



University Medical Center Groningen

UNIVERSITAIR MEDISCH CENTRUM GRONINGEN





Do antibiotic resistant bacteria
increase the burden of BSI?

Hajo Grundmann,
University Medical Centre Groningen,
The Netherlands



ESCMID Online Lecture Library
© by author

No!



Does antibiotic resistance increase the Burden of Disease (BoD) caused by BSI?

or

Costs and burden: What is the excess population attributable fraction of antibiotic resistance in BSI?



Topics

- Costs and Burden
- published estimates
- own data

ESCMID Online Lecture Library
© by author



Cost and Burden

ESCMID Online Lecture Library
© by author



Cost categories

- Direct costs
 - charged or required for a specific project or product
- Indirect costs
 - incurred for common or joint objectives and therefore difficult to identify with a specific project or product



Perspectives

- Hospitals
- Patients
- Society

ESCMID Online Lecture Library
© by author



Cost categories and perspectives

Direct costs

Indirect costs

Hospitals

Patients

Society

ESCMID Online Lecture Library
© by author



Cost categories and perspectives

Direct costs

Indirect costs

Hospitals

Medical care

Patients

Society

ESCMID Online Lecture Library
© by author



Cost categories and perspectives

Direct costs

Indirect costs

Hospitals

Medical care

Maintenance of
structures and
functions

Patients

Society

ESCMID Online Lecture Library
© by author



Cost categories and perspectives

	Direct costs	Indirect costs
Hospitals	Medical care	Maintenance of structures and functions
Patients	Out of pocket charges for health care and medicines	
Society		



Cost categories and perspectives

	Direct costs	Indirect costs
Hospitals	Medical care	Maintenance of structures and functions
Patients	Out of pocket charges for health care and medicines	Opportunity loss, lost functionality
Society		



Cost categories and perspectives

	Direct costs	Indirect costs
Hospitals	Medical care	Maintenance of structures and functions
Patients	Out of pocket charges for health care and medicines	Opportunity loss, lost functionality
Society	Health care expenditure	



Cost categories and perspectives

	Direct costs	Indirect costs
Hospitals	Medical care	Maintenance of structures and functions
Patients	Out of pocket charges for health care and medicines	Opportunity loss, lost functionality
Society	Health care expenditure	Loss of productivity



Burden of Disease (BoD) studies

- Combine morbidity and mortality into a single measurement (DALY)
- Measure healthy life years lost due to premature death or disability
- Against an objective reference point
 - - Average life expectancy in a low-mortality population



BoD studies on AMR

- Don't combine morbidity and mortality into a single measurement
- Measure excess morbidity and mortality due to antibiotic resistance
- Against a counterfactual reference point
 - infection with susceptible pathogen



Published Estimates

ESCMID Online Lecture Library
© by author



Cost and Burden estimates in the EU

Human and economic impact of antimicrobial resistance*



Each year, in EU countries...

25,000 deaths directly attributable to multidrug-resistant infections

Extra in-hospital costs	Extra outpatient costs	Productivity losses due to absence from work	Productivity losses due to patients who died from their infection	TOTAL
€ 927.8 million	€ 10 million	€ 150.4 million	€ 445.9 million	€ 1.5 billion

Source – *The bacterial challenge: time to react*, Joint Technical Report from ECDC and EMA, Stockholm, September 2009. Available online at: http://ecdc.europa.eu/en/publications/Publications/Forms/ECDC_DispForm.aspx?ID=444

*Estimates for 5 common multidrug-resistant bacteria (EU Member States, Norway and Iceland, 2007)

