Infezioni opportunistiche di ritorno in Late-Presenters PWH

Pandora-Virtual 2025

Antonio Di Biagio

COMPUTED TOMOGRAPHY OF THE CENTRAL NERVOUS SYSTEM

A symposium entitled "Update on Computed Tomography of the Central Nervous System" will be held at the Acapulco Princess Hotel in Acapulco, Mexico, February 25-March 2. The fee is $385.

Contact the Program Coordinator, Office of Continuing Education, Upstate Medical Ctr., State University of New York, 750 E. Adams St., Syracuse, NY 13210; or call (315) 473-4304.

PEDIATRIC DERMATOLOGY

The Ninth Annual Pediatric Dermatology Seminar will be held at the Carillon Beach Hotel in Miami Beach, Fla., February 25-28. The fee is $190.

Contact Dr. Guinter Kahn, 16800 N.W. 2d Ave., Miami, FL 33169; or call (305) 652-8600.

CLINICAL GENETICS

A symposium entitled "Clinical Genetics for Primary Care Physicians" will be held at the University of Wisconsin in Madison on February 26 and 27. The fee is $180.

Contact Sarah Z. Aslakson, Continuing Medical Education, 465B WARF Bldg., 610 Walnut St., Madison, WI 53706; or call (608) 263-2856.

SPECIAL REPORT

EPIDEMIOLOGIC ASPECTS OF THE CURRENT OUTBREAK OF KAPOSI'S SARCOMA AND OPPORTUNISTIC INFECTIONS*

SINCE June 1981, the Centers for Disease Control (CDC) has learned of an increased occurrence of Kaposi's sarcoma, *Pneumocystis carinii* pneumonia, and other serious opportunistic infections concentrated among homosexual men in the United States. After receiving the initial reports,[1,2] the CDC formed a task force to undertake surveillance for these disorders and conduct epidemiologic and laboratory investigations. This report describes these surveillance activities and summarizes current knowledge of the epidemiologic aspects of this outbreak.

Clinical Infectious Diseases
MAJOR ARTICLE
IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD

Time Trends in Causes of Death in People With Human Immunodeficiency Virus: Insights From the Swiss HIV Cohort Study

M. S. R. Weber,[1,2] J. J. Duran Ramirez,[1,2] M. Hentzien,[3,4,5] M. Cavassini,[6] E. Bernasconi,[7] E. Hofma
H. Kovari,[9] M. Stöckle,[10] P. Schmid,[11] D. Haerry,[12] D. L. Braun,[1,2,a] H. F. Günthard,[1,2,a] K. Kusejko[1,2,a]

[1]Department of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, Zurich, Switzerland; [2]Institute of Medical Vi
Unit, Department of Infectious Diseases, University Hospital Geneva, Geneva, Switzerland; [4]Department of Medicine, University of Ge
Ardenne University, Reims, France; [6]Department of Infectious Diseases, Lausanne University Hospital, University of Lausanne, Lausanne
Hospital Lugano EOC, University of Geneva and University of Southern Switzerland, Lugano, Switzerland; [8]Department of Infectious Disea
Bern, Switzerland; [9]Center for Infectious Diseases, Klinik im Park, Zürich, Switzerland; [10]Division of Infectious Diseases and Hospital E
Basel, Switzerland; [11]Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital St Gallen, St Gallen, Switzerland;

2024

Non-AIDS cancers now the leading cause of death

AIDS and liver complications have dropped dramatically

RUOLO DELLA ART !!

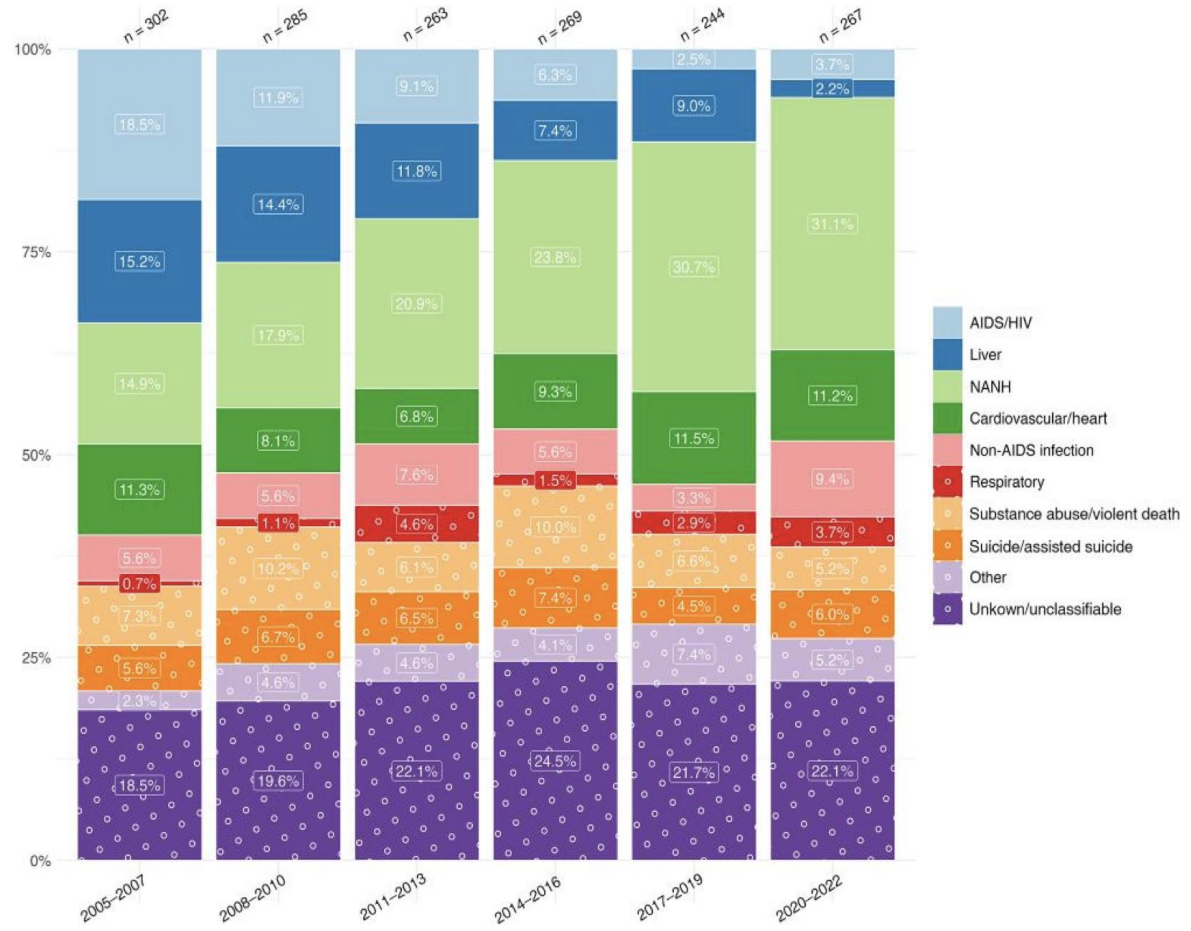
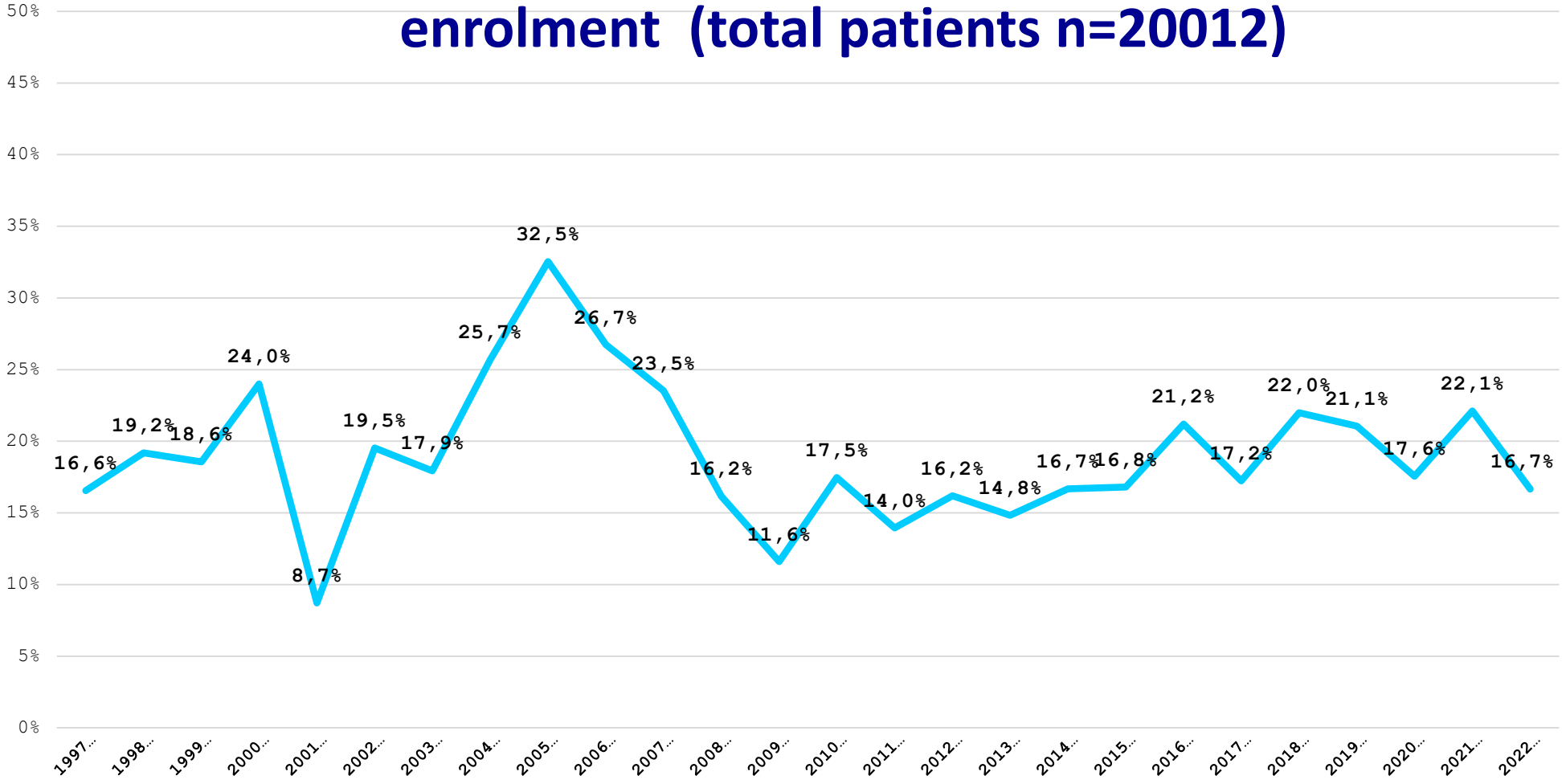


Figure 1 Time trends in causes of death from 2005 to 2022, stratified by 3-year periods. Single causes of death are categorized into broader categories as outlined in Table 1. The x-axis includes time periods from 2005 to 2022, grouped into 3-year intervals; y-axis, the percentage distribution for each cause-of-death category; number above bar, the total reported deaths for the corresponding 3-year period. Abbreviations: HIV, human immunodeficiency virus; NANH, non-AIDS, non-hepatic.

