



Global Overview of Mycetoma and Treatment Gaps

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ECTMIH
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Mycetoma: addressing the unbearable treatment gap

Content

- Global overview
- Definition
- Epidemiology
- Transmission
- Treatment gaps

Epidemiology - history

1694: First description of mycetoma

1842: Gill - Madura foot (Madurai, India)

1860: Van Dyke Carter – Mycetoma: ‘mykes’ and ‘oma’

Mycetoma

Definition: **chronic infection of subcutaneous tissues**

Clinical triad

- swelling
- sinuses
- grains



Actinomycetoma
(bacteria)

Eumycetoma
(fungi)

Mycetoma

Definition: **chronic infection of subcutaneous tissues**

Actinomycetoma
(*bacteria*)

Nocardia brasiliensis
Streptomyces somaliensis
Nocardia asteroides
Actinomadura madurae
Actinomadura pelletieri

Eumycetoma
(*fungi*)

Madurella mycetomatis
Falciformispora senegalensis
Trematosphaeria grisea
Scedosporium apiospermum
Acremonium spp.

Mycetoma

Definition: **chronic infection of subcutaneous tissues**

Similar presentation

Actinomycetoma
(bacteria)

Eumycetoma
(fungi)



Mycetoma

Definition: **chronic infection of subcutaneous tissues**

Actinomycetoma
(bacteria)

Eumycetoma
(fungi)

