European Burden of Disease Network – COST Action

MEASURING THE IMPACT OF COMMUNICABLE DISEASES: METHODOLOGIES, CHALLENGES AND LESSONS LEARNED

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World Health Organization

World Health Organization

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Initiation of the project

- Funding by the European Centre for Disease Prevention and Control
- Project lasted 6 years
- Initiated by ECDC Director Zsuzsanna Jakab

- Jakab Z. Why a burden of disease study?. Euro Surveill. 2007;12(12):pii=750. https://doi.org/10.2807/esm.12.12.00750-en
- van Lier EA, Havelaar AH (2007) Disease burden of infectious diseases in Europe: a pilot study. RIVM report 215011001. Bilthoven: National Institute for Public Health and the Environment (RIVM), Available: http://www.rivm.nl/bibliotheek/rapporten/215011001.pdf
- van Lier EA, Havelaar AH, Nanda A (2007) The burden of infectious diseases in Europe: a pilot study. Euro Surveill 12(12): E3–4.

Burden of Communicable Diseases in Europe project (BCoDE)

The BCoDE study will allow assessment of the comparative impact of infectious diseases

- Objective: to introduce an evidence-based approach to health description
- Objective: to foster an overview of surveillance data quality and availability
- Objective: to facilitate the communication of complex information to decision makers
- Objective: to provide a tool for planning and prioritisation

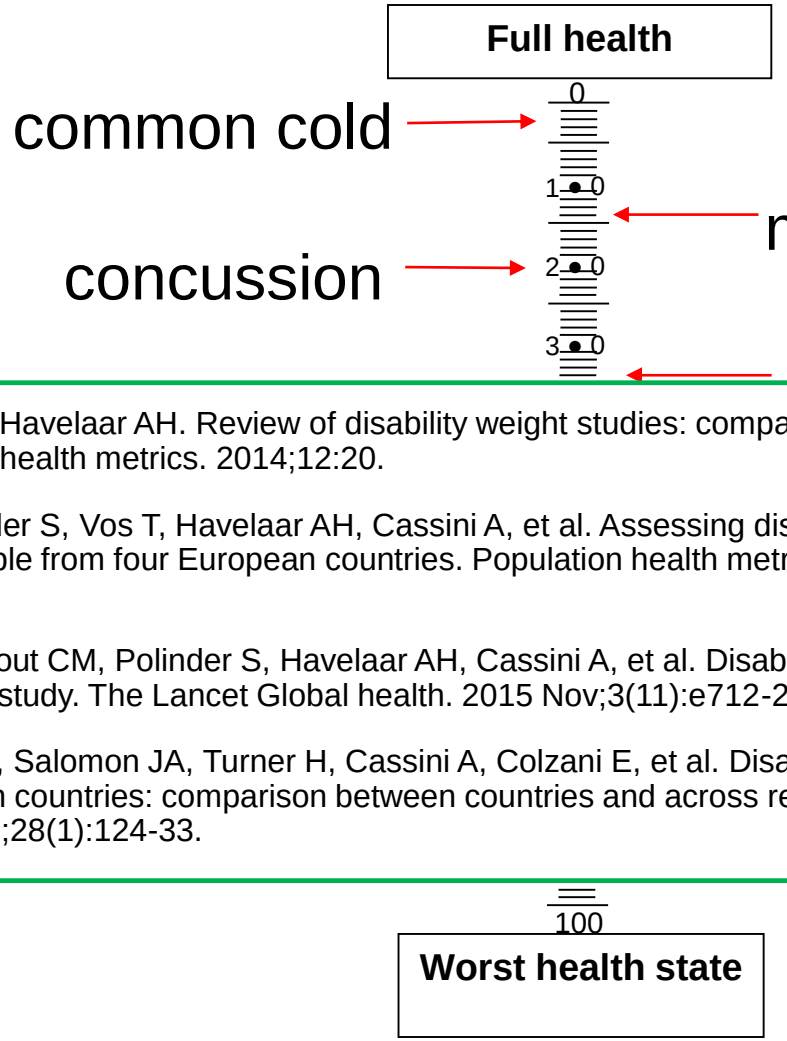
Apples and pears

Choice of a common currency
to compare impact of diseases and their sequelae

Disability-adjusted life years (DALYs)

- Kretzschmar M, Mangen MJ, Pinheiro P, Jahn B, Fèvre EM, Longhi S, Lai T, Havelaar AH, Stein C, Cassini A, Kramarz P; BCoDE consortium. New methodology for estimating the burden of infectious diseases in Europe. PLoS Med. 2012;9(4):e1001205.
- Mangen MJ, Plass D, Havelaar AH, Gibbons CL, Cassini A, Mühlberger N, van Lier A, Haagsma JA, Brooke RJ, Lai T, de Waure C, Kramarz P, Kretzschmar ME; BCoDE consortium. The pathogen- and incidence-based DALY approach: an appropriate [corrected] methodology for estimating the burden of infectious diseases. PLoS One. 2013 Nov 20;8(11):e79740. Erratum in: PLoS One. 2013;8(12).

Disability weights

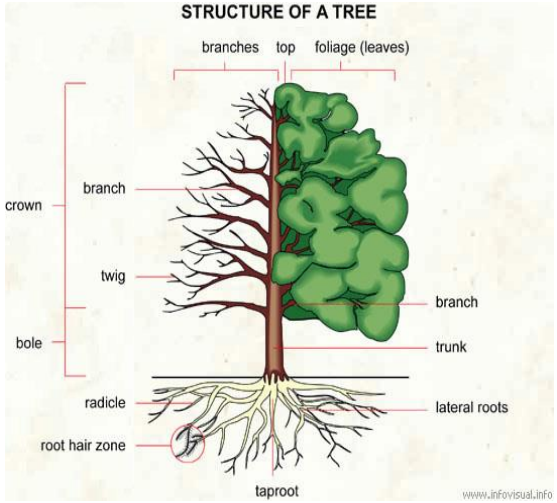


- Haagsma JA, Polinder S, Cassini A, Colzani E, Havelaar AH. Review of disability weight studies: comparison of methodological choices and values. Population health metrics. 2014;12:20.
- Haagsma JA, Maertens de Noordhout C, Polinder S, Vos T, Havelaar AH, Cassini A, et al. Assessing disability weights based on the responses of 30,660 people from four European countries. Population health metrics. 2015;13:10.
- Salomon JA, Haagsma JA, Davis A, de Noordhout CM, Polinder S, Havelaar AH, Cassini A, et al. Disability weights for the Global Burden of Disease 2013 study. The Lancet Global health. 2015 Nov;3(11):e712-23.
- Maertens de Noordhout C, Devleesschauwer B, Salomon JA, Turner H, Cassini A, Colzani E, et al. Disability weights for infectious diseases in four European countries: comparison between countries and across respondent characteristics. Eur J Public Health. 2018 Feb 1;28(1):124-33.

How is a disease represented?

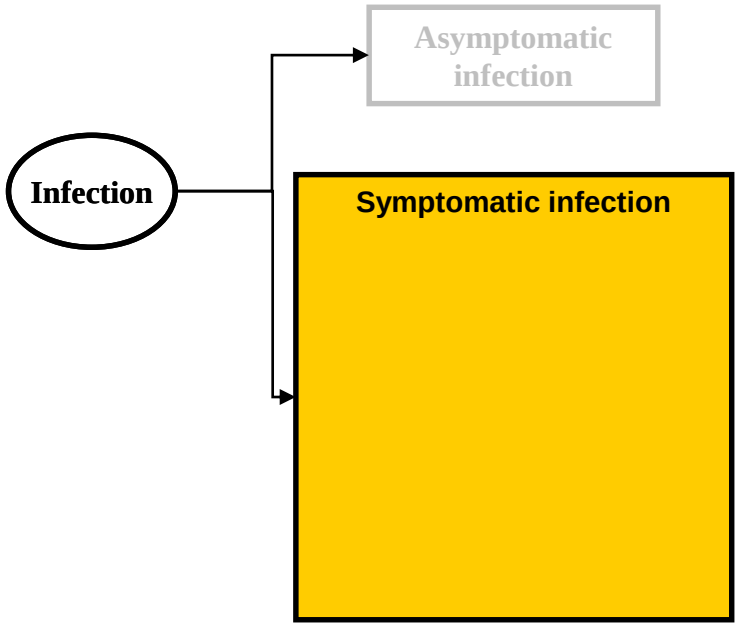
- An outcome tree is a qualitative representation of the progression of a disease in time by ordering relevant health outcomes following infection and illustrating their conditional dependency.

- Several variables need to input the outcome tree

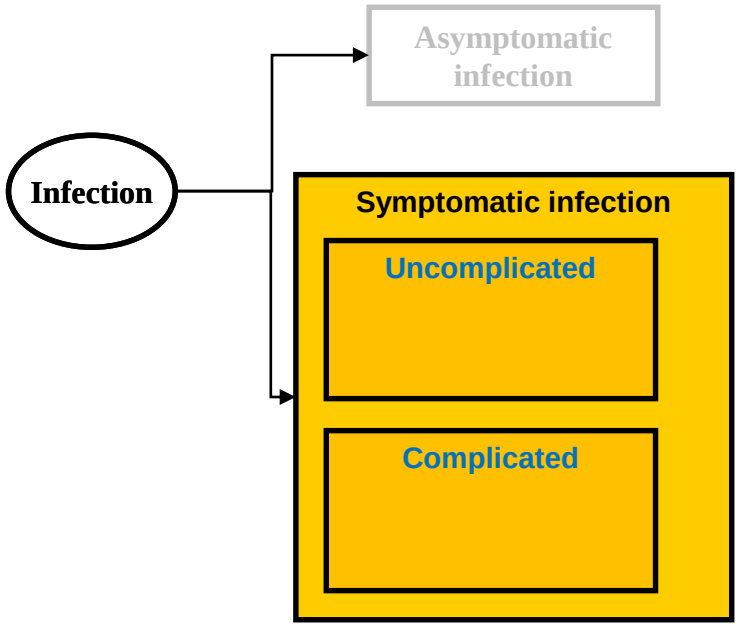


Representing progression of diseases: building outcome trees

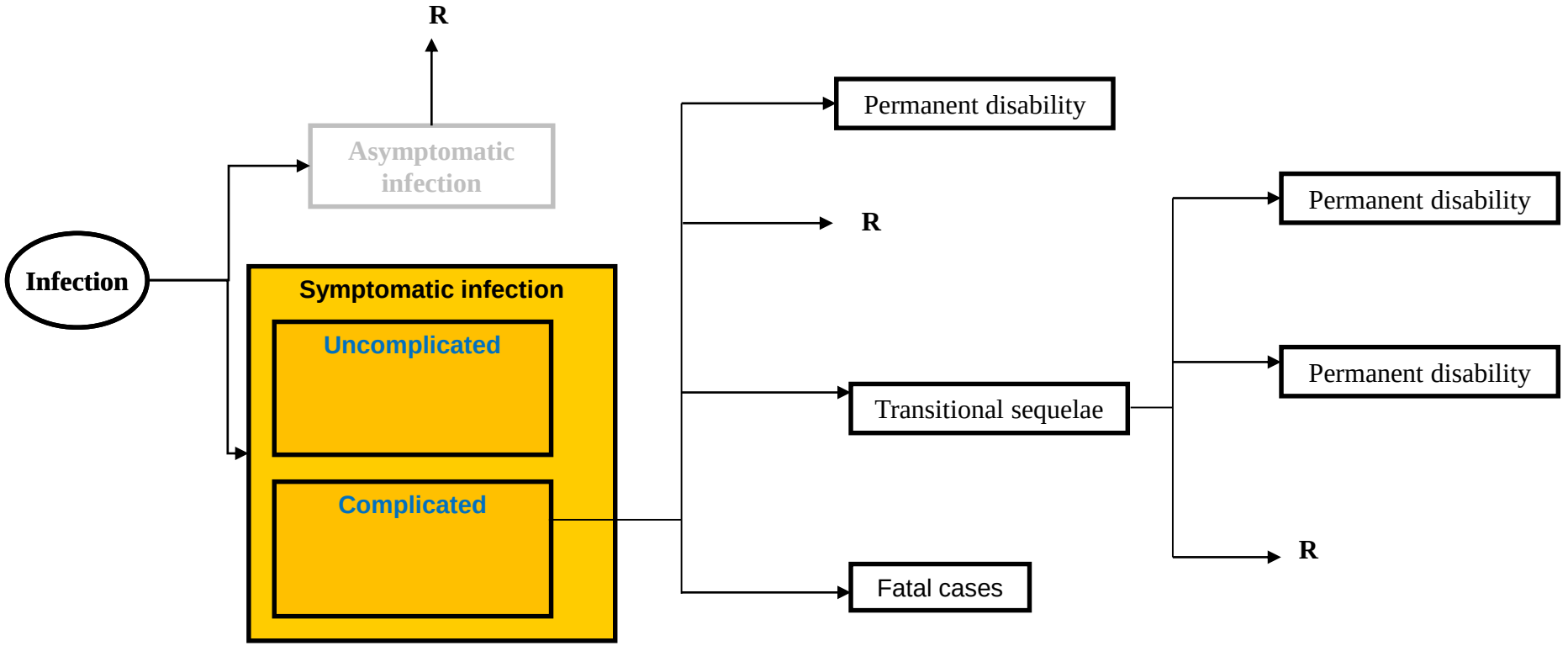
Representing progression of diseases: building outcome trees



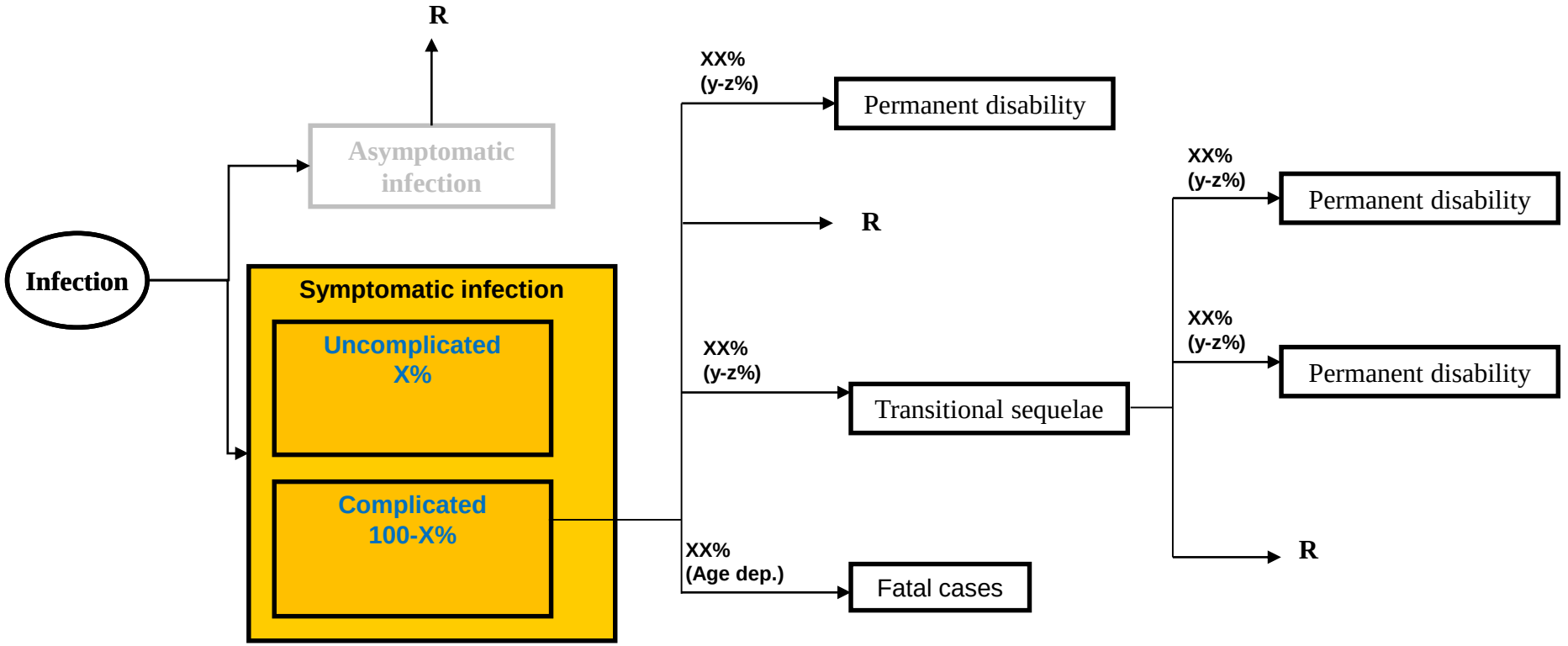
Representing progression of diseases: building outcome trees



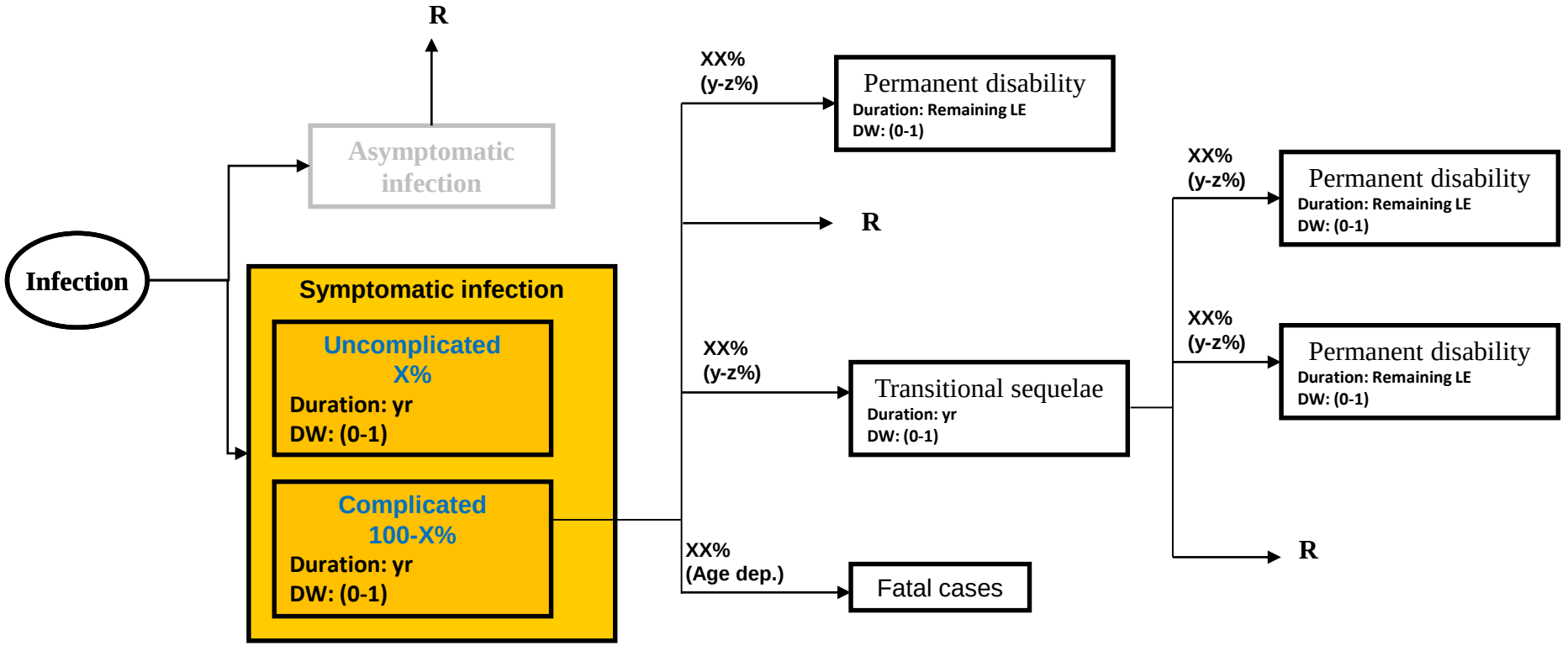
Representing progression of diseases: building outcome trees



Representing progression of diseases: building outcome trees

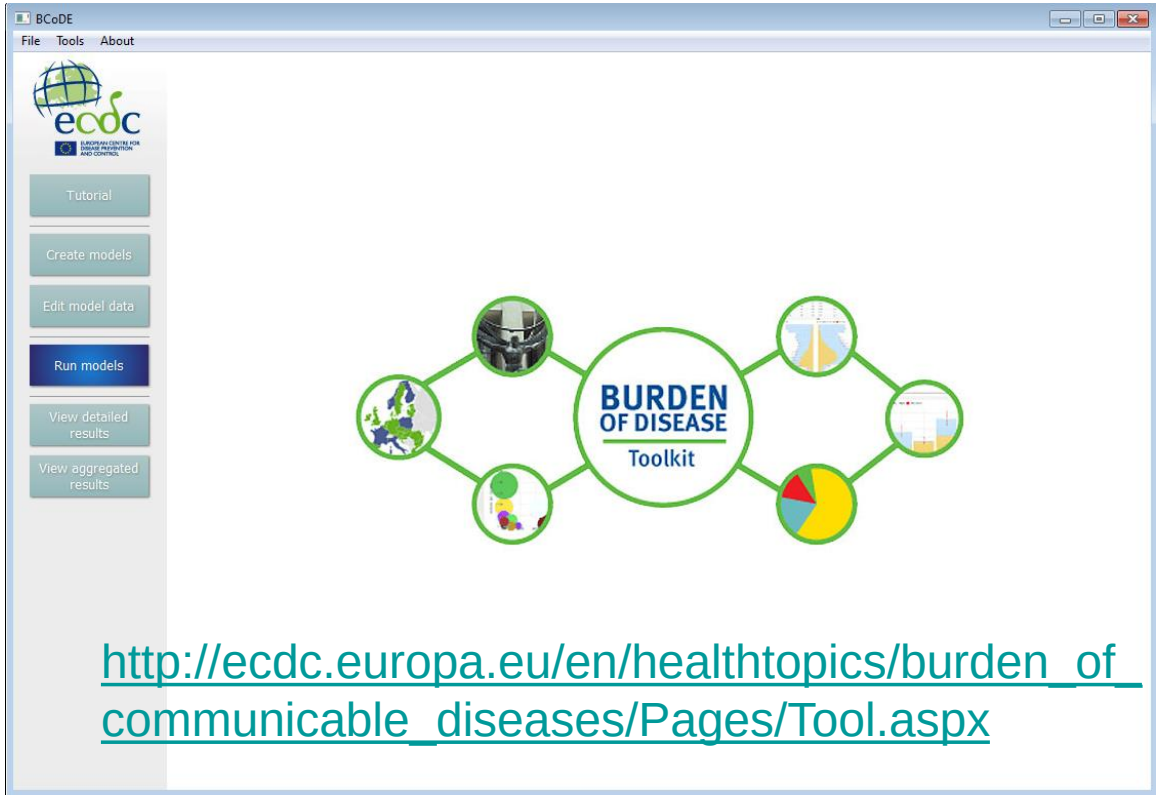


Representing progression of diseases: building outcome trees



Calculating DALYs: the BCoDE toolkit

- User-friendly, stand-alone & free
- Flexible
- No age weighting
- Incidence-based approach
- Pathogen-based
- Time discounting as an option
- Monte Carlo simulations
- Option to choose number of iterations



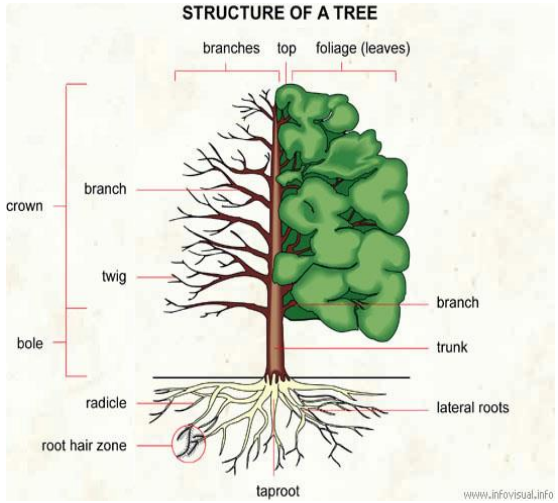
http://ecdc.europa.eu/en/healthtopics/burden_of_communicable_diseases/Pages/Tool.aspx

Colzani E and Cassini A, et al. A Software Tool for Estimation of Burden of Infectious Diseases in Europe Using Incidence-Based Disability Adjusted Life Years. PLoS One. 2017;12(1):e0170662.