Prevalence of AIDS presenters (n=3615) according to calendar year at enrolment (total patients n=20012)

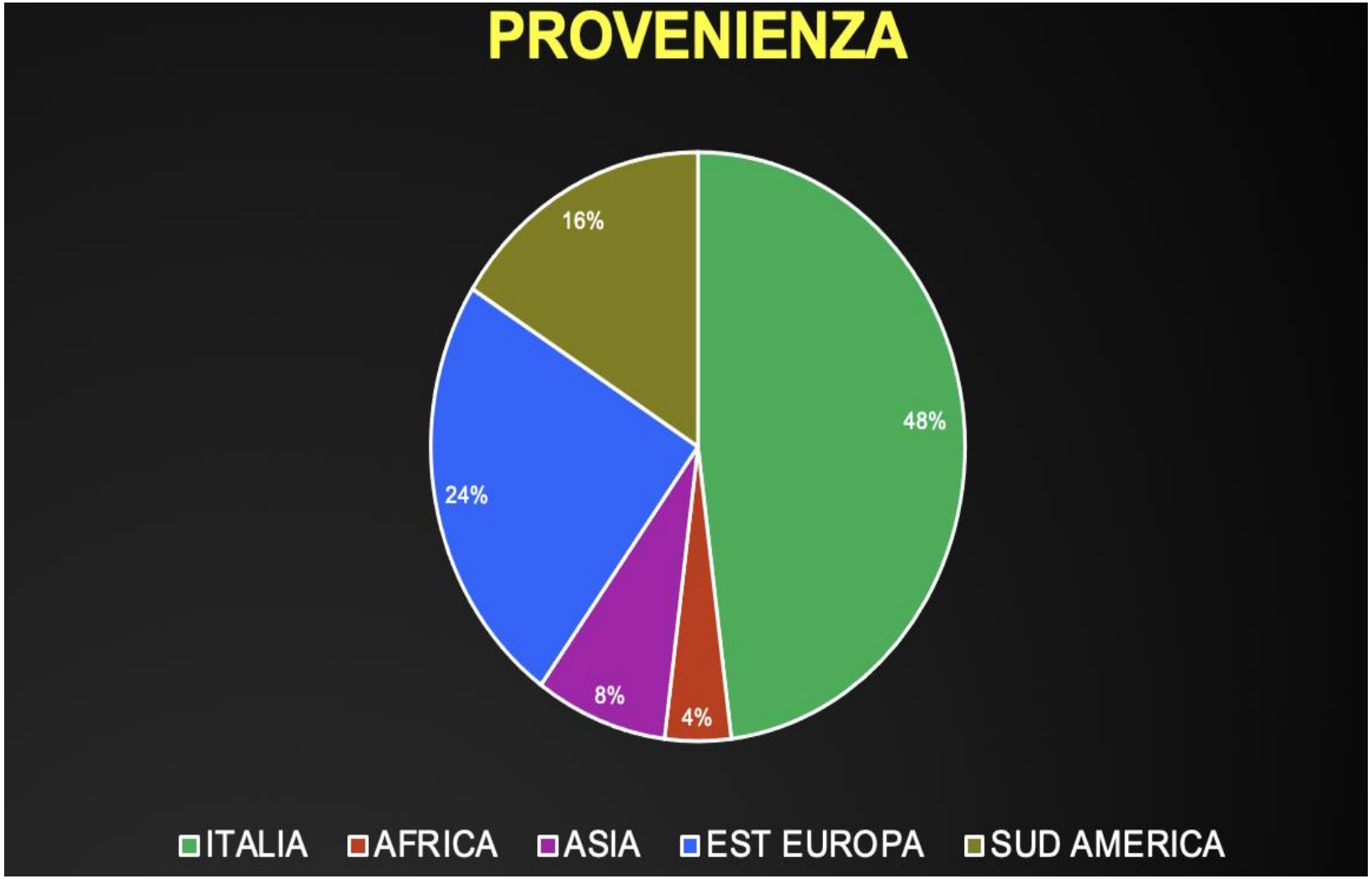


Jan 2023 Report

Dati demografici

- **Nuove diagnosi: 25**
  - Età media: 41,6
  - F=7 M=18

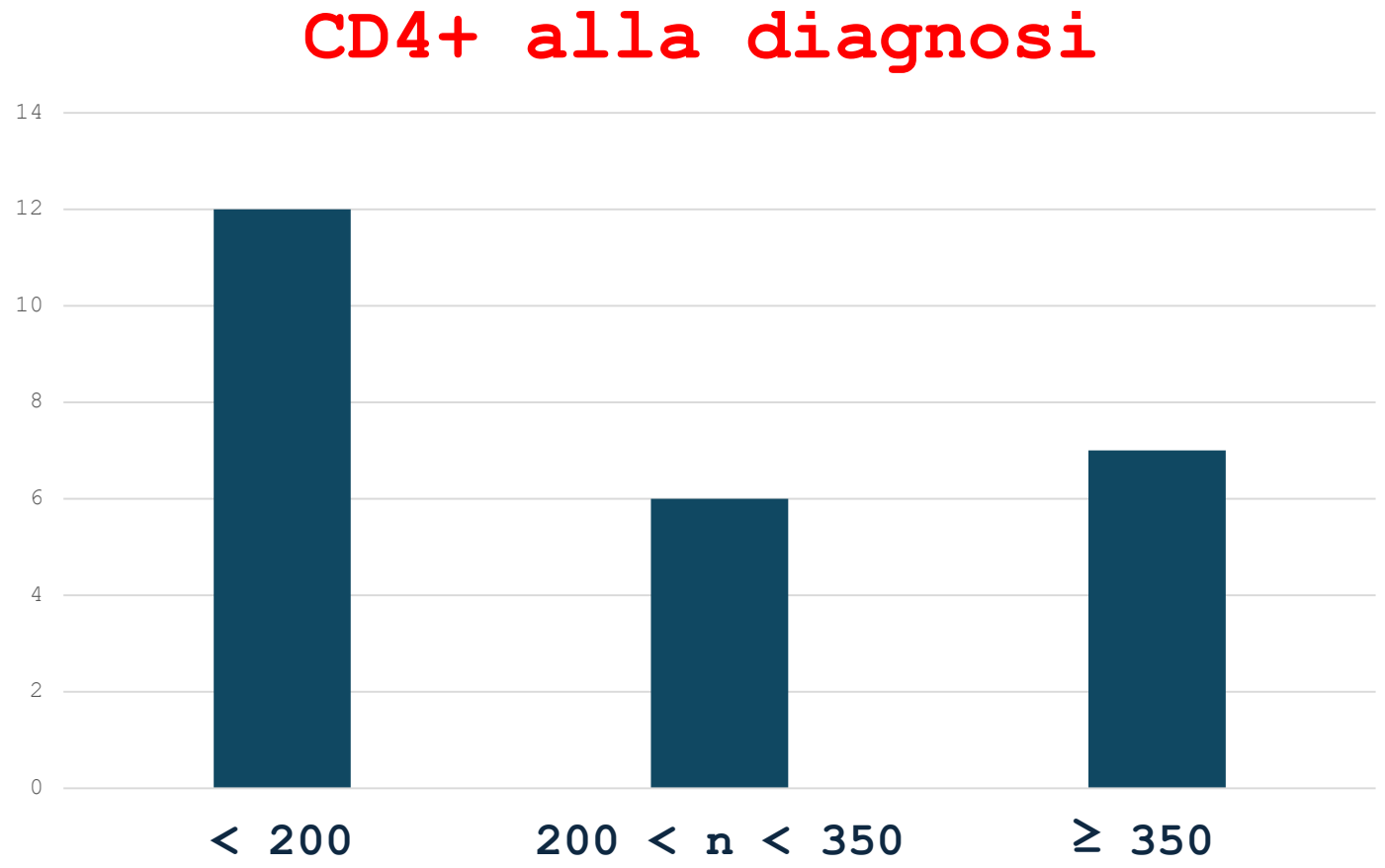
  - **AIDS: 7**
  - **LATE PRESENTER: 11**



