MMTN
MEDICAL MYCOLOGY TRAINING NETWORK

Know your fungal landscape in Vietnam

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ASIA FUNGAL WORKING GROUP
an ISHAM working group

ISHAM
INTERNATIONAL SOCIETY FOR HUMAN AND ANIMAL MYCOLOGY

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Know Your Fungal Landscape in Viet Nam

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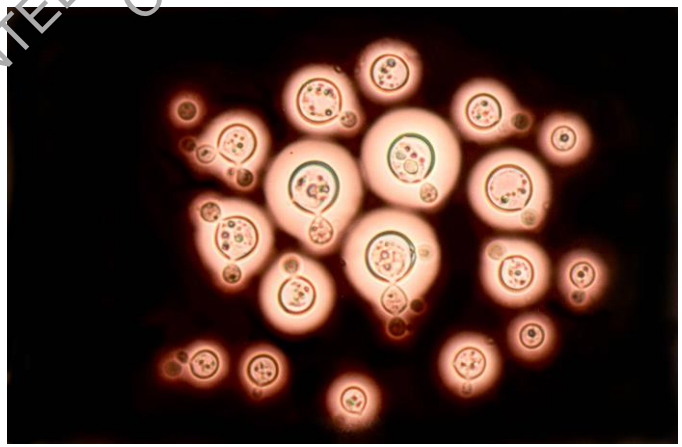


Invasive Fungal Infections

Invasive Fungal Infections

Global perspective – the big 5…

Situation in Viet Nam

What are the challenges?

Questions

Global Perspective

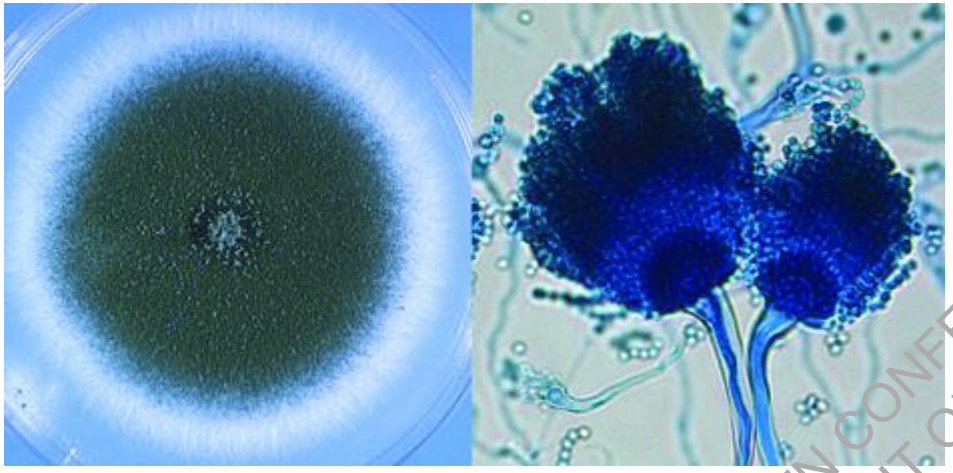
Invasive fungal infections have poor prognoses

More than 2 million life threatening infections each year

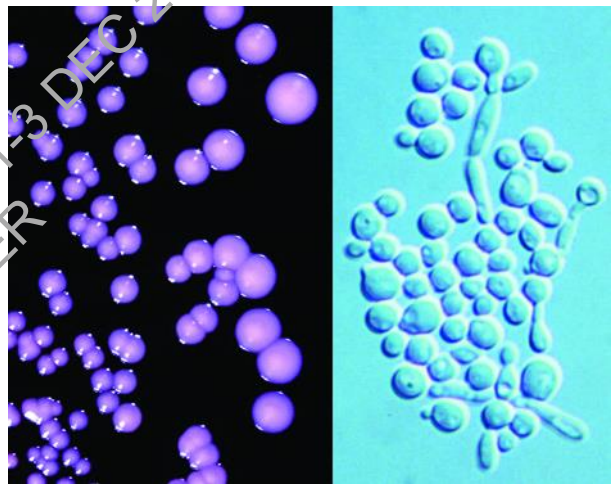
90% of all deaths attributed to

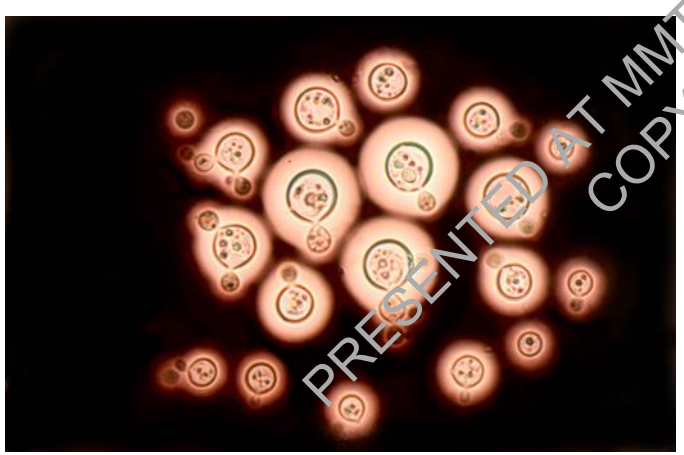
- Aspergillus
- Candida
- Cryptococcus
- Pneumocystis

