Histoplasmosis

Alessandro C. Pasqualotto, MD PhD MBA FECMM

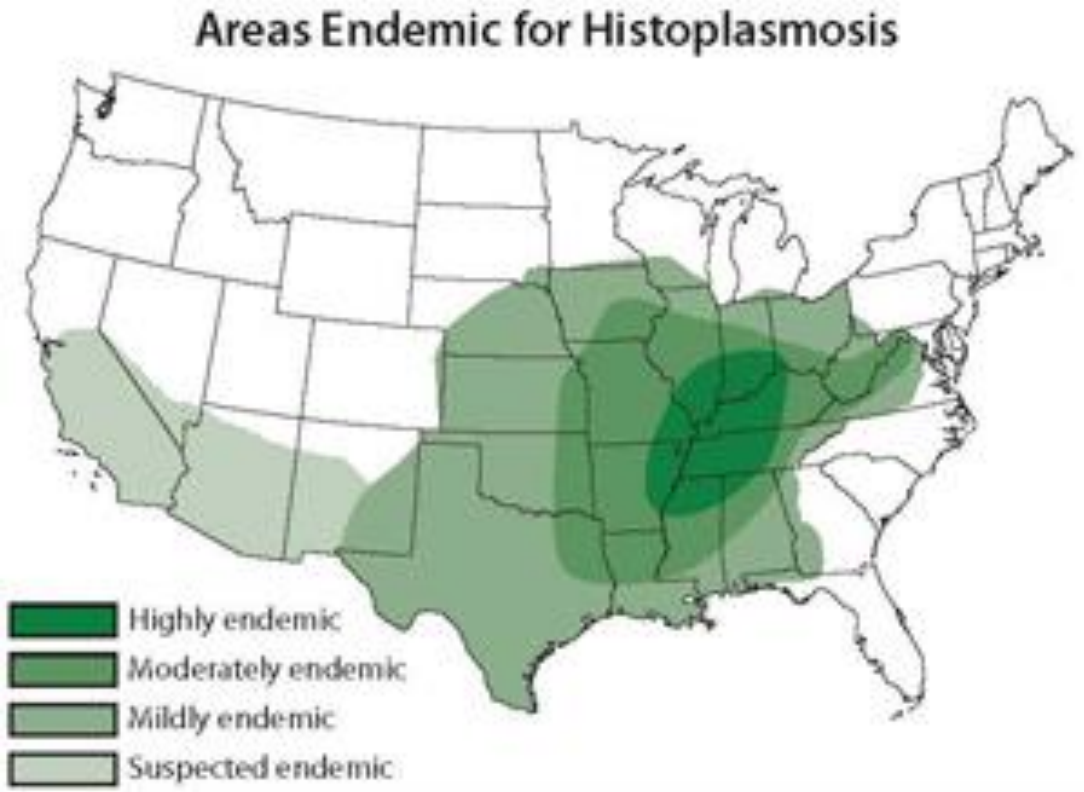
Porto Alegre, Brazil

Why opportunistic infections still matter in the HIV response - Part 1

Virtual meeting, April 29th, 2025

Epidemiology

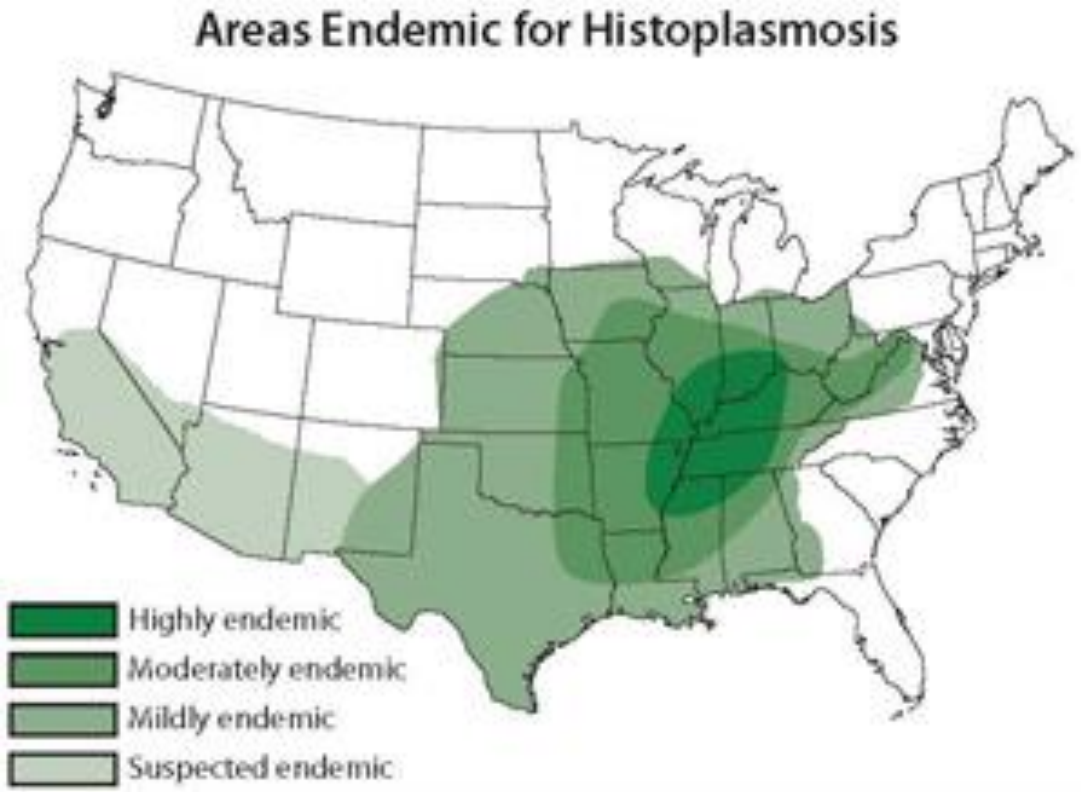
IAS Endemic in the US



Previously

Maiga AW, et al. Emerg Infect Dis 2018; 24: 1835-9

IAS Endemic in the US



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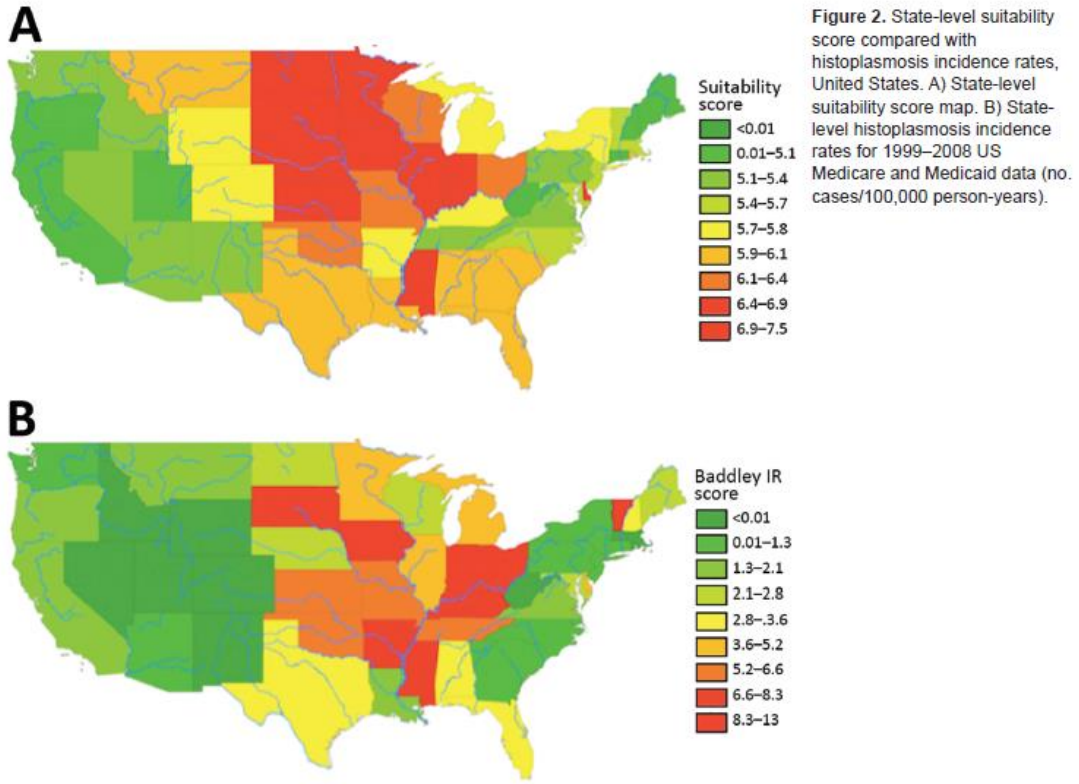
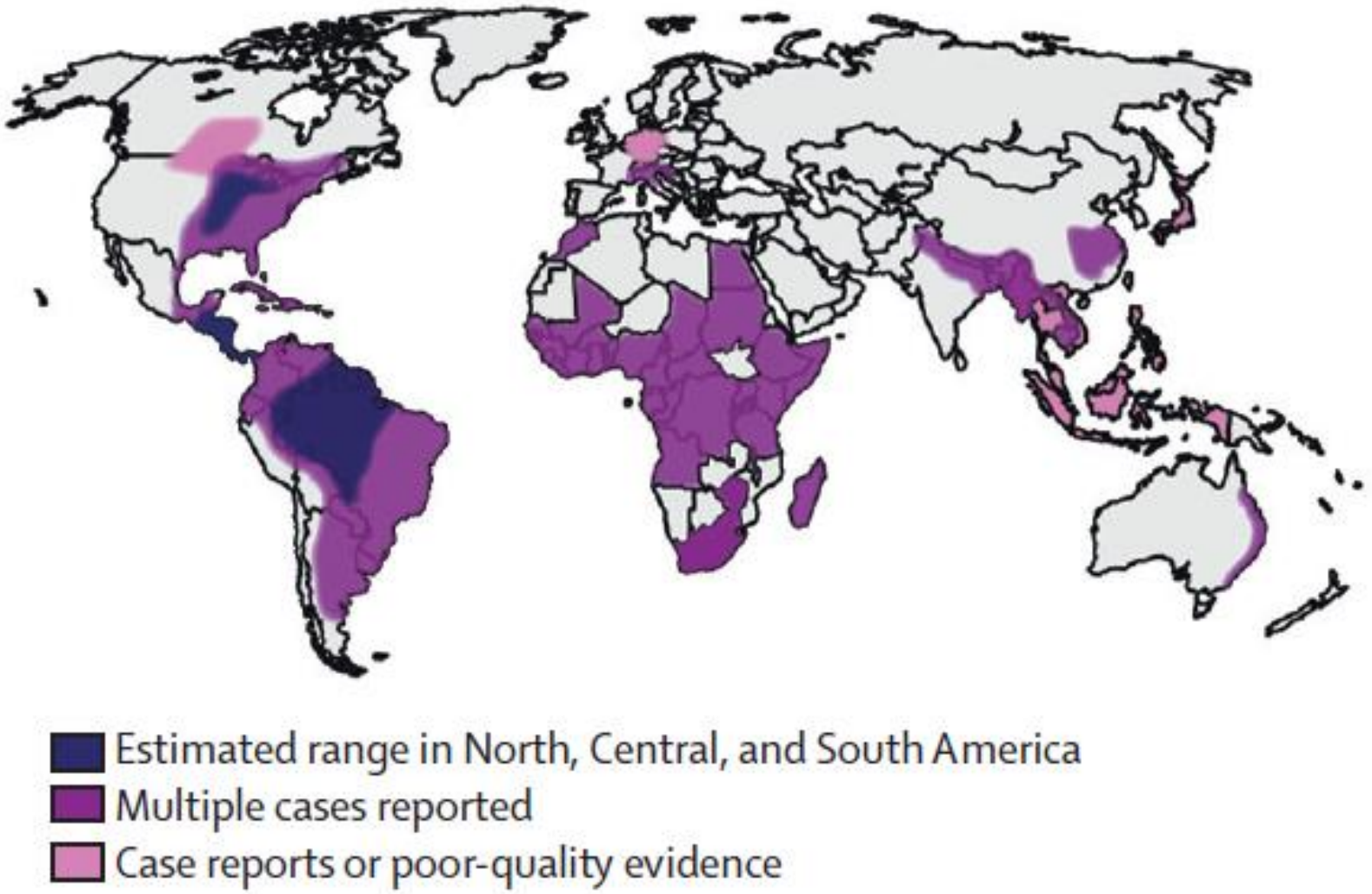