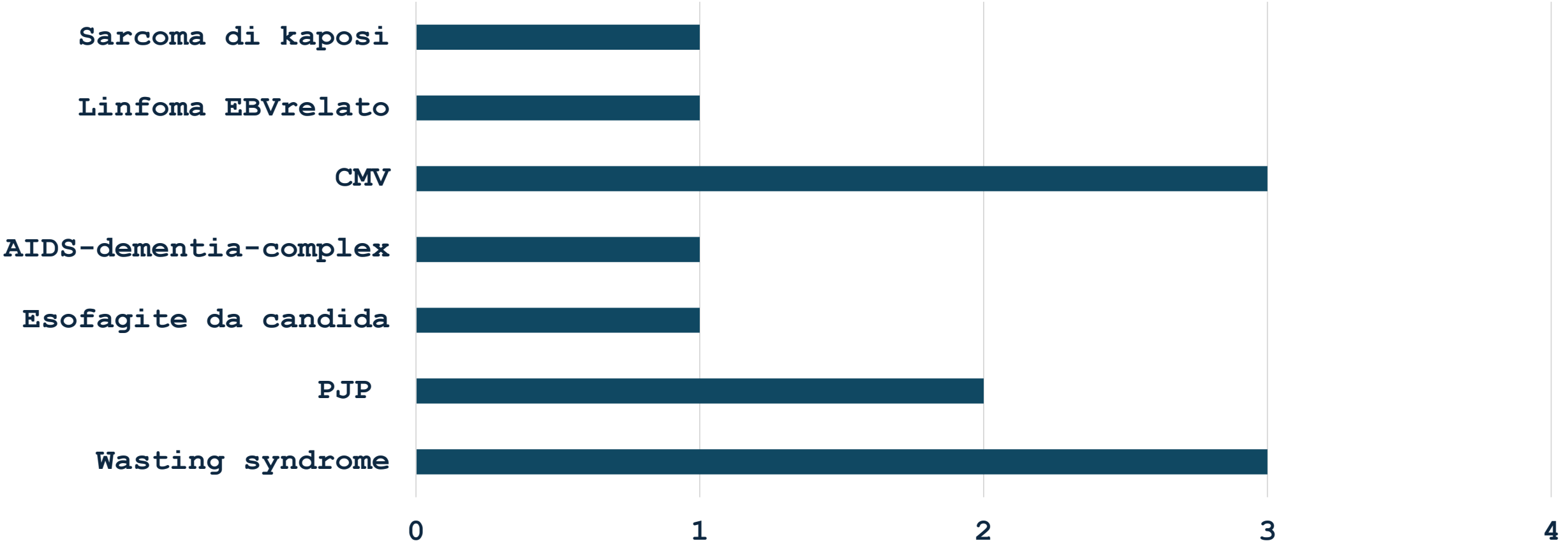
Linfociti T CD4+ alla diagnosi

MEDIANA CD4+: 293/mmc

- Valore più basso: 5/mmc
- Valore più alto: 1000/mmc



Condizioni AIDS-definenti



Demographic and viroimmunological characteristics

Advanced naive of total diagnosis, n (%)	199/575 (35%)
Sex, n (%)	
Male	150 (75%)
Female	46 (23%)
Transgender people	3 (2%)
Age, years, mean (-/+ sd)	
45 (33-57)	
Mode of transmission, n (%)	
Heterosexual	**115 (58%)**
MSM	65 (33%)
IDU	13 (7%)
Other	6 (3%)

Years of diagnosis, n (%)	
2019	44 (22%)
2020	35 (18%)
2021	33 (17%)
2022	38 (19%)
2023	49 (25%)
AIDS presenters baseline, n, (%)	
108 (54%)	
CD4 baseline	
Median (IQR)	52 (22,5-117)
CD4 < 50 cell/mm^3	**96 (48)**
VL baseline	
Median (IQR)	267600 (82758-980000)
> 100.000 cp/ml, n (%)	**141 (71%)**

Presenting Author: Arianna Narducci, UNIFG

Symptoms and hospitalizations before the diagnosis

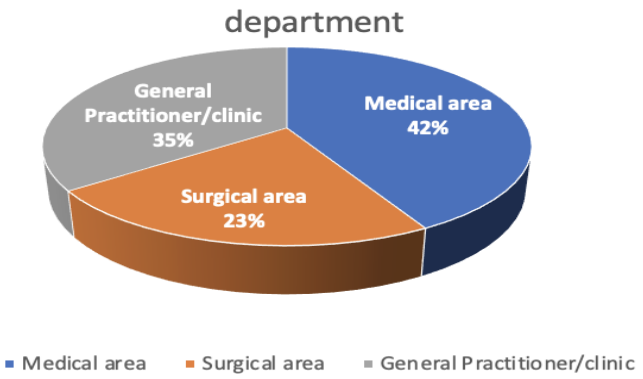
58/199 (29%) advanced naive were admitted two years before HIV diagnosis:

General practitioner

Internal medicine

Emergency room

General surgery



But also: Urology, Ematology, Intensive Care Unit, Infectious Disease, Cardiology, Gastroenterology, Ob/Gyn, Dermatology, Ophthalmology, Oncology, Reumtology, Otolaryngology

- **Mononucleosis-like illness (44%)**
- **Leukocytopenia/thrombocytopenia, anemia (7%)**
- **Lymphadenopathy (7%)**
- **Cutaneous lesion (7%)**
- **Pneumonia (5%)**
- **Gastroenteritis (5%)**
- **Oral candidiasis**
- **Genital herpes**
- **Seborrheic dermatitis**
- **Leishmania**
- **Other (20%)**

Advanced HIV as a Neglected Disease

Nathan Ford, D.Sc., Peter Ehrenkranz, M.D., and Joseph Jarvis, M.B., B.S.

PERCHE???

1) it is estimated that more than 4 million people have advanced HIV disease
2) Each year more than 600,000 of them are expected to die

……with limited attention paid to either consistently using existing tools or finding new tools for preventing AIDS-related deaths.

…..Pneumocystic pneumonia, cryptococcal diseases, and histoplasmosis….

NEJM, 8 febbraio 2024

Recent Trends in Opportunistic Infections at ART Initiation in the NA-ACCORD of IeDEA, 2017-2021

Jonas Kulakauskas[1], Kate Buchacz[2], John T Brooks[2], Jennifer Lam[3], M John Gill[4], Michael Horberg[5], Maile Karris[6], Emily C Williams[7], Kathleen McGinnis[8], Catherine Lesko[1], Richard Moore[1], **Keri N Althoff**[1], for the NA-ACCORD of IeDEA

1. Johns Hopkins University, Baltimore, Maryland, USA; 2. US Centers for Disease Control and Prevention, Atlanta, GA, USA; 3. Kaiser Permanente Northern California, Pleasanton, CA, USA; 4. University of Calgary, Alberta, Calgary, Canada; 5. Kaiser Permanente Mid-Atlantic States, Washington DC, USA; 6. University of California, San Diego, CA, USA; 7. University of Washington, Seattle, WA, USA; 8. VA Connecticut Healthcare System, US Department of Veterans Affairs, West Haven, CT, USA

981
Contact: Keri Althoff
kalthoff@jhu.edu

BACKGROUND

- Understanding the prevalence and consequences of opportunistic infections (OIs) at antiretroviral therapy (ART) initiation remains critical for informing HIV testing and care strategies that reduce the likelihood of late presentation for care
- **We assessed trends in OIs at ART initiation and their association with 1-year survival in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) from 2017 – 2021**

METHODS

- **Study population**: adults (≥18 years) with detectable viral loads (>200 copies/mL) initiating ART from 1 Jan 2017 to 31 Dec 2021 (study period)
- **Opportunistic infection (OI)** diagnoses were measured six months prior to two weeks after ART initiation
- **Death** was measured via clinical tracking and linkages to death registries
- **Covariates** (measured at ART initiation) included sex, race and ethnicity, HIV acquisition risk group, HIV viral load, CD4 count, and contributing cohort
- **Statistical Analyses**
  - Trends in the annual prevalence of OI at ART initiation were estimated and correlates identified using log binomial model to estimate crude and adjusted prevalence ratios (PR) and 95% confidence intervals
  - 1-year cumulative incidence of death by OI status was estimated using Kaplan-Meier curves and a log-rank test
  - Cox proportional hazards models were used to estimate the crude (HR) and adjusted (aHR) hazard ratios and 95% confidence intervals for death

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RESULTS

N=6,923 people with HIV starting ART from 2017-2021

- 25% >50-years-old, 15% female, 71% non-White or Hispanic, 41% men who have sex with men, 27% with CD4 <200 cells/mm^3, 91% initiated ART with integrase inhibitors

n=374 (5.4%) initiated ART with an OI from 2017-2021

- Pneumocystis pneumonia was most common (44%) followed by:
  - esophageal candidiasis (23%)
  - pulmonary tuberculosis (6%)
  - cryptococcal meningitis (5%)
  - other OIs accounted for <4%

n=94 deaths in the first year after ART initiation from 2017-2021

- n=75 deaths in those without an OI
- n=19 deaths in those with an OI

Table 1: Crude and adjusted prevalence ratios (PR) and 95% confidence intervals (95% CI) of OI at ART initiation

Characteristic	Crude PR (95% CI)	Adjusted PR (95% CI)
Age group (years)		
18-30	Ref	Ref
31-40	**2.02 (1.47, 2.77)**	**2.17 (1.57, 3.00)**
41-50	**2.90 (2.11, 3.99)**	**3.05 (2.19, 4.26)**
51-60	**2.03 (1.43, 2.89)**	**2.20 (1.52, 3.19)**
61-70	**2.75 (1.84, 4.12)**	**3.24 (2.11, 4.98)**
≥70	**3.95 (2.33, 6.71)**	**4.86 (2.78, 5.81)**
Sex		
Male	Ref	Ref
Female	1.14 (0.87, 1.47)	0.91 (0.67, 1.24)
Race and ethnicity		
Non-Hispanic White	Ref	Ref
Non-Hispanic Black	0.88 (0.70, 1.11)	0.97 (0.76, 1.25)
Hispanic	1.18 (0.88, 1.60)	1.27 (0.93, 1.73)
Non-Hispanic Other	0.99 (0.66, 1.43)	1.08 (0.73, 1.59)
HIV acquisition risk		
MSM	Ref	Ref
Heterosexual	**1.55 (1.20, 1.99)**	**1.36 (1.00, 1.83)**
IDU	1.45 (0.83, 2.35)	1.16 (0.68, 1.97)
Other/missing	1.22 (0.96, 1.54)	1.19 (0.81, 1.74)

Bold indicates p<0.05. Adjusted model 1 includes all the variables in the table and contributing cohort.