Parameter	Unit	Value	Reference
No. MRSA ^a from LRTI ^b / from BSI ^b	Ratio	1.25	[21]
No. MRSA from SSTI ^b / from BSI	Ratio	5.25	[21]
No. MRSA from UTI ^b / from BSI	Ratio	0.75	[21]
Attributable mortality of MRSA BSI	%	9.8	[26]
Attributable mortality of MRSA LRTI	%	7.0	[26-27]
Attributable mortality of MRSA SSTI	%	1.4	[26-27]
Attributable mortality of MRSA UTI	%	0.2	[26-27]
Extra length of hospital stay for MRSA BSI	Days	8	[29]
Extra length of hospital stay for MRSA LRTI	Days	9.4	[29]
Extra length of hospital stay for MRSA SSTI	Days	5	[29]
Extra length of hospital stay for MRSA UTI	Days	6.1	[28]
No. VRE ^c from wound infection / from BSI	Ratio	4.67	[23]
No. VRE from intra-abdominal infection / from BSI	Ratio	1.89	[23]
No. VRE from UTI / from BSI	Ratio	3.44	[23]
Attributable mortality of VRE BSI	%	25	[23]
Attributable mortality of VRE wound infection	%	6	[23]
Attributable mortality of VRE intra-abdominal infection	%	3	[23]
Attributable mortality of VRE UTI	%	9	[23]
Extra length of hospital stay for VRE BSI	Days	15	[23]
Extra length of hospital stay for VRE wound infection	Days	6.2	[23]
Extra length of hospital stay for VRE intra-abdominal infection	Days	2.6	[23]
Extra length of hospital stay for VRE UTI	Days	5.4	[23]
No. penicillin-resistant <i>Streptococcus pneumoniae</i> from respiratory tract infection/ from BSI	Ratio	2.7	[24]
No. third-generation cephalosporin-resistant <i>Klebsiella pneumoniae</i> from LRTI / from BSI ^d	Ratio	1.19	[22]



Recent Cost and Burden estimates in the EU

Table 2. Estimated yearly human burden of infections due to the selected antibiotic-resistant bacteria and percentage of this burden due to bloodstream infections, EU Member States, Iceland and Norway, 2007.

Antibiotic-resistant bacteria^a	No. cases of infection (four main types)^b (% bloodstream infections)	No. extra deaths (% from bloodstream infections)	No. extra hospital days (% from bloodstream infections)
<i>Antibiotic-resistant Gram-positive bacteria</i>			
Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)	171 200 (12%)	5 400 (37%)	1 050 000 (16%)
Vancomycin-resistant <i>Enterococcus faecium</i>	18 100 (9%)	1 500 (28%)	111 000 (22%)
Penicillin-resistant <i>Streptococcus pneumoniae</i> ^c	3 500 (27%)	–	–
<i>Sub-total</i>	<i>192 800 (12%)</i>	<i>6 900 (35%)</i>	<i>1 161 000 (16%)</i>
<i>Antibiotic-resistant Gram-negative bacteria</i>			
Third-generation cephalosporin-resistant <i>Escherichia coli</i> ^d	32 500 (27%)	5 100 (52%)	358 000 (27%)
Third-generation cephalosporin-resistant <i>Klebsiella pneumoniae</i>	18 900 (27%)	2 900 (52%)	208 000 (27%)
Carbapenem-resistant <i>Pseudomonas aeruginosa</i> ^e	141 900 (3%)	10 200 (7%)	809 000 (3%)
<i>Sub-total</i>	<i>193 300 (9%)</i>	<i>18 200 (27%)</i>	<i>1 375 000 (13%)</i>
Total	386 100 (11%)	25 100 (29%)	2 536 000 (14%)



Recent Cost and Burden estimates in the EU

Table 3. Estimated yearly economic burden of infections (four main types^a) due to the selected antibiotic-resistant bacteria, EU Member States, Iceland and Norway, 2007.

Antibiotic-resistant bacteria ^b	Extra in-hospital costs (EUR)	Extra outpatient costs ^c (EUR)	Productivity losses due to absence from work (EUR)	Productivity losses due to patients who died from their infection (EUR)	Overall costs (EUR)
<i>Antibiotic-resistant Gram-positive bacteria</i>	424 700 000	5 500 000	91 100 000	145 600 000	666 900 000
<i>Antibiotic-resistant Gram-negative bacteria</i>	503 100 000	4 500 000	59 300 000	300 300 000	867 200 000
Total	927 800 000	10 000 000	150 400 000	445 900 000	1 534 100 000



