	Prostate adenoma, 2
Skin	499/626 (79.7)	17 (3.4)	Skin biopsy, 12 (2.4)	Non-melanoma skin cancer[f], 3 (0.6)	Melanocytic nevus, 3; dermatofibroma, 2; keratosis, 2.

Abbreviations: ASCUS, atypical squamous cells of undetermined significance; CRC, colorectal cancer; CT, computed tomography; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; MRI, magnetic resonance imaging.

[a]n/N (%), denotes participating in each screening (n) out of those eligible (N) as defined by the study protocol.

[b]Of those participating in each screening.

[c]Abnormal anal cytologies: ASCUS, 117; HSIL, 16; LSIL, 42.

[d]Abnormal cervical cytology: ASCUS, 11; LSIL, 6.

[e]Suprarenal adenoma, 2; lung infiltrate, 1; atelectasis, 1; cholelithiasis, 1; nephrolithiasis, 1; hiatus hernia, 1.

[f]Basal cell carcinoma, 2; squamous cell carcinoma, 1.

Acceptability, Appropriateness, and Feasibility of the Program

Thirty-five fully completed surveys were received from HIV providers across the 23 participating centers in the IMPAC-Neo protocol. Table 4 shows the proportions of responses given to the measured attributes of readiness for implementation. The composite scores showed that the screening protocol was perceived as acceptable, appropriate, and feasible by 97.1%, 91.4%, and 77.1% of the respondents, respectively. At the individual item level, a predominant majority selected "agree" or "completely agree" in response to each item.

DISCUSSION

In this contemporary cohort of PWH receiving effective ART, a comprehensive cancer screening protocol integrated into routine medical care for HIV revealed a significant proportion of persons having cancer precursor lesions. Moreover, the study identified a small number of early-stage malignancies, facilitating timely diagnosis and the initiation of early treatment interventions. This approach is particularly crucial as early treatment has the potential to improve outcomes for selected individuals. To our knowledge, this study represents the first investigation into the screening results derived from a comprehensive cancer surveillance, focusing on precancer and cancer, among asymptomatic individuals with HIV on ART. The high adherence to the screening protocol and the positive reception from the providers suggest that it may be implementable in real-world healthcare settings.

Anal and colorectal screening exhibited the highest performance in our investigation. Early intervention targeting HSIL, a precursor to invasive carcinoma, has the potential to alter the natural progression of anal cancer [22], the malignancy with the highest excess incidence and mortality among all non-AIDS defining malignancies [1, 2] and the leading non-AIDS cancer contributing to years of life lost in PWH in the United States [23]. Our study observed an overall prevalence of anal lesions, determined through anal cytology, of 39%, aligning with findings in other studies [24], and 13% of individuals with abnormal cytology presented with HSIL. Following the completion of the cancer screening cascade with HRA, 5% of subjects undergoing anal cancer screening exhibited HSIL, identified through either cytology or biopsy. Moreover, 13.9% displayed LSIL additional abnormalities, which can evolve over time [25, 26].

Much like with anal cancer, the identification and early removal of precancerous lesions, such as premalignant adenomas or sessile serrated lesions, constitute a highly effective strategy for preventing CRC [27, 28]. Despite the acknowledged benefits of early screening, CRC continues to rank third in incidence and as cause of cancer-related mortality for both men and women in the United States [29]. The overall incidence of CRC in PWH appears comparable to the general population [2, 30, 31] but several studies indicate that PWH are diagnosed with CRC at younger ages compared to individuals without HIV [32, 33], with potentially more aggressive clinical progression, poorer outcomes and increased mortality [2, 34–37].

Although guidelines recommend initiating CRC screening in the general population at age 50, with earlier and more frequent screenings for high-risk patients [38], there is as yet no conclusive evidence supporting the benefits of enhanced screening in

