WHO is afraid of fungus

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World Health Organization

Disclosures

No conflicts of interest

Outline

- WHO
  - Who is WHO?
  - Who decides what WHO should do?
  - What drives decision?
- Global agenda opportunity: antimicrobial resistance
  - The Global Action Plan on AMR
  - Fungal antimicrobial resistance: need for data
- Summary WHO current initiatives on fungal infection
- Conclusions

World Health Organization:

Who we are and What we do?

World Health Organization

Objective of WHO

The objective of the World Health Organization shall be the attainment by all people of the highest possible level of health

WHO Constitution,1948

Main Function of WHO

To act as the directing and coordinating authority on international health work

WHO Constitution,1948

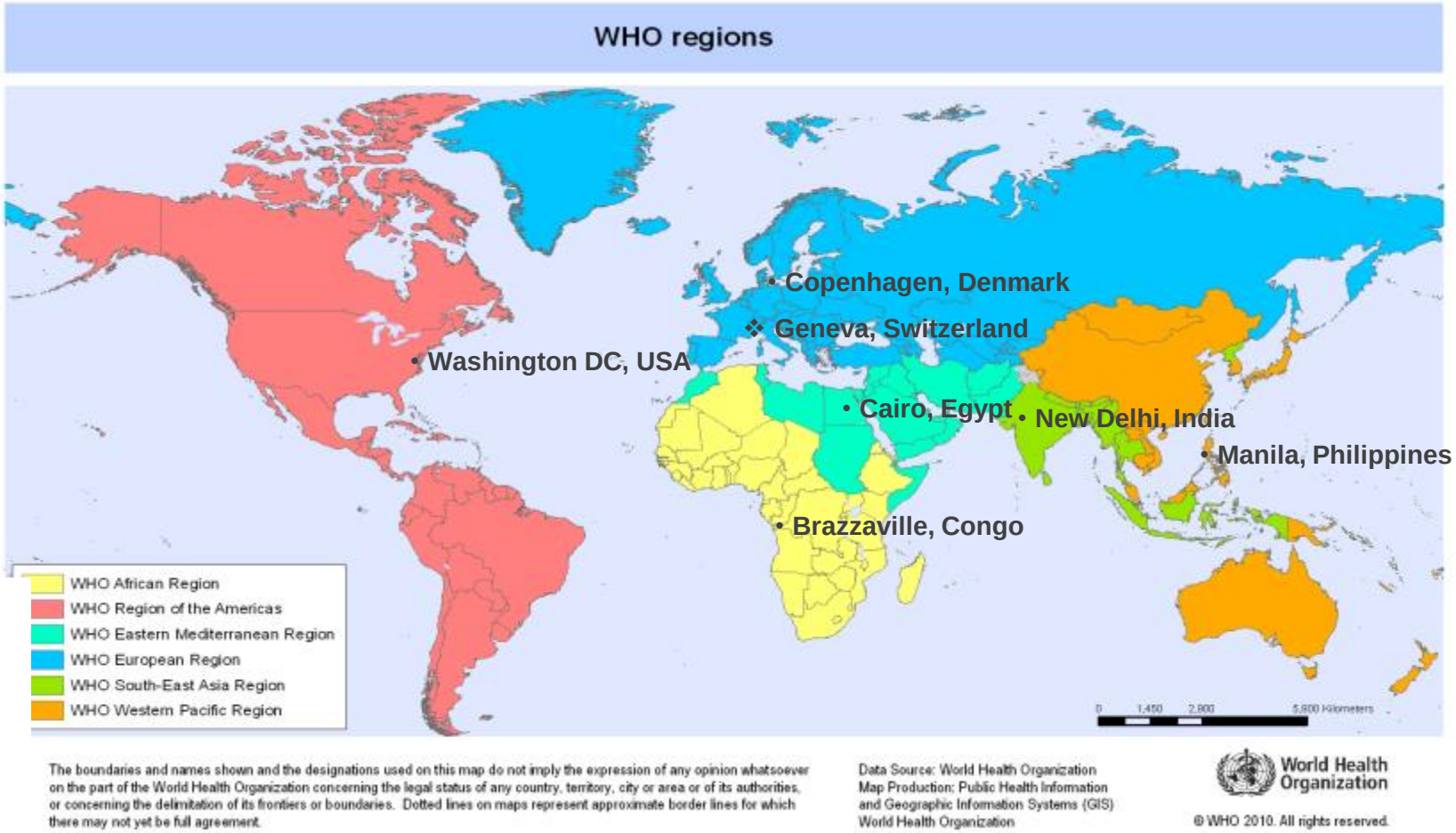
What is WHO?

- UN specialized agency for health (1948)
- 194 countries (Ministries of Health)
- Headquarters in Geneva, 6 regional offices, 151 country offices
- Secretariat is staffed by some 7500 health and other experts and support staff
- Budget: US$ 4,421.5 million (2018/19)

- Director-General: Dr Tedros Adhanom Ghebreyesus

World Health Organization

WHO Headquarters and Regions



World Health Organization

Our main goals

- Promote health development: Give priority to health outcomes in poor, disadvantaged or vulnerable groups
- WHO Global Plan of Work 2019-2023 priorities
  - achieving universal health coverage
  - addressing health emergencies
  - promoting healthier populations

World Health Organization

Our main goals

- Promote **health security:** Addressing common threats and vulnerability we are facing
  - Prevent, control and manage outbreaks, epidemics and pandemics
  - Respond to humanitarian crises (natural disasters, conflicts)

World Health Organization

Our approach – WHO core functions

- **Providing leadership** on matters critical to health and engaging in partnerships
- **Setting norms and standards** and promoting and monitoring their implementation
- Use **evidence** and **research** to frame ethical policy options for countries to improve people's health

Supporting countries

- Technical support to countries that do no have sufficient capacity of their own
- Monitor and assess global health trends hand-in-hand with national and regional agencies
- Strengthening health systems

Milestones

- 1948, Disease classification systematized
- Eradication programs: smallpox eradicated (1980), guinea worm is nearing eradication
- Ongoing: leprosy, malaria, onchocerciasis, TB, AIDS and polio
- WHO Framework Convention on Tobacco Control (2005)

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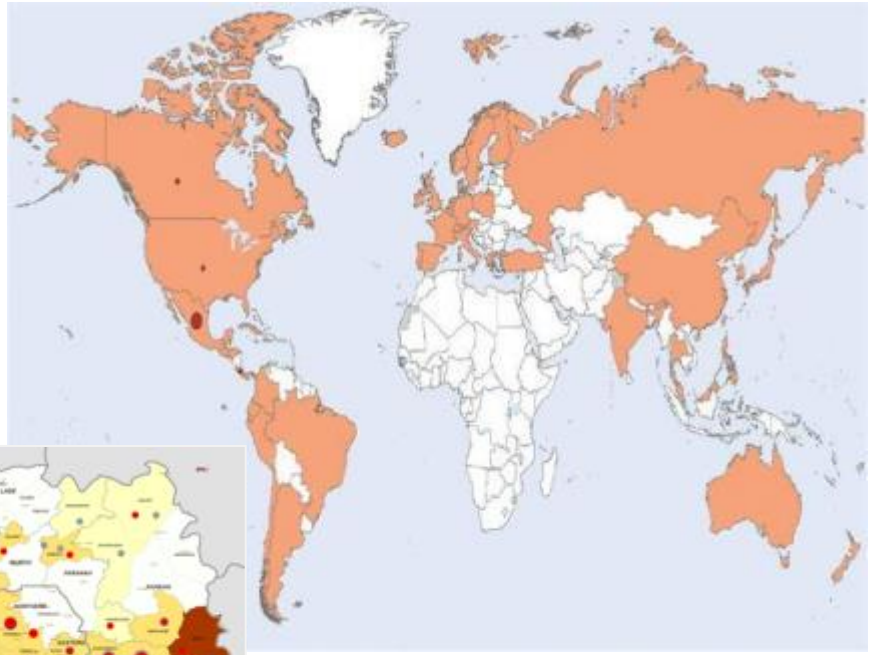
Milestones

Health humanitarian response systems

- International Health Regulations - IHR updated (2005)
- SARS (2003)
- Influenza A (H1N1): First pandemic of 21st century (2009)
- Ebola crisis in West Africa (2014)

27 May 2009 Pandemic (H1N1) 2009



Ebola crisis 2014-2015

World Health Organization

World Health Organization:

Who decides on What WHO does?

World Health Organization

Governance of WHO

World Health Assembly (WHA)

The supreme decision-making body, determines the policies of the Organization, meets once a year in Geneva: **194 Member States**

Executive Board (EB)

Main functions are to give effect to the decisions and policies of the World Health Assembly and advise the WHA. Members elected for three-year terms: **34 members**

Has WHA ever addressed fungal infection?

- ❑ Yes
- ❑ No

Has WHA ever addressed fungal infection?

