Talaromycosis: A Neglected Tropical Disease in Southeast Asia

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TROPICAL MEDICINE RESEARCH CENTER For TALAROMYCOSIS

Duke UNIVERSITY

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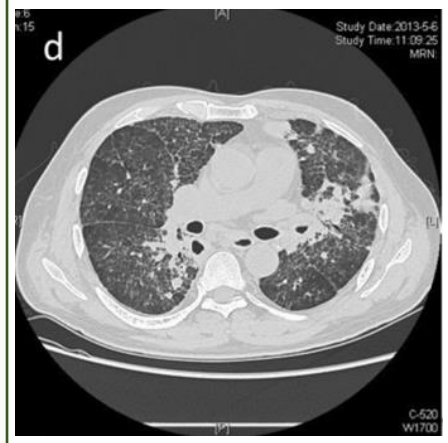
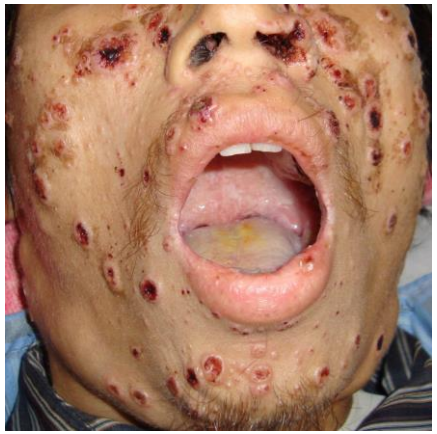
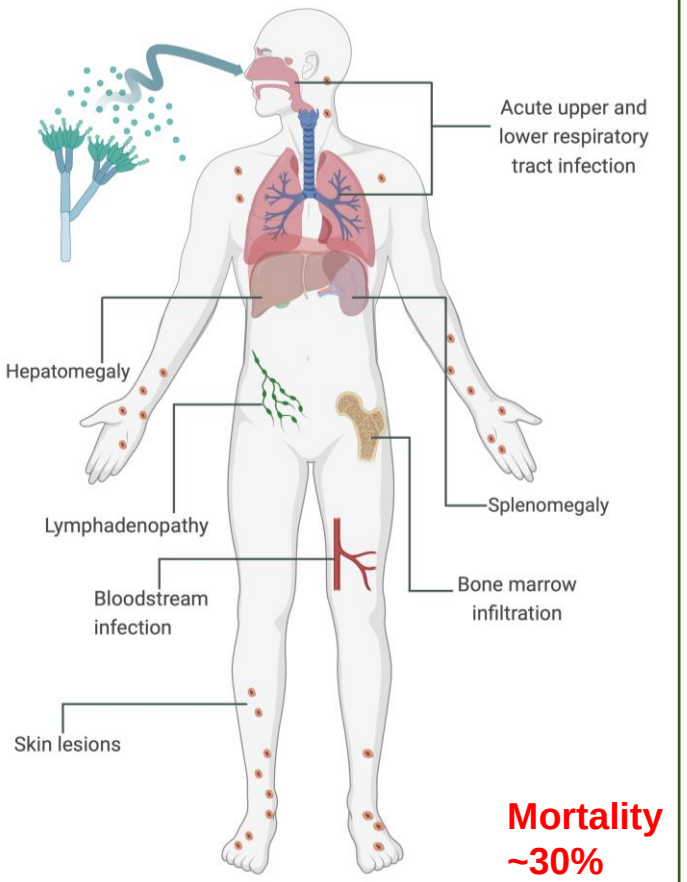
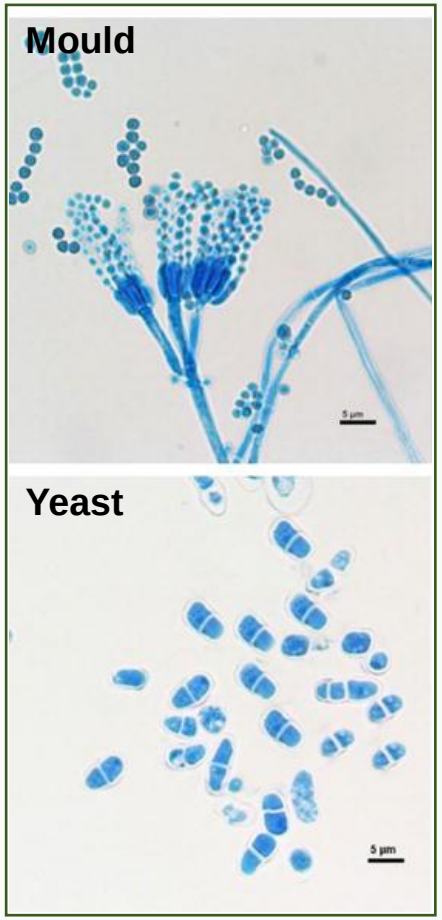
The Severe Fungal Disease **Talaromycosis**

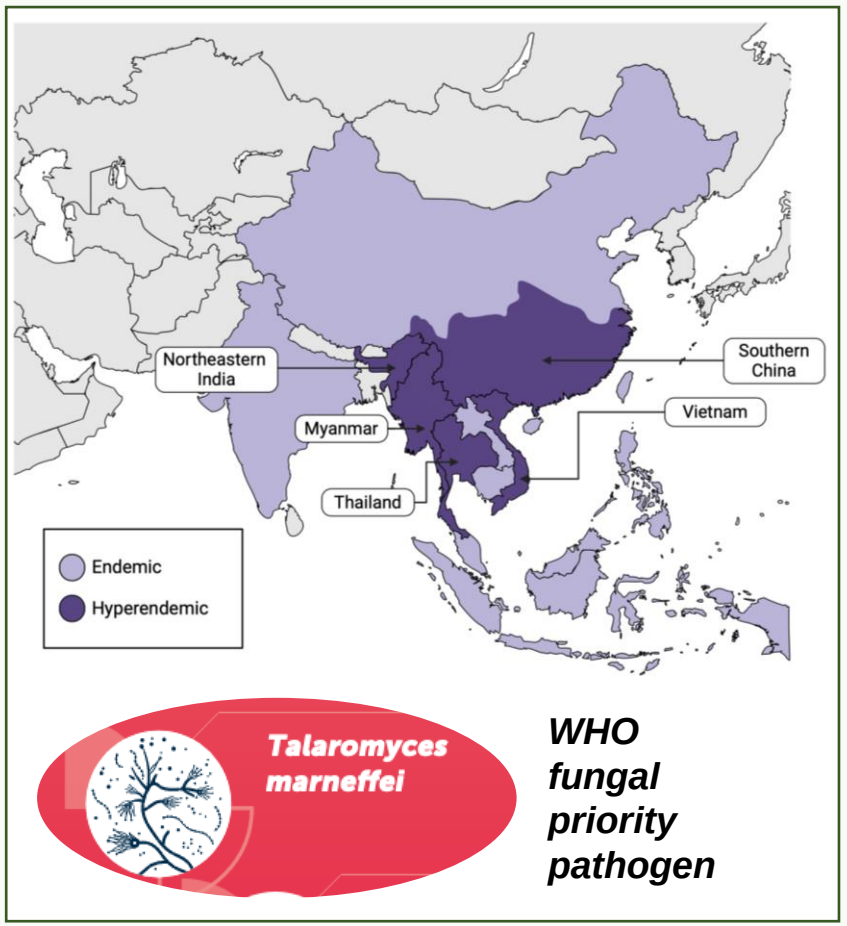




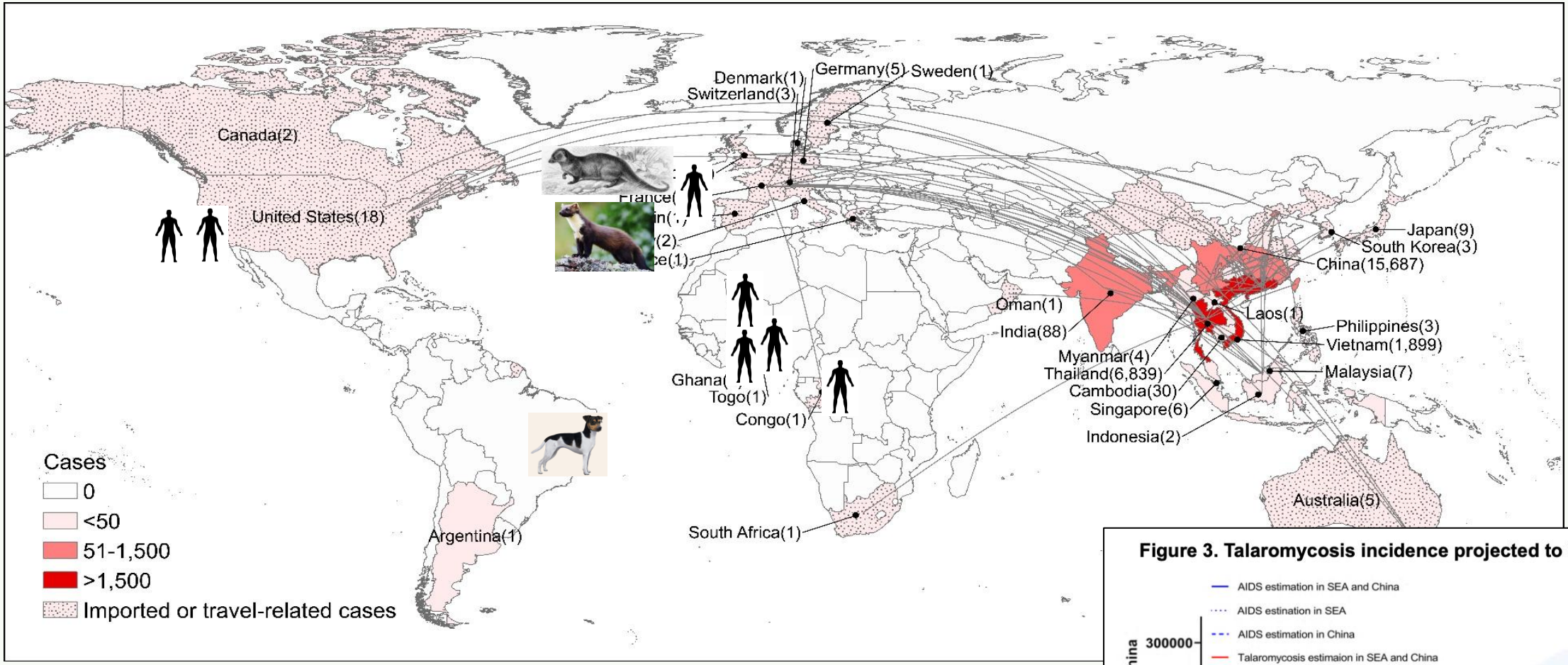


Mortality ~30%





Figures: L. Brown, T. Le *et al* (2025)



Chuanyi Ning, PhD

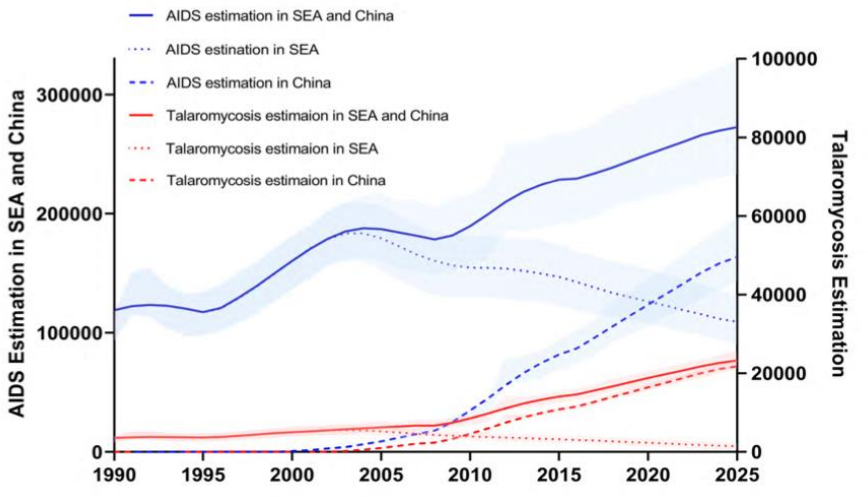
Estimated 25,000 cases per year

90% HIV-infected

China (60.3%), Thailand (30.4%), and Vietnam (8.4%)

Rising incidence and expanding geography (32 countries)