Aspergillus spp



Candida spp





Cryptococcus spp

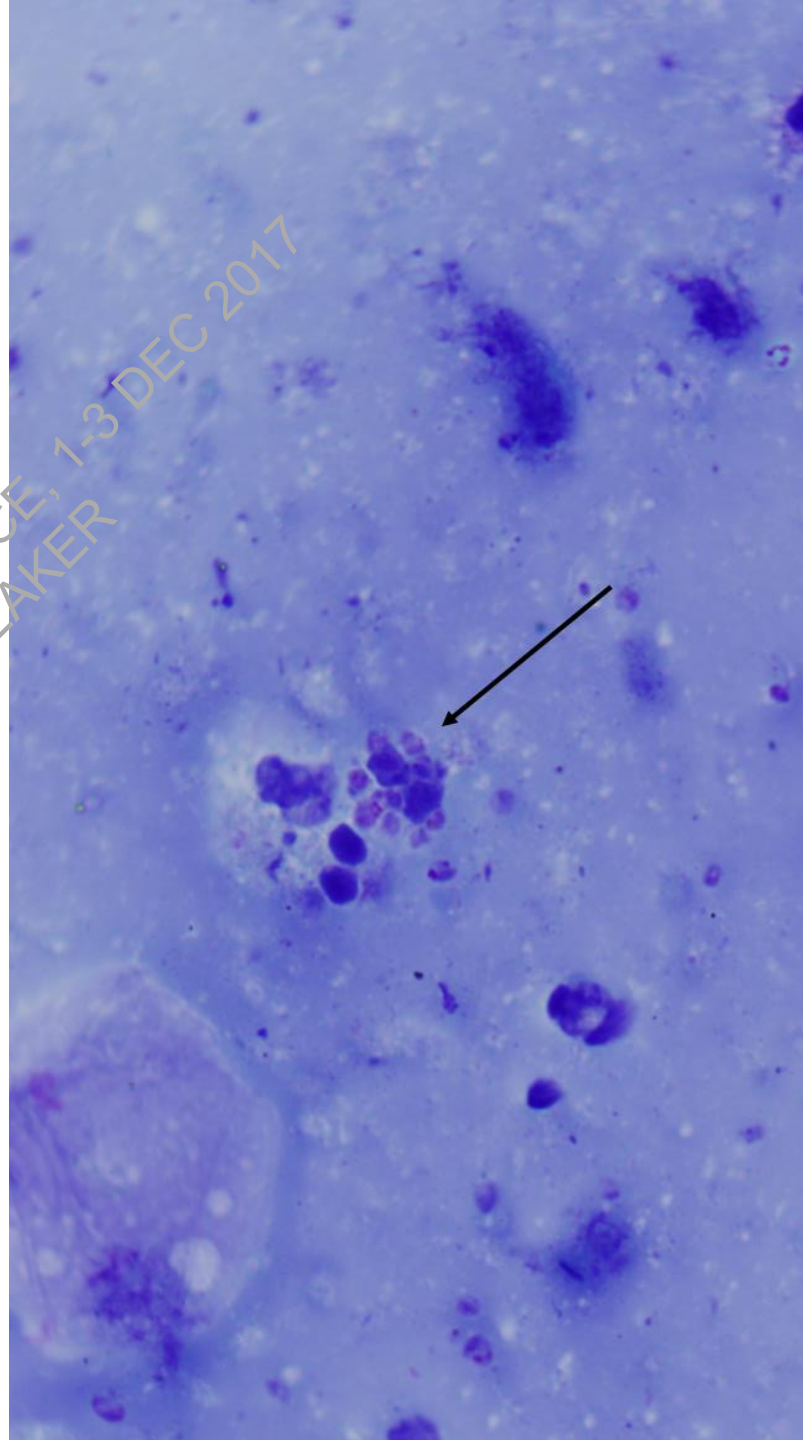
Pneumocystis

https://mycology.adelaide.edu.au/

http://www.microbiologybook.org/mycology/

No 5 - Asia

Talaromyces marneffei



Disease driven by closely associated co-morbidities:

HIV

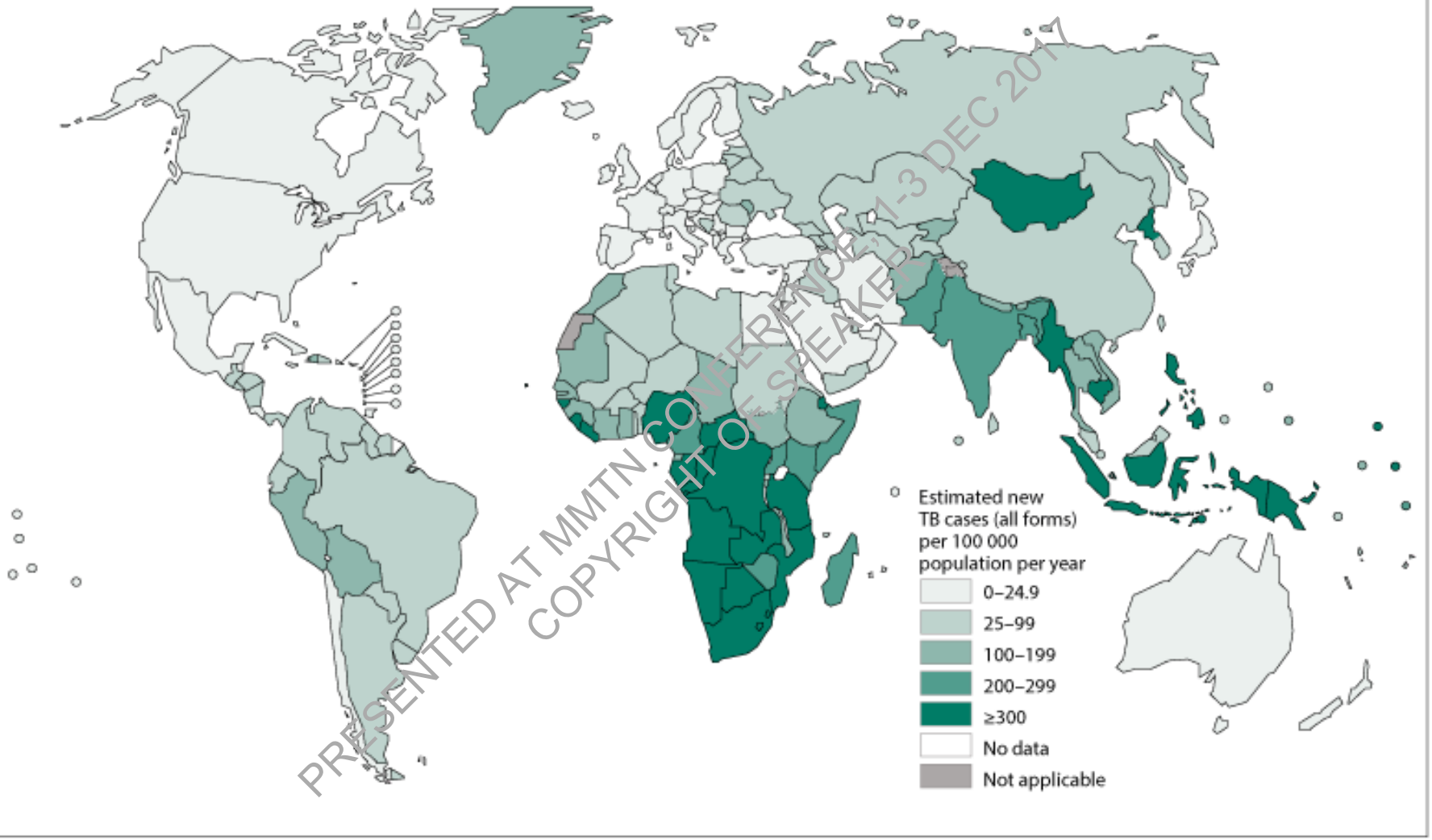
Lung diseases

- Pulmonary TB
- COPD

Serious intercurrent illness

- intensive care
- chemotherapy
- iatrogenic immunosuppression

Estimated TB incidence rates, 2015

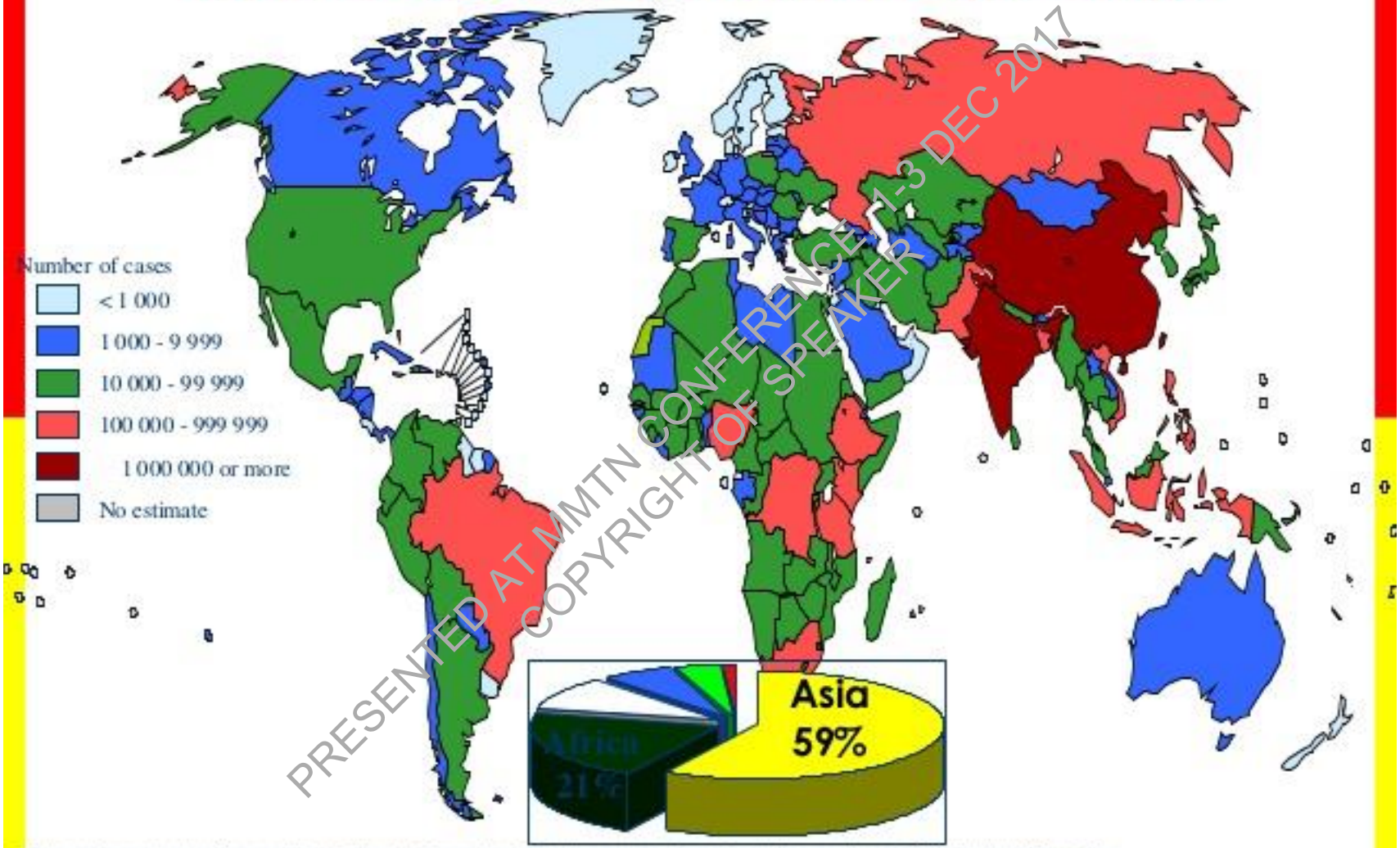


The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: *Global Tuberculosis Report 2016*. WHO, 2016.