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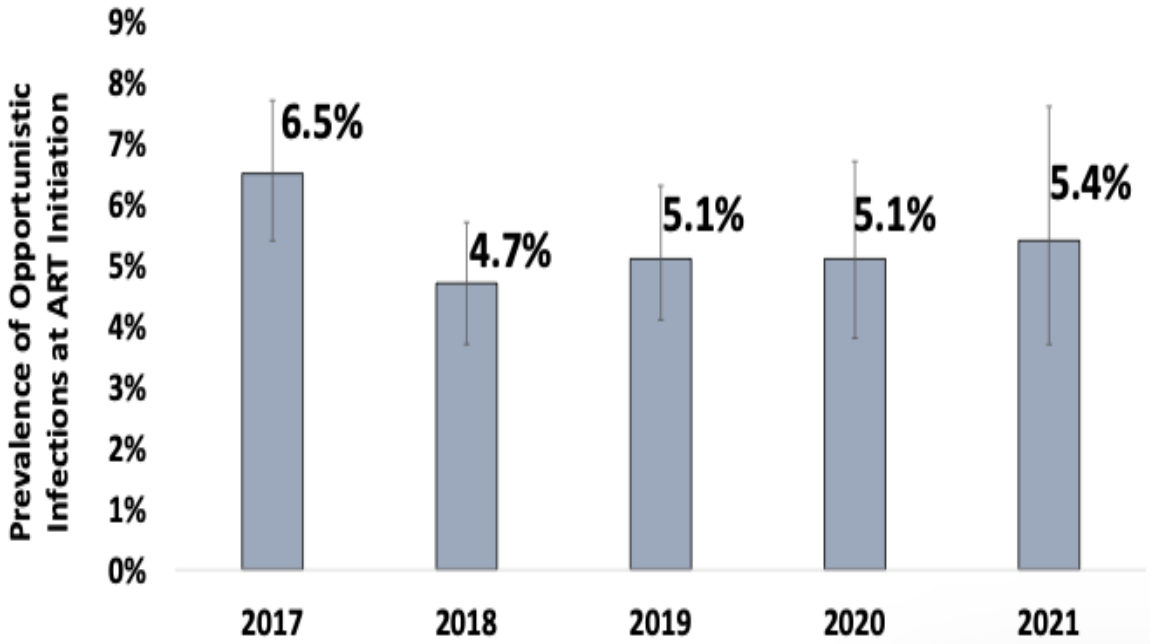
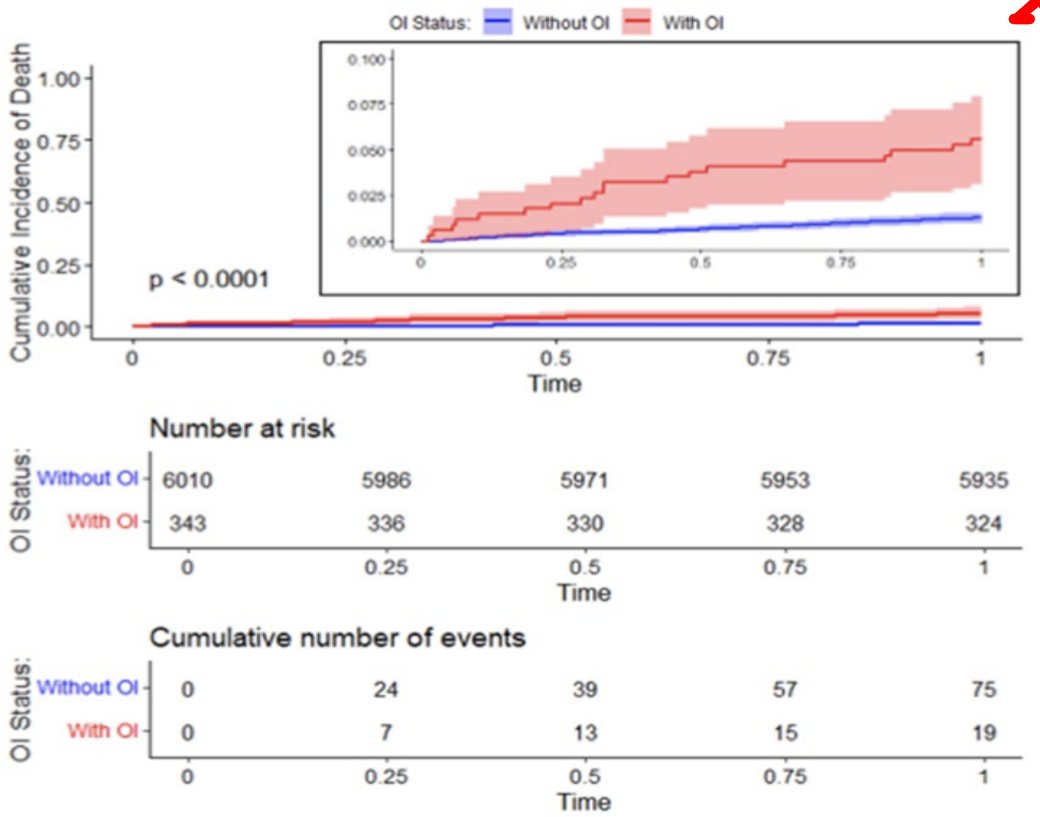
Figure 1: Annual trends in the prevalence of opportunistic infections at ART initiation, 2017-2021



Bars indicate 95% confidence intervals.

Figure 2: Cumulative incidence (and shaded 95% confidence interval) of death in the first year after ART initiation



There was a 4.5-fold increase in the risk of death among those with vs. without an OI at ART initiation (HR=4.55 [95% CI 3.09, 7.10]). The risk was nearly 2-fold after adjustment for age, sex, race and ethnicity, HIV acquisition risk group, viral load, CD4 and cohort (aHR=1.85 [95% CI 1.03, 3.34]).

A low but persistent proportion (≈5%) of PWH are starting ART with an opportunistic infection in the United States and Canada. Test-and-treat strategies focusing on those at highest risk for delayed ART initiation may assure optimal care and a reduction in mortality.

Burden of Opportunistic Infections and Causes of Death in Hospitalized Patients With AHD in Vietnam

983

Nam Xuan Ha[1*], Vu Quoc Dat[1,2*], Nguyen Quang Dieu[1], Vo Trieu Ly[3,4], Pham Ngoc Thach[5], Do Duy Cuong[6], Nguyen Thi Hao[1], Trinh Thi Men[1], Phan Thi Hong Dao[1], Tran Thi Hong Chau[1], Trinh Le Phuong[1], Dang Hoang Khanh[1], Thu Nguyen[8], H Rogier van Doorn[1,7#], Thuy Le[8,9#], and the Talaromycosis Study Group.

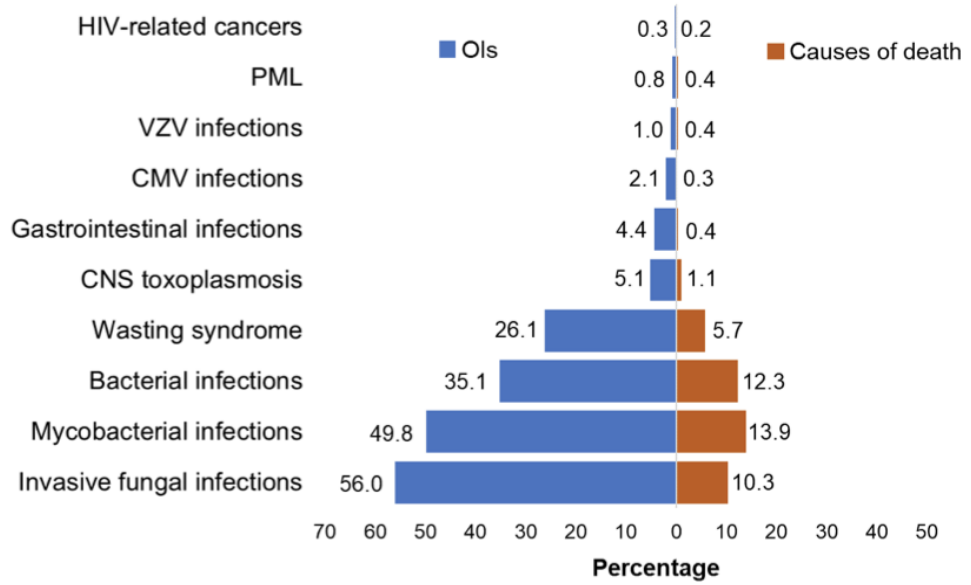
[1]Oxford University Clinical Research Unit, Hanoi/ Ho Chi Minh City, Vietnam, [2]Hanoi Medical University, Hanoi, [3]University of Medicine and Pharmacy at Ho Chi Minh City, [4]Hospital for Tropical Diseases, Ho Chi Minh City, [5]National Hospital for Tropical Diseases, Hanoi, [6]Bach Mai Hospital, Hanoi, [7]Nuffield Department of Medicine, University of Oxford, UK, [8]Duke University School of Medicine, Durham, NC, USA, [9]Tropical Medicine Research Center for Talaromycosis at Pham Ngoc Thach University of Medicine, Ho Chi Minh City ***(* and # authors contribute equally)***

- The **leading OIs** in hospitalized patients with AHD were: 1) **Invasive fungal infections** (505, 56.0%), 2) **Mycobacterial infections** (449, 49.8%); 3) **Severe bacterial infections** (316, 35.1%).
- The **leading causes of death** were **mycobacterial infections** (125, 13.9%), followed by **severe bacterial infections** (111, 12.3%), and **invasive fungal infections** (93, 10.3%).
- The **highest mortality** was in patients with **severe bacterial infections** (37.0%), followed by **mycobacterial infections** (29.4%), and **invasive fungal infections** (23.2%).

RESULTS

Figure 4. Percentage of causes of death, Vietnam (N=901)

(All percentages were calculated with a denominator of 901)



Notes: ART: Antiretroviral therapy, PCP: Pneumocystis pneumonia, TB: Tuberculosis, NTM: Nontuberculous mycobacteria, CNS: Central nervous system; CMV: Cytomegalovirus; HSV: Herpes simplex virus, VZV: Varicella-zoster virus; PML: Progressive multifocal leukoencephalopathy.

CONCLUSIONS

- Mycobacterial, bacterial, and invasive fungal infections are the leading causes of HIV death in Vietnam, collectively claiming lives of 21.1% of hospitalized patients with AHD.
- Our data highlight the need for a package of screen and treat strategy targeting these pathogens, and post-discharge interventions to reduce AIDS mortality.

Burden of Opportunistic Infections and Causes of Death in Hospitalized Patients With AHD in Vietnam

983

Nam Xuan Ha[1*], Vu Quoc Dat[1,2*], Nguyen Quang Dieu[1], Vo Trieu Ly[3,4], Pham Ngoc Thach[5], Do Duy Cuong[6], Nguyen Thi Hao[1], Trinh Thi Men[1], Phan Thi Hong Dao[1], Tran Thi Hong Chau[1], Trinh Le Phuong[1], Dang Hoang Khanh[1], Thu Nguyen[8], H Rogier van Doorn[1,7#], Thuy Le[8,9#], and the Talaromycosis Study Group.