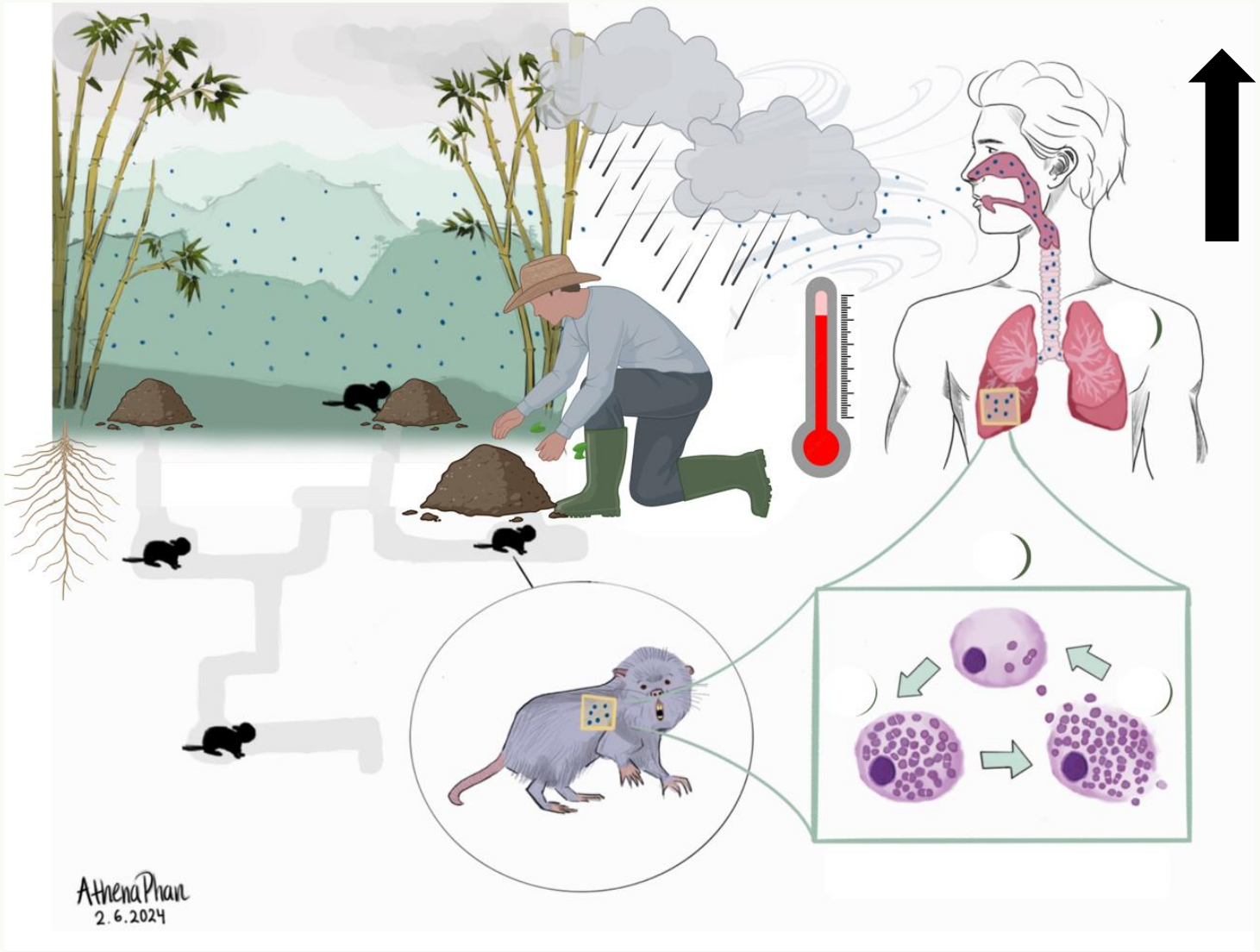
Figure 3. Talaromycosis incidence projected to 2025



C. Ning CROI (2020)

Ecology of Talaromycosis

The Bamboo Rat



Temperature
Humidity
Rainfall

Figure by Prof Le's daughter Tuong-Vy Athena Phan (2024)

T. Le *et al* CID (2011), Bulterys, T. Le *et al* CID (2013), Chariyalertsak *et al* JID (1996)

Risk Factors for Talaromycosis in Vietnam: **A case-control study**

- **Case-control** study of individuals with advanced HIV disease across 2 major hospitals in Vietnam **(n = 610)**, **matched** in a 2:1 ratio
- Data on **13** pre-defined exposure variables collected by face-to-face questionnaires
- **Geographical mapping** of cases and controls

Characteristics	All patients (N = 610)	Cases (N = 205)	Controls (N =405)
Age (years)	34 (31 – 38)	33 (30 – 38)	34 (31 – 39)
Sex (male)	456 (74.8%)	154 (75.1%)	302 (74.6%)
CD4 (cells/μL)	N = 194 16.5 (7.0 – 36.0)	N = 66 9.0 (5.0 – 18.8)	N = 128 25.5 (9.0 – 54.3)
Absolute Lymphocyte (cells/μL)	N = 585 520 (300 – 750)	N = 197 410 (230 – 600)	N = 388 570 (380 – 810)
WHO stage 1 2 3 4	N = 606 3 (0.5%) 16 (2.6%) 146 (24.1%) 441 (72.8%)	N = 204 0 (0%) 0 (0%) 0 (0%) 204 (100%)	N = 402 3 (0.7%)* 16 (4.0%)* 146 (36.3%)* 237 (59.0%)
Inpatient Outpatient	573 (93.9%) 37 (6.1%)	205 (100%) 0 (0%)	368 (90.9%) 37 (9.1%)

All controls diagnosed with another OI

L. Brown, B. Jonat *et al*, in press EID (2025)

Behavioral and exposure risk factors for talaromycosis

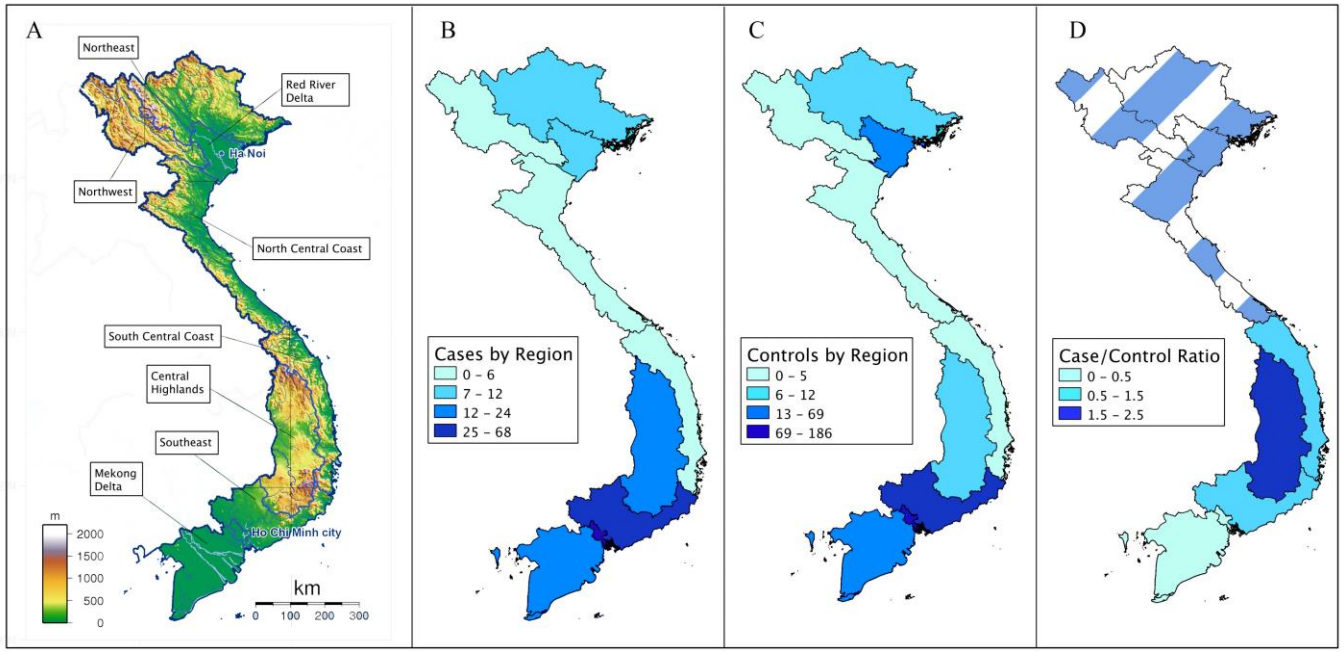
Exposure Covariates	All (N = 610)	Cases (N = 205)	Controls (N = 405)	Univariate effect OR (95% CI), *P*-value	Multivariate effect OR (95% CI), *P*-value
Antiretroviral therapy	250/610 (41.0)	72/205 (35.1)	178/405 (44.0)	**0.68 (0.47 to 0.97), *P* = 0.04**	0.75 (0.50 to 1.13), *P* = 0.17
Fluconazole prophylaxis	61/596 (10.2)	15/198 (7.6)	46/398 (11.6)	0.59 (0.31 to 1.11), *P* = 0.10	0.68 (0.35 to 1.34), p =0.27
Cigarette smoking	413/610 (67.7)	130/205 (63.4)	283/405 (69.9)	0.65 (0.42 to 1.01), *P* = 0.06	0.71 (0.43 to 1.18), *P* = 0.19
Injection drug use	232/610 (38.0)	71/205 (34.6)	161/405 (39.8)	0.79 (0.54 to 1.15), *P* = 0.21	0.85 (0.54 to 1.35), *P* = 0.50
Outdoor occupation	263/610 (43.1)	100/205 (48.8)	163/405 (40.2)	**1.47 (1.03 to 2.09), *P* = 0.04**	1.23 (0.81 to 1.87), *P* = 0.34
Soil exposure	409/610 (67.0)	143/205 (69.8)	266/405 (65.7)	1.22 (0.85 to 1.75), *P* = 0.29	1.06 (0.69 to 1.63), *P* = 0.80
Natural water exposure	285/610 (46.7)	90/205 (43.9)	195/405 (48.1)	0.83 (0.58 to 1.19), *P* = 0.31	0.76 (0.51 to 1.13), *P* = 0.18
Tropical plant exposure	218/610 (35.7)	90/205 (43.9)	128/405 (31.6)	**1.75 (1.22 to 2.56), *P* = 0.002**	**1.84 (1.17 to 2.90), *P* = 0.008**
Highland plant exposure	49/610 (8.0)	25/205 (12.2)	24/405 (5.9)	**2.25 (1.24 to 4.01), *P* = 0.008**	1.71 (0.86 to 3.41), *P* = 0.13
Bamboo rat exposure	6/610 (1.0)	3/205 (1.5)	3/405 (0.7)	2.00 (0.40 to 9.91), *P* = 0.40	1.71 (0.33 to 8.87), *P* = 0.53
Farming animal exposure	93/610 (15.2)	40/205 (19.5)	53/405 (13.1)	**1.60 (1.02 to 2.51) *P* = 0.04**	**2.03 (1.18 to 3.49) *P* = 0.010**
Domestic animal Exposure	170/610 (27.9)	57/205 (27.8)	113/405 (27.9)	1.01 (0.67 to 1.51) *P* = 0.97	1.39 (0.87 to 2.22) *P* = 0.17
Raw animal consumption	411/610 (67.4)	132/205 (64.4)	279/405 (68.9)	0.82 (0.57 to 1.18) *P* = 0.28	0.91 (0.60 to 1.37) *P* = 0.64

In our **multivariable analysis**, independent factors for talaromycosis included:

1. **Exposure to tropical plants** (rice, bamboo, sugarcane)
2. **Exposure to farmed animals**

L. Brown, B. Jonat *et al*, in press EID (2025)

Geographical risk factors for talaromycosis



Region	Number of cases	Number of controls	Case to control ratio	OR (95% CI), *P*-value
Mekong	17	69	0.25	Reference category
HCMC	60	185	0.32	1.31 (0.56-3.03); *P* = 0.91
Southeast	68	78	0.87	3.42 (1.44-8.10); *P* = 0.001
South Central Coast	6	5	1.20	8.76 (1.25-61.56); *P* = 0.02
Central Highlands	24	11	2.18	11.36 (2.92-44.24); *P* < 0.0001

- Patients in the **highland and surrounding regions** were significantly more likely to develop talaromycosis than those residing in the Mekong Delta or HCMC

- In addition, patients with **previous residence** or **travel** to these regions were at increased risk
  OR (95% CI): **3.15** (1.49 – 6.64), *P* = 0.003

L. Brown, B. Jonat *et al*, in press review EID (2025)

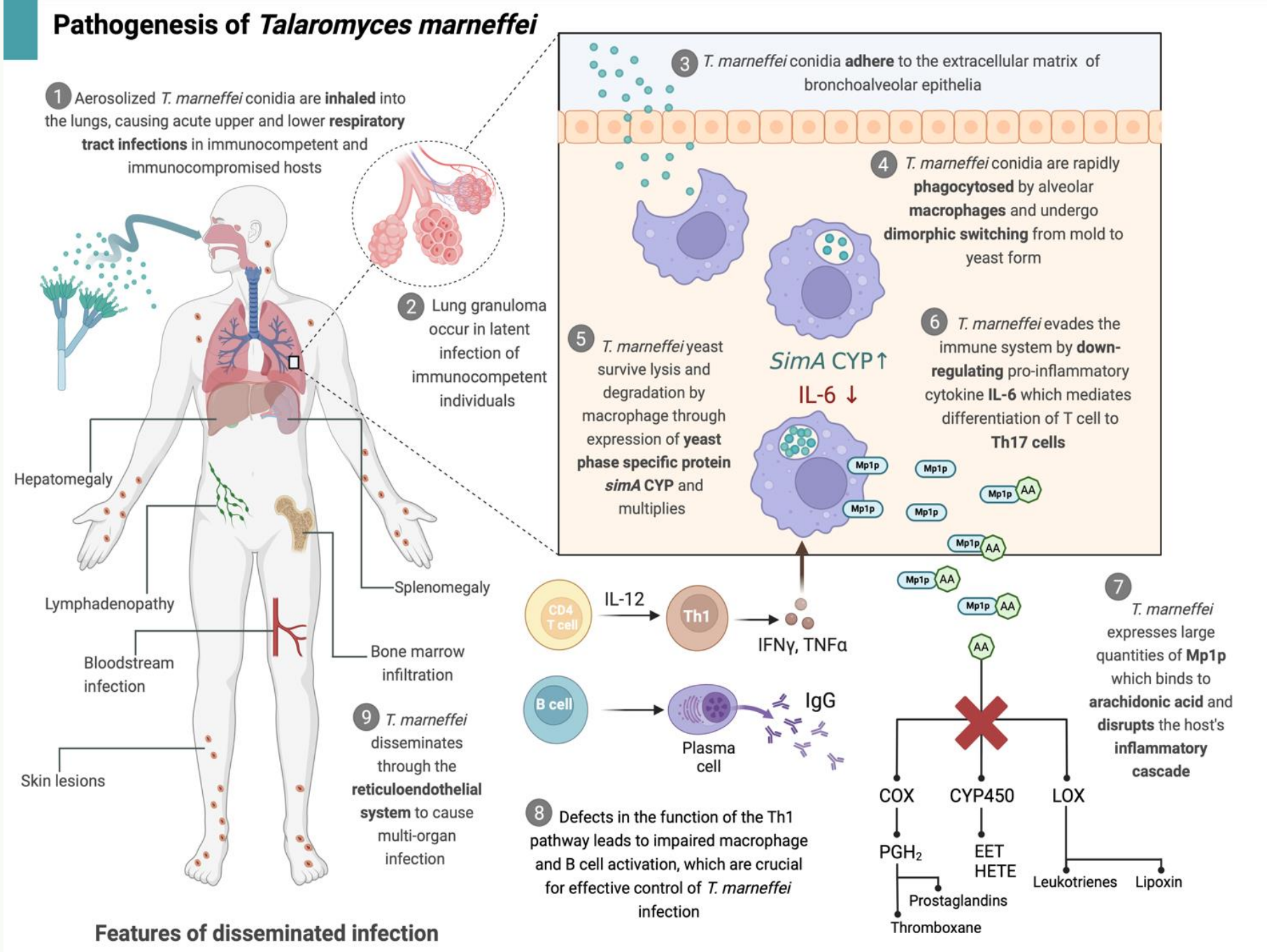
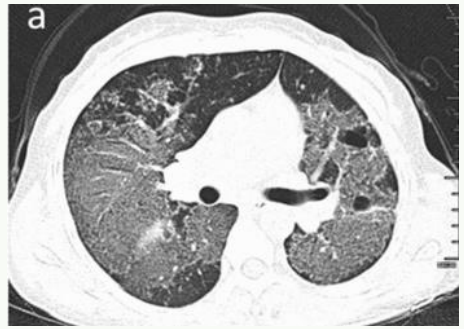