How is a disease represented?

Several variables need to input the outcome tree:

- Health outcomes √
- Percentage that develop the health outcome √
- Duration of health outcomes √
- Disability weights √
- …and finally: Number of cases

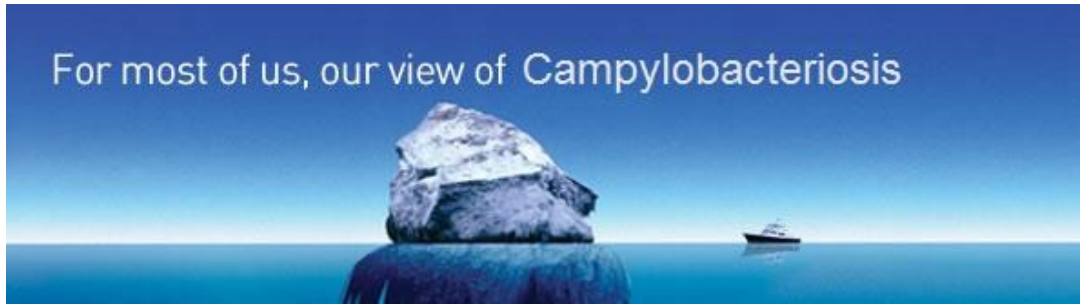


Estimating incidence

Ranking of diseases: notified cases to ECDC

1	Chlamydia
2	Campylobacteriosis
3	Salmonellosis
4	Tuberculosis
5	Gonococcal infections
6	HIV
7	Toxoplasmosis (congenital and acquired)
8	Giardiasis
9	Pertussis
10	Mumps
11	Syphilis
12	Rubella
13	Invasive pneumococcal infections
14	Measles
15	Hepatitis A
16	Cryptosporidiosis
17	Shigellosis
18	Infection with VTEC/STEC
19	Legionnaires'disease
20	Invasive meningococcal disease
21	HBV
22	Q fever
23	Invasive Haemophilus influenza disease
24	Listeriosis
25	Tetanus
26	Diphtheria

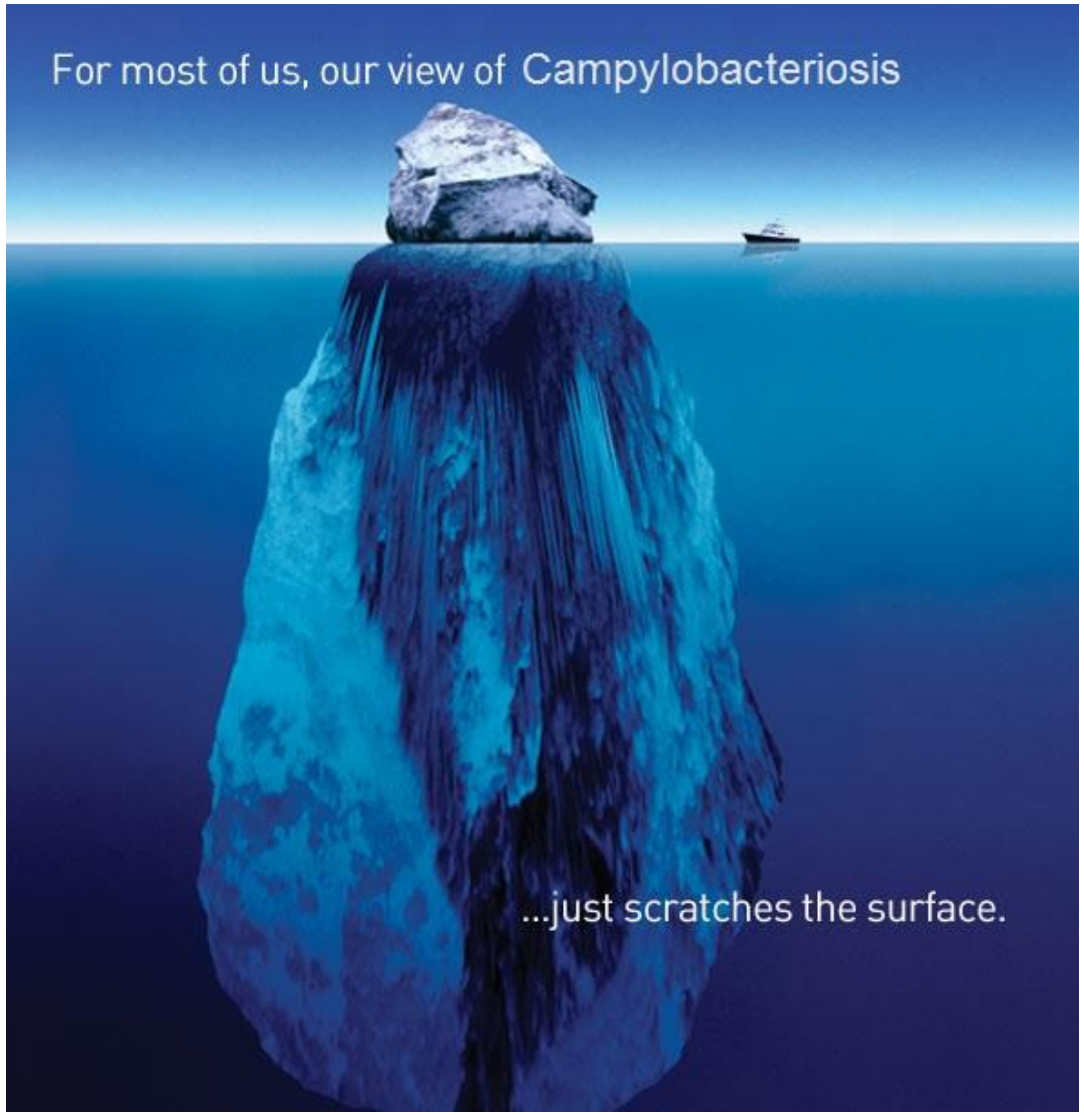
Not all diseases are reported case-based



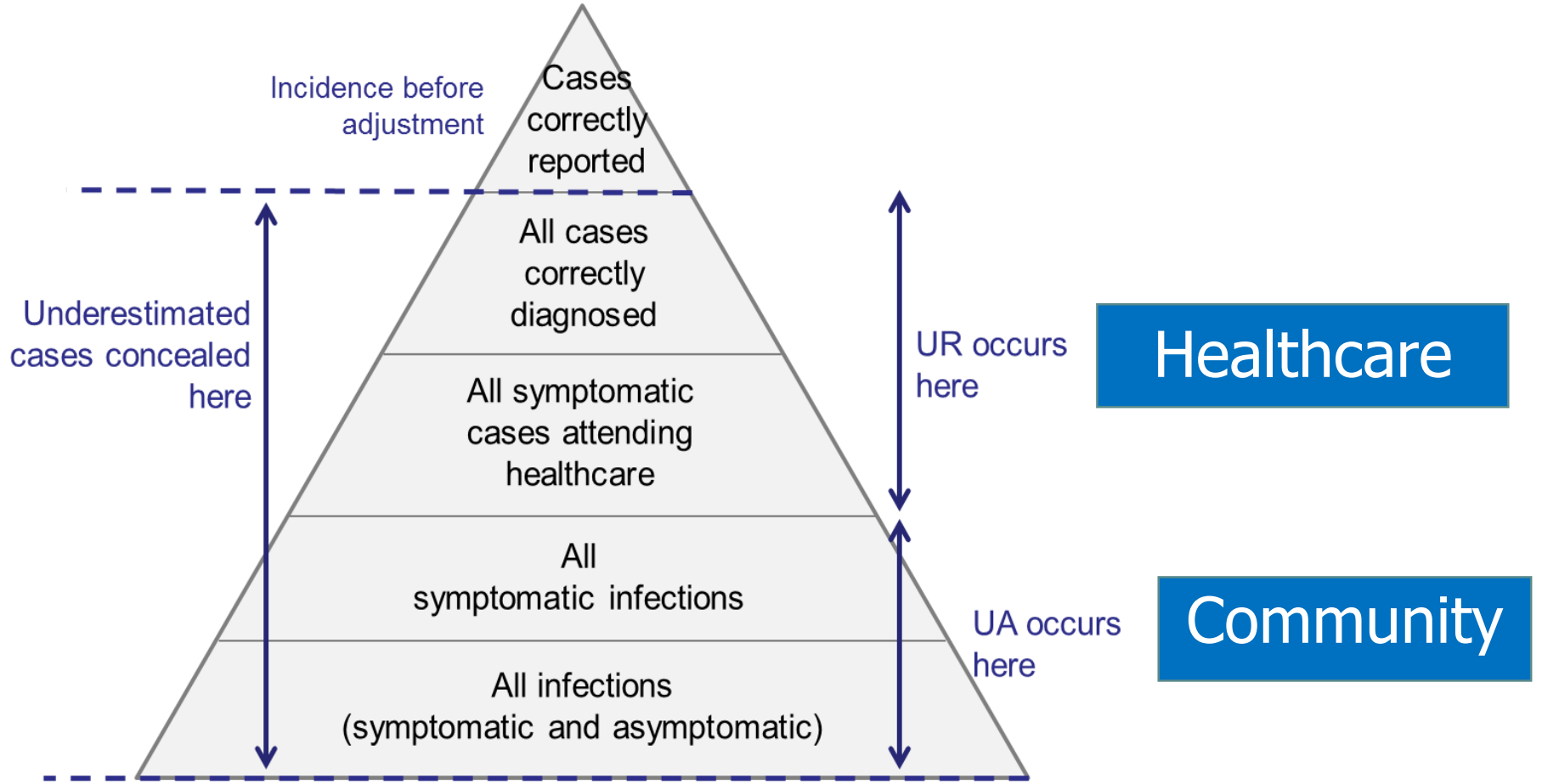
Iceberg ahead…

World Health Organization

…but it`s only the tip!



The surveillance pyramid: the issue of under-estimation in surveillance



Gibbons CL, Mangen MJ, Plass D, Havelaar AH, Brooke RJ, Kramarz P, Peterson KL, Stuurman AL, Cassini A, Fèvre EM, Kretzschmar ME; Burden of Communicable diseases in Europe (BCoDE) consortium. Measuring underreporting and under-ascertainment in infectious disease datasets: a comparison of methods. BMC Public Health. 2014 Feb 11;14(1):147.

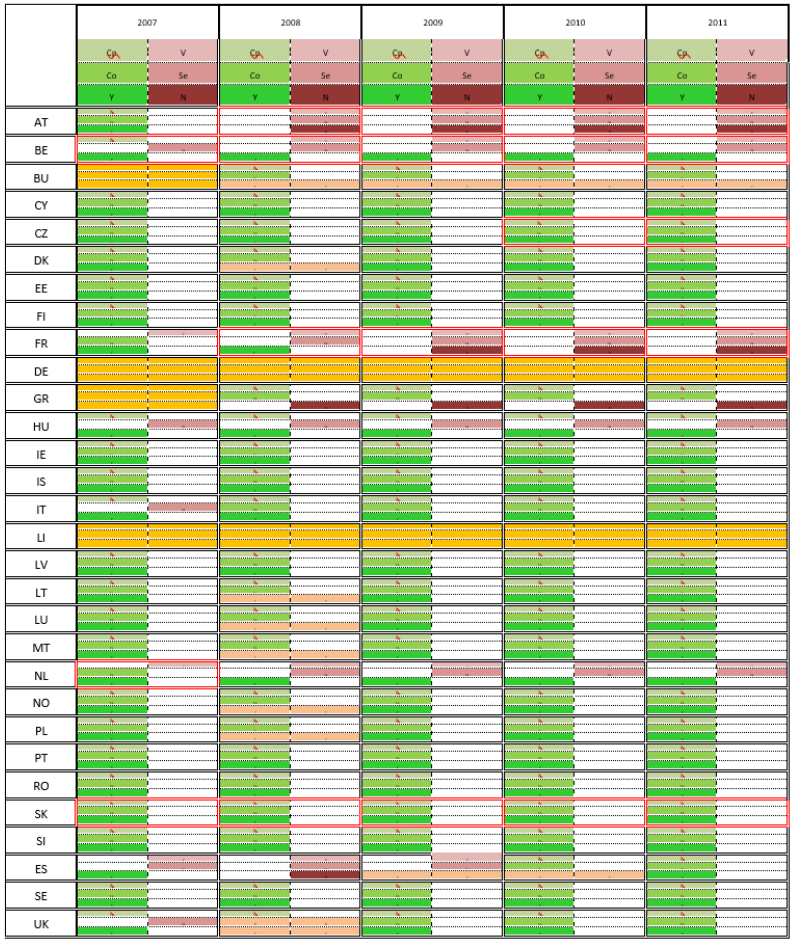
Assessing data availability and quality

	2007 (5/2/08)	2008 (7/1/09)	2009 (15/1/10)	2010 (22/3/11)	2011
AT	EU Case Def.	EU Case Def.	EU 2008	EU 2008	EU 2008
BE	EU Case Def.	EU Case Def.			Unknown
BU			EU 2002	EU 2002	EU 2002
CY	EU Case Def.	EU Case Def.	EU 2002	EU 2008	EU 2008
CZ	Other	Other	Other	Other	EU 2008
DK	Other	Other	Other	Other	Other
EE	EU Case Def.	EU Case Def.	EU Case Def.	EU 2008	EU 2008
EL			EU 2008	EU 2008	EU 2008
FI	EU Case Def.	EU Case Def.			Unknown
FR	Other	EU Case Def.	EU Case Def.		Unknown
DE					
HU	EU Case Def.	EU Case Def.		EU 2008	EU 2008
IE	EU Case Def.	EU Case Def.	EU 2002	EU 2002	EU 2002
IS	EU Case Def.		EU 2008	EU 2008	EU 2008
IT		EU Case Def.		Other	Other
LV	EU Case Def.	EU Case Def.	EU 2008	EU 2008	EU 2008
LIE					
LT	EU Case Def.	EU Case Def.			Unknown
LU	Unknown	Unknown	None	None	Unknown
MT	EU Case Def.	EU Case Def.	EU 2008	EU 2008	EU 2008
NL	Other	Other	Other	Other	Other
NO	EU Case Def.	EU Case Def.			Unknown
PL	EU Case Def.	EU Case Def.		Unknown	Unknown
PO	Other	Other	Other	Other	EU 2008
RO		EU Case Def.			
SK	EU Case Def.	EU Case Def.			
SI	EU Case Def.	EU Case Def.			
ES	EU Case Def.	EU Case Def.			
SE	Other	Other			
UK	Other	Other			

DATA AVAILABILITY

YEARS	Countries that did not report	Countries that reported nil cases	Countries that report but for which we do not have the incidence	Countries that report aggregated cases
2007	DE; LI		AU; BE; CY; FR; HU; IT; NL;	HU; IE
2008	DE; LI		AU; BE; CY; FR; HU; IT; NL;	BU; GR; HU; IE; PL; RO; UK
2009	DE; LI		AU; BE; CY; FR; HU; IT; NL;	BU; GR; HU; IE; RO; ES
2010	DE; LI		AU; BE; CY; FR; HU; IT; NL;	BU; GR; HU; IE; RO; ES; UK
2011	DE; LI		AU; BE; CY; FR; HU; IT; NL;	BU; GR; HU; IE; RO; ES; UK

SURVEILLANCE OVERVIEW



Cp= compulsory, V=voluntary, Co=comprehensive, Se=Sentinel, Y=national coverage, N=non-national coverage. Red frame: Active surveillance system. Yellow-filled square: no data.

Source: Annual epidemiological report (2009-201

Assessing rates and correcting for under-estimation

RATE OF DISEASE IN EU/EEA 2007-2011.

Countries	2007	2008	2009	2010	2011	Rate average	MFs	Real incidence
EEA	10.6	9.6	9.9	10.4	10.54	10.21	1.01-3.85	10.31-39.30
AT								
BE	5.31*1.63= 8.65	6.52*1.63= 10.6	6.46*1.63= 10.52	7.04*1.63= 11.47	7.65*1.63= 12.46	10.74	1.01-3.85	10.8-41.76
BU	1.9	2.3	2.5	1.5	2.62	2.16	1.01-3.85	2.19-8.33
CY	0.44*2-4= 0.88-1.76	0.17*2-4= 0.34-0.64	0.62*2-4= 1.24-2.48	2.05*2-4= 4.1-8.2	0.98*2-4= 1.9-3.8	1.7-3.4	1.01-3.85	1.7-6.54
CZ	10.8	7.8	6.8	7.1	6.68	7.84	1.01-3.85	7.91-30.17
DK	6.5	7.5	10.2	8.7	9.01	8.38	1.01-3.85	8.47-32.27
EE	13.1	10.9	9.4	8.1	12.39	10.78	1.01-3.85	10.89-41.5
FI	3.6	3.7	4.4	4.8	5.38	4.38	1.01-3.85	4.42-16.85
FR								
DE								
GR	1.8	1.9	1.5	2.8	3.34	2.27	1.01-3.85	2.29-8.73
HU								
IE	9.7	10.1	9.7	13.7	13.99	11.44	1.01-3.85	11.55-44.04
IS	7.8	7.9	14.7	5.7	5.67	8.35	1.01-3.85	8.44-32.16
IT	1*10= 10	0.86*10= 8.6	1.16*10= 11.6	0.65*10= 6.5	0.66*10= 6.6	8.66	1.01-3.85	8.7-33.67
LIE								
LV	29.4	22	19.1	15.3	15.52	20.26	1.01-3.85	20.47-78.02
LT	13.9	15.8	11.7	9.5	9.46	12.07	1.01-3.85	12.19-46.48
LU	0.2	3.7	1.2	0.6	0.6	1.26	1.01-3.85	1.27-4.85
MT	12.8	12.2	15	11.4	11.5	12.58	1.01-3.85	12.71-48.43
NL								
NO	5.1	6.4	5.6	8.5	8.48	6.82	1.01-3.85	6.88-26.24
PL	0.9	0.7	1.1	0.8	0.79	0.86	1.01-3.85	0.87-3.3
PT	0.7	0.6	1.1	0.8	0.84	0.81	1.01-3.85	0.82-3.11
RO*see notes	3.8	2.9	2.9	2.2	2.23	2.81	1.01-3.85	2.83-10.8
SK	1.5	2.8	3.2	2.3	2.43	2.45	1.01-3.85	2.47-9.42
SI	2.1	2	1.5	2.1	2.15	1.97	1.01-3.85	1.99-7.58
ES	3.8	4.2	4.3	4.2	5.01	4.3	1.01-3.85	4.35-16.56
SE	7	7.9	6.6	9	9.08	7.92	1.01-3.85	8-30.48
UK*see notes	30.7	26.9	28.2	30	29.95	29.15	1.01-3.85	29.44-112.23

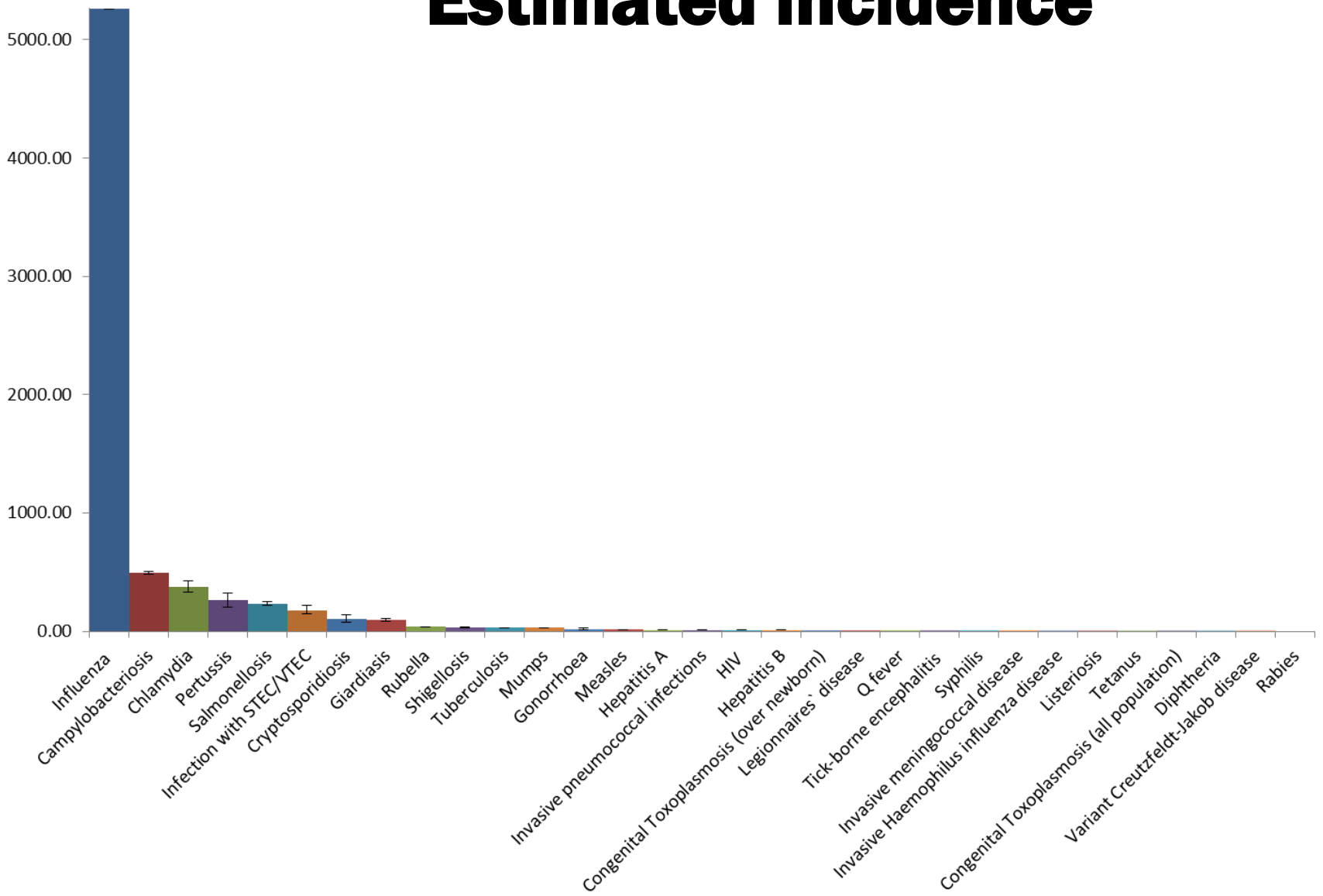
CORRECTING FOR UNDER-ASCERTAINMENT AND UNDER-REPORTING:

EXCLUSION CRITERIA:

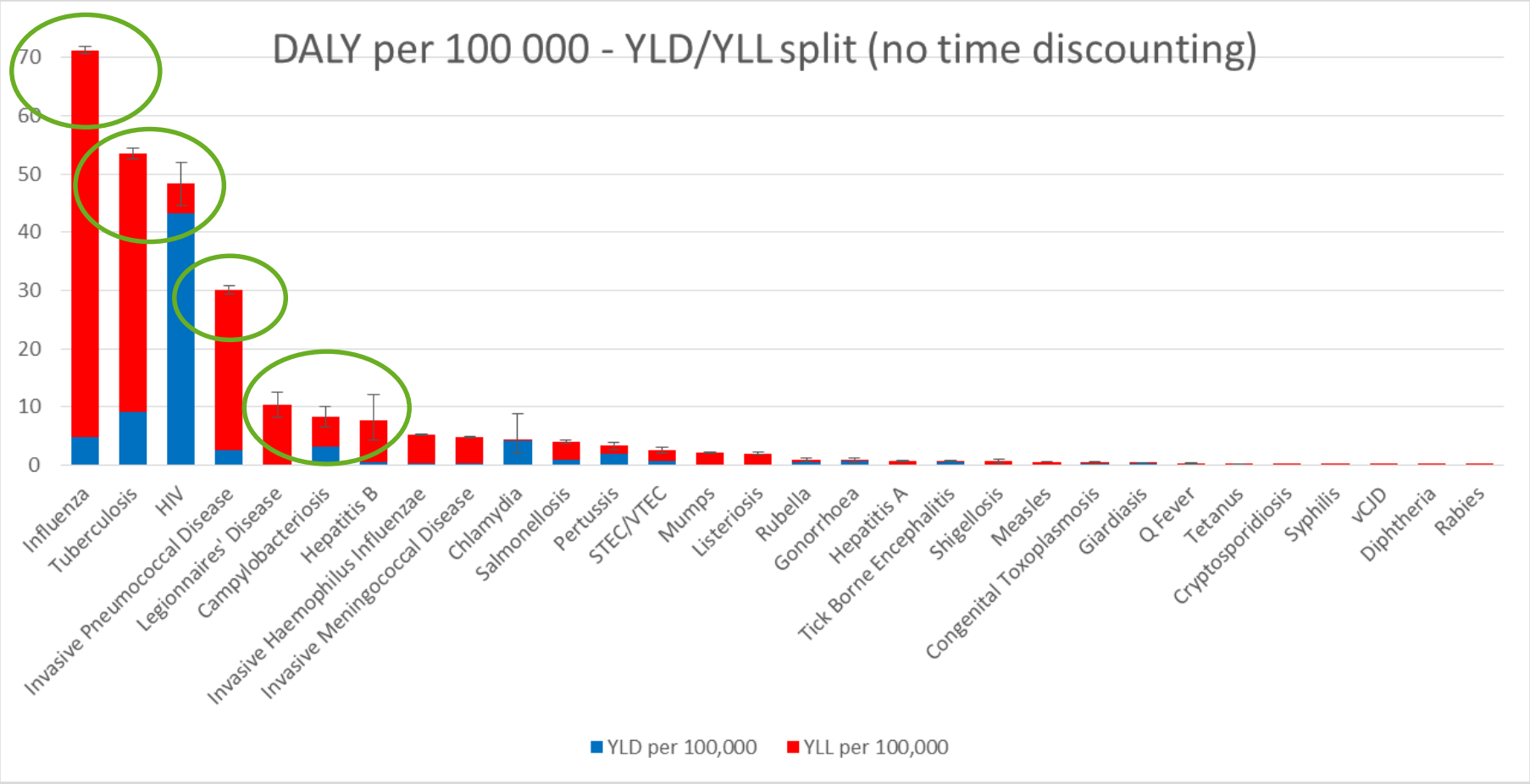
- Studies published before 2000
- Studies using data from the '80 or before
- Studies not conducted in Europe

N'	Criteria	Article		Appraisal
13	☺	•No information on UR: France, Germany, Netherlands •Low rate of reporting: Austria •Very low rate of reporting: Belgium, Portugal, Spain Country: estimated reporting; MF •Denmark: 26-50%; **MF = 2-3.85** •Finland: 76-99%; **MF = 1.01-1.32** •Greece: 51-75%; **MF = 1.33-1.96** •Ireland: 76-99%; **MF = 1.01-1.32** •Italy: 26-50%; **MF = 2-3.85** •Norway: 76-99%; **MF = 1.01-1.32** •Sweden: 76-99%; **MF = 1.01-1.32** United Kingdom: 76-99%; **MF = 1.01-1.32**	**Lowndes' study (Pub 2004; European Union)** **Surveillance systems for STI'S in the European Union: facing a changing epidemiology** **Study aim:** To characterize the nature, content, and performance characteristics of existing national STI surveillance systems in the EU and Norway, to facilitate collection of comparable surveillance data •Study was carried out as part of a European Commission funded project on European Surveillance of STIs •Cross sectional survey in 14 member states of the EU and Norway using a structured questionnaire (November 2002 – July 2003) •Coverage of case reporting by mandatory STI case reporting systems was investigated **Pro:** •Data on underreporting for different countries in Europe **Con: (?)** **MY COMMENTS:** Study carried out as a part of a european commission funded project on European surveillance of STI. Limitations: it does not include UA of symptomatic cases and does nor the component of UR that referred to mis-diagnosis. Another weakness is the lack of clear description from where data on sensitivity of SS come from.	☺
16	☹	**MF UR (NNS) (4,902/1,425) = 3.44** CI [3.01-3.87] **MF UR (STD-MHS) (4,902/917) = 5.34** CI [4.68-6.02]	**Reintjes' study (Pub in 1999; Netherlands)** **Assessgin the sensitivity of STD surveillance in the Netherlands: an application of the capture-recapture method** **Study aim:** To assess the sensitivity of two national STD surveillance system of the country •Capture-recapture method was used to estimate the sensitivity of gonorrhoea case finding in two STD surveillance systems: (1) STD registration at municipal health services (STD-MHS), (2) statutory notification by clinicians (NNS) •National notification system (NNS) is based on statutory notification by general practitioners and physicians •Confirmed cases are notified anonymously; cases have to be confirmed by laboratory testing •STD registration at MHS is based on voluntary data collection by public-health nurses working in STD control in MHS and six STD clinics •Cases are defined on the basis of the diagnosis made by a medical doctor •Gonorrhoea cases are confirmed by laboratory test •1,425 cases of Gonorrhoea were notified in the NNS vs. 917 cases notified in STD-MHS; based on 162 matches a total number of 4,902 actual cases (95% CI: 4,288-5,518) with gonorrhoea were estimated **Pro:** •European study •capture-recapture analysis **Con:** •only two source capture-recapture	:/
3	☹	**Women: MF UA asymptomatic (100/40) = 2.50**	**Borges-Costa's study (Pub 2011;Portugal)** **Sexually transmitted infections in pregnant adolescents: prevalence and association with maternal and foetal morbidity** **Study aim:** To assess the prevalence of sexually transmitted infections in pregnant adolescents and the associations between these infections and adverse birth outcomes •Assessment of the prevalence of gonorrhoea and chlamydia during pregnancy in a population of pregnant adolescents (11-19 years) in Lisbon, Portugal (n=204) •60% of cases were asymptomatic **Pro:** •European study **Con:** •Only pregnant adolescents (STI prevalence in teenagers is higher in those that are pregnant)	☹ **The populati on is not represen tative of the country**
4	☹	**Men: MF UA asymptomatic (100/21) = 4.76**	**Forni's study (Pub 2009, UK)** **Microscopy detection of rectal gonorrhoeae in asymptomatic men** **Study aim:** To determine the usefulness of microscopy to detect presumptive rectal gonorrhoea infection in asymptomatic men who have sex with men (MSM) •Retrospective audit of health records (January 2005 to March 2007) •Data from MSM attending a central London genitourinary medicine clinic (n=300) •79% of cases reported no symptoms **Pro:** •European study **Con:** •Only MSM	:/ **Populati on is not represen tative**
6	☺	**Men: MF UA asymptomatic (100/90) = 1.11**	**Pittrof's study (Pub 2009; UK)** **Questioning the value of screening for gonorrhoeae in symptomless heterosexual men** **Study aim:** To discuss whether gonorrhoea screening of asymptomatic heterosexual men with no contact history should continue in UK genitourinary clinics •Health Protection Agency Data •STI-screenings for	☹

Estimated incidence



Results from BCoDE 2009-2013 (no time discounting)



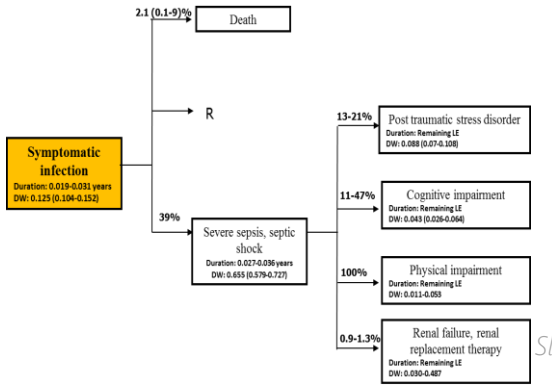
Cassini A, Colzani E, Pini A, Mangen M-JJ, Plass D, McDonald SA, et al. Impact of infectious diseases on population health using incidence-based disability-adjusted life years (DALYs): results from the Burden of Communicable Diseases in Europe study, European Union and European Economic Area countries, 2009 to 2013. Eurosurveillance. 2018;23(16):17-00454.

Is it possible to estimate the burden of HAIs?

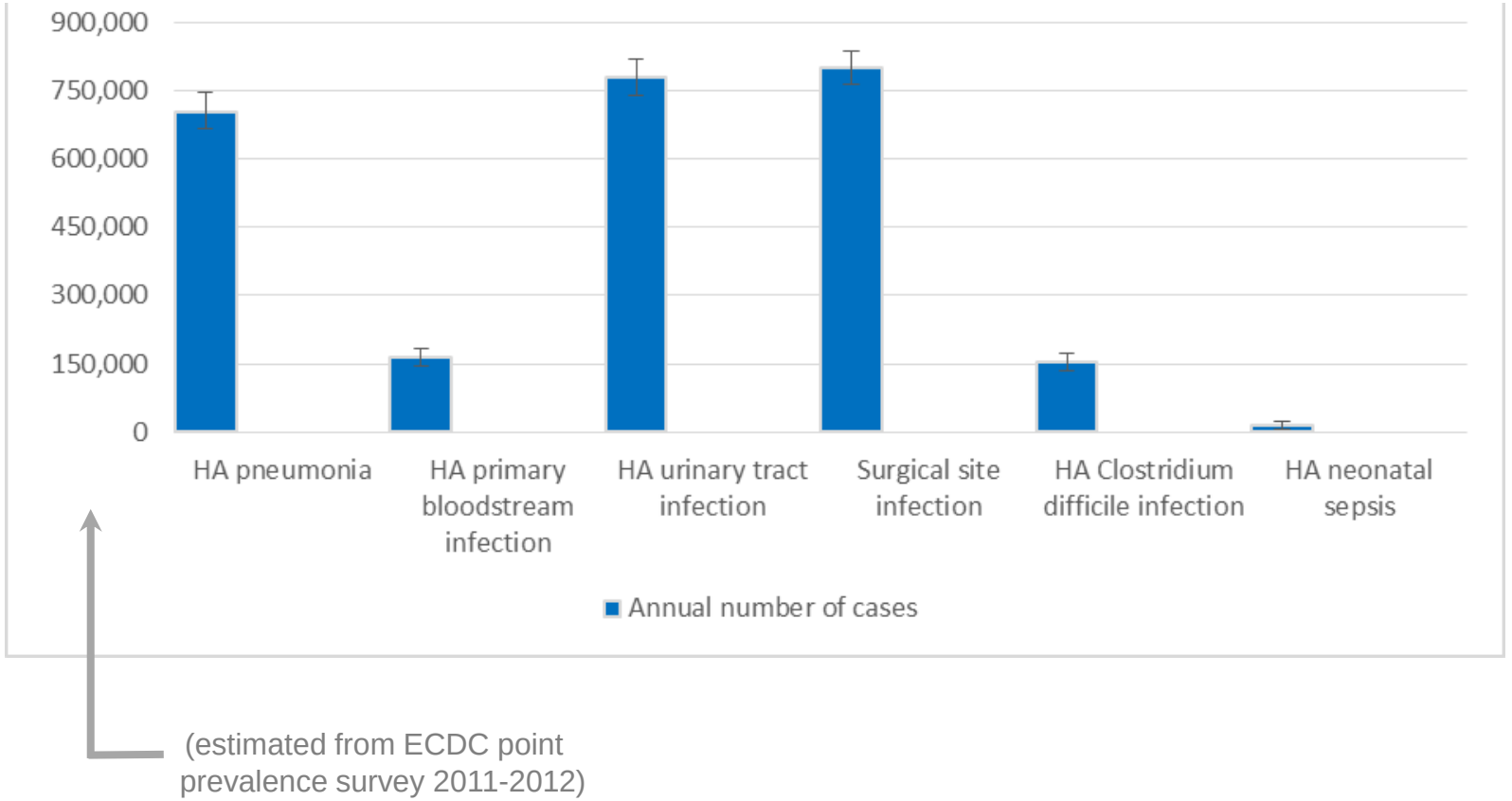
- HAIs are always associated with comorbidities that contribute to morbidity and mortality
- Administrative hospital discharge data do not accurately reflect the burden of HAIs
- The burden of HAIs has not been studied adequately despite a significant proportion being preventable

Methodology builds on a number of studies + specific adjustments

- Attributable mortality, sequelae and length of stay: Systematic review of the literature. Berlin: RKI; 2016. http://www.rki.de/DE/Content/Institut/OrgEinheiten/Abt3/FG37/Research_Report_BHAI.pdf?__blob=publicationFile
- Incidence data: Age-group and sex prevalent number of HAIs from the PPS converted into annual incidence rates applying the Rhame and Sudderth formula. Point prevalence survey of Healthcare-associated infections and antimicrobial use in European acute care hospitals. Stockholm: ECDC; 2013.
- Adjusting for impact of co-morbidities on life expectancy: Standard life expectancy table. McCabe score stratification of cases according to remaining life expectancy; comparison with standard life expectancy

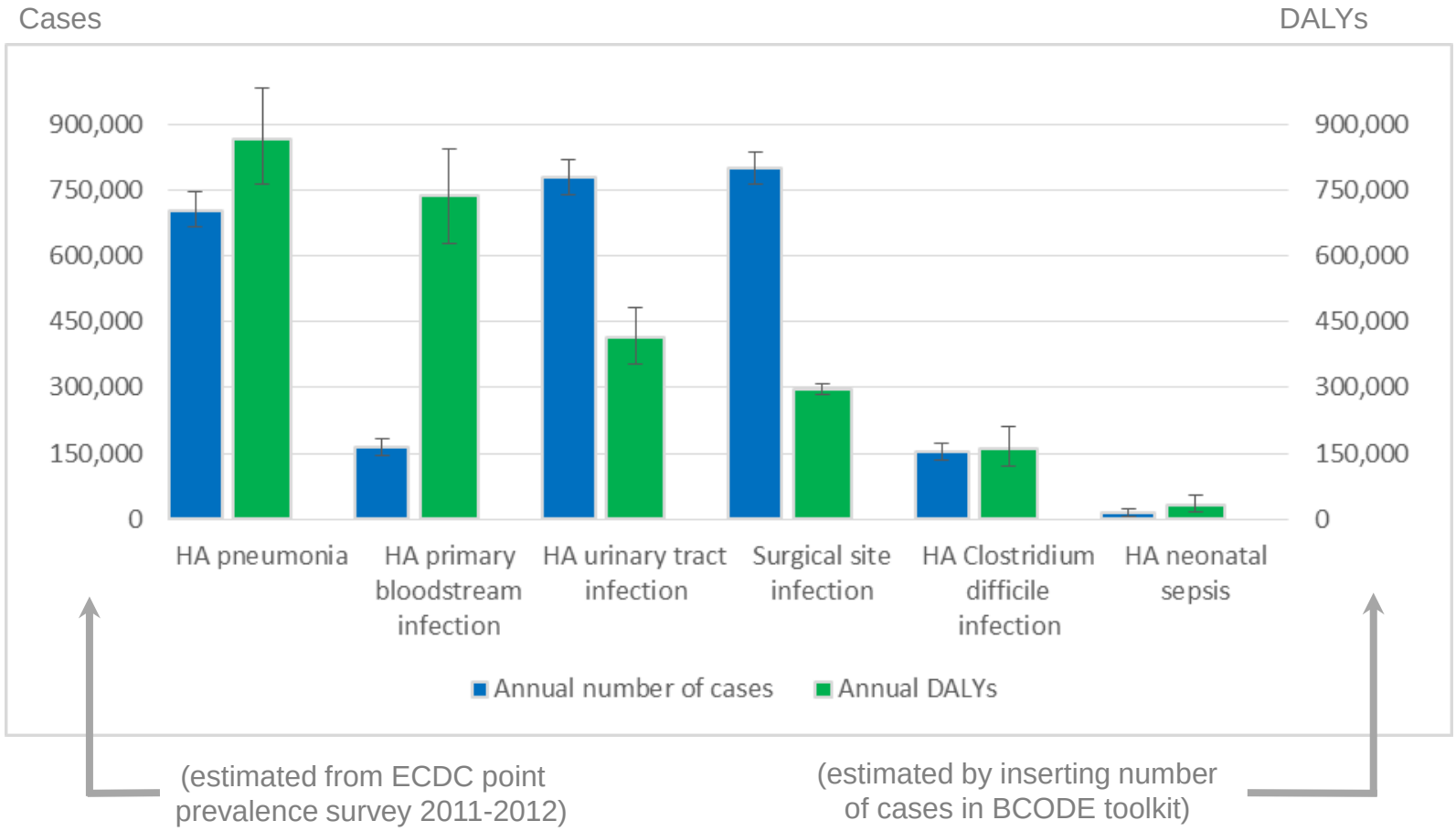


- Age-group and sex prevalent number of HAIs from the PPS was converted into annual incidence rates applying the Rhame and Sudderth formula
- 2.6 million annual number of cases of HAIs estimated in the EU/EEA (95% UI: 1,624,140 - 4,084,550)



Cassini A and Plachouras D, Eckmanns T, Abu Sin M, Blank H-P, Ducomble T, et al. Burden of Six Healthcare-Associated Infections on European Population Health: Estimating Incidence-Based Disability-Adjusted Life Years through a Population Prevalence-Based Modelling Study. PLoS medicine. 2016;13(10):e1002150.

- 2.6 million annual number of cases of HAIs are associated with more than 91,000 deaths (76,000 to 108,000)
- Incidence and prevalence do not provide the full picture



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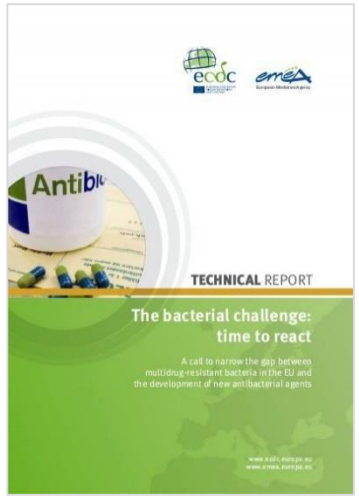
Objectives of the study

To provide estimates of:

- Incidence
- Attributable deaths
- Attributable length of hospital stay
- Impact on the health of the population

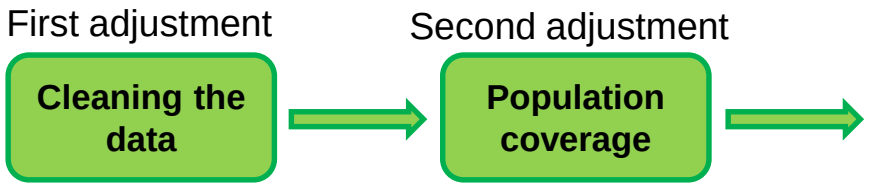


of infections with antibiotic-resistant bacteria

To refresh previous estimates ("Time to react") and improve methodology

- Based on EARS-Net data 2015
- All EU/EEA countries

Estimating incidence

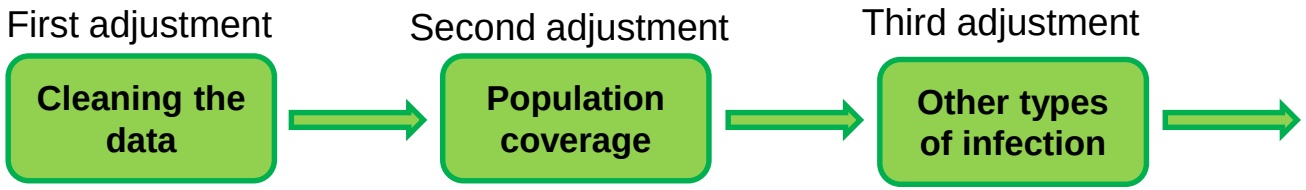


1. EARS-Net age-group and sex-specific number of cases, per country. Unknown age and sex were re-distributed
2. National designated collaborator provided a country coverage factor for each bacterium

Country	*S. pneumoniae*	*S. aureus*	*Enterococci*	*E. coli*	*K. pneumoniae*	*P. aeruginosa*	*Acinetobacter* spp
Austria	90	90	90	90	90	90	90
Belgium	87	24	24	24	23	24	8
Bulgaria	28-29-30	28-29-30	28-29-30	28-29-30	28-29-31	28-29-32	28-29-33
Cyprus	82.5-85-87.5	82.5-85-87.	82.5-85-87.5	82.5-85-87	82.5-85-87.5	82.5-85-87.5	82.5-85-87.5
Czech Republic	90	85	85	85	85	85	85
Germany	20-25-30	20-25-30	20-25-30	20-25-30	20-25-30	20-25-30	20-25-30
Denmark	100	100	100	100	100	100	100
Estonia	100	100	100	100	100	100	100
Greece	NA	57	54	60	53	52	60
Spain	27.8-31.05-34.3	27.8-31.05-	27.8-31.05-34	27.8-31.05	27.8-31.05-34.3	27.8-31.05-34.3	27.8-31.05-34.3
Finland	97-98-99	97-98-99	98-99-100	97-98-99	97-98-99	98-99-100	94-95-96
France	67.2	12.6-18-18	12.6-18-18	12.6-18-18	12.6-18-18	12.6-18-18	12.6-18-18
Croatia	85-90-95	85-90-95	85-90-95	85-90-95	85-90-95	85-90-95	85-90-95
Hungary	90	90	90	90	90	90	90
Ireland	97	97	97	97	97	97	97
Iceland	100	100	100	100	100	100	100
Italy	10-15-20	10-15-20	10-15-20	10-15-20	10-15-20	10-15-20	10-15-20
Lithuania	90	90	90	90	90	90	90
Luxembourg	100	100	100	100	100	100	100
Latvia	90	90	90	90	90	90	90
Malta	95	95	95	95	95	95	95
Netherlands	65	65	65	65	65	65	65
Norway	100	100	100	100	100	100	100
Poland	14	14	14	14	14	14	14
Portugal	95	96.1	96	95.2	96.5	95.3	91.2
Romania	12-15-17	12-15-17	12-15-17	12-15-17	12-15-17	12-15-17	12-15-17
Sweden	75-77.5-80	75-77.5-80	75-77.5-80	75-77.5-80	75-77.5-80	75-77.5-80	60
Slovenia	99.1	97.9	98.8	99.3	99.6	97.9	100
Slovakia	75	75	75	75	75	75	75
United Kingdom	21	26	12	12	12	12	12

Estimated population country coverage per organism

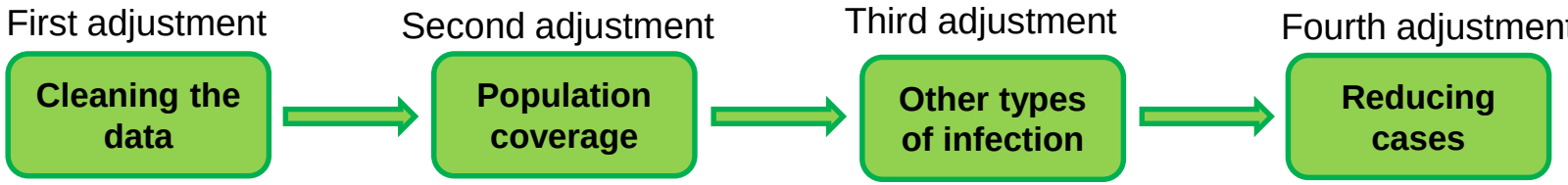
Estimating incidence



1. EARS-Net age-group and sex-specific number of cases, per country. Unknown age and sex were re-distributed
2. National designated collaborator provided a country coverage factor for each bacterium
3. Applying a BSI to non-BSI ratio – from PPS 2011-2012 (except for *S. pneumoniae*)