Similar presentation

More aggressive

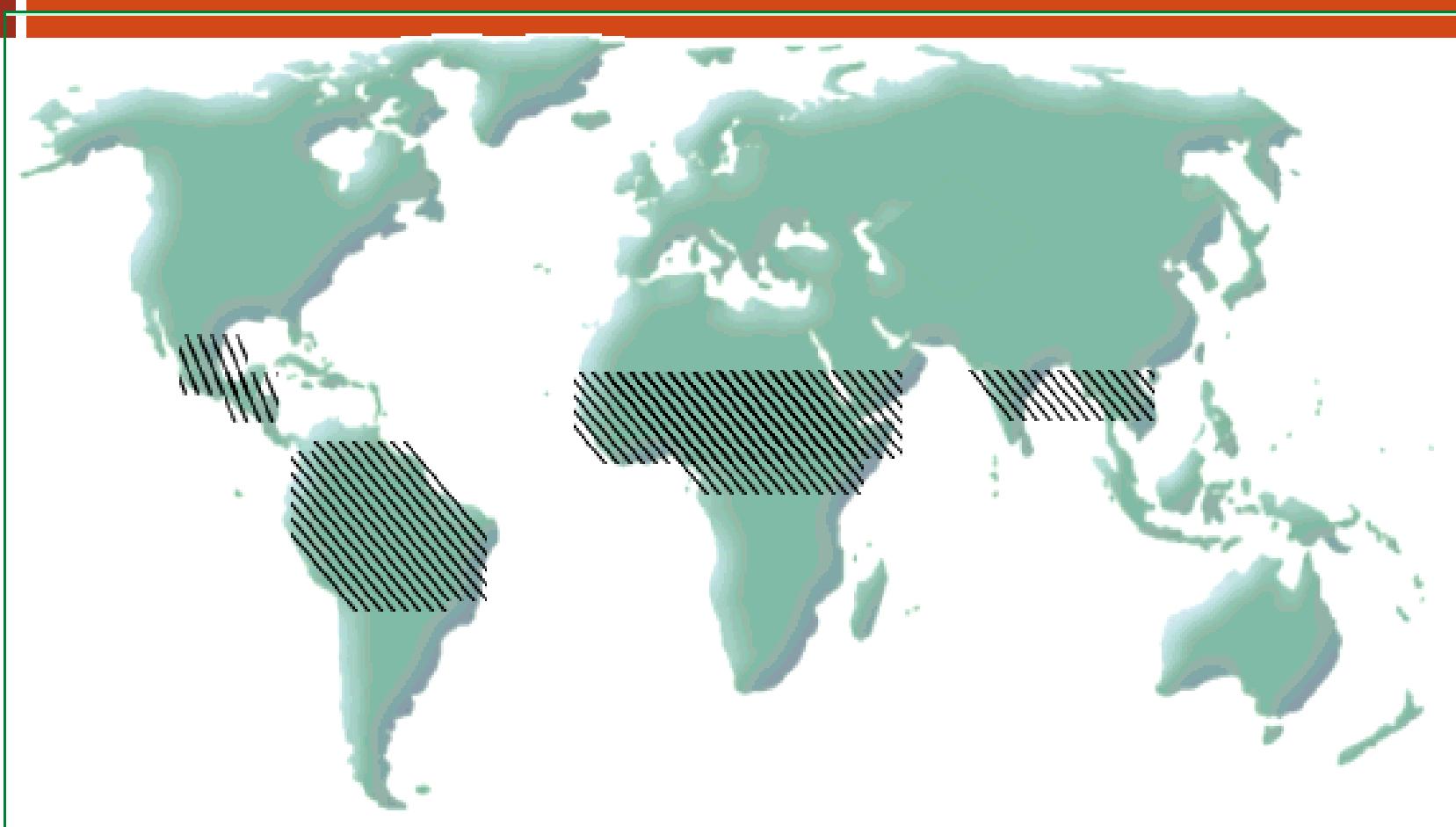
Treatment with antibacterial agents

Slow progression