Figure: L. Brown, T. Le *et al* (2025)

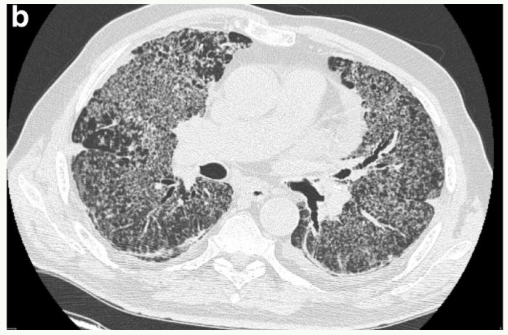
Diagnostic Challenges

- **Non-specific** clinical features that **vary** according to **host factors** and **overlap** with other OIs

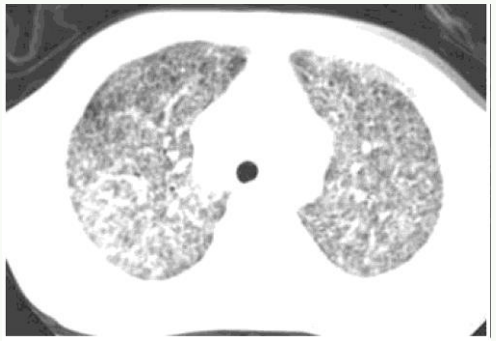
- Initiation of **empirical therapy** is **not recommended** due to broad differentials, antifungal drug duration and toxicity and drug-drug interactions



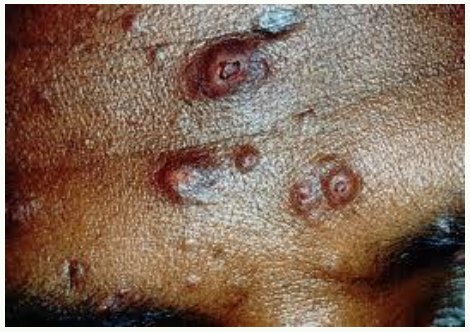
Talaromycosis

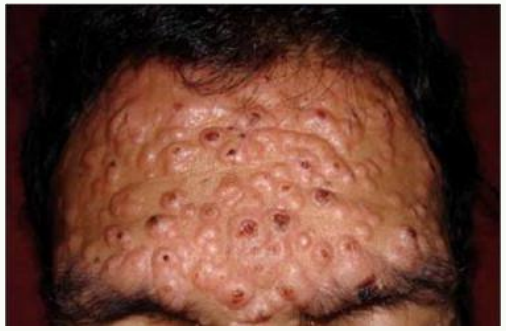


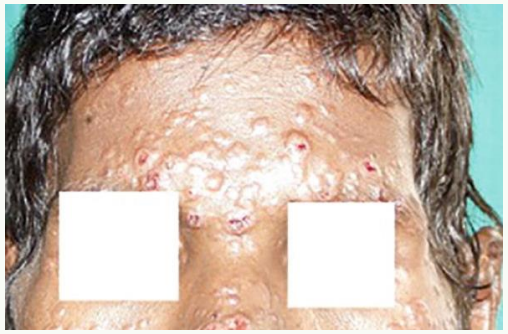
Histoplasmosis



Cryptococcosis



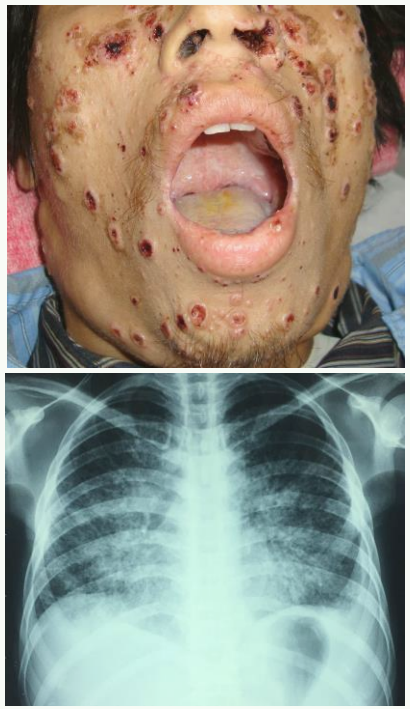




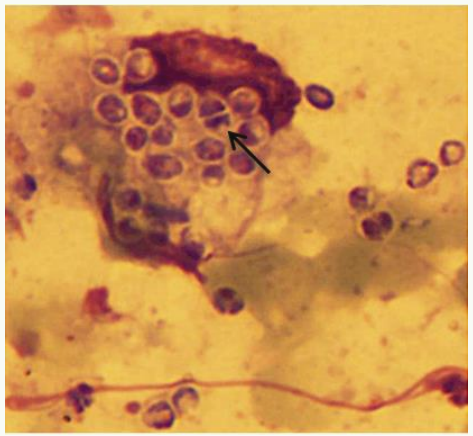
Mortality increases from 25% to 50% with late diagnosis

Hu Y. *et al*, Mycopathologia (2013)

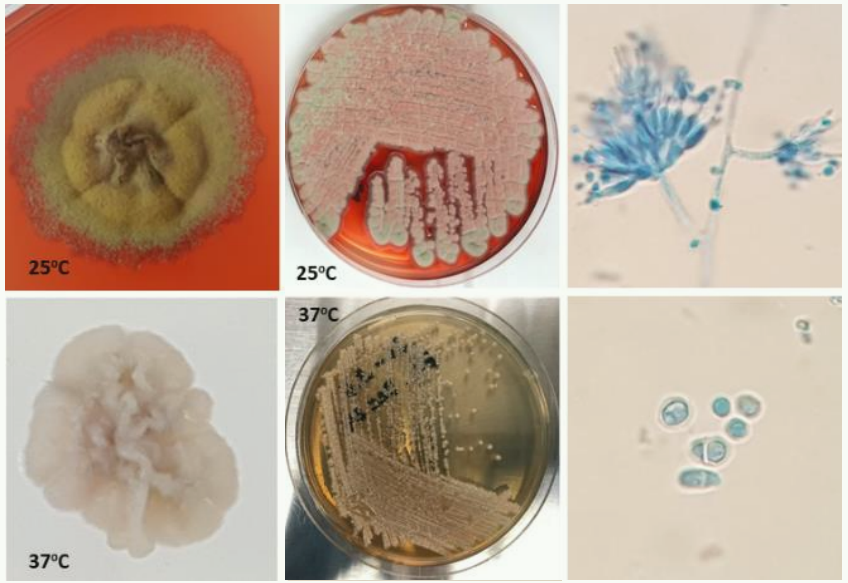
Diagnostic Challenges



Symptoms onset
Up to 6 months



Giemsa stain of skin smear
Skin lesions absent in 50%
Late-stage infection



Culture
Takes 5 – 28 days
Sensitivity: 50% to 70% in blood
Late-stage infection

Mortality increases from 25% to 50% with late diagnosis

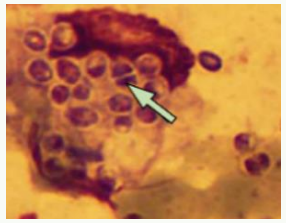
Hu Y. *et al*, Mycopathologia (2013)