Colistin-/carbapenem/third generation cephalosporin-resistant *E. coli**			
	Ratio	Lower CI	Upper CI
BSI	1.00	0.74	1.56
UTI	4.68	2.10	7.25
RESP	0.53	0.08	0.97
SSI	1.24	0.43	2.05
OTH	0.60	0.14	1.07

Estimating incidence



1. EARS-Net age-group and sex-specific number of cases, per country. Unknown age and sex were re-distributed
2. National designated collaborator provided a country coverage factor for each bacterium
3. Applying a BSI to non-BSI ratio – from PPS 2011-2012 (except for *S. pneumoniae*)
4. Reduce the number of non-BSIs according to risk of S-BSI (to avoid double-counting)

Colistin-/carbapenem-resistant *E. coli*	
BSI	1
UTI	0.25
RESP	0.00
SSI	0.00
OTH	0.00

Determining attributable mortality and attributable length of stay

Systematic literature review

>360 publications identified

- Infection type specific
- Bug-drug specific

Criteria scoring

All papers were scored

- Study type
- Sample size
- Representativeness
- Matching
- Controlling for confounders

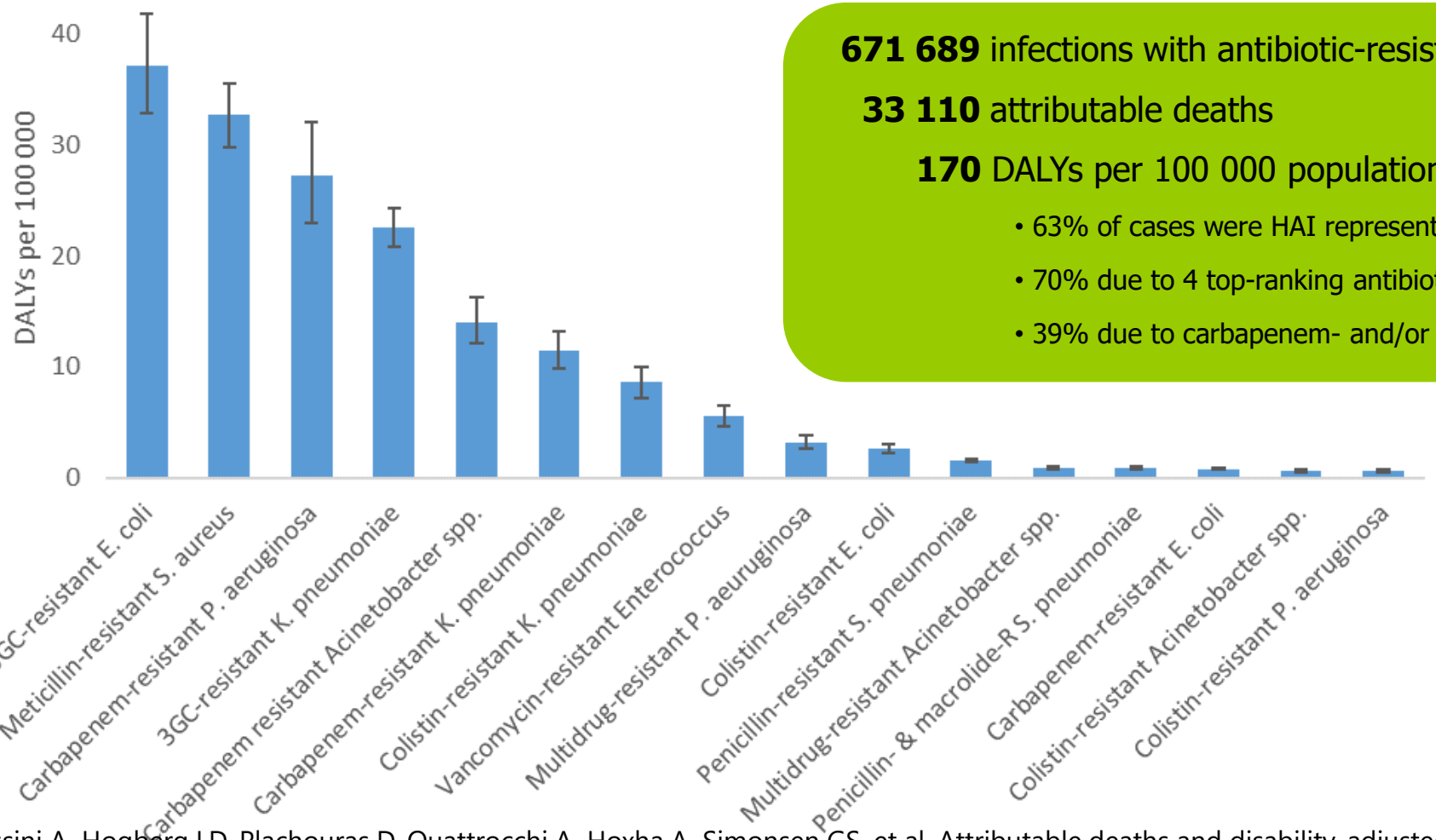
Final decisions

Final disease models

- Built on consensus
- Baseline models from HAIs

	Baseline model	*Klebsiella pneumoniae*			*Escherichia coli*			*Acinetobacter* spp.			*Pseudomonas aeruginosa*			*Staphylococcus aureus*	*Enterococcus faecalis* and *E. faecium*	*Streptococcus pneumoniae*	
		3GCRKP	CRKP	ColRKP	3GCREC	CREC	ColREC	MDRACI	CRACI	ColRACI	MDRPA	CRPA	ColRPA	MRSA	VRE	PRSP	PMRSP
BSI																	
Case fatality proportion (%)	7.1-20.3	14.4-19	20-51.3	32-88.8	17.1 (9.5-26)	20-51.3	32-88.8	7.1-32.9	7.1-34	7.1-34	7.1-35.2	7.1-38.7	7.1-38.7	17.9 (14.4-21.8)	22.9 (21.8-23.8)	15.7-20.3	15.7-20.3
Duration (days)	5.87-11.5	9.28 (9.20–9.35)	15-35	15-39.1	6-18.5	15-35	15-39.1	5.87-20.1	5.87-20.1	5.87-20.1	14.87-21.5	14.87-21.5	14.87-21.5	8.99-14.62	6.97-18.3	Baseline	Baseline
RESP																	
Case fatality proportion (%)	3.6 (2.7-4.5)	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	2.7-9.8	2.7-10.5	2.7-10.5	Baseline	Baseline	Baseline	Baseline
Duration (days)	7-14	13.6-18.1	13.6-18.1	13.6-18.1	Baseline	13.6-18.1	13.6-18.1	Baseline	Baseline	Baseline	10-17	15-22	15-22	Baseline	Baseline	Baseline	Baseline
UTI																	
Case fatality proportion (%)	0	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	N/A	N/A
Duration (days)	7 (4-11)	7 (5-12)	7.5 (4-14)	7.5 (4-14)	7 (5-12)	7.5 (4-14)	7.5 (4-14)	8 (4-11)	8 (4-11)	8 (4-11)	8 (4-11)	8 (4-11)	8 (4-11)	Baseline	Baseline	N/A	N/A
SSI																	
Case fatality proportion (%)	0.9<65; 3.6>64	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	N/A	N/A
Duration (days)	8.5 (0-15.2)	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	N/A	N/A
OTHER																	
Case fatality proportion (%)	0	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline	0	0
Duration (days)	6 (3-11)	12 (8-21)	12 (6-27)	12 (6-27)	12 (8-21)	12 (6-27)	12 (6-27)	14.5 (9-19)	14.5 (9-19)	14.5 (9-19)	14.5 (9-19)	14 (9-19)	14.5 (9-19)	12 (8-19)	Baseline	5-10	5-10

Estimated burden of infections with antibiotic-resistant bacteria, EU/EEA, 2015



671 689 infections with antibiotic-resistant bacteria

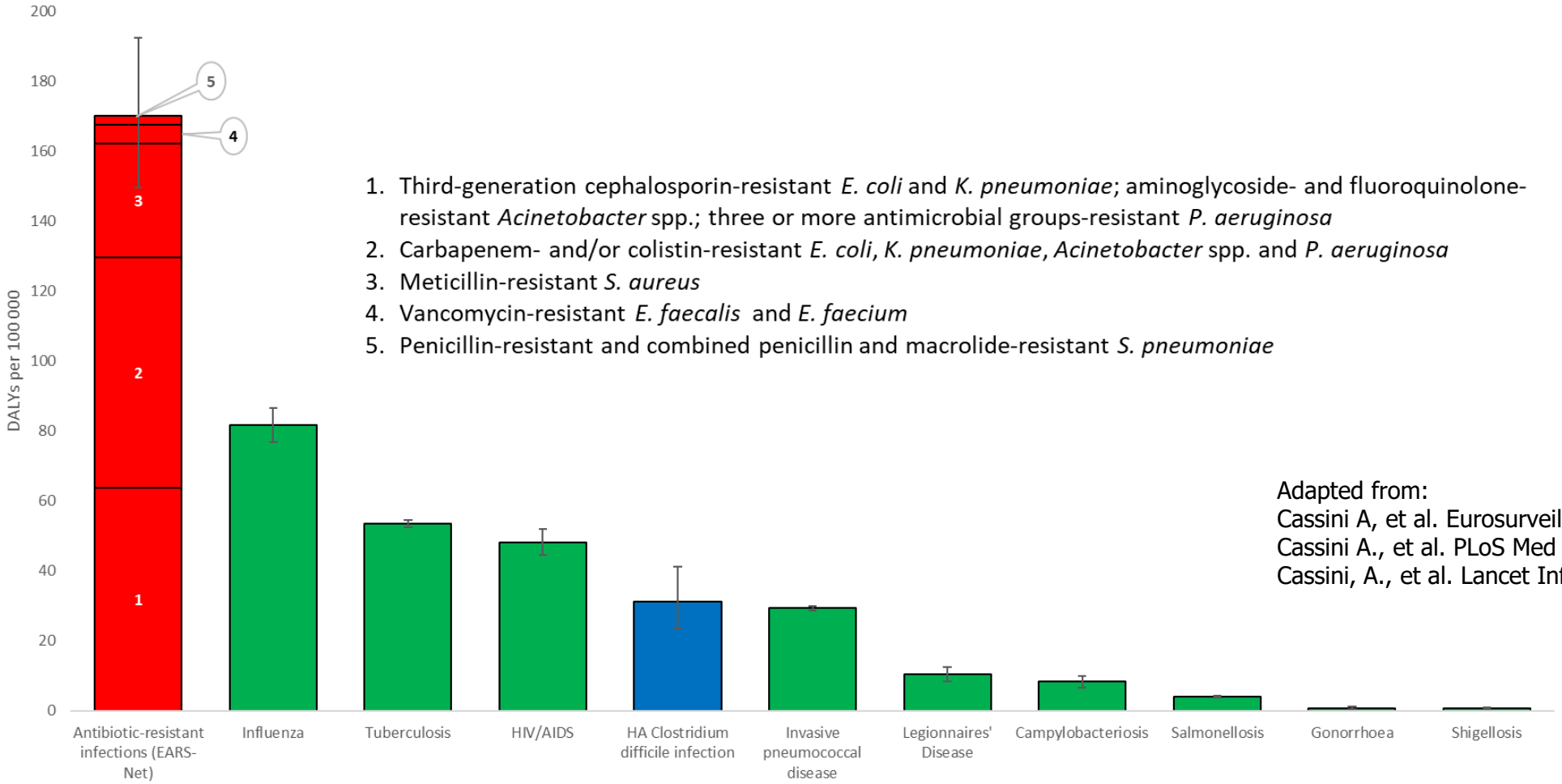
33 110 attributable deaths

170 DALYs per 100 000 population

- 63% of cases were HAI representing 75% of total burden (DALYs)
- 70% due to 4 top-ranking antibiotic-resistant bacteria
- 39% due to carbapenem- and/or colistin resistance

Cassini A, Hogberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS, et al. 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. Lancet Infect Dis. 2019;19(1):56-66.

Burden of AMR is comparable to the combined burden of influenza, TB & HIV/AIDS

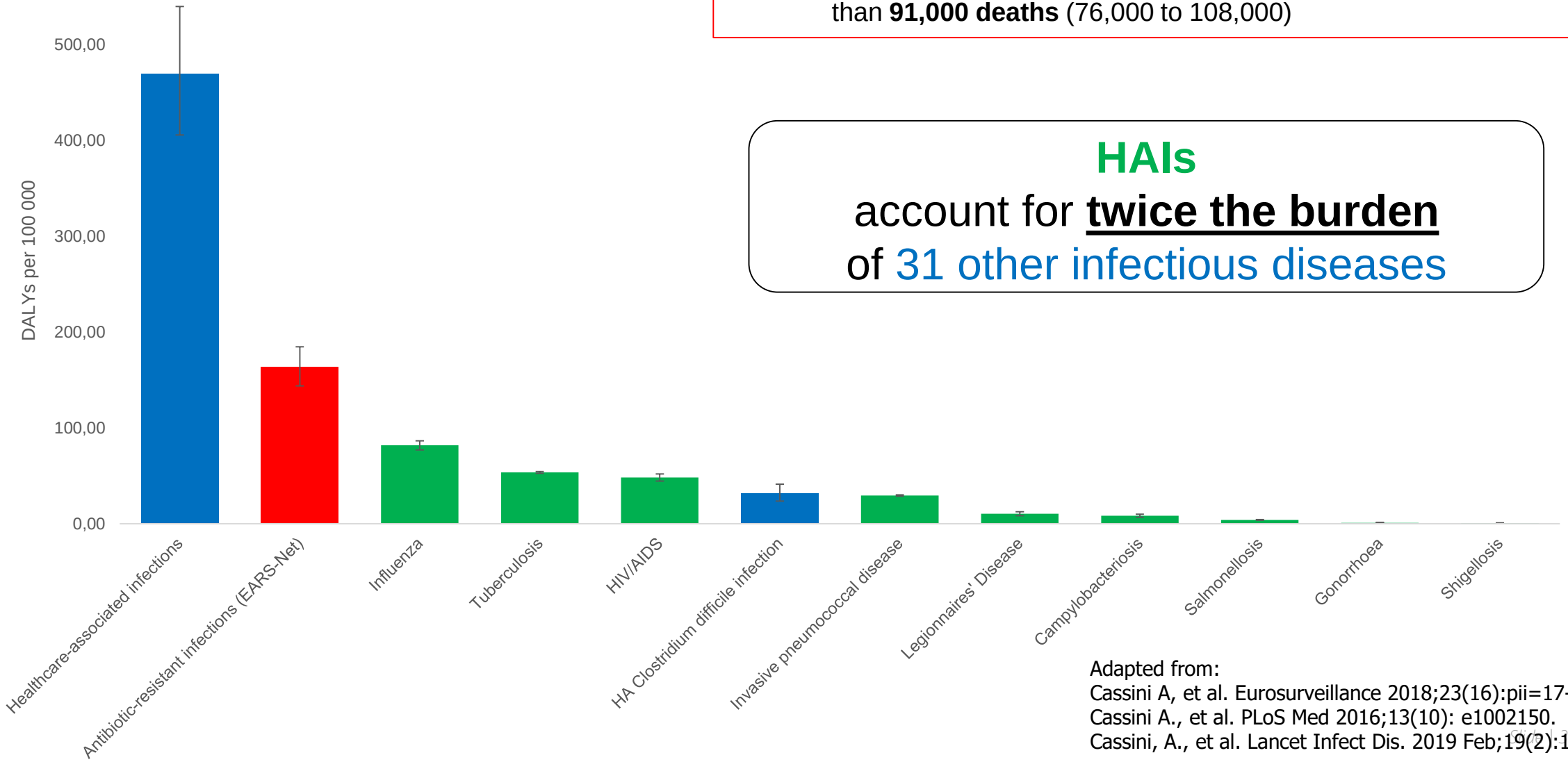


1. Third-generation cephalosporin-resistant *E. coli* and *K. pneumoniae*; aminoglycoside- and fluoroquinolone-resistant *Acinetobacter* spp.; three or more antimicrobial groups-resistant *P. aeruginosa*
2. Carbapenem- and/or colistin-resistant *E. coli*, *K. pneumoniae*, *Acinetobacter* spp. and *P. aeruginosa*
3. Meticillin-resistant *S. aureus*
4. Vancomycin-resistant *E. faecalis* and *E. faecium*
5. Penicillin-resistant and combined penicillin and macrolide-resistant *S. pneumoniae*

Adapted from:
Cassini A, et al. Eurosurveillance 2018;23(16):pii=17-00454
Cassini A., et al. PLoS Med 2016;13(10): e1002150.
Cassini, A., et al. Lancet Infect Dis. 2019 Feb;19(2):129-130.

Burden of HAIs

2.6 million annual number of cases of HAIs are associated with more than **91,000 deaths** (76,000 to 108,000)

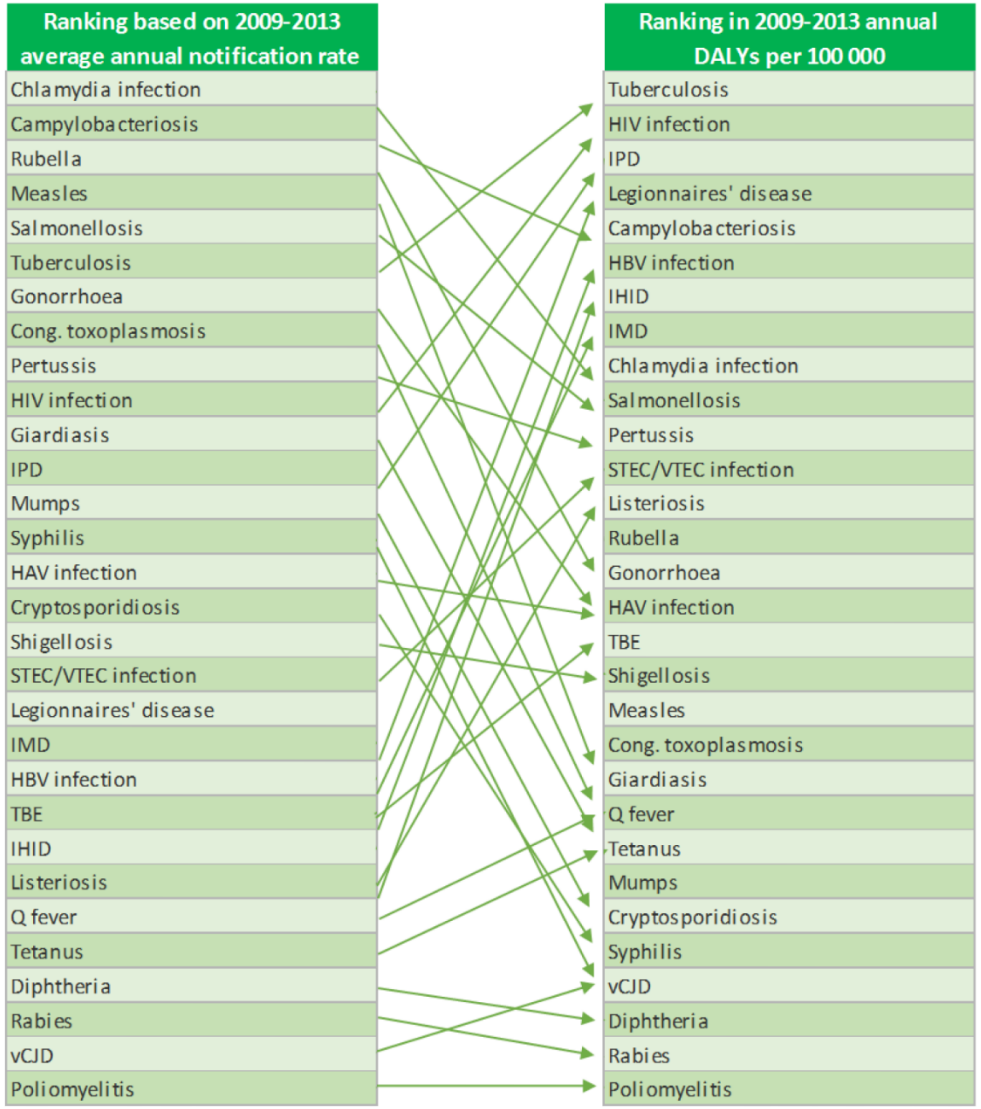


HAIs
account for **twice the burden**
of 31 other infectious diseases

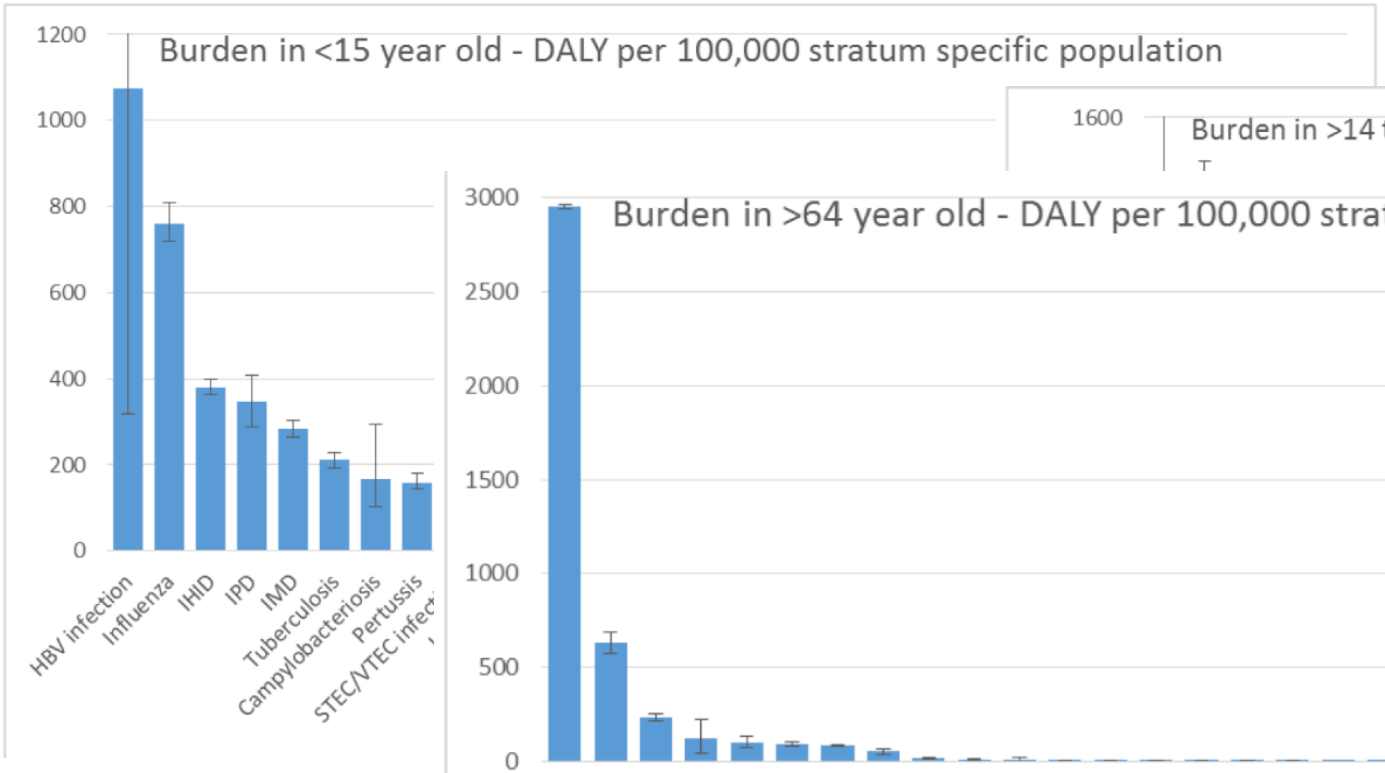
Adapted from:
Cassini A, et al. Eurosurveillance 2018;23(16):pii=17-00454
Cassini A., et al. PLoS Med 2016;13(10): e1002150.
Cassini, A., et al. Lancet Infect Dis. 2019 Feb;19(2):129-130.

