



HIV and Leishmaniasis co-infection

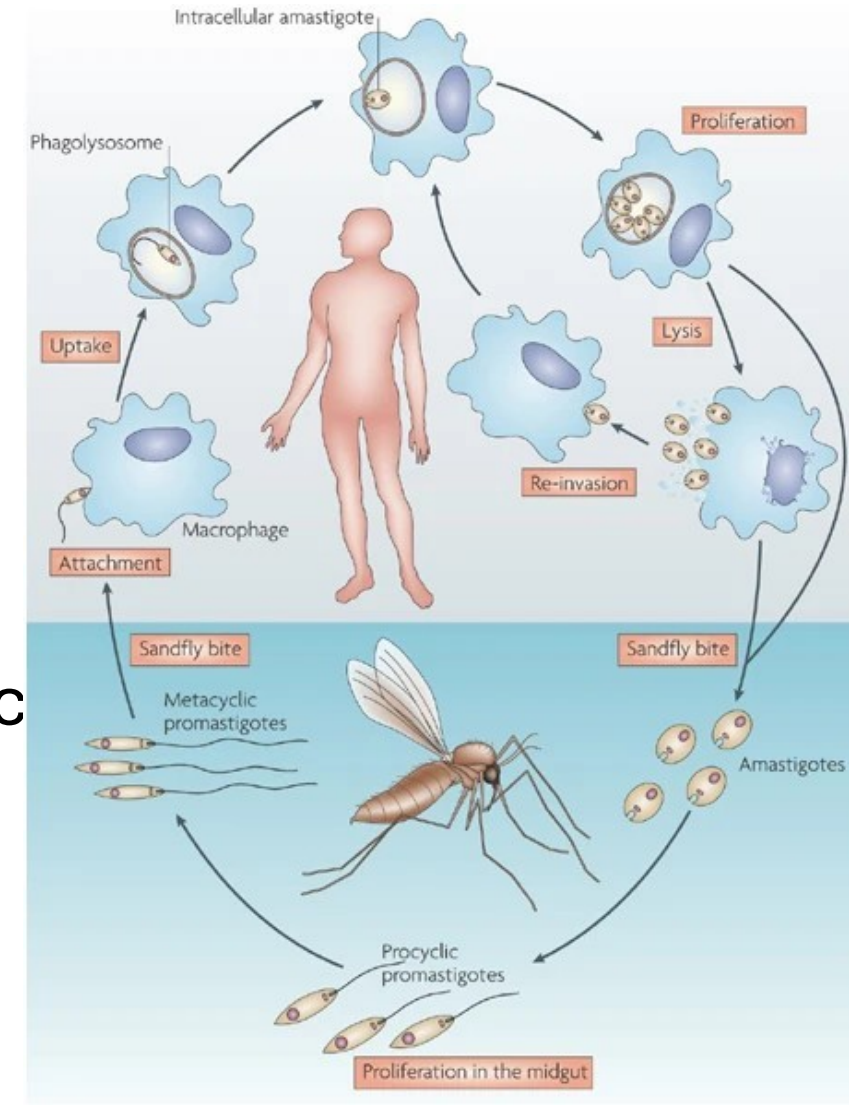
Prof. Esayas Kebede Gudina (MD, DTMH, PhD)
Department of Internal Medicine

Jimma University, Ethiopia

28 July 2026

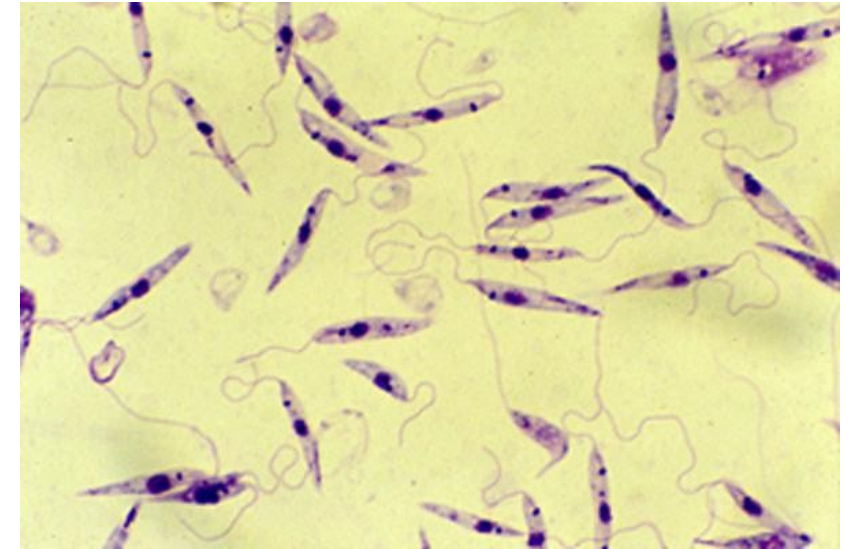
Presentation outline

- Burden of VL
- HIV-VL Syndemic
- East Africa – The Epicenter of HIV-VL syndemic
- Clinical challenges
- Management strategies
- Public health implication



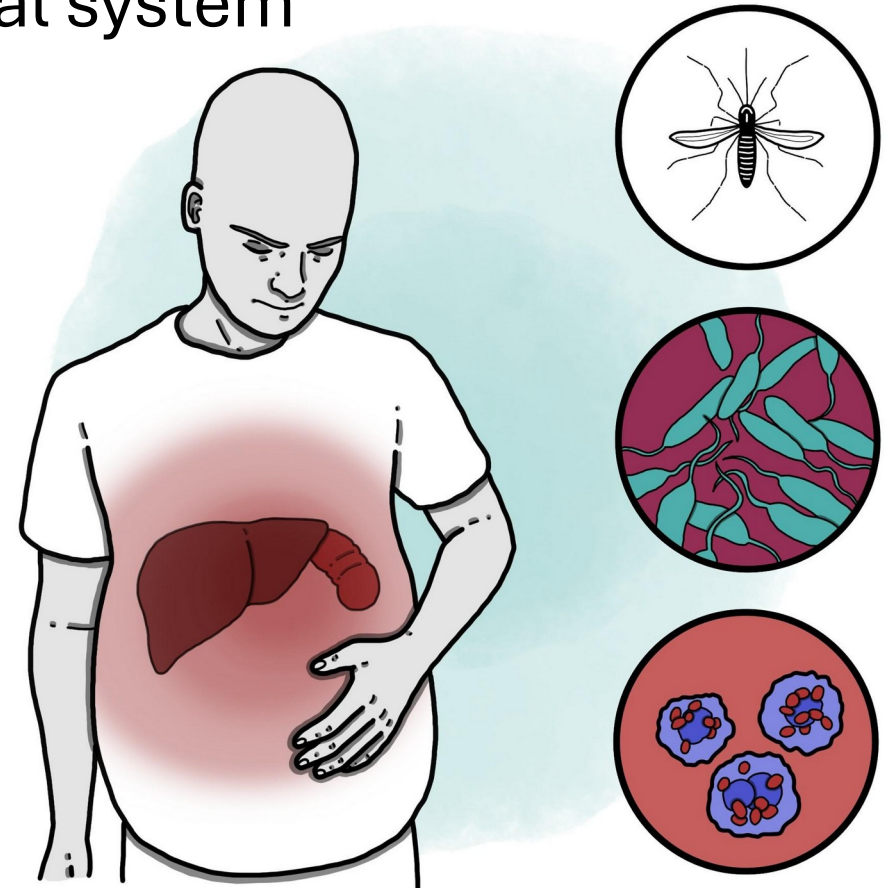
Leishmaniasis at a glance

- Vector-borne protozoan infection
- Caused by *Leishmania* species
- Spread by the bite of infected female phlebotomine sandflies
- One of the NTDs
- Major forms:
 - Visceral leishmaniasis (VL, kala-azar)
 - Cutaneous leishmaniasis (CL)
 - Mucocutaneous leishmaniasis (MCL)



Visceral leishmaniasis

- Affects predominantly reticuloendothelial system
 - Spleen
 - Liver
 - Bone marrow
- Potentially fatal if untreated