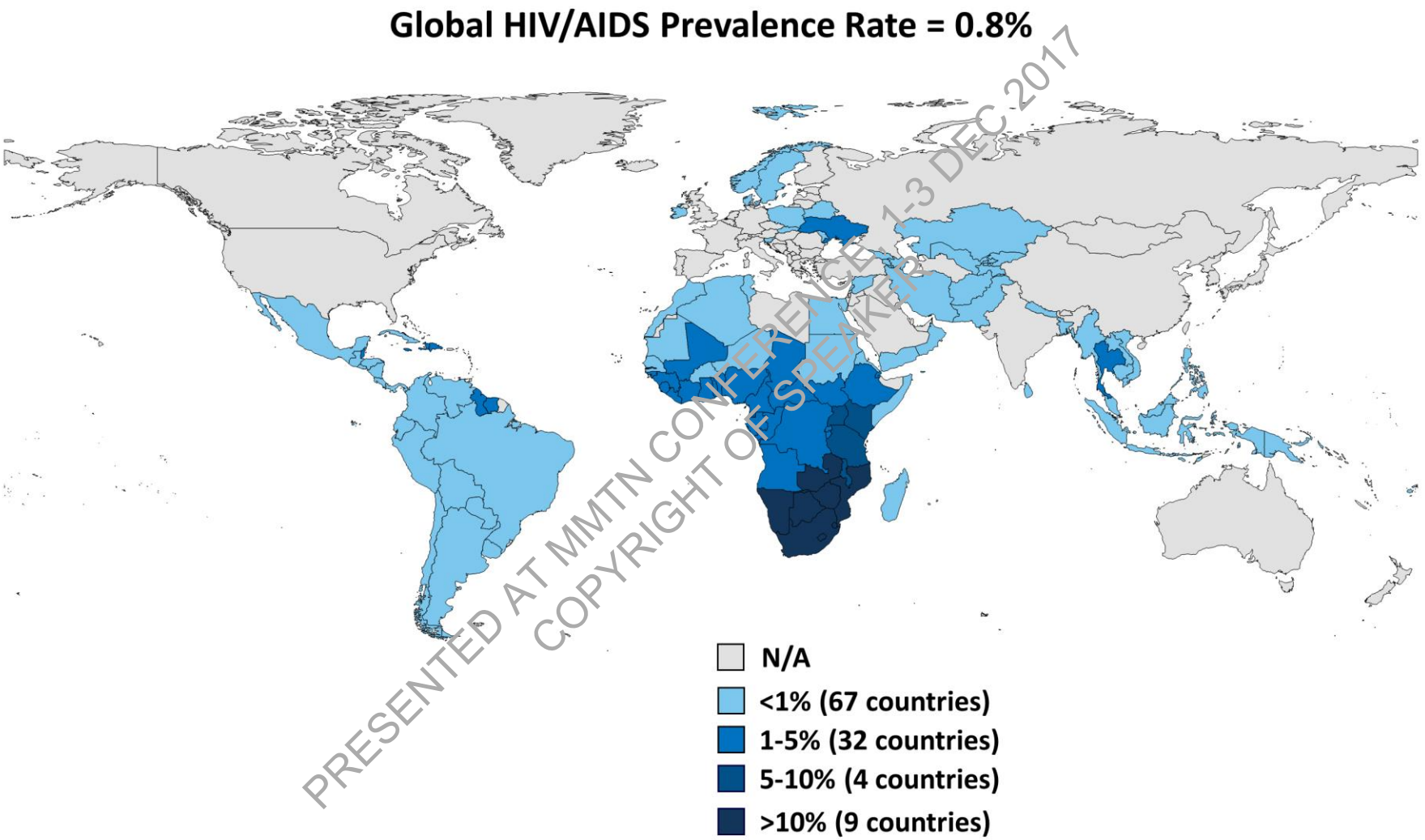
World Health Organization

Most TB cases were in India and China



WHO/HTM/TB/2004.331

Adult HIV Prevalence Rate, 2014



NOTES: Data are estimates. Prevalence rates include adults ages 15-49.
SOURCE: Kaiser Family Foundation, based on UNAIDS, How AIDS Changed Everything; 2015.

Therefore, the vast burden of disease occurs where these diseases are prevalent

Viet Nam:

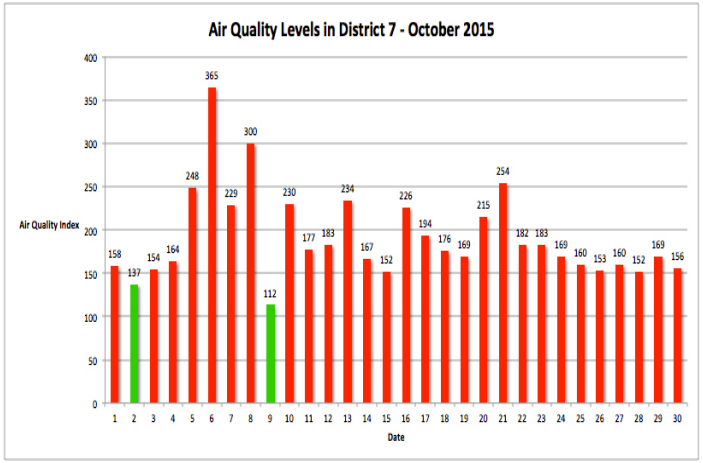
TB prevalence

13th highest burden country, incidence 189/100 000 pa

HIV prevalence

<0.5%

Air pollution…



Estimating the burden of fungal diseases in Viet Nam

Beardsley J, Denning DW, Chau NV, Chau NTB, Crump JA,
Day JN: Estimating the burden of fungal disease in Vietnam. **Mycoses**, 2015, 58 (Suppl. S5), 101–106

