

Rischio infettivologico nella persona che vive con HIV

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Inflammation Strikes Again: Frailty and HIV

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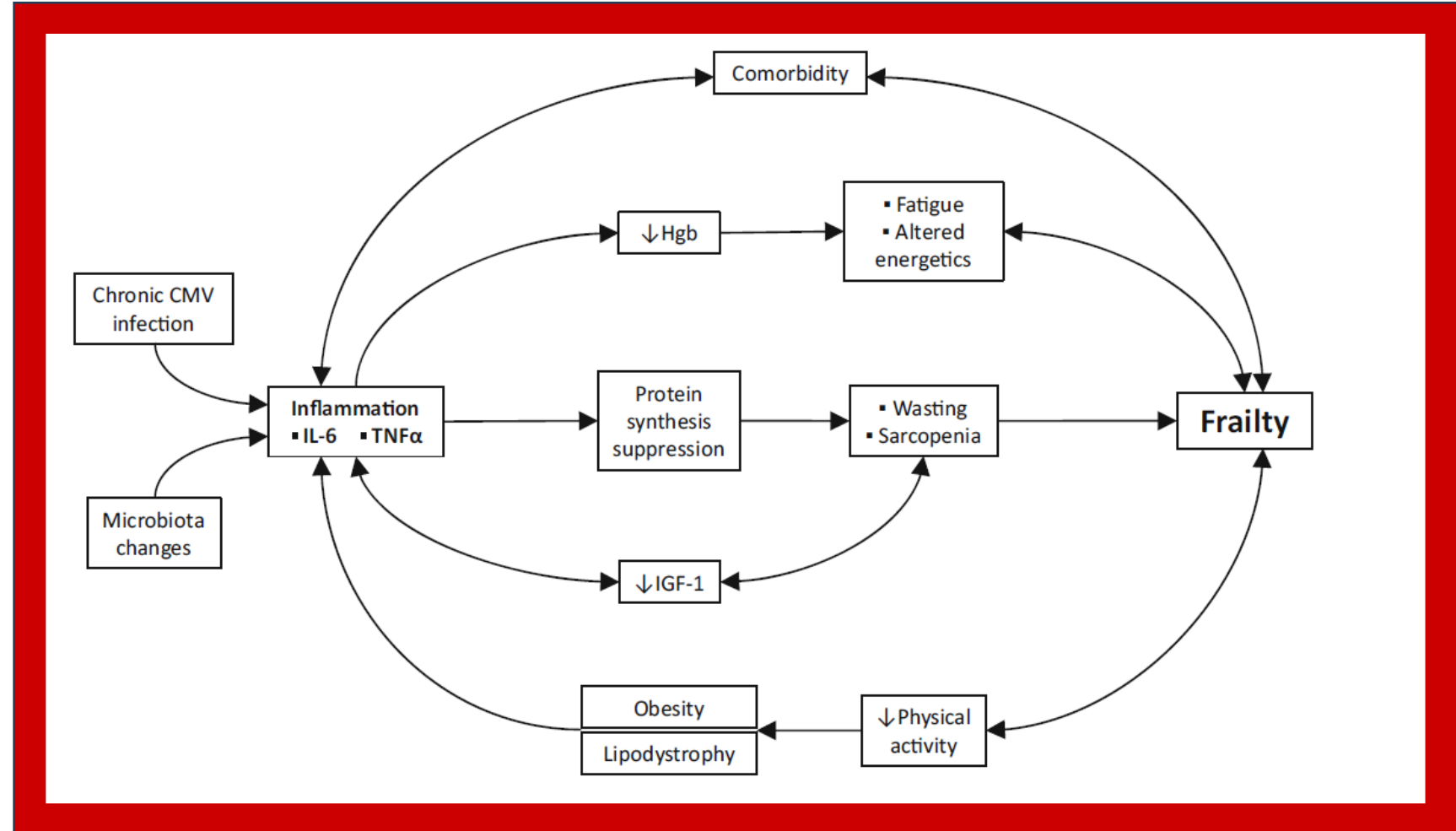
Stephanie M. Fukui

Damani A. Piggott

Kristine M. Erlandson

Potential pathways of frailty pathogenesis from dysregulated inflammation in HIV.

These proposed interactions are not all-inclusive, but demonstrate a potential framework for understanding the role of inflammation in the development of frailty in the context of HIV. Hgb, hemoglobin; IGF-1, insulin-like growth factor 1



Frailty = state of an increased vulnerability

- Lack of consensus regarding the definition of frailty
- Frailty is a multidimensional concept affecting physical, cognitive, psychological, and social domains, and the more domains that are affected, the worse the prognosis.