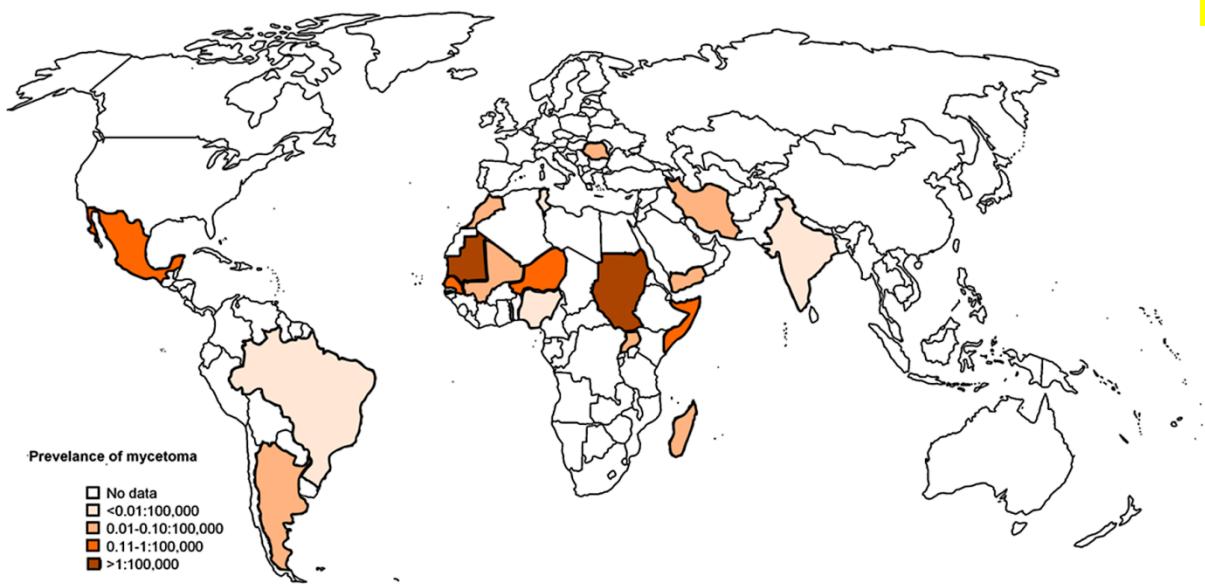
Treatment with antifungals

Mycetoma belt

Between latitude 30° North and 15° South

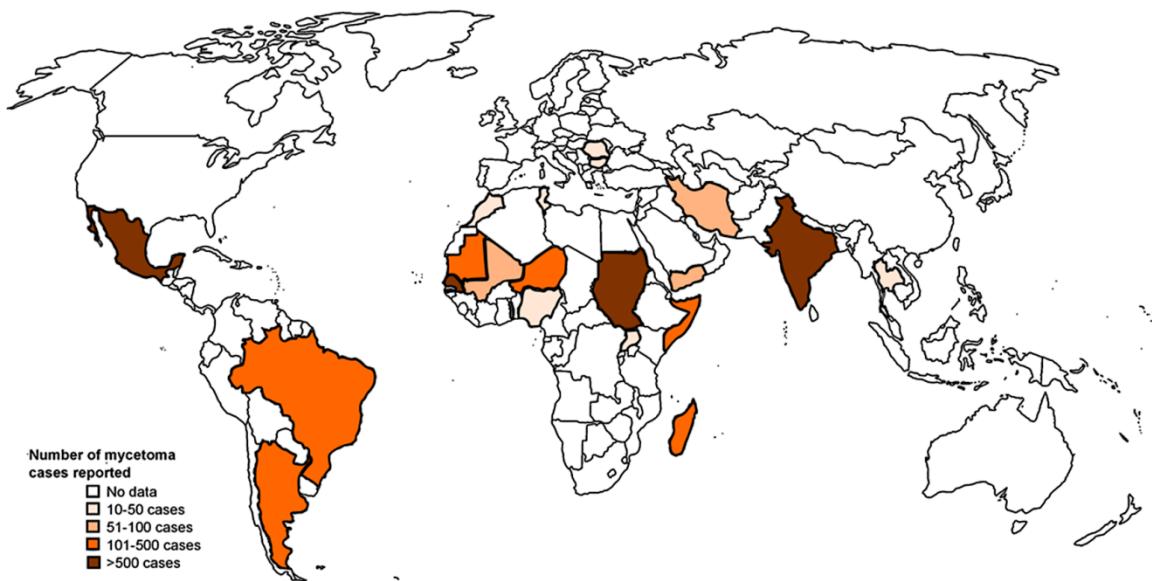