Determining disease burdens

1. National surveillance programmes
    1. Gold standard
    2. Expensive
2. Sentinel Surveillance
    1. More cost effective
    2. Complex in highly urbanised areas with multiple health care providers (e.g. Viet Nam)
3. Actuarial Approach

Actuarial Approach

- Foundational data based upon population structure (WHO, Vietnam census data)
- Literature search to identify data describing incidence in country, neighbouring countries or globally
- Literature search to identify prevalences of known risk factors in country, neighbouring countries or globally

Viet Nam

- Population structure
- 91M 2012

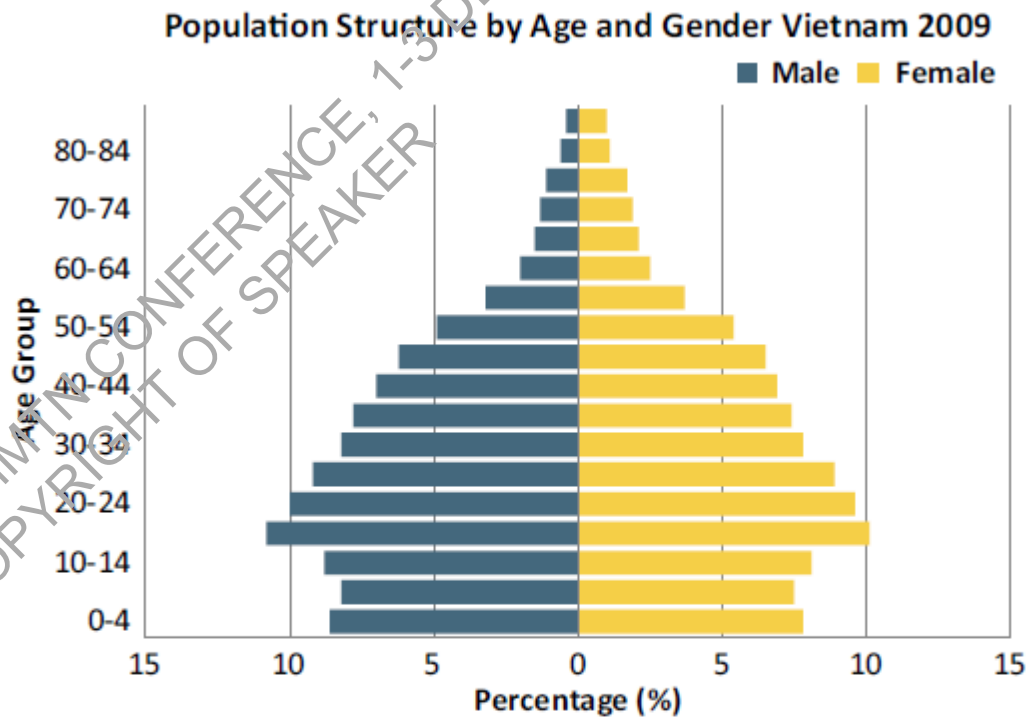


Figure 1 Population structure by age and gender in Vietnam, 2009.

Estimates – Risk Factors

- HIV: 250 000 infected, ~50% receiving ARVs, 4500 new cases of AIDS
- TB burden: annual incidence 218/100 000
- COPD/Asthma – population prevalence 6.7% and 1% (~350 000 acute admissions)
- Haematological cancer and transplants: AML incidence 5/100 000; ~25 BMTs, ~130 kidney transplants
- ICU bed numbers derived from Viet Nam General Statistics Office

Results

Aspergillosis

Disease	Estimation	Total number	Case prevalence /100k
Invasive Aspergillosis	3.9% severe COPD 10% AML 10% other haem maligancy 6% heart transplants, 0.5% Kidney transplants	14 523 (3,745-18,556)	15.99
Allergic Bronchopulmonary Aspergillosis	2.5% of adult asthmatics; 15% of adults with cystic fibrosis	23 607 (4,981-66,208)	26
Severe Asthma with Fungal Sensitisation	33% of the most severe 10% of adult asthmatics	31 161 (8,538-181,599)	34
Chronic pulmonary aspergillosis	22% of cases of cavitary pulmonaryTB; 2% of non-cavitary cases	55 509 (9,162-127,519)	61

AIDS associated Mycoses

Disease	Estimation	Total number	Case prevalence /100k
Cryptococcal meningitis	3% of new AIDS diagnoses	140 (23-1319)	0.15
Pneumocystis pneumonia	13% of new AIDS diagnoses	608 (281-2748)	0.67
Talaromycosis	4% of new AIDS diagnoses	206 (159-594)	0.23

Chau *et al. BMC Infectious Diseases* 2010, 10:199
http://www.biomedcentral.com/1471-2334/10/199

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

A prospective descriptive study of cryptococcal meningitis in HIV uninfected patients in Vietnam - high prevalence of *Cryptococcus neoformans var grubii* in the absence of underlying disease