Impact on action

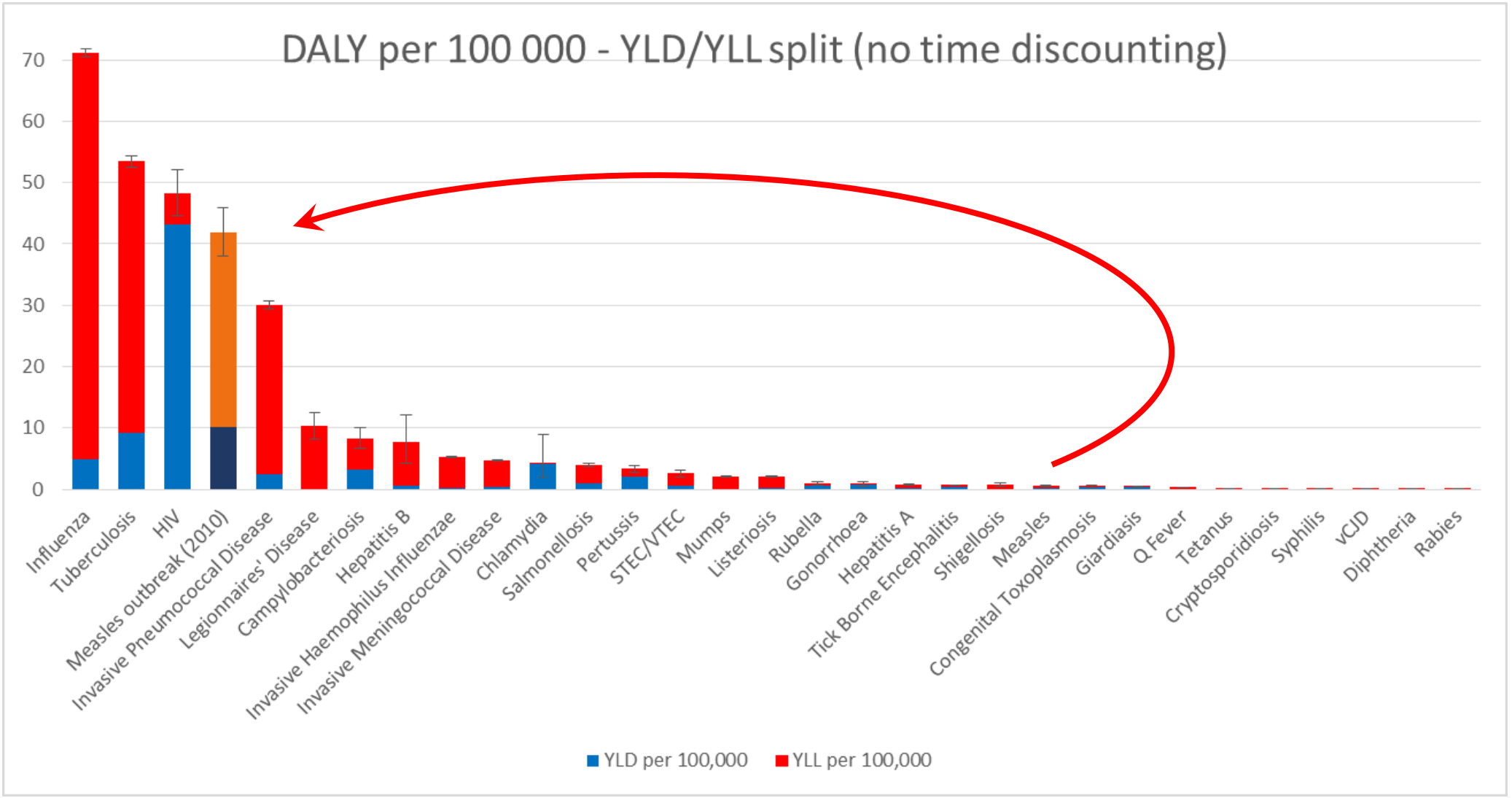
Ranking of diseases: all positions change



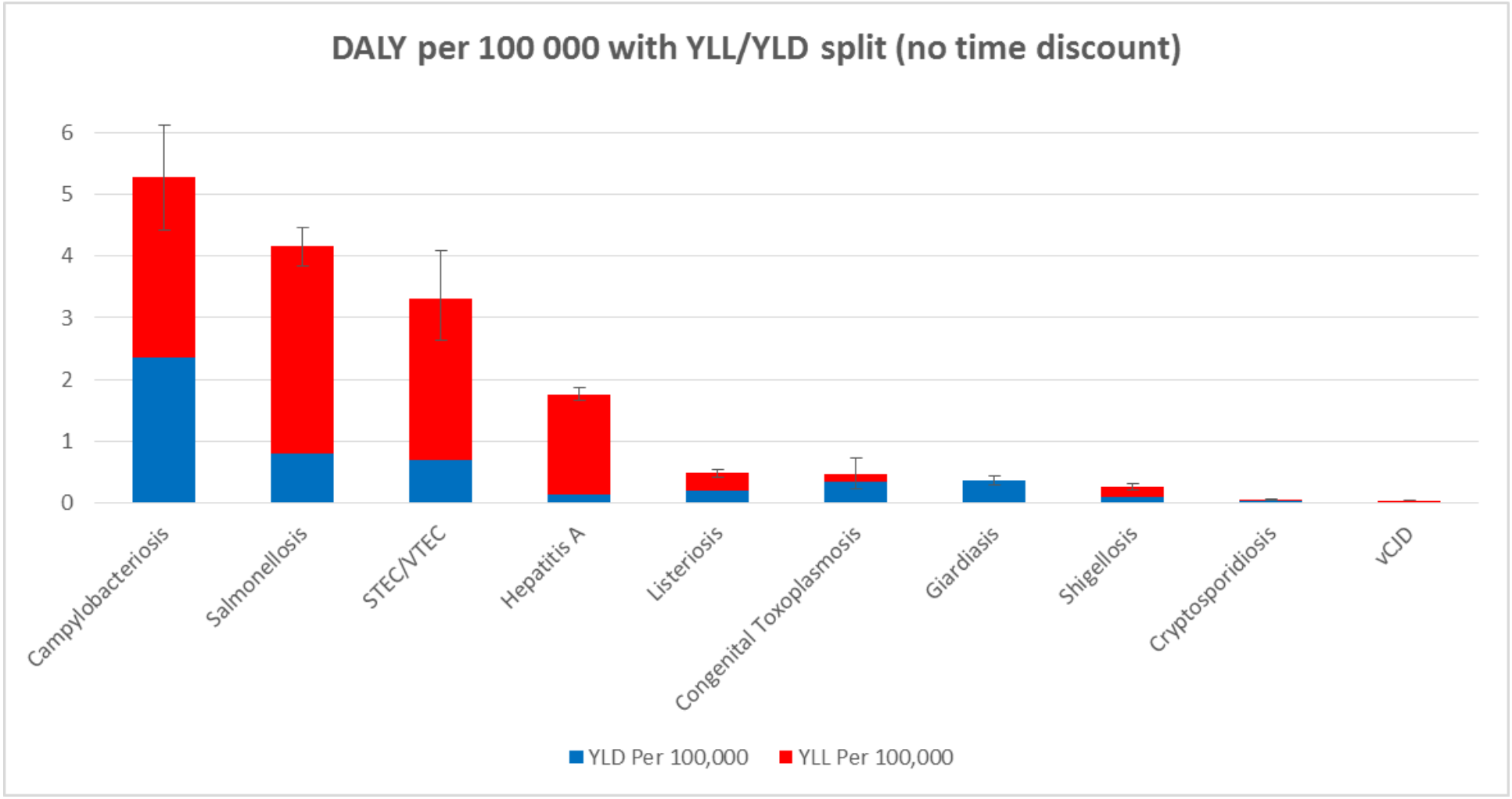
Splitting the population



Burden and outbreaks

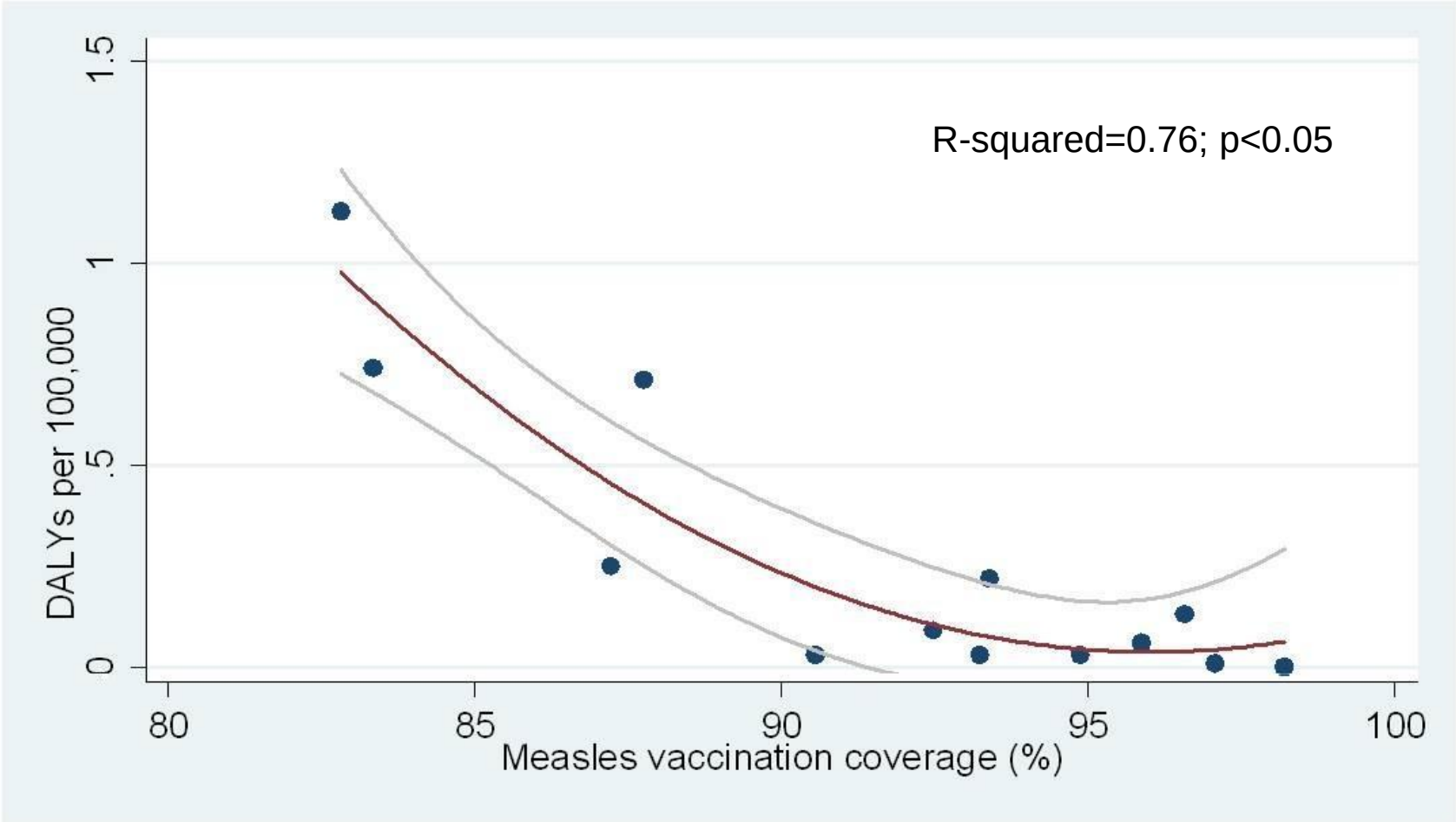


Campylobacteriosis has the highest impact amongst FWD



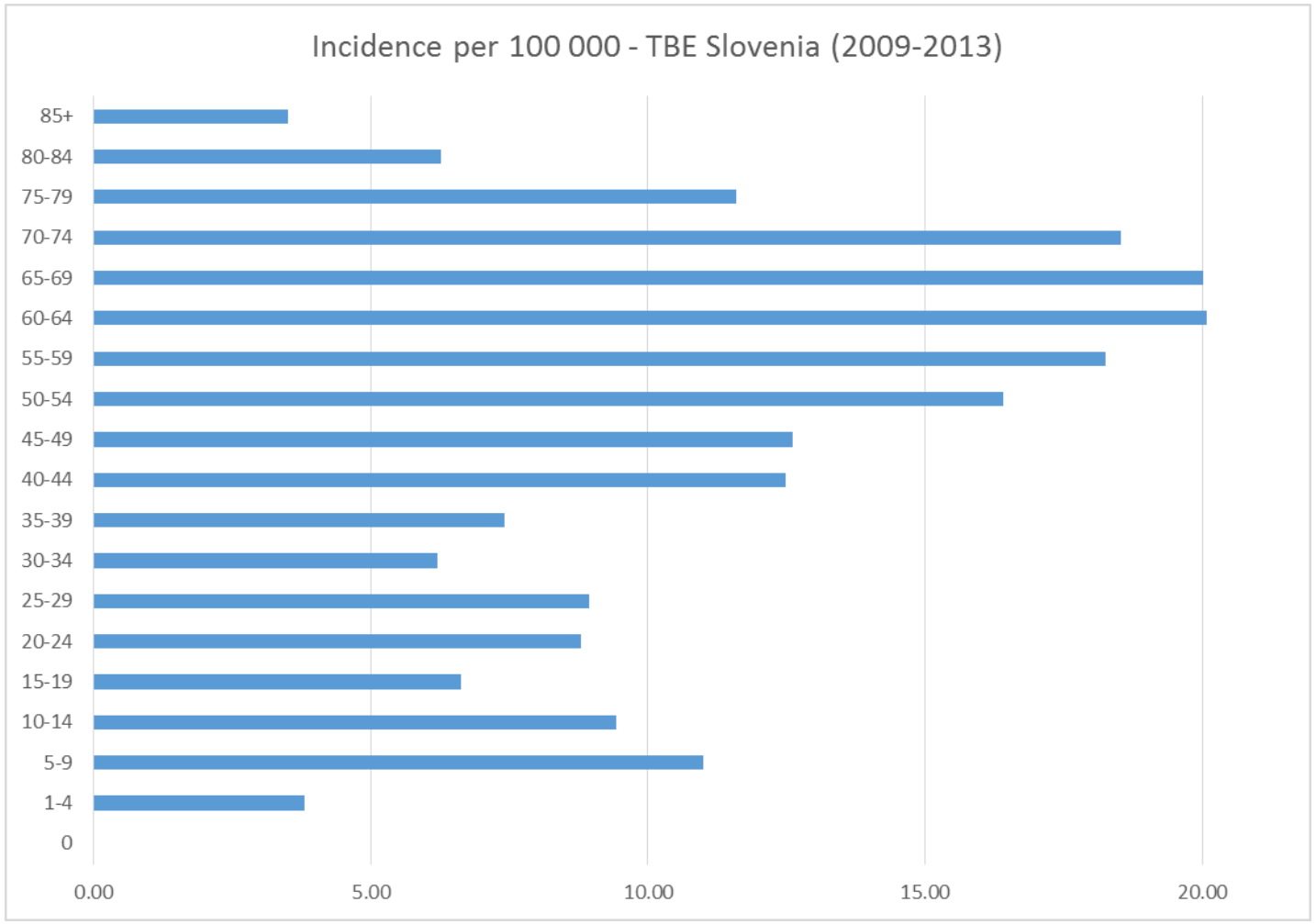
Cassini A, Colzani E, Kramarz P, Kretzschmar M, Takkinen J. Impact of food and water-borne diseases on European population health. Current Opinion in Food Science. 2016;12:21-9.

Quadratic correlation between vaccination coverage and burden of measles in different Member States



Colzani E, McDonald SA, Carrillo-Santisteve P, Busana MC, Lopalco P, Cassini A. Impact of measles national vaccination coverage on burden of measles across 29 Member States of the European Union and European Economic Area, 2006-2011. Vaccine. 2014 Feb 13. pii: S0264-410X(14)00157-1.

Tick-borne encephalitis in Slovenia



Fafangel M, Cassini A, Colzani E, Klavs I, Grgic Vitek M, Ucakar V, et al. Estimating the annual burden of tick-borne encephalitis to inform vaccination policy, Slovenia, 2009 to 2013. Euro Surveill. 2017;22(16).

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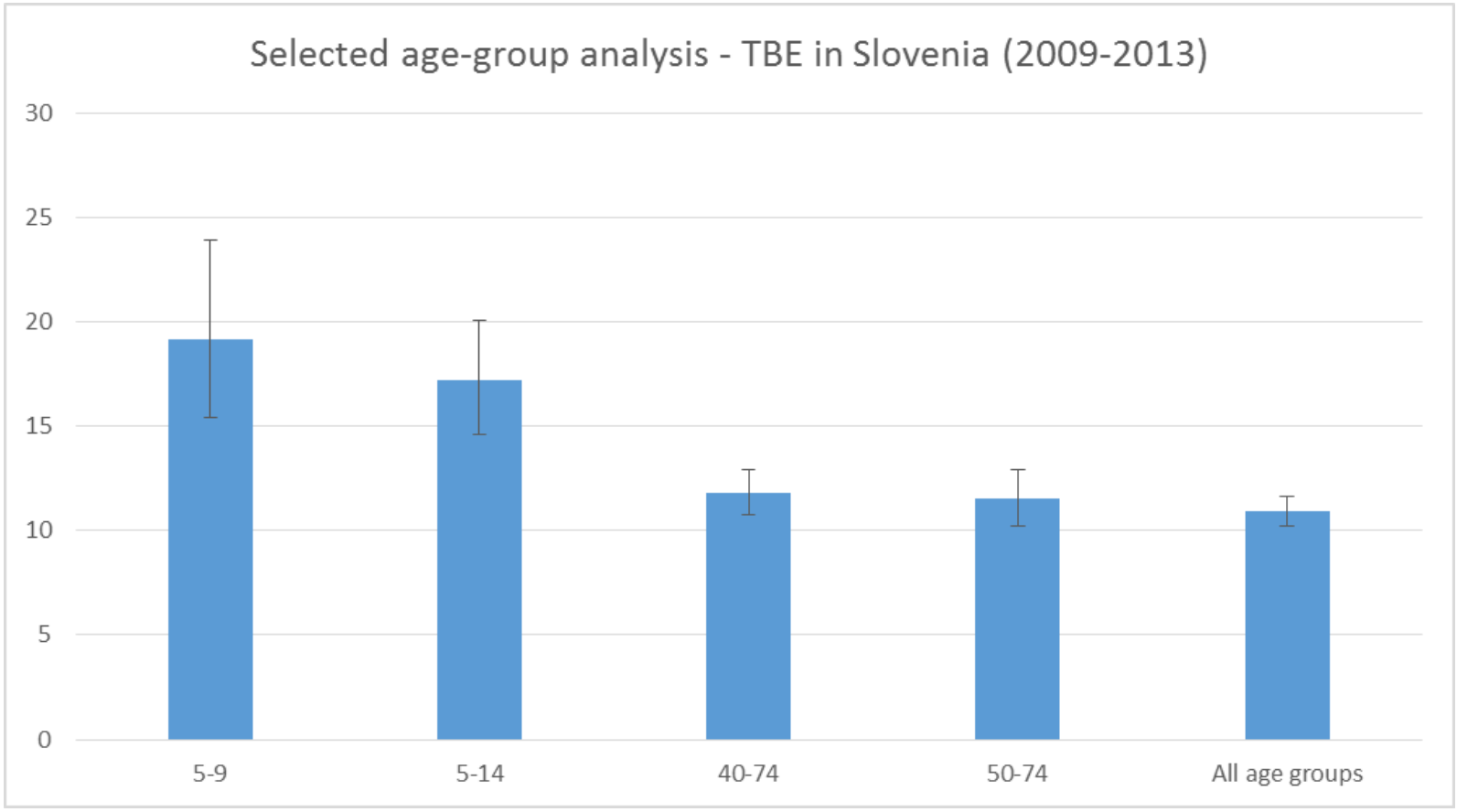
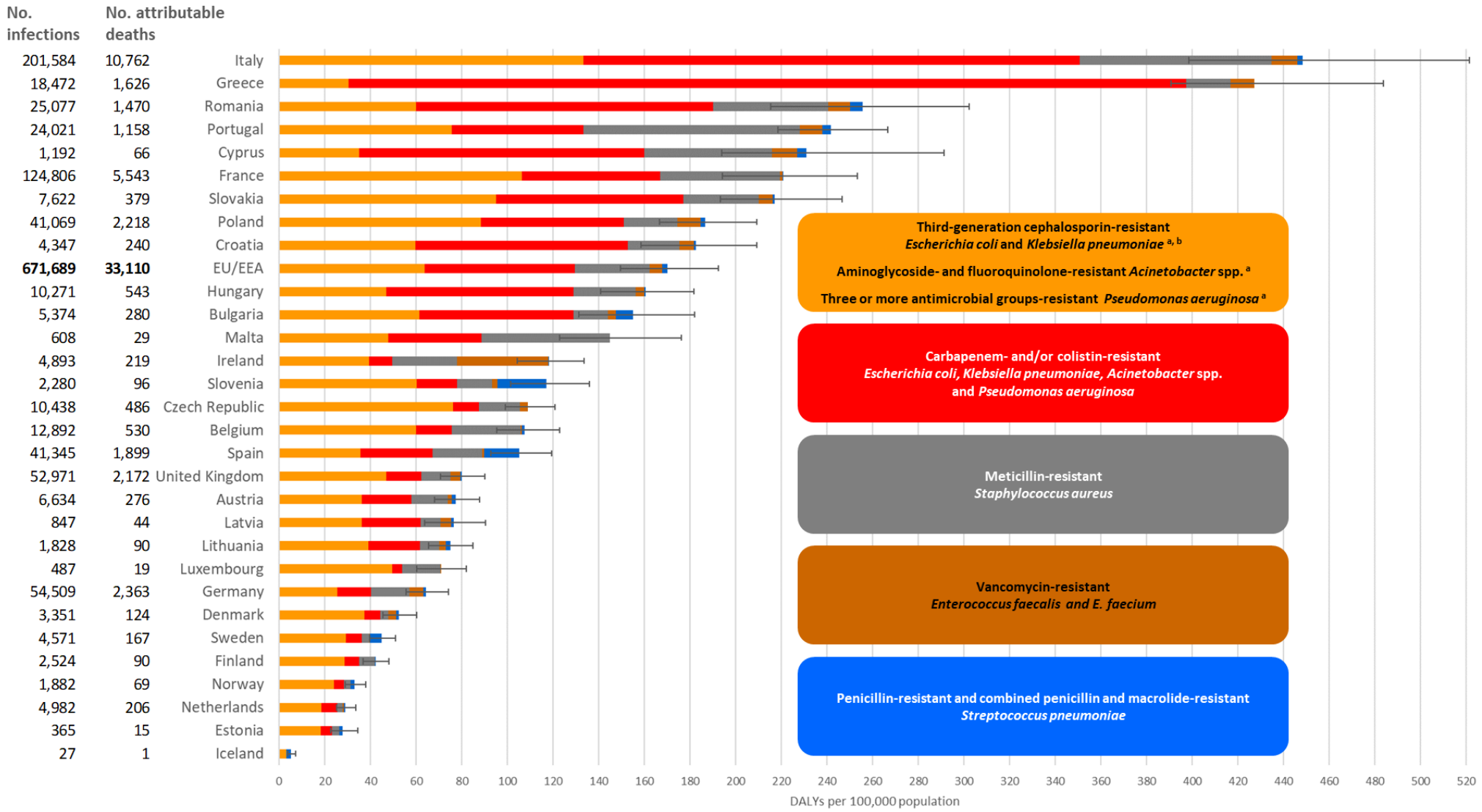


- Fafangel M, Cassini A, Colzani E, Klavs I, Grgic Vitek M, Ucakar V, et al. Estimating the annual burden of tick-borne encephalitis to inform vaccination policy, Slovenia, 2009 to 2013. Euro Surveill. 2017;22(16).
- Fafangel M, Grgic Vitek M, Klavs I. Letter to the editor: Applying incidence-based disability-adjusted life years (DALYs) disease burden estimates to foster change in national vaccination policy, Slovenia, 2017 to 2018. Euro Surveill. 2018;23(27).