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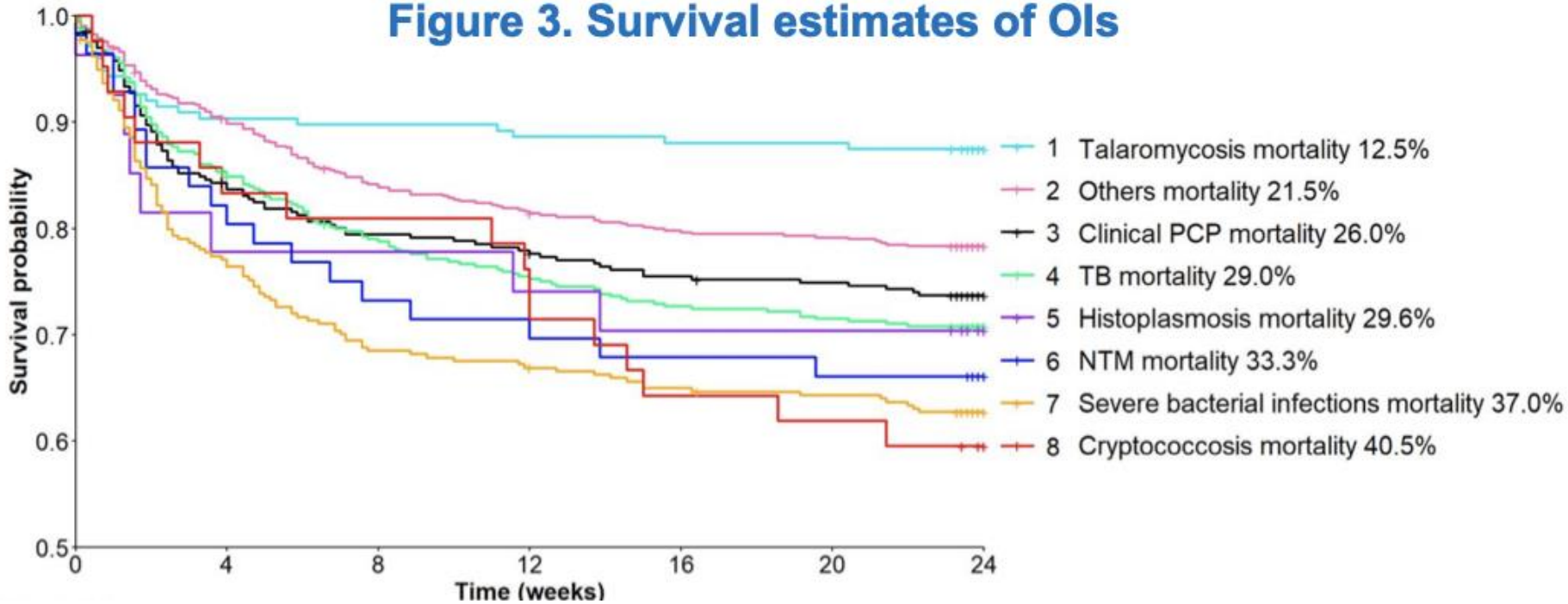
Figure 3. Survival estimates of OIs



RESULTS

- 83% were male. Age (years) was 36 (IQR: 30-44).
- CD4 count (cells/mm^3) was 19 (IQR: 9-45).
- 847 (94.0%) had at least one OI; 439 (48.7%) had ≥ 3 OIs.
- Median time to death (days) was 26 (IQR: 11.0-58.8), 174/218 (79.8%) of deaths occurred within first 2 months.

HIV-Replication as Risk Factor for Three Opportunistic Infections

Poster 799

Hansjakob Furrer*, on behalf of the Opportunistic Infections Project Team of COHERE in EuroCoord
*Department of Infectious Diseases, Bern University Hospital, University of Bern, Switzerland.

Introduction

- To evaluate risk of primary and recurrent cytomegalovirus retinitis (CMVR), extrapulmonary cryptococcosis (CRC) and disseminated *Mycobacterium avium* disease (MAC) in patients off prophylaxis at different CD4 and HIV-RNA levels within the European multi-cohort collaboration COHERE.
- Evaluate appropriateness of current guidelines for secondary prophylaxis.

Table 1. EACS stopping guidelines for primary and secondary prophylaxis

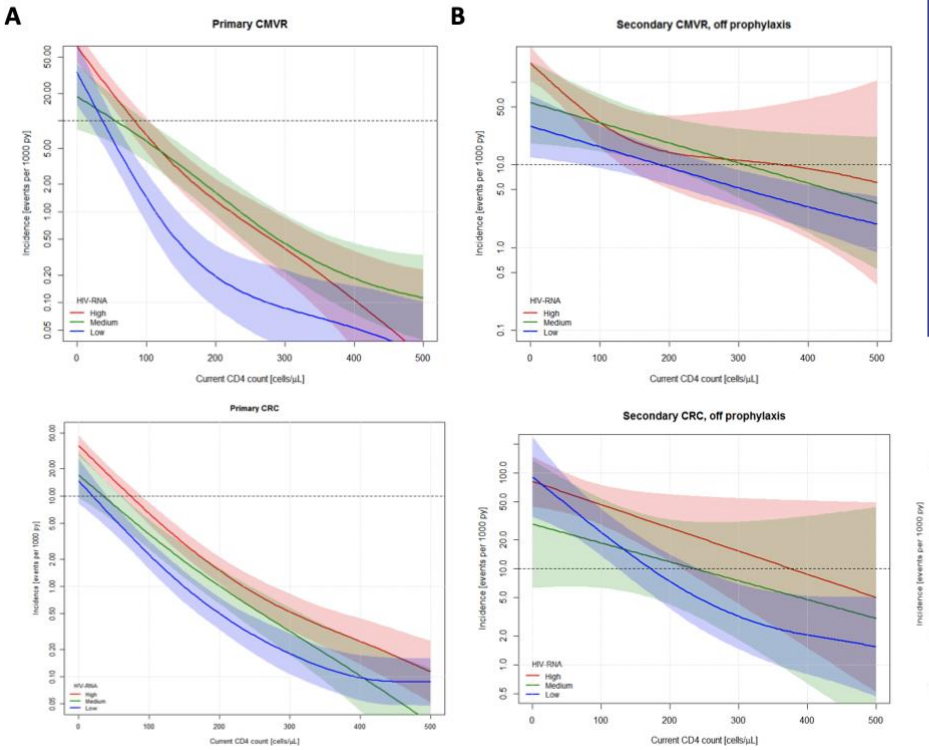
EACS	Primary	Secondary
CMVR	-	> **200** over **3** mths
CRCO	-	>**100** for at least **3** mths
MAC	> **100** over **3** mths	> **100** cells/µL over **6** mths **and** MAC treatment for at least **12** mths

www.eacsociety.org/guidelines/eacs-guidance/eacs-guidance.html

Methods

- After 1.1.98, on and off cART, > 15 yrs, without a previous diagnosis or with one previous diagnosis ("primary" or "secondary"); excluding CD4 count > 3000.
- Incidence of 1st and 2nd events of CMVR, CRC and MAC in patients off primary or secondary prophylaxis in COHERE (up to 2015), fitting CD4 using cubic splines.

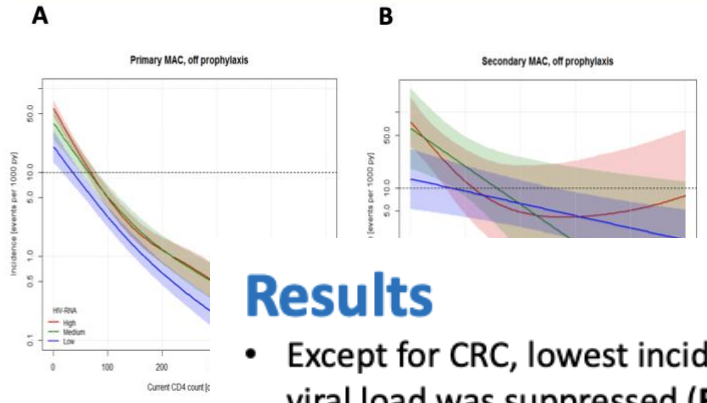
Figure 1. Primary (**A**) and recurrent (**B**) CMVR, CRC and MAC in patients off prophylaxis for CD4 level stratified by RNA strata (low <400 in blue, medium 400-10'000 in green, high >10'000 copies/mL in red); 95% confidence intervals for each of the different plasma HIV-RNA strata shaded



Poisson GAM model with CD4 modelled by a restricted cubic spline and HIV-RNA stratified as low (< 400), medium (400-10'000) or high (>10'000c/mL).

Table 2. Number of events and incidence per 1000 py. with primary and secondary prophylaxis for CMVR, CRC and MAC

	CMVR Primary	CMVR Secondary	CRC Primary	CRC Secondary	MAC primary	MAC secondary
Patients	33548	1054	131151	871	131003	1248
Cases	195	74	394	73	634	81
Follow-up [py]	264532	6358	861753	5461	859057	8032
Incidence	**0.7**	**11.6**	**0.5**	**13.3**	**0.7**	**10.1**
[95% CI]	[0.6, 0.9]	[9.1, 14.6]	[0.4, 0.5]	[10.5, 16.8]	[0.7, 0.8]	[8.0, 12.5]



Results

- Except for CRC, lowest incidence in patients with low CD4 counts was found when viral load was suppressed (**Figure 1**)
- Incidence of secondary events in patients with suppressed viral load crossed 10/1000py at CD4 of 87 (MAC), 186 (CMVR) and 172/µL (CRC).