Long hot season, short heavy rainy season

A

Case series ≥ 10 patients

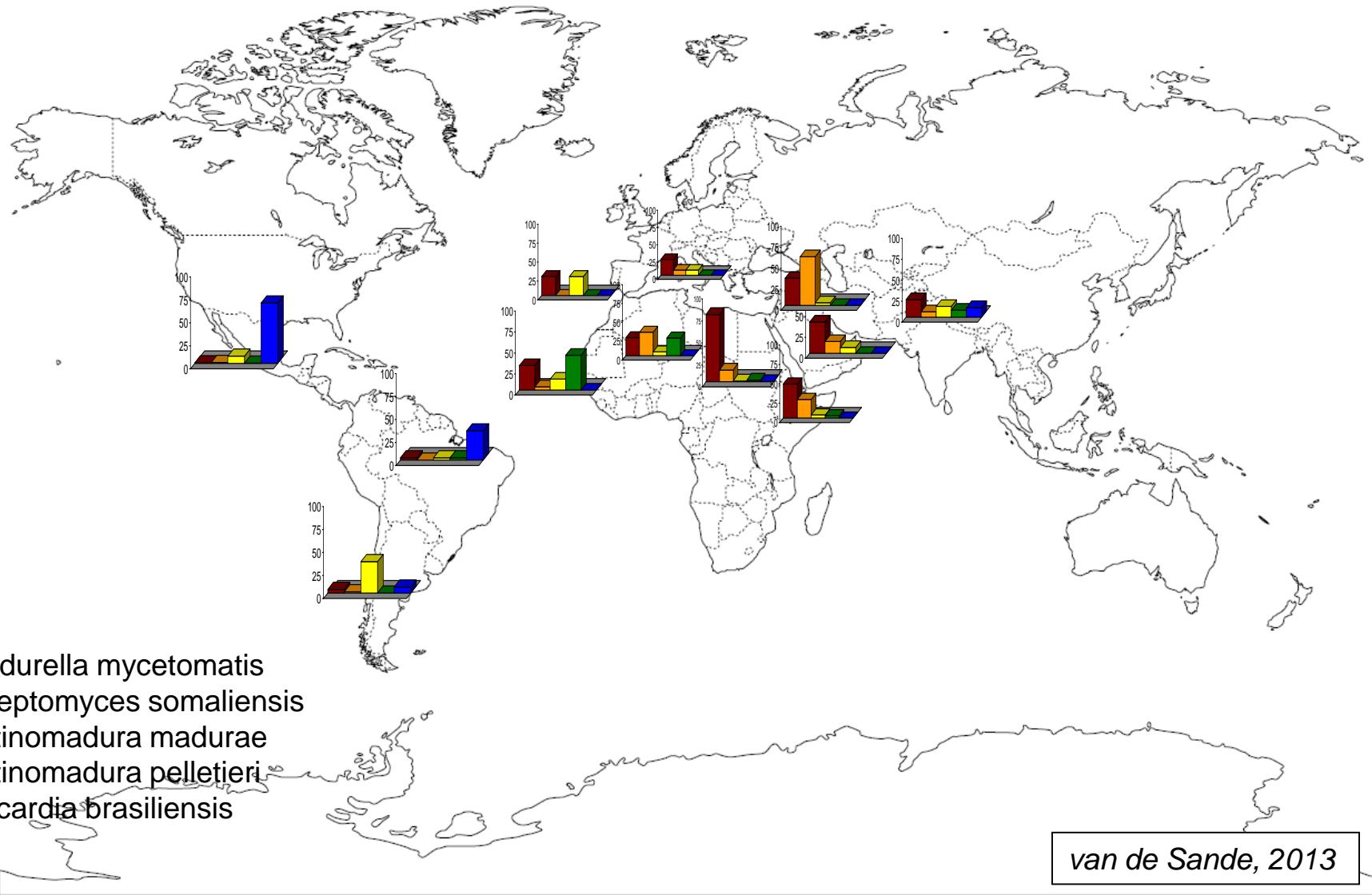
Prevalence
calculated as
cases/population