World Health Organization

Estimated burden of AMR, age-group standardised, EU/EEA, 2015

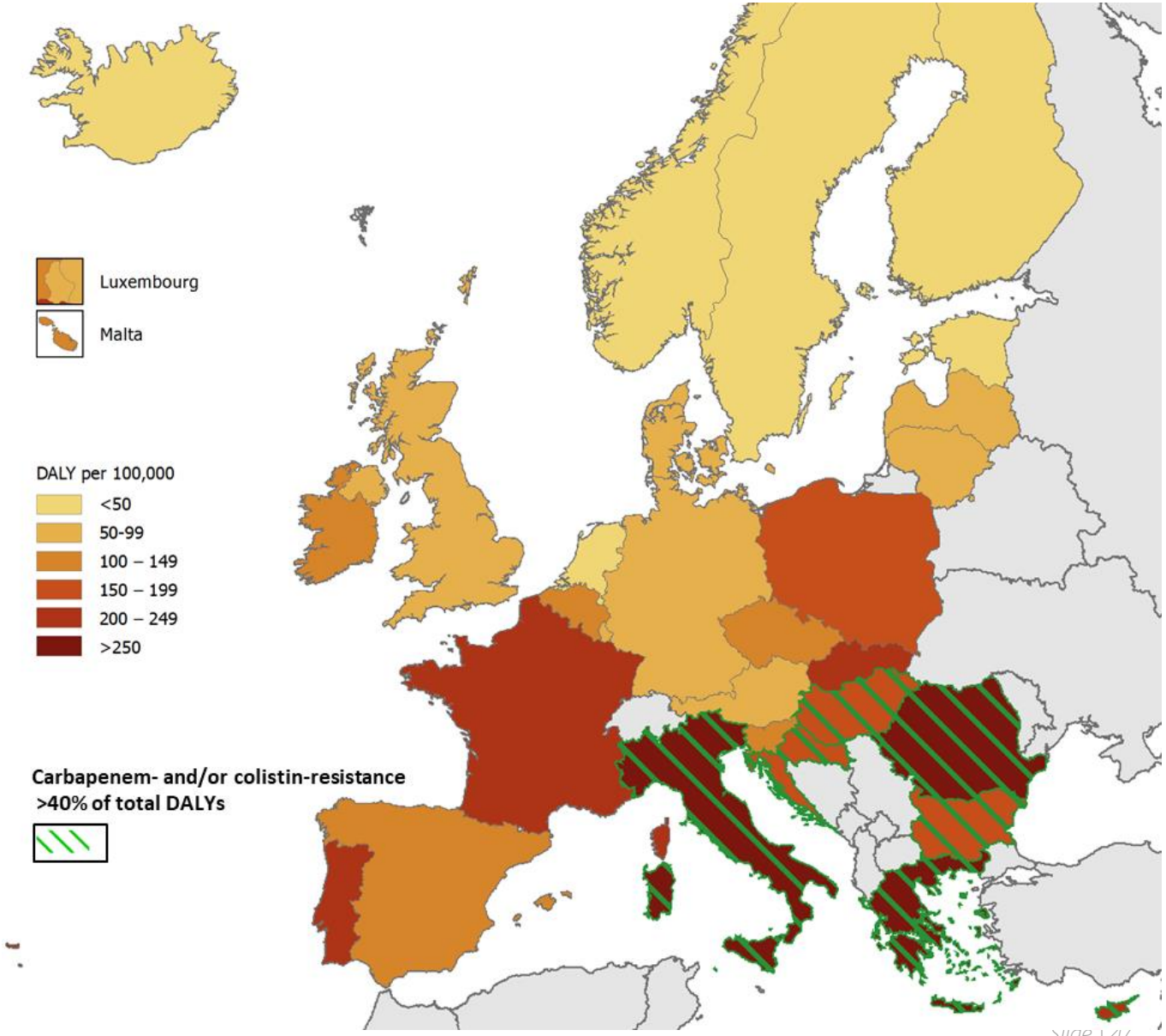


Burden of AMR, per country – carbapenem-resistance

63% of cases were HAI representing 75% of total burden (DALYs)

70% due to 4 top-ranking antibiotic-resistant bacteria

39% due to carbapenem- and/or colistin resistance

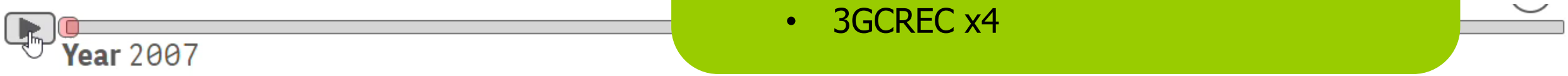


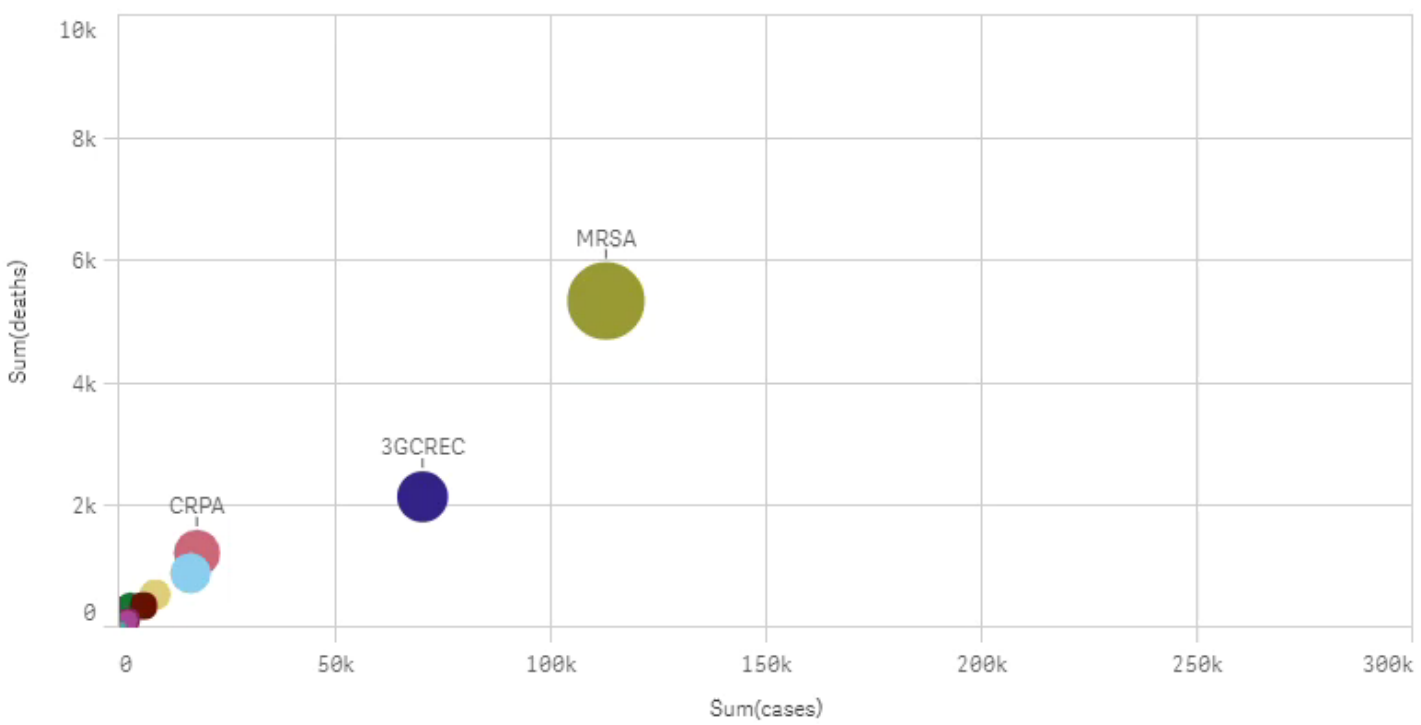
From 2007 to 2015

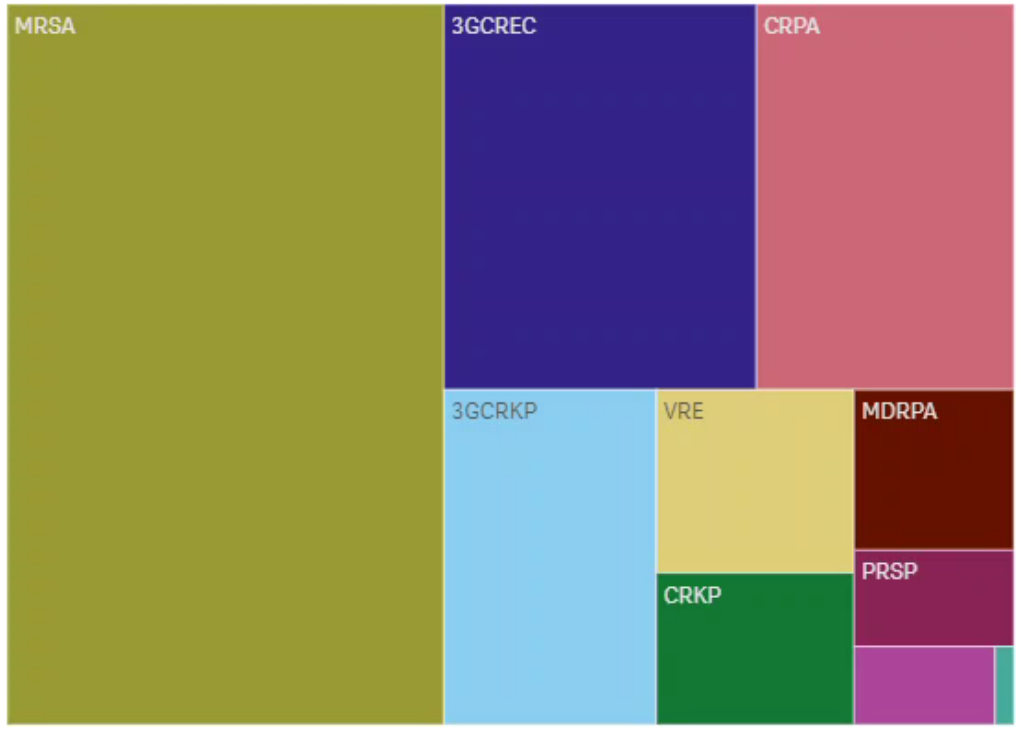
Total number of deaths more than doubled

Increase in number of deaths due to:

- CRKP x6
- 3GCREC x4







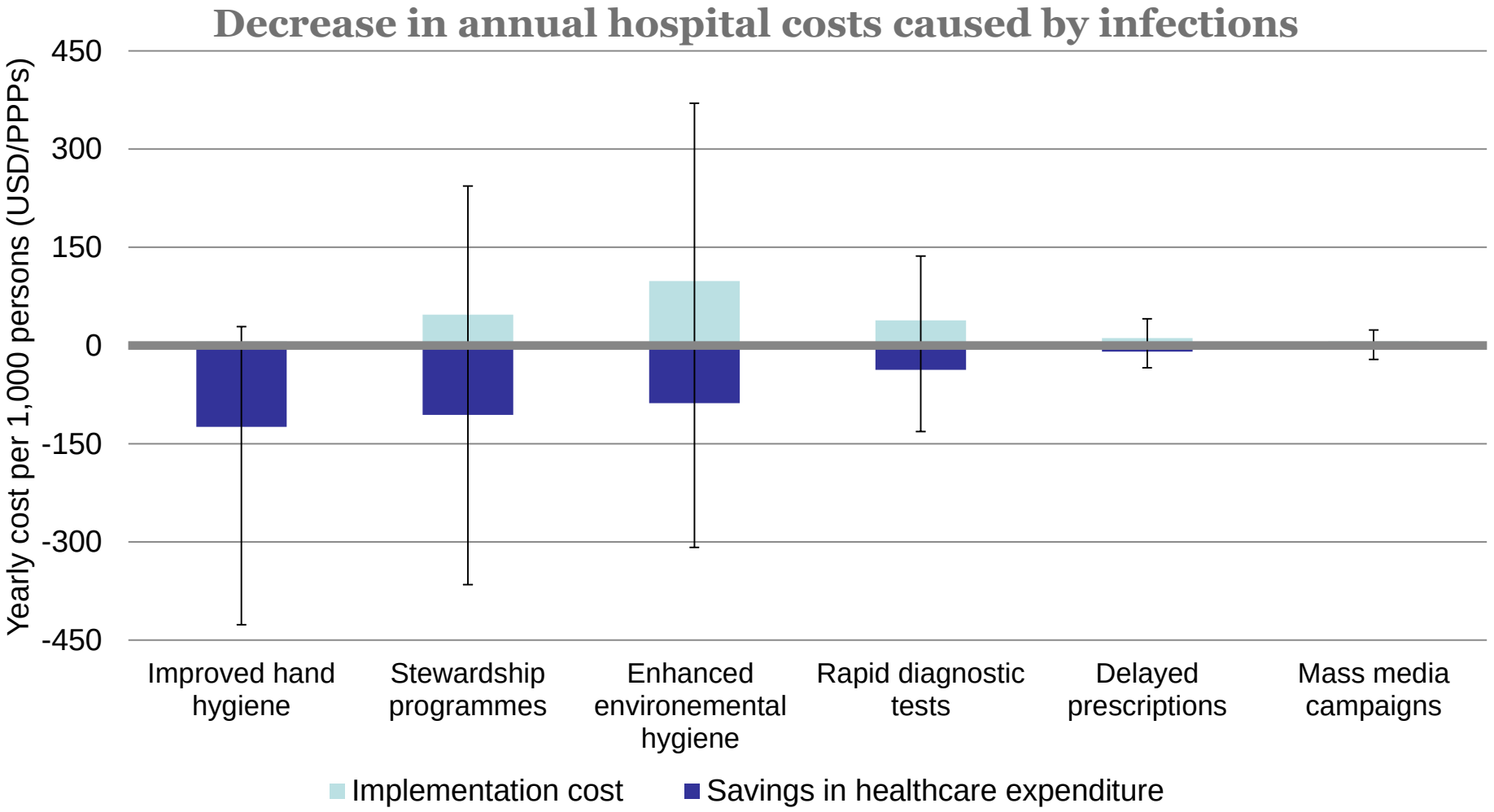
La risposta: PNCAR

PROGRAMMA	TARGET	PRINCIPALI OBIETTIVI	
		A BREVE TERMINE (2017-2018)	A LUNGO TERMINE (2019-2020)
SORVEGLIANZA AMR	Umano	Sistema nazionale di sorveglianza dell'AMR con la partecipazione di tutte le Regioni	Consolidare le sorveglianze "dedicate" (es. CPE), valutare la sorveglianza per nuovi cloni emergenti e tendere verso un modello di sorveglianza esaustivo e non più sentinella
	Veterinario	Rafforzare la *performance* del sistema di sorveglianza e monitoraggio dell'AMR	Sorvegliare nuovi cloni antibiotico-resistenti
SORVEGLIANZA DELLE INFEZIONI CORRELATE ALL'ASSISTENZA (ICA)	Umano	Sviluppare un piano nazionale di sorveglianza delle ICA	Applicare il piano nazionale di sorveglianza delle ICA in tutte le Regioni
SORVEGLIANZA DEL CONSUMO DEGLI ANTIBIOTICI	Umano	Ottimizzare il monitoraggio del consumo degli antibiotici prescritti a livello nazionale	Promuovere lo sviluppo di sistemi regionali per il monitoraggio dell'appropriatezza prescrittiva
	Veterinario	Rendere la prescrizione veterinaria elettronica obbligatoria su tutto il territorio nazionale. Promuovere lo sviluppo di modelli di classificazione delle aziende sulla base della valutazione del rischio di sviluppo di AMR e consumo di antibiotici (miglioramento dei controlli ufficiali)	Misurare i dati di prescrizione e di consumo degli antibiotici e non soltanto quelli di vendita
RESIDUI DI ANTIBIOTICI	Veterinario	Aggiornamento annuale del piano di monitoraggio dei residui in animali e alimenti di origine animale, con rivalutazione periodica delle ricerche	Aggiornamento annuale del piano di monitoraggio dei residui in animali e alimenti di origine animale, con rivalutazione periodica delle ricerche
PREVENZIONE DELLE INFEZIONI CORRELATE ALL'ASSISTENZA (ICA)	Umano	Armonizzare le strategie per la prevenzione e il controllo delle ICA, integrandole con quelle per l'uso appropriato di antibiotici	Migliorare e adeguare costantemente alle evidenze scientifiche le misure di prevenzione e controllo delle ICA
PREVENZIONE DELLE MALATTIE INFETTIVE E DELLE ZOONOSI	Veterinario	Sviluppare programmi di buone pratiche nella corretta gestione degli allevamenti e strategie di prevenzione della malattie infettive	Ridurre il rischio infettivo nelle aziende zootecniche
USO CORRETTO E PRUDENTE DEGLI ANTIBIOTICI	Umano	Armonizzare le strategie sull'uso appropriato di antibiotici, integrandole con quelle di controllo delle ICA. Rendere specifici e sostenibili i programmi di *antimicrobial stewardship*. Migliorare conoscenze e consapevolezza negli operatori sanitari e nei cittadini	Migliorare e aggiornare costantemente le indicazioni nazionali sull'uso appropriato di antibiotici. Promuovere interventi utili a ridurre il fenomeno dell'utilizzo di antibiotici "avanzati" a domicilio
	Veterinario	Predisporre Linee guida per l'uso prudente di antibiotici in animali produttori di alimenti e animali da compagnia	Rafforzare la cooperazione con Industria farmaceutica, Associazioni e Organizzazioni sull'uso prudente
COMUNICAZIONE	Umano e Veterinario	Promuovere programmi di comunicazione per aumentare la consapevolezza del fenomeno AMR e le buone pratiche di uso degli antibiotici	Coinvolgere nelle iniziative tutti gli operatori sanitari, le società scientifiche, le associazioni: dai cittadini agli operatori sanitari
FORMAZIONE		Promuovere la formazione degli operatori sanitari nei diversi ambiti, secondo il principio *One Health*	Educare e promuovere lo scambio di buone pratiche di formazione sull'uso corretto e prudente degli antibiotici
RICERCA E SVILUPPO		Identificare il tema AMR e delle ICA come area prioritaria nell'ambito della ricerca	Promuovere il trasferimento dei risultati della ricerca

Courtesy of Michele Cecchini, OECD (Michele.CECCHINI@oecd.org)

World Health Organization

… And Decrease Healthcare Expenditure

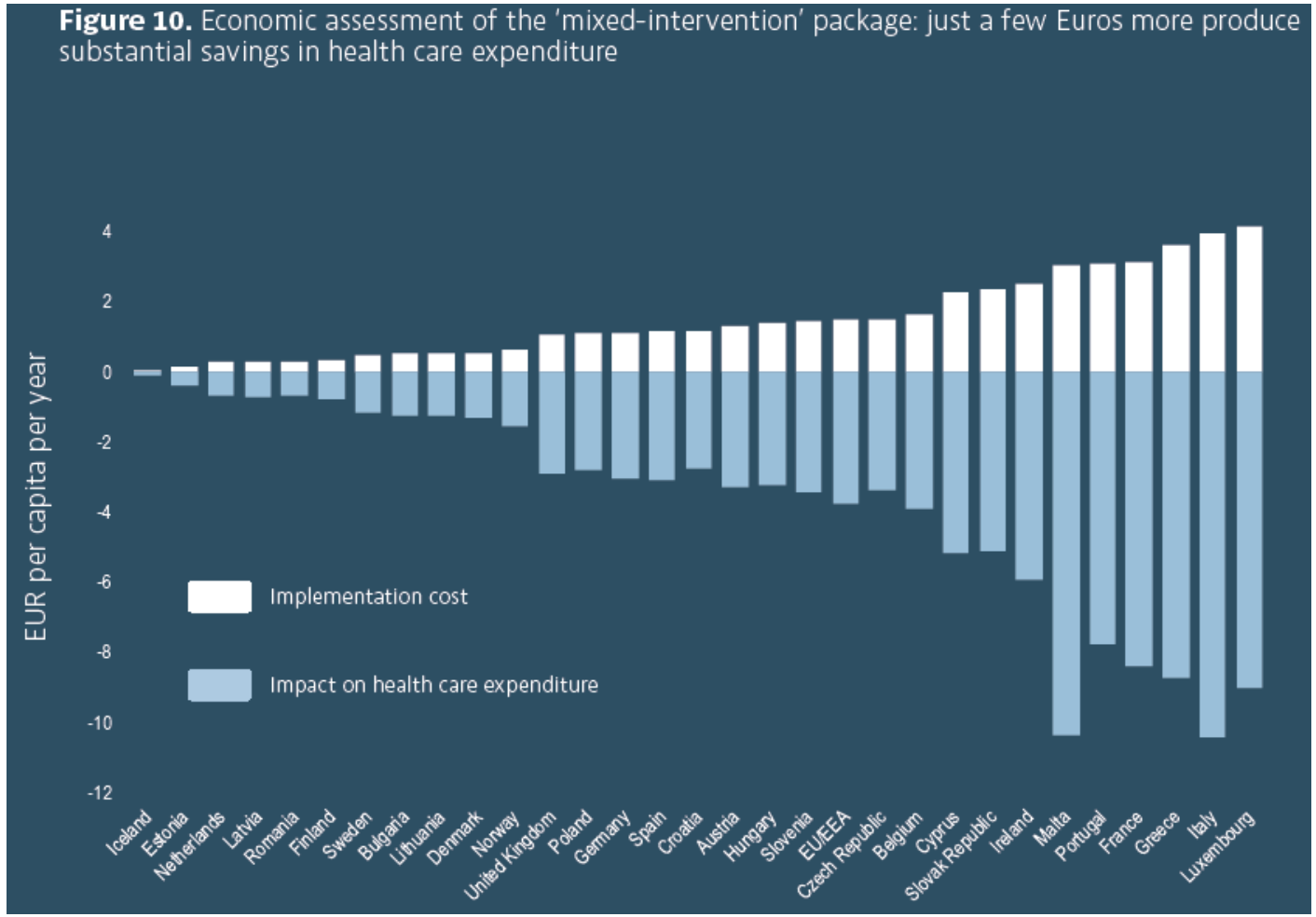


Note: columns show the median value across 33 OECD and EU countries; whiskers show min and max values

"Although some policies require major investments and involve complex implementation, a number of policies such as hygiene interventions can be effectively implemented in resource-constrained settings."

"The first intervention would be to improve hygiene in healthcare facilities, including promotion of hand hygiene and better hospital hygiene."

