



Burden of antimicrobial resistance in Germany

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Content

- AMR - why burden estimation is challenging
- Incidence based burden estimates
- Project: burden of bloodstream infections of Vancomycin-resistant Enterococcus faecium and Methicillin-resistant Staphylococcus aureus
- Project: AMR burden Germany - comparison GBD versus BCODE
- Outlook to country comparison project



What is antimicrobial resistance (AMR) and why are we so concerned about it?

- Antimicrobial drugs – medicines active against infections caused by bacteria (antibiotics), viruses (antivirals), fungi (antifungals) and parasites
- Resistance: when micro-organisms survive exposure to antimicrobials that would normally kill them or stop growth.
- Increasing problem due to overuse of antimicrobials.

=> Simple infections may become life threatening

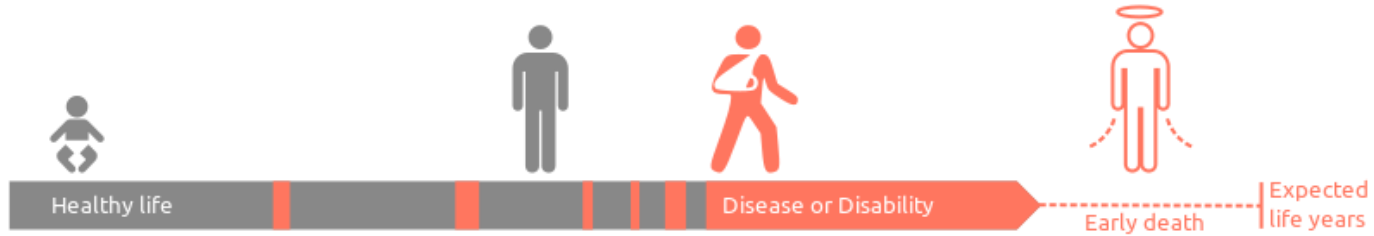


DALY

Disability Adjusted Life Years is a measure of overall disease burden, expressed as the cumulative number of years lost due to ill-health, disability or early death

$$= \text{YLD} + \text{YLL}$$

Years Lived with Disability + Years of Life Lost



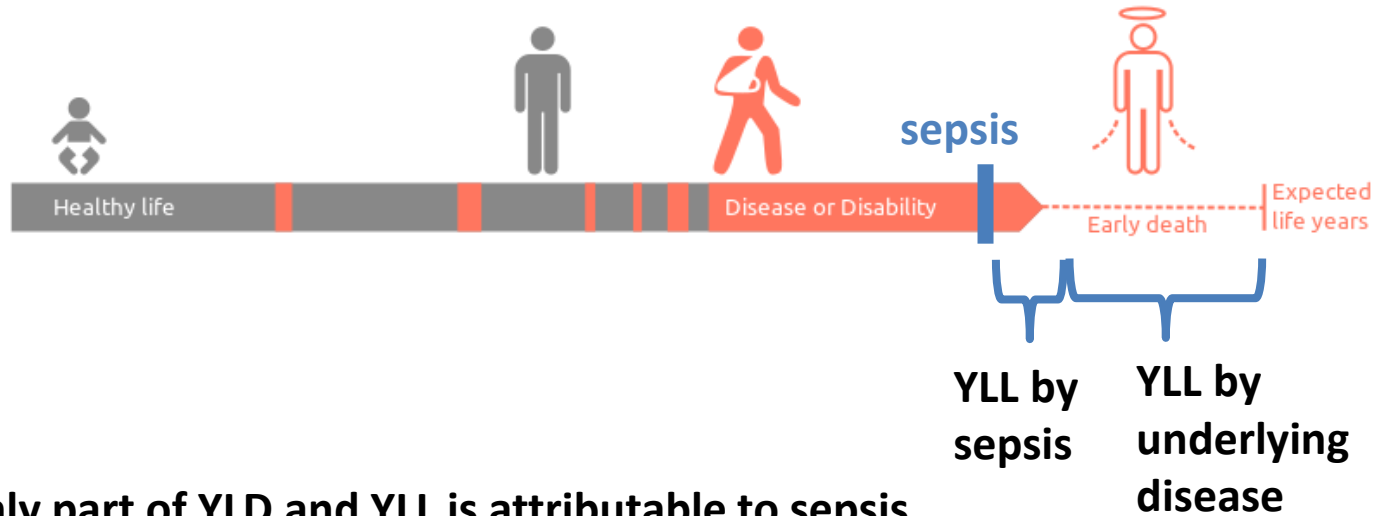


DALY

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$$= \text{YLD} + \text{YLL}$$

Years Lived with Disability + Years of Life Lost



Only part of YLD and YLL is attributable to sepsis and/or underlying disease



Burden of Healthcare Associated Infections

- Urinary tract infection
- Neonatal sepsis (in preterm born babies)
- Primary sepsis (non-neoantal)
- *Clostridium difficile* infection
- Healthcare associated pneumonia
- Surgical site infection

=> **13 systematic reviews**

- a) attributable mortality
- b) attributable morbidity
- c) Length of disease



RESEARCH ARTICLE

Burden of Six Healthcare-Associated Infections on European Population Health: Estimating Incidence-Based Disability-Adjusted Life Years through a Population Prevalence-Based Modelling Study