Figure 2. State-level suitability score compared with histoplasmosis incidence rates, United States. A) State-level suitability score map. B) State-level histoplasmosis incidence rates for 1999–2008 US Medicare and Medicaid data (no. cases/100,000 person-years).

More recently

Maiga AW, et al. Emerg Infect Dis 2018; 24: 1835-9

Histo is a global disease



Thompson GR 3rd, et al. Lancet Infect Dis 2021; S1473-3099(21)00191-2

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Open Forum Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

Histoplasmosis, An Underdiagnosed Disease Affecting People Living With HIV/AIDS in Brazil: Results of a Multicenter Prospective Cohort Study Using Both Classical Mycology Tests and *Histoplasma* Urine Antigen Detection

Diego R. Falci,[1,2] Alexandre A. Monteiro,[3] Cassia Ferreira Braz Caurio,[3,4] Tulio C. O. Magalhães,[1] Melissa O. Xavier,[5] Rossana P. Basso,[5] Marineide Melo,[6] Alexandre V. Schwarzbold,[7] Paulo Roberto Abrão Ferreira,[8] Jose Ernesto Vidal,[9] João Paulo Marochi,[9] Cassia Silva de Miranda Godoy,[10] Renata de Bastos Ascenco Soares,[10] Aurea Paste,[11] Monica B. Bay,[12] Vera Lucia Pereira-Chiccola,[13] Lisandra Serra Damasceno,[14] Terezinha do Menino Jesus Silva Leitão,[14] and Alessandro C. Pasqualotto[3,4]

Falci DR, et al. Open Forum Infect Dis 2019; 6: ofz073

Histo frequency in Brazil

- **570 patients with AHD were screened**
  - ✓ 11 centres in Brazil

Falci DR, et al. Open Forum Infect Dis 2019; 6: ofz073

Histo frequency in Brazil

- **570 patients with AHD were screened**
  - ✓ 11 centres in Brazil
- **21.6% had histoplasmosis**
  - ✓Urinary antigen (IMMY Clarus) increased diagnosis by **53.8%**

Falci DR, et al. Open Forum Infect Dis 2019; 6: ofz073

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IN THE AMERICAS
HISTOPLASMOSIS
KILLS MORE PEOPLE
WITH AIDS THAN
TUBERCULOSIS
The Histoplasma antigen test
now endorsed by the WHO
as an Essential Diagnostic
is a game changer for
avoidable deaths
gaffi
GLOBAL ACTION FUND FOR FUNGAL INFECTIONS
WWW.GAFFI.ORG
#FIGHT FUNGUS

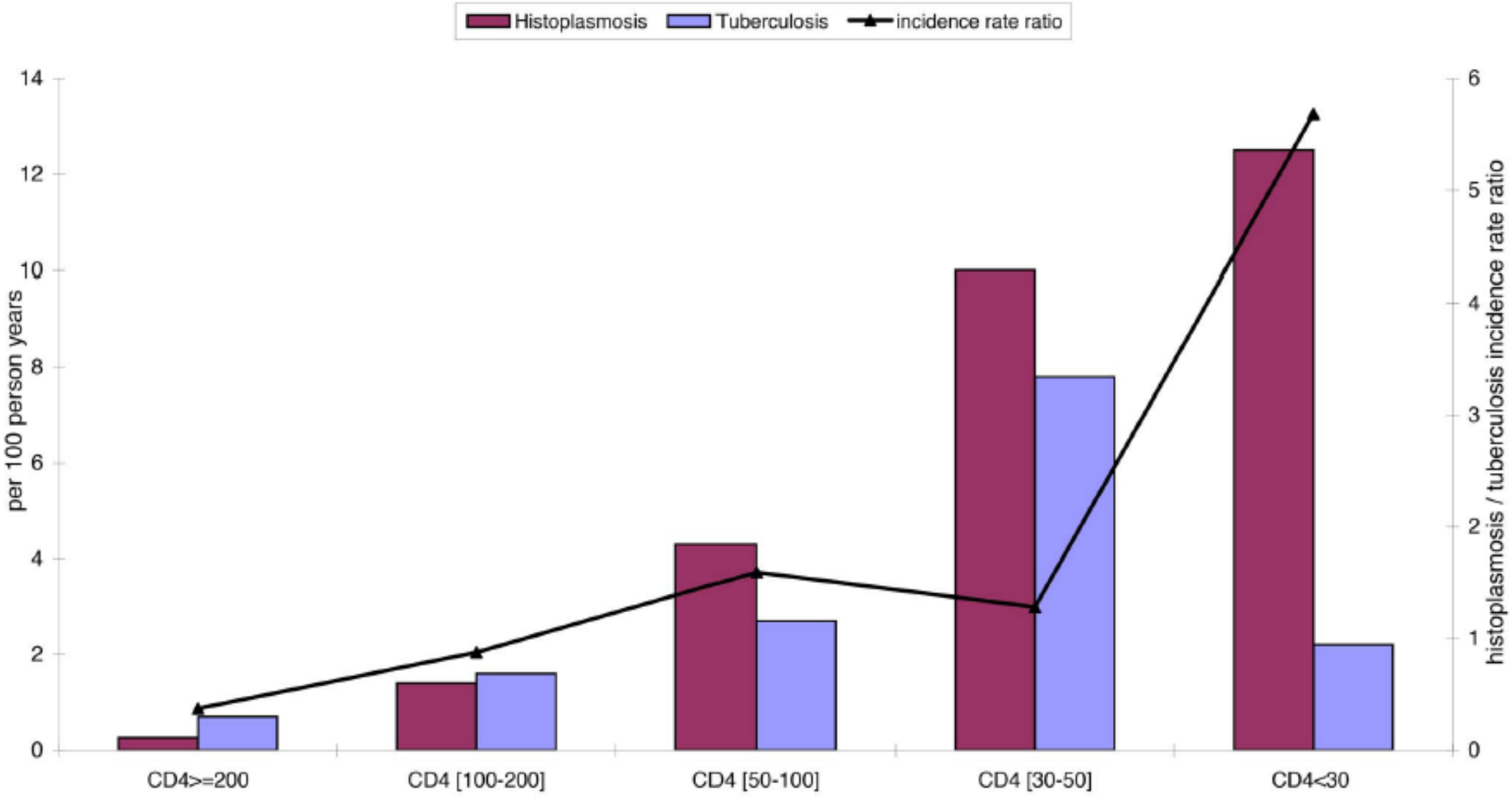

Figure 1. Shows the incidence rate for tuberculosis and histoplasmosis for different CD4 strata.
doi:10.1371/journal.pntd.0003290.g001