Conclusions

- **HIV replication is a major risk factor for 1st and 2nd events of MAC and CMVR and primary CRC, but not for recurrent CRC in low CD4 strata (IRIS?).**
- **Our data support current guidelines for stopping secondary prophylaxes in patients with suppressed plasma HIV replication.**
- **Patients with unsuppressed HIV load may need continuation of maintenance treatment above currently recommended CD4 thresholds.**

Poster 0754

Risks of Opportunistic Infections for HIV+ and Uninfected Veterans Undergoing Cancer Chemotherapy

Alain Makinson[1], Lesley S. Park[2], Kimberly Stone[3], Maria Rodriguez-Barradas[4], Sheldon T. Brown[5], Roxanne Wadia[6], Kristina Crothers[7], Cynthia L. Gibert[8], Roger Bedimo[9], Matthew B. Goetz[10], Fatma Shebl[11], Jacques Reynes[1], Vincent Le Moing[1], Keith M. Sigel[3]

[1]University Hospital Montpellier, Montpellier, France, [2]Stanford University, Stanford, CA, USA, [3]Icahn School of Medicine at Mt Sinai, New York, NY, USA, [4]Baylor College of Medicine, Houston, TX, USA, [5]James J. Peters VA Medical Center, Bronx, NY, USA, [6]VA Connecticut Healthcare System, West Haven, CT, USA, [7]University of Washington, Seattle, WA, USA, [8]Washington DC VA Medical Center, Washington, DC, USA, [9]VA North Texas Health Care Center, Dallas, TX, USA, [10]VA Greater Los Angeles Health Care System, Los Angeles, CA, USA, [11]Massachusetts General Hospital, Boston, MA, USA

BACKGROUND

- Cancer is a leading cause of morbidity and mortality for persons with HIV (PWH)
- PWH with malignancies treated with chemotherapy may be at enhanced risk of opportunistic infections (OIs)
- We sought to clarify risks associated with OIs in PWH undergoing chemotherapy, using data from a large, national cohort of Veterans

METHODS

Population

- Data from the Virtual Cohort of Veterans Aging Cohort Study (VACS)
- Tumor site was collected from linked cancer registry data
- PWH and HIV-negative veterans who were diagnosed with malignancy between 01/01/1996 and 12/31/2018, and received at least one chemotherapy infusion

Outcome

- incidence of OIs 14 days to 6 months after first chemotherapy treatment

Analysis

- We calculated inverse probability weights of HIV infection, using the conditional probability of being a PWH given the baseline characteristics of age, sex, tumor site, race/ethnicity, year of cancer diagnosis, smoking status and alcohol use
- We used inverse probability weighted Poisson models to evaluate the association between HIV and OI risk overall, then stratified by hematological and non-hematological malignancies
- We assessed the risk of OIs in PWH, stratified by CD4 count at cancer diagnosis and by PCP prophylaxis use.

Table 1 : Baseline characteristics according to HIV-status in Veterans with malignancies treated by chemotherapy.

Characteristics	PWH (n=2,135)	Without HIV (n=3,031)	p-value
Age (median, IQR)	56 (49-62)	59 (54-64)	<0.001
Male, n (%)	2,105 (98.6)	2,962 (97.7%)	0.02
Race/Ethnicity, n (%)			<0.001
White	960 (45.0)	1,201 (39.6)	
African-American	973 (45.6)	1,562 (51.5)	
Hispanic	149 (7.0)	217 (7.2)	
Other	53 (2.5)	51 (1.7)	
Smoking, n (%)			<0.001
Never	395 (18.5)	458 (15.1)	
Current	1,146 (53.7)	1,757 (58.0)	
Former	327 (15.3)	554 (18.3)	
Unknown	267 (12.5)	262 (8.6)	
Charlson comorbidity index (median, IQR)	6 (4-8)	1 (0-2)	<0.001
Alcohol Use, n (%)	300 (14.1)	586 (19.3)	<0.001
Malignancies, n (%)			<0.001
Hematologic	645 (30.2)	479 (15.8)	
Non-hematologic	1,490 (69.8)	2,552 (84.2)	
PCP prophylaxis use, n (%)	640 (30.0)	126 (4.2)	<0.001
HIV-related characteristics			
Recent CD4, cells/mm3, median (IQR)	289 (141-512)	NA	
Controlled viremia	1,327 (69.0)	NA	

Table 2 : Opportunities infections by HIV-status among hematologic and non-hematologic malignancies

Types of OI	Hematologic Malignancies		Non-hematologic Malignancies		Total
	PWH (n=645)	Without HIV (n=479)	PWH (n=1,490)	Without HIV (n=2,552)	
Candida oesophagitis	11 (1.7)	1 (0.2)	22 (1.5)	9 (0.4)	43
Zoster	10 (1.6)	2 (0.4)	11 (0.7)	7 (0.3)	30
CMV	9 (1.4)	1 (0.2)	1 (0.07)	0 (0)	11
PCP	8 (1.2)	0 (0)	3 (0.2)	0 (0)	11
Atypical Mycobacterium	2 (0.3)	0 (0)	3 (0.2)	1 (0.04)	6
Cryptococcus	2 (0.3)	0 (0)	1 (0.07)	0 (0)	3
Salmonella bacteremia	0 (0)	0 (0)	0 (0)	1 (0.04)	1
Histoplasmosis	1 (0.2)	0 (0)	0 (0)	0 (0)	1

Table 3 : OI incidence rates/1000 p-y by cancer group

Types of Malignancies	OI Incidence rate/1000 p-y (95%CI)		Incidence rate ratio (95% CI)
	PWH	Without HIV	
All	94.4 (75.3-117.8)	17.5 (11.6-26.4)	4.6 (2.5-8.8)
Hematologic	163.6 (118.4-220.3)	18.6 (7.0-49.5)	10.0 (3.1-32.6)
Non-hematologic	65.3 (48.1-88.7)	17.3 (11.0-27.1)	3.3 (1.5-7.6)

- HIV was associated with increased rate ratio for OI:
  - 4.3 (95% CI 2.3-8.1) for all malignancies
  - 9.8 (95% CI 3.1-31.3) for hematologic malignancies
  - 3.1 (95% CI 1.4-7.0) for non-hematologic malignancies
- Among patients with CD4 levels >200/mm^3 at diagnosis:
  - 3 of 3,613 non-hematological cancers (0.08%) were treated for possible PCP (no definitive case)
  - 2 of the 3,375 non-hematological cancers (0.06%) without PCP prophylaxis at cancer diagnosis were treated for possible PCP OIs. No toxoplasmosis occurred.

- OIs were significantly increased in PWH with malignancies undergoing chemotherapy
- 39% of OIs in PWH were Candida esophagitis
- Our study does not support systematic PCP prophylaxis in PWH with non- hematological malignancies and controlled HIV-disease, as ASCO recommends implementation for risks >3.5%

CASO CLINICO
LATE PRESENTER OGGI

Anamnesi

- 41 aa, Camerun
- Nel 2018 in Turchia, Grecia ed infine Italia nel Dicembre 2019 (ONG).
- Due figlie, una in Camerun di 16aa ed una in Italia nata nel 2019 in Grecia
- Nel 2020-21 ripetuti accessi negli ospedali per mastite
- Tra il 2019 ed il 2021 la bambina viene presa in carico dai servizi territoriali per eseguire le vaccinazioni di legge Italiana
- Vaccinata 2 dosi SARS CoV-2

A ottobre 2021 riceve una telefonata dal Camerun che l'avvisa che suo marito è deceduto per AIDS

Almeno 2 occasioni mancate.
QUALI ?

Almeno 2 occasioni mancate. QUALI ?

- Donna di origine africana non viene mai testata in due anni per HIV nonostante frequenti visite in ospedali e sia ospite di una ONG con permesso di soggiorno regolare
- Bambina <3 anni, nata da una donna africana, con migrazione e soggiorno in due campi per profughi vengono seguite regolari vaccinazioni secondo Piano Vaccinale: DTP-polio-Hib-HBV, Men b, MMRV, PCV13, Men ACWY senza aver controllato mai HIV

Mamma 11 ottobre 2021: test HIV positivo

- HIV RNA 9,600 copie/mL (arrivato il 19 ottobre)
- CD4 + 6 cell/mmc (arrivati il 18 ottobre)
- Ratio 0,6
- Herpes simplex sacrale, candidosi orale
  - Riferiti persistenti da alcuni mesi ma attribuiti a stress
- Pregressa HBV, HBsAg negativo, IgG positive per toxoplasma e CMV
- Criptococco e quantiferon negativi
- Inizia INSTI based regimen in STR (3 farmaci)

Pochi giorni dopo, in un ospedale periferico

- Dispnea, tosse
- A domicilio Levofloxacina ed Enoxaparina
- 26 ottobre per il peggioramento va in Ospedale: pO2: 52mmHg in aa, TNF SARS-COV-2 negativo, TC torace polmonite interstiziale a vetro smerigliato (85% di interessamento polmonare).
- 11 Hgb, PCR 234, cre 0,5, LDH 647, Sierologia per Mycoplamsa IgM negativa.

Almeno 2 errori. QUALI ?

- Levofloxacina e Enoxaparina (SARS-CoV-2?) per 10 giorni
- Sierologia per Micoplasma, non per fare la diagnosi di polmonite

Trasferita a Malattie Infettive

- Beta d-Glucano fuori scala >523 pg/mL
- Inizia TMP/SMX 3 fiale QID
- EGDS: Candidosi esofagea e lesioni multiple di colorito rosso vinoso stomaco e duodeno di dimensioni variabili tra 5 e 25-30 mm
- Fluconazolo
- Diarrea Cronica, dolore addominale, biopsia del colon: CMV, fundus oculi negativo
- CMV DNA PCR 35,379 UI/ml
- Inizia Valganciclovir
- Eseguita biopsia: Sarcoma di Kaposi
- Doxorubicina 30mg/15ml previa valutazione cardiologica ed ECG

Peculiarità del caso clinico

- **Missed opportunities**
  - **In Italia da 2 anni, mai test HIV**
- **HIV/AIDS**
  - **Polmonite da P. jiroveci; S.Kaposi, CMV, Candidosi Esofagea**
- **Bimba??**

Novembre 2021

- 2 anni e 2 mesi, nata tramite parto cesareo da madre sieropositiva non in ART, in campo profughi in Grecia.
- EO: Normale sviluppo psicomotorio (barriera linguistica), peso 15 kg, diarrea ricorrente e dermatite cronica
- EE: Hb 10.9 g/dl, non piastrinopenia né leucopenia
- Stadiazione: CD4+ 242 N/mmc (4%, R 0.1), HIV-RNA 2.5x10^6 cp/ml

Sistema immunitario nel bambino con HIV

2 MODELLI:

1. Progressione lenta (maggior parte) deterioramento clinico e immunologico da 5 a 10 anni di vita. Primo anno di vita comparsa di segni e sintomi lievi e non specifici (p. es., linfoadenopatia, epatosplenomegalia, parotite), seguiti da deterioramento clinico e immunologico.
2. Rapida progressione (minoranza) infezioni opportunistiche ed encefalopatia entro il 1 anno di vita.