B

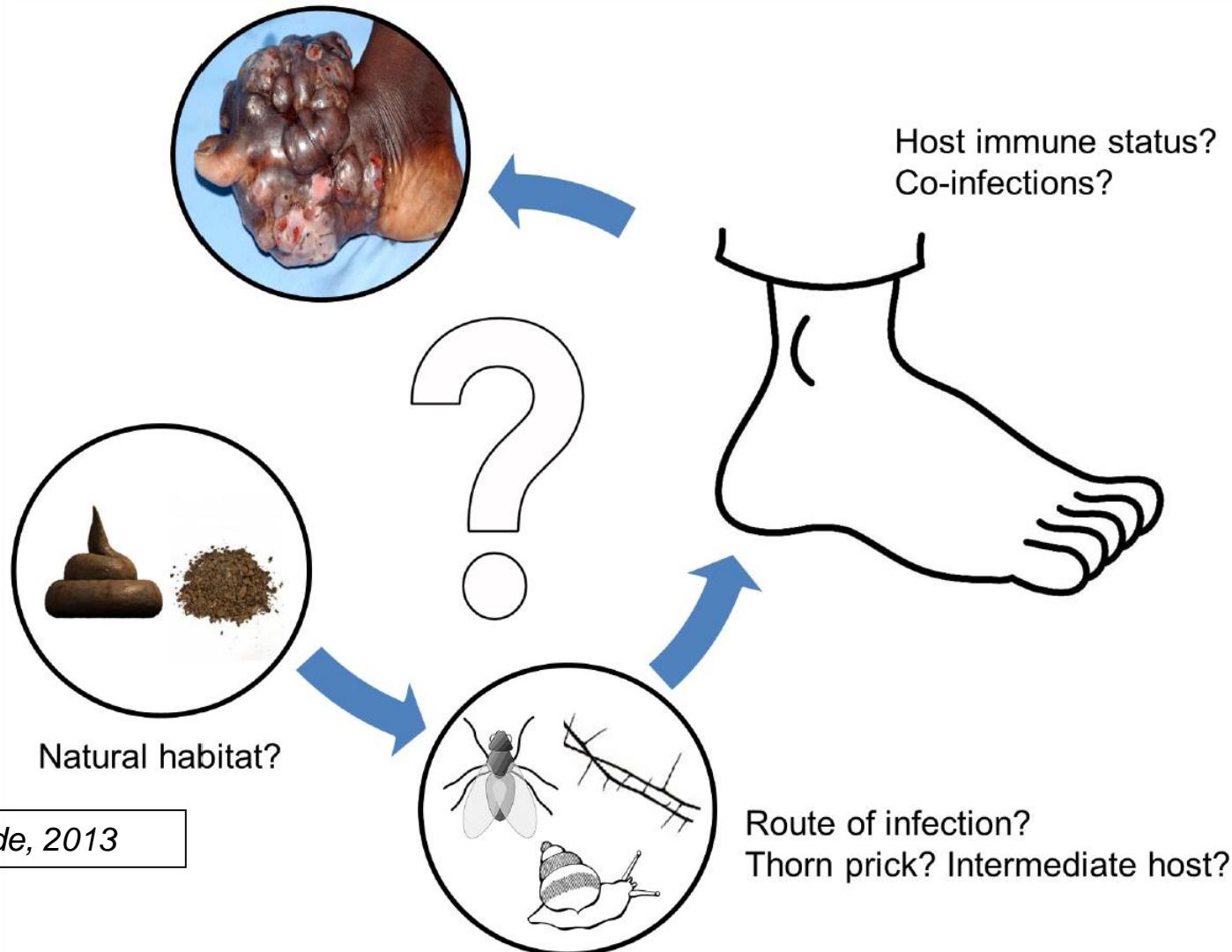
Number of cases
reported

van de Sande, 2013

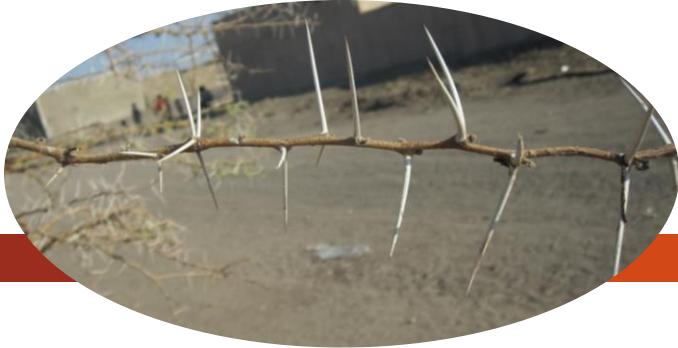
Incidence, prevalence and mapping of mycetoma