- ☑ Yes
- ☐ No

WHA 1975 on mycotic diseases

WHA28.55 Mycotic diseases

The Twenty-eighth World Health Assembly,

Having examined the programme budget submitted by the Director-General for the financial years 1976 and 1977;

Noting with satisfaction the important place given in this programme budget to the control of communicable diseases in general;

Considering that superficial and deep mycotic infections are extremely widespread in both industrial and developing countries, and that they amount to an important medicosocial problem,

1. INVITES the health authorities of Member States to give mycotic infections the attention warranted by their prevalence and medicosocial importance;

2. REQUESTS the Director-General to provide assistance within the Organization's programmes to epidemiological studies on superficial and deep mycotic infections and to provide Member States with appropriate technical advice on their control; and

3. REQUESTS the Director-General to report to the Twenty-ninth World Health Assembly on the public health importance of mycotic diseases in WHO Member States.

Handb. Res., Vol. II, 1.8.3

Twelfth plenary meeting, 28 May 1975
(Committee A, first report)

World Health Assembly, 28. (1975). Mycotic diseases. World Health Organization. http://www.who.int/iris/handle/10665/92993

World Health Organization

WHA 1976 on mycotic diseases

The Twenty-ninth World Health Assembly,

Thanking the Director-General for his report on mycotic diseases submitted in pursuance of resolution WHA28.55;

Noting with appreciation the contribution of governments in reporting on mycotic diseases in their respective countries;

Realizing the important place these diseases have in human pathology, in spite of the scarcity of data regarding their prevalence and incidence;

Stressing the fact that the control of some mycotic infections is feasible with the tools now available,

1. RECOMMENDS that Member States build up specialized expertise within their health services to enable an adequate assessment to be made of the prevalence and incidence of mycotic diseases and, subsequently, of their public health importance;

2. REQUESTS the Director-General:

(1) to assist Member States in training technical personnel for the application of available diagnostic and treatment procedures;

(2) to promote the establishment of an up-to-date nomenclature of mycotic disorders;

(3) to stimulate research on mycotic infections, with particular emphasis on simple diagnostic techniques and chemotherapy.

A29/B/SR/13 – 15 May 1976

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WHA 2016: resolution on mycetoma

SIXTY-NINTH WORLD HEALTH ASSEMBLY WHA69.21

Agenda item 15.3 28 May 2016

Addressing the burden of mycetoma

The Sixty-ninth World Health Assembly,

Having considered the report on mycetoma,[1]

Deeply concerned about the impact of mycetoma, especially among children and young a
of working age, and the public health and socioeconomic burdens that the disease places on poor,
communities;

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Report of the Tenth Meeting of the WHO Strategic and Technical Advisory Group for Neglected Tropical Diseases

29–30 March 2017 WHO, Geneva

Recommendation:
Chromoblastomycosis to be added to the Neglected Tropical Diseases portfolio in category B together with mycetoma and other deep mycoses.

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Neglected tropical diseases

Neglected tropical diseases
About us
Diseases
Preventive chemotherapy and transmission control
Innovative and intensified disease management
Vector ecology and management
Neglected zoonotic diseases
Water, sanitation and hygiene

Mycetoma, chromoblastomycosis and other deep mycoses

Mycetoma

Mycetoma is a chronic, progressively destructive morbid inflammatory disease usually of the foot but any part of the body can be affected. Infection is most probably acquired by traumatic inoculation of certain fungi or bacteria into the subcutaneous tissue. Mycetoma was described in the modern literature in 1694 but was first reported in the mid-19th century in the Indian town of Madura, and hence was initially called Madura foot.

Mycetoma commonly affects young adults, particularly males aged between 20 and 40 years, mostly in developing countries. People of low socioeconomic status and manual workers such as agriculturalists, labourers and herdsmen are the worst affected.

Mycetoma has numerous adverse medical, health and socioeconomic impacts on patients, communities and health authorities.

As mycetoma is a badly neglected disease, accurate data on its incidence and prevalence are not available.

Distribution

The causative organisms of *mycetoma* are distributed worldwide but are endemic in tropical and subtropical areas in the '*Mycetoma* belt', which includes the Bolivarian Republic of Venezuela, Chad, Ethiopia, India, Mauritania, Mexico, Senegal, Somalia, Sudan and Yemen.

Transmission

Transmission occurs when the causative organism enters the body through minor trauma or a penetrating injury, commonly thorn pricks. There is a clear relationship between mycetoma and individuals who walk barefooted and are manual workers. The disease is common among barefoot populations who live in rural areas in endemic regions but no person is exempted.

Clinical picture

1. Mycetoma
2. Chromoblastomycosis

Related links

- Fact sheet on mycetoma

World Health Assembly (WHA) Resolutions on Mycetoma

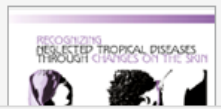
- Addressing the burden of mycetoma, 2016 [pdf 139kb]
- Réduction de la charge du mycétome [pdf 79kb]
- Reducción de la carga de micetoma [pdf 141kb]

Clinical cases

View pictures of clinical cases

- Massive foot mycetoma
  High Resolution picture
- Massive thigh mycetoma with native treatment complication
  High Resolution picture

Related publication



World Health Organization:

What drives decision?

World Health Organization

What drives Member States decisions?

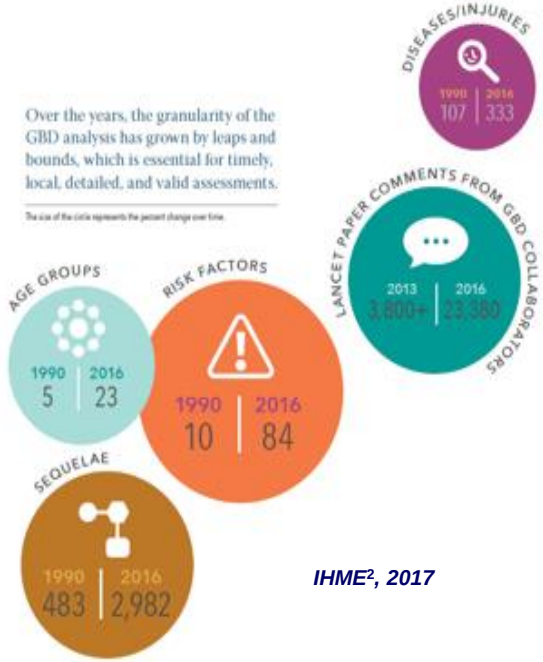
- Burden of disease
- Perception of threat to health security
- Global agendas for development of mankind

Information on burden of disease

- What metrics?
- How does fungal infection burden compare to other health issues?

Global Burden of Disease (GBD)

The WHO Global Burden of Disease (GBD) project provides a framework for integrating, validating, analysing and disseminating information to assess the comparative importance of diseases, injuries and risk factors in causing premature death, loss of health and disability in different populations.



IHME[2], 2017

GBD has introduced a new metric – disability-adjusted life-years (DALY) – as a single measure to quantify the burden of diseases (BOD).

http://www.who.int/healthinfo/global_burden_disease/about/en/

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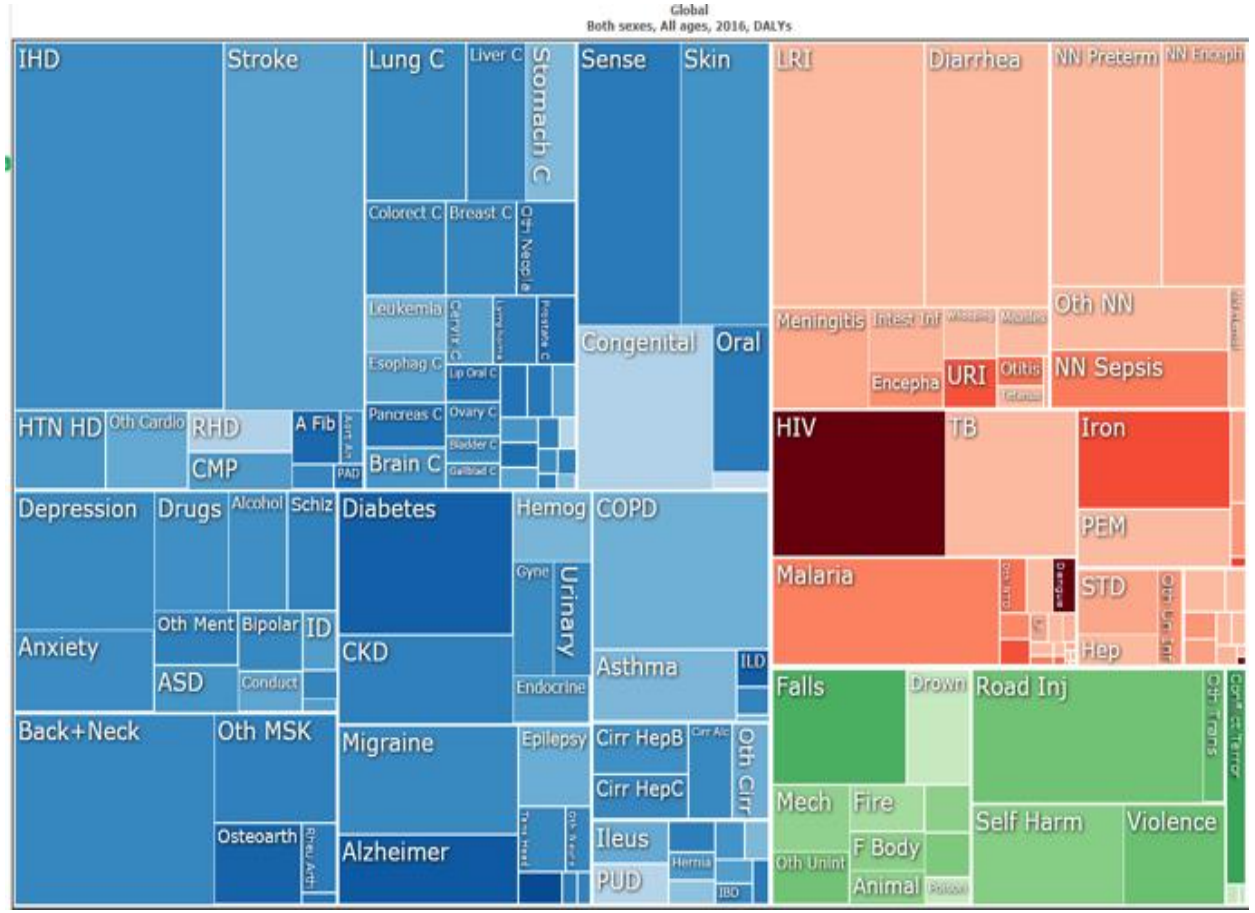
GBD tools: examples