Talaromycosis Diagnostics

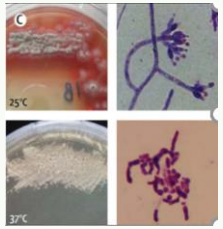
Confidence

DIRECT METHODS
Pathogen Detection

INDIRECT METHODS
Host-Based Detection



Microscopy

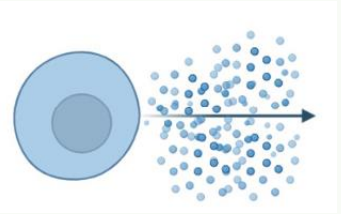


Culture

Genome Detection

Antigen Detection

Host Transcriptomics



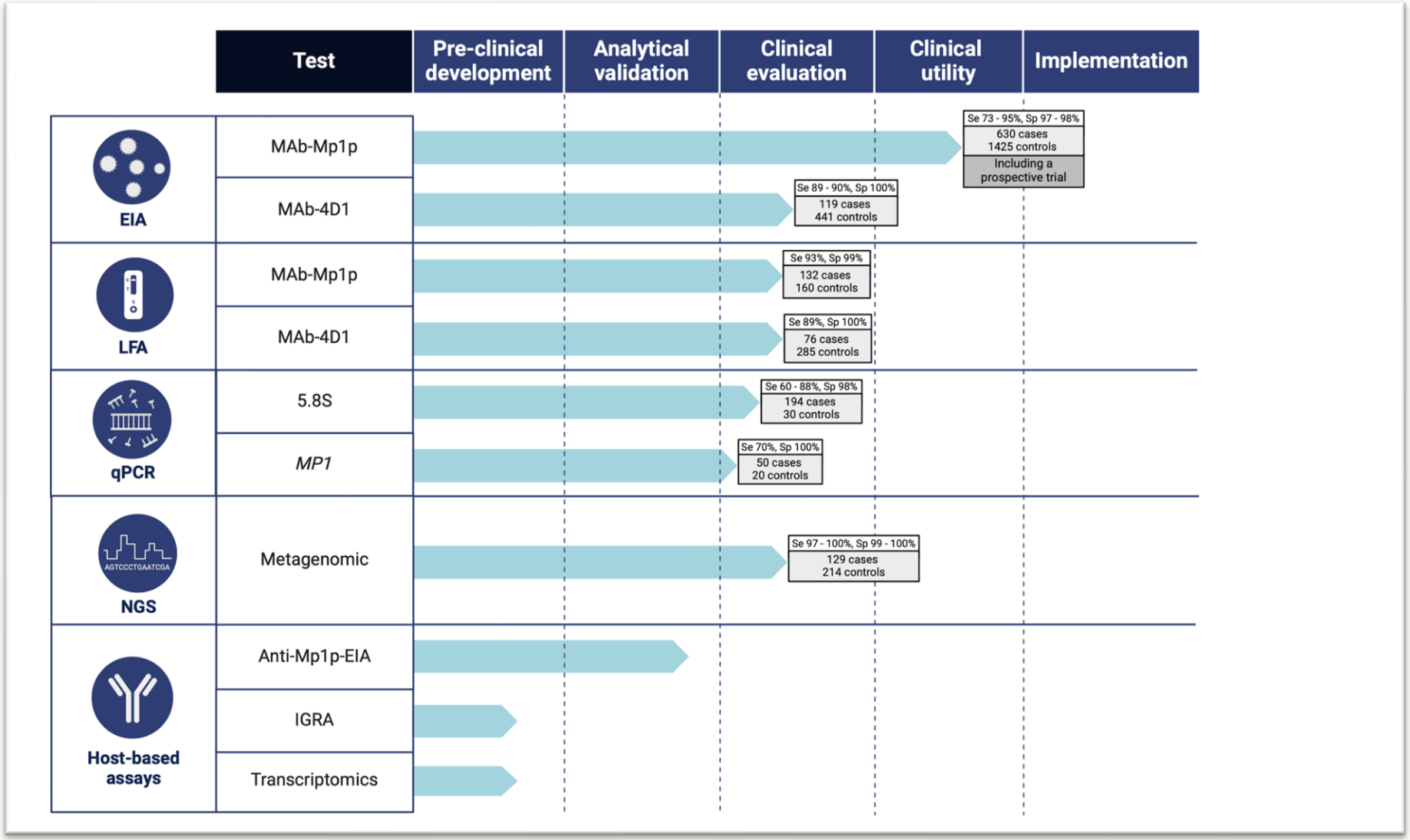
IFN-gamma Release

Serology IgG

Ease of detection

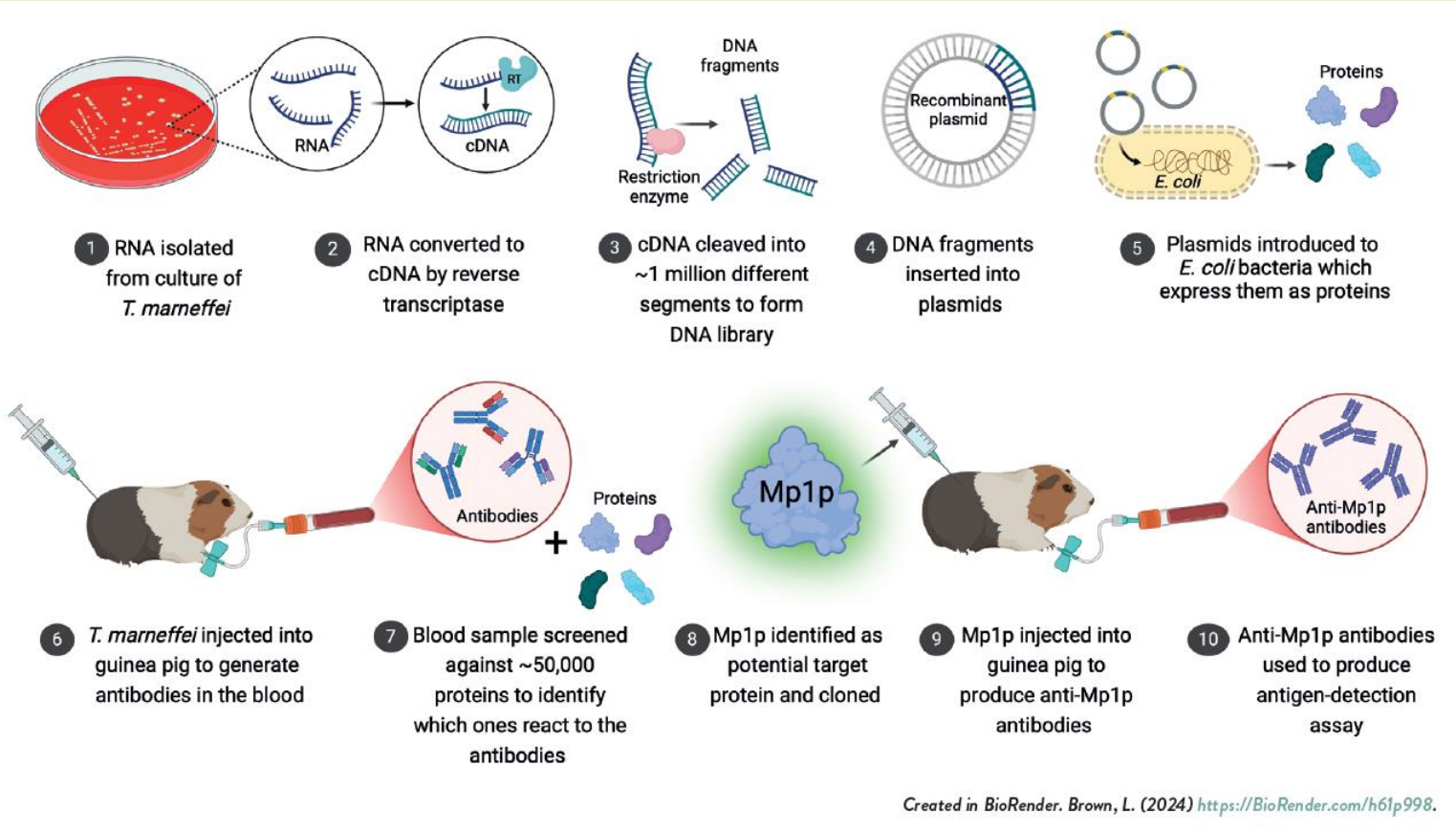
Time to Result: Weeks Days Hours Minutes

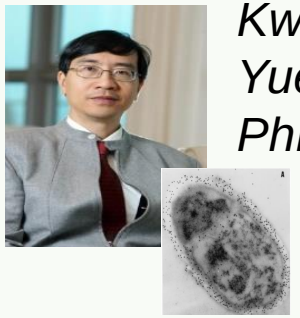
The Novel Diagnostic Pipeline



Figures: [1]Brown *et al* under review in CID (2025)

Mp1p antigen enzyme immunoassays (EIA)



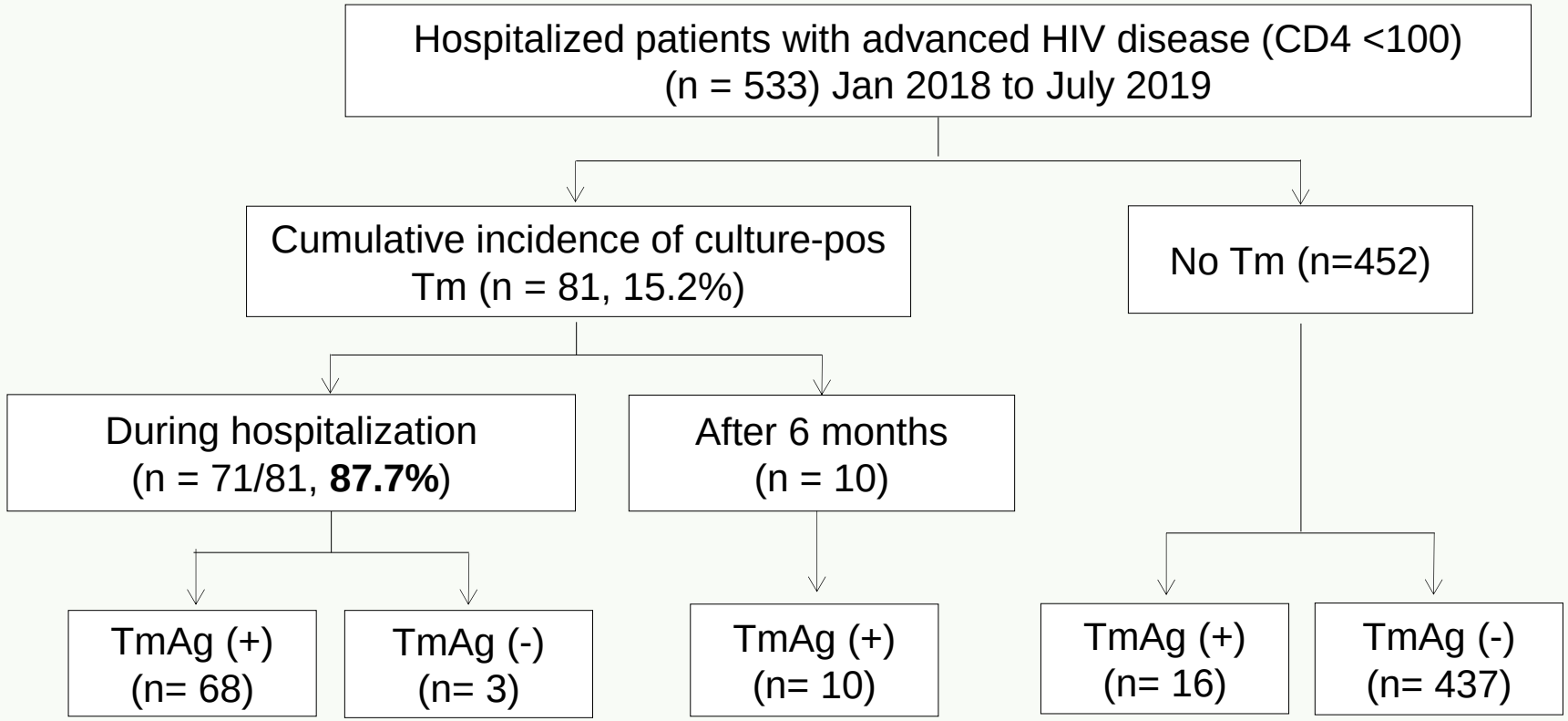


Kwok-Yung Yuen, MD, PhD

Study	Country	Cases / Controls (n)	Specimen type	Sens (%)	Spec (%)
Thu (2020)	Southern Vietnam	372 cases, 517 controls	Plasma, urine	86	98
Chen (2022)	China	93 cases, 190 controls	Serum	72	97
Gong (2023)	China	350 cases, 255 controls	Serum	72	98

Figure: L. Brown, T. Le *et al* (2025)

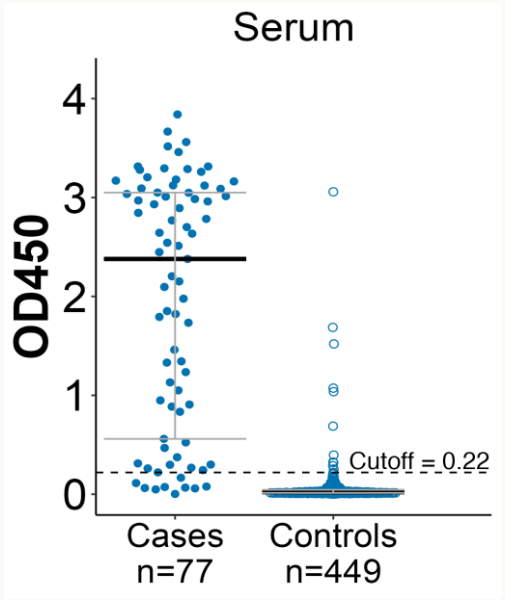
Mp1p EIA prospective validation in hospitalized patients with AHD

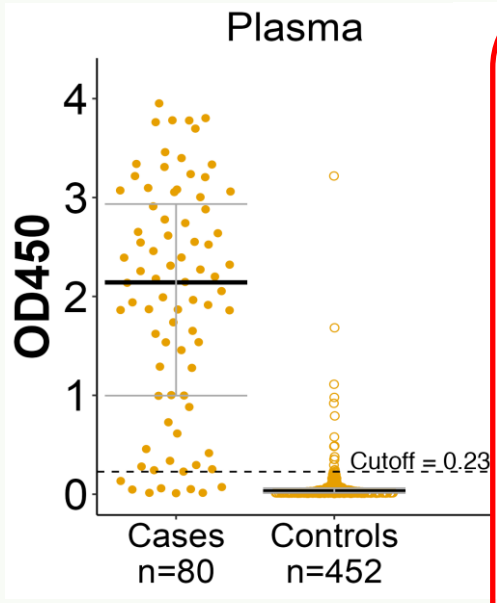


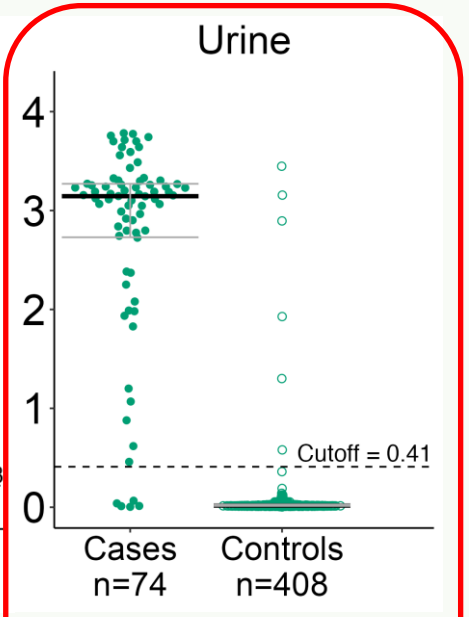
Sensitivity 96.2%
78/81 (95% CI: 88.7 – 99.0%)

Specificity 96.7%
437/452 (95% CI: 94.6 – 98.1%)

Ly VT, *et al.* Vietnam J of Infect Dis (2023)







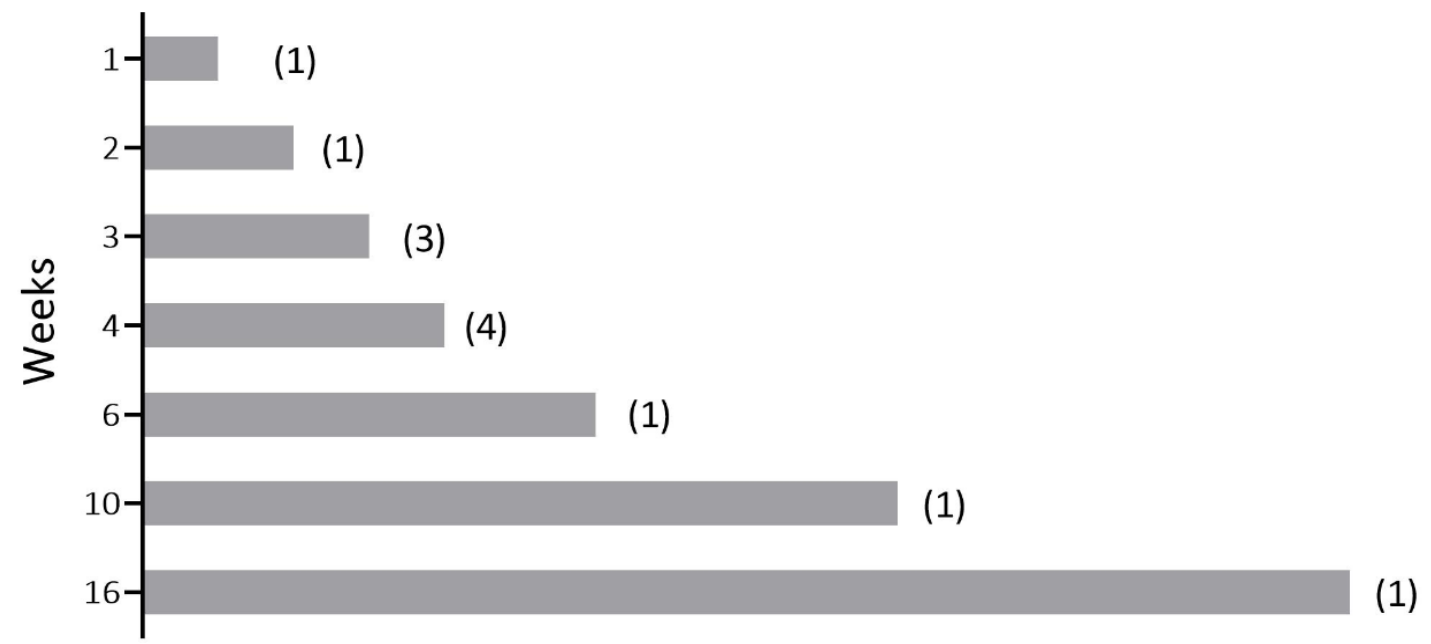
	Serum (n = 526)		Plasma (n = 532)		Urine (n = 482)	
	Tm (n = 77)	No Tm (n = 449)	Tm (n = 80)	No Tm (n = 452)	Tm (n = 74)	No Tm (n = 408)
TmAg Pos	68	11	72	15	69	6
TmAg Neg	9	438	8	437	5	402
Sensitivity	88.3% [79.0 – 94.5]		90.0% [81.2 – 95.6]		93.2% [84.9 – 97.8]	
Specificity	97.6% [95.7 – 98.8]		96.7% [94.6 – 98.1]		98.5% [96.8 – 99.5]	
PPV	86.1% [76.5 – 92.8]		82.8% [73.2 – 90.0]		92.0% [83.4 – 97.0]	
NPV	98.0% [96.2 – 99.1]		98.2% [96.5 – 99.2]		98.8% [97.2 – 99.6]	

Ly VT, *et al.* Vietnam J of Infect Dis (2023)

Mp1p EIA performance when testing plasma and urine together

	Cases (n = 81)	Controls (n = 452)	Row Sum
TmAg positive	78	15 (FP)	93
TmAg negative	3 (FN)	437	440
Column sum	81	452	533
Sensitivity	96.3% (95% CI 89.6– 99.2)		
Specificity	96.7% (95% CI 94.6 – 98.1)		
Positive predictive value	83.9% (95% CI 74.8– 90.7)		
Negative predictive value	99.3% (95% CI 98.0 - 99.9)		

Ly VT, *et al.* Vietnam J of Infect Dis (2023)



Mp1p antigenemia precedes blood culture positivity by up to **16 weeks**

Ly VT, *et al.* Vietnam J of Infect Dis (2023)

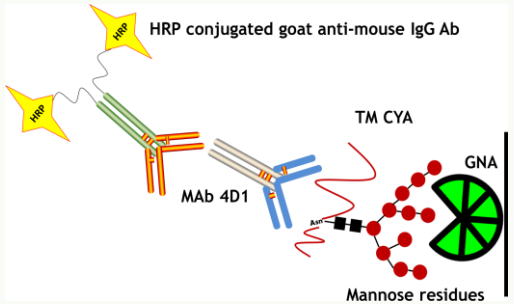
Three point-of-care antigen tests

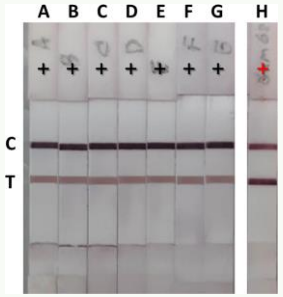
IMMY Mp1p LFA

IMMY/Uni HK

Sens = 91%
Spec = 99%
239 cases, 160 controls

4D1 LFA

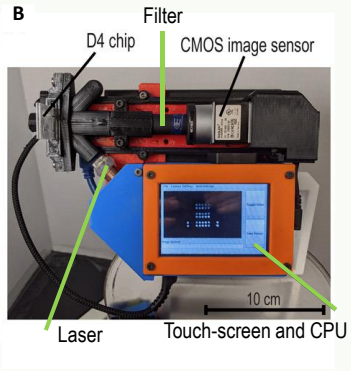




Sirida Youngchim,
Chiangmai Uni.