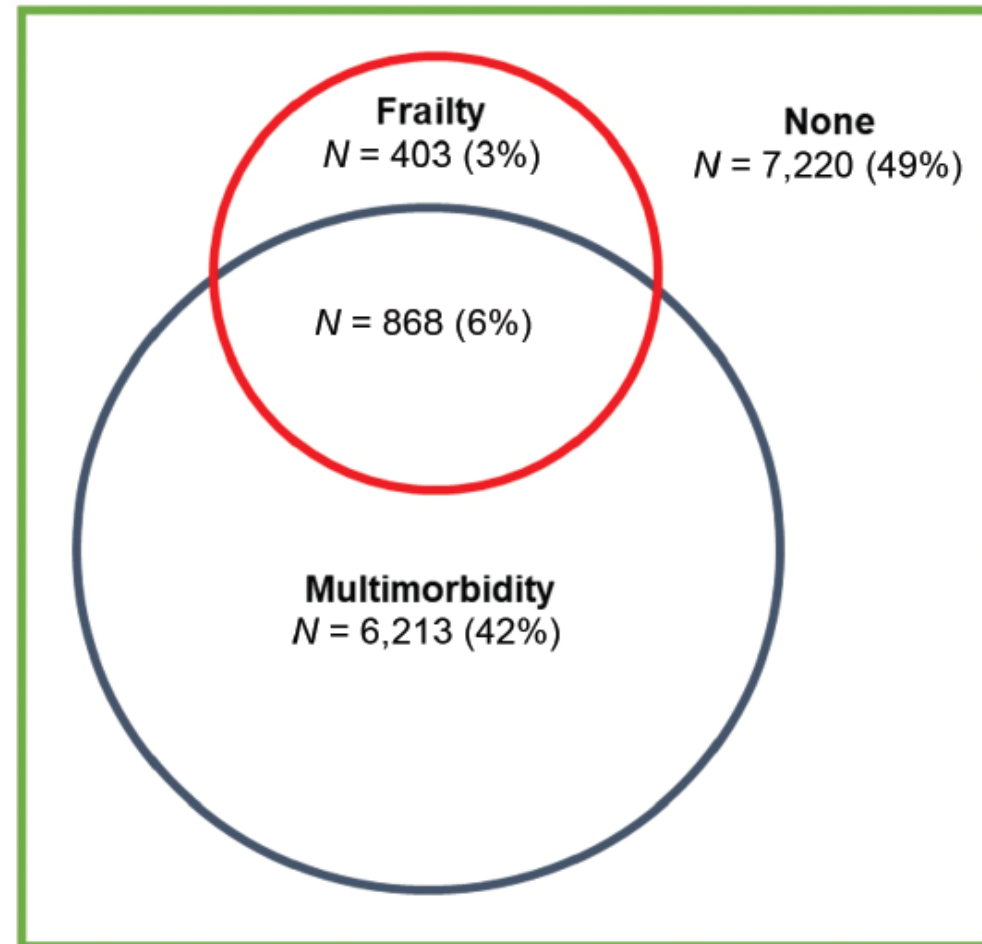


Figure 2. Overlap of frailty and multimorbidity (pooled data from nine studies including community-dwelling people; $N = 14,704$). Frailty was defined according to the Cardiovascular Health Study (CHS) criteria (by Fried and colleagues) and multimorbidity as 2+ diseases.

Vaccine preventable disease: HBV

Worldwide spread of HBV



360M

Approximately **360 million** individuals **worldwide** are chronically infected with **hepatitis B virus (HBV)**.

Approximately **10%** of all **HIV-infected people** are also chronically **coinfected with HBV**.

HIV/HBV coinfection: Liver damage

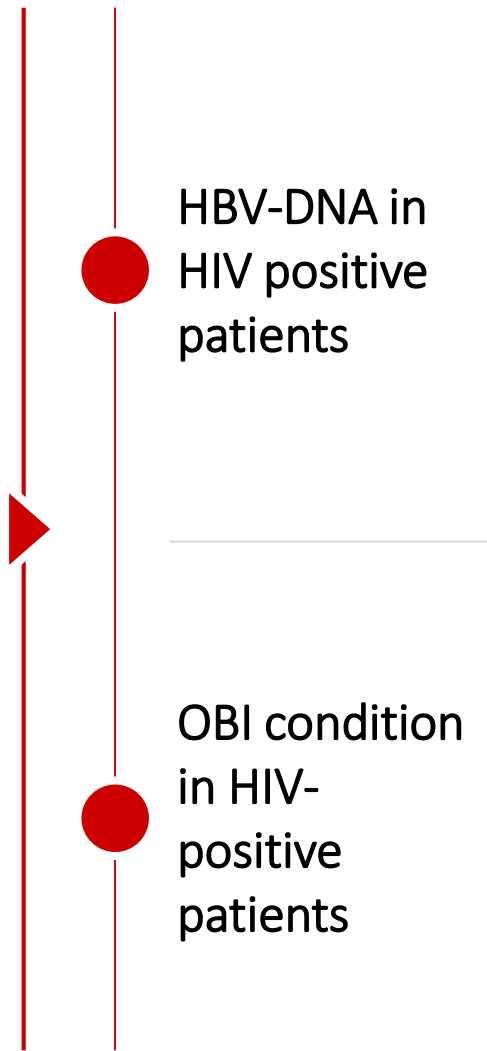
In **patients with HIV/HBV**, the **coinfection accelerates HBV-related liver damage**, with **faster liver fibrosis progression** and more frequent development of **ESLD** and **HCC** compared to HBV monoinfected patients.

HIV/HBV coinfection: Viro-immunological status

Conversely, the **presence of a simultaneously active HBV infection** affects the **viro-immunological status of HIV/HBV-coinfected patients**, which is usually characterized by a **lower CD4-positive lymphocyte count** at the onset and a **slower CD4 cell count recovery** after the start of cART

Vaccine preventable disease: HBV

The differences in the outcome between HIV monoinfected and HIV/HBV coinfectd populations persist despite cART



HBV-DNA in HIV positive patients

Even the condition of resolved HBV infection (presence of anti Hepatitis B c antigen [anti-HBc] in the absence of Hepatitis B surface antigen [HBsAg]) can often be associated with the appearance of detectable HBV-DNA in HIV-positive patients (occult HBV infection (OBI)).