Own Data

ESCMID Online Lecture Library
© by author



Objectives

Determine incident and expected (BSI):

total no. of events

total no. of excess deaths

total no. of excess bed-days

for 13 European Countries

3rd gen. cephalosporin-resistant *E. coli* (G3CREC)

methicillin-resistant *S. aureus* (MRSA)



Data for 2007

BURDEN study*

ORs for 30-day mortality

mean excess length of stay

ESCMID Online Lecture Library
© by author



Cohort studies 2007

Country (beds/hospital)	Patient days at risk (12 month observation)
AT (2137)	65,7268
BE (856)	29,0790
DE (1234)	39,1258
GR (949)	29,3632
HR (1724)	47,9528
IE (819)	23,8166
IT (912)	29,2150
LV (1029)	30,7006
MT (835)	25,2488
RO (1109)	42,7666
SC (877)	25,5215
SI (2344)	61,4353
UK (1210)	29,2030
Overall	4,791,550

ESCAAD Online Lecture Library
© by author



Data for 2007

BURDEN study*

ORs for 30-day mortality

mean excess length of stay

EARSS

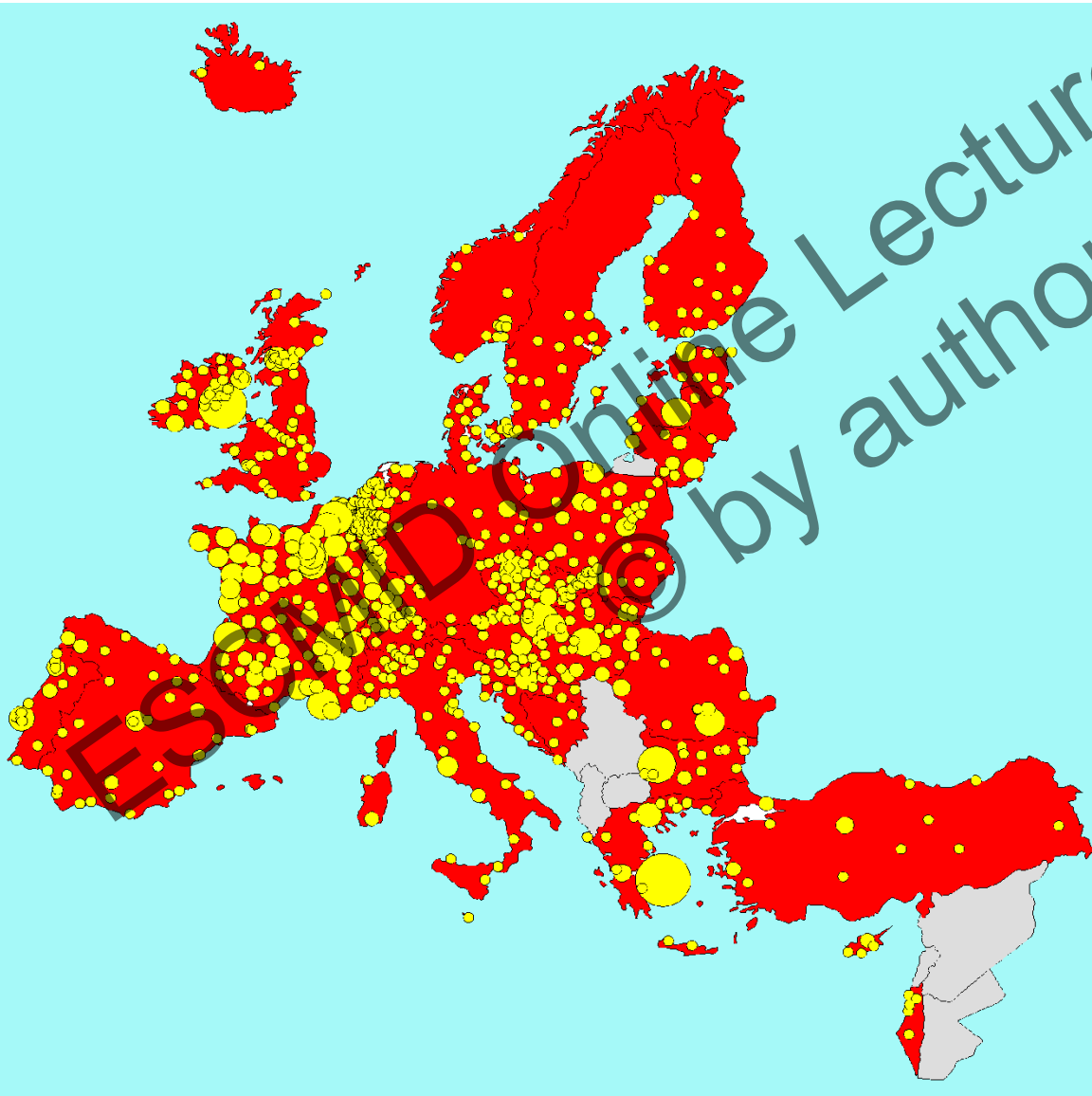
frequency BSI

acute care hospital beds

ESCMID Online Lecture Library © by author



EARSS/EARS-net data 2007



33 countries

774 laboratories

1380 hospitals



Data for 2007

BURDEN study*

ORs for 30-day mortality

mean excess length of stay

EARSS

frequency BSI

acute care hospital beds

Eurostat/OECD database

national acute care beds

WHO CHOICE

Cost model for determining unit hospital costs by care category and country



BoD estimates for the EU (1)

	MRSA	G3C REC
BSI (cases)	28,000	15,000
Ex Mort (cases)	5,500	2,700
Ex LoS (days)	256,000	120,000
Ex Hosp Cost	44,000,000 €	18,000,000 €