Investing 1.5 Euros per capita per year in a package 3 of mixed public health interventions **would avoid about 27 000 deaths per year** in EU/EEA countries.



Package 1, for hospitals: hand hygiene, antibiotic stewardship programmes and enhanced environmental hygiene = 85%

Package 2, for community settings: delayed antibiotic prescriptions, mass media campaigns and the use of rapid diagnostic tests = 23%

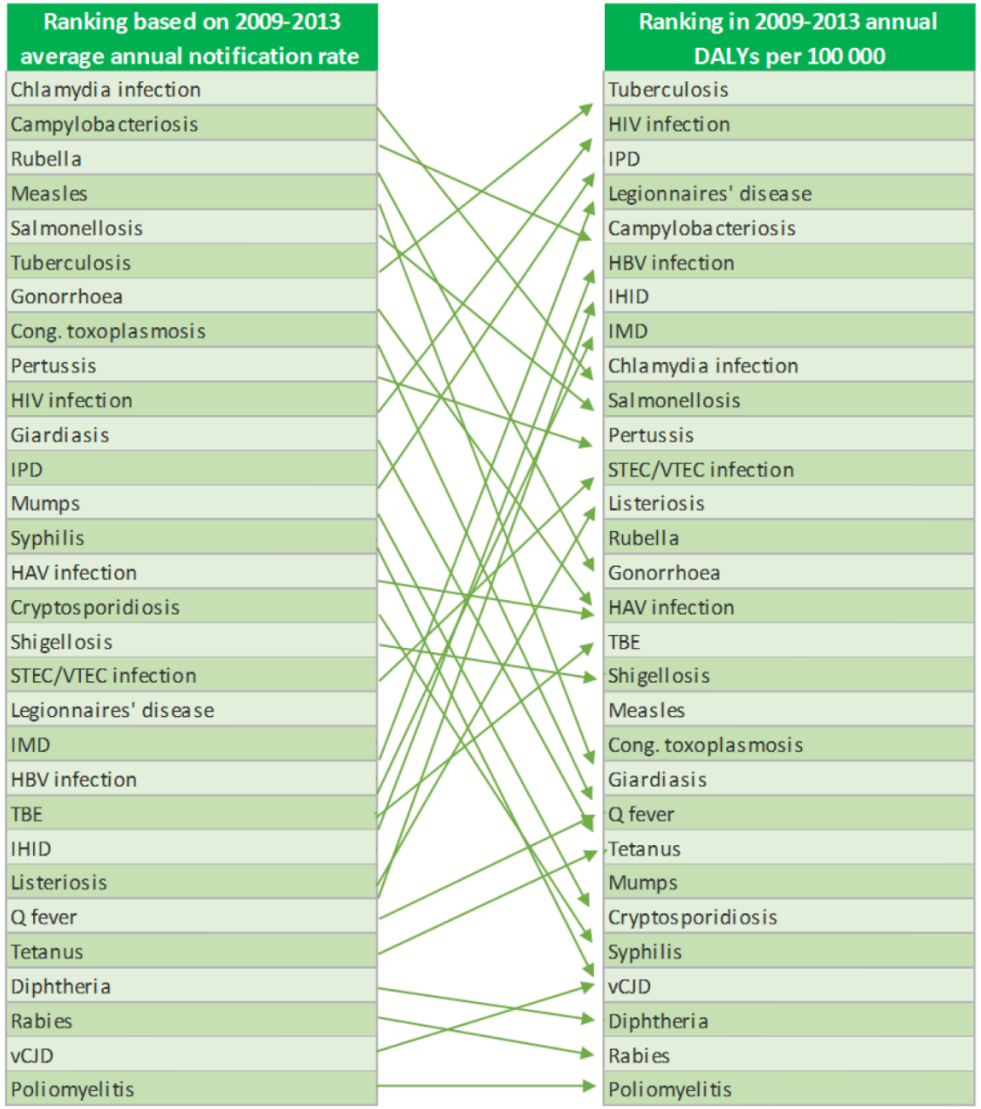
Package 3, mix of interventions = 73%

Savings of 3, 0.7 and 2 Euros per capita per year

Source: OECD & ECDC (2019): Antimicrobial Resistance, Tackling the Burden in the European Union. Briefing note for EU/EEA countries.

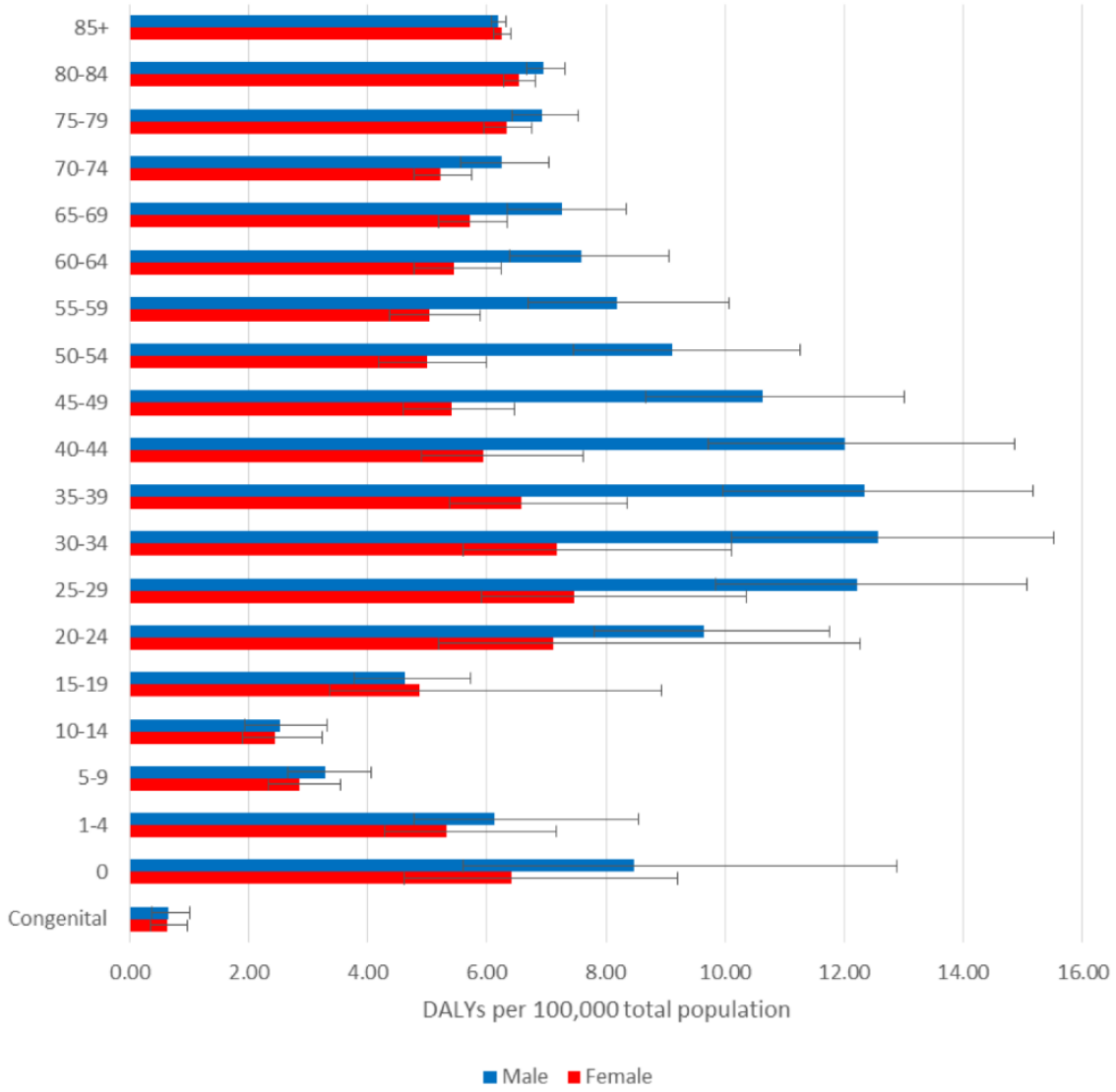
Visualisation of data

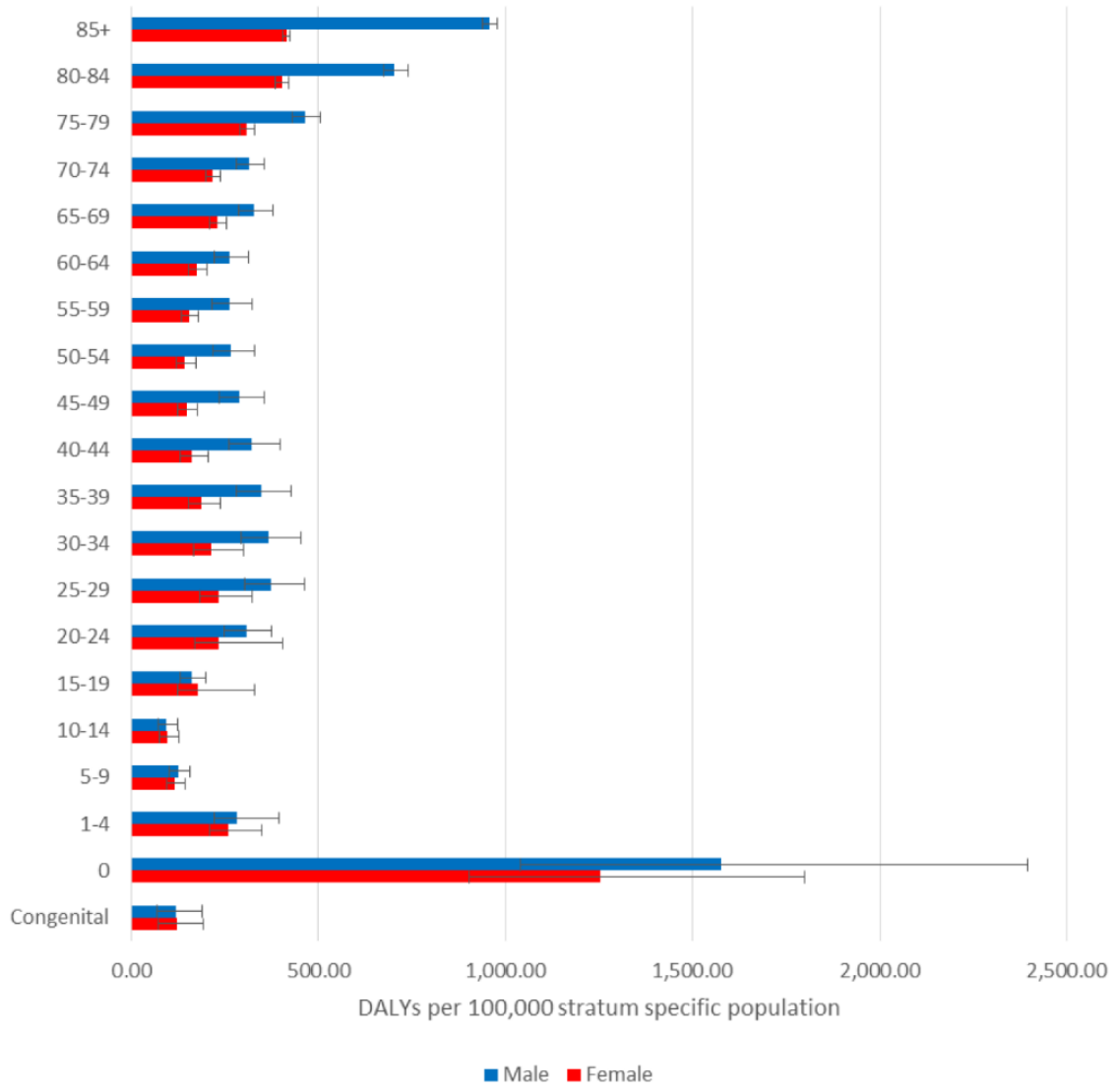
Ranking of diseases: all positions change



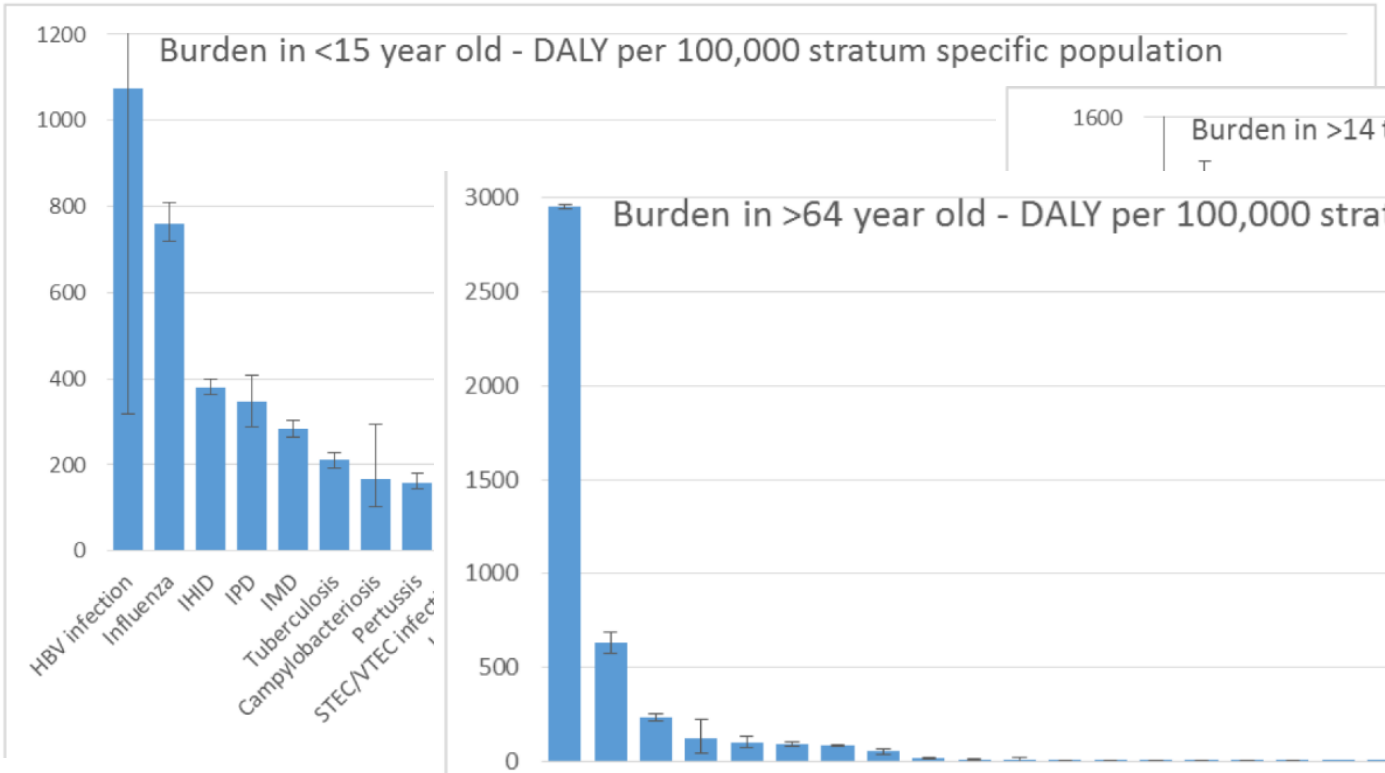
World Health Organization

DALYs per 100,000 total population or age-group adjusted?