Countries can combine the evidence expressed by DALYs, along with information about policies and costs to decide & set the health agenda.

Institute for Health Metrics and Evaluation: http://www.healthdata.org/data-visualization/gbd-compare
IHME , 2018

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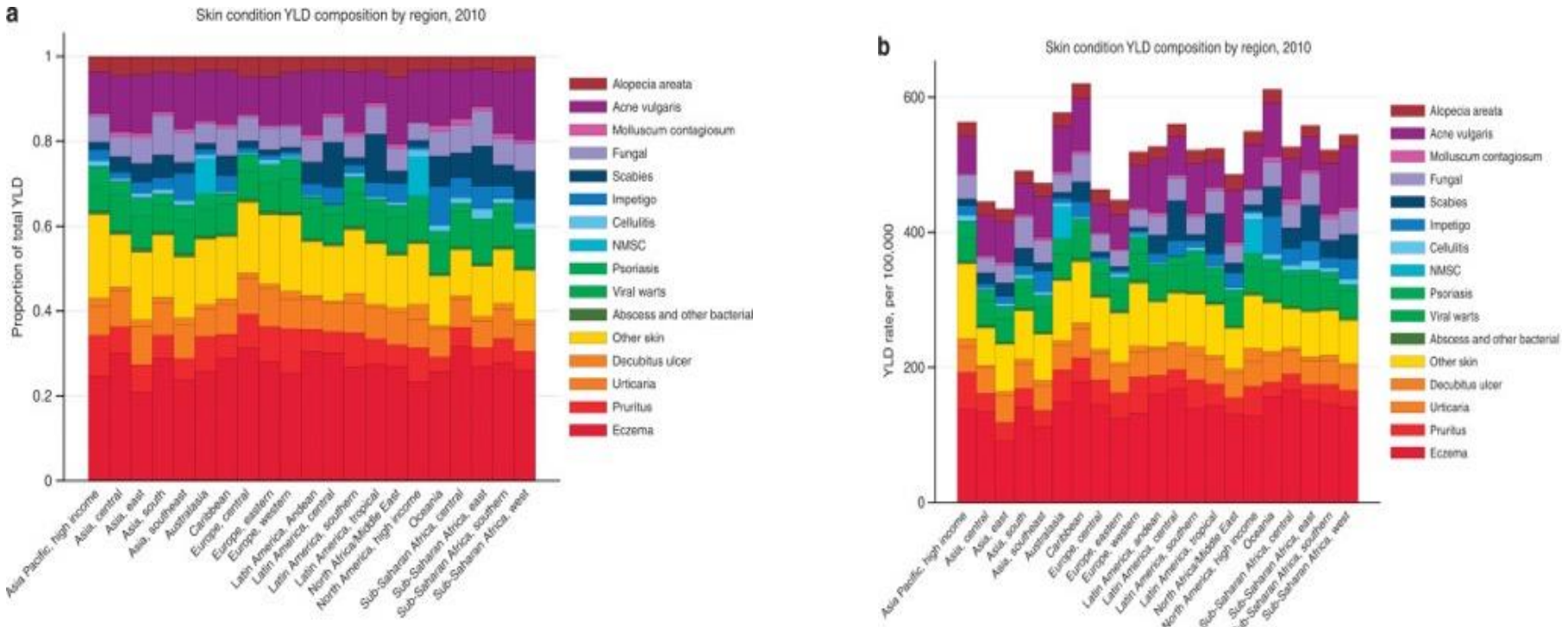
Example: burden of fungal skin conditions

Skin condition years lost due to disability (YLD) composition by region, 2010. (a) Proportion of total YLD, (b) YLD rate per 100,000. NMSC, non-melanoma skin cancer.



- **In the Global Burden of Disease project 2010 update fungal skin diseases were the fourth most common health problem affecting 985 million people after dental caries, tension-type headache and migraine.**

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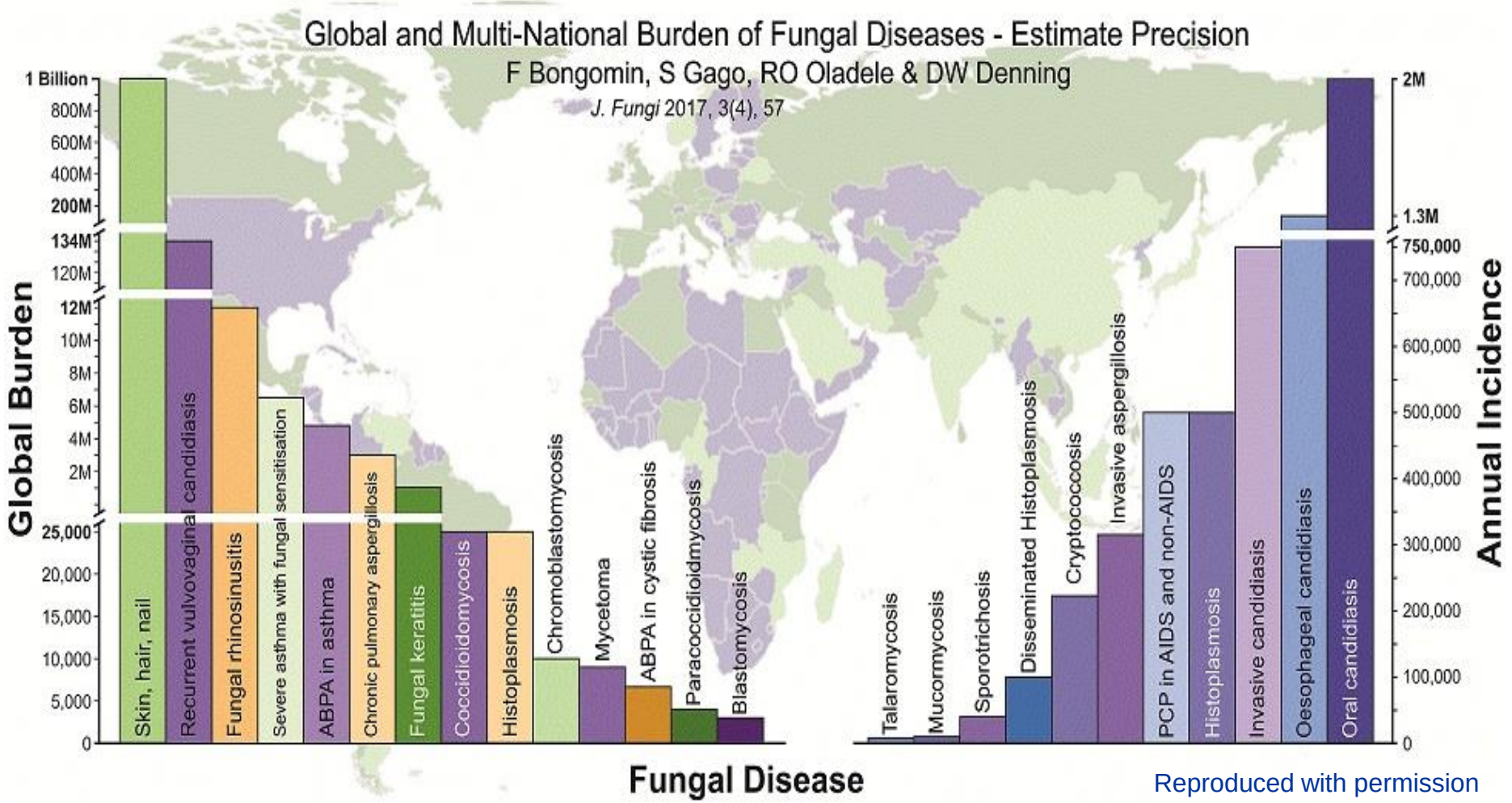
Global estimates of fungal diseases burden