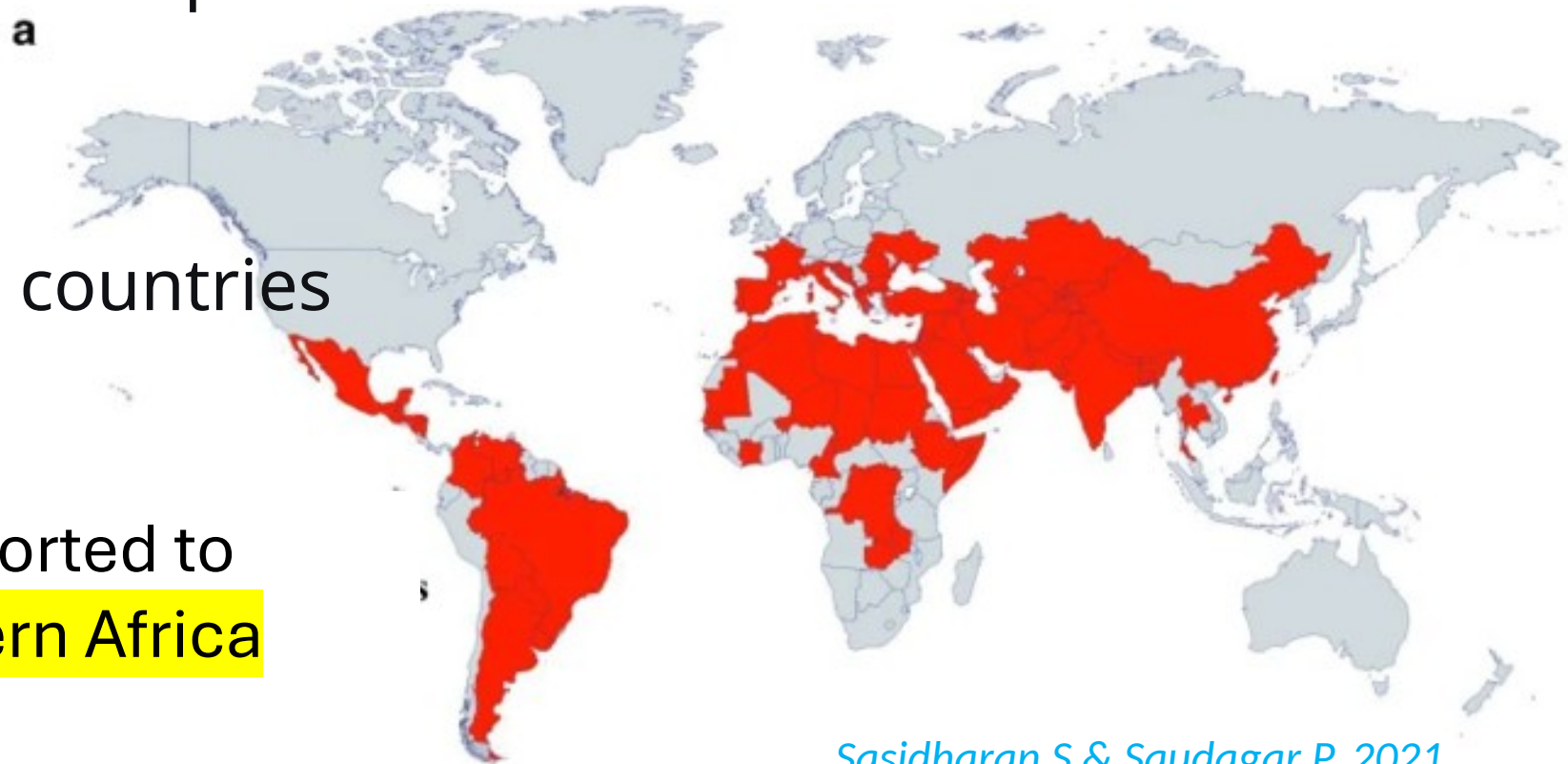


Global Burden of VL

- 50,000–90,000 new cases annually worldwide
- Only **25-45%** of cases reported to WHO