The mode of transmission



van de Sande, 2013



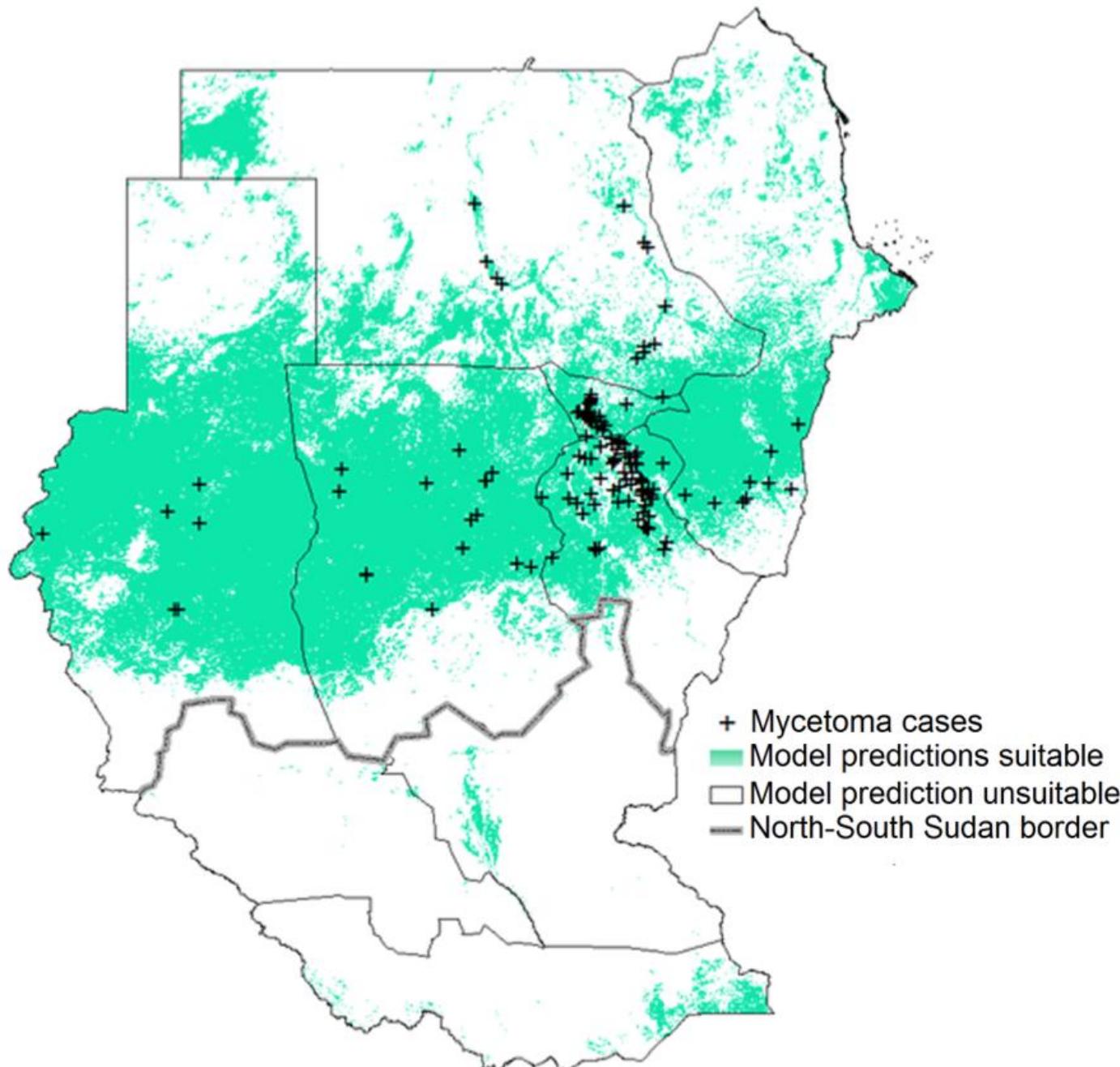
Sudan

- Transmission:
 - ▣ Thorn prick, (micro-)trauma
 - ▣ most cases on feet, but not exclusively
 - ▣ People often barefooted

- Reservoir: unknown
 - ▣ Plants, soil, animal dung, other?



Mycetoma in Sudan



Samy, 2014

Possible reservoirs

Natural infection in animals

- Cats, cows, parrots, dolphins, dogs, goats, hamsters, horses
- Pathology similar
- Organisms: same or different

Ecological study to detect habitat of *M. mycetomatis*

Soil, thorn samples from Sudan – (*M. mycetomatis* >90% of cases)

- Direct isolation by culture: – all negative
- PCR RFLP (Restriction Fragment Length Polymorphism)
 - soil: positive in 17 / 74 (23%)
 - thorn: positive in 1 / 22 (5%)
 - identical to PCR products of clinical isolates

A. Ahmed, 2002

Occupation, gender, age

- Occupation
 - ▣ Herdsman, farmers
- Age
 - ▣ Age group 20-40 years most affected
 - ▣ Children 5%
- Gender
 - ▣ Hospital-based M : F = 4 : 1
 - ▣ Field (Sudan) M : F = 1.6 : 1

Mycetoma - treatment

	Actinomycetoma	Eumycetoma
Treatment	antibiotics	antifungal + surgery
Current regimen	cycle 5 weeks amikacin (IV) + cotrim (PO) 2-3 cycles	ketoconazole, itraconazole 12 M (!), + removal of mass
Cure rate	> 90%	37%

Eumycetoma: treatment failure results in progressive amputations or spread beyond surgical intervention