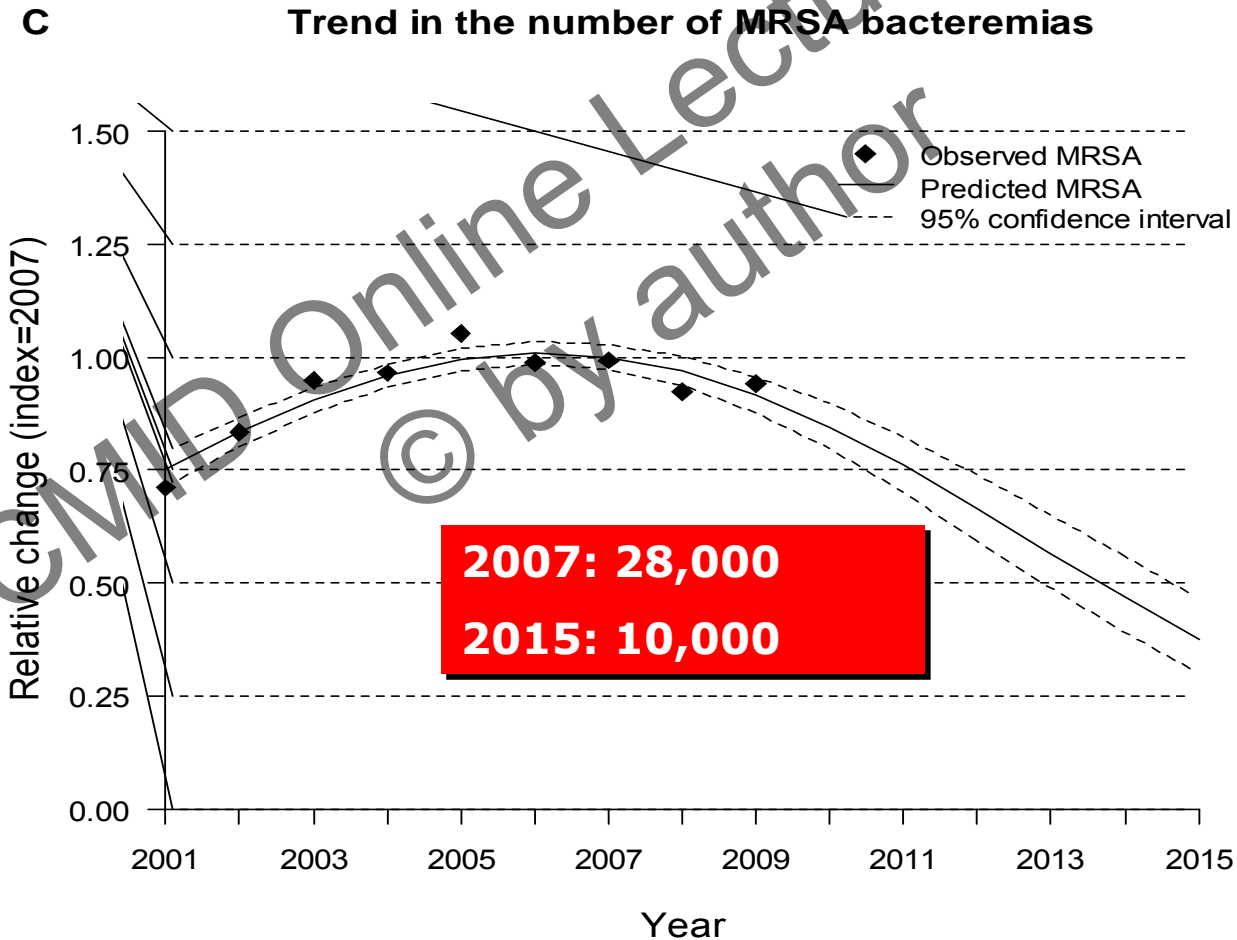


BoD estimates for the EU (2)

	total
BSI (cases)	43,000
Ex Mort (cases)	8,200
Ex LoS (days)	376,000
Ex Hosp Cost	62,000,000 €