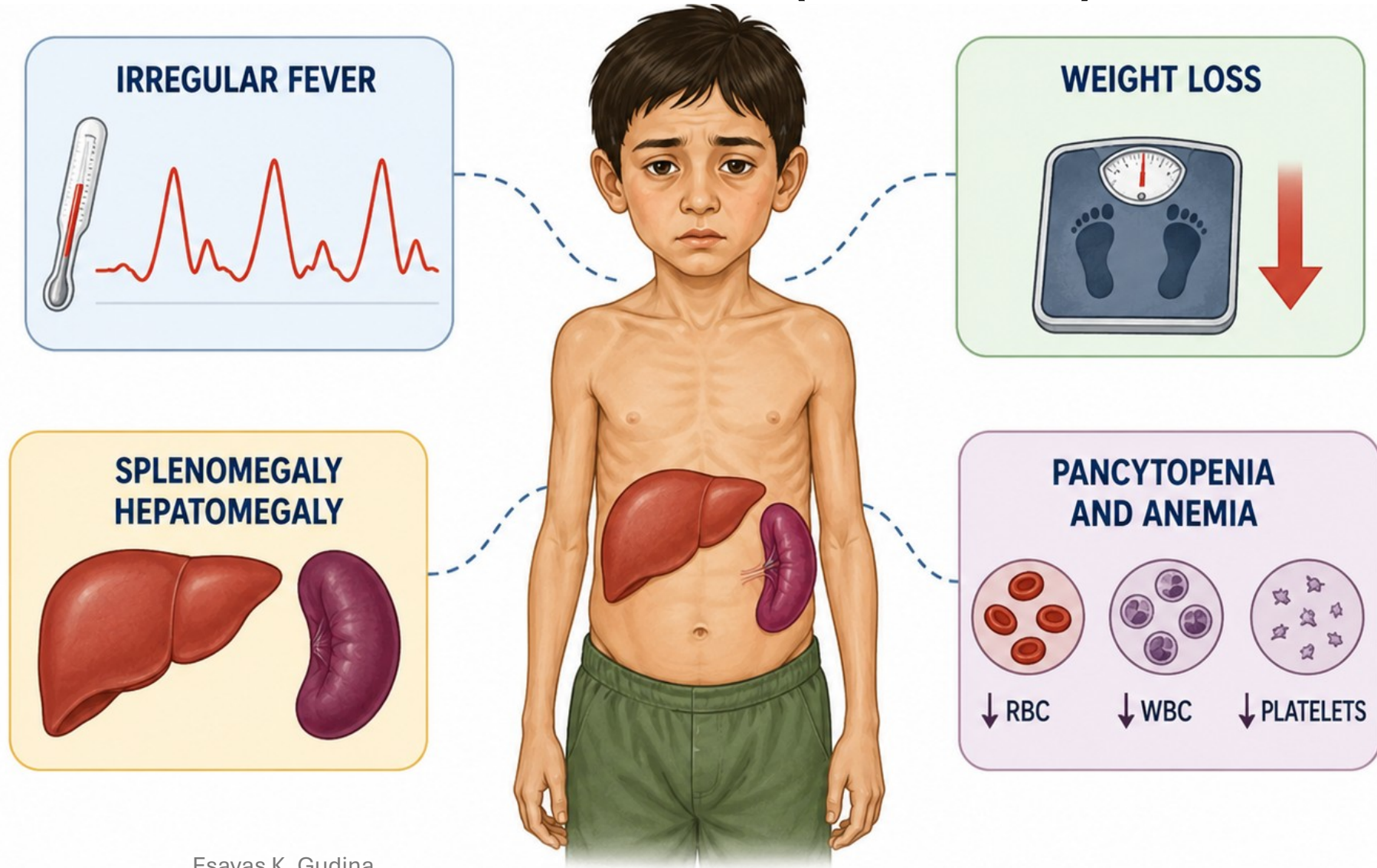
- **90%** of cases in 10 countries

- **66%** of VL cases reported to WHO are from **Eastern Africa**



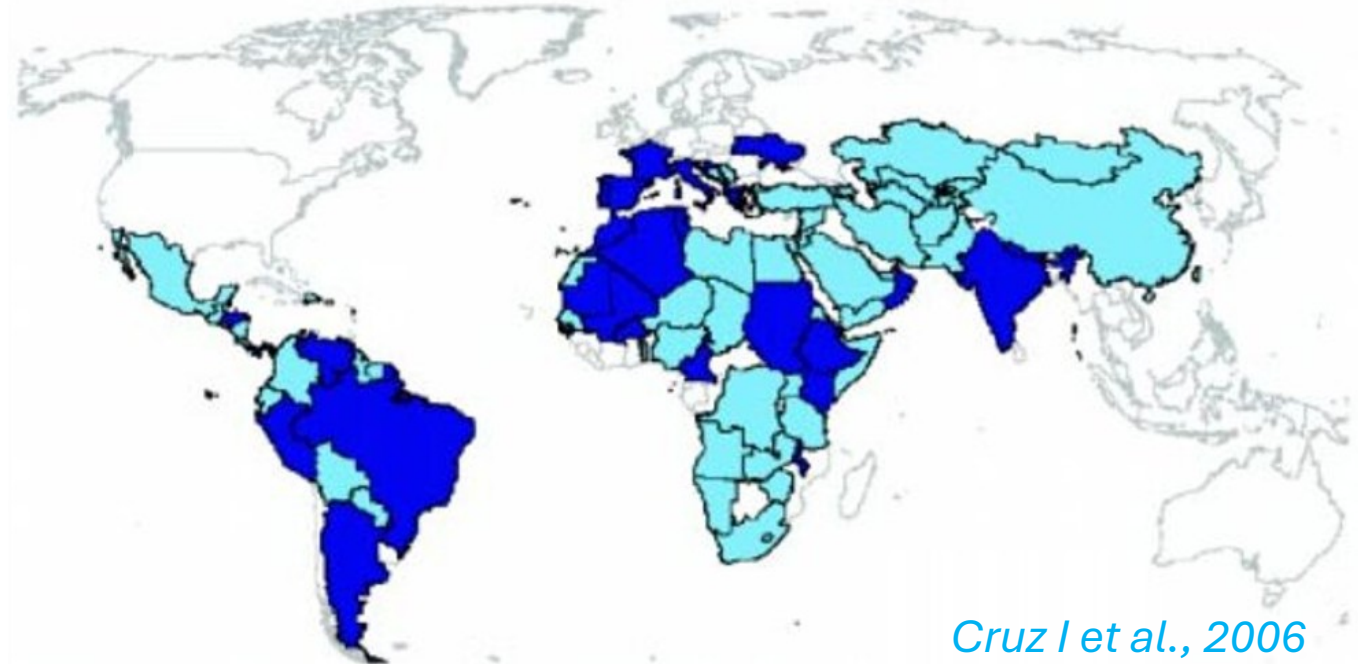
Sasidharan S & Saudagar P. 2021

Clinical Manifestations (Classic)

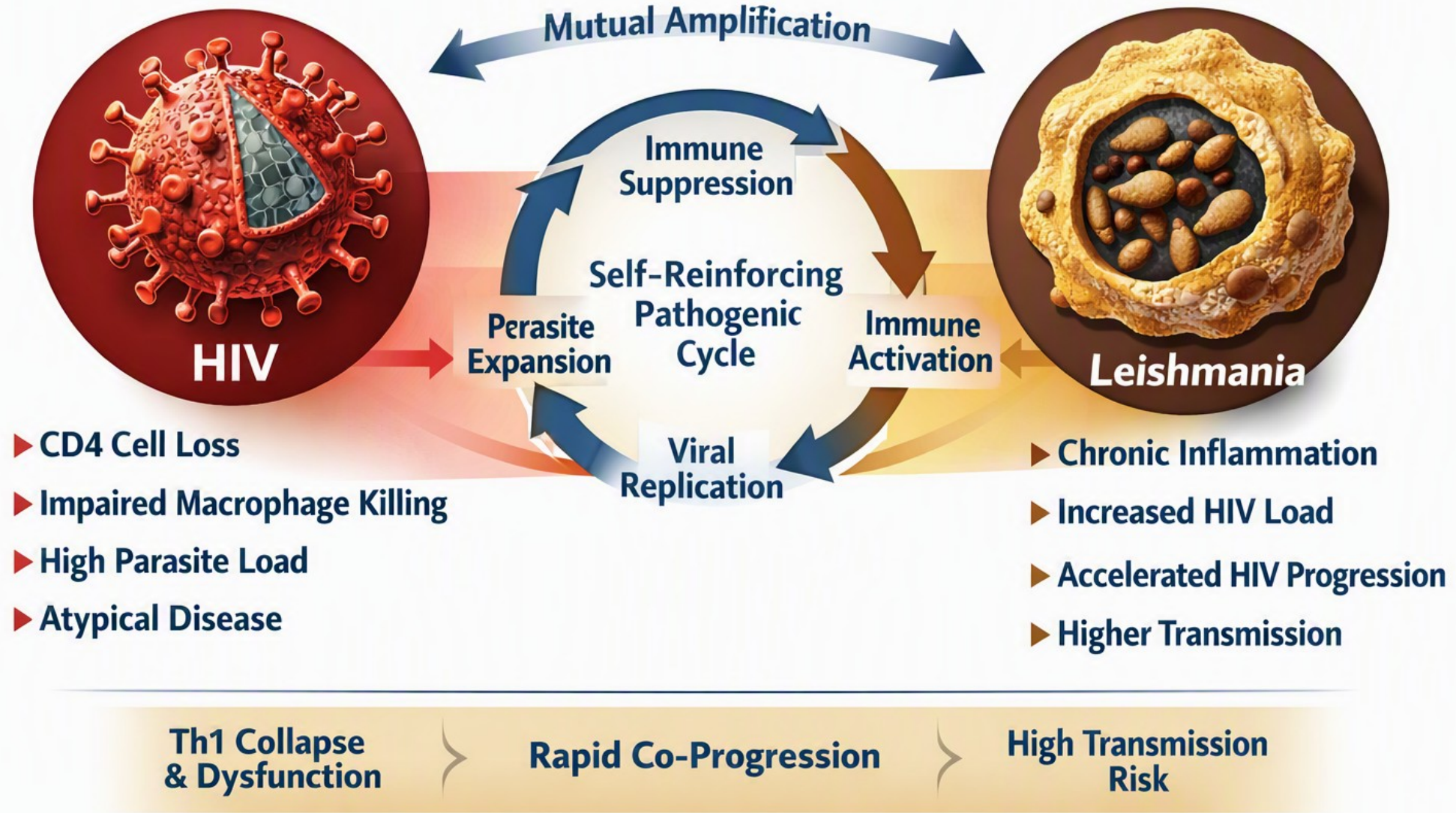


The HIV-VL Coinfection Syndemic

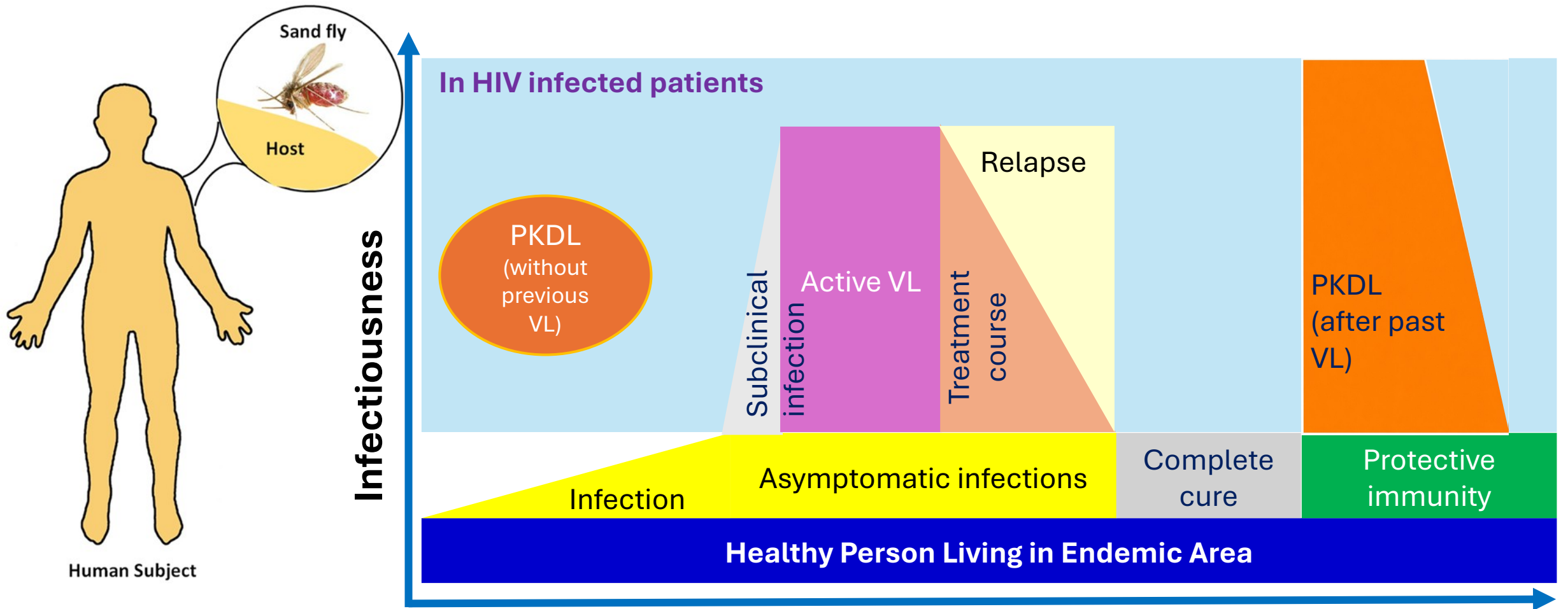
- **First Reported in southern Europe (mid-1980s):**
 - Spain: up to 60% HIV prevalence among VL patients in IV drug users
- Now documented in **45 countries** worldwide
- Global prevalence of VL in PLH is 6% (*Kantzanou M et al., 2023*)
- High rates reported from:
 - Brazil
 - Ethiopia
 - India