Nacher M, et al. PLOS Negl Trop Dis 2014: 8: e3290

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Review

Histoplasmosis and Tuberculosis Co-Occurrence in People with Advanced HIV

Diego H. Caceres [1,2,*,†] and Audrey Valdes [3,*,†]

Labs should test for both TB and histo in advanced AIDS (median CD4 count: 30)

Caceres DH, Valdes A. J Fungi 2019; 5:73

Clinical manifestations

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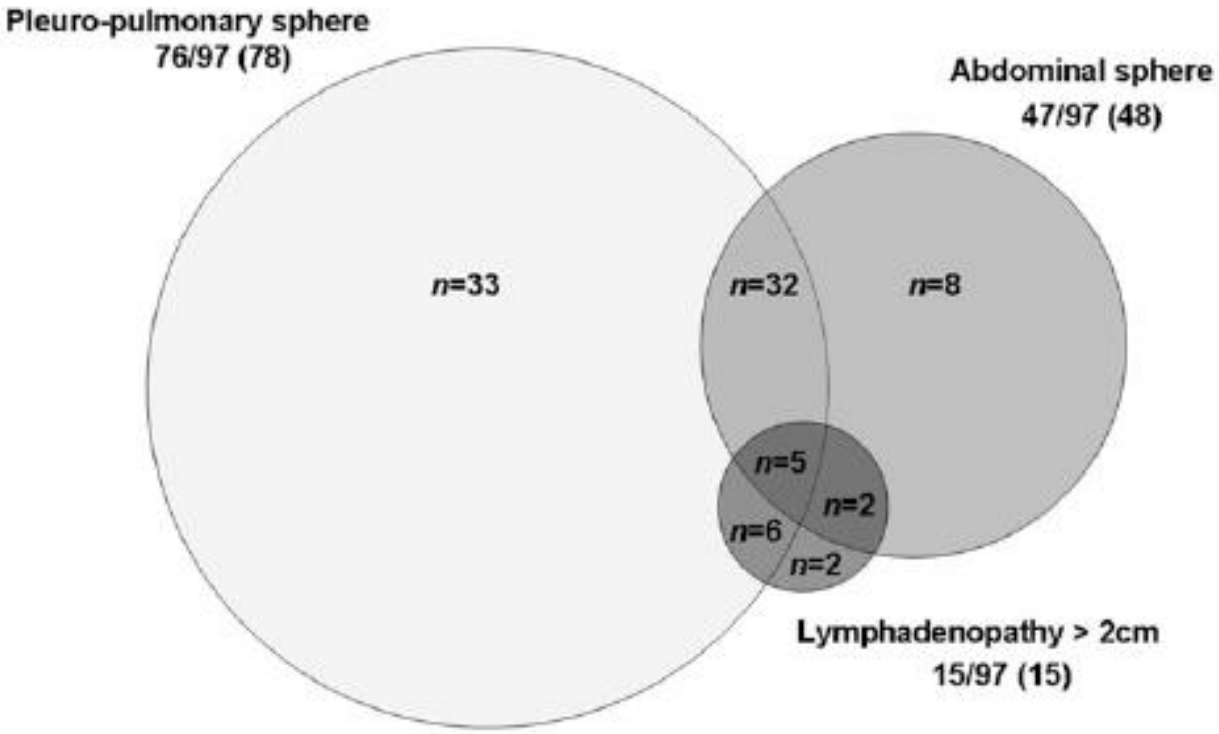
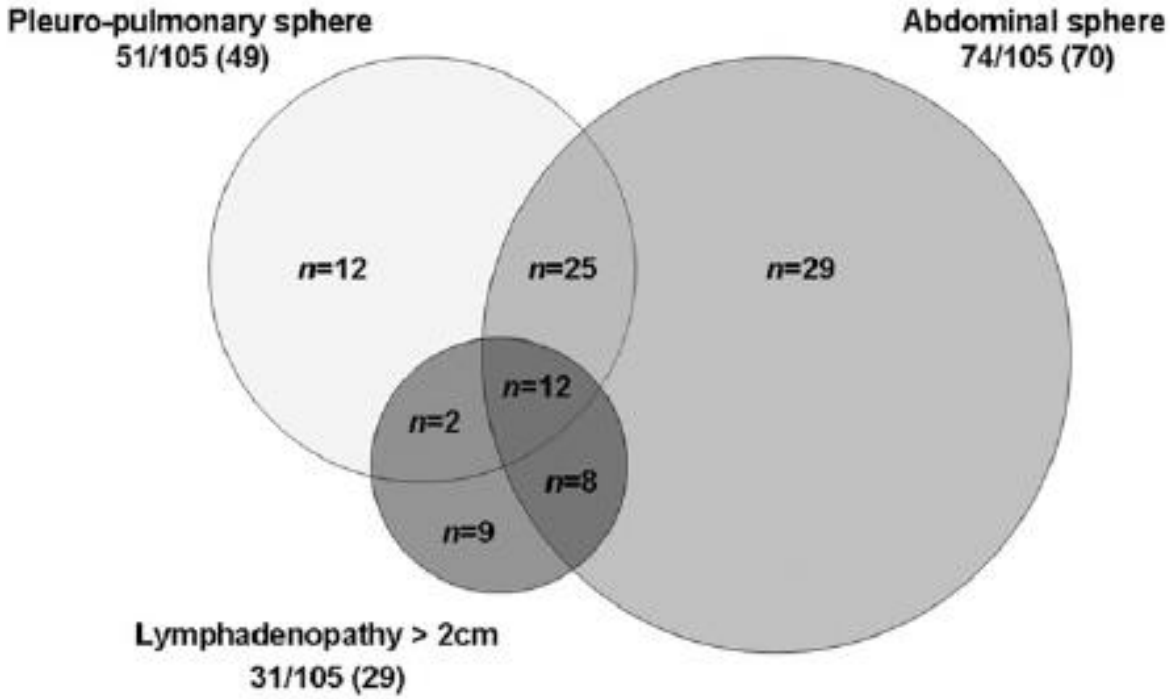
Tuberculosis : clinical aspects