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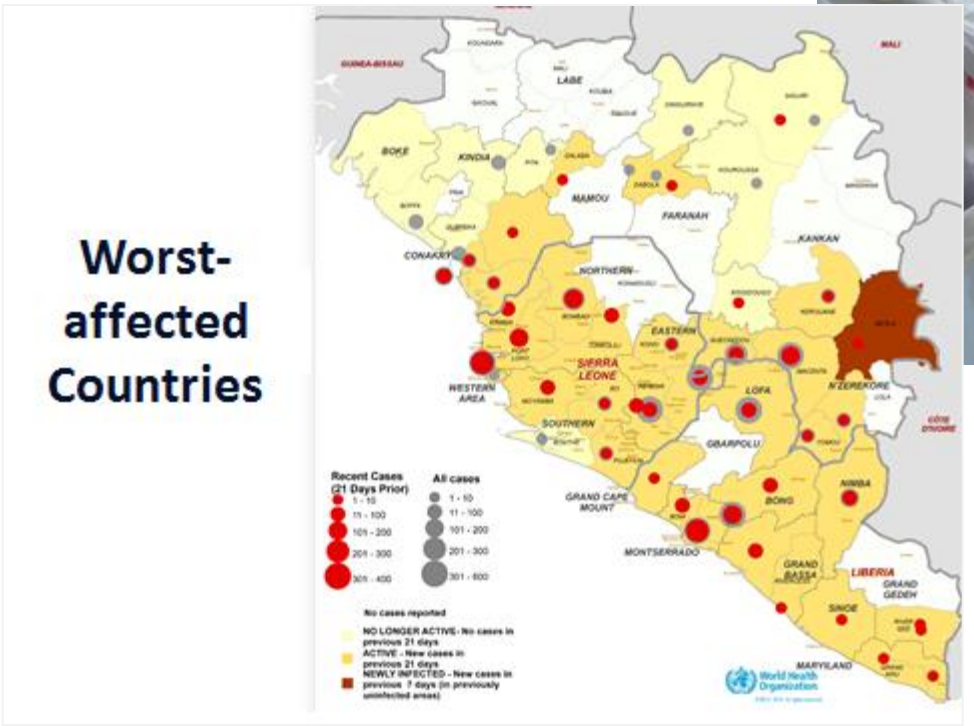
What drives Member States decisions?

- Burden of disease
- Perception of threat to health security
- Global agendas for development of mankind

Perception of threat

- SARS, influenza, Ebola…
- …next emerging pathogen.



2014-2015 Ebola crisis in west Africa

World Health Organization

Perception of threat about fungus?

The Unexpected and Troubling Rise of *Candida auris*

Tom Chiller, MD

DISCLOSURES | August 24, 2017

EDITORIAL COLLABORATION Medscape & CDC

Schelenz et al. Antimicrobial Resistance and Infection Control (2016) 5:35
DOI 10.1186/s13756-016-0132-5

RESEARCH

First hospital outbreak of t emerging *Candida auris* in hospital

Silke Schelenz[1,3*], Ferry Hagen[2], Johanna L. Rhodes[3], Alire Lisa Ryan[1], Joanne Shackleton[1], Richard Trimlett[5], Jacques F and Matthew C. Fisher[3]

Abstract

Background: *Candida auris* is a globally emerging multidrug r We report an ongoing outbreak of *C. auris* in a London cardio-t the first report of *C. auris* in Europe and the largest outbreak so implementation of control measures.

Methods: Data on *C. auris* case demographics, environmental s measures, and antifungal susceptibility of patient isolates were Speciation of *C. auris* was performed by MALDI-TOF and typing length polymorphism (AFLP).

Results: This report describes an ongoing outbreak of 50 *C. aur* within a single Hospital Trust in London. A total of 44 % ($n = 22$ infection with a candidaemia rate of 18 % ($n = 9/50$). Environme around bed space areas. Implementation of strict infectior of cases and their contacts, wearing of personal protective patients on affected wards, skin decontamination with chl based reagents and hydrogen peroxide vapour. Genotypir the same geographic region clustered.

Conclusion: This ongoing outbreak with genotypically closel appropriate species identification and rapid detection of cases

Keywords: *Candida auris*, Outbreak, Healthcare-associated infe

Antimicrobial Resistance

ecdc

RAPID RISK ASSESSMENT

Candida auris in healthcare settings – Europe

First update, 23 April 2018

Main conclusions and options for response

Candida auris poses a risk for patients in healthcare facilities across Europe due to its propensity to cause outbreaks and its antifungal resistance. Difficulties with laboratory identification and lack of awareness of this *Candida* species may delay early detection increasing the potential for horizontal transmission. *C. auris* was first identified in 2009 and within a few years has emerged as a cause of healthcare-associated infections. Outbreaks have been reported in countries in five continents. The number of reported *C. auris* cases in European countries has increased significantly since the last ECDC rapid risk assessment on *C. auris* in December 2016. There continues to be a need to raise awareness of *C. auris* in European healthcare facilities, so that they may adapt their laboratory testing strategies and implement enhanced infection prevention and control measures where necessary.

Options to reduce identified risks: prevention of transmission of *C. auris* in healthcare settings