Why does HIV increase the risk of VL?



HIV positive individuals are at higher risk of developing VL once infected



Clinical Consequences

VL is an **AIDS-defining** condition characterized by:

- Atypical disease presentations
 - Higher rates of treatment failure and relapse
 - Increased drug toxicity
- 
- More severe morbidity
 - Higher mortality rates

Public Health Significance

- Coinfected patients carry high parasite loads (*'effective reservoir'*)
→ highly infectious to sandflies → increased transmission
- Repeated treatment with the same medicines → drug-resistant *Leishmania* strains



Coinfected patients are difficult to cure



A major threat to VL control and elimination

East Africa: The Global Epicenter

- Estimated annual incidence: **29,400–56,700** cases
- Highest VL-HIV coinfection rate in the world
- HIV prevalence among VL patients in Northwest Ethiopia **20-41%**

Alvar J et al., 2008

Mengistu G & Ayele B, 2007

- **24.4%** of all VL patients admitted to Gondar Hospital were HIV coinfectd

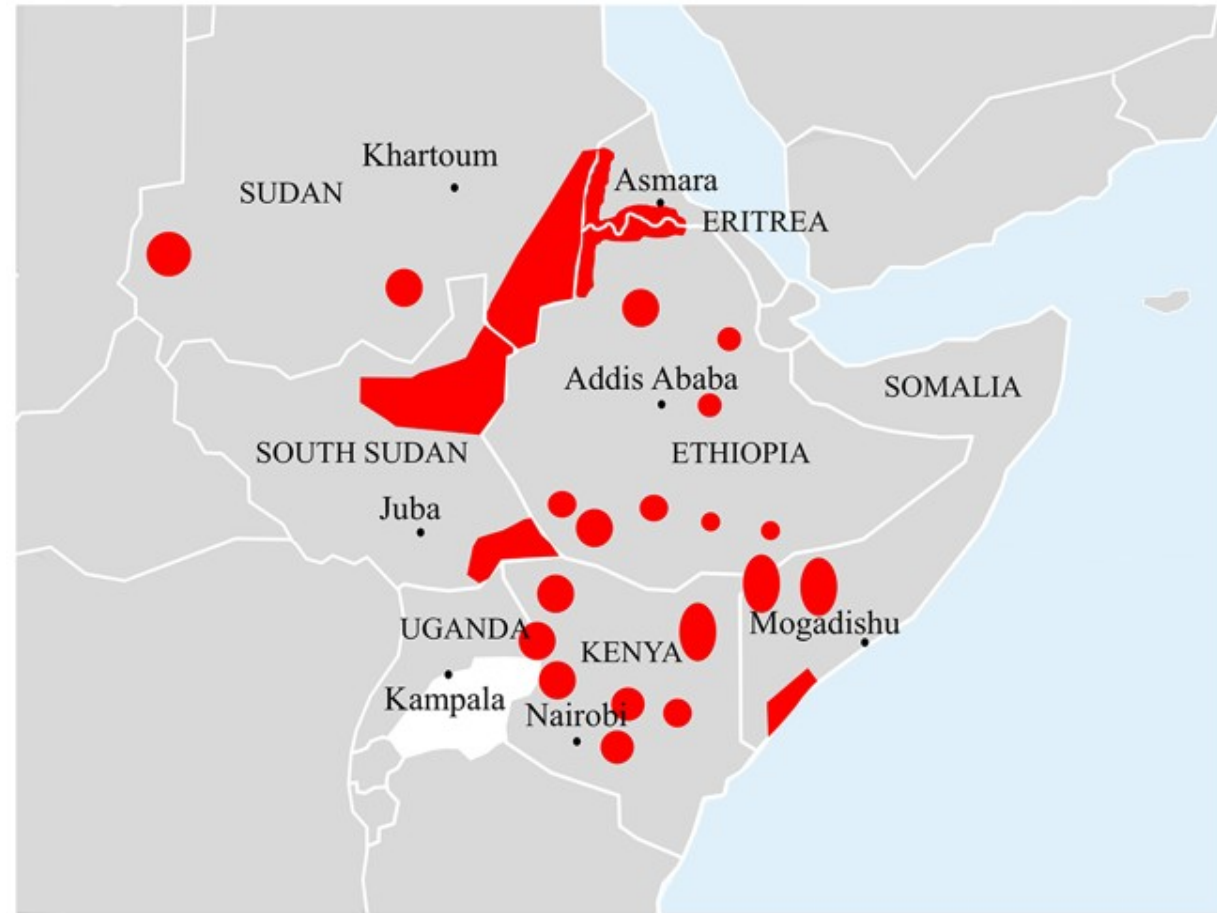
Diro E et al., 2014

Prevalence of HIV in VL cases in East Africa

Ethiopia
Sudan
South
Sudan
Kenya

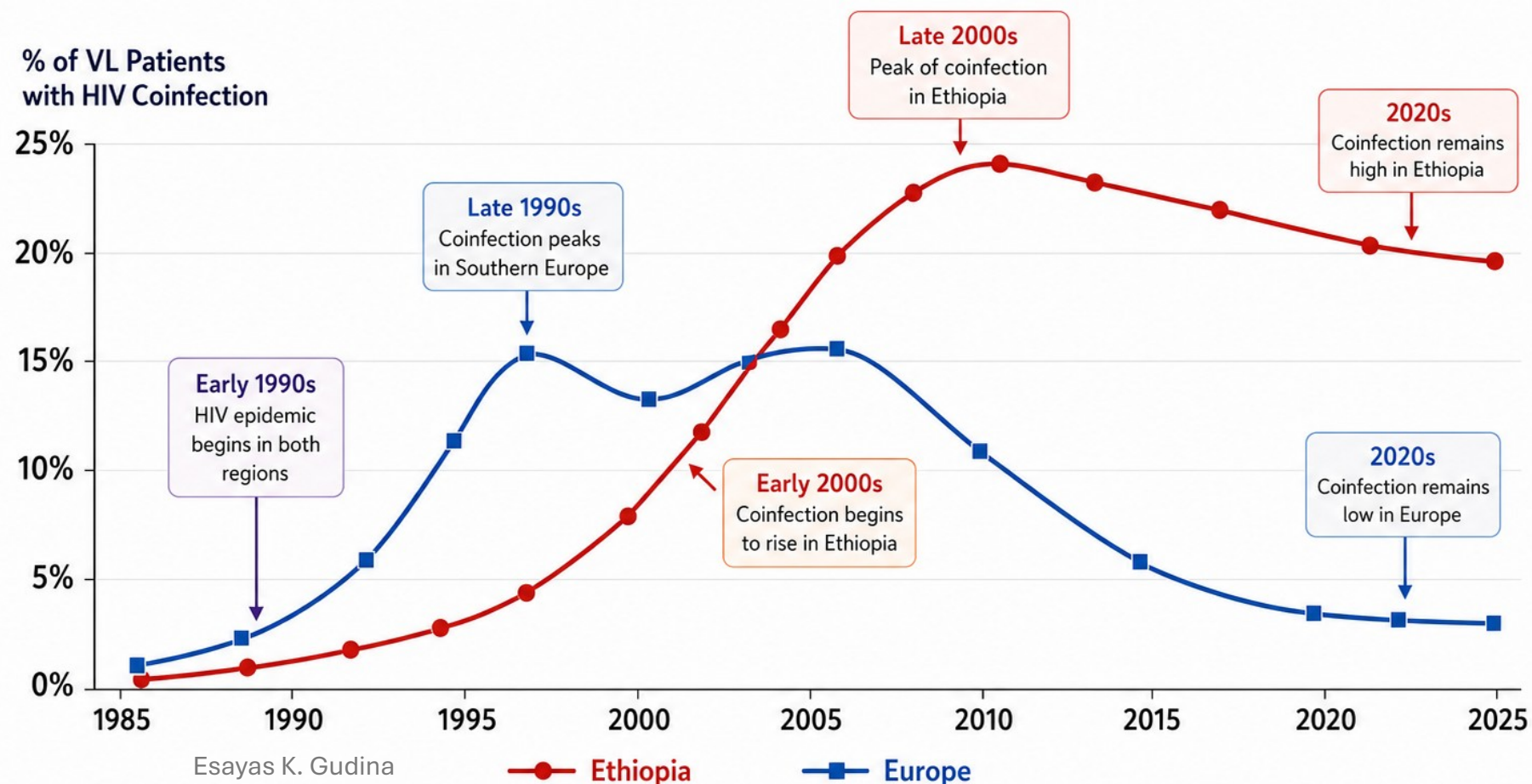
18.7%
1.3%
2.5%
1.4%

(MSF Data, 2009-2012)



East Africa's Unique Trajectory

- Unlike Europe where ART reduced HIV-VL coinfection, East Africa continues to face high rates.



Drivers of the Epidemic in East Africa

Population Mobility (seasonal migration):

- Highlanders moving to VL-endemic lowlands for seasonal work
- Non-immune individuals become exposed and infected

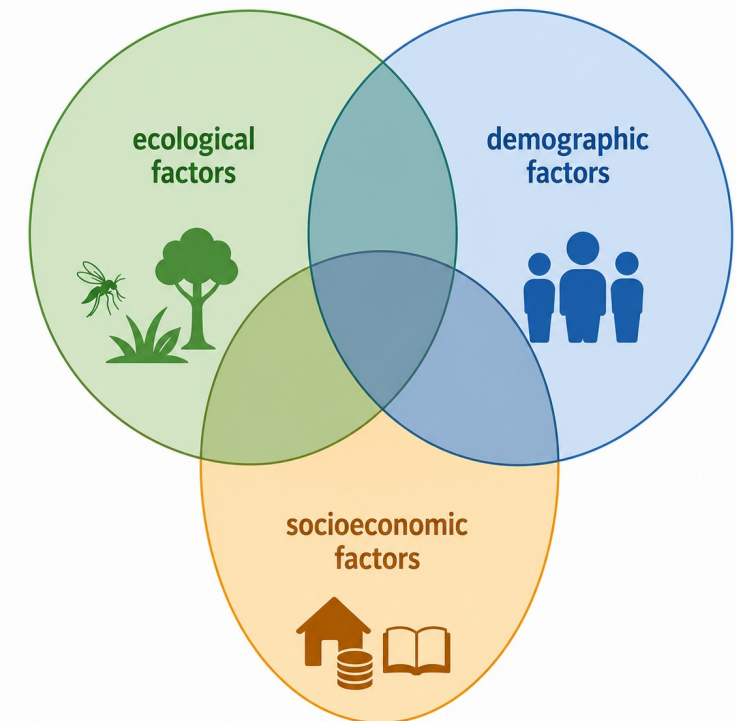
Socioeconomic Factors:

- Poor communities in remote areas
- Weak healthcare infrastructure
- Limited access to diagnosis and treatment