OBI condition in HIV-positive patients

In HIV-positive subjects, the OBI condition has been associated with a low number of CD4-positive lymphocytes, elevation of alanine aminotransferase and more frequent AIDS-defining illnesses

RESEARCH

Open Access



Sero-prevalence of human immunodeficiency virus–hepatitis B virus (HIV–HBV) co-infection among pregnant women attending antenatal care (ANC) in sub-Saharan Africa (SSA) and the associated risk factors: a systematic review and meta-analysis

Hussein Mukasa Kafeero^{1,2*} , Dorothy Ndagire³, Ponsiano Ocama⁴, Abdul Walusansa² and Hakim Sendagire^{1,2}

HBV infected children born to HBV–HIV co-infected mothers are at an **increased risk of liver complications and liver diseases related death** than those born from HBV mono-infected mothers

HBV–HIV co-infection **escalates HBV replication** and hepatitis B pre-core antigen (HBeAg) sero-positivity increasing viral load

90–95% of the children who acquire HBV through the perinatal route progress to chronic infection

Vaccine preventable disease: HAV

- ▶ While studies conducted in countries of high HAV endemicity showed no differences in the HAV seroprevalence between HIV-positive and HIV-negative individuals, **the seroprevalence in countries of low endemicity was higher among HIV-positive individuals compared to HIV-negative individuals.**
- ▶ Among HIV-positive individuals, older age and injecting drug use were identified as the independent factors associated with seropositivity for HAV.
- ▶ The **duration of HAV viremia and stool shedding of HAV may be longer in HIV-positive individuals**, increasing the window of opportunity for wider transmission of HAV.

No specific disease manifestations in immunocompromised hosts or PWH have been described.

Vaccine preventable disease: Meningococcal diseases

- **5- to 24-fold increased risk of meningococcal disease in people with HIV compared with people without HIV**
- **Several outbreaks were associated with clubs and bathhouses.**

Some public health jurisdictions now recommend meningococcal vaccine for all men who have sex with men, regardless of HIV status

Vaccine preventable disease: Meningococcal diseases

- Estimates the incidence of laboratory-confirmed meningococcal bacteremia and meningitis in HIV-infected and uninfected individuals in Gauteng Province, South Africa in 2005
 - Evaluated whether HIV was a risk factor for mortality amongst patients with meningococcal disease from 2003 to 2007.
 - Evaluated whether HIV is associated with an increased risk of bacteremia.
- **1336 meningococcal cases.** Of 504 patients with known outcome, 308 (61%) had HIV serostatus data (138 HIV positive)
 - The estimated incidence in HIV-infected individuals was higher compared to incidence in HIV-uninfected individuals (CI 3.7–5.7, $P < 0.001$)
 - The case-fatality ratio (CFR) was 20% (27/138) amongst HIV-infected and 11% (18/170) amongst HIV-uninfected individuals [odds ratio (OR) 2.1, 95% CI 1.1–3.9].
 - HIV infection was associated with increased odds of bacteremia (OR 2.7, 95% CI 1.5–5.0).

Vaccine preventable disease: Varicella Zoster Virus

More than 95% of adults (aged >20 years) born in the United States have immunity to VZV, mostly due to primary VZV infection

Before the availability of ART, the incidence of herpes zoster was **more than 15-fold higher among PLW than among age matched controls without**. However, the risk of herpes zoster remains **threefold higher in adults with HIV** than in the general population

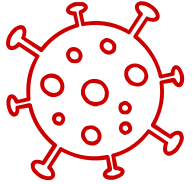
Herpes zoster can occur in adults with HIV at any CD4 T lymphocyte (CD4) cell count, but with CD4 counts <200 cells/mm³, the risk of disease is higher

The risk of herpes zoster in PLWH is increased in the 6-month period immediately after initiation of ART, possibly because of an immune reconstitution **inflammatory syndrome (IRIS)**-related mechanism.

PLW with CD4 <200 are at highest risk of herpes zoster–related complications, including **disseminated herpes zoster**.

The central nervous system (CNS) is a target organ for herpes zoster dissemination in patients coinfecting with HIV. Various VZV-related neurologic syndromes occur in people with HIV, including CNS vasculitis, multifocal leukoencephalitis, ventriculitis, myelitis and myeloradiculitis, optic neuritis, cranial nerve palsies and aseptic meningitis.

Vaccine preventable disease: HPV



Human papillomavirus prevalence has been reportedly **higher in HIV-positive women.**



Inability of HIV compromised immune system to control the replication and expression of HPV in the body and this may lead to **faster progression of invasive cancer** than in normal individuals.



In **HIV-positive patients, HPV infection appears to persist longer** than among healthy individuals, **thus increasing the risk of developing cancer.**



Females with multiple HR-HPV type infections are more susceptible to HIV infection, on the other hand, females positive for HIV are prone to acquiring HPV infection

From: **High-grade Dysplasia in Anogenital Warts of HIV-Positive Men**

JAMA Dermatol. 2016;152(11):1225-1230. doi:10.1001/jamadermatol.2016.2503

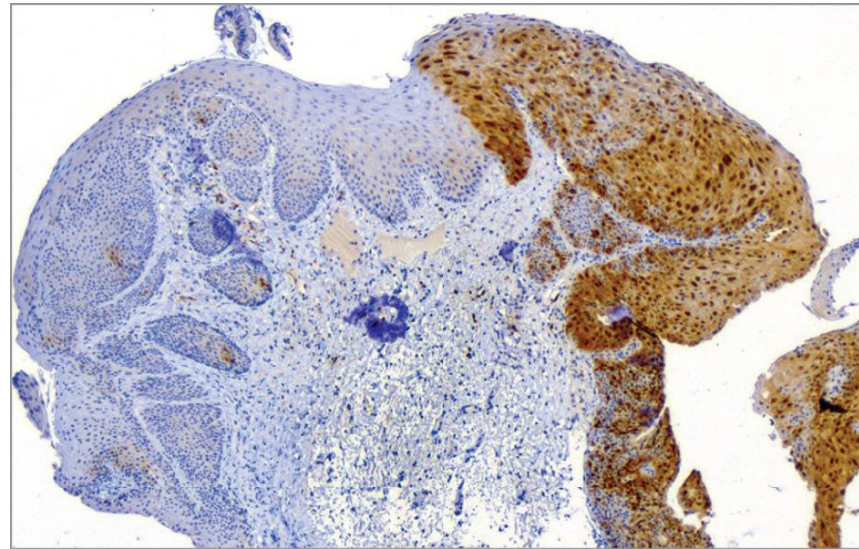


Figure Legend:

Immunohistochemical Analysis of p16^{INK4a} Expression in an Intraanal Lesion that Clinically Appeared as Anogenital Warts, but Histopathologically Revealed Focal Areas of High-Grade Dysplasia. The lesion clinically appeared as an anogenital wart, but histopathologically revealed focal areas of high-grade dysplasia. p16^{INK4a} is an indirect marker of high-risk human papillomavirus E7 oncogene expression. Strong nuclear and cytoplasmic p16^{INK4a} expression is present in the areas of high-grade dysplasia, whereas p16^{INK4a} staining is negative in the anogenital wart part of the lesion (hematoxylin-eosin, original magnification × 1000)

Vaccine preventable disease: HPV

- Recent evidence indicates that **anogenital lesions of patients who are HIV+ morphologically appearing as benign AGWs** may harbor focal areas of high-grade dysplasia
- 
- **HPV analyses** including **genotyping, viral load determination, and immunohistochemical analysis** of such lesions in comparison to similar-looking AGWs of immunocompetent individuals.
 - In contrast to AGWs of HIV+ MSM, **none of the evaluated lesions of immunocompetent patients harbored focal areas of low-grade or high-grade dysplasia.**
- 
- In contrast to patients who are **HIV–**, **AGWs of HIV+ MSM** may harbor high-grade dysplasia or even cancer, although the clinical appearance is that of classical AGWs.
 - Accordingly, **all HPV-induced anogenital lesions of high-risk patients such as HIV+ MSM should be evaluated histopathologically and by p16INK4a and/or Ki67 immunohistochemical analysis and HPV genotyping should be considered** if areas of dysplasia are detected.

Vaccine preventable disease: *S. pneumoniae*

PLWHA have a higher risk of noninvasive and invasive pneumococcal disease.

Study of episodes of IPD in PLWHA in a reference institute for Infectious Diseases in Rio de Janeiro, Brazil, from 2005 to 2020

Comparison of demographic, clinical, and laboratory features of control patients, selected based on age, gender, and healthcare scenario

- ✓ Patients with HIV and IPD had a higher median CD4 count compared with the control group (267 cells/mm³ vs. 140 cells/mm³), although both groups could be considered immunosuppressed.
- ✓ Alcoholism, hepatic cirrhosis, and lower nadir CD4 count were associated with the risk of death in patients with IPD.
- ✓ **The vaccination rate was less than 20%**, which leads us to reinforce the recommendation of vaccination
- ✓ Nadir CD4 counts were lower in PLWHA and IPD who died

Vaccine preventable disease: Influenza

Some studies of influenza have noted higher hospitalization rates and increased mortality among people with HIV however, these findings have not been observed in all settings:

People with HIV are at high risk of serious influenza-related complications, particularly in low-and-middle income country settings

Clin Infect Dis. 2020;70(10):2121-2130; Influenza Other Respir Viruses. 2018;12(1):22-29.

Vs

The prognosis of patients on well-controlled cART was similar to uninfected population

Increased morbidity may be greatest for people with HIV not on antiretrovirals (ARV) or with advanced disease.

Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. National Institutes of Health, Centers for Disease. Reviewed January 10, 2024

Vaccine preventable disease: SARS-COV2

- PWH are at a **higher risk of severe illness, hospitalization, and death** from COVID-19 than their uninfected peers, when adjusted for age, comorbidities, and sociodemographic factors.
- **More advanced immunosuppression and detectable viremia** have been associated with poorer outcomes; antiretroviral therapy appears protective
- **Intersecting social and structural determinants of health, older biological age, and greater frequency of age associated comorbidities** are associated with worse outcomes for PWH with COVID-19

Less clear whether PWH are at a higher risk of acquiring COVID-19, in the absence of additional risk factors.

British HIV Association guidelines on the use of vaccines in HIV-positive adults 2015

© 2015 British HIV Association



- It is envisaged that the **HIV specialist** should **provide overall guidance on vaccine use** and enlist the help of primary care physicians for vaccine administration.



- **Education of healthcare providers** and **good communication** are **key requirements** to ensure **successful implementation** of this guidance.



- **Despite evidence** that **HIV-positive persons benefit from vaccination**, there are **persisting perceptions** about disease incidence and burden, and vaccine effectiveness and safety, which **affect vaccination practices** among health professionals caring for HIV-positive patients.