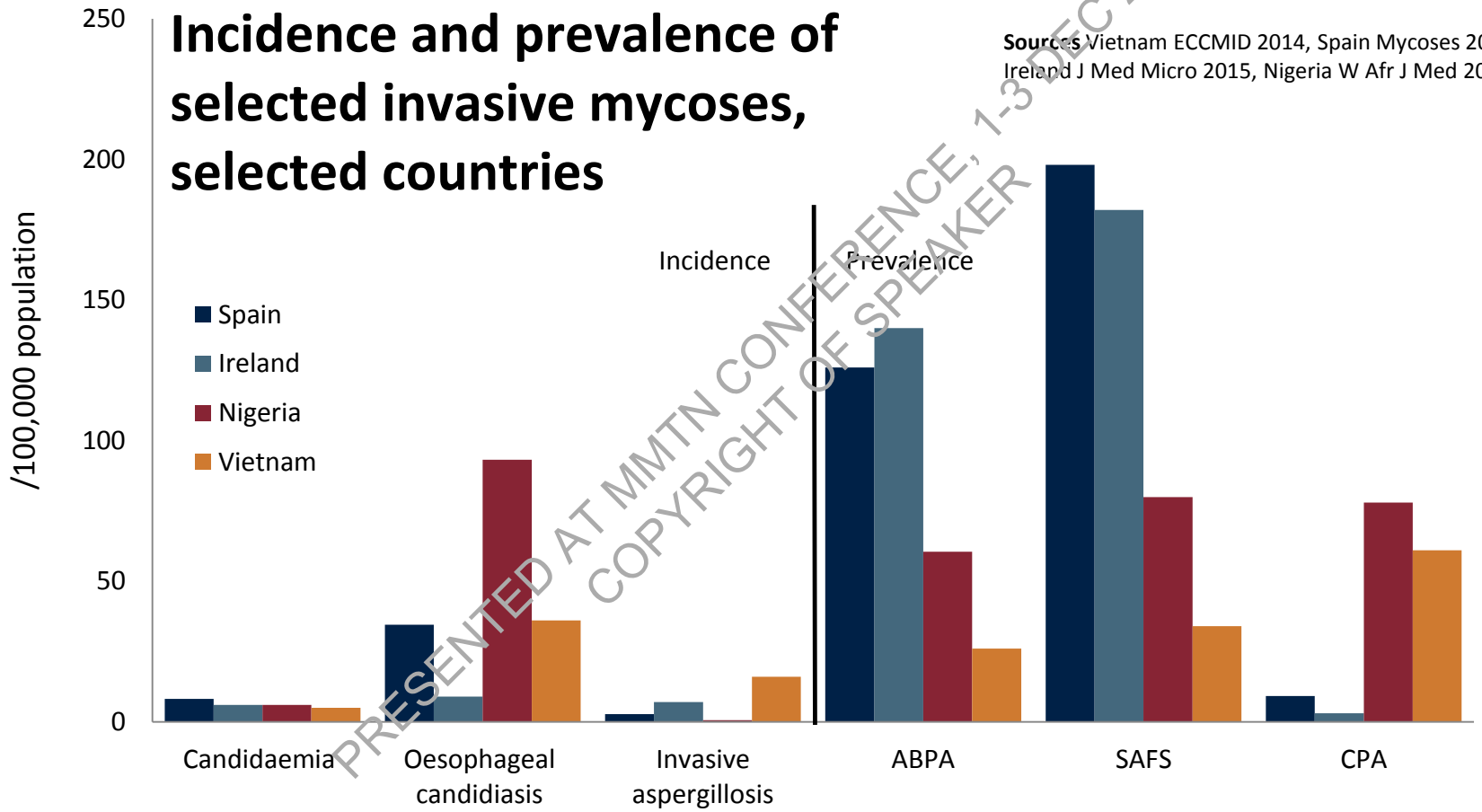
Tran TH Chau[1], Nguyen H Mai[1], Nguyen H Phu[1], Ho D Nghia[1], Ly V Chuong[1], Dinh X Sinh[1], Van A Duong[2], Pham T Diep[2], James I Campbell[2,3], Stephen Baker[2,3], Tran T Hien[1], David G Lalloo[4], Jeremy J Farrar[2,3] and Jeremy N Day*[2,3]

Candidiasis

Disease	Estimation	Total number	Prevalence /100k
Candidaemia	5/100,000 general population: 3.5 in ICU patients, 1.5 in non-ICU patients	4,540 (1,735-10,150)	5
Oesophageal Candidiasis	20% of HIV patients not on ARVs; 5% of those on ARVs	33,107 (9,524-61,173)	36
Oral Candidiasis	90% of HIV positive not on ARVs	121,590 (7,454-260,028)	132
Recurrent vaginal candidiasis >4/times/year	6% of adult women	1,767,581 (1,194,070-3,229,512)	3,893