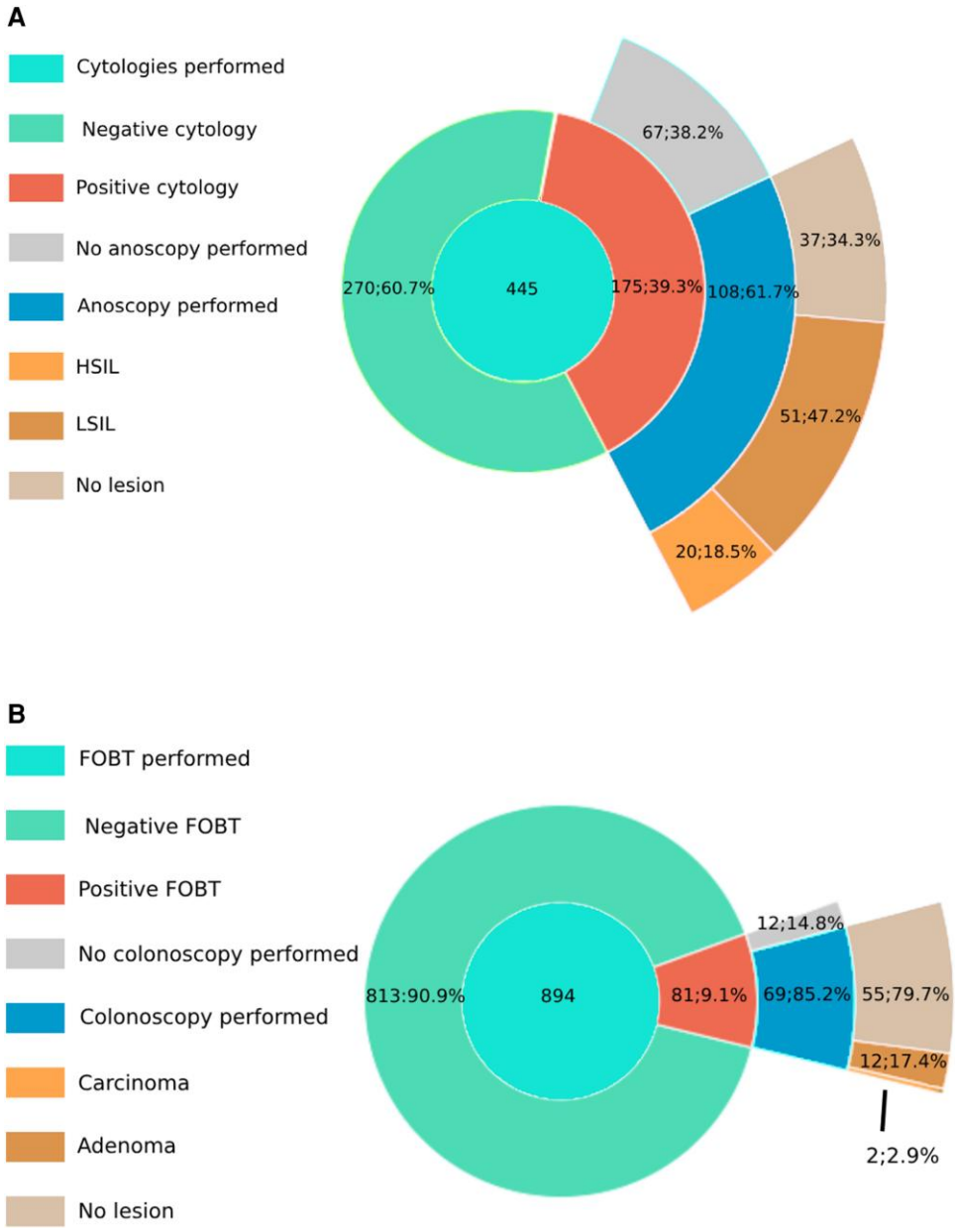

Figure 1. Participants undergoing anal (n = 445; panel *A*) and colorectal cancer screenings (n = 894; panel *B*) and the outcomes of the screening cascade at baseline. Abbreviations: FOBT, fecal occult blood test; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion.

PWH. Current HIV/AIDS guidelines endorse the general recommendations for persons at average risk [20]. These typically involve a FOBT or structural examination followed by colonoscopy if positive, screening modalities proven effective in reducing CRC incidence and mortality in randomized controlled trials [38]. Data on CRC screening practices and outcomes in PWH are limited, with some studies reporting higher adenoma detection rates in PWH [31, 37, 39–41]. In our study, PWH whose initial screening event was a FOBT yielded positive results in 9% of cases. Among those subsequently undergoing colonoscopy, adenomas or carcinomas were detected in 20% (1.6% of the PWH undergoing CRC screening). The prevalence rates in our study slightly exceeded those documented in an observational study conducted in California [31] and were higher than expected, given that Spain operates a national population-based CRC screening program, making most participants in the IMPAC-Neo study eligible and potentially open to participation.