Alessandro Cassini^{1,2*}, Diamantis Plachouras^{1*}, Tim Eckmanns³, Muna Abu Sin³, Hans-Peter Blank³, Tanja Ducombe³, Sebastian Haller³, Thomas Harder³, Anja Klingeberg³, Madlen Sixtensson³, Edward Velasco³, Bettina Weiß³, Piotr Kramarz¹, Dominique L. Monnet¹, Mirjam E. Kretzschmar^{2,4}, Carl Suetens¹

¹ European Centre for Disease Prevention and Control, Stockholm, Sweden, ² Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands, ³ Robert Koch Institute, Berlin, Germany, ⁴ Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, The Netherlands

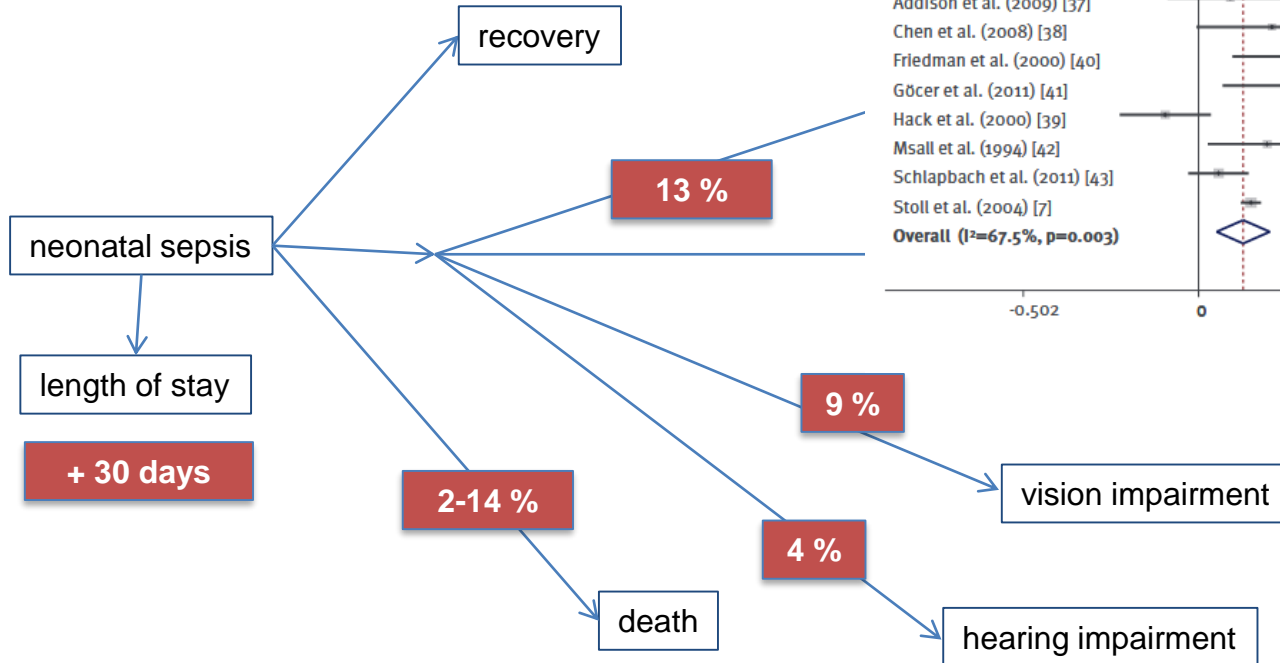


RESEARCH

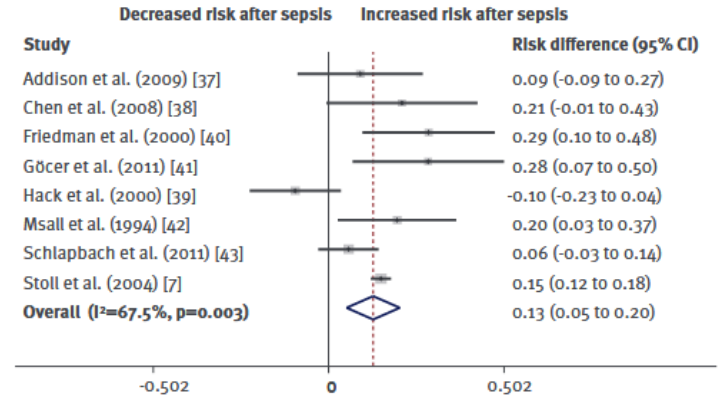
Application of a new methodology and R package reveals a high burden of healthcare-associated infections (HAI) in Germany compared to the average in the European Union/European Economic Area, 2011 to 2012

Benedikt Zacher^{1,2}, Sebastian Haller^{1,2}, Niklas Willrich¹, Jan Walter¹, Muna Abu Sin¹, Alessandro Cassini¹, Diamantis Plachouras³, Carl Suetens³, Michael Behnke⁴, Petra Gastmeller⁴, Lothar H. Wieler¹, Tim Eckmanns¹