Convergent Risk Factors:

- Migration → both VL and HIV exposure
- HIV-infected individuals develop active VL more rapidly
- HIV prevalence among migrant workers at Humera and Mekele

12%



More explosive transmission in East Africa

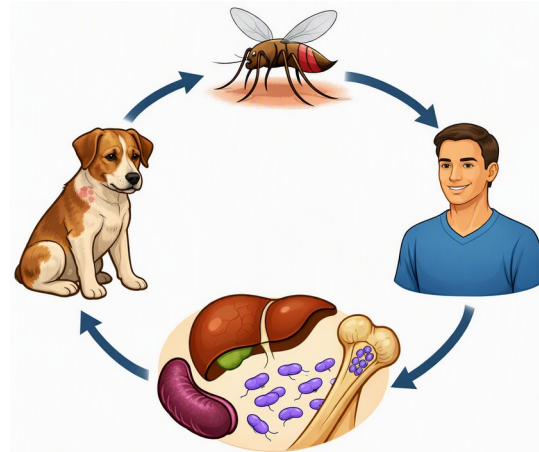
Mediterranean region

Etiology

- *L. infantum*
- Zoonotic
→ Animal reservoir

Vectors

- *P. perniciosus*, *P. perfiliewi*
- Highly zoophilic
→ Prefer biting dogs/canines



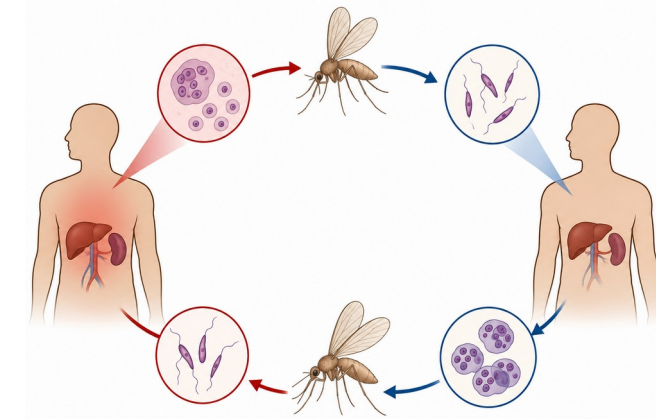
East Africa

Etiology

- *L. donovani*
- Anthroponotic
→ Human-to-human transmission

Vectors

- *P. orientalis*, *P. martini*
- Highly anthropophilic
→ Prefer biting humans



More virulent and difficult to manage

- Response to drugs varies between regions
 - Paromomycin shows lower efficacy in Ethiopia vs. Sudan

Implication:

- ✎ Treatment protocols from Europe cannot be directly extrapolated
- ✎ Region-specific treatment recommendations needed

Atypical presentation of VL in HIV

- High parasite loads in peripheral locations
 - Skin, GI tract, lungs, peripheral blood, peritoneal fluid
- Gastrointestinal involvement is common
- Skin lesions may be misdiagnosed as Kaposi sarcoma
- Oral lesions may mimic other opportunistic infections
- ➔ Miss-diagnosis and delayed diagnosis is common

Post-Kala-Azar Dermal Leishmaniasis (PKDL) in HIV

- Maculopapular or nodular rash following VL treatment
- More frequent in HIV patients (**27.3%** vs. **13.3%** in HIV-negative)
- Can occur **during** VL (**para-KDL**) in HIV patients
- These presentations may be missed in resource-poor settings relying on syndromic approaches



Non-HIV VL



Fever

Prolonged, irregular fever



Weight loss

Common, progressive



Splenomegaly

Marked (usually massive)