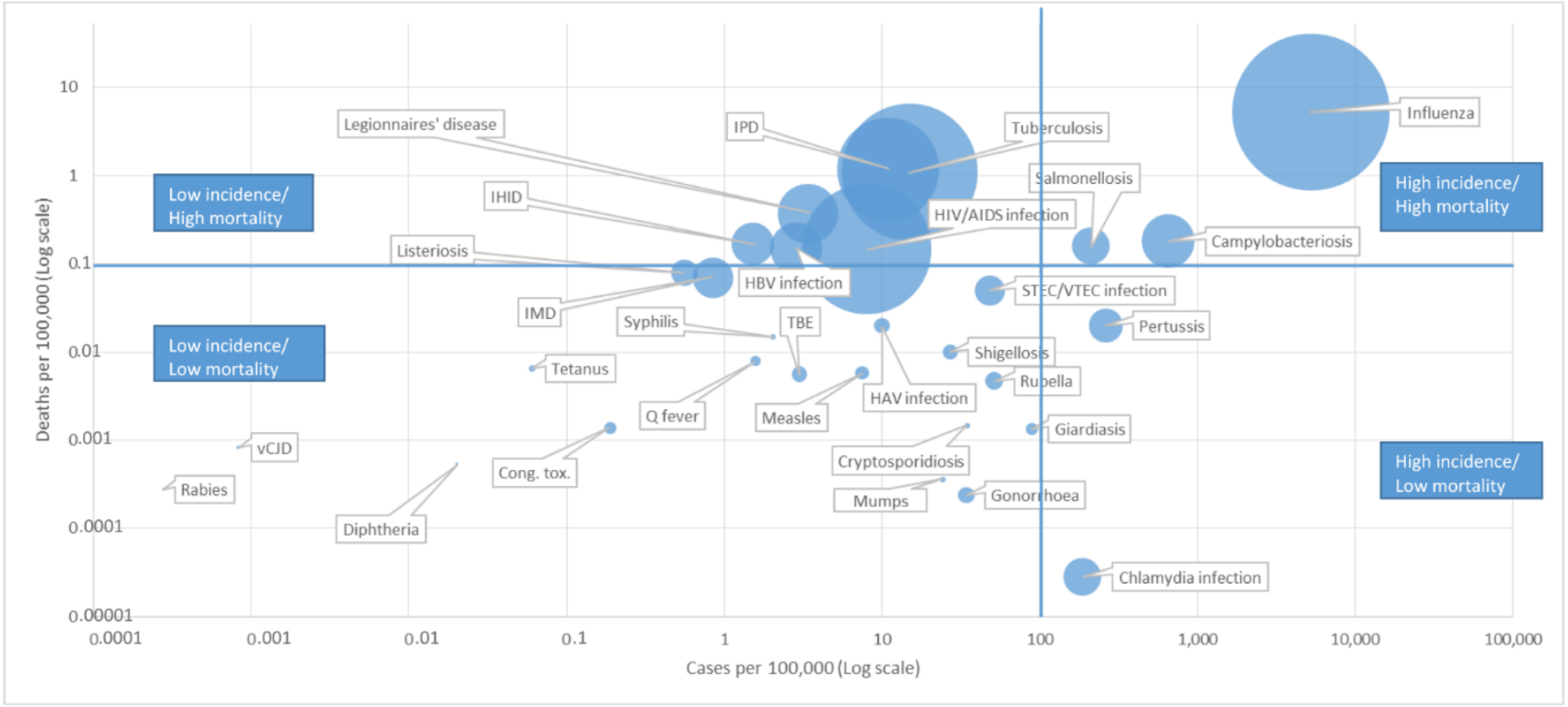


Splitting the population

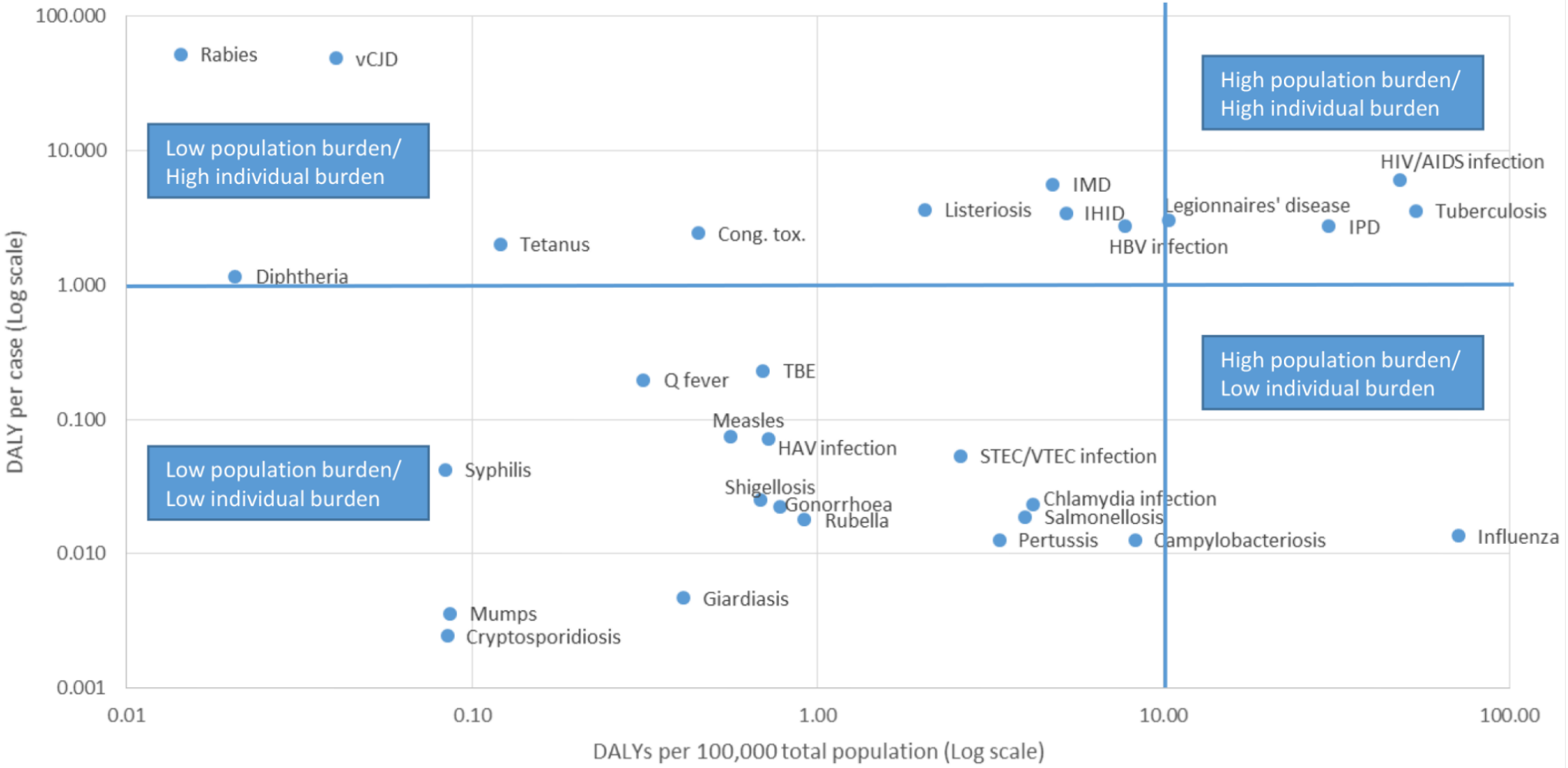


World Health Organization

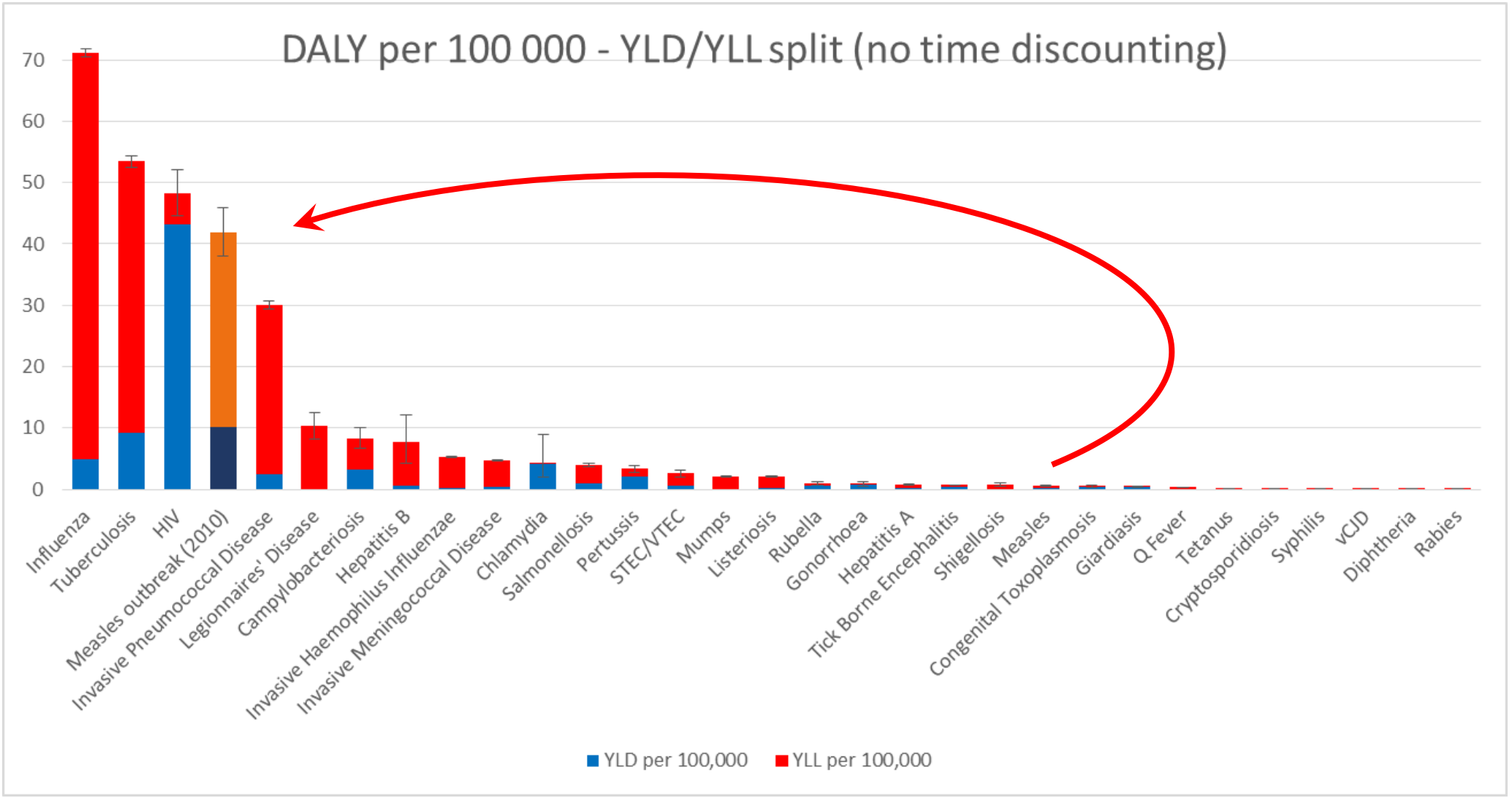
Making sense of the general results



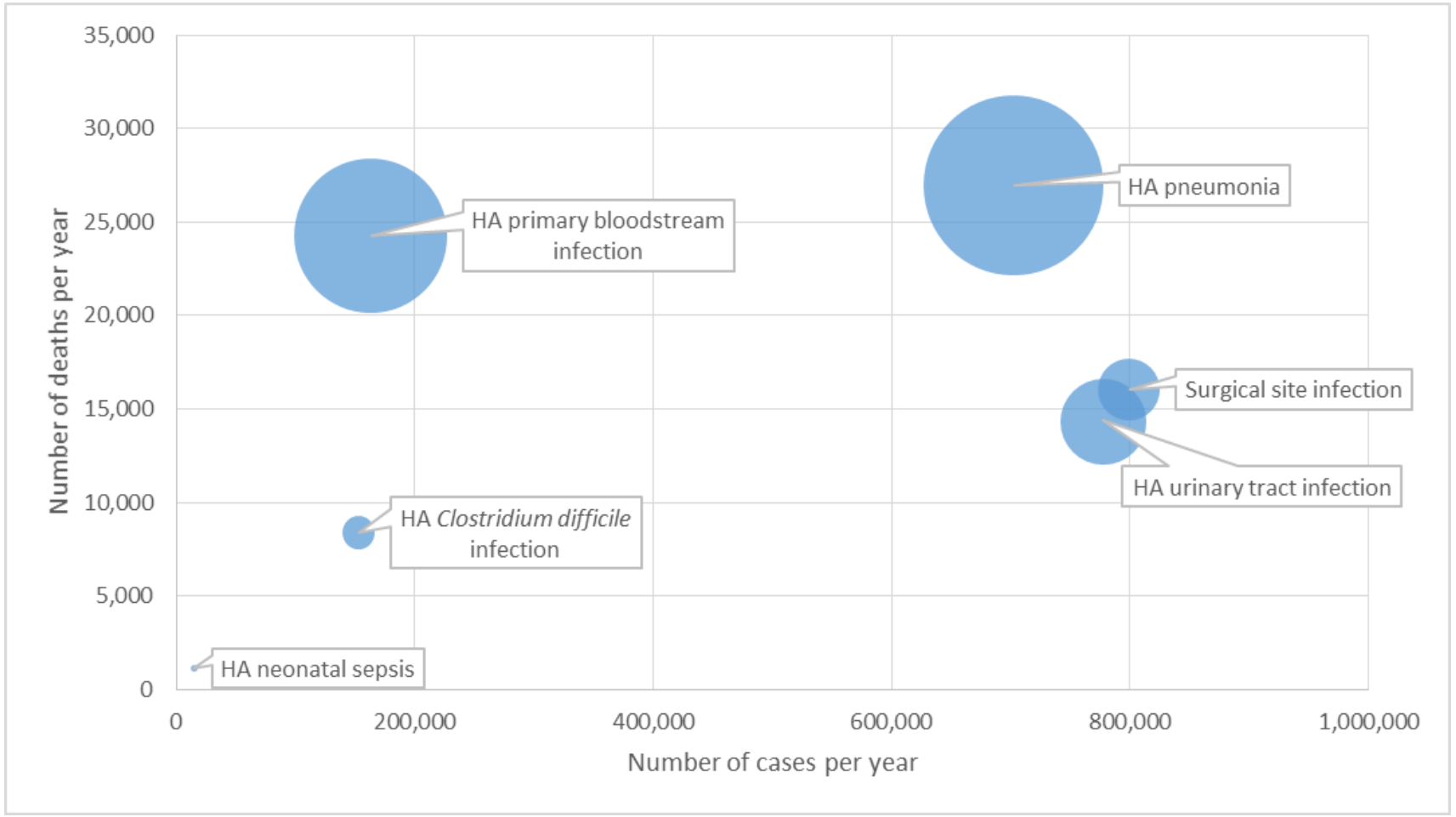
Personal burden vs. population burden



Burden and outbreaks



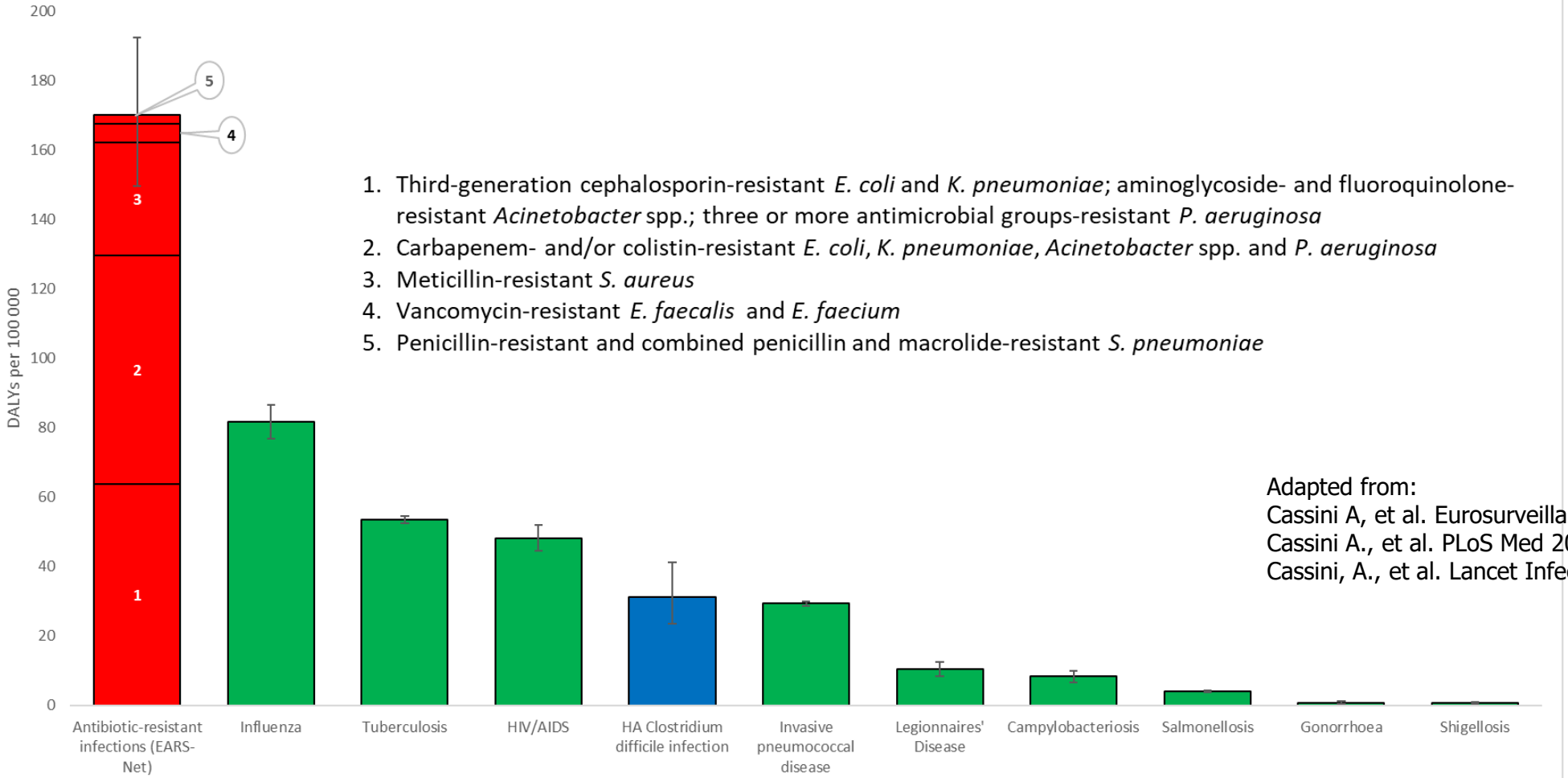
Contribution of incidence and mortality to the burden of HAIs



Burden of HAIs in EU/EEA Member States – 2011-2012
Diameter of bubble reflects DALYs per 100,000.

Cassini A and Plachouras D, Eckmanns T, Abu Sin M, Blank H-P, Ducomble T, et al. Burden of Six Healthcare-Associated Infections on European Population Health: Estimating Incidence-Based Disability-Adjusted Life Years through a Population Prevalence-Based Modelling Study. PLoS medicine. 2016;13(10):e1002150.

Burden of AMR is comparable to the combined burden of influenza, TB & HIV/AIDS

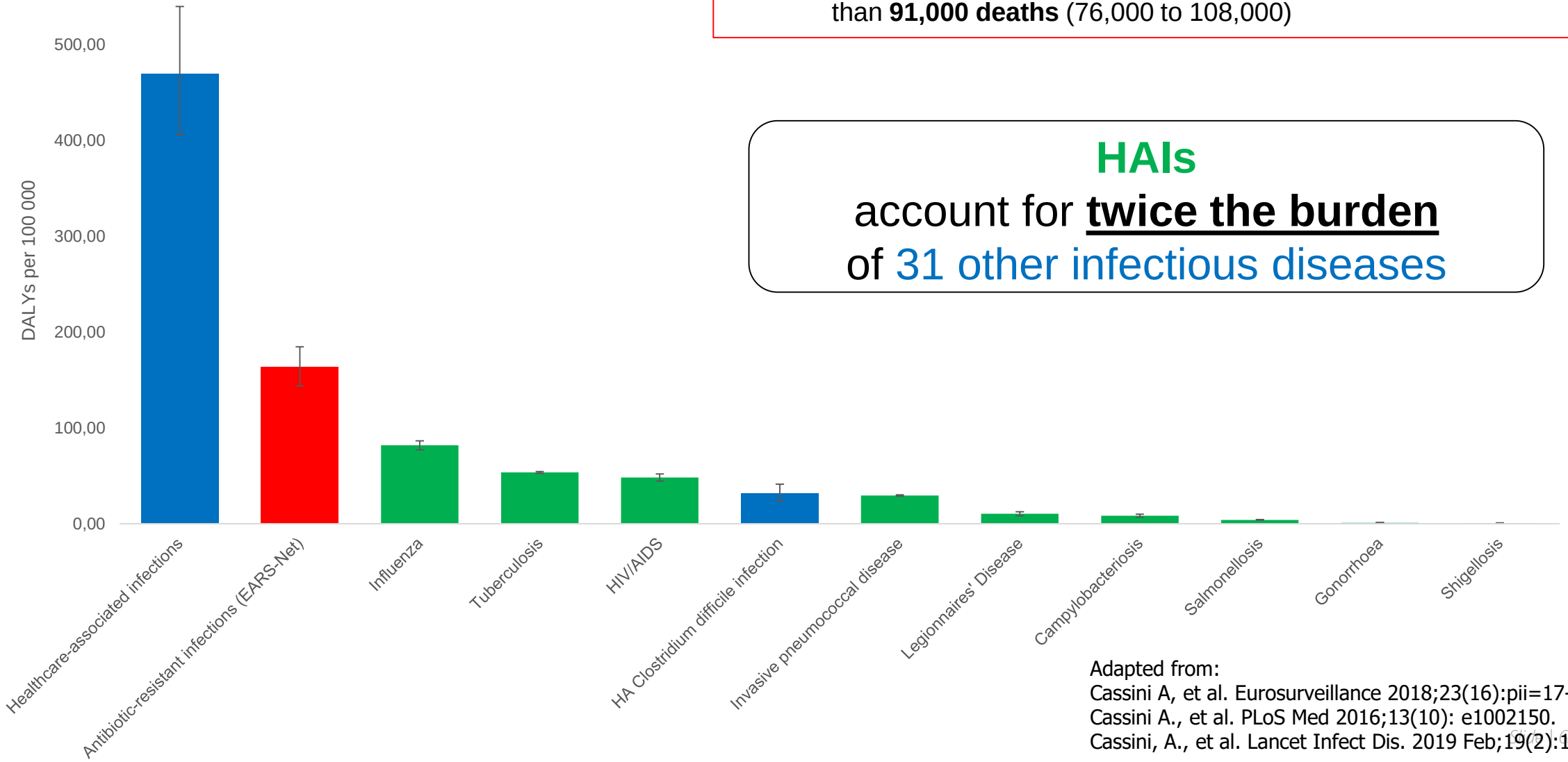


1. Third-generation cephalosporin-resistant *E. coli* and *K. pneumoniae*; aminoglycoside- and fluoroquinolone-resistant *Acinetobacter* spp.; three or more antimicrobial groups-resistant *P. aeruginosa*
2. Carbapenem- and/or colistin-resistant *E. coli*, *K. pneumoniae*, *Acinetobacter* spp. and *P. aeruginosa*
3. Meticillin-resistant *S. aureus*
4. Vancomycin-resistant *E. faecalis* and *E. faecium*
5. Penicillin-resistant and combined penicillin and macrolide-resistant *S. pneumoniae*

Adapted from:
Cassini A, et al. Eurosurveillance 2018;23(16):pii=17-00454
Cassini A., et al. PLoS Med 2016;13(10): e1002150.
Cassini, A., et al. Lancet Infect Dis. 2019 Feb;19(2):129-130.

Burden of HAIs

2.6 million annual number of cases of HAIs are associated with more than **91,000 deaths** (76,000 to 108,000)



HAIs
account for **twice the burden**
of 31 other infectious diseases

Adapted from:
Cassini A, et al. Eurosurveillance 2018;23(16):pii=17-00454
Cassini A., et al. PLoS Med 2016;13(10): e1002150.
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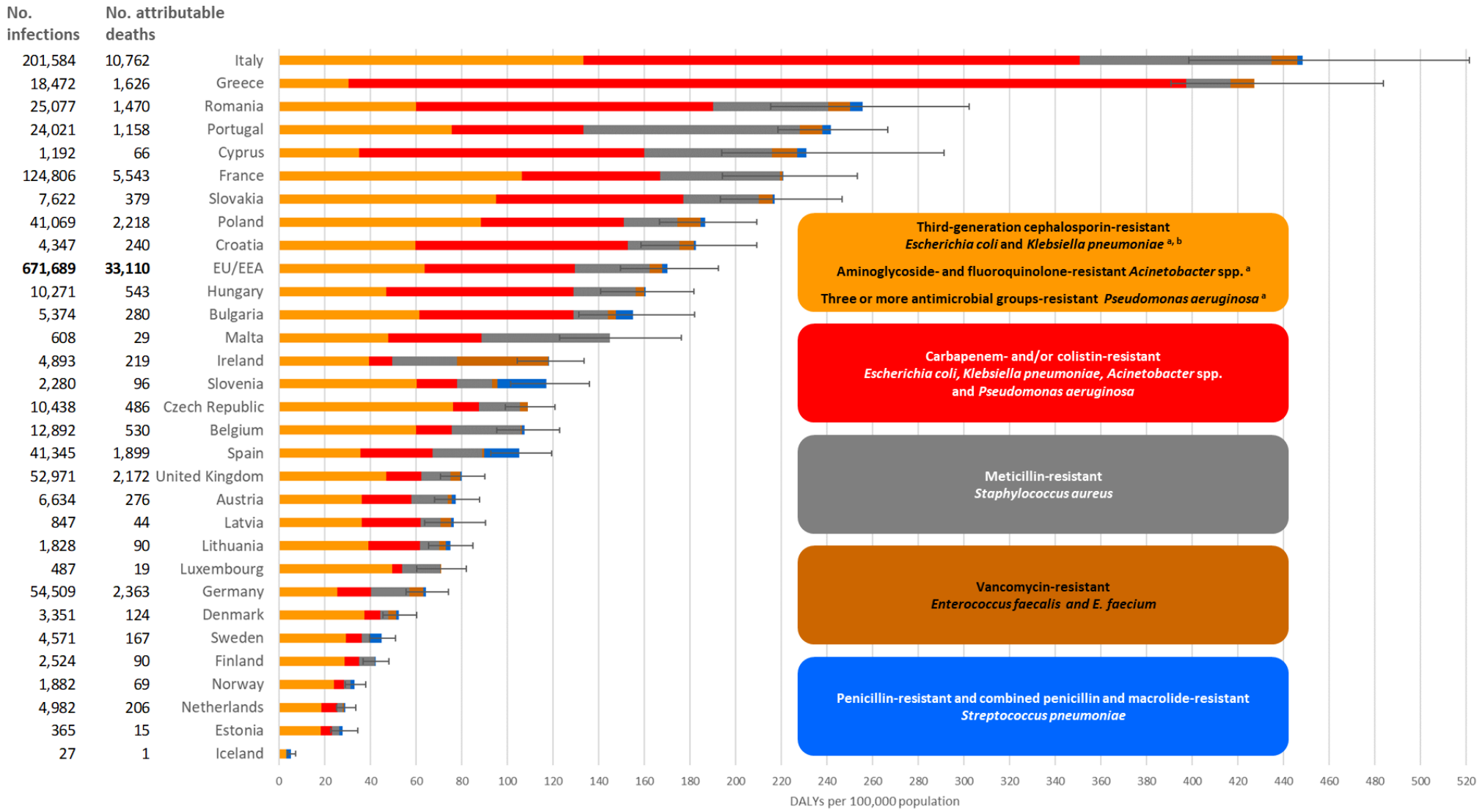
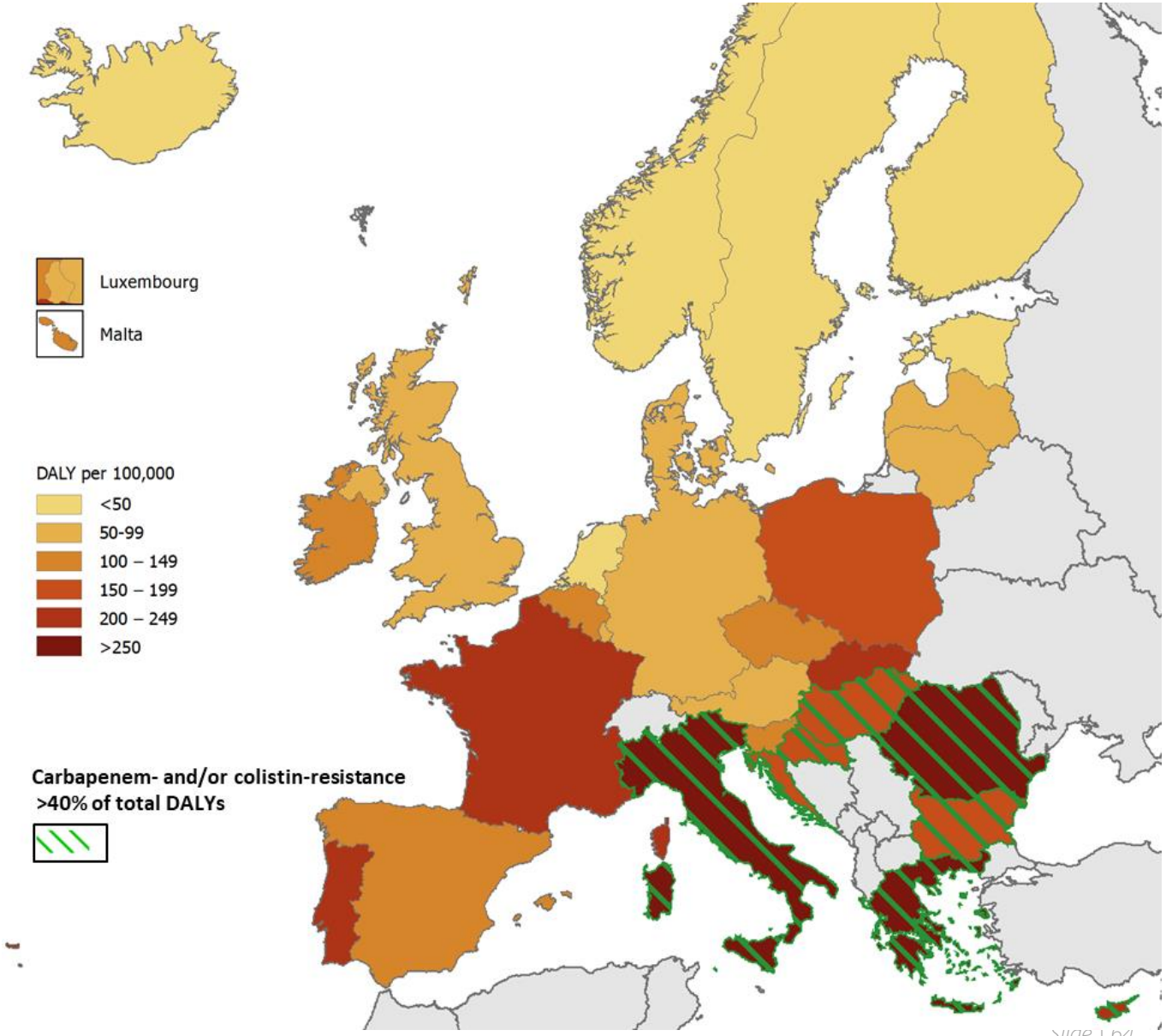
World Health Organization

Estimated burden of AMR, age-group standardised, EU/EEA, 2015



Burden of AMR, per country – carbapenem-resistance



Large number of people involved

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Cassini A, Hogberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS, et al. 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. Lancet Infect Dis. 2019;19(1):56-66.

Thank you

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