Outcome Tree Neonatal Sepsis in preterm born babies



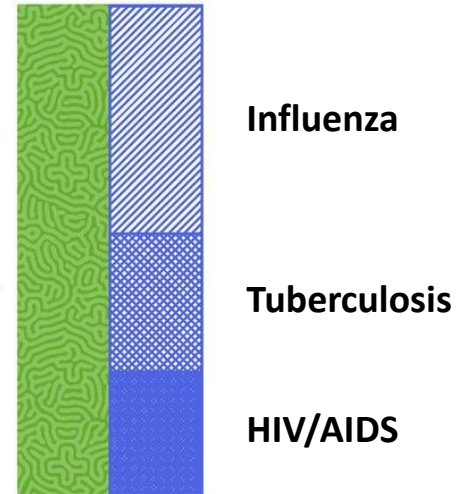
Forest Plot neuro impairment



Burden of infections with bacteria resistant to antibiotics 2015 EU

- 33 000 Deaths / year
- 875 000 DALYs: highest burden in infants <1 yr & ≥ 65 yrs
- 75% Healthcare-associated infections

Antibiotic resistance



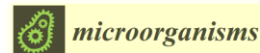
Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis



Burden of Bloodstream Infections: Vancomycin-resistant *Enterococcus faecium* and Methicillin-resistant *Staphylococcus aureus*, Germany, 2015-2022

■ Objective:

To estimate burden of BSI due to VREfm and MRSA in Disability-Adjusted Life-Years and attributable deaths, Germany from 2015 to 2022, to describe changes and identify potential risk groups for both pathogens



Article

Germany's Burden of Disease of Bloodstream Infections Due to Vancomycin-Resistant *Enterococcus faecium* between 2015–2020

Simon Brinkwirth ^{1,2,3,*}, Sofie Martins ⁴, Olaniyi Ayobami ¹, Marcel Feig ⁵, Ines Noll ¹, Benedikt Zacher ⁶, Tim Eckmanns ¹, Guido Werner ⁷, Niklas Willrich ^{1,†} and Sebastian Haller ^{1,*†}



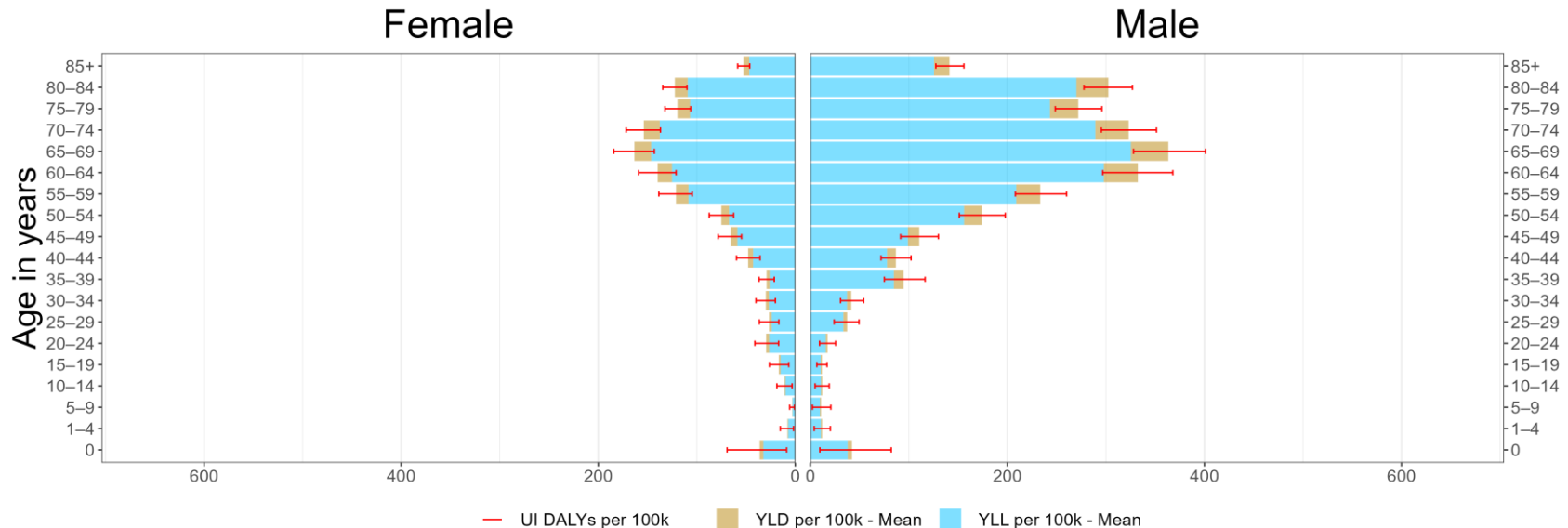
Burden of VRE and MRSA – Methods

- Data source: Antibiotic Resistance Surveillance (ARS) laboratory-based surveillance system, Germany
 - Coverage: approximately 30% of all hospitals
 - Data collection: 2015-2022
 - Case Definition: BSI defined as a blood culture isolates of VRE and MRSA
1. Incidence estimation of VREfm and MRSA BSI per 100,000 inhabitants stratified by age group and sex
 2. Estimated incidences were used as an input to the Burden of Communicable Disease in Europe (BCODE) toolkit to obtain DALYs and attributable deaths