Eumycetoma

M. mycetomatis: in vitro susceptibility - azoles

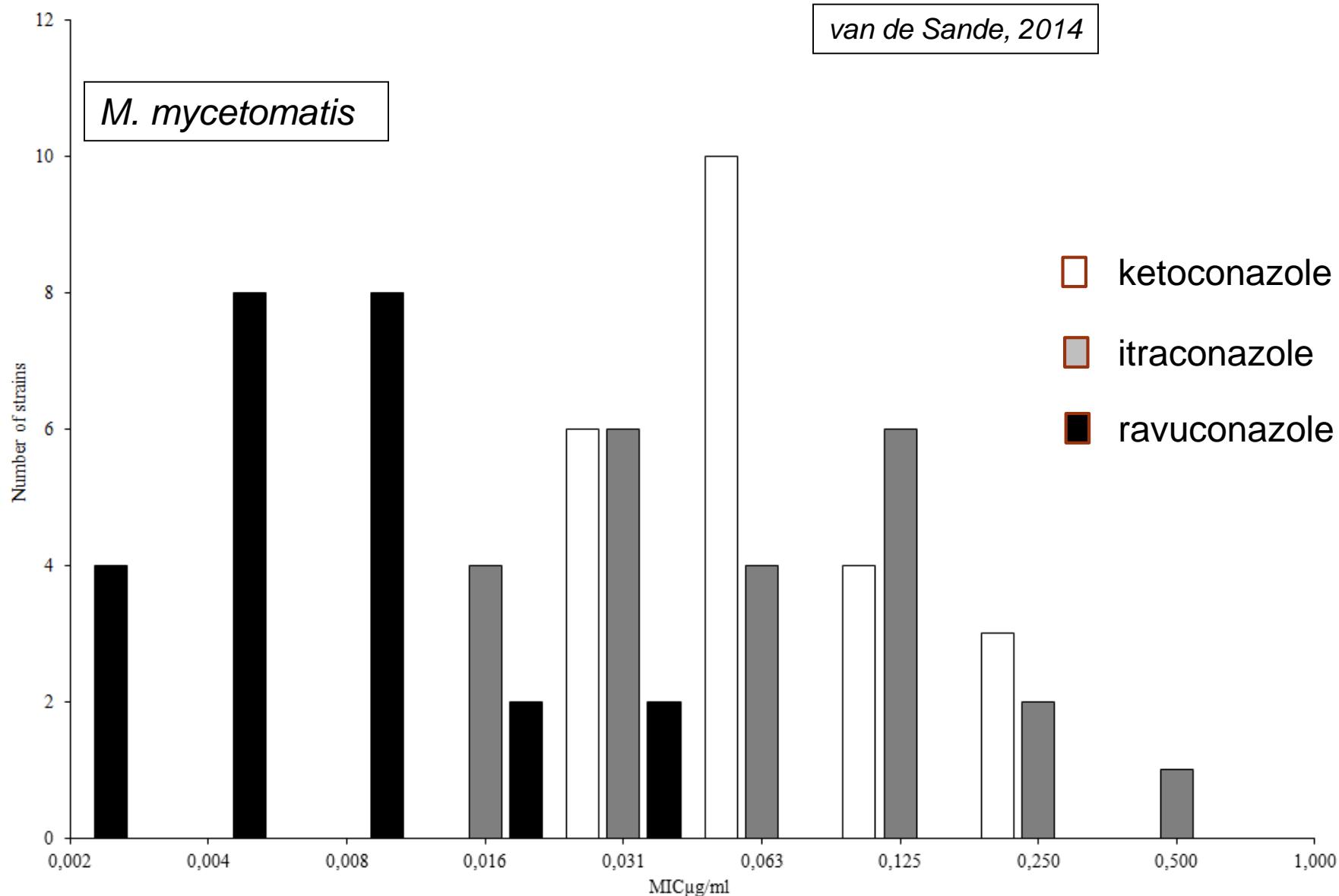
	MIC ₉₀ µg/ml	Range
□ Ketoconazole	0.125	<0.01 -1
□ Fluconazole	128	0.25 - > 128
□ Itraconazole	0.064	< 0.01-0.5
□ Voriconazole	0.125	< 0.01-1
□ Posaconazole	0.06	< 0.03 -0.125
□ Isavuconazole	0.06	< 0.01- 0.125

van de Sande, 2005
Kloezen, 2012

Eumycetoma

M. mycetomatis: *in vitro* susceptibility – other drugs

	MIC ₉₀ µg/ml	Range
Amphotericin B	2	<0.01 – 4
5-Flucytosine	>128	>128
Terbinafine	8	1- >16
Echinocandins		
▪ anidulofungin	>128	0.5 - >128
▪ caspofungin	128	8 - >128
▪ micafungin	>128	16 - >128



MICs of raruconazole
(E1224: fosraruconazole - pro-drug of raruconazole)

Conclusions – gaps in knowledge

- Global epidemiology
 - ▣ burden of disease
 - ▣ global collection of strains: typing, drug sensitivity
- Transmission
 - ▣ need for ecological study
 - ▣ shoe wearing project
- Treatment gap

Conclusions: Eumycetoma – treatment gap

- Short term: ravyconazole
- Medium term: voriconazole, isavuconazole
- Long term: pipe-line is empty!
screen existing libraries for new compounds

Thank you for your attention