The study revealed asymptomatic cases of the most prevalent cancers in the general population, including breast cancer, liver cancer, and prostate cancer, all of which were screened in all participants. Additionally, in individuals randomized to the enhanced arm, we identified several cases of skin cancer and 1

Table 3. Variables Linked to Anal Squamous Intraepithelial Lesion Subsequent to the Completion of the Screening Cascade Among Individuals Engaged in Anal Cancer Screening

Characteristic	Anal Squamous Intraepithelial Lesion: No n, (%)	Anal Squamous Intraepithelial Lesion: Yes n, (%)	Unadjusted OR	*P* Value	Adjusted OR	*P* Value
Age						
<50	106 (74.6)	36 (25.4)	Ref.			
50–70	172 (78.9)	46 (21.1)	0.79 (0.48–1.30)	.347		
>70	6 (75.0)	2 (25.0)	1.03 (0.13–4.87)	.982		
Gender						
Female	48 (92.3)	4 (7.7)	Ref.			
Male	236 (74.7)	80 (25.3)	3.92 (1.53–13.6)	.005	3.37 (1.27–11.77)	.029
Smoking status						
Never	172 (78.9)	46 (21.1)	Ref.			
Former/current	104 (75.9)	33 (24.1)	1.19 (0.71–1.97)	.510		
Current CD4 cells/uL						
>500	218 (80.4)	53 (19.4)	Ref.			
350–500	40 (81.6)	9 (18.4)	0.94 (0.40–1.98)	.846	0.83 (0.35–1.79)	.648
<350	13 (59.1)	9 (40.9)	2.85 (1.11–7.03)	.018	2.95 (1.09–7.81)	.028
CD4/CD8 ratio						
>1	111 (87.4)	16 (12.6)	Ref.			
<1	153 (74.6)	52 (25.4)	2.34 (1.29–4.44)	.005	2.09 (1.13–4.05)	.021
Nadir CD4 count, cells/uL						
>350	62 (82.7)	13 (17.3)	Ref.			
200–350	58 (79.5)	15 (20.5)	1.23 (0.53–2.86)	.618		
<200	63 (75.9)	20 (24.1)	1.50 (0.69–3.38)	.296		

Abbreviation: OR, odds ratio.

Table 4. Proportion of Responses Provided by Human Immunodeficiency Virus (HIV) Providers Participating in the IMPAC-Neo Trial (n = 35) Regarding the Assessed Attributes of Readiness for Implementing a Cancer Screening Protocol Integrated into Routine HIV Care

	Completely Disagree (%)	Disagree (%)	Neutral (%)	Agree (%)	Completely Agree (%)	Cronbach's Alpha	Composite Score[a]
Feasibility						0.87	77.1%
Seems implementable	0	8.8	14.7	35.3	41.2		
Seems possible	0	11.4	11.4	34.3	42.9		
Seems doable	0	8.6	20	34.3	37.1		
Seems easy to use	11.4	17.1	14.3	22.9	34.3		
Acceptability						0.95	97.1%
Meets my approval	2.9	0	2.9	25.7	68.6		
It is appealing to me	0	2.9	2.9	25.7	68.6		
I like it	0	2.9	2.9	23.5	70.6		
I welcome it	0	2.9	8.6	25.7	62.9		
Appropriateness						0.89	91.4%
Seems fitting	2.9	0	5.7	34.3	57.1		
Seems suitable	0	2.9	2.9	28.6	65.7		
Seems applicable	0	8.6	17.1	28.6	45.7		
Seems like a good match	0	2.9	8.8	23.5	64.7		

[a]The responses for each of the 4 items in every measurement were assigned ordinal values ranging from 1 to 5, indicating "completely disagree" to "completely agree," respectively. The cumulative score was derived by aggregating these values across the 4 items, yielding a score range from 4 to 20. This composite score was then dichotomized using the neutral attitude value, which was established by summing the responses for the 4 items in each measure (ie, 12), thereby serving as the midpoint. Scores falling within the range of 4–12 were construed as indicative of disagreement with the measure, whereas scores within the range of 13–20 were regarded as reflective of agreement with the measure. Subsequently, the proportions of respondents expressing disagreement or agreement were calculated based on these score intervals.

case of early-stage lung cancer, the most lethal cancer [42] and a leading cause of death among PWH [2, 3]. Although PWH are likely to derive substantial benefits from lung cancer screening, limited data exist characterizing real-world lung cancer screening outcomes among this population [43, 44] and concerns have been raised on potential harms associated with subsequent invasive procedures derived of false-positive screening, particularly in patients with low CD4 cell counts [45]. However, contrary to initial hypotheses, the frequency of false-positive results apparently is not higher in PWH [43–46]. Among participants in the IMPAC-Neo protocol undergoing lung cancer screening, radiological abnormalities were prevalent. However, only 1 case necessitated a prompt invasive diagnostic procedure during the baseline assessment, ultimately revealing an early-stage adenocarcinoma.