Minimal prevalence of HPV vaccination and common occurrence of high-risk HPV types in pregnant women with HIV: data from a national study in Italy

European Journal of Clinical Microbiology & Infectious Diseases (2022) 41:505–509

Marco Floridia · Giulia Masuelli · Beatrice Tassis · Marina Ravizza et Al. on behalf of The Italian Group on Surveillance of Antiretroviral Treatment in Pregnancy

Only 8 women
(1.1%) had
been
vaccinated
prior to the
current
pregnancy

Table 1 Clinical and demographic information

	All	Vaccinated	Not vaccinated	P value
Age (years) (median, IQR) (n: 731)	33 (28–37)	36 (27.5–39.5)	33 (28–37)	0.504
Months from HIV diagnosis (median, IQR) (n: 724)	57.5 (12.25–115)	72 (43.5–165)	57 (12–115)	0.373
HIV already diagnosed before pregnancy (%; n/N) (n: 728)	80.8 (588/728)	100 (7/7)	80.6 (581/721)	0.223
African ethnicity (%; n/N) (n: 728)	44.6 (325/728)	37.5 (3/8)	44.7 (322/720)	0.485
History of intravenous drug use (%; n/N) (n: 726)	2.9 (21/726)	0 (0/8)	2.9 (21/718)	0.790
History of sexually transmitted diseases* (%; n/N) (n: 706)	25.6 (181/706)	12.5 (1/8)	25.8 (180/698)	0.350
HBV-coinfected (%; n/N) (n: 711)	11.7 (83/711)	12.5 (1/8)	11.7 (82/703)	0.631
HCV-antibody positive (%; n/N) (n: 708)	6.4 (45/708)	25 (2/8)	6.1 (43/700)	0.087
Primiparous (%; n/N) (n: 729)	41.6 (303/729)	37.5 (3/8)	41.6 (300/721)	0.558
Recent substance use** (%; n/N) (n: 707)	4.0 (28/707)	0 (0/8)	4.0 (28/699)	0.723
Alcohol abuse*** (%; n/N) (n: 711)	0.4 (3/711)	0 (0/8)	0.4 (3/703)	0.967
Smoking, any (%; n/N) (n: 718)	17.5 (126/718)	25 (2/8)	17.5 (124/710)	0.423
Smoking, moderate/heavy (> 10 cigarettes per day) (%; n/N) (n: 718)	9.2 (66/718)	12.5 (1/8)	9.2 (65/710)	0.539
HIV symptomatic disease (CDC disease stage B or C) (%; n/N) (n: 719)	6.5 (47/719)	0 (0/8)	6.6 (47/711)	0.581
CD4 count/mm ³ at first visit in pregnancy (median, IQR) (n: 681)	543 (397.5–703)	455 (405.75–757)	545 (396–703)	0.560
CD4<200/mm ³ at first visit in pregnancy (%; n/N) (n: 681)	7.6 (52/681)	12.5 (1/8)	7.6 (51/673)	0.472
HIV-negative partner (serodiscordant couple) (%; n/N) (n: 722)	47.4 (342/722)	0 (0/8)	47.9 (342/714)	0.013
On ART at conception (%; n/N) (n: 728)	69.0 (502/728)	75 (6/8)	68.9 (496/720)	0.525
On protease inhibitors at conception (%; n/N) (n: 725)	41.5 (301/725)	62.5 (5/8)	41.3 (296/717)	0.197
On nonnucleoside reverse transcriptase inhibitors at conception (%; n/N) (n: 725)	18.6 (135/725)	0 (0/8)	18.8 (135/717)	0.191
On integrase inhibitors at conception (%; n/N) (n: 725)	11.7 (85/725)	12.5 (1/8)	11.7 (84/717)	0.633
Body mass index (BMI, kg/m ²) (median, IQR) (n: 615)	23.2 (20.8–26.1)	22.8 (20.9–25.6)	23.1 (20.8–26.1)	0.883

Implementation of EACS vaccination recommendations among people living with HIV

Infection (2022) 50:1491–1497

Sven Breitschwerdt · Carolynne Schwarze-Zander · Ahmad Al Tayy et Al.

**No central recording of vaccination coverages
has been set up in Germany**

305 PLWH (82.3% male, 17.7% female)

CD4 + T cell count was 543 (IQR 304–770), and for 297 (97.4%) PLWH CD4 + T cell count was $\geq$ 200/ul.

The viral load was undetectable (< 40 copies/ml) in 289 (94.8%) cases.

Highest vaccination rates were observed for HAV (87.4%), *Streptococcus pneumoniae* (77.4%) and Influenza (76.5%). 64.3% PLWH got vaccinated against HBV (64%).

Lowest vaccination rates were detected for HPV (0%) and *Neisseria meningitidis* (3.0%)

Vaccination rates among PLWH are **higher compared to the general German population.**

Implementation of EACS guidelines into daily routine though is not fully executed and the need for improving vaccination rates has to be emphasized.

Centrally organized vaccination registers as well as electronic medical records could be helpful

Potenziali barriere a un'adeguata copertura vaccinale nelle persone con infezione da HIV

Legate al paziente e a condizioni ambientali

- **Popolazioni “Hard to reach”**
- **Vaccine hesitancy**

Legate alla pratica medica

- **Scarsa conoscenza della condizione di fragilità del paziente**
- **Scarsa consapevolezza dell'importanza della vaccinazione come strumento di prevenzione**
- **Scarsa consapevolezza dell'efficacia e sicurezza dei vaccini anche in persone fragili**
- **Complessità della gestione del paziente fragile (i.e. necessità di schedule vaccinali ad hoc)**



Hard To Reach

Meccanismi che intervengono in determinate circostanze sociali ed ambientali e che precludono una corretta copertura vaccinale a determinati soggetti

DEMAND	High	Hard to reach	Easy to reach AND Easy to vaccinate
	Low	Hard to reach AND Hard to vaccinate	Hard to vaccinate
		Low	High
	SUPPLY		

HARD-TO-REACH POPULATIONS

“Those facing supply-side barriers to vaccination due to geography by distance or terrain, transient or nomadic movement, healthcare provider discrimination, lack of healthcare provider recommendations, inadequate vaccination systems, war and conflict, home births or other home-bound mobility limitations, or legal restrictions”

HARD-TO-VACCINATE POPULATIONS

“those who are reachable but difficult to vaccinate because of demand-side barriers such as distrust, religious beliefs, lack of awareness, poverty or low-socioeconomic status, lack of time, or gender-based discrimination”

THIS POPULATION SEEMS AWFULLY HARD TO REACH.