Conta CD4+ diversa per fascia d'età: 2500-4000 N/mmc neonato VS 400-1500 adulto

Fluctuations in symptoms in human immunodeficiency virus-infected children: the first 10 years of life. Gray L, Newell ML, Thorne C, Peckham C, Levy J, European Collaborative Study. Pediatrics. 2001;108(1):116.

Prima Considerazione sui Vaccini Bambino HIV+ e Piano vaccinale

- MPR: sicuro da somministrare ai bambini con HIV, a meno che non abbiano un sistema immunitario gravemente indebolito.
- DTP: sicuro da somministrare a neonati e bambini con HIV.
- Hib e Hep B sono sicuri da somministrare ai bambini con HIV.
- VZIG (immunoglobulina della varicella) deve essere presa in considerazione per i bambini sieropositivi noti, a seconda del loro stato immunitario.
- Vaccinazione antinfluenzale è raccomandato
- Pneumococco sicuro

CDC stage in children

Class P-0. Indeterminate infection

Class P-1. Asymptomatic infection

- Subclass A. Normal immune function
- Subclass B. Abnormal immune function
- Subclass C. Immune function not tested

Class P-2. Symptomatic infection

- Subclass A. Nonspecific findings
- Subclass B. Progressive neurologic disease
- Subclass C. Lymphoid interstitial pneumonitis
- Subclass D. Secondary infectious diseases
  - Category D-1. Specified secondary infectious diseases listed in the CDC surveillance definition for AIDS
  - Category D-2. Recurrent serious bacterial infections
  - Category D-3. Other specified secondary infectious diseases
- Subclass E. Secondary cancers
  - Category E-1. Specified secondary cancers listed in the CDC surveillance definition for AIDS
  - Category E-2. Other cancers possibly secondary to HIV infection
- Subclass F. Other diseases possibly due to HIV infection

Table 1.2. CDC Classification System for HIV in Children

CLASS P-0. INDETERMINATE INFECTION
Infants <15 months born to infected mothers but without definitive evidence of HIV infection or AIDS

CLASS P-1. ASYMPTOMATIC INFECTION
Subclass A. Normal immune function
Subclass B. Abnormal immune function
Hypergammaglobulinemia, T4 lymphopenia, decreased T4-to-T8 ratio, or absolute lymphopenia
Subclass C. Immune function not tested

CLASS P-2. SYMPTOMATIC INFECTION
Subclass A. Nonspecific findings (at least two for ≥2 months)
Fever, failure to thrive, generalized lymphadenopathy, hepatomegaly, splenomegaly, enlarged parotid glands, persistent or recurrent diarrhea
Subclass B. Progressive neurologic disease
Loss of developmental milestones or intellectual ability, impaired brain growth, or progressive symmetrical motor deficits
Subclass C. Lymphoid interstitial pneumonitis
Subclass D. Secondary infectious diseases
Category D-1. Opportunistic infections in CDC case definition
Bacterial: mycobacterial infection (noncutaneous, extrapulmonary, or disseminated); nocardiosis
Fungal: candidiasis (esophageal, bronchial, or pulmonary), coccidioidomycosis, disseminated histoplasmosis, extrapulmonary cryptococcosis
Parasitic: P. carinii pneumonia, disseminated toxoplasmosis with onset ≥1 month of age, chronic crytosporidiosis or isosporiasis, extraintestinal strongyloidiasis
Viral: cytomegalovirus disease (onset ≥1 month of age), chronic mucocutaneous/disseminated herpes (onset ≥1 month age), progressive multifocal leukoencephalopathy
Category D-2. Unexplained, recurrent, serious bacterial infections (two or more in 2 years)
Sepsis, meningitis, pneumonia, abscess of an internal organ, bone/joint infections
Category D-3. Other infectious diseases
Includes persistent oral candidiasis, recurrent herpes stomatitis (at least two episodes in 1 year), multidermatomal or disseminated herpes zoster
Subclass E. Secondary cancers
Category E-1. Cancers in AIDS case definition
Kaposi's sarcoma, B cell non-Hodgkin's lymphoma, or primary lymphoma of brain
Category E-2. Other malignancies possibly associated with HIV
Subclass F. Other conditions possibly caused by HIV
Includes hepatitis, cardiopathy, nephropathy, hematologic disorders, dermatologic diseases

Pediatric AIDS second edition (Pizzo, Wilfert)

CLASS P-2: malattia sintomatica

Stage	Age at time of CD4+ T-lymphocyte test*					
	<1 year		1 to 5 years		≥6 years	
	Cells/microL	Percent	Cells/microL	Percent	Cells/microL	Percent
0[¶]	NA	NA	NA	NA	NA	NA
1	≥1500	≥34	≥1000	≥30	≥500	≥26
2	750 to 1499	23 to 33	500 to 999	22 to 29	200 to 499	14 to 25
3 (AIDS)[Δ]	<750	<26	<500	<22	<200	<14
Unknown[◇]	NA	NA	NA	NA	NA	NA

CDC: Centers for Disease Control and Prevention; NA: not applicable; AIDS: acquired immunodeficiency syndrome.

Acquired immune deficiency syndrome (AIDS)-defining conditions

Bacterial infections, multiple or recurrent*
Candidiasis of bronchi, trachea, or lungs
Candidiasis of esophagus
Cervical cancer, invasive[¶]
Coccidioidomycosis, disseminated or extrapulmonary
Cryptococcosis, extrapulmonary
Cryptosporidiosis, chronic intestinal (>1 month's duration)
Cytomegalovirus disease (other than liver, spleen, or nodes), onset at age >1 month
Cytomegalovirus retinitis (with loss of vision)
Encephalopathy, HIV-related[Δ]
Herpes simplex – Chronic ulcers (>1 month's duration) or bronchitis, pneumonitis, or esophagitis (onset at age >1 month)
Histoplasmosis, disseminated or extrapulmonary
Isosporiasis, chronic intestinal (>1 month's duration)
Kaposi sarcoma
Lymphoma, Burkitt (or equivalent term)
Lymphoma, immunoblastic (or equivalent term)
Lymphoma, primary, of brain
Mycobacterium avium complex or *Mycobacterium kansasii*, disseminated or extrapulmonary
Mycobacterium tuberculosis of any site, pulmonary[¶], disseminated, or extrapulmonary
Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
Pneumocystis jirovecii pneumonia
Pneumonia, recurrent[¶]
Progressive multifocal leukoencephalopathy
Salmonella septicemia, recurrent
Toxoplasmosis of brain, onset at age >1 month
Wasting syndrome attributed to HIV[Δ]

OMS raccomanda di iniziare rapidamente ART

- Stadio 2-3 OMS
- Età <2 anni
- Età da 2 a 5 anni con conta CD4 ≤750 N/mmc o percentuale CD4 <25%
- Età ≥5 anni con conta CD4 ≤350 N/mmc

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)

Preferred Initial Regimens Based on Age and Weight			
Age	**Weight Restriction**	**Regimens**	**FDC Available** (see Appendix A, Table 1)
Newborns, Birth to Age <14 Days[a,b]	None	Two NRTIs **plus** NVP	No
	≥2 kg	Two NRTIs **plus** RAL[c]	No
Neonates ≥14 Days to Age <4 weeks	None	Two NRTIs **plus** LPV/r[b]	No
	≥2 kg	Two NRTIs **plus** RAL[c]	No
Infants and children Aged ≥4 Weeks to <6 Years	≥3 kg	Two NRTIs **plus** DTG[d]	No
Children Aged ≥6 Years	≥25 kg	Two NRTIs **plus** BIC[e]	Yes
		Two NRTIs **plus** DTG[d]	Yes
Adolescents Aged ≥12 Years with SMRs of 4 or 5	Refer to the Adult and Adolescent Antiretroviral Guidelines		Yes

Oggi HIV-RNA <30 copie/mL

ABC+3TC+RAL
(Primi 6 mesi)
Sciroppi + CPR
pediatriche su Kg

Lamivudina+Dolute
gravir
150 mg + 25 mg

Syndrome Approach to Opportunistic Infections

Initial Risk Assessment

Assess for severity of illness (hemodynamic instability, sepsis, altered mentation) History: Symptoms, ART and prophylaxis adherence, prior OIs, travel, sexual history, possible exposures
Exam: Pulmonary, abdominal, eye, skin/mucosa, anogenital, lymph node, neuro exams
Labs: CBC with diff, complete metabolic panel, urinalysis, CD4 count and HIV viral load (if not recently obtained)

Ocular Symptoms

DDx: CMV, VZV, HSV, *Bartonella*, syphilis, TB, *toxoplasma*, bacterial or fungal keratitis, microsporidiosis, HIV retinopathy

Work-up: **Urgent ophthalmologic eval for all acute vision loss or eye pain**
Herpesvirus serologies +/- PCR, RPR with treponemal Ab, Toxo IgG, Corneal biopsy or vitreal tap for path and Cx

Respiratory Symptoms

CD4 > 250 DDx: TB, bacterial pneumonia, *Coccidioides*, respiratory viruses, lymphoma, pulmonary edema, non- infectious causes (e.g., PE)

CD4 < 250 DDx: PCP, endemic fungi (*Histoplasma*, *Cryptococcus*, *Coccidioides*), mycobacterial, lymphoma, KS

Work-up in low CD4: Imaging (CXR +/- CT scan); Bacterial, fungal and AFB blood and sputum Cx, TB PCR sputum, PCP DFA x3, LDH, ABG, serum cryptococcal Ag, urine *Histoplasma* Ag, respiratory viral panel
Consider early bronchoscopy if initial work-up (-) or clinical worsening.