Histoplasmosis : clinical aspects



Adenis A, et al. Am J Trop Med Hyg 2014; 90: 216-23

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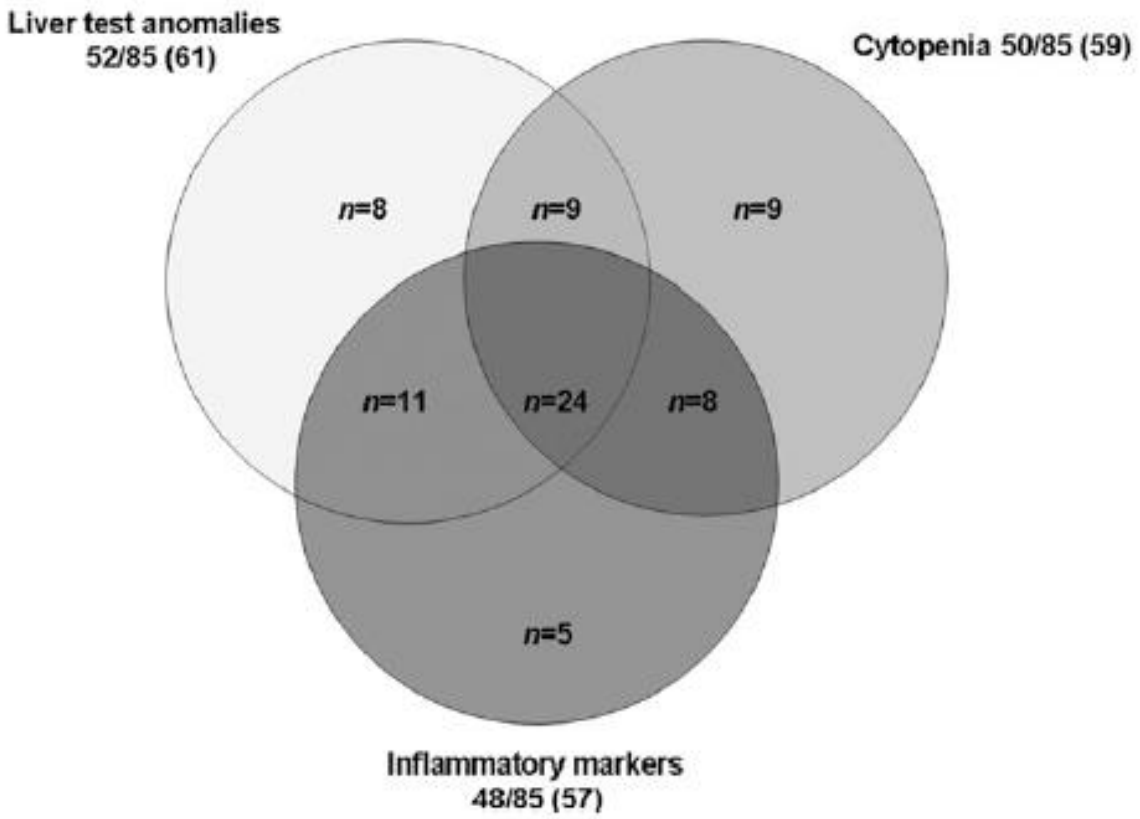
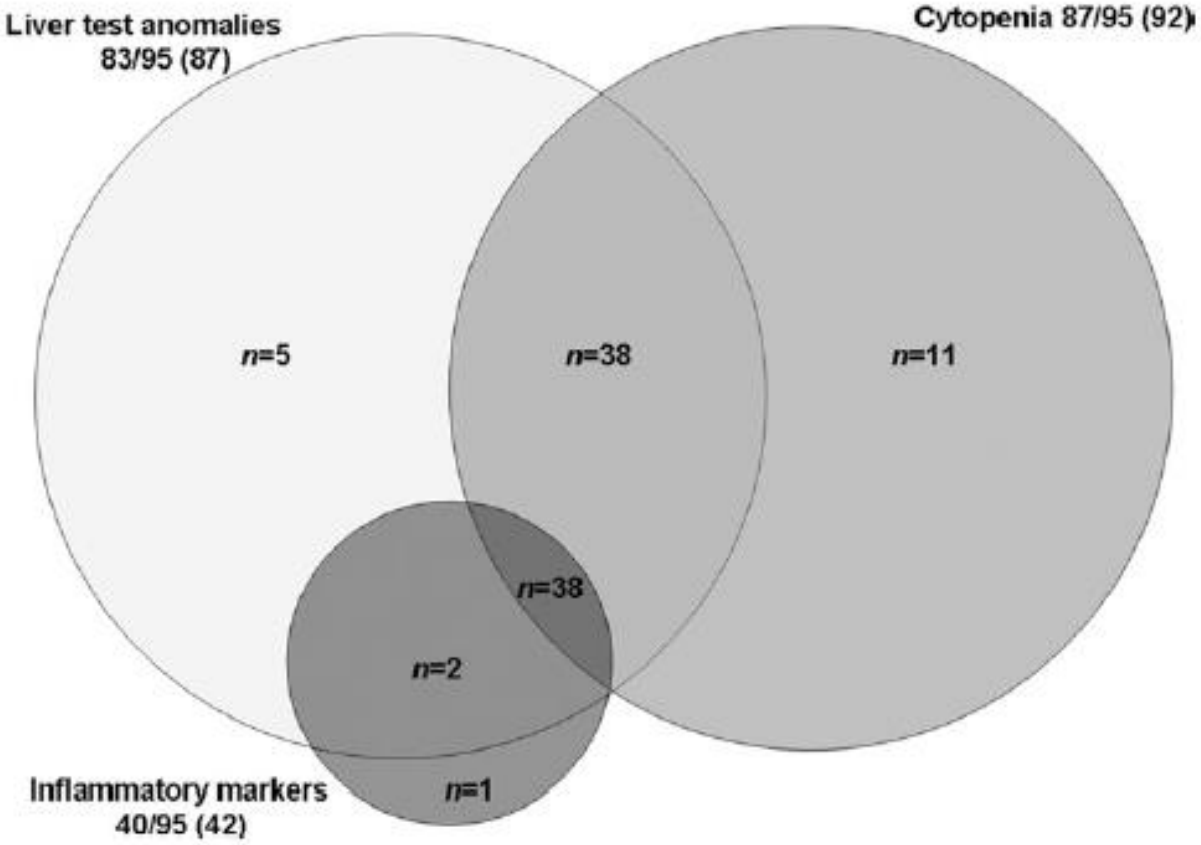
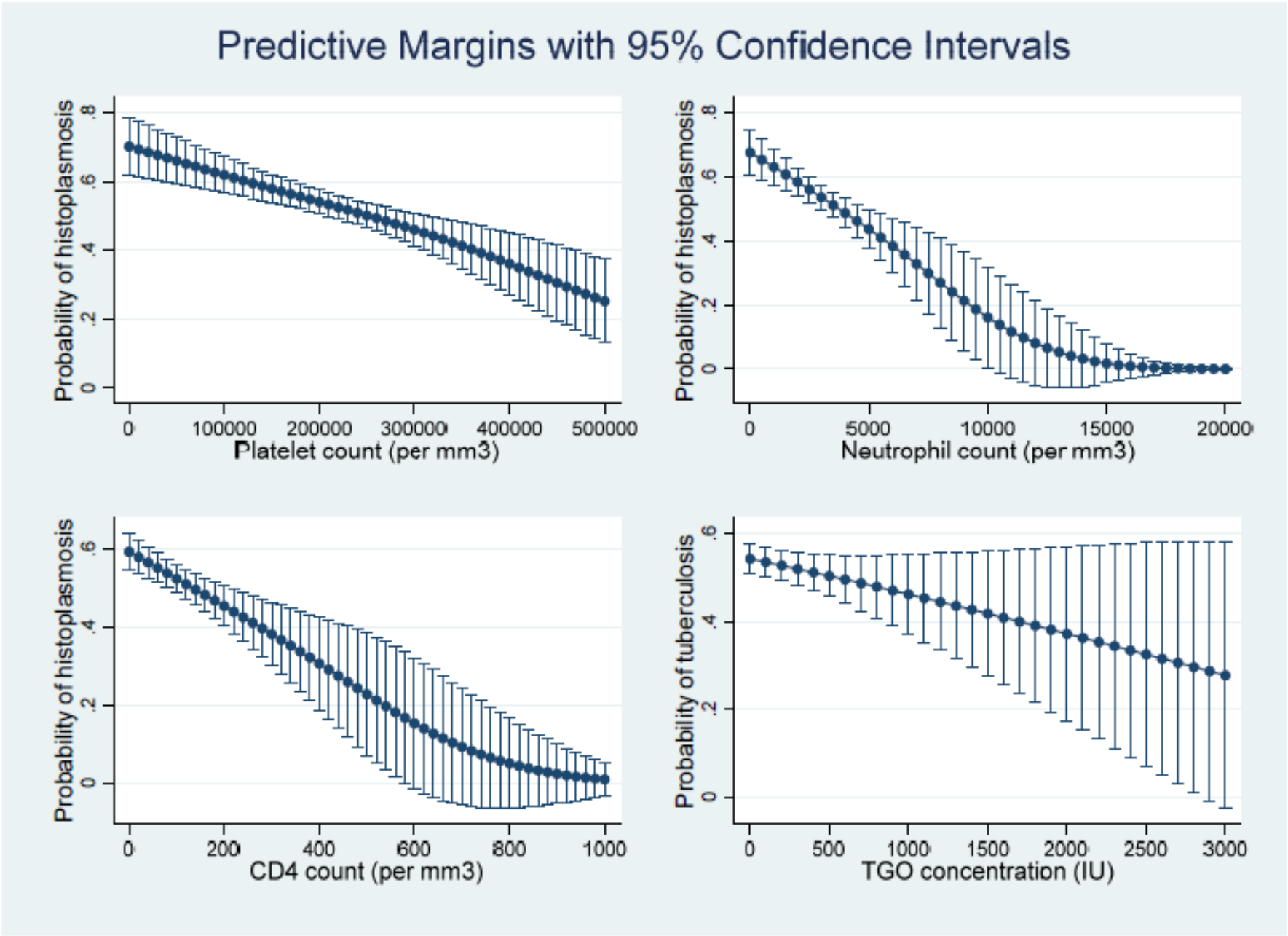
Tuberculosis : biological aspects



Histoplasmosis : biological aspects



Adenis A, et al. Am J Trop Med Hyg 2014; 90: 216-23



Nacher M, et al. J Fungi 2022; 8:16

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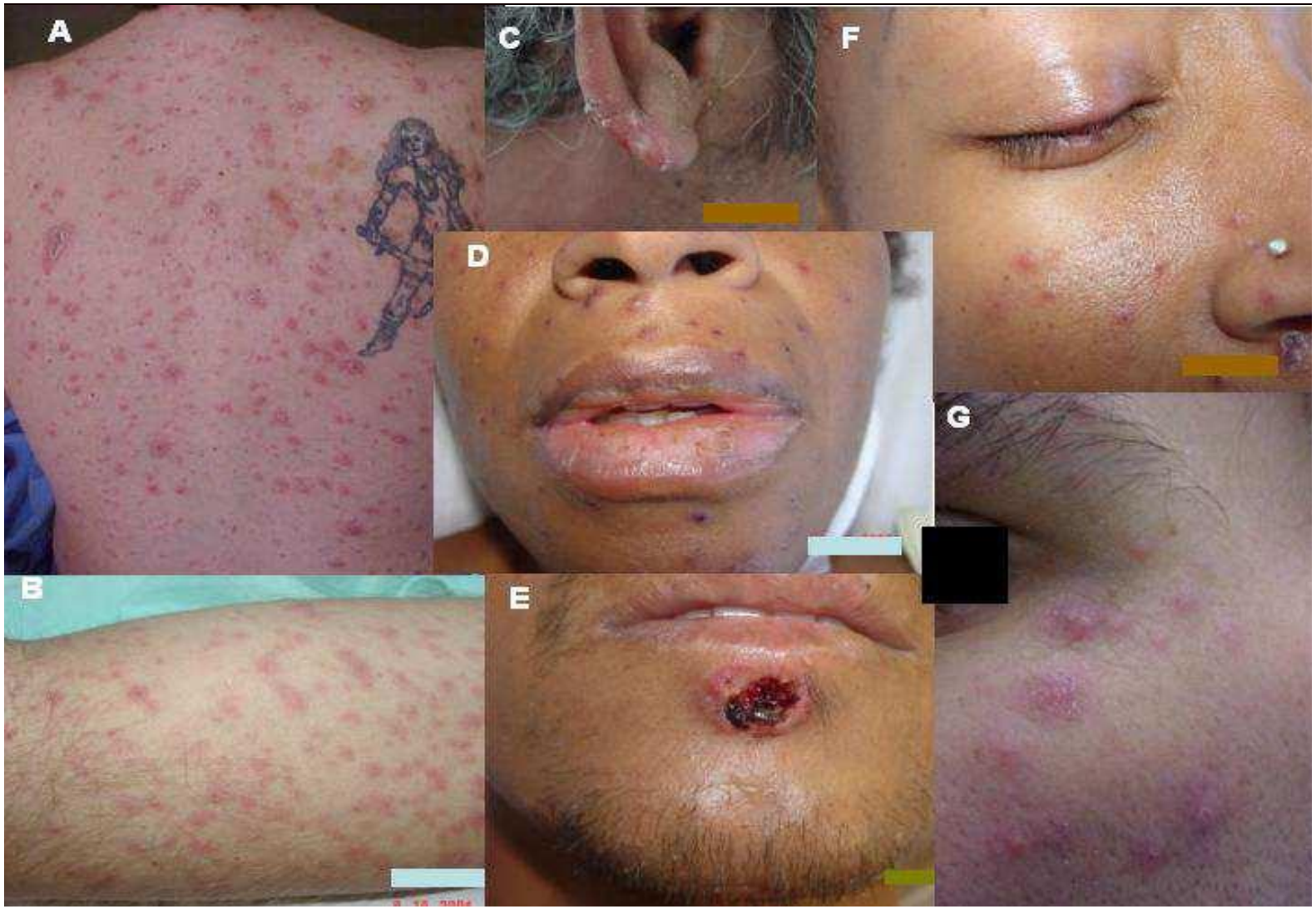
Table 1 Clinical predictors for histoplasmosis, according to different gold standards: CDC test, IMMY assay and classic methods (culture/histopathology).