WE'RE RIGHT HERE... ALL
YOU NEED TO DO IS TRY!



Review

Immunogenicity and Efficacy of Vaccination in People Living with Human Immunodeficiency Virus

Eeva Tortellini ^{1,*} , Yann Collins Fosso Nguangue ¹, Federica Dominelli ¹ , Mariasilvia Guardiani ¹ , Carmen Falvino ¹, Fabio Mengoni ¹, Anna Carraro ¹ , Raffaella Marocco ², Patrizia Pasculli ¹ , Claudio Maria Mastroianni ¹ , Maria Rosa Ciardi ¹, Miriam Lichtner ^{2,3}  and Maria Antonella Zingaropoli ¹

	Humoral and Cellular Immunity	Clinical efficacy
 HAV	A slight decrease in antibody titres over time. CD4+ T-cells are critical for long-term vaccine-induced protection	Increasing the number of doses (from 2 to 3) would increase the rate of seroconversion
 HBV	HBsAb titers decrease over time. The magnitude of the IFN- γ - and TNF- α -based T-cell responses to HBsAg were not too high after the completion of the vaccination schedule	Depending on absolute CD4+ T-cell count
 HPV	A decline in antibody titres between 2–5 years after the last dose vaccination	Depending on absolute CD4+ T-cell count
 Influenza	Only 60% developed protective antibody titers after immunization. CTL response magnitude is inversely correlated with disease severity	Increasing the number of doses improved protection
 MPXV	Higher and longer lasting antibody response after the third dose	Depending on absolute CD4+ T-cell count
 SARS-CoV-2	Booster dose is able to induce a robust B-cell memory response. Cellular immunity contributes to the vaccine's effectiveness against viral variants and to protect from severe forms	Depending on absolute CD4+ T-cell count
 <i>S. pneumoniae</i>	PCV13 induces a specific antibodies and memory B-cells and a T-cell-dependent response providing long-lasting protection. PPSV3 induces a T-cell-independent humoral response	Less immunogenic in PLWH as compared to general population due to a mitigated immune response
 VZV	Antibody response after 1 dose. Higher memory T-cell responses	Depening on cell-mediated immunodeficiency and immunocompromised state

Immunogenicità dei vaccini nelle persone con infezione da HIV

- Immunogenicità dei vaccini anti **SARS COV 2** in pazienti con infezione ben controllata comparabile alla popolazione generale ([AIDS](#). 2023 Jan 1; 37(1))
- **Pneumococco**: riduzione dei casi di malattia invasiva grazie a vaccinazione PCV (*British HIV Association guidelines on the use of vaccines in HIV-positive adults 2015*)
- **HBV**: maggiore risposta per schedule a 4 dosi rispetto a 3 dosi e per CD4 più elevati ([Front Immunol.](#) 2021; 12: 745541.)
- **HAV**: risposta potenzialmente subottimale per pazienti immunodepressi, con possibili strategie ad HOC (es. booster a 5 anni, completare schedula vaccinale di 3 dosi entro 12 mesi) (*British HIV Association guidelines on the use of vaccines in HIV-positive adults 2015*)
- **HPV**: sieroconversione vicina al 100% in uomini e donne (seppure mancanza di dati sulla progressione delle lesioni verso lesioni cancerose) ([Sci Rep.](#) 2021; 11: 4954.)

EACS (European AIDS Clinical Society) guidelines

- ▶ Vaccinate according to national guidelines for healthy population, **preferably after having achieved suppressed viraemia and immune reconstitution** (CD4 count ≥ 200 cells/ μ L or $\geq 15\%$)
- ▶ Consider repeating vaccinations performed at CD4 count < 200 cells μ L (or $< 15\%$) or unsuppressed viraemia once adequate immune reconstitution is achieved (HIV VL undetectable and CD4 count ≥ 200 cells/ μ L or $\geq 15\%$)
- ▶ As vaccine responses may be significantly lower in persons with HIV, do not use rapid schedules and consider antibody titres to assess their effectiveness if vaccinated at CD4 count < 200 cells/ μ L ($< 15\%$) or unsuppressed viremia. Observe boosters and all post-exposure measures (particularly after potential rabies exposure)
- ▶ Avoid polysaccharide vaccination

For **attenuated live vaccines*** (in addition to restrictions for general population):

- Contraindicated if CD4 count < 200 cells/ μ L ($< 15\%$) and/or AIDS. Impaired protection after vaccination with unsuppressed viraemia. Administer immunoglobulins if exposed and not yet vaccinated
- **Oral live typhoid** Preferred if CD4 count ≥ 200 cells/ μ L ($\geq 15\%$). Contraindicated if CD4 count < 200 cells/ μ L ($< 15\%$): then give inactivated parenteral polysaccharide vaccine