Neurologic Symptoms

Meningoencephalitis: Bacterial meningitis, Neurosyphilis, TB, *Cryptococcus*, other endemic fungi, HSV, VZV, CMV, PML (JC virus), HIV encephalopathy
CNS mass lesion: *Toxoplasma*, PCNSL (EBV- associated), TB, endemic fungi, *Nocardia*, brain abscess, Syphilitic gumma, CNS Chagas disease, primary brain tumor

Work-up: Contrasted neuroimaging (CT scan or MRI), LP (opening pressure, cell count, diff, glucose, protein, Gm stain/Cx)

Based on initial studies, can obtain additional serum (e.g., Toxo IgG, RPR, Crypto Ag) or CSF studies (e.g., fungal Cx and serologies, Crypto Ag, AFB Cx, TB PCR, VDRL, viral PCR)

Undifferentiated fever (FUO)/Multiorgan Disease

DDx: Bacterial sepsis, TB, MAC, *Brucella*, *Bartonella*, endemic fungi, CMV, EBV, HHV-8 (Multicentric Castleman's), Parvovirus B19, Malaria, visceral leishmaniasis, lymphoma, disseminated KS, HLH

Work-up: Bacterial, AFB and fungal blood Cx; Fungal serologies, Crypto Ag, urine Histo Ag, CMV PCR, HHV-8 PCR, LDH, ferritin, blood smear Consider CT scan of chest, abdomen/pelvis Consider biopsy of bone marrow, lymph node or liver for path and Cx

Hepatobiliary Symptoms

DDx: Viral hepatitis (A, B, C, E), lymphoma or HCC, MAC, TB, syphilis, *Bartonella*, *Histoplasma*, CMV, cryptosporidiosis, microsporidiosis, AIDS cholangiopathy, DILI

Work-up: Pattern of LFT instructive; Viral hepatitis Ab, routine and AFB blood Cx, CMV PCR, fungal Ab, RPR; Hepatic imaging (US +/- CT) followed by ERCP or liver biopsy if indicated

Gastrointestinal Symptoms

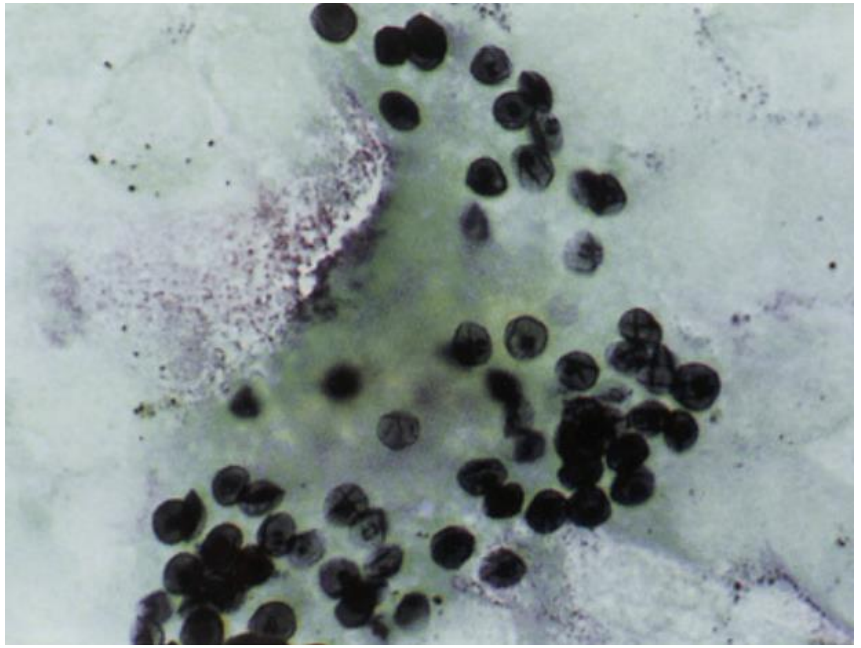
Upper GI (dysphagia, pain): Candidiasis, CMV, HSV, aphthous ulcers, KS, lymphoma or carcinoma

Lower GI (diarrhea): Bacterial enterics, C. difficile, *Giardia*, Cryptosporidiosis, *Cyclospora*, Microsporidiosis, Cystoisospora, CMV, MAC, KS, Lymphoma

Work-up
Upper GI: empiric *Candida* Rx if thrush present; endoscopy for biopsy with stains, Cx and PCR
Lower GI: Stool for routine Cx, C. diff, *Giardia/Cryptosporidia* Ag, O&P, Modified AFB, Trichrome stains; AFB blood and stool Cx, blood CMV PCR
Consider endoscopy with biopsy if initial work-up (-) or high concern for CMV colitis

Pneumocystis jirovecii

- Fungus
- Low virulence
- Found in lungs of humans and other mammals
- Lacks ergosterol in the plasma membrane, not sensitive to antifungals that target this pathway
- Airborne transmission



Triage / Disease Severity

- MILD

- Room air arterial oxygen PaO_2 ≥70 mm Hg or alveolar-arterial PAO_2-PaO_2 gradient <35 mm Hg
- Consideration for outpatient management
- Oral treatment regimen

- MODERATE/SEVERE

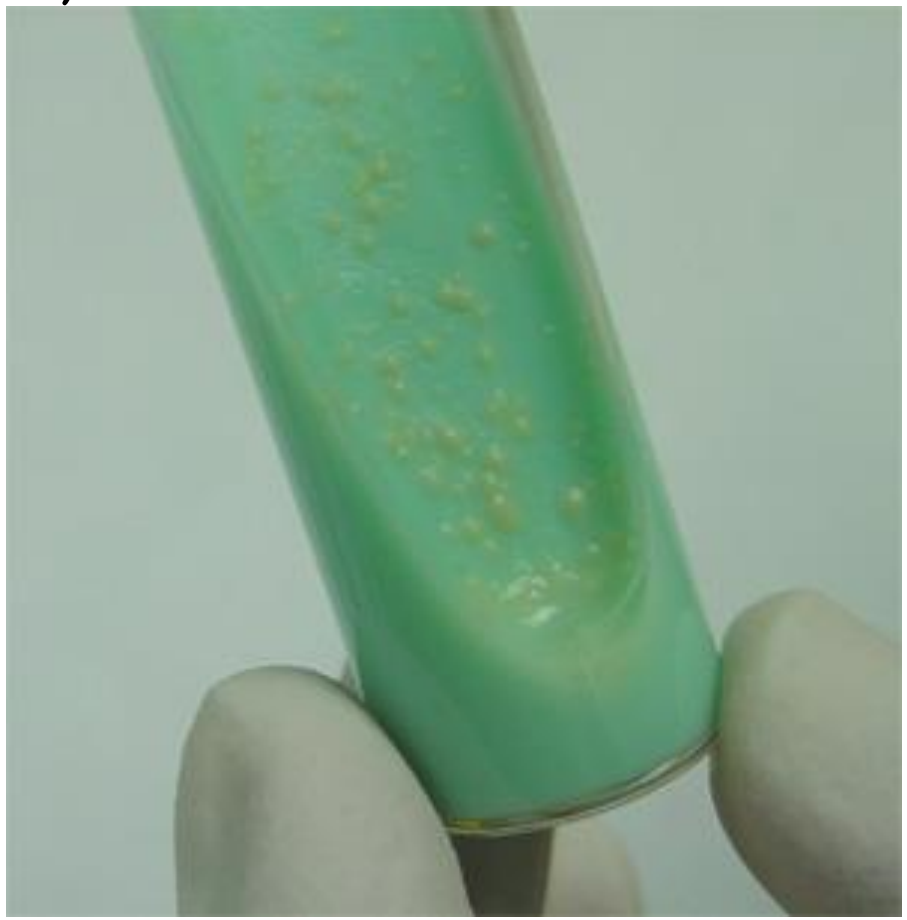
  - PAO_2-PaO_2 ≥35 to <45 mm Hg
  - PAO_2-PaO_2 ≥45 mm Hg
  - Inpatient management
  - Initial IV treatment regimen and close monitoring

Treatment

- Preferred:
  - TMP/SMX dose 15-20 mg/kg TMP component IV/PO daily divided every 6 or 8 hours for 21 days
- Adjunctive corticosteroids:
  - Room air PaO2<70 mm Hg or A-a gradient >35 mm Hg
  - Prednisone 21-day taper starting at 40 mg twice daily
  - IV methylprednisolone at 75% of prednisone dose
- Alternative:
  - Mild Disease: primaquine + clindamycin or atovaquone
  - Severe Disease: pentamidine or primaquine + clindamycin
- ART should be initiated within 2 weeks if not already started

Mycobacterium avium Complex (MAC)

- Environmental organism found in soil, water
- Low virulence
- Colonizes respiratory and GI tracts
- Disseminated infection in CD4 <50



Treatment

- At least 2 drugs as initial therapy to prevent emergence of resistance
- Clarithromycin 500 mg PO twice daily + ethambutol 15 mg/kg PO daily
- Azithromycin 500 mg + ethambutol 15 mg/kg PO daily when drug interactions or intolerance precludes the use of clarithromycin
- +/- rifabutin 300 mg PO daily (high mycobacterial loads, absence of effective ART, etc.)

CMV Retinitis

- Most common Cytomegalovirus Retinitis (CMV) manifestation in HIV (CD4 <50)
- Estimated 30% of patients with Stage 3 HIV/AIDS had CMV retinitis prior to potent ART
- Clinical:
  - Decreased visual acuity, “floaters,” vision loss; mostly unilateral
- Exam:
  - Characteristic perivascular fluffy, yellow-white retinal infiltrates associated with hemorrhages
- Diagnosis:
  - Retinal changes observed in dilated pupil exam by ophthalmologist, PCR of aqueous or vitreous humor, response to empiric anti-CMV therapy

Other CMV Disease

- Diagnostic approach: consistent clinical manifestations and evidence of the virus in tissue
- Colitis:
  - 5-10% of patients
  - Weight loss, abdominal pain, diarrhea, fever
- Esophagitis:
  - Small percentage of patients
  - Odynophagia, nausea, epigastric discomfort
- Pneumonitis:
  - Uncommon in PWH
  - CMV PCR from BAL specimen with limited diagnostic value
- Neurologic disease:
  - Dementia, ventriculoencephalitis (acute)

Treatment

- Site-Threatening Lesions:
  - Ganciclovir 5 mg/kg IV q12h for 14–21 days, then 5 mg/kg IV daily
  - Ganciclovir 5 mg/kg IV q12h for 14–21 days, then valganciclovir 900 mg PO daily
  - Valganciclovir 900 mg PO q12h for 14–21 days, then 900 mg once daily
  - +/- Intravitreous injections of ganciclovir or foscarnet repeat weekly until lesion inactivity is achieved
- Peripheral Lesions:
  - Valganciclovir 900 mg PO q12h for 14–21 days, then 900 mg once daily for 3–6 months