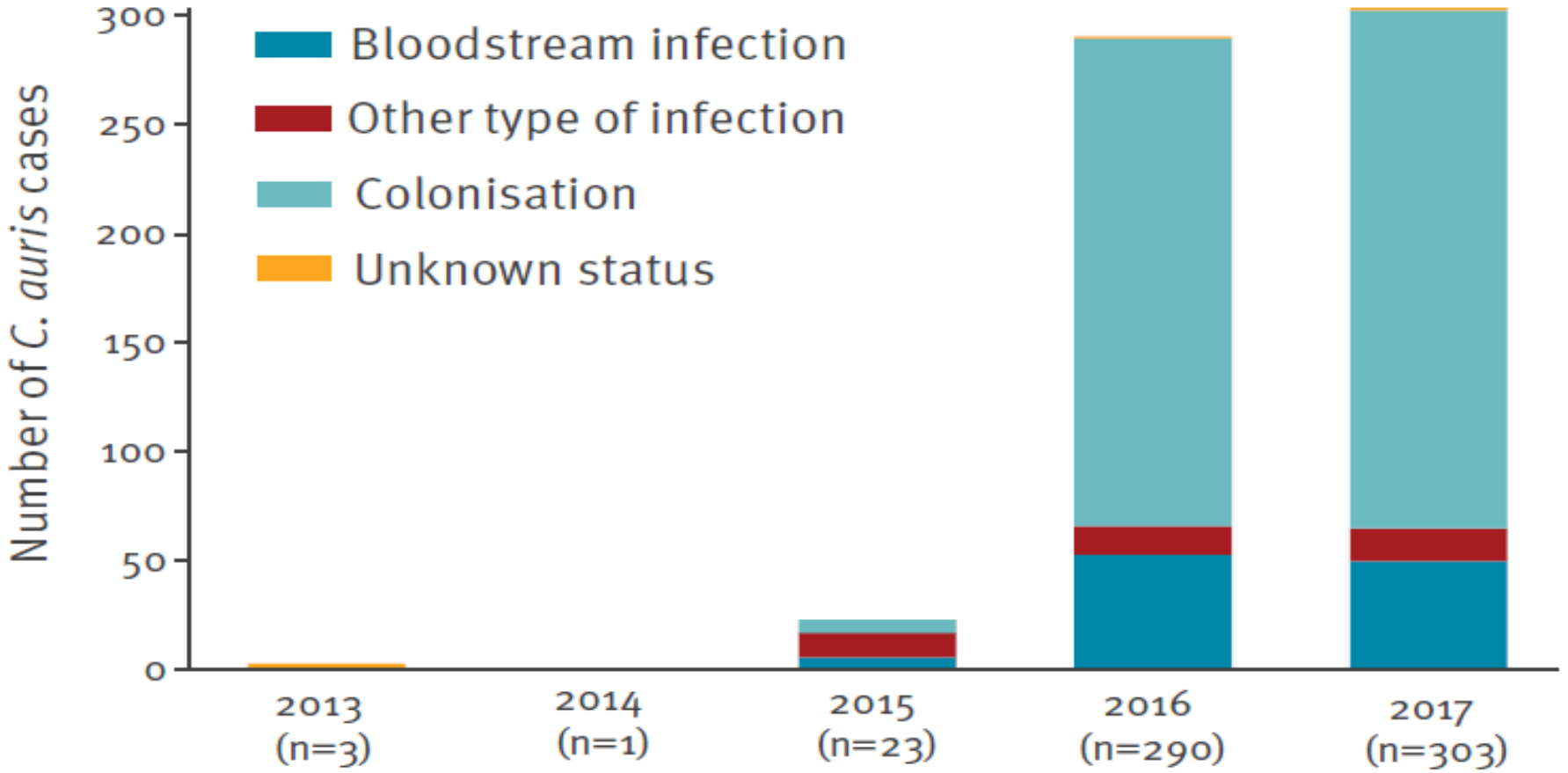
Laboratory detection of *C. auris*

Recognition of *C. auris* requires that isolates of *Candida* species from invasive infections are accurately identified to the species level. A correct identification of *C. auris* is possible using either Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry, provided that *C. auris* is included in the reference profile database, or DNA sequencing of specific domains of the ribosomal genes. When these tests are not available at clinical laboratory level, referral of non-*albicans Candida* spp. invasive isolates to a reference mycology laboratory is advisable, especially if identified by biochemical tests as *Candida haemulonii*, *Candida famata*, *Candida sake*, *Rhodotorula* species or *Saccharomyces* species. This is particularly important for hospitals with an increased incidence of infection by non-*albicans Candida* species or those that admit patients transferred from a facility reporting a *C. auris* outbreak. Where *Candida* species isolates are tested for antifungal susceptibility, resistance to fluconazole is another characteristic that should prompt tests to speciate the *Candida* isolate.

Standard infection control measures

Good standard infection control, including environmental cleaning, adequate cleaning and reprocessing of medical devices, and adequate capacity of microbiological laboratories, as well as sufficient capacity of

Reported *Candida auris* cases, EU/EEA countries, 2013-2017 (n=620*)



*** One additional case detected in Austria in January 2018 is not included in the figure.**

Source: Kohlenberg A, et al. Eurosurveillance 2018 Mar;23(13):pii=18-00136.

Slide credits: ECDC

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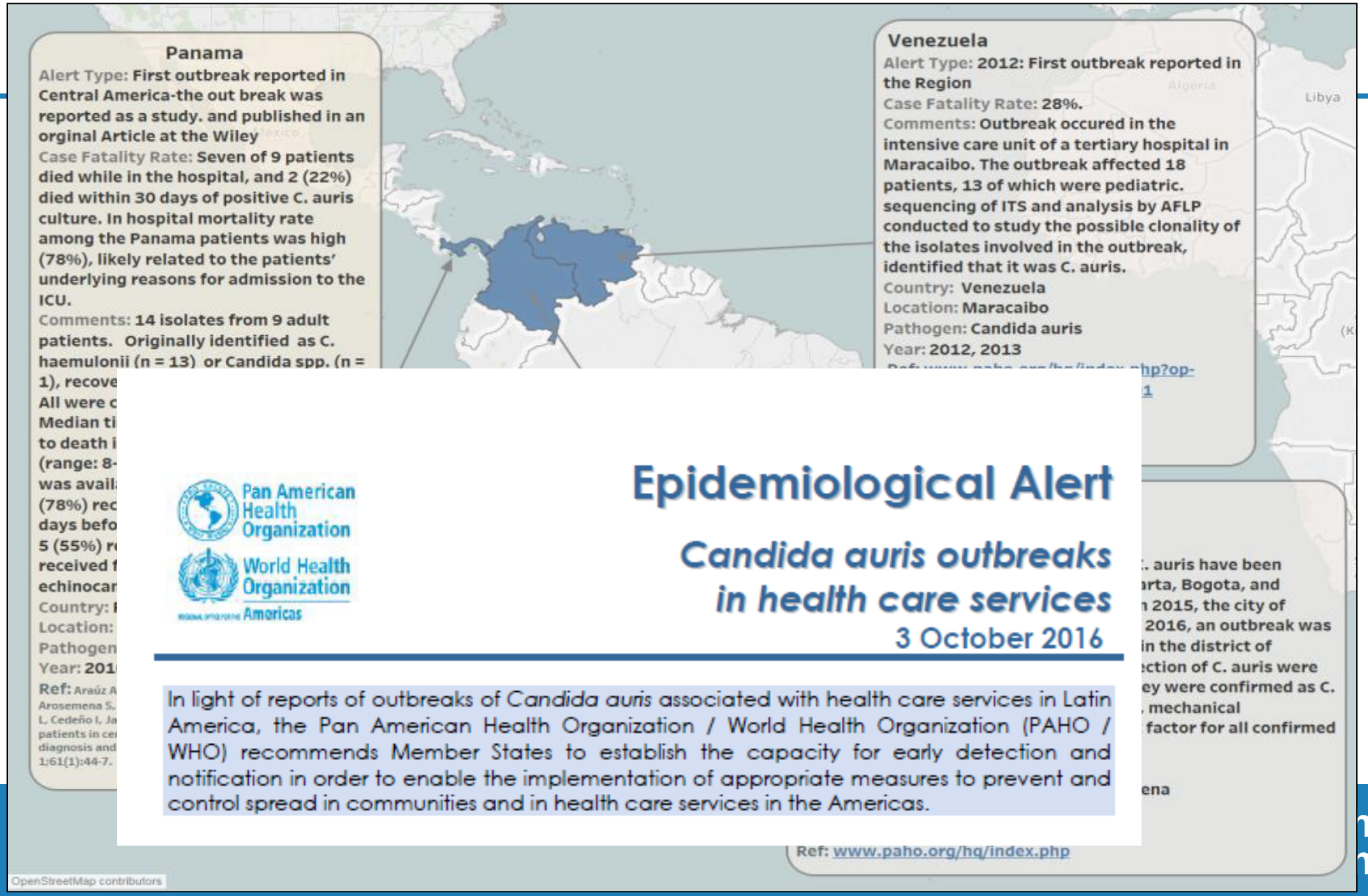
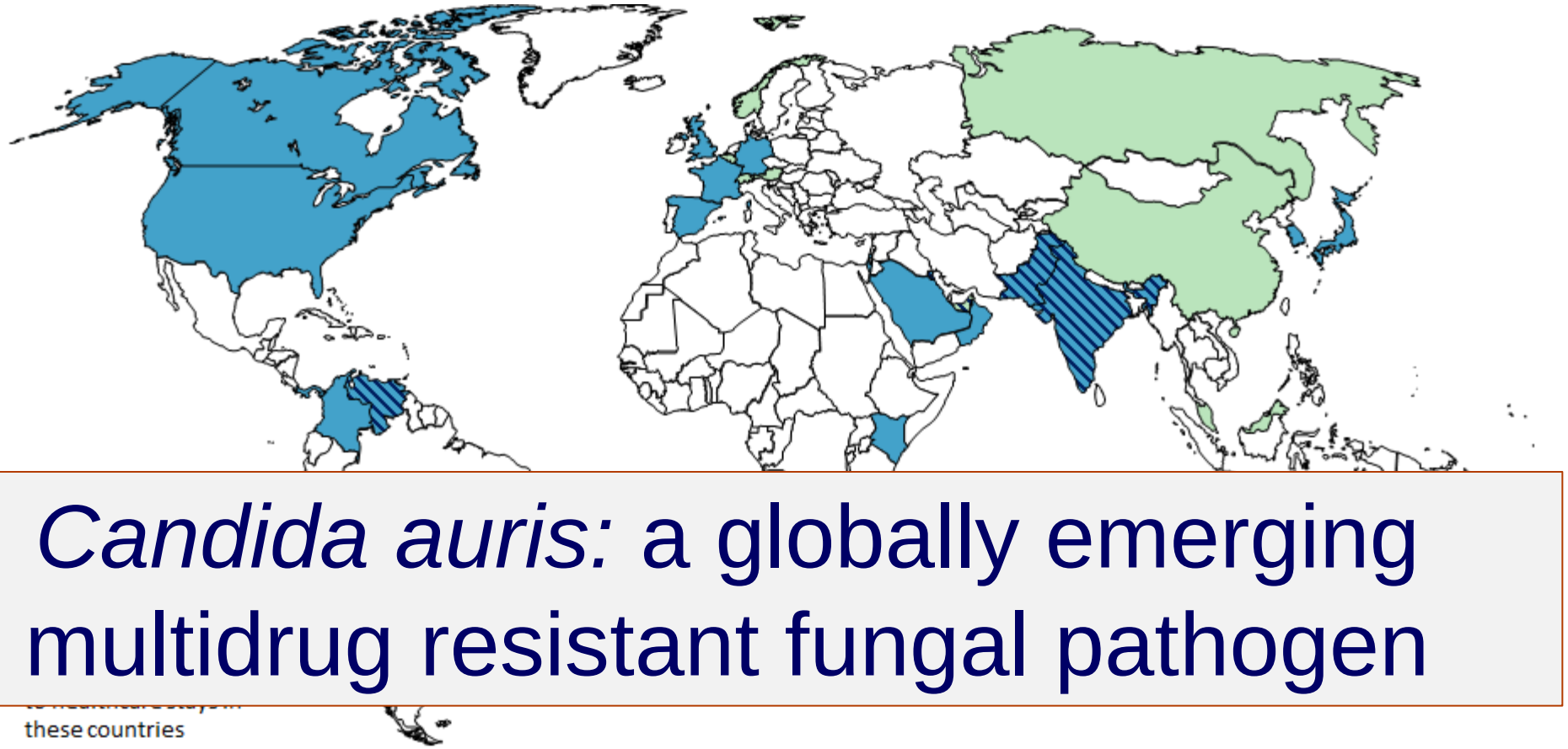
Health Emergency Alerts Involving AMR Mycoses



Countries from which *Candida auris* cases have been reported, as of June 15, 2018



Candida auris: a globally emerging multidrug resistant fungal pathogen

Source: CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™ At https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html

World Health Organization

What drives Member States decisions?