	Gold standard against which variable was compared			
	IMMY®		Classic methods	
Clinical findings	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Oral ulcers	9.5 (2.1–43.0)	0.001	13.0 (2.5–68.2)	<0.001
Pulmonary symptoms	3.9 (0.5–32.5)	0.227	1.32 (1.2–1.5)	0.189
Papules	7.0 (1.9–27.2)	0.002	1.8 (0.3–10.0)	0.614
Mediastinal lymphadenopathy	3.9 (1.0–14.6)	0.035	6.0 (1.3–28.0)	0.013

CDC, Centers for Disease Control and Prevention; CI, confidence interval; OR, odds ratio.

Hoffmann ER, et al. Mycoses 2017; 60: 20-24

Syphilis of the fungal world



Cunha VS, et al. Clin Experiment Dermatol 2007; 32: 250-5

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Diagnosis

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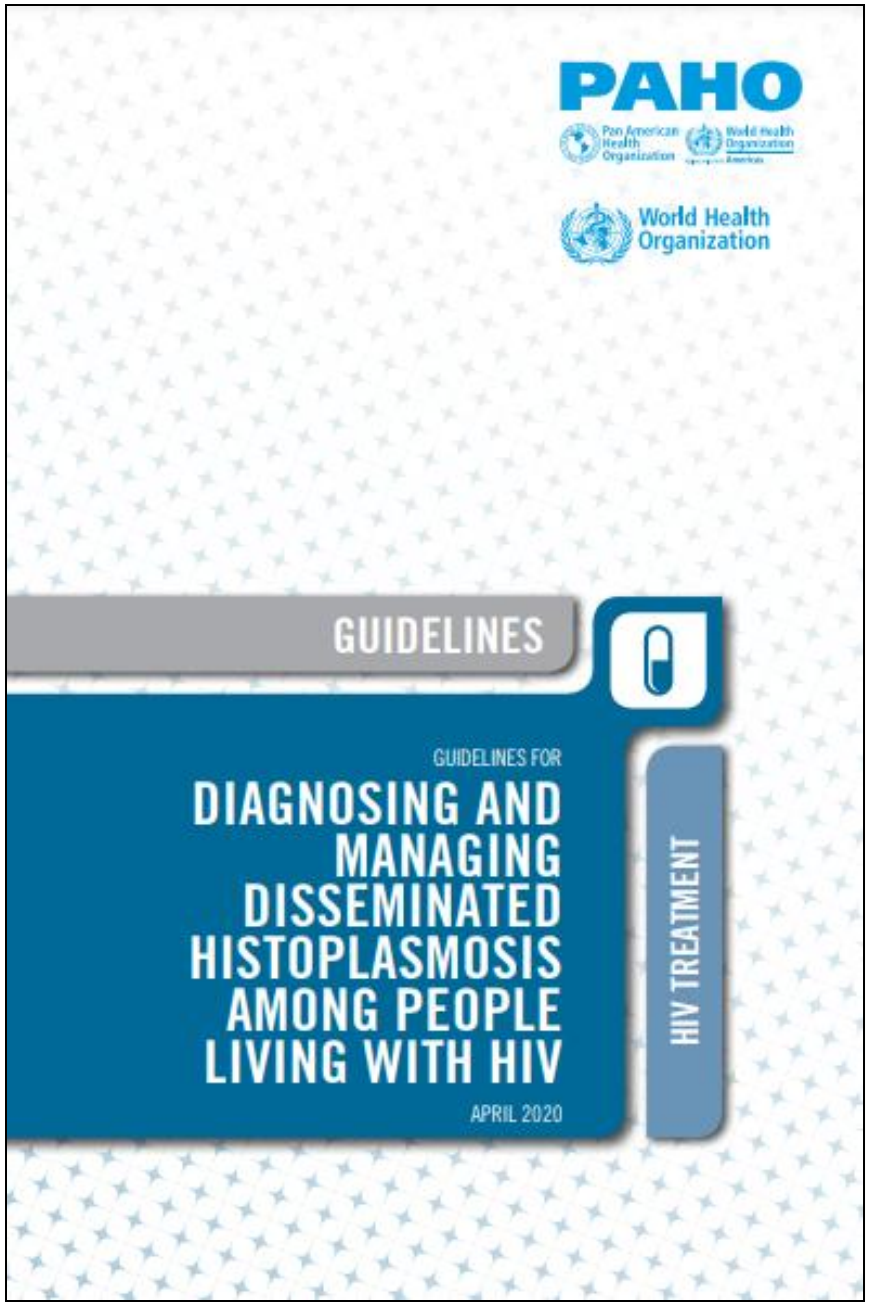

Perez F, et al. J Fungi 2021; 7:134

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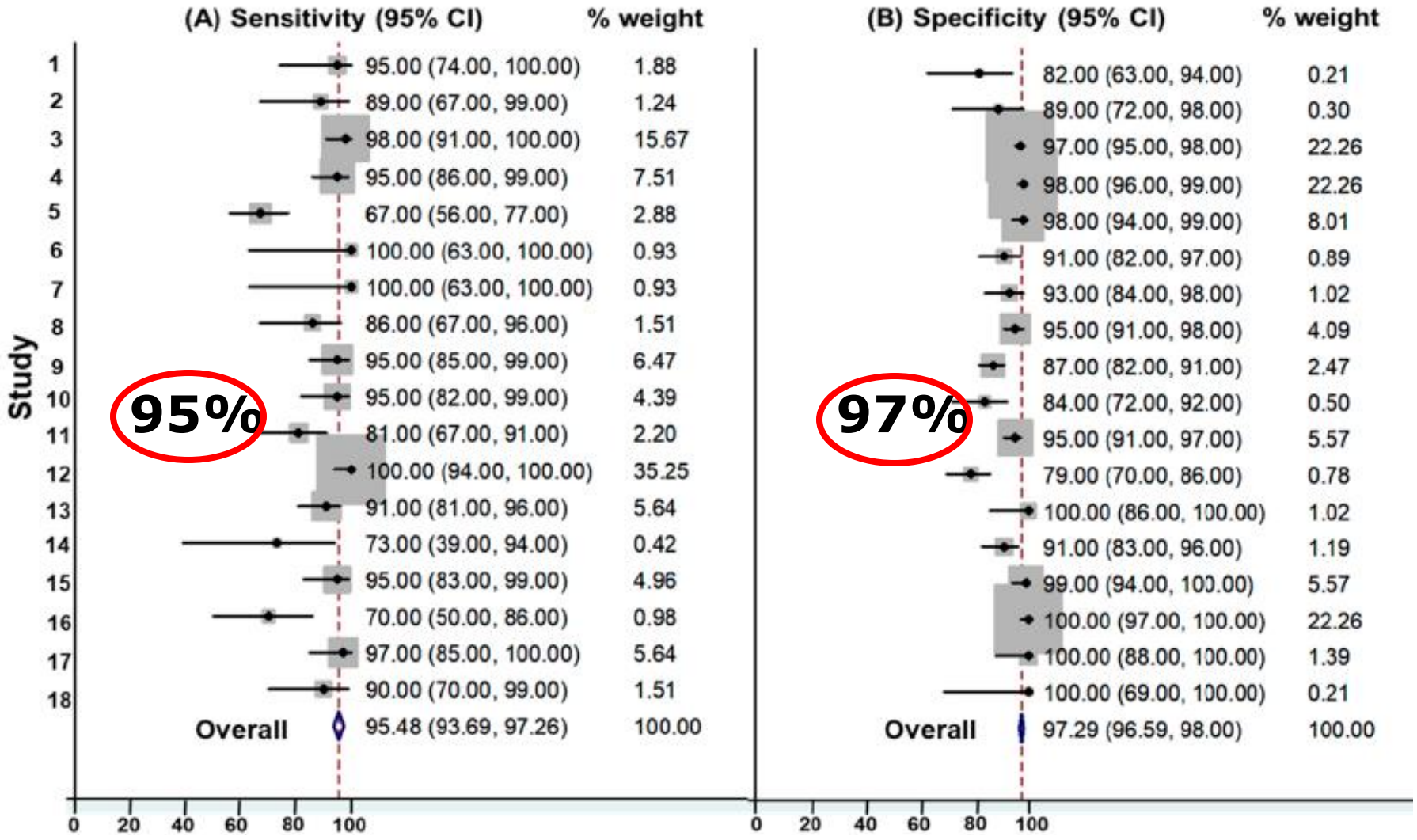
1 Diagnosis of histoplasmosis