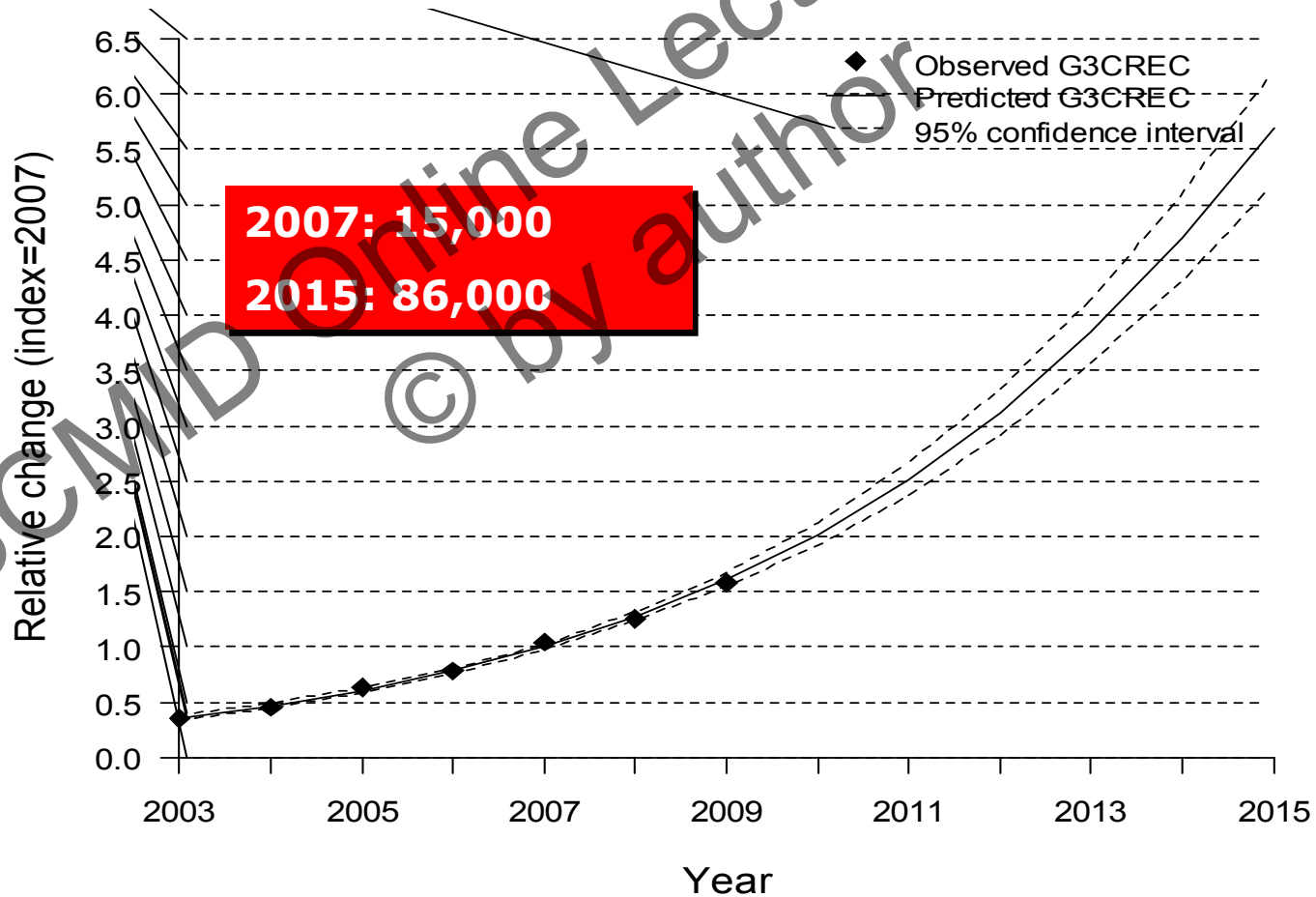
MRSA: trend analysis





G3CREC: trend analysis

F Trend in the number of G3CREC bacteremias





BoD estimates for the EU (3)

	2007	2015
BSI (cases)	43,000	96,000
Ex Mort (cases)	8,200	17,000



Cause-specific mortality in EU (cases per 100,000)

LRTI	29.5
HIV	1.5
MRSA/REC BSI	1.5
TB	1.0

ESCMID Online Lecture Library
© by author



Cause-specific mortality in EU

(cases per 100,000)

	2007	2015
LRTI	29.5	
HIV	1.5	
MRSA/REC BSI	1.5	4.3
TB	1.0	
CVD	373	
RTA	8.5	
ECDC 2010	4.9	



Appraisal (1)

- i. No studies have so far addressed cost and burden from all relevant perspectives
- ii. Current figures from ECDC/EMA are based on multiple assumptions
- iii. Most studies determine risk estimates for single pathogens/infections in single centres and don't provide population-based estimates
- iv. The BURDEN study estimates PAF for antibiotic resistance among BSI caused by the two important AMR pathogens across Europe



Appraisal (2)

- v. Global estimates require the inclusion of the paediatric segment in low resource countries to obtain valid DALY estimates
- vi. Surrogate markers such as drug effectiveness indices may be good approximations of BoD