- Burden of disease
- Perception of threat to health security
- Global agendas for development of mankind

SUSTAINABLE DEVELOPMENT GOALS

17 GOALS TO TRANSFORM OUR WORLD

UN agenda for 2030: 17 sustainable development goals

Antimicrobial resistance (AMR) threats 7 out of 17 goals!

World Health Organization

Global agenda opportunity: antimicrobial resistance

- The Global Action Plan on Antimicrobial Resistance (AMR)
- Fungal antimicrobial resistance: need for data

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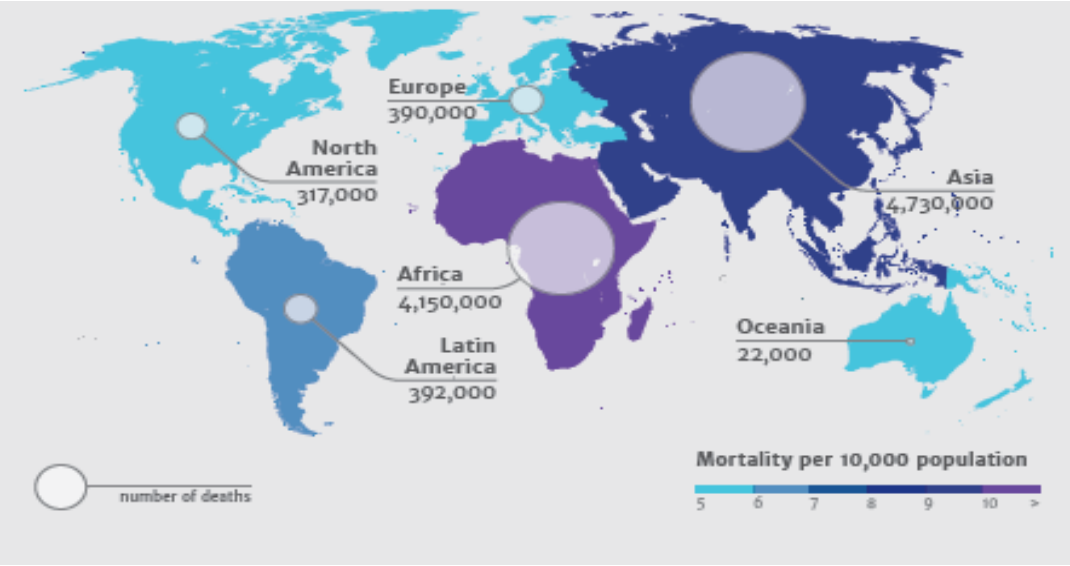
AMR Growing Awareness & Political Commitment

Mortality & Economic impact

- By 2050, lead to 10 million deaths/year
- Reduction of 2 to 3.5 percent in GDP
- Costing the world up to $100 trillion

Deaths attributable to AMR every year by 2050



J. O'Neil, 2014. Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations.

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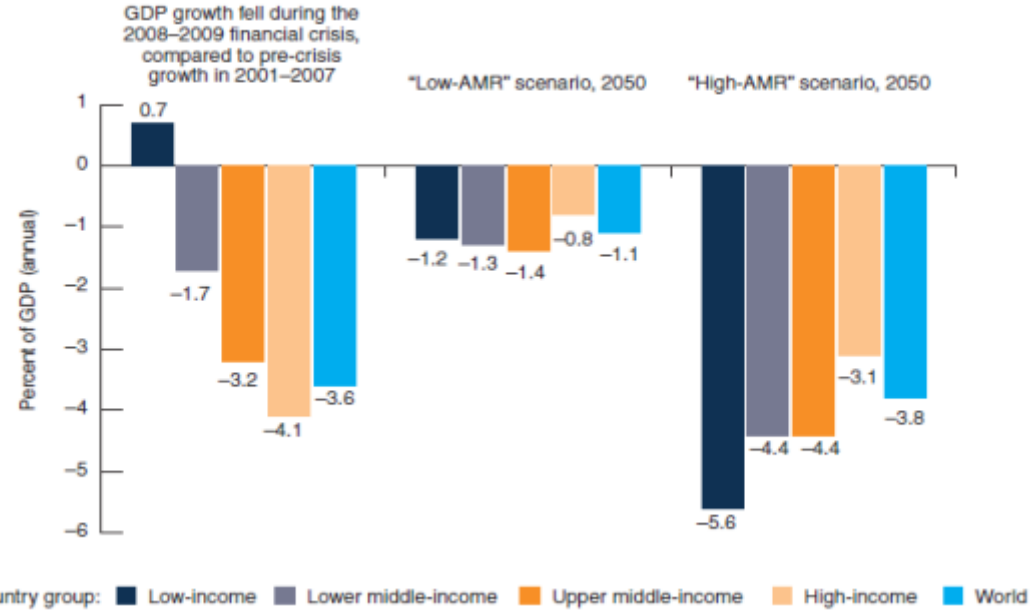
Economic Impact

- Economic Costs of AMR May Be as Severe as During the Financial Crisis
- AMR could reduce GDP substantially, but unlike in the recent financial crisis, the damage could last longer and affect low-income countries the most.



Source: World Bank, March 2017. Drug-Resistant Infections: A threat to our economic future

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AMR is now considered a major threat to modern medicine & global economy

- Profound worldwide adverse health consequences
- Long-term threat with no end in sight unless fundamental changes are made
- Economic implications
- A true **intersectoral** issue

AMR: Need for a One Health strategy

Clinical Infectious Diseases

BRIEF REPORT

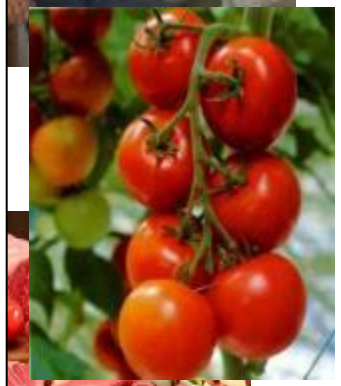
Intercountry Transfer of Triazole-Resistant *Aspergillus fumigatus* on Plant Bulbs

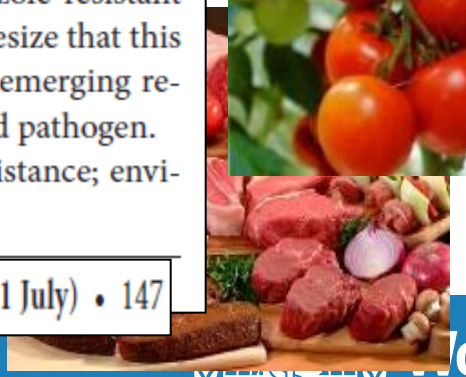
Katie Dunne,[1] Ferry Hagen,[2,3] Niamh Pomeroy,[1] Jacques F. Meis,[2,3] and Thomas R. Rogers[1]

[1]Department of Clinical Microbiology, Trinity College Dublin, Ireland; [2]Department of Medical Microbiology and Infectious Diseases, Canisius Wilhelmina Hospital, and [3]Centre of Expertise in Mycology, Radboud University Medical Center/Canisius Wilhelmina Hospital, Nijmegen, The Netherlands

We investigated whether plants imported to Ireland from the Netherlands might harbor triazole-resistant *Aspergillus fumigatus*. Samples of plant bulbs were positive for triazole-resistant *A. fumigatus* with *CYP51A* mutations. We hypothesize that this represents a route for intercountry transfer of an emerging resistance mechanism in a major opportunistic mold pathogen.

Keywords. *Aspergillus fumigatus*; triazole resistance; environment; intercountry transfer.