Overall, adherence to the screening protocol was high, and the initial tests and subsequent procedures associated with the screening cascade were well-accepted by the participants. Compliance remains a substantial challenge in the implementation of cancer screening among PWH, frequently trailing behind the general population [14–17, 47, 48]. Previous research has identified patient- and provider-related barriers as significant factors influencing adherence to screening. These barriers encompass decision-making complexities in the context of medical comorbidity, competing patient priorities, limited access to required resources, and shortage of skilled personnel to conduct tests. Additionally, the lack of clarity on which provider specialty should take ownership of screening responsibilities contributes to the challenges [49].

An inherent strength of our research lies in its comprehensive collection of extensive data from multiple medical centers nationwide, implemented within an organized, pragmatic, and comprehensive cancer screening program integrated into routine HIV medical care. Our findings on readiness for implementation suggest the program's feasibility and favourable acceptance of the screening protocol within real-world healthcare settings. In addition to the cross-sectional nature of the analyses, several study limitations should be noticed. Although the investigation benefits from the high overall uptake of cancer screening, enabling the evaluation of numerous screening outcomes, the limited number of positive screens and malignancies diagnosed poses a challenge. This constraint hindered the derivation of accurate reliable estimates for cancer prevalence. The programme included enhanced screening for neoplasms that have not shown a greater incidence compared to the general population. However, the worse prognosis and younger ages at diagnosis observed with some of these cancers in PWH led us to explore alternative strategies to the standard approach. Targeted screening approaches may be necessary to address these differences and optimize cancer care. Despite the well-established evidence supporting the life-saving potential of early detection of cancer, there remains a crucial need for the estimation of the long-term benefits and potential harms associated with the screening protocols in PWH. Additionally, economic assessments play a pivotal role in endorsing decisions to incorporate and implement these protocols, especially in low- and middle-income countries, emphasizing the importance of identifying the most cost-effective strategies. Several of these objectives align with the specific goals of the IMPAC-Neo trial. Screening guidelines evolve, and some screenings, such as those for lung cancer in the enhanced arm, are now considered standard of care according to the recommendations of the European Commission. Even as guidelines continue to shift, they are still in the process of being widely implemented and may not yet be considered standard of care across all clinical settings and countries. Our study aimed to demonstrate the feasibility and impact of comprehensive screening protocols, which surpass current standard practices in many regions, particularly in PWH.

In summary, the baseline assessment of the IMPAC-Neo cohort unveiled a noteworthy proportion of PWH who exhibited cancer precursor lesions and detected asymptomatic cases of the most prevalent cancers in the general population that were identified at an early stage. The feasibility and positive reception of the comprehensive cancer screening protocol implemented in clinical practice environments suggest that devising tailored and inclusive programs integrated into routine care services could prove to be an effective strategy to augment screening uptake in this unique population that requires special attention and effort. Forthcoming findings from longitudinal analyses and cost-effectiveness assessments within the IMPAC-Neo framework stand to provide valuable insights guiding decisions regarding cancer screening for individuals with HIV.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author F. G.

Notes

Author contributions. F. G.: conceptualization (lead), methodology (lead), writing—original draft (lead), funding acquisition, project administration, supervision; L. L.: project administration (supporting), formal analysis (supporting), writing—review and editing (equal); C. G.: data curation (supporting); writing—review and editing (equal); JT: data curation (supporting); writing—review and editing (equal); L. G. F.: data curation (supporting); writing—review and editing (equal); M. G. T.: data curation (supporting); writing—review and editing (equal); E. B.: data curation (supporting); writing—review and editing (equal); A. R.: data curation (supporting); writing—review and editing (equal); JGA: data curation (supporting); writing—review and editing (equal): J. F.: data curation (supporting); writing—review and editing (equal): A. G. C.: data curation (supporting); writing—review and editing (equal); O. M.: data curation (supporting); writing—review and editing (equal); J. B.: data curation (supporting); writing—review and editing (equal); D. R.: data curation (supporting); writing—review and editing (equal); M. M.: data curation

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Data sharing statement. The data that support this work are available from the corresponding author, F. G., upon reasonable request.

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