Sens = 89%
Spec = 100%
76 cases, 265 controls

Mp1p D4 POCT



Duke/Uni HK

Sens = 92%
Spec = 100%
26 cases, 8 controls

Thu, Venugopalan *et al* (in preparation), Pruksaphon *et al* PLOS NTD (2021), Kinnamon *et al* ACS Sens (2023)

The Mp1p LFA

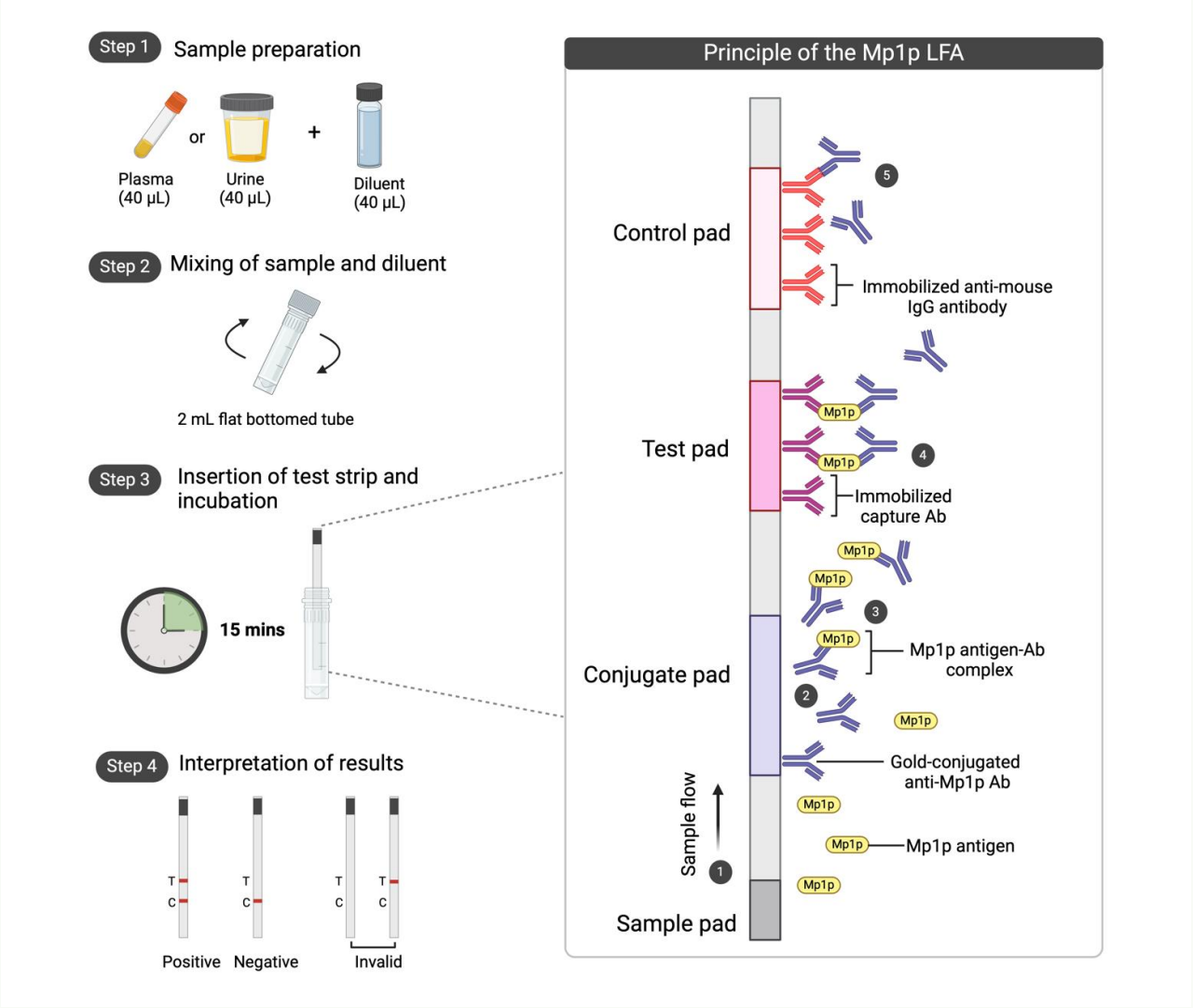
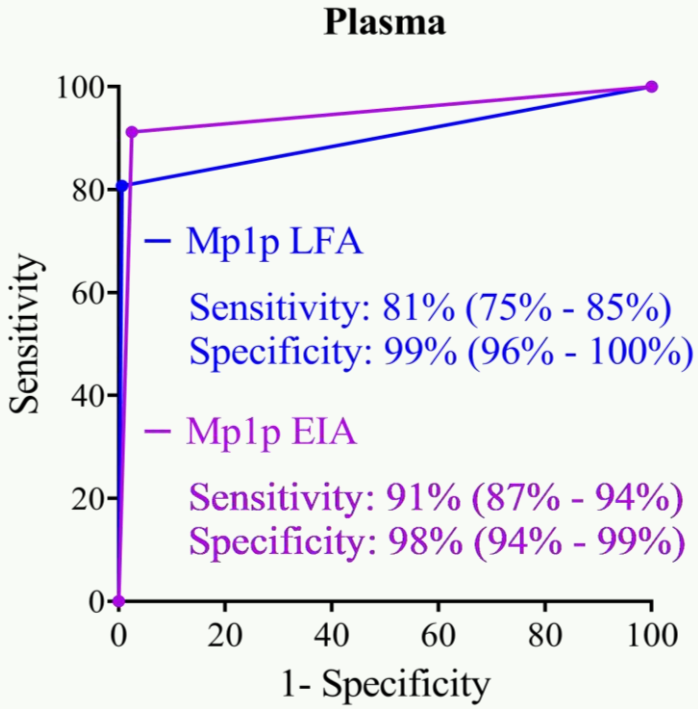
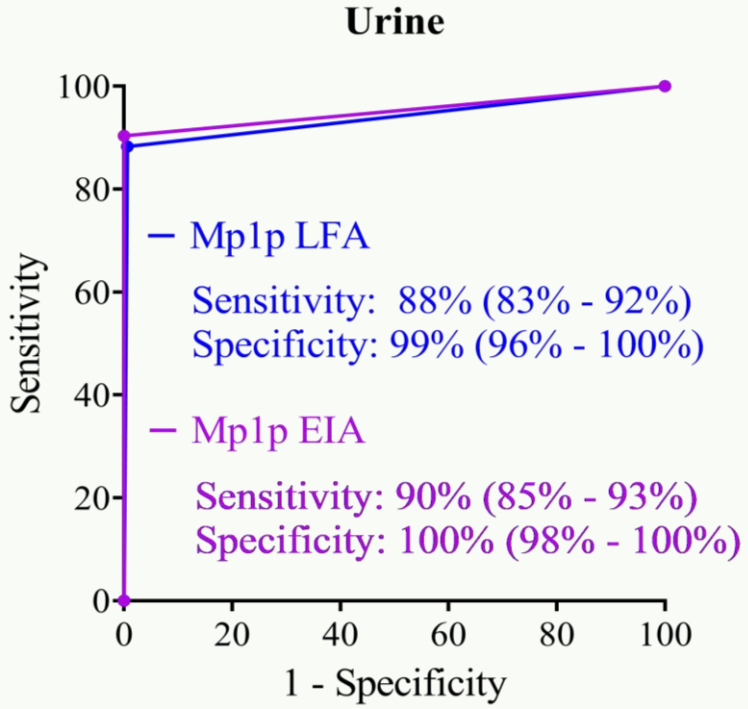


Figure: L. Brown, T. Le *et al* (2025)

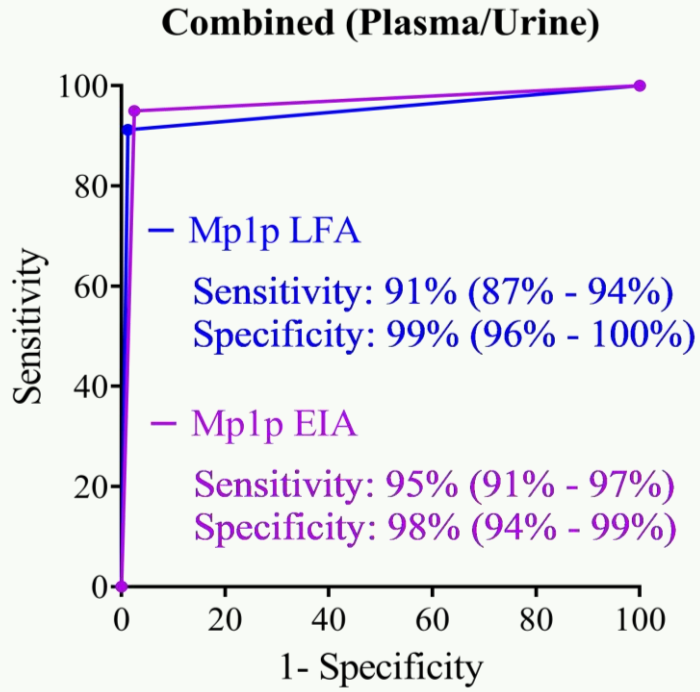
Performance of **IMMY Mp1p LFA vs. Mp1p EIA** (239 talaromycosis case and 160 control patients with AHD)



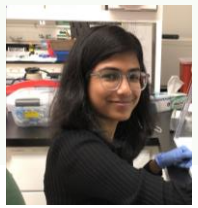
Sensitivity LFA vs EIA, $P < 0.001$
Specificity LFA vs EIA, $P = 0.37$



Sensitivity LFA vs EIA, $P = 0.27$
Specificity LFA vs EIA, $P = 1.00$



Sensitivity LFA vs EIA, $P = 0.02$
Specificity LFA vs EIA, $P = 0.68$



EIA (95%) > LFA (91%) >> blood culture (55%)

Thu NTM and Venugopalan S (in preparation)

Triple fungal screen-and-treat strategy in advanced HIV disease

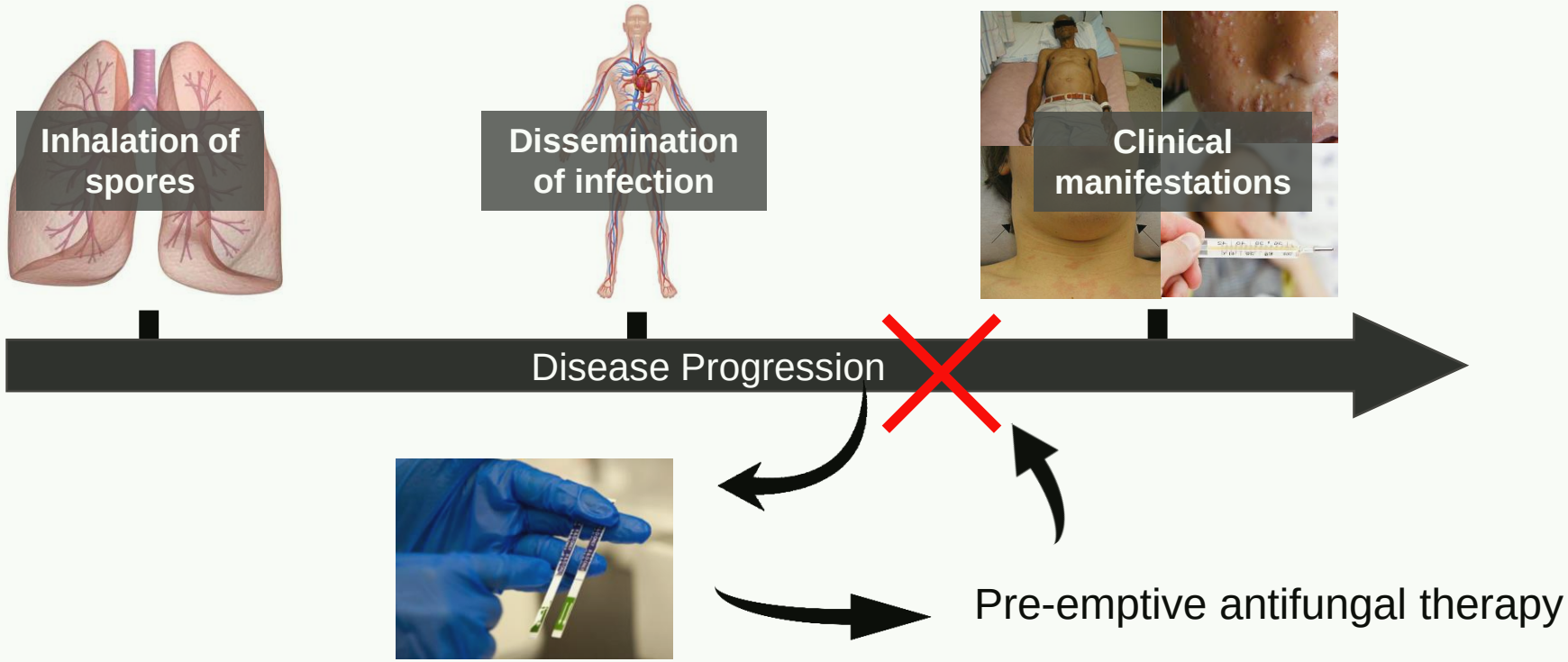


Figure: T. Le (2025)