Burden of VRE – Results

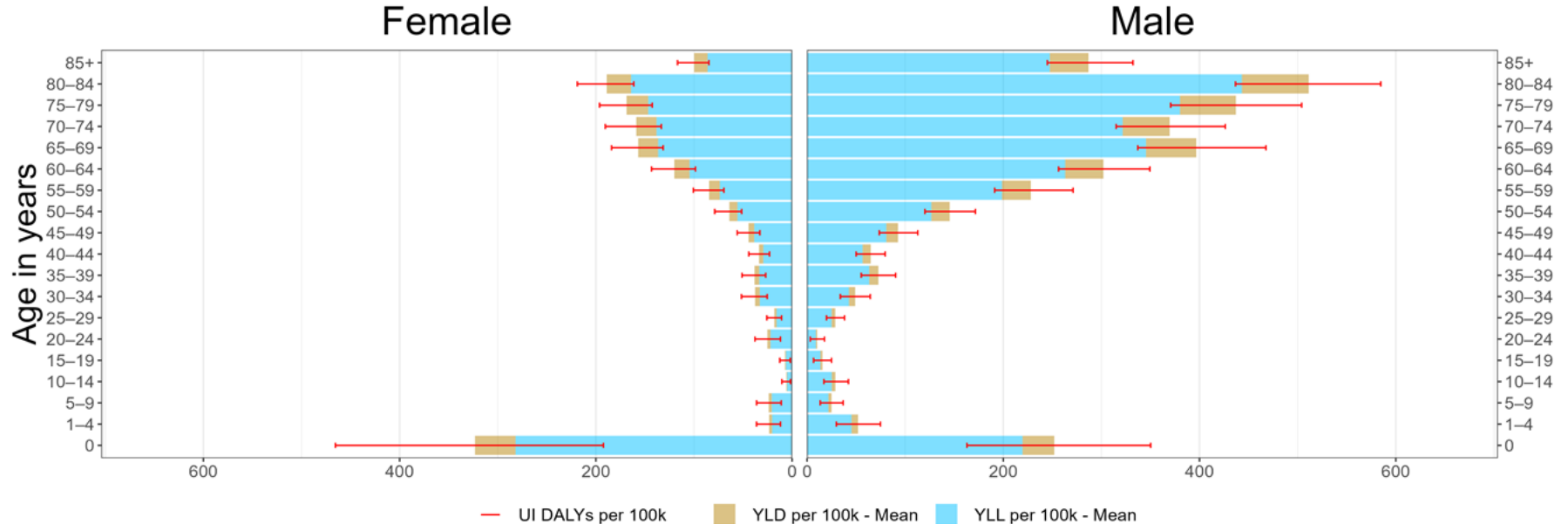
- The estimation is based on 5,367 isolates from 528 hospitals
- The incidence per 100,000 increased from 1.4 to 2.5
- Attributable deaths 263 - 483





Burden of MRSA – Results

- The estimation is based on 7,572 isolates from 638 hospitals
- The incidence per 100,000 decreased from 5.3 to 2.0
- Attributable deaths 830 - 303





<https://vizhub.healthdata.org/microbe>



69% of **sepsis** deaths in **Germany** were caused by **bacterial infection**. The remaining 31% were caused by other pathogens such as viruses, fungi, and parasites.

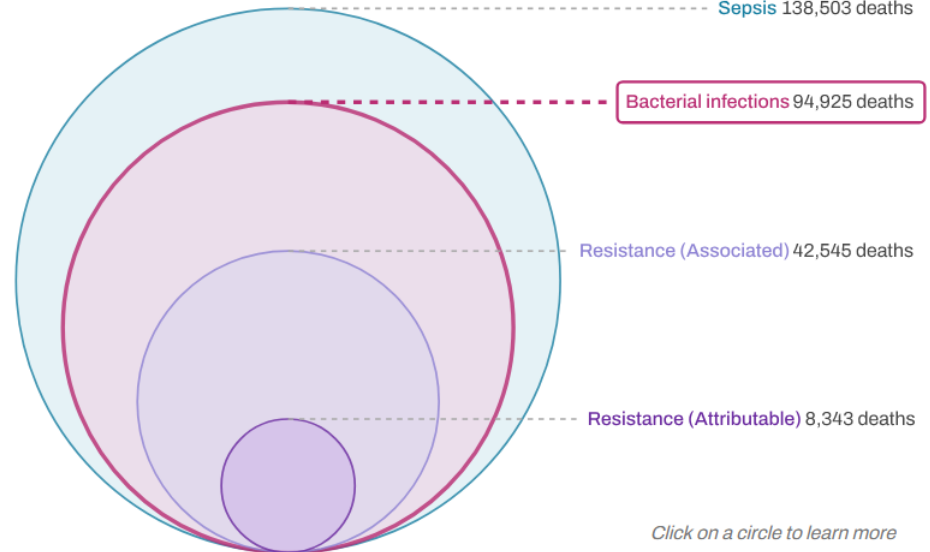
Key terms

Bacteria

Causes infection ⇒ *sepsis* ⇒ *death or disability*

Single-celled microorganisms capable of independent reproduction. They can be beneficial or cause disease, in which case they are referred to as bacterial pathogens.