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AMR Global Action Plan

- Adopted by World Health Assembly in May 2015
- Endorsed by the UN General Assembly in September 2016
- One Health approach => close collaboration with FAO and OIE
- Blueprint developed by the international community
  - Countries
  - International organizations, civil society and others
- Stepwise approach to implementation of actions
- Provides framework actions
  - By WHO
  - By Member States
  - By international partners

http://www.who.int/antimicrobial-resistance/global-action-plan/en/

World Health Organization

AMR Global Action Plan 5 strategic objectives

1. Improve awareness and understanding
2. Strengthen knowledge through surveillance & research
3. Reduce incidence of infection
4. Optimize use of antimicrobial medicines
5. Ensure sustainable investment for R&D and implementation of control measures

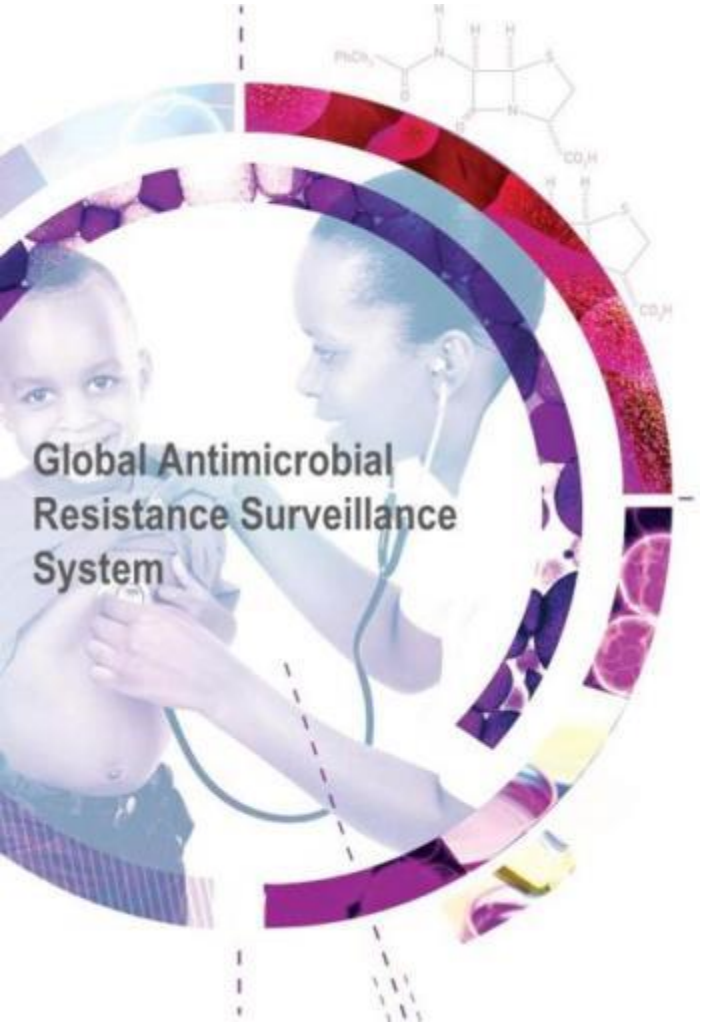
All countries to build & implement national action plans!

WHO current initiative to address AMR in invasive fungal infection

- Surveillance of AMR in invasive *Candida* infection
- Platform: Global AMR Surveillance System (GLASS)

World Health Organization

WHO Global AMR Surveillance System – GLASS

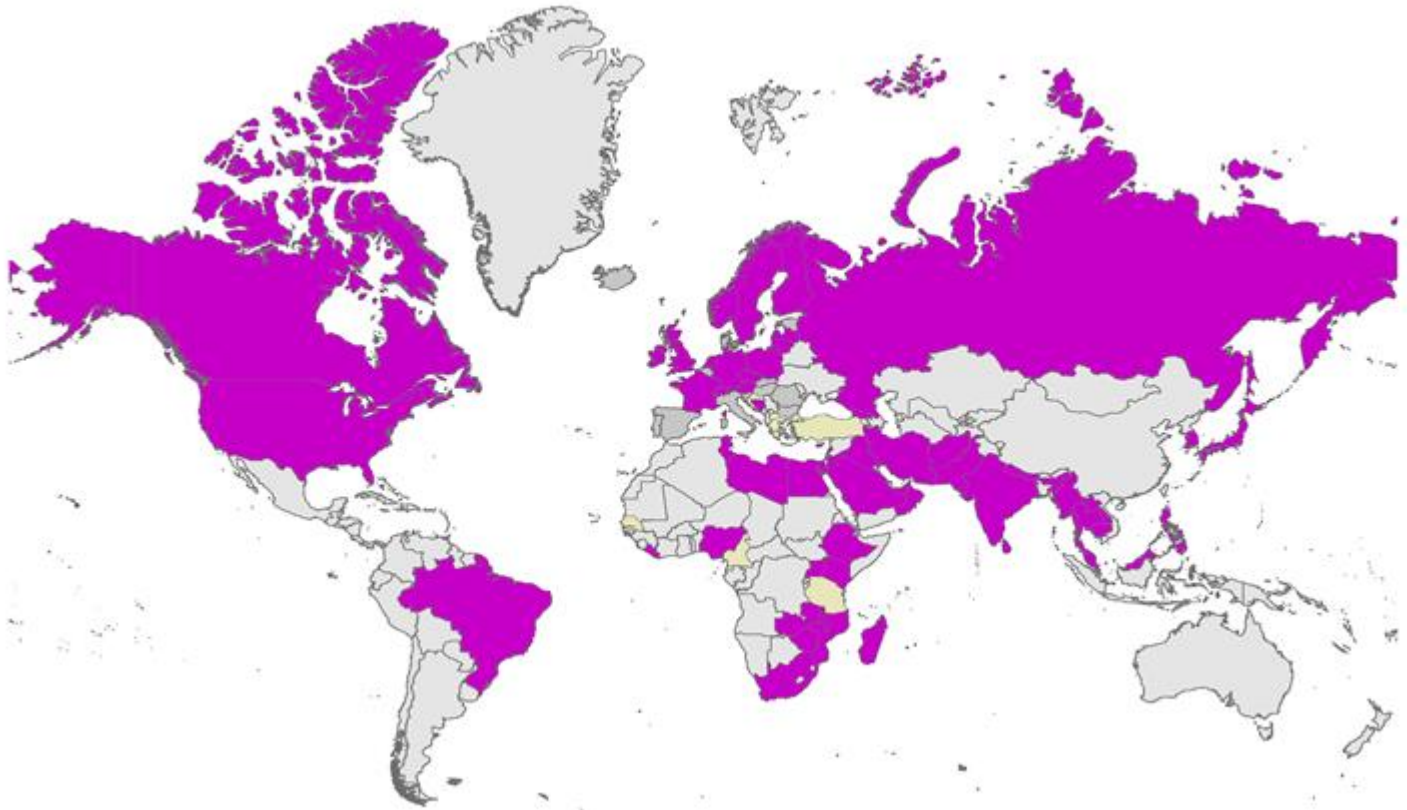


- To support AMR Global Action Plan.
- To foster national AMR surveillance systems through harmonized global standards.
- Initial focus on human bacterial pathogens
- March 2016: country enrolment started

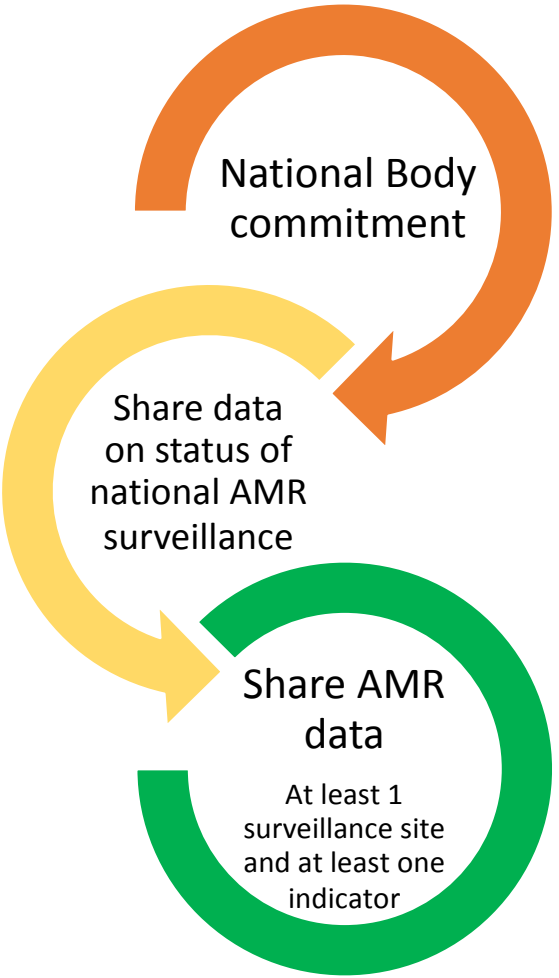
World Health Organization

Countries enrolled in GLASS

*As of 28 June 2018**



Enrolment completed (n=62) Enrolment in progress (n=7)