Triple fungal and mycobacterial screening study flow

Figure 1. Study population and schema

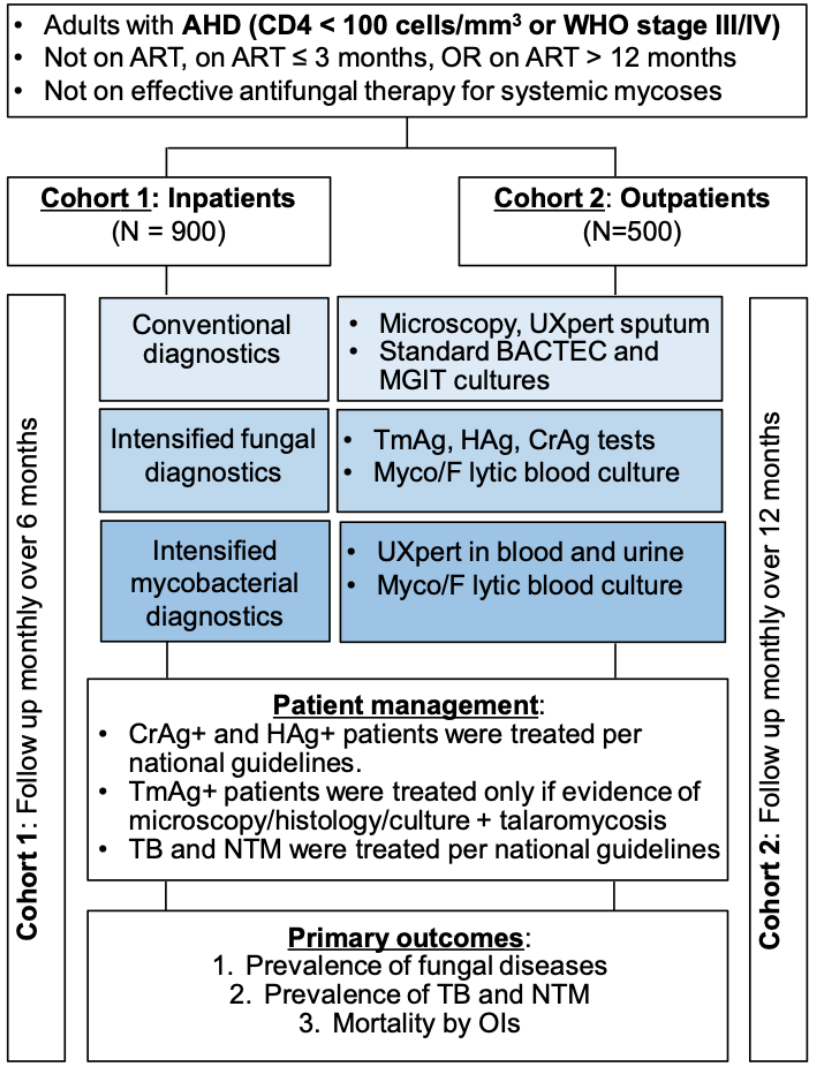
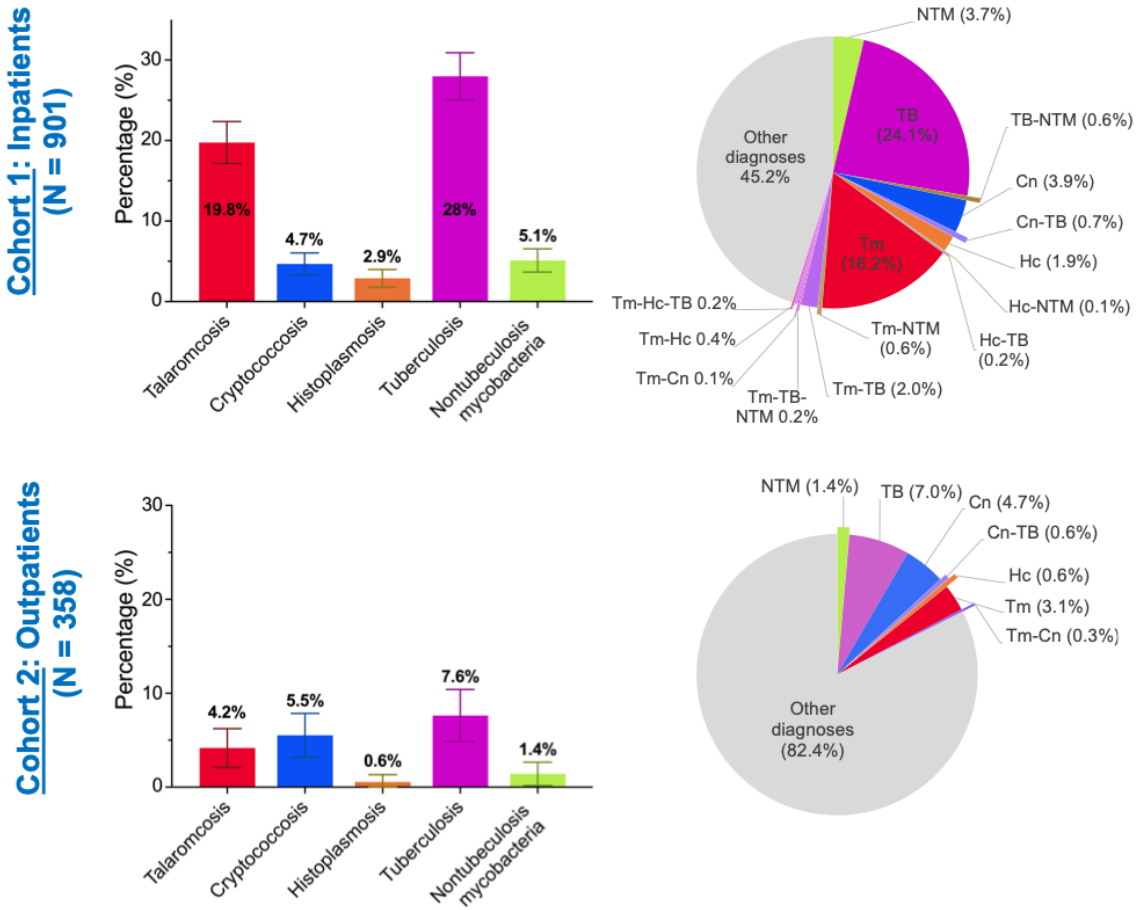


Figure 2. Prevalence of three mycoses and mycobacterial infections in inpatients and outpatients with ADH



Note: Tm: Talaromycosis; Cn: Cryptococcosis, Hc: Histoplasmosis, TB: Tuberculosis, NTM: non-tuberculosis mycobacteria

Figure: Vu Quoc Dat *et al* CROI (2024)

qPCR assays

1994 — Lobuglio: Conventional PCR, Amplify ITS region

1998 — Vanittanakom: Conventional PCR/ hybridization isolates

2002 — Vanittanakom: Nested PCR, 26 isolates

2003 — Prariyachatigul: One-tube seminested PCR, 2 clinical samples

2009 — Vanittanakom: Nested PCR, **Serum**, **Sens 68% (24/34)**

Pornprasert: 5.8s rRNA qPCR, **Whole blood**, **Sens 60% (12/20)**

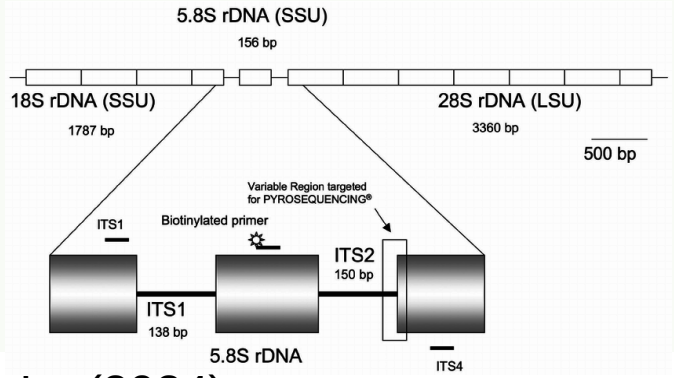
2016 — Hien: Real-time PCR, *MP1* gene, **Plasma**, **Sens 70% (19/27)**

Lu: Real-time PCR, **Serum**, **Sensitivity 77% (23/30)**

2019 — Li: Real-time PCR, 5.8S, **Serum**, **Sens 86% (31/36)**

2024 — Khanh *et al*: 5.8s qPCR, **Whole blood**, **Sens 99% (101/102) w/ fungemia**, **55.6% (20/36) w/o fungemia**

rRNA (18S, 28S, 5.8S)



Tm Mp1p glycomannoprotein

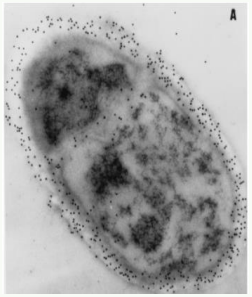
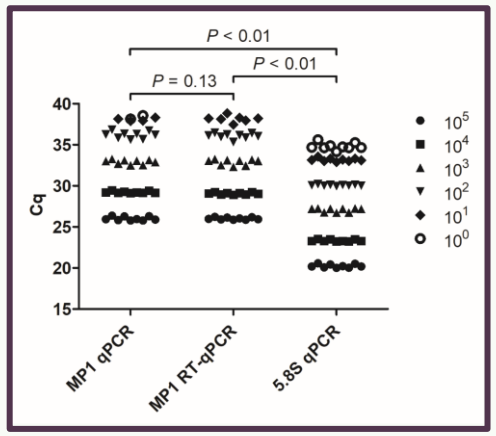
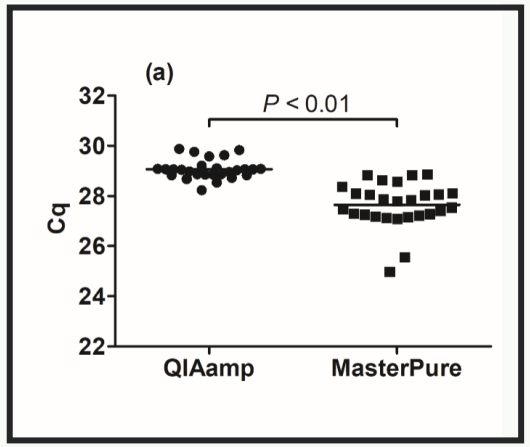


Figure: T. Le (2024)

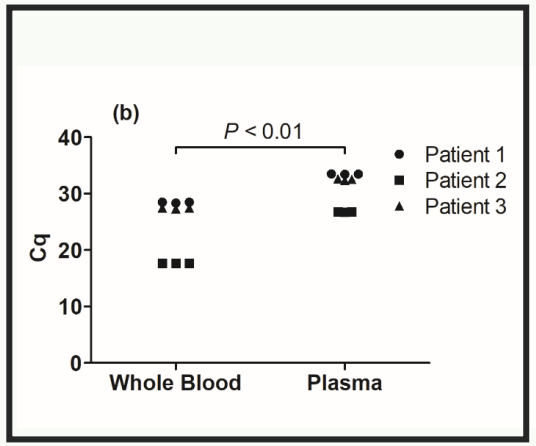
Optimization of the 5.8S qPCR assay



5.8S primers



DNA extraction by MasterPure



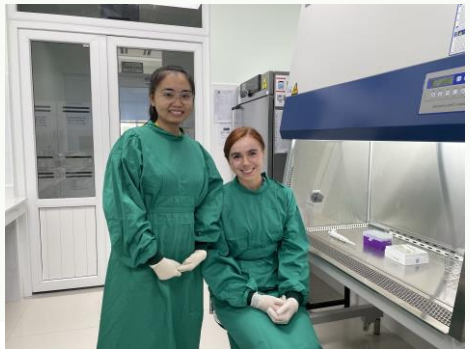
Whole blood (1mL)

No cross-reactivity with 15 clinically-related species

- *Candida albicans*
- *Candida tropicalis*
- *Candida krusei*
- *Candida parasilopsis*
- *Aspergillus fumigatus*
- *Aspergillus terreus*
- *Aspergillus flavus*
- *Cryptococcus neoformans*
- *Histoplasma capsulatum*
- *Penicillium chrysogenum*
- *Penicillium aurantiogriseum*
- *Penicillium citrinum*
- *Penicillium crustosum*
- *Penicillium expansum*
- *Penicillium glabrum*