Composition of infection-related deaths in Germany



THE LANCET

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ARTICLES | VOLUME 395, ISSUE 10325, P629-655, FEBRUARY 12, 2022

Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis

Antimicrobial Resistance Collaborators¹ · Show footnotes

Open Access · Published: January 19, 2022 · DOI: [https://doi.org/10.1016/S0140-6736\(21\)03724-0](https://doi.org/10.1016/S0140-6736(21)03724-0)

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Summary

Background

Antimicrobial resistance (AMR) poses a major threat to human health around the world. Previous publications have estimated the effect of AMR on incidence, deaths, hospital length of stay, and health-care costs for specific pathogen–drug combinations in select locations. To our knowledge, this study presents the most comprehensive estimates of AMR burden to date.

Methods

We estimated deaths and disability-adjusted life-years (DALYs) attributable to and associated with bacterial AMR for 23 pathogens and 88 pathogen–drug combinations in 204 countries and territories in 2019. We obtained data from systematic literature reviews,

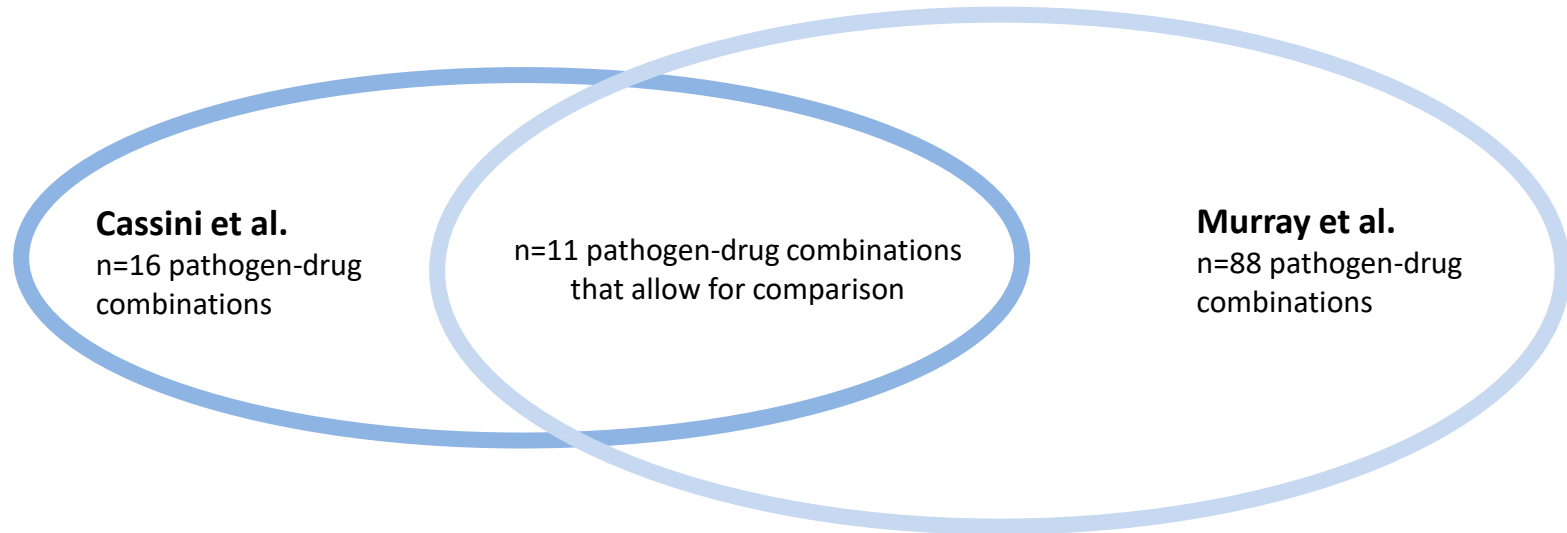


AMR burden in Germany – comparison of estimates different study questions

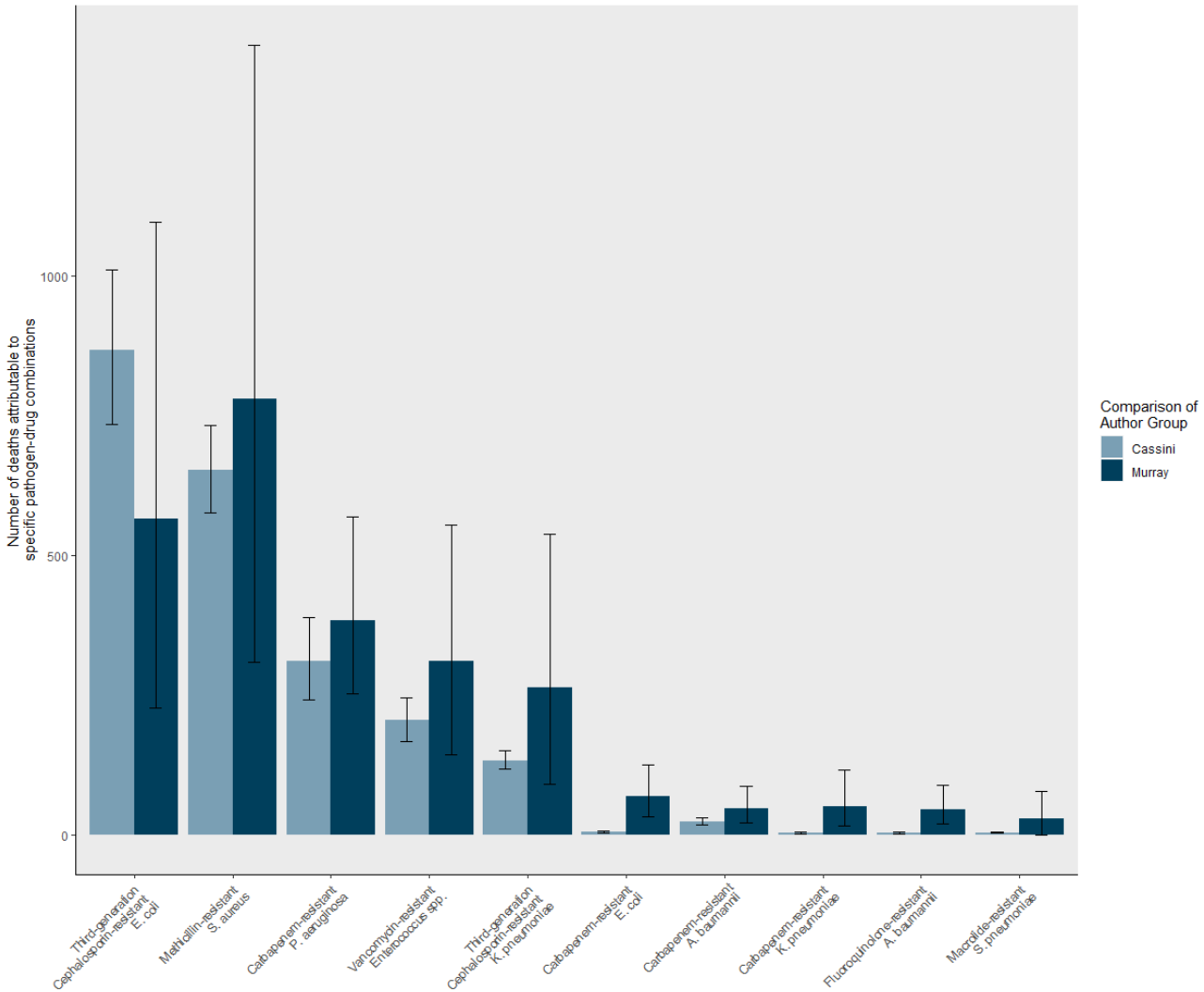
- What is the burden of antimicrobial resistant bacteria? **GBD**
- What is the burden due to a specific group of drug-pathogen combinations in certain infections? **BCODE**
- What is the burden only due to antimicrobial resistance/lack of treatment options? **GBD**
- ...



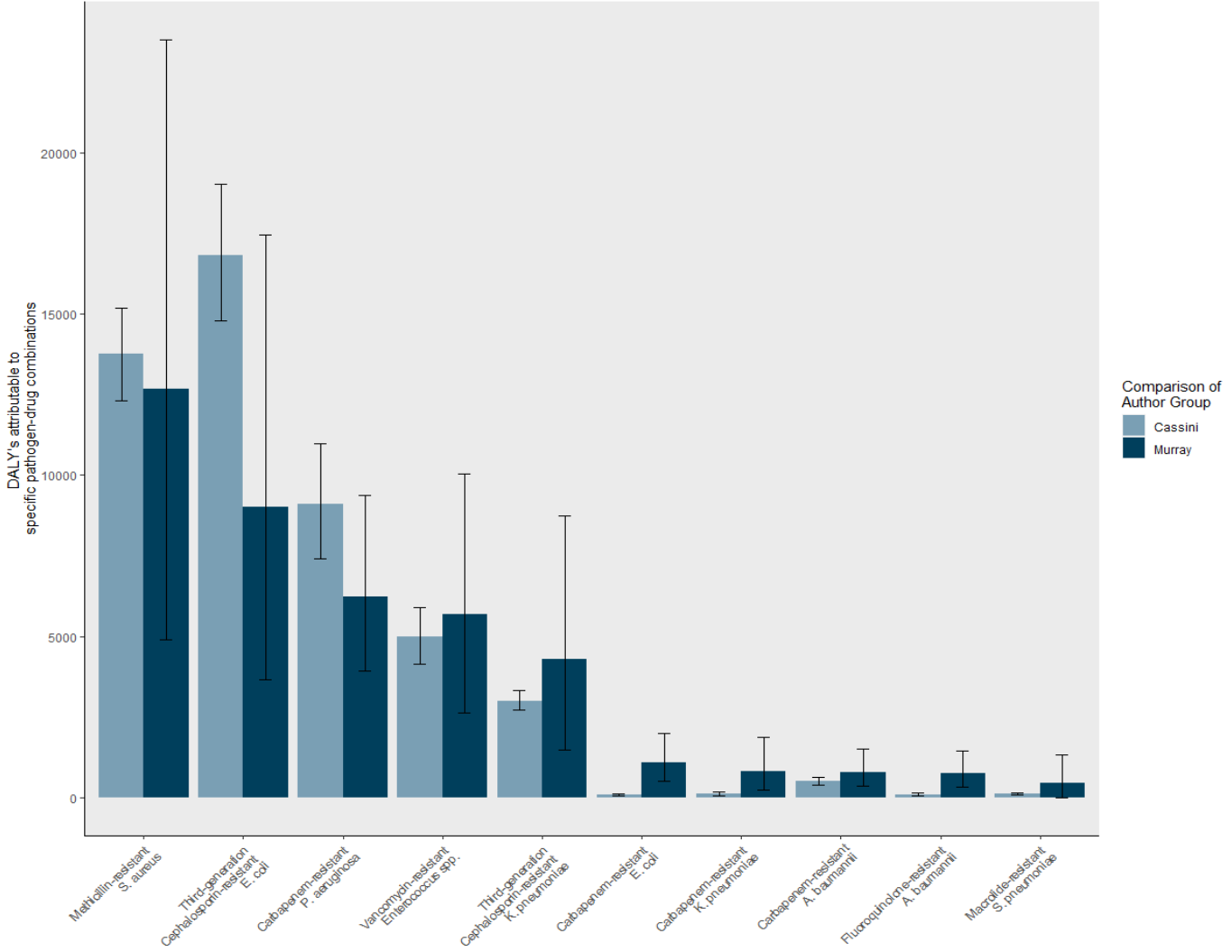
AMR burden in Germany – comparison of estimates drug-pathogen combinations