Hepatomegaly

Common



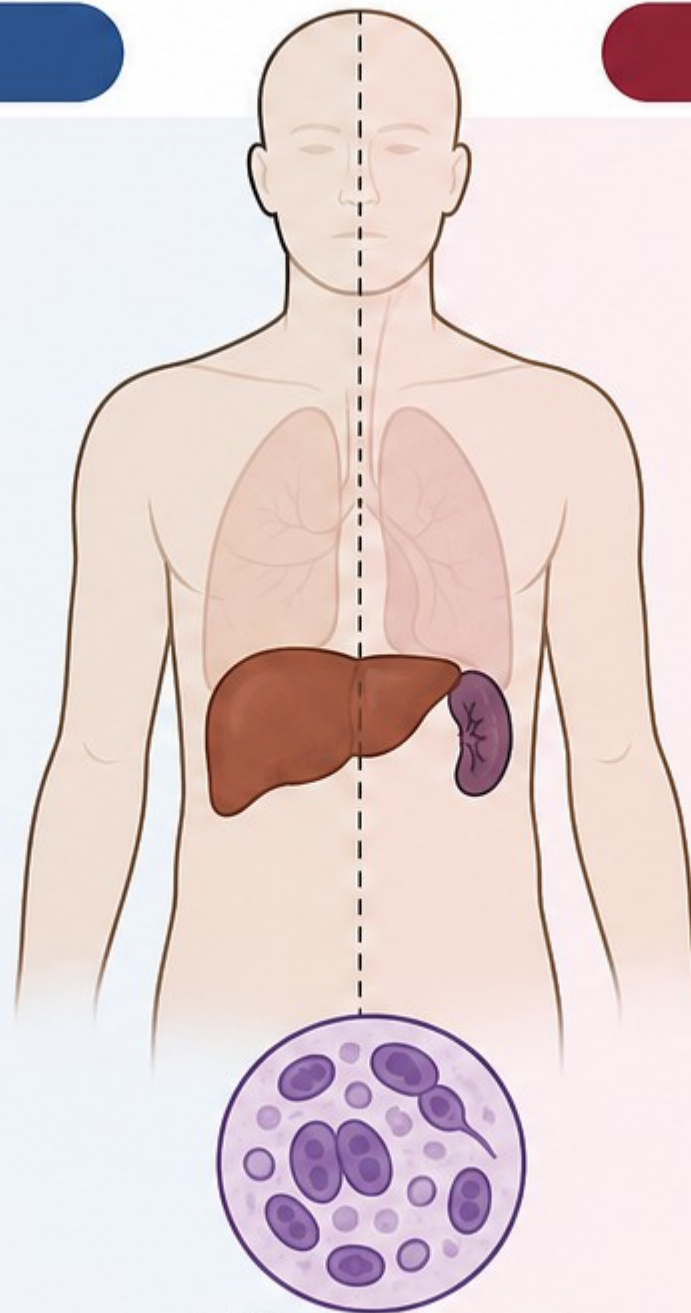
Pancytopenia

Common and pronounced



General condition

Usually poor



Leishmania donovani
amastigotes in macrophage

HIV-associated VL

Fever
May be absent or low-grade



Weight loss
Common, may be less pronounced



Splenomegaly
Absent or mild



Hepatomegaly
Absent or mild



Pancytopenia
Less frequent; anemia may predominate



General condition
Variable; may be less severe



Diagnostic challenges

All serological tests have suboptimal performance in HIV patients.

Test type	Brand	Target antibody	Target antigen	Sensitivity %		Specificity %
				HIV+	HIV-	
DAT						
≥800	ITM	Total antibodies	L. donovani promastigote	70.6	82.5	NA
≥3200				64.7	75.0	
ELISA IgG						
rK39 IgG	Serion	IgG	Leishmania spp rK39	84.3	100.0	97.5
RDTs						
IT Leish	BioRad	IgG	rK39	88.2	95.0	100
Kalazar Detect	InBios	IgG	rK39	84.3	95.0	92.5
rK39 IgG1	Coris	IgG1	rK39	74.5	80.0	100
rK28 IgG1	Coris	IgG1	rK28	70.6	82.5	97.5
Kalazar Antigen ICT	Xinjier	antigen	NA	88.2	90.0	20.0 ²¹
G-Sit	CTK	Total antibodies	rK39	88.2	100	97.5

Implication:

HIV patients need invasive tissue aspiration for parasitological diagnosis



Risk for potentially fatal bleeding

Diagnostic challenges....

Combining **DAT** and the **rK39** test improves VL diagnosis in HIV patients.

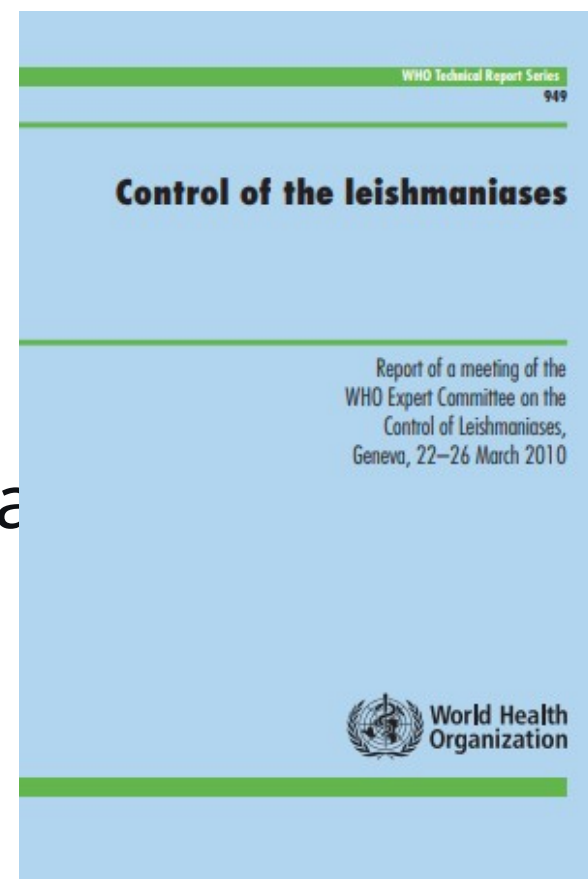
Test type	Sensitivity	
	HIV+	HIV-
rK39 DiaMed-IT-Leish [®] test	77.3	86.9
DAT (titer $\geq$ 1:3,200)	88.6	95.2
rK39 test plus DAT	97.7	98.8

ter Horst R et al., 2009

Treatment challenges

2010 WHO Guidelines:

- Main focus on liposomal amphotericin monotherapy
- Based on European experience with *L. infantum*
- Limited evidence for East Africa
- L-AmB monotherapy efficacy only **55% D58** in HIV co-infected patients in Ethiopia



Diro E et al., 2019

Treatment challenges

Older regimens are less effective & more toxic in HIV co-infected VL patients

Treatment	Issues
Pentavalent antimonials (SSG)	○ High toxicity in HIV patients ○ 4-10x higher death rate vs. HIV-negative ○ 30% parasitological failure
L-AmB monotherapy	○ 16% failure in primary VL ○ 56% failure in relapse cases
Miltefosine monotherapy	○ 17.5% parasitological failure
SSG + paromomycin	○ Limited experience in HIV coinfectd

New WHO Guidelines (The game-changer)

- New evidence from India and Ethiopia showed improved relapse-free survival with the new regimen.

	Previous (AmBisom monotherapy)	Current (AmBisome + miltefosin)
India ¹	88%	96%
Ethiopia ²	55%	88%

¹Burza E et al. 2022

²Diro E et. 2019

WHO GUIDELINE
for the treatment of visceral
leishmaniasis in HIV co-infected
patients in East Africa and
South-East Asia



The new regimen

L-AMB (up to a cumulative treatment dose of **30 mg/kg** body weight, given as 5 mg/kg on each treatment day **1, 3, 5, 7, 9, 11**)

PLUS

Miltefosine (100 mg/day for **28** days)

Insead of:

AmBisome infusion at a dose of 3–5 mg/kg daily or in 10 intermittent doses (on days **1–5, 10, 17, 24, 31 and 38**) to a total dose of **40 mg/kg**.

Impact of the new regimen

Outcome	Combination Therapy	Monotherapy
Treatment success (D58)	Higher	Lower
Relapse-free survival	Superior	-
Initial cure rate	83.8%	-
Parasitological failure	3.5%	Higher

It allows a lower total dose of amphotericin.