***varicella, measles, mumps, rubella, yellow fever**

Vaccination

- | | |
|---|---|
| <ul style="list-style-type: none">• Vaccinate according to national guidelines for healthy population, preferably after having achieved suppressed viraemia and immune reconstitution (CD4 count ≥ 200 cells/μL or $\geq 15\%$)• Consider repeating vaccinations performed at CD4 count < 200 cells/μL (or $< 15\%$) or unsuppressed viraemia once adequate immune reconstitution is achieved (HIV VL undetectable and CD4 count ≥ 200 cells/μL or $\geq 15\%$)• As vaccine responses may be significantly lower in persons with HIV (i.e. lower seroconversion rates, faster titre decline), do not use rapid schedules (e.g. rabies, tick-borne encephalitis, HAV/HBV) and consider antibody titres to assess their effectiveness if vaccinated at CD4 count < 200 cells/μL ($< 15\%$) or unsuppressed viraemia (e.g. rabies, tick-borne encephalitis, HAV, meningococci). Be attentive to observe boosters and all post-exposure measures (particularly after potential rabies exposure)• Avoid polysaccharide vaccination• For background data, see www.bhiva.org/vaccination-guidelines.aspx and www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf | <ul style="list-style-type: none">• For attenuated live vaccines⁽ⁱ⁾
(in addition to restrictions for general population):<ul style="list-style-type: none">• *Varicella, measles, mumps, rubella, yellow fever
Contraindicated if CD4 count < 200 cells/μL ($< 15\%$) and/or AIDS. Impaired protection after vaccination with unsuppressed viraemia. Administer immunoglobulins if exposed and not yet vaccinated• Oral live typhoid
Preferred if CD4 count ≥ 200 cells/μL ($\geq 15\%$). Contraindicated if CD4 count < 200 cells/μL ($< 15\%$): then give inactivated parenteral polysaccharide vaccine• Mpox (Jynneos, Imvamune® or Imvanex®)
This live but attenuated non-replicating modified vaccinia Ankara (MVA) strain vaccine is safe in persons with HIV, although effectiveness may be lower if CD4 count < 200 cells/μL ($< 15\%$) and/or people living with unsuppressed HIV |
|---|---|

- Tutti i pazienti HIV-positivi, preferibilmente se $CD > 200/mm^3$ ed HIV-RNA < 50 cp/mL sono da valutare per vaccinazioni.
- Ai pazienti che nonostante soppressione RNA restano indefinitamente con $CD4 < 200/mm^3$ (“immunological non responders”), andrebbero comunque offerte le vaccinazioni per pneumococco e influenza

Living with HIV and Getting Vaccinated: A Narrative Review

Andrea De Vito 1, Agnese Colpani , Mattia Trunfio, Vito Fiore , Giulia Moi , Marco Fois , Nicola Leoni , Stefano Ruii , Sergio Babudieri , Andrea Calcagno and Giordano Madeddu



vaccines

Table 7. Comparison of five HIV guideline recommendations for the *Neisseria meningitidis* vaccine administration.

	BHIVA [22,25]	EACS [24]	NIH [23]	SIMIT [27]	WHO [26]
Who to vaccinate?	All aged < 25 if not already vaccinated or if they received the last MenC doses below the age of 10 years; Presence of specific risk factors: asplenia or persistent complement component deficiency; Risk of exposure through travel	According to the risk profile: - Travel - MSM - Contact with Children	All aged > 18 years if not already vaccinated	All people	Recommended for children in some high-risk populations
Type of vaccine	MenC, MenACWY, Men B in people < 25 years MenC, MenB, and/or MenACWY for high-risk people; MenACWY: exposed to travel	MenACWY; MenB according to national guidelines	MenACWY; MenB not indicated	MenACWY; MenB	NP
Interval doses	Two doses with 2 months interval	Two doses with 2 months interval	Two doses with 2 months interval	MenACWY: two doses with 2–3 months interval MenB: two doses with at least one-month interval	NP
Booster	MenACWY every five years if ongoing risk through travel or due to underlying condition	NP	Repeat vaccination every 5 years throughout life	Considerer repeat vaccination with MenACWY every 5 years to keep high immunity	NP

NP: not present.

Table 2. Comparison of five HIV guideline recommendations for the HBV vaccine administration.

	BHIVA [22,25]	EACS [24]	NIH [23]	SIMIT [27]	WHO [26]
Who to vaccinate?	All if seronegative	All if seronegative	All if seronegative	All if seronegative	All if seronegative
Type of vaccine and doses	Yeast-based: 40 µg Adjuvanted: 20 µg Four doses: 0, 1, 2, 6 months	According to national guidelines	Yeast-based: 40 µg Adjuvanted: 20 µg Three doses	Yeast-based: 40 µg Adjuvanted (preferred): 20 µg Three doses	Suggest using double doses
Target IgG	>100 UI/L 8 weeks after the last doses	>100 UI/L	≥10 mIU/mL 8 weeks after the last doses	>100 UI/L	>100 UI/L
Occult HBV*	One dose; check HBsAb two weeks later; if HBsAg < 10 IU/L, offer full vaccination	NP	NP	One dose; check HBsAb two weeks later; if HBsAg < 10 IU/L, offer full vaccination	NP
Differences for people with low CD4/mm ³	No differences in doses; repeat HBsAb screening more frequently if CD4 cell/mm ³ < 350	For people with “particularly low CD4”, consider a double dose (40 µg) or use a more immunogenetic vaccine	No difference in doses. For non-responder people with CD4/mm ³ < 200: delay re-vaccination until CD4 > 200/mm ³	No difference in doses. For non-responder people with CD4/mm ³ < 500: delay re-vaccination until CD4 > 500/mm ³	NP
Boosting	People with HBsAg < 10 UI/L: three more doses People with HBsAg < 100 UI/L but >10 UI/L: one dose	People with HBsAg < 10 UI/L: three more doses People with HBsAg < 100 UI/L but >10 UI/L: one dose	Non-responder: revaccinate with 3–4 doses For people whose HBsAg level fall below 10 UI/L: one dose if not receiving tenofovir-based regimen	People with HBsAg < 10 UI/L: three more doses People with HBsAg < 100 UI/L but >10 UI/L: one dose	People with HBsAg < 10 UI/L: three more doses People with HBsAg < 100 UI/L but >10 UI/L: one dose