"Among people living with HIV, disseminated histoplasmosis should be diagnosed by detecting circulating Histoplasma antigens"
(conditional recommendation; low-certainty evidence)

Perez F, et al. J Fungi 2021; 7:134

IAS Meta-analysis of Ag detection



Caceres D, et al. J Fungi 2019; 5: 76

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RESEARCH ARTICLE

Cost-effectiveness evaluation of routine histoplasmosis screening among people living with advanced HIV disease in Latin America and the Caribbean

Radha Rajasingham[1], Narda Medina[2], Gabriel T. Mousquer[3], Diego H. Caceres[4,5], Alexander Jordan[6], Mathieu Nacher[7], Diego R. Falci[8,9], Ayanna Sebro[10], Alessandro C. Pasqualotto[11,12], Omar Sued[13], Tom Chiller[6], Freddy Perez[11,13]*

Routine Histoplasma antigen screening avoids an estimated 17% of deaths in persons with advanced HIV disease, and is cost-effective compared to no histoplasmosis screening, with an ICER of $26/LYS.

Rajasingham R, et al. PLoS Public Health 2023; 3:e0001861

IAS

Impact of the introduction of a package of care involving early detection of opportunistic infections, a prospective multicenter cohort study of people living with HIV/AIDS in Brazil

Alessandro C. Pasqualotto,[a,b] Omar Sued,[c,j] Nicole Reis,[a,d] Larissa R. Silva,[a] Renata B. A. Soares,[e,f] Cassia S. M. Godoy,[e,f] Marineide G. Melo,[g] Nayla A. Hatem,[a] Bruna Regis Razzolini,[d] Andressa Noal,[g] Tarsila Vieceli,[a,b] Diego R. Falci,[h,i] and Freddy Perez[a,c,j,*]

[a]Federal University of Health Sciences of Porto Alegre, R. Sarmento Leite, 245 - Centro Histórico, Porto Alegre, RS, 90050-170, Brazil
[b]Santa Casa de Porto Alegre, Porto Alegre, RS, Brazil
[c]Pan American Health Organization (PAHO), 525 23 ST NW, Washington DC, 20037, USA
[d]Hospital Vila Nova, R. Catarino Andreatta, 155 - Bairro Vila Nova, Porto Alegre, RS, 91750-040, Brazil
[e]Hospital Estadual de Doenças Tropicais Dr Anuar Auad, Alameda do Contorno, 3556, Jardim Bela Vista, Goiânia, GO, 74850-400, Brazil
[f]Pontifícia Universidade Católica de Goiás, Goiânia, GO, Brazil
[g]Grupo Hospitalar Conceição, Av. Francisco Trein, 596 - Cristo Redentor, Porto Alegre, RS, 91350-200, Brazil
[h]Hospital de Clínicas de Porto Alegre, Rua Ramiro Barcelos, 2350 Bloco A, Av. Protásio Alves, 211 - Bloco B e C - Santa Cecília, Porto Alegre, RS, 90035-903, Brazil
[i]Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre, RS, Brazil

The Lancet Regional Health - Americas 2025;45: 101085
Published Online xxx
https://doi.org/10.1016/j.lana.2025.101085

Summary

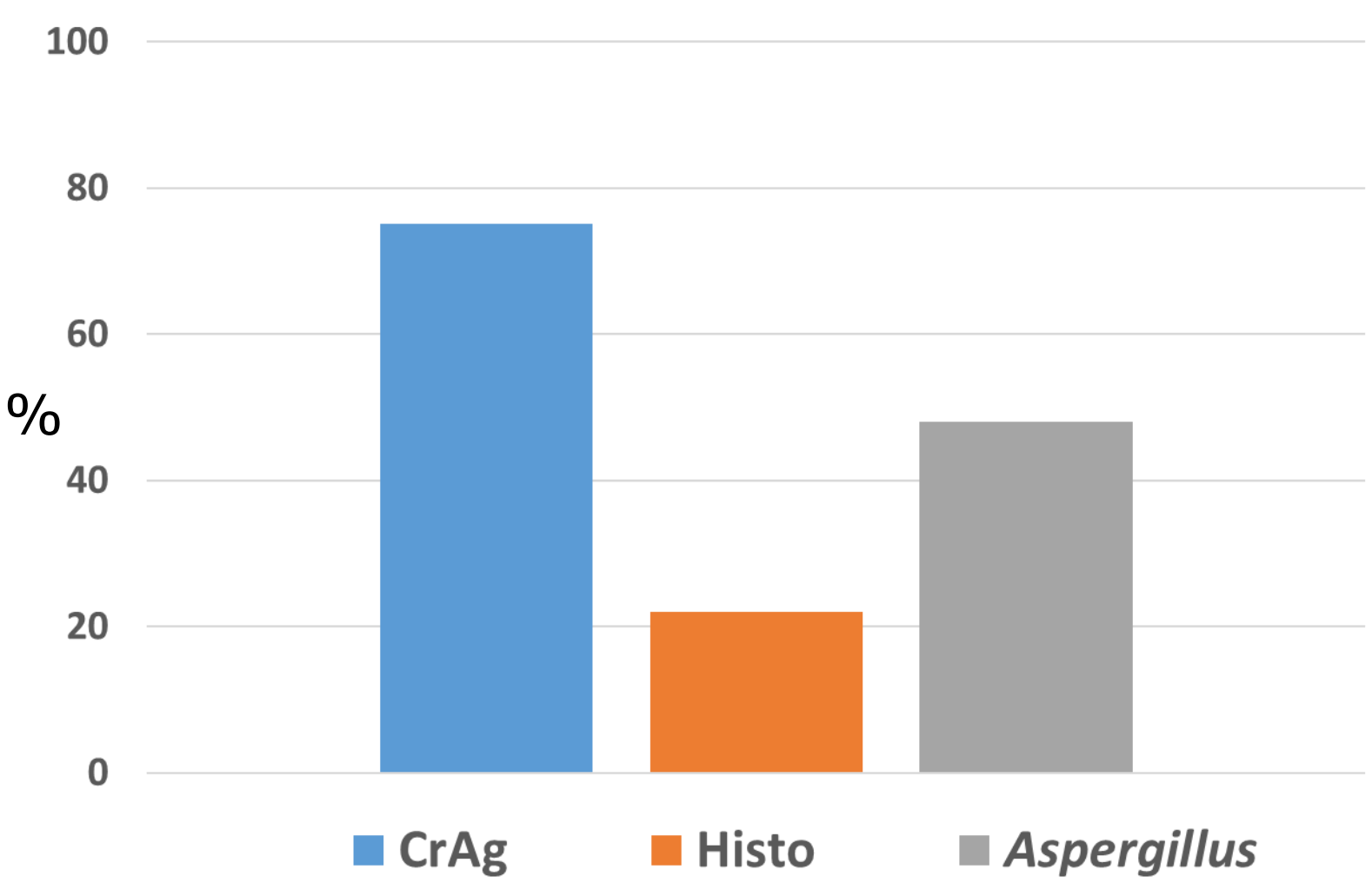
Background Opportunistic infections (OIs) significantly contribute to morbidity and mortality in advanced HIV disease. This study evaluates the efficacy of point-of-care (POC) diagnostics for tuberculosis (TB), histoplasmosis, and cryptococcosis in routine HIV care in Brazil.

Methods A prospective multicenter cohort study was conducted across five hospitals enrolling people living with HIV (PLHIV) with CD4+ T-cell count <200 cells/mm^3 or OI symptoms, regardless of CD4 count, HIV-naïve patients, those initiating treatment, and individuals with unsuppressed viral load lost to follow-up (>3 months). POC tests included VISITECT CD4 Advanced Disease, TB LAM Ag (Abbott), GeneXpert MTB/RIF (Cepheid), Histoplasma antigen LFA (MiraVista), and CrAg LFA (IMMY). Patients were followed at 30 and 90 days. Retrospective data for six months pre-study was collected for comparison.

Findings Among 419 PLHIV (55% cisgender men, 44% cisgender women, 1% transgender; mean age: 42 years, SD ± 11.1), 46% had confirmed OIs: TB (34%), cryptococcosis (12%), histoplasmosis (10%). Co-infections were frequent, with TB and histoplasmosis (44%). Cryptococcal meningitis and severe histoplasmosis were diagnosed in 5% and 6%, respectively. TB LAM was positive in 27% of tested patients, with 74% having disseminated TB. POC testing increased detection rates for TB, (1.8-fold) cryptococcosis (2.8-fold), and histoplasmosis (2.8-fold) compared to historical data. Survival rates were 87% at 30 days and 80% at 90 days, with cryptococcal antigenemia associated with higher mortality.