AMR-attributable deaths for selected pathogen-drug combinations (Germany)



AMR-attributable DALYs for selected pathogen-drug combinations (Germany)





Summary: comparison of German AMR burden estimates

- When stratified to similar drug-pathogen combinations results are highly comparable despite:
 - different observation periods
 - differing methodology
 - incomplete pathogen-drug matching
 - differing study questions



Country comparisons with stratified GBD 2019 data

- Project financed by WHO-Hub Berlin and RKI in cooperation with IHME
- Aim: may GBD AMR burden differences between neighbouring countries be used to identify:
 - best practice examples?
 - particular challenges?
 - risk groups?

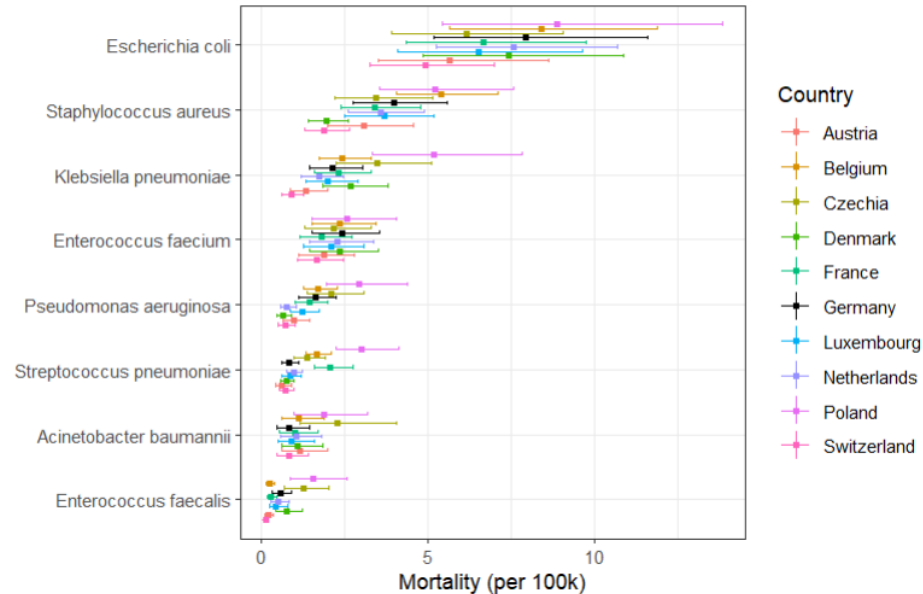
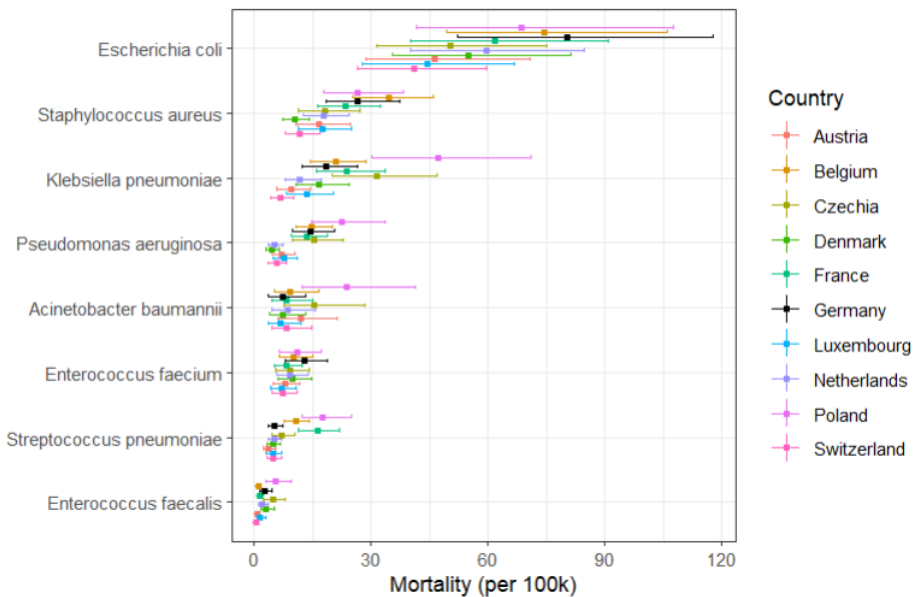
Country comparison by species