*** Call for country enrolment issued on 21 March 2016**

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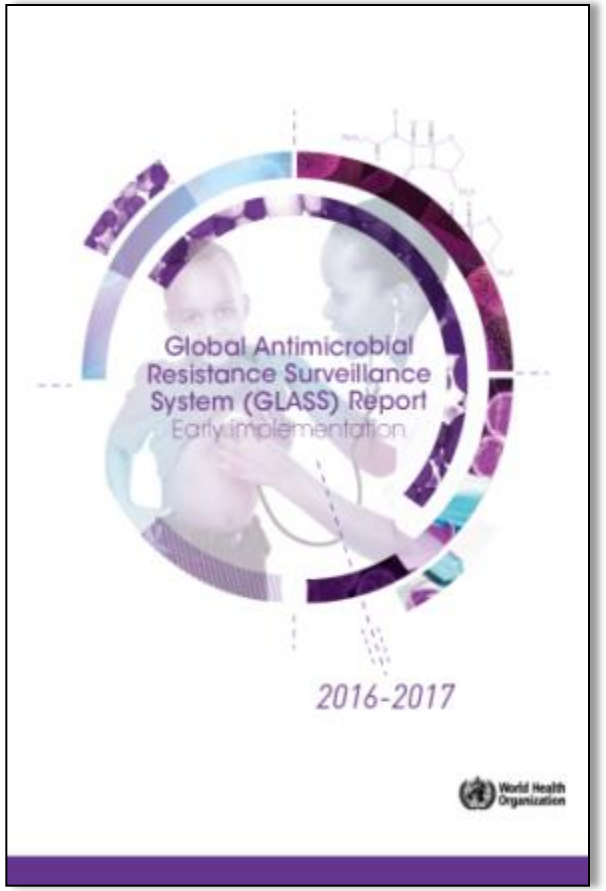
First GLASS report: 2016 data
Published in January 2018



AMR data reported by 22 countries

Reported to GLASS

Number of sites	
Hospitals	466
Outpatients clinics	139
Other institutions	124
Total	**729**

Number of patients with suspected infection	
Blood stream	81,920
Urinary tract	415,679
Gastro-intestinal	7,477
Sexually transmitted	2,847
Total	**507,923**

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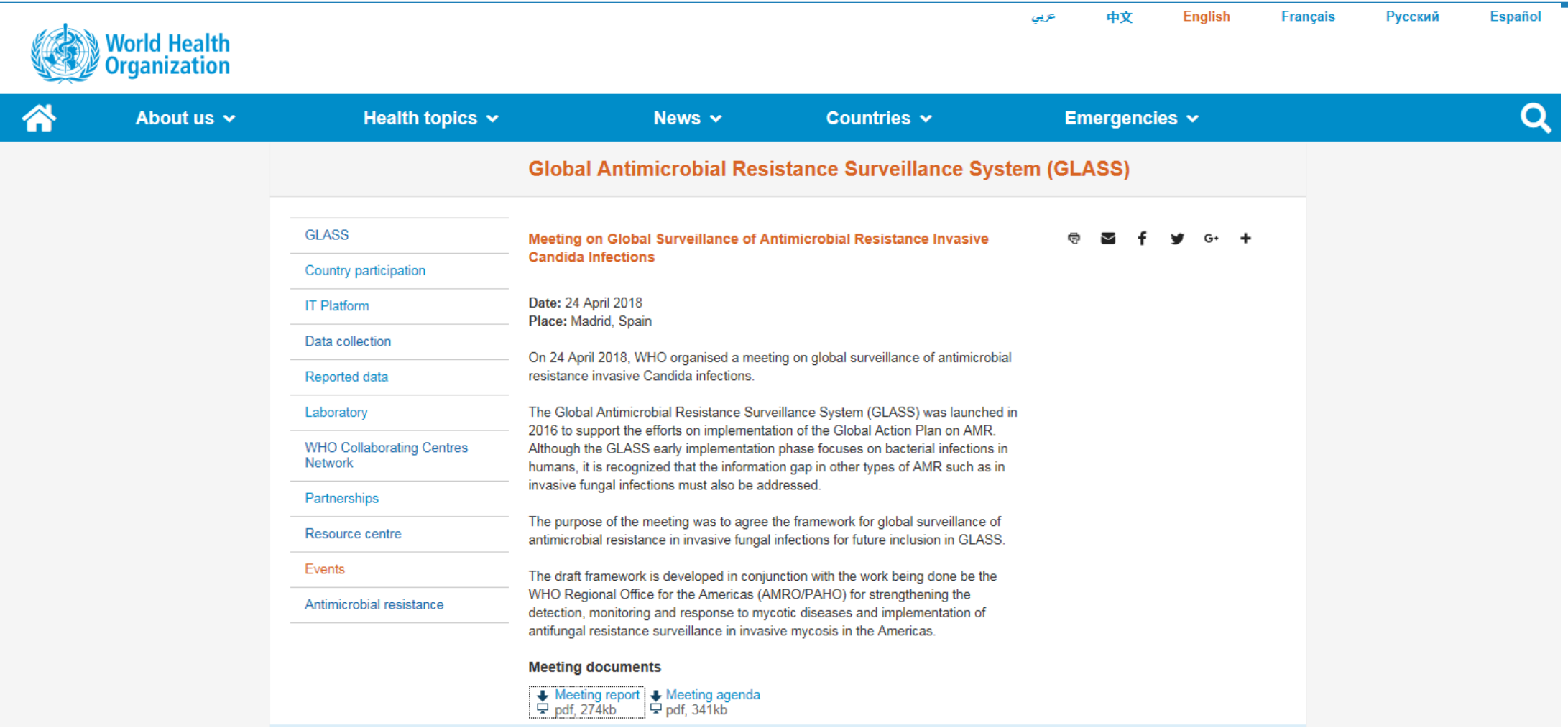
Development of framework for global surveillance of AMR invasive *Candida* infection



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World Health Organization

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Global Antimicrobial Resistance Surveillance System (GLASS)

- GLASS
- Country participation
- IT Platform
- Data collection
- Reported data
- Laboratory
- WHO Collaborating Centres Network
- Partnerships
- Resource centre
- Events
- Antimicrobial resistance

Meeting on Global Surveillance of Antimicrobial Resistance Invasive Candida Infections

Date: 24 April 2018
Place: Madrid, Spain

On 24 April 2018, WHO organised a meeting on global surveillance of antimicrobial resistance invasive Candida infections.

The Global Antimicrobial Resistance Surveillance System (GLASS) was launched in 2016 to support the efforts on implementation of the Global Action Plan on AMR. Although the GLASS early implementation phase focuses on bacterial infections in humans, it is recognized that the information gap in other types of AMR such as in invasive fungal infections must also be addressed.

The purpose of the meeting was to agree the framework for global surveillance of antimicrobial resistance in invasive fungal infections for future inclusion in GLASS.

The draft framework is developed in conjunction with the work being done be the WHO Regional Office for the Americas (AMRO/PAHO) for strengthening the detection, monitoring and response to mycotic diseases and implementation of antifungal resistance surveillance in invasive mycosis in the Americas.

Meeting documents

Meeting report pdf, 274kb | Meeting agenda pdf, 341kb

World Health Organization

ECDC survey on preparedness for *Candida auris*, 29 EU/EEA countries, 2018

Preparedness for *C. auris*	No. countries
Mycology reference laboratory available	21
Laboratory alert issued	18
Clinical alert issued	10
Offer for reference identification to hospital laboratories	13
Preparation of guidance for laboratory testing	7
Preparation of guidance for clinical management	4
Preparation of guidance for infection control	4
Retrospective surveillance in place	8
Prospective surveillance in place	7

Source: Kohlenberg A, et al. Eurosurveillance 2018 Mar;23(13):pii=18-00136.

Slide credits: ECDC

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Steps for the development of framework

1. Develop and pilot a tool for assessment of the laboratory capacity for identification and AST of candidemia
2. Develop IT tools for data entry and submission to GLASS
3. Definition of sentinel sites at country level
4. Pilot testing of the framework
5. Summarize & publish pilot results
6. **Dec 2019:** framework for global AMR surveillance of bloddstream infection due to *Candida* spp

Support from WHO Collaborating Centres

- **Dr Tom Chiller**: WHO Collaborating Centre for Surveillance, Epidemiology and Control of Salmonella and other Foodborne Diseases, CDC, Atlanta, USA.

- **Prof Arunaloke Chakrabarti**: WHO Collaborating Centre on Reference and Research on Fungi of Medical Importance, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

Current WHO Initiatives on fungal infection

- HIV Department have recommendation for screening, treatment, prevention of:
  - Pneumocystis pneumonia (PCP) yeast-like fungus *P. jirovecii*
  - *Cryptococcus neoformans*
  - *Candida* (thrush)
- Neglected Tropical Disease
  - Mycetoma
  - Chromoblastomycosis
- Antimicrobial resistance
  - Surveillance of bloodstream infection due to *Candida* spp

Conclusions

- To date, the global response to infectious diseases has focused on pathogens other than fungi (e.g., bacteria and viruses).
- One of the major limitations in addressing the threat of antifungal resistant fungi is a lack of data at the global level.
- Global advocacy on the importance of fungal diseases must be intensified.
- Links between fungal disease and global agendas offer an window of opportunity for advocacy and action.
- AMR agenda is providing an opportunity for global surveillance of invasive *Candida* spp.

Thank you!

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