Interpretation POC testing improved OI diagnosis, aligning with WHO guidelines. These findings highlight the importance of integrating rapid diagnostics into HIV programs and the need for further research on long-term outcomes.

IAS Dx capabilities in Latin Am



Falci DR, Pasqualotto AC. Mycoses 2019; 62: 368-72

Treatment

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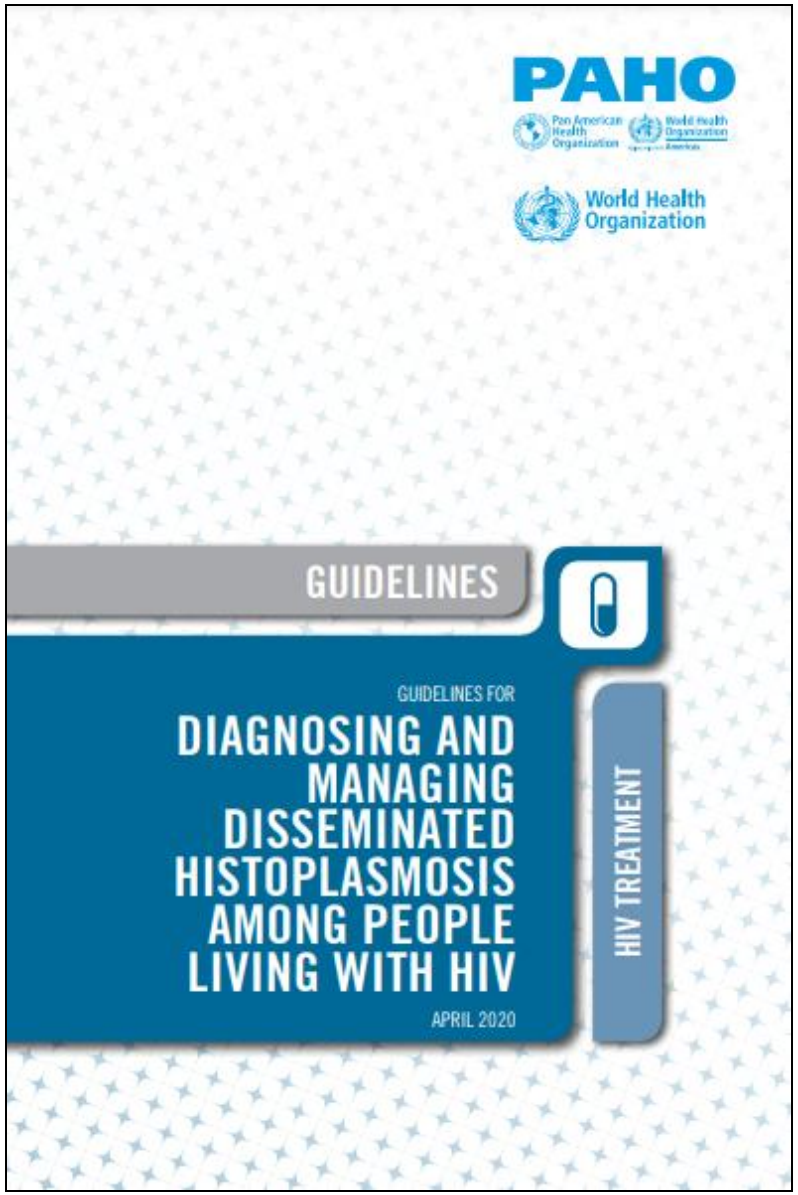

Global guideline for the diagnosis and management of the endemic mycoses: an initiative of the European Confederation of Medical Mycology in cooperation with the International Society for Human and Animal Mycology

George R Thompson III, Thuy Le, Ariya Chindamporn, Carol A Kauffman, Ana Alastruey-Izquierdo, Neil M Ampel, David R Andes, Darius Armstrong-James, Olusola Ayanlowo, John W Baddley, Bridget M Barker, Leila Lopes Bezerra, Maria J Buitrago, Leili Chamani-Tabriz, Jasper F W Chan, Methee Chayakulkeeree, Oliver A Cornely, Cao Cunwei, Jean-Pierre Gangneux, Nelesh P Govender, Ferry Hagen, Mohammad T Hedayati, Tobias M Hohl, Grégory Jouvion, Chris Kenyon, Christopher C Kibbler, Nikolai Klimko, David C M Kong, Robert Krause, Low Lee Lee, Graeme Meintjes, Marisa H Miceli, Peter-Michael Rath, Andrej Spec, Flavio Queiroz-Telles, Ebrahim Variava, Paul E Verweij, Ilan S Schwartz, Alessandro C Pasqualotto

Thompson GR 3rd, et al. Lancet Infect Dis 2021; S1473-3099(21)00191-2

Perez F, et al. J Fungi 2021; 7:134

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2 Treatment of histoplasmosis

2.1. Induction therapy (first line treatment): "Liposomal amphotericin B, 3.0 mg/kg for two weeks is the preferred treatment for severe or moderately severe disease." (conditional recommendation; very-low-certainty evidence)

Alternative Induction therapy: *"In settings where liposomal amphotericin B is unavailable, deoxycholate amphotericin B, 0.7– 1.0 mg/kg, is recommended for two weeks"*

2.2. Maintenance therapy: *"Itraconazole 200 mg three times daily for three days and then 200 mg twice daily is recommended for treating mild to moderate disease"* (conditional recommendation; very-low-certainty evidence)

"Less than 12 months of therapy can be considered when the person is clinically stable, receiving antiretroviral therapy, has suppressed viral loads, and the immune status has improved" (conditional recommendation, very-low-certainty evidence)

Perez F, et al. J Fungi 2021; 7:134

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Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

Single High Dose of Liposomal Amphotericin B in Human Immunodeficiency Virus/AIDS-Related Disseminated Histoplasmosis: A Randomized Trial

Alessandro C. Pasqualotto,[1,2] Daiane Dalla Lana,[1] Cassia S. M. Godoy,[3,4] Terezinha do Menino Jesus Silva Leitão,[5,6] Monica B. Bay,[7,8] Lisandra Serra Damasceno,[5,6] Renata B. A. Soares,[3,4] Roger Kist,[2] Larissa R. Silva,[1] Denusa Wiltgen,[1,2] Marineide Melo,[9] Taiguara F. Guimarães,[3] Marilia R. Guimarães,[10] Hareton T. Vechi,[7] Jacó R. L. de Mesquita,[5] Gloria Regina de G. Monteiro,[7,8] Antoine Adenis,[11] Nathan C. Bahr,[12] Andrej Spec,[13] David R. Boulware,[14] Dennis Israelski,[15] Tom Chiller,[16] and Diego R. Falci[17,18]

[1]Department of Clinical Medicine and Post-Graduation Program in Pathology, Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, Brazil; [2]Infectious Diseases and Internal Medicine Services, Santa Casa de Misericórdia de Porto Alegre, Porto Alegre, Brazil; [3]Infectious Diseases Service, Hospital de Doenças Tropicais, Goiânia, Brazil; [4]Department of Research and Education, Pontifícia Universidade Católica de Goiás, Goiânia, Brazil; [5]Infectious Diseases Service, Hospital São José de Doenças Infecciosas, Fortaleza, Brazil; [6]Department of Public Health, Federal University of Ceará, Fortaleza, Brazil; [7]Department of Infectious Diseases, Federal University of Rio Grande do Norte, Natal, Brazil; [8]Infectious Diseases Service, Giselda Trigueiro Hospital and Instituto de Medicina Tropical do Rio Grande do Norte, Natal, Brazil; [9]Infectious Diseases Service, Hospital Nossa Senhora da Conceição, Porto Alegre, Brazil; [10]Department of Nephrology, Universidade de São Paulo, São Paulo, Brazil; [11]Centre d'Investigation Clinique Antilles Guyane Inserm CIC1424, Centre Hospitalier de Cayenne, Cayenne, France; [12]Division of Infectious Diseases, Department of Medicine, University of Kansas Medical Center, Kansas City, Kansas, USA; [13]Division of Infectious Disease, Washington University in St. Louis School of Medicine, St. Louis, Missouri, USA; [14]Division of Infectious Diseases and International Medicine, Department of Medicine, University of Minnesota, Minnesota, USA; [15]International Medical Affairs, Global Patient Solutions, Gilead Sciences, San Francisco, California, USA; [16]Mycotic Division, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; [17]Infectious Diseases Service, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil; and [18]Department of Clinical Medicine, Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre, Brazil

Single High-dose of Liposomal Amphotericin B in HIV/AIDS-related Disseminated Histoplasmosis: a Randomized Trial