not age-standardized

age-standardized

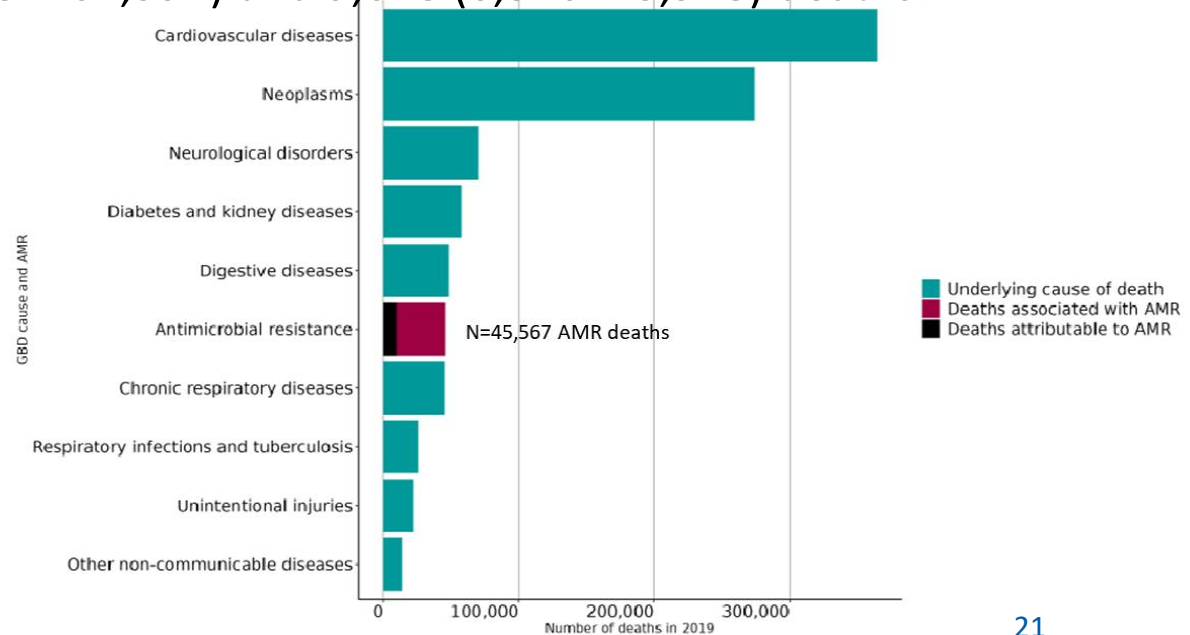
AMR-associated mortality for selected species

AMR-associated ASMR for selected species



Summary of German AMR Burden

- Different methods – similar results
- Total burden of associated and attributable mortality due to bacterial AMR in Germany was 45,692 (31,281–64,591) and 9,648 (6,520–13,918) deaths.
- Largest fatal burden of AMR from bloodstream infections, followed by respiratory and intraabdominal infections.



The length of each bar states the number of deaths by GBD cause and those associated with/attribution to AMR in 2019.

Die Entwicklung des Robert Koch-Instituts

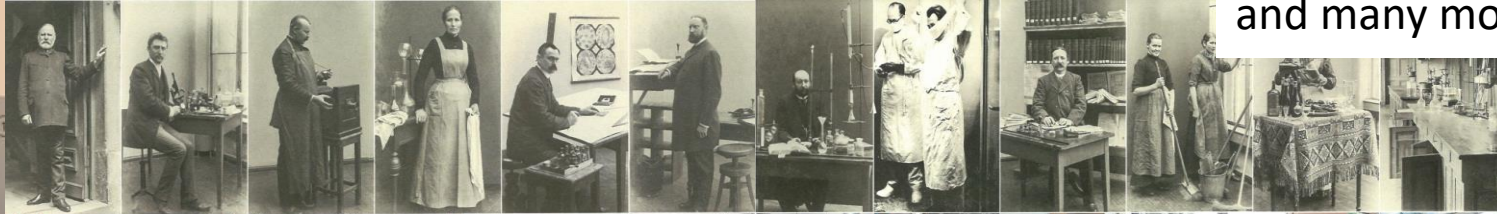
The Development of the Robert Koch Institute

6 Neubau



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1891



2015