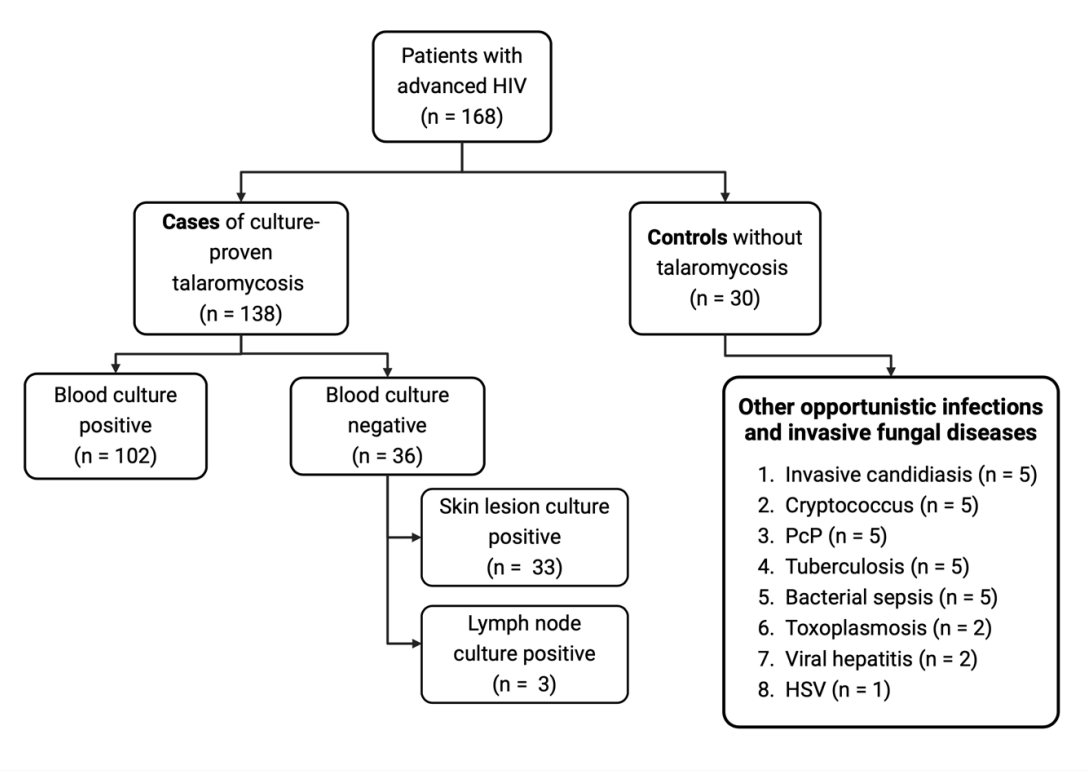
Achieved highest analytical sensitivity to date (1 cell per mL)

Khanh, Ha My et al



[1]Khanh, Brown *et al* Medical Mycology (2025)

Clinical evaluation of the 5.8S qPCR assay



Overall sensitivity = 88%

- In blood-culture-positive = 99%
- In blood-culture-negative = 56%

Overall specificity = 97%

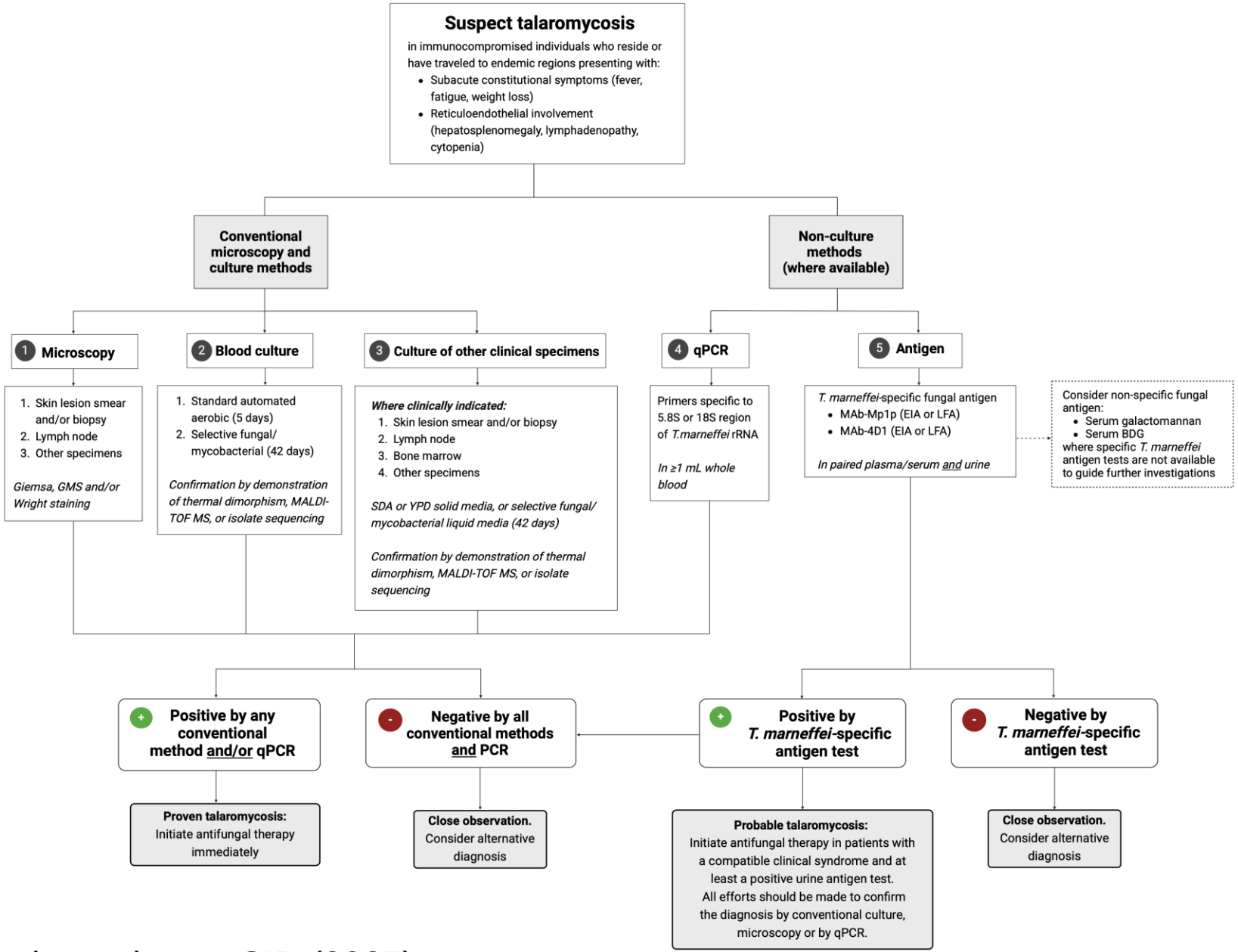
Further optimization:

- Higher volumes of whole blood
- Smaller elution volumes
- ddPCR

	5.8S qPCR	Blood culture	P value
Blood culture-positive cases (n = 102)	101 (99.0%) 95% CI: 94.6 – 99.9%	102 (100%)	1.00
Blood culture-negative cases (n = 36)	20 (55.6%) 95% CI: 38.1 - 72%	-	
Total cases	121 (87.7%) 95% CI: 80.7 - 92.5%	102 (73.9%) 95% CI: 65.6 - 80.8%	<0.01

[1]Khanh, Brown *et al* Medical Mycology (2025)

Diagnostic Algorithm for Talaromycosis



Figures: [1]Brown *et al* under review at CID (2025)

In vitro activity against *T. marneffei*

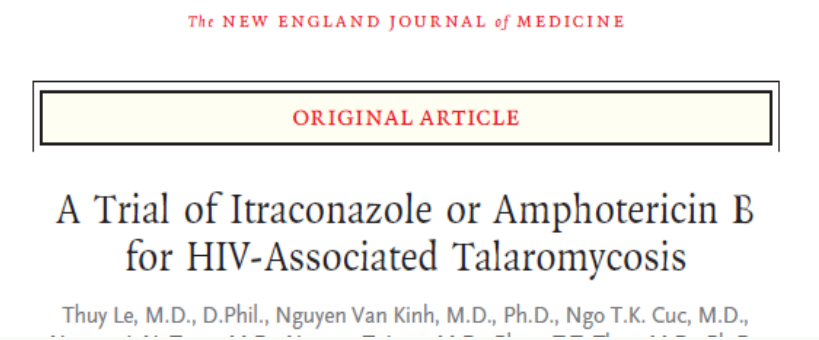
Fluconazole	
Itraconazole	
Voriconazole	
Posaconazole	
Isavuconazole	
Terbinafine	
5-FC	
AmB*	
Caspofungin	
Andulafungin	
Micafungin	
Olorofim	
Fosmanogepix	
Oteseconazole	

**Not correlated with clinical efficacy*

Potent	
Variable	
Limited	

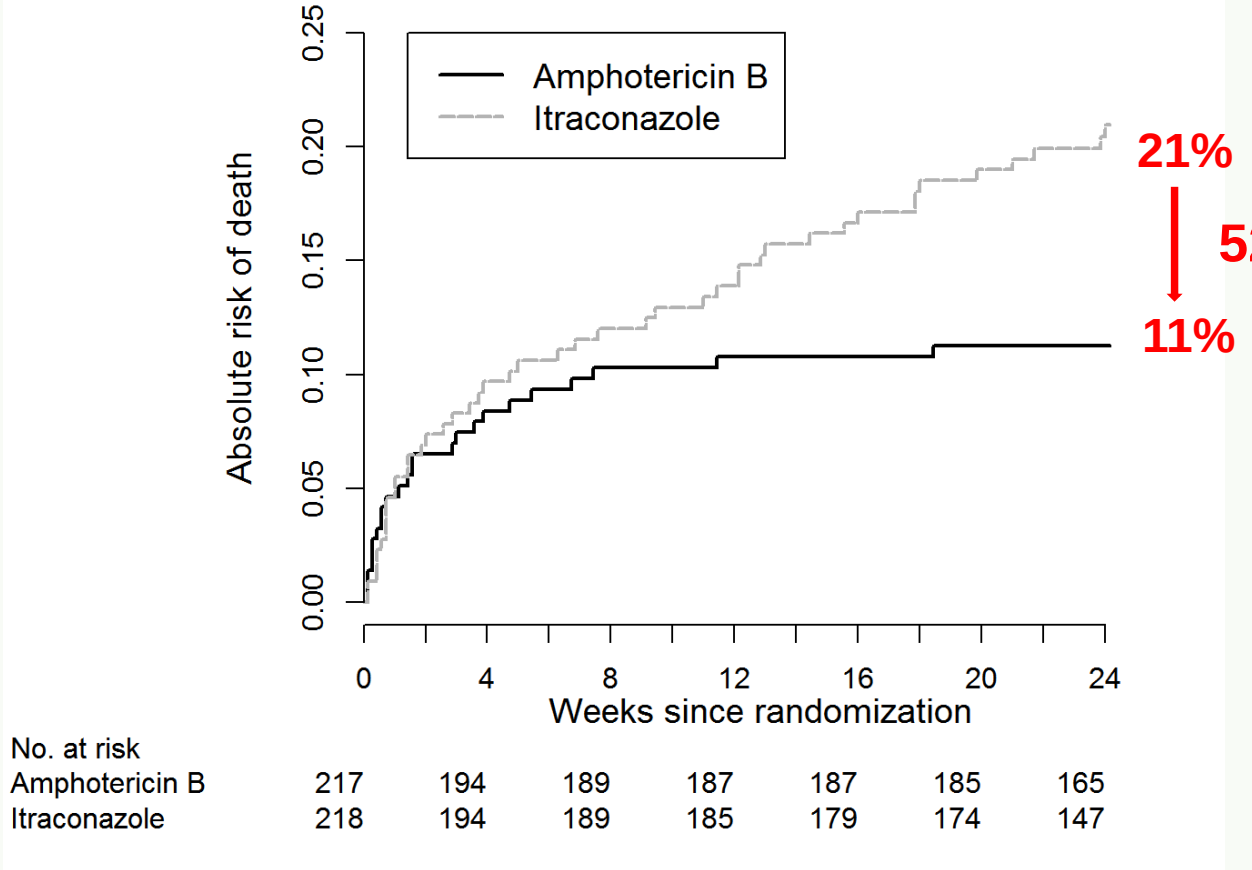
[1]Fang *et al* (2021) + [2]Tan *et al* (2022) Infect Drug Resist, [3]Guo et al (2022) Chin Med J