Secondary prophylaxis

Rationale

- VL relapse is common in HIV patients (particularly if CD4 <100 cells/ μ L)
- Secondary prophylaxis reduces relapse risk by $\geq 50\%$

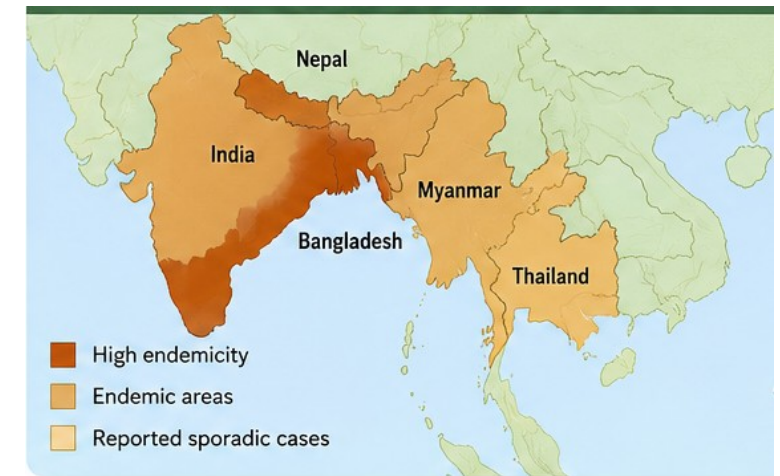
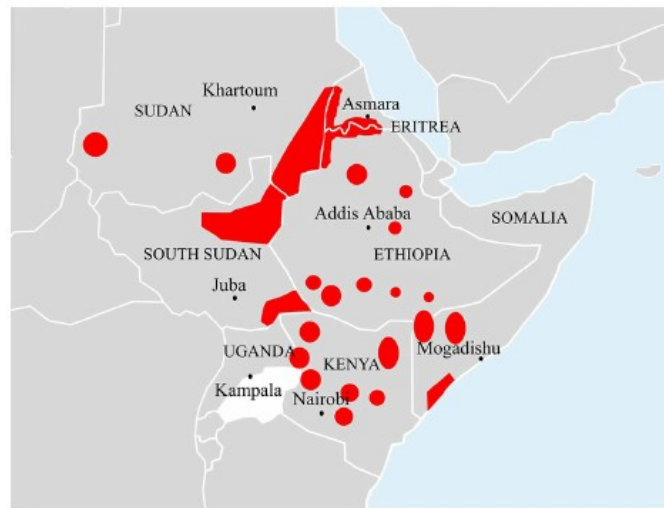
Recommended regimen

- EA – Pentamidine isethionate (4 mg/kg IV) every 3 to 4 weeks
- SEA – Amphotericin B every three to four weeks

Concern

- Prophylaxis in anthroponotic transmission may promote drug resistance

Different Epidemiological Contexts



Aspect	East Africa	South-East Asia
Parasite	<i>L. donovani</i>	<i>L. donovani</i>
Transmission cycle	Anthroponotic	Anthroponotic
HIV coinfection rate	Highest in world (20-40%)	5-7% in India
Key drivers	Migration, agricultural labor	Urban/rural mixing
Treatment efficacy	88%	96%
Main challenge	High relapse rates, diagnostic access	Sustaining elimination gains

➔ Region-specific guidelines are essential due to differing epidemiology, parasite strains, and treatment responses.

Antiretroviral Therapy recommendation

- Early HIV diagnosis and retention in care critical
- Initiate ART as soon as clinically stable (typically week 2 of VL treatment)
- **Protease Inhibitors (PIs):** May have direct anti-leishmanial effects
 - Requires further research
 - PI-based ART could be explored as an option in VL-endemic regions

Diro E et al., 2019

Predictors of Poor VL Outcome in HIV

- Age >40 years
- Hemoglobin ≤ 6.5 g/dL
- Tuberculosis coinfection at VL diagnosis

Abongomera et al., 2017

Immune Reconstitution Inflammatory Syndrome (IRIS)

A Rare but important phenomenon

- Only very few clear-cut cases reported globally

The paradox:

- VL-IRIS appears to be an **exception** in TB-HIV

Possible Reasons for low IRIS:

- *Leishmania* may dampen the immune system, reducing IRIS risk
- **PKDL** may represent an IRIS manifestation

PKDL and Transmission Potential

- Reported in **up to 50%** of VL-treated patients in Sudan

• More frequent in HIV patients (**27.3%** incidence vs. **13.3%**)

- HIV patients have **higher tissue parasite loads**
- PKDL lesions in HIV patients contain **abundant parasites**
- Potential role as **reservoirs** for *L. donovani* transmission

van Griensven J et al., 2024

Drug Resistance Threat:

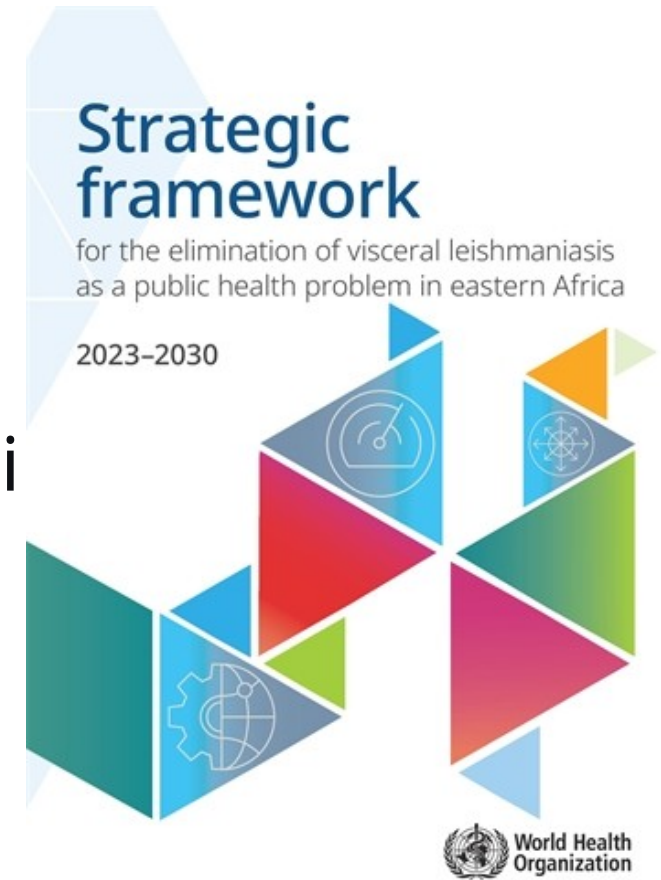
- High treatment failure & relapse rates
- Repeated drug exposure
- Increased risk **drug-resistant parasites**
- Potential to spread resistant strains



There is a need for Xenodiagnosis studies to assess transmission potential

Public Health Implications of VL-HIV co-infection

- HIV coinfection is a **major obstacle**
- Coinfected patients serve as potential reservoir
- Drug resistance can emerge and spread
- Undermines elimination programs



Integrated Approach Needed for elimination

Prevention

- Target high-risk migrant populations with health education
- Evaluate vector control measures

Diagnosis

- Routine HIV testing for all VL patients and vice versa
- Improved diagnostic algorithms for HIV patients

Treatment

- Implement new WHO guidelines
- Ensure ART access at VL treatment sites

Research

- More clinical trials in East Africa
- Basic immunology research

Clinical Practice recommendation for East Africa

Diagnosis

- Use serial serological testing (**rK39 + DAT**) for initial screening
- Maintain low threshold for parasitological diagnosis in HIV patients
- **Screen for TB** coinfection

Treatment

- Based on 2022 WHO Guidelines
 - First-line: **L-AmB + Miltefosine**
- Initiate ART as soon as clinically stable
- Consider secondary prophylaxis with pentamidine in

Monitoring

- Close follow-up for relapse (especially in low CD4 patients)
- Monitor for PKDL development

Future Research Priorities

Diagnostics

- Non-invasive diagnostic methods (*peripheral blood microscopy, PCR*)
- Better tests for monitoring treatment response and detecting relapse
- Validated antigen tests for East African populations

Treatment

- Confirm combination therapy efficacy in larger clinical trials
- Optimal duration of secondary prophylaxis
- Role of **Protease Inhibitors** in VL treatment
- Drug resistance monitoring