Pasqualotto et al., 2023 | *Clinical Infectious Diseases*

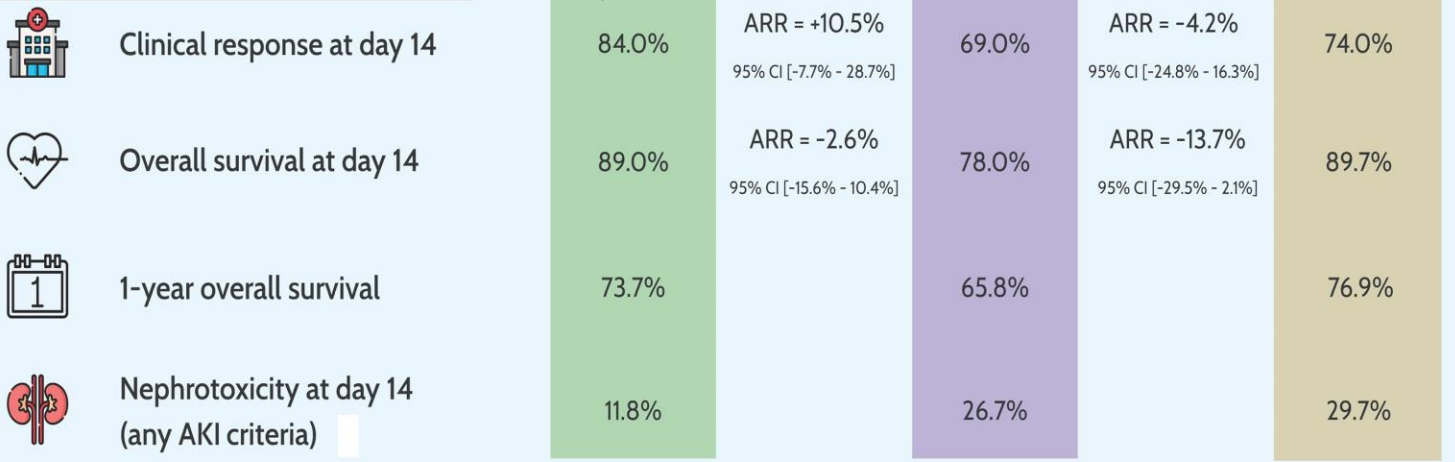
Infectious Diseases Society of America

Liposomal amphotericin is the drug of choice for disseminated histoplasmosis, but access is limited due to the high costs of the conventional long regimens.

PARTICIPANTS: Adult people living with HIV, hospitalized and diagnosed with disseminated histoplasmosis, in six Brazilian tertiary medical centers.

METHODS

Prospective randomized multicenter open-label trial. Interventions: One or two-dose induction L-AmB therapy versus control (three arms), all followed by oral itraconazole therapy.

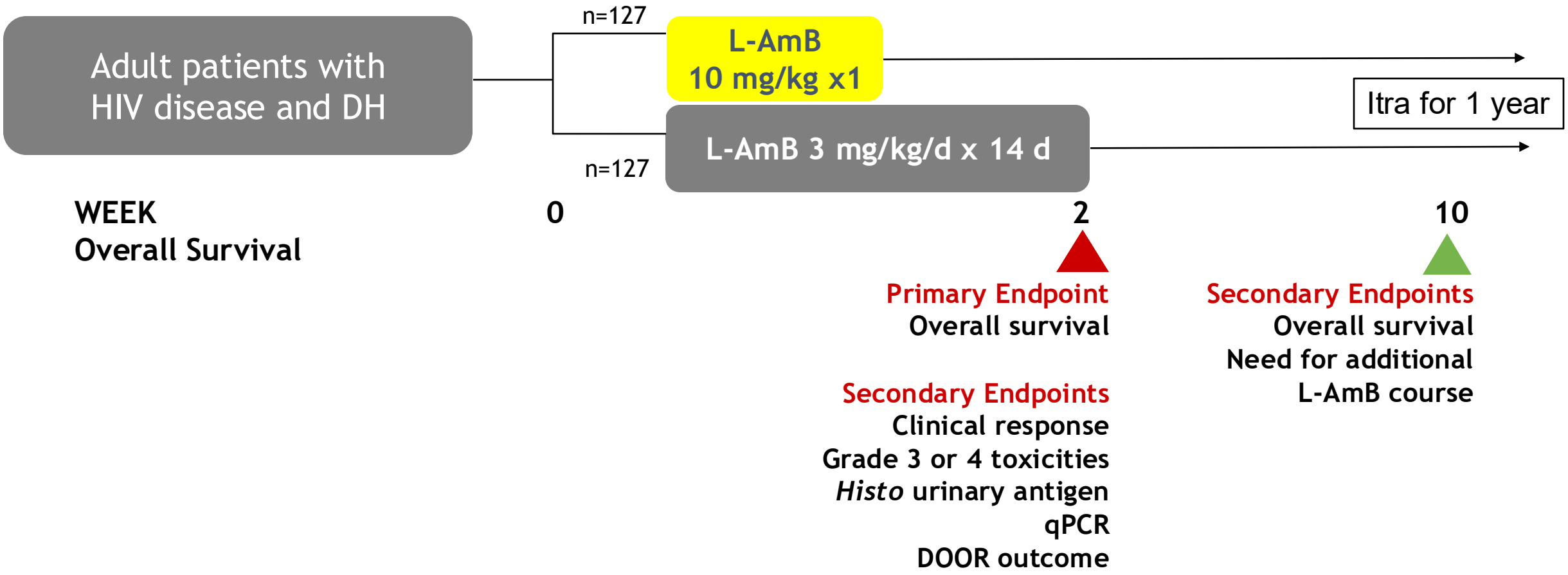


One day induction therapy with 10 mg/kg of L-AmB in AIDS-related histoplasmosis was safe. A phase III clinical trial is needed to confirm clinical response. A single-dose regimen would markedly reduce drug-acquisition costs and shorten and simplify treatment, which are key points in terms of increased access.

Clinical Infectious Diseases https://doi.org/10.1093/cid/ciad313

IAS Induction trial

Randomized, multicenter (16 centers), open-label study in Brazil



Non-inferiority trial with a 90% power to detect a margin of 10% with a two-tailed p-alpha of 5%
If non-inferiority is reached, the study will be tested for superiority

IAS DOOR outcome - Secondary endpoint

- Evaluated on D14 by a blinded external committee

  (i) Death within the first 2 weeks of randomization

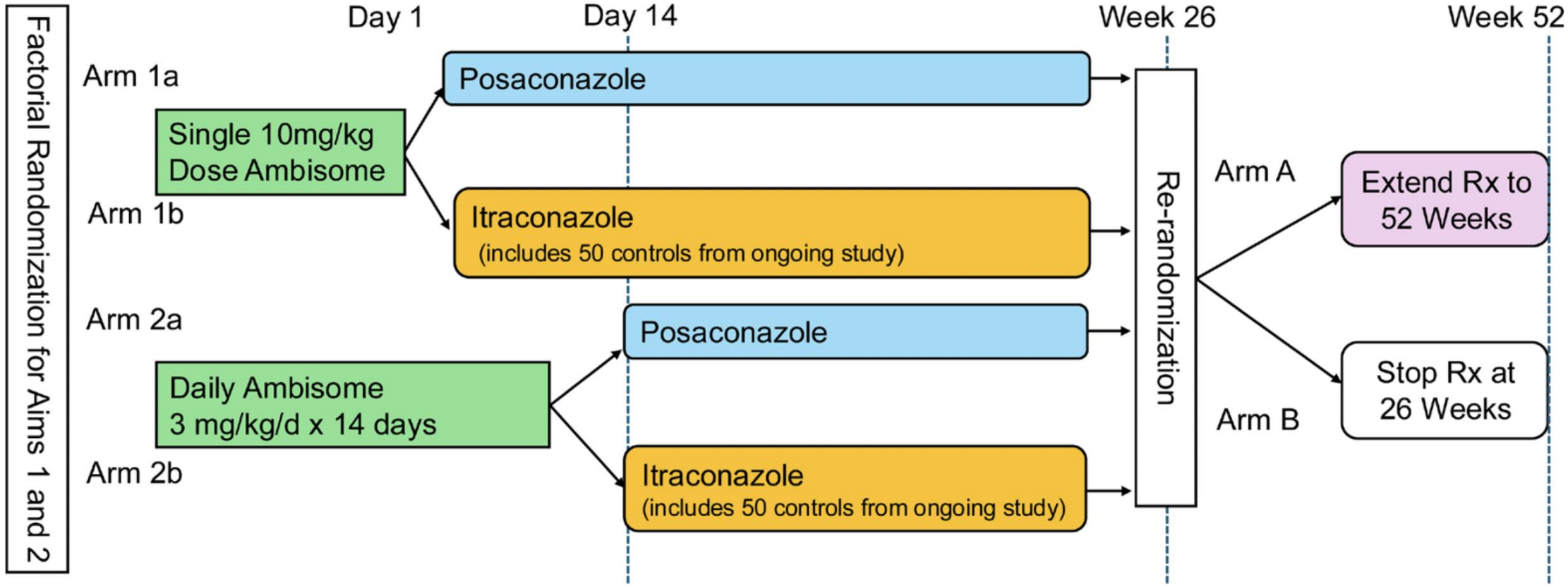
  (ii) Death within the 10-week follow-up period

  (iii) Grade 4 laboratory abnormality in the first 2 week

  (iv) Grade 3 laboratory abnormality in the first 2 weeks

  (v) Survival at week 10

IAS Factorial trial



n=664

Study PIs: Nathan Bahr and Alessandro C. Pasqualotto

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CORRESPONDENCE

Fungal diseases are not in the radar of main international HIV conferences

do Nascimento, Anderson A.A.[a]; Pasqualotto, Alessandro C.[a,b]

Author Information

AIDS 39(1):p 99-100, January 01, 2025. | ***DOI:*** 10.1097/QAD.0000000000004060

0.8% only

International AIDS Conference

IAS Conference

CROI

EACS

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Thank you

pasqualotto@ufcspa.edu.br

+55 51 999951614

Twitter: @PasqualottoAle