Current Treatment Options for Talaromycosis



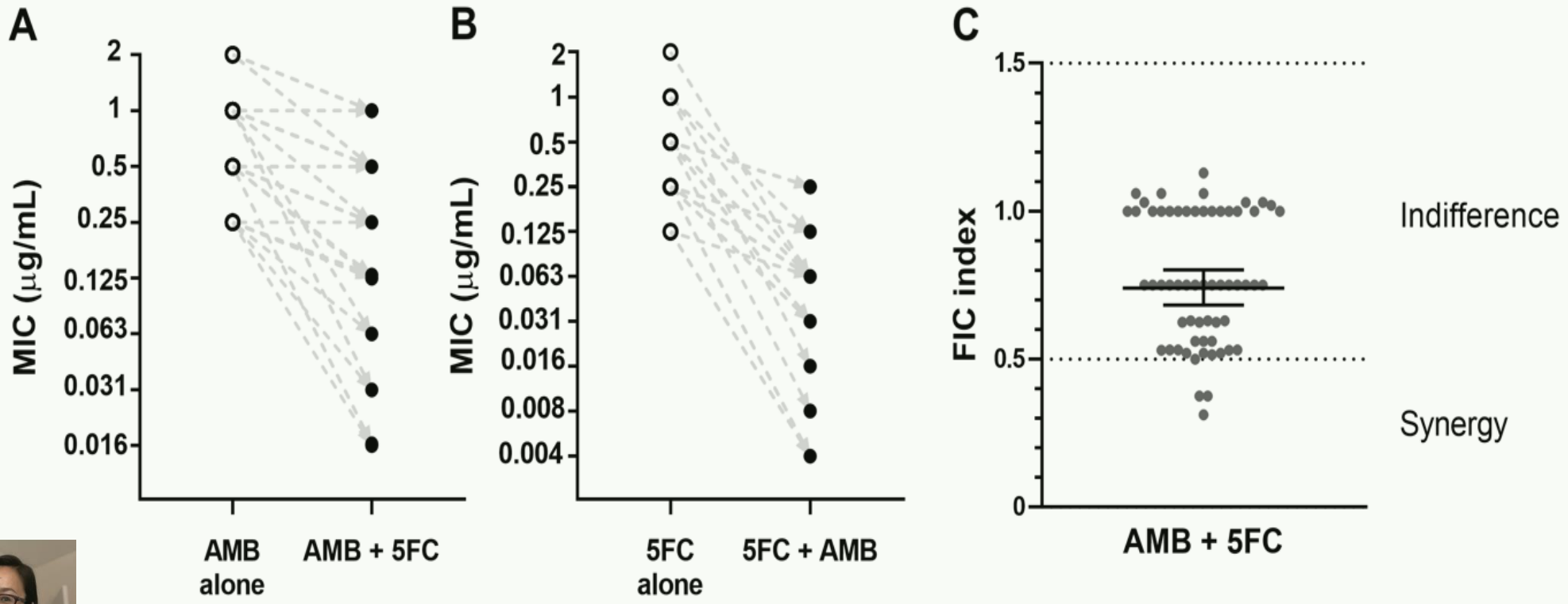
DAmB – *highly potent but highly toxic*

55% grade 3 AEs or higher



Le T *et al* NEJM *(2017)*

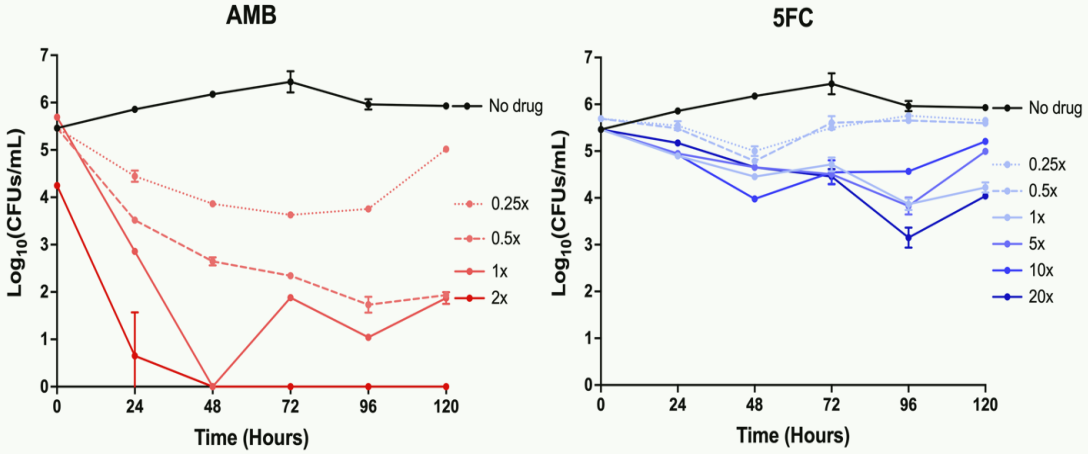
Partial synergy between Amphotericin B and 5FC against Tm in 60 clinical isolates

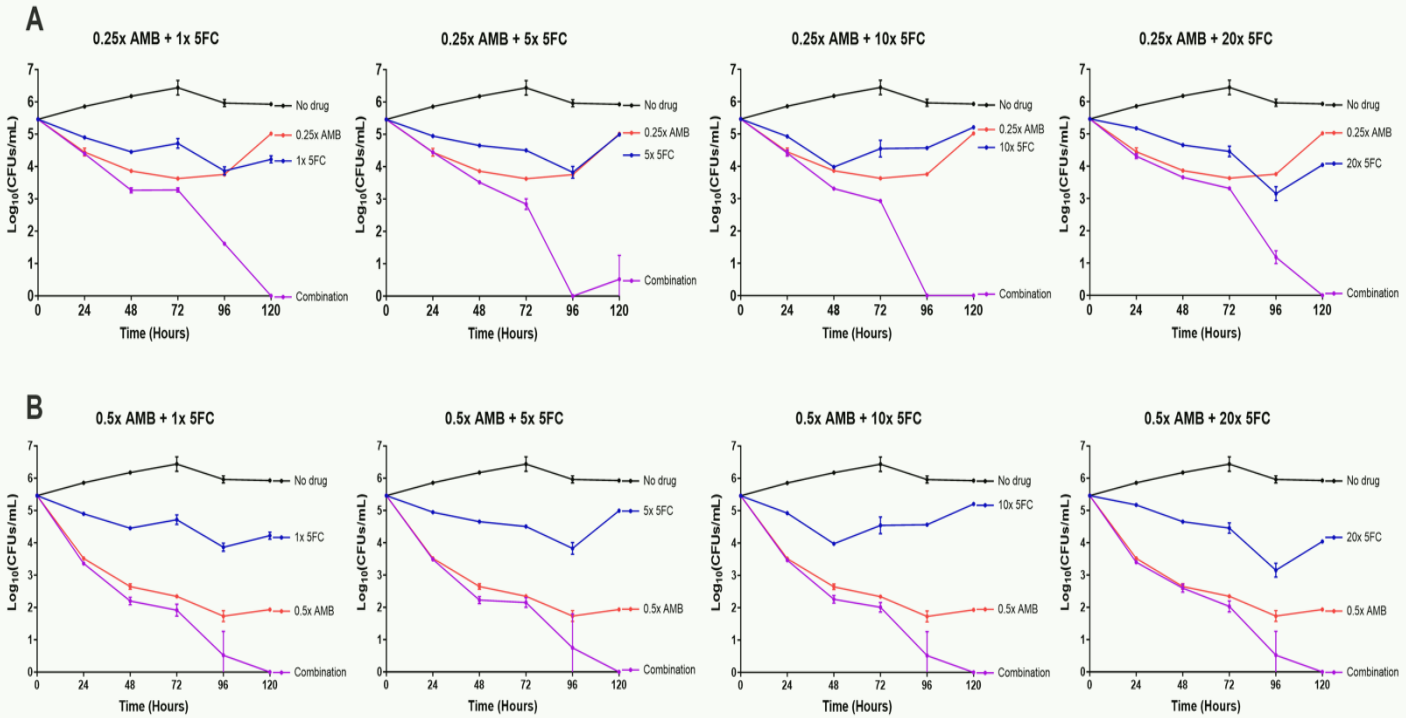


Vitsupakorn S, *et al*. Unpublished

Duke UNIVERSITY

Full synergy between Amphotericin B and 5FC against Tm - time kill curve experiments





Vitsupakorn S, *et al*. Unpublished

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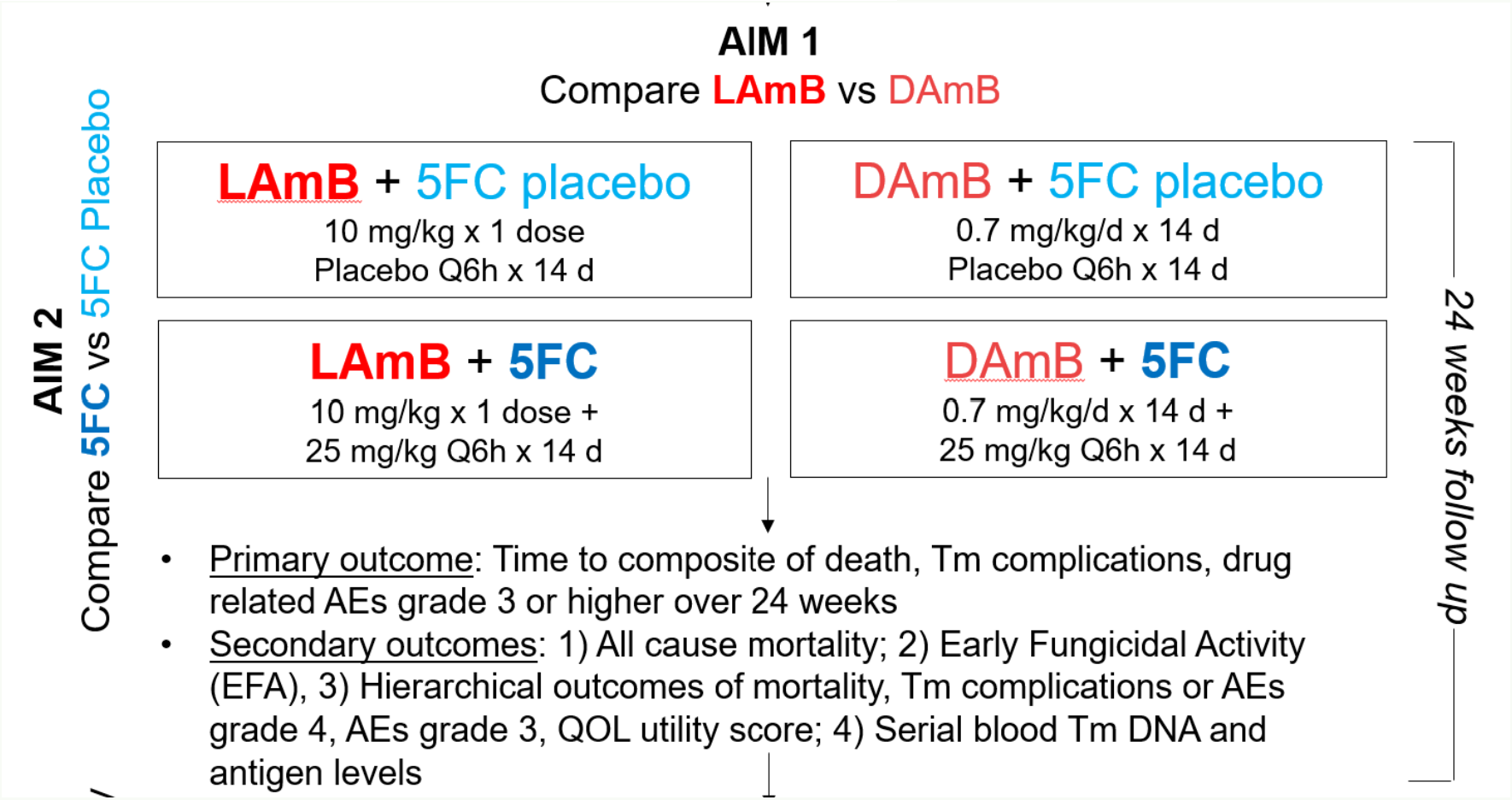
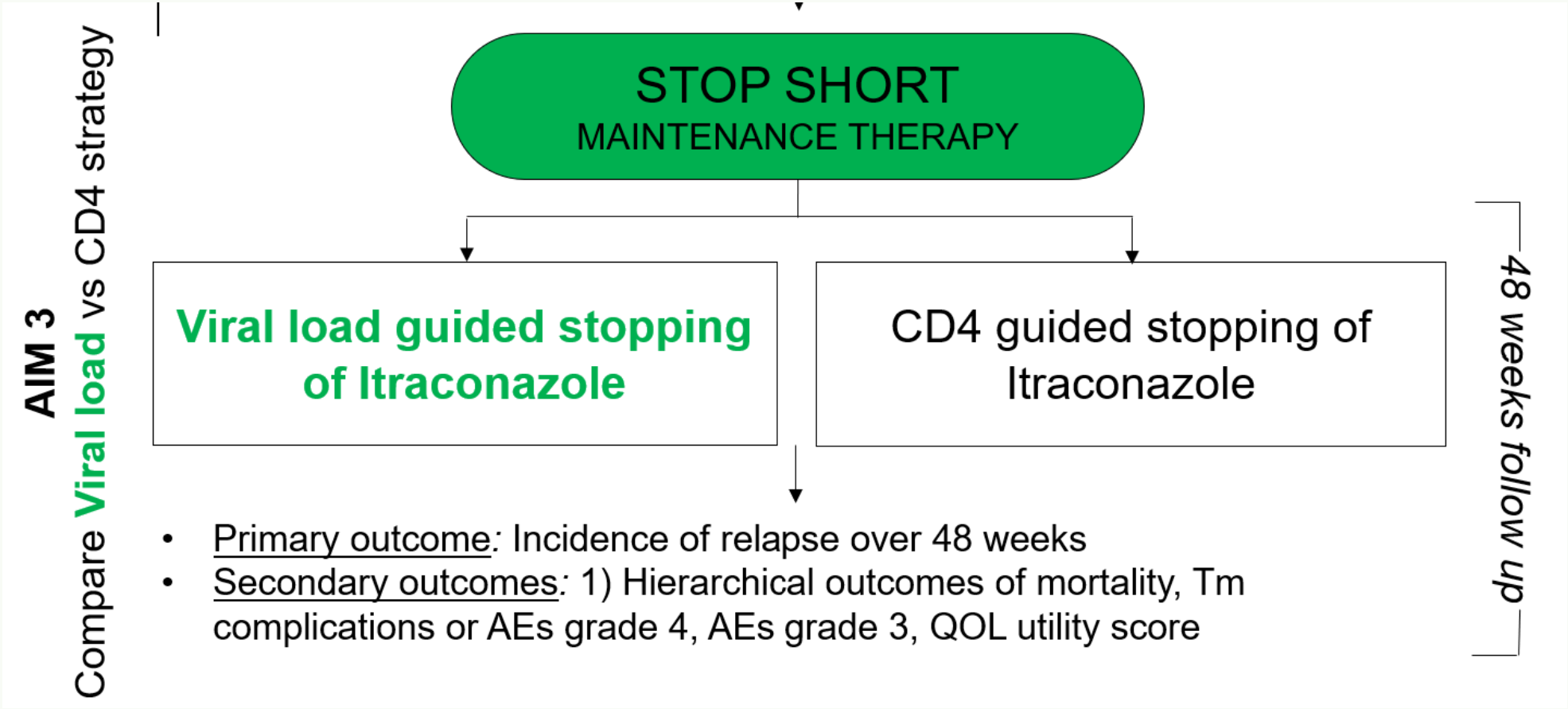
LAmB–FAST

Liposomal Amphotericin B - Flucytosine Antifungal Strategies for Talaromycosis



National Institute of Allergy and Infectious Diseases

When is it safe to stop maintenance antifungal therapy?



National Institute of Allergy and Infectious Diseases

LAmB–FAST

Liposomal Amphotericin B - Flucytosine Antifungal Strategies for Talaromycosis

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Shenzhen 3rd Hospital, Shenzhen, China
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Yun He, MD PhD

NIH NIAID

Summary, insights, research directions

Diagnosis

1. qPCR and antigen assays offer excellent rapid rule in and rule out tests
2. Urine is an excellent sample for antigen detection
3. There is the potential for antigen and qPCR testing to be used to prognosticate and follow treatment response
4. Host-based diagnostics will expand our understanding of disease spectrum, identify people at risk for disease reactivation disease, and improve patient management

Treatment

1. Induction therapy:
   - LAmB-FAST trial
   - Liposomal ampho B +/- 5FC
   - Other antifungals?

2. Consolidation and maintenance: STOP SHORT trial testing viral load guided strategy

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