Infection	Vaccination rationale	Comment
Influenza Virus	Higher rate of pneumonia. Explicitly recommended in all persons with HIV	Yearly, use 4-valent vaccine if available
Human Papilloma Virus (HPV)	Shared risk with HIV of contracting infection. Higher rate of cervical and anal cancer	Vaccinate with 3 doses between ages 9 and 45 (health insurance coverage differs by country according to age, sex, sexual orientation). Use 9-valent vaccine if available. Persons treated for high grade dysplasia could benefit from a full course vaccination for secondary prevention
Hepatitis B Virus (HBV)	Shared risk with HIV of contracting infection. Untreated HIV accelerates progression of liver disease	Vaccinate if seronegative. Repeat doses until anti-HBs antibodies ≥ 10 IU/L / ≥ 100 IU/L according to national Guidelines. In order to reach ≥ 100 IU/L in non-responders repeat 3 doses if anti-HBs < 10 IU/L, 1 dose if anti-HBs < 100 IU; ⁽⁹⁾ consider double dose (40 µg) or use more immunogenic vaccines in particular with low CD4 count and high HIV VL. No benefit for intradermal application. See page 127
Hepatitis A Virus (HAV)	According to risk profile (travel, close contact with children, MSM, IVU, active hepatitis B or C infection, chronic liver disease)	Vaccinate if seronegative. Consider checking antibody titres in persons at high risk. Weaker immune response expected with HAV/HBV co-vaccine. See page 127
<i>Neisseria meningitidis</i>	According to risk profile (travel, close contact with children, MSM)	Use conjugated ⁽¹⁰⁾ 4-valent vaccine (for serotypes A, C, W-135, Y; 2 doses 1-2 months apart) if available. Booster every five years if exposure continues. Polysaccharide vaccine no longer recommended. Vaccinate against Meningococcus serotype B according to national guidelines
<i>Streptococcus pneumoniae</i>	Higher rate and severity of invasive disease. Vaccine explicitly recommended for all persons with HIV	One dose of a conjugated vaccine: PCV-13, PCV-15 or PCV-20a for all persons according to availability and national guidelines, also if pre-vaccinated with PPV-23 polysaccharide vaccine. For patients vaccinated with PCV-13 or PCV-15, one dose of PPV-23 at least 2 months after the conjugate vaccine may be considered in some national guidelines for all persons with HIV
Varicella Zoster Virus (VZV)	Higher rate and severity of both chicken-pox and zoster	Perform serology if exposure history negative. Vaccinate if seronegative. For contraindications, see*. To prevent shingles, preferably use adjuvant recombinant sub-unit vaccine over live-attenuated vaccine according to national guidelines
Yellow Fever Virus	Mandatory for travel to selected countries (provide exemption letter if no true risk of exposure)	Contraindicated if past or current haematological neoplasia or thymus affection (thymoma, resection/radiation) For other contraindications, see*. Booster every 10 years
Rabies		If pre-exposure rabies vaccination is administered in persons with CD4 ≥ 200 cells/ μ L, 2-dose (days 0 and 7) IM schedule is recommended. For persons with CD4 count < 200 cells/ μ L or detectable viremia, consider pre-exposure vaccination with 3 doses (0, 7, 21 or 28 days) and antibody titre measurement 14 days later. In case of rabies postexposure prophylaxis (PEP) in unvaccinated persons, perform immediate wound cleaning, infiltration of human rabies immunoglobulin (HRIG) within and around the wound and days 0, 3, 7 and 14 IM administration of rabies vaccine in people with HIV with CD4 ≥ 200 cells/ μ L. In people with HIV with CD4 < 200 cells/ μ L or detectable viremia, PEP should comprise a 5-dose vaccination regimen (days 0, 3, 7, 14, and 28), with one dose of HRIG and additional vaccine dose is recommended if rabies serology demonstrates inadequate titers during the follow-up (antibody levels < 0.5 IU/mL). In vaccinated people with HIV, the PEP recommendation for a 2/3-dose vaccination series has not changed

***Vademecum per le vaccinazioni
dell'adulto "a rischio"
(per condizione o patologia).***

Edizione 1.0

VACCINAZIONI INDICATE

<u>Anti-pneumococcica</u>
<u>Anti-zoster (RZV)</u>
<u>Anti-meningococcica</u> MCV4: 1 o 2 dosi (seconda dose dopo 4-8 sett) MenB: 2 o 3 dosi (schedula differente, a seconda che si utilizzi 4CMenB o MenB-fHbp)
<u>Antinfluenzale</u>
<u>COVID</u> : secondo indicazioni ministeriali (di solito con vaccino antinfluenzale)
<u>HPV</u> : in particolare, nei soggetti tra 18 e 45 anni oppure se AIN2 e/o CIN2 e oltre
<u>Anti-Haemophilus</u> : se mai vaccinato, Hib 1 dose (non indicata da tutti)
<u>dTap</u> : richiamo come per popolazione generale
<u>HBV</u> : se non immune
<u>HAV</u> : se non immune
<u>HMPX</u> : se ad elevato rischio di trasmissione
<u>MPR</u> : se non immune
<u>Varicella</u> : se non immune

Grazie dell'attenzione