- vii. Additional studies will provide a more comprehensive estimate (more pathogens more infections, better ascertainment of costs)



EARSS National Representatives, data managers and laboratories

BURDEN study group: Walter Koller, Jutta Berger, Jan Nagler, Claudine Icket, Smilja Kalenic, Jasminka Horvatic, David Turner, Louise Lansbury, Harald Seifert, Achim Kaasch, Olga Paniara, Athena Argyropoulous, Maria Bompola, Edmond Smyth, Mairead Skally, Annibale Raglio, Arta Balode, Agita Melbarde Kelmere, Michael Borg, Debbie Xuereb, Mihaela Ghita, Peter Davey, Michelle Noble, Jana Kolman, Stanko Grabljevec

Health Protection Agency UK NOW Public Health England: John Davies, Miranda Murray, Mark Lillie, Elizabeth Sheridan, Ruth Blackburn and Katherine Henderson

NHS National Services Scotland: Julie Wilson and Camilla Wiuff

Welsh Healthcare Associated Infection Programme: Mari Morgan

Public Health Agency Northern Ireland: Health Care Associated Infections (HCAI) Team

Swedish institute for Infection Control Sweden: Johan Struwe

Tel Aviv Sourasky Medical Centre Israel: Yehuda Carmeli

Mater Dei hospital Malta: Michael Borg and Elizabeth Scicluna

Iceland: Karl Kristinsson and Linda Helgadottir

Finland: Pelanteri Simo and Outi Lyytikainen