International Context

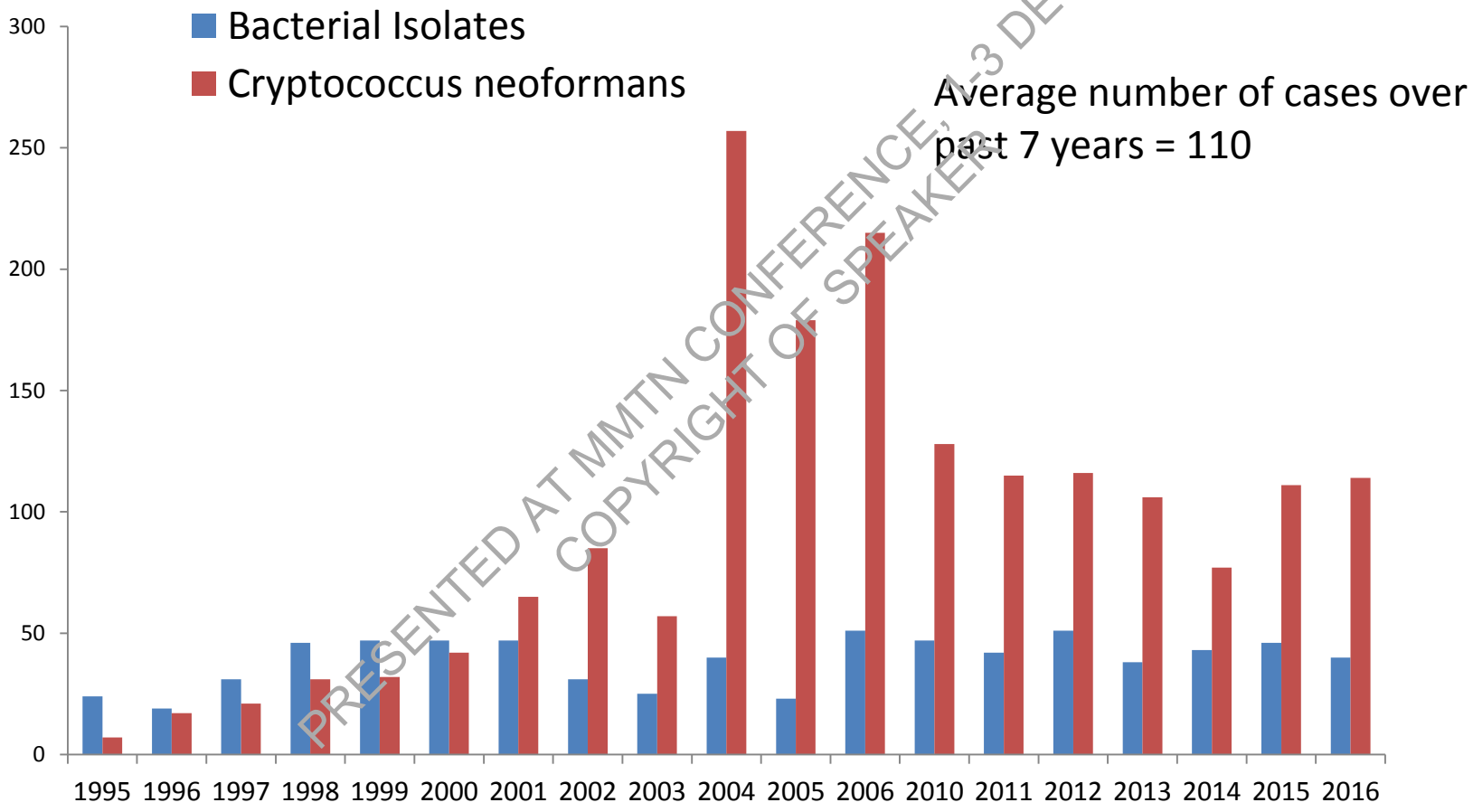
Incidence and prevalence of selected invasive mycoses, selected countries



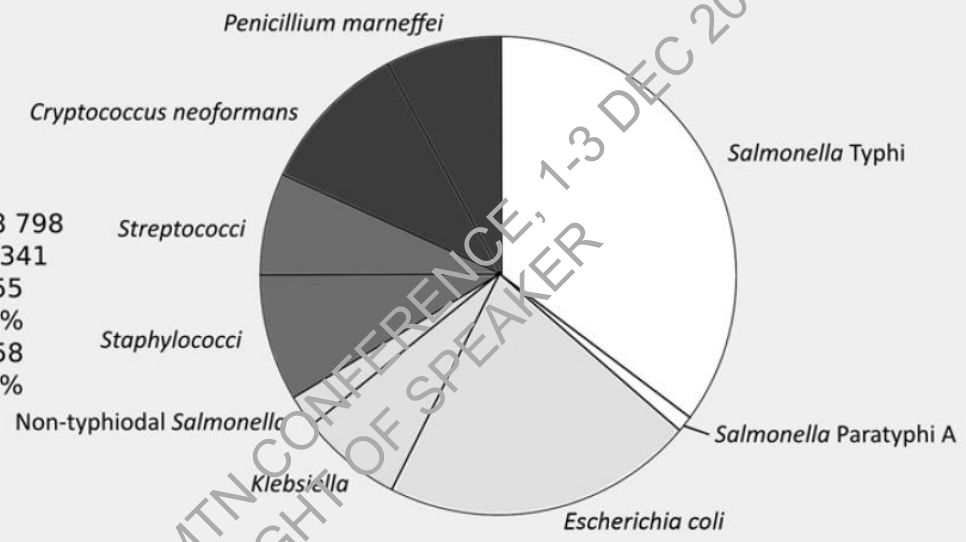
Sources Vietnam ECCMID 2014, Spain Mycoses 2014, Ireland J Med Micro 2015, Nigeria W Afr J Med 2014

Are our estimates accurate?

Pyogenic bacterial meningitis isolates and *Cryptococcus neoformans* isolates 1995 - 2016, Hospital for Tropical Diseases, HCMC