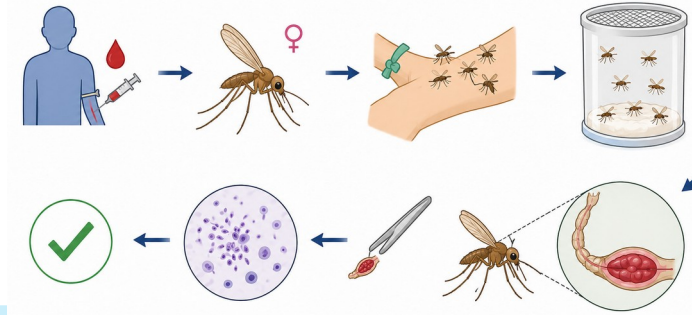
Future Research Priorities

Immunology

- Interaction between HIV and *Leishmania* at the cellular level
- Mechanisms of IRIS and paradoxical reactions
- Role of immune modulation

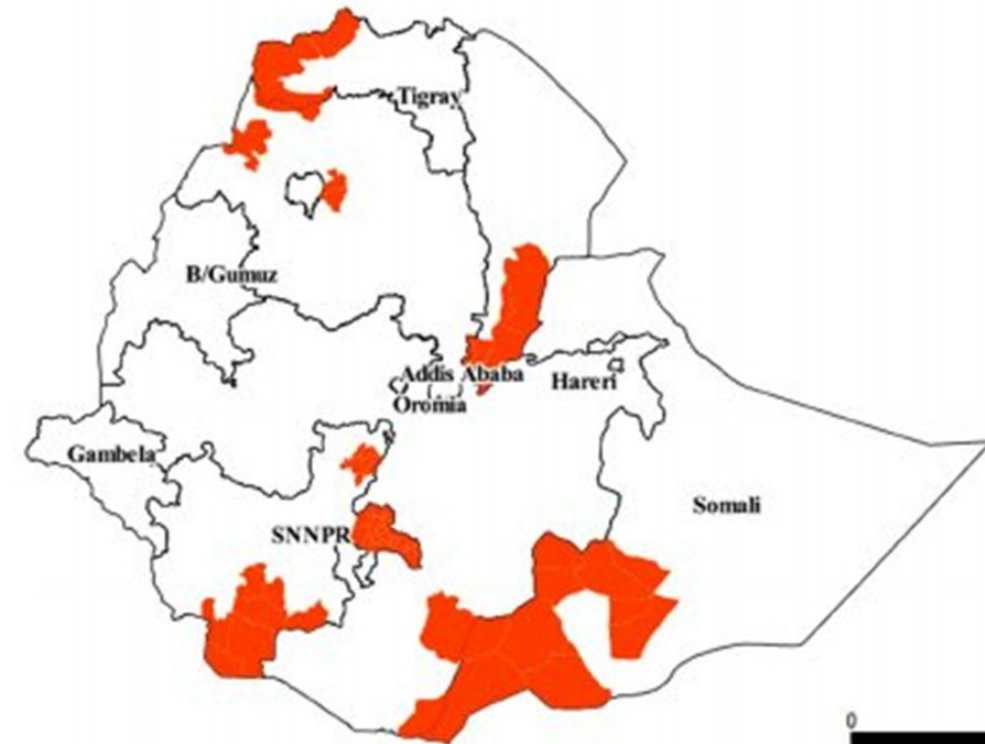
Epidemiology

- Transmission potential of coinfecting patients (xenodiagnosis)
- Impact of population migration on transmission dynamics
- Surveillance of drug resistance



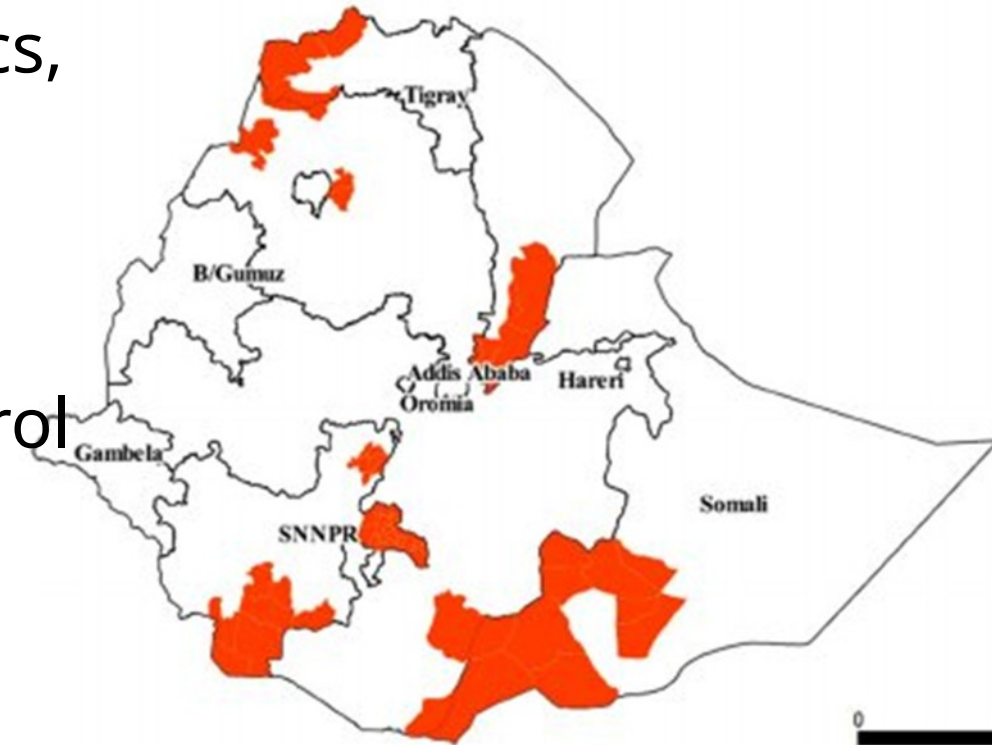
Summary (1)

- East Africa (Ethiopia) has the highest VL-HIV coinfection rate globally (20-40%)
- Coinfection challenges VL elimination through increased treatment failure, relapse, and potential drug resistance
- Atypical clinical presentations and poor serological test performance complicate diagnosis in HIV patients
- L-AmB + miltefosine for East Africa improving cure rates from 55% to 88%

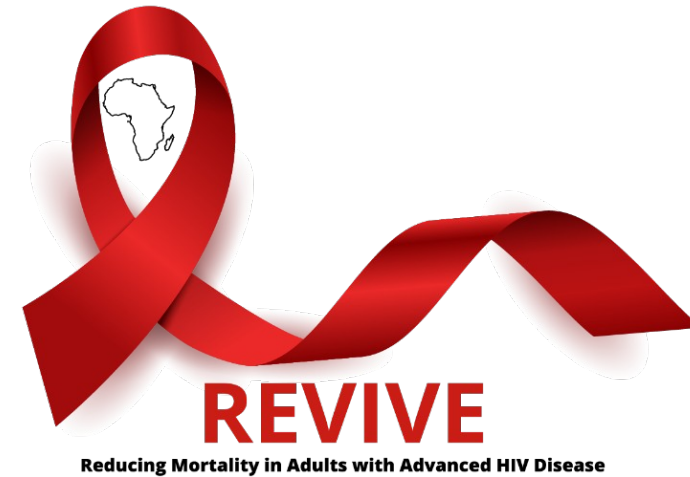
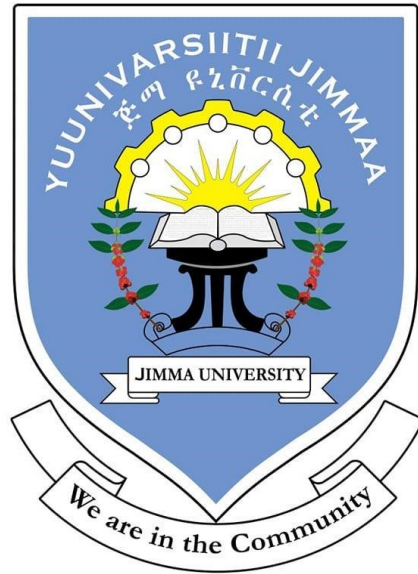


Summary (2)

- Comprehensive management requires Early ART initiation, Secondary prophylaxis for high-risk patients, Active TB screening
- Critical research gaps remain in diagnostics, optimal treatment strategies, and understanding transmission potential
- Integrated public health approaches are essential to address both HIV and VL control



Thank you!



Contact @:

esayas.gudina@ju.edu.et

ORCID: <https://orcid.org/0000-0002-6264-9695>