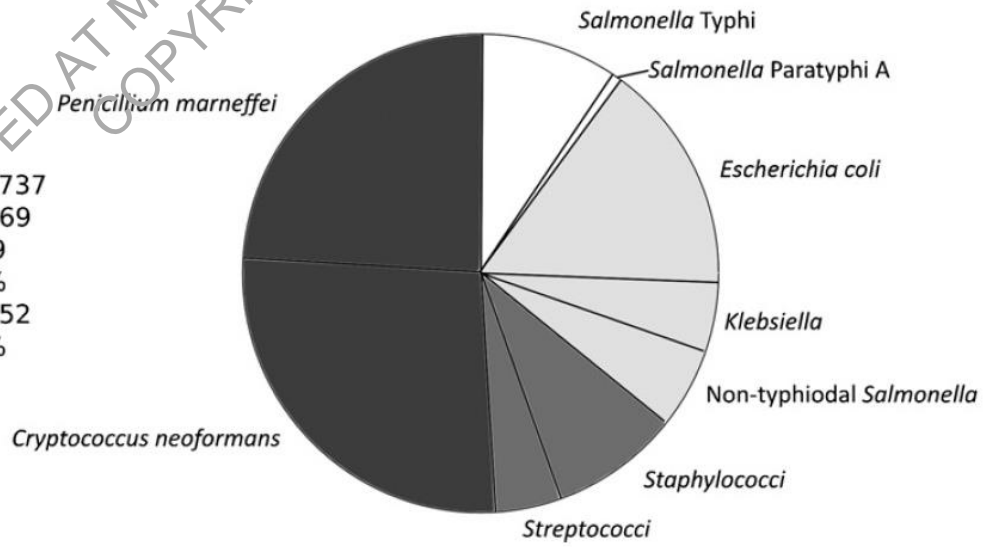


1999 - 2003



Hospital admissions : 138 798
Blood cultures : 18 341
Positive blood cultures : 1755
Positive culture rate : 9.6%
HIV seropositive : 4758
HIV rate/admissions : 3.4%

2004 - 2008



Hospital admissions : 152 737
Blood cultures : 26 669
Positive blood cultures : 2559
Positive culture rate : 9.6%
HIV seropositive : 12 552
HIV rate/admissions : 8.2%

What were my learning points?

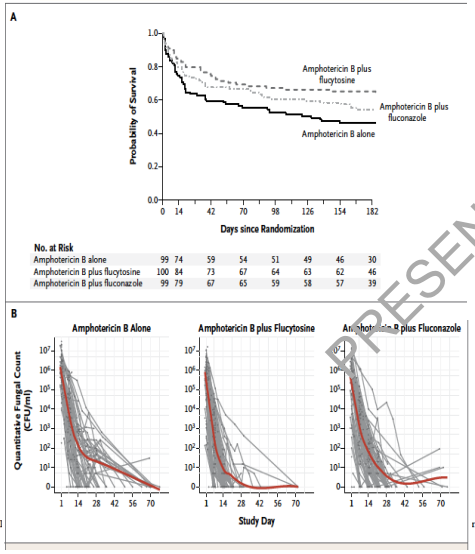
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Combination Antifungal Therapy for Cryptococcal Meningitis

Jeremy N. Day, M.D., Ph.D., Tran T.H. Chau, M.D., Ph.D., Marcel Wolbers, Ph.D., Pham P. Mai, M.D., Nguyen T. Dung, M.D., Nguyen H. Mai, M.D., Ph.D., Nguyen H. Phu, M.D., Ph.D., Ho D. Nghia, M.D., Ph.D., Nguyen D. Phong, M.D., Ph.D., Cao Q. Thai, M.D., Le H. Thai, M.D., Ly V. Chuong, M.D., Dinh X. Sinh, M.D., Van A. Duong, B.Sc., Thu N. Hoang, M.Sc., Pham T. Diep, B.Sc., James I. Campbell, M.I.B.M.S., Tran P.M. Sieu, M.D., Stephen G. Baker, Ph.D., Nguyen V.V. Chau, M.D., Ph.D., Tran T. Hien, M.D., Ph.D., David G. Lalloo, M.D., and Jeremy J. Farrar, M.D., D.Phil.

ABSTRACT



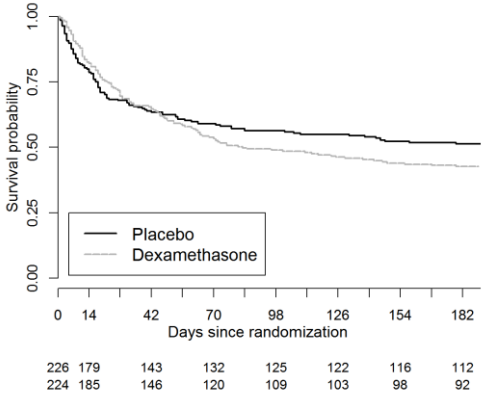
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjunctive Dexamethasone in HIV-Associated Cryptococcal Meningitis

J. Beardsley, M. Wolbers, F.M. Kibengo, A.-B.M. Ggayi, A. Kamali, N.T.K. Cuc, T.Q. Binh, N.V.V. Chau, J. Farrar, L. Merson, L. Phuong, G. Thwaites, N. Van Kinh, P.T. Thuy, W. Chierakul, S. Siriboon, E. Thiansukhon, S. Onsanit, W. Supphamongkholchaikul, A.K. Chan, R. Heyderman, E. Mwinjiwa, J.J. van Oosterhout, D. Imran, H. Basri, M. Mayxay, D. Dance, P. Phimmasone, S. Rattanavong, D.G. Lalloo, and J.N. Day, for the CryptoDex Investigators*

ABSTRACT



N ENGL J MED 374;6 NEJM.ORG FEBRUARY 11, 2016

Main challenges

- We lack high quality data on the burden of fungal disease in Vietnam
- There is likely a large unrecognised burden of disease
  - Aspergillosis – is this being misdiagnosed as poorly responsive TB?
  - Candidaemia and other candidiasis
- As medical treatment gets more sophisticated, fungal infections likely to become more important
- As pollution worsens, likely to see more pulmonary fungal disease
- Cryptococcosis is not going away...
- Need to improve our fungal diagnostics
- Need to improve our fungal reporting

The Wellcome Trust (Intermediate Fellowship)

Thanks!

OUCRU:
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Nguyen Van Vinh Chau
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Nick Hunt – University of Sydney
Joon-sup Lee – University of Sydney
David Dance - LOMWRU
Sayaphet Rattanavong - LOMWRU
Freddie Kibengo – MRC Uganda
Anatoli Kamali – MRC Uganda
Wirongrong Chierakul - MORU
Adrienne Chan – Dignitas International
Cryptodex Investigators
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Niranjan Nagarajan - GIS