Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in Switzerland

On the basis of data from the European Antimicrobial Resistance Surveillance Network and the European Centre for Disease Prevention and Control (ECDC) point prevalence survey (PPS) of health-care-associated infections and antimicrobial use in 2011–12,[1] Alessandro Cassini and colleagues[2] estimated the burden of disease due to infections with 16 antibiotic resistance-bacterium combinations in 2015 in the EU or European Economic Area (EEA).[2] Switzerland is not an EU or EEA country and, thus, was not part of this project.

We applied the same methodology to estimate the number of infections with antibiotic-resistant bacteria and the resulting number of attributable deaths and disability-adjusted life-years (DALYs) in Switzerland for 2015. The data source for bloodstream infections was the Swiss national antibiotic resistance database of the Swiss Centre for Antibiotic Resistance. Because the Swiss PPS of 2017 had a small sample size for each antibiotic resistance-bacterium combination,[3] bloodstream infection or non-bloodstream infection conversion factors were based on the ECDC PPS of 2011–12. As Cassini and colleagues did, we used the Burden of Communicable Disease in Europe toolkit for the estimation of the outputs,[4] based on 10 000 Monte Carlo simulations, without time discounting.

We estimated that 7156 (95% uncertainty interval [UI] 6825–7488) cases of infections with antibiotic-resistant bacteria occurred in 2015, which accounted for 276 (95% UI 261–292) attributable deaths and 7400 (95% UI 7073–7753) DALYs. These estimates correspond to estimates of 85·0 (95% UI 81·1–88·9) infections per 100 000 people, 3·28 (95% UI 3·10–3·47) attributable deaths per 100 000, and 87·8 (95% UI 83·9–92·0) DALYs per 100 000 (table).

The number of DALYs per 100 000 in Switzerland was lower than the EU or EAA average of 170·1 (95% UI 149·5–192·4) and, compared with individual EU or EEA countries,[2] Switzerland ranked between the UK (79·9, 95% UI 70·2–90·1) and Spain (105·1, 95% UI 92·3–119·3).

In 2015, in Switzerland, the highest proportion of the total burden of disease due to infections with antibiotic-resistant bacteria (49·1 [55·9%, 95% UI 52·5–59·8] of 87·8) was caused by third-generation cephalosporin-resistant *Escherichia coli* and *Klebsiella pneumoniae*. Infections with carbapenem-resistant or colistin-resistant *E coli, K pneumoniae, Acinetobacter* spp, and *Pseudomonas aeruginosa* contributed to 20·8 (23·7%, 95% UI 21·0–26·6) of the total burden of 87·8 DALYs per 100 000, which was lower than the EU or EEA average of 65·9 (38·7%, 32·9–45·1) of 170·1 DALYs per 100 000.

The methodology developed by ECDC to estimate the burden of infections with antibiotic-resistant bacteria proved valuable for Switzerland and for benchmarking with other European countries. We conclude that other

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	Infections per year (95% UI)	Infections per 100 000 (95% UI)	DALYs (95% UI)	DALYs per 100 000 (95% UI)	Attributable deaths per year (95% UI)	Attributable mortality per 100 000 (95% UI)
Third-generation cephalosporin-resistant *Escherichia coli**	5107 (4770–5439)	60·7 (56·7–64·6)	3550 (3301–3827)	42·2 (39·2–45·5)	156 (143–171)	1·86 (1·70–2·03)
Carbapenem-resistant *Pseudomonas aeruginosa*†	641 (597–687)	7·6 (7·1–8·2)	1580 (1377–1794)	18·7 (16·3–21·3)	43 (37–50)	0·51 (0·44–0·59)
Meticillin-resistant *Staphylococcus aureus*	608 (579–637)	7·2 (6·9–7·6)	745 (711–782)	8·9 (8·4–9·3)	29 (27–30)	0·34 (0·32–0·36)
Third-generation cephalosporin-resistant *Klebsiella pneumoniae**	413 (393–433)	4·9 (4·7–5·1)	587 (555–621)	7·0 (6·6–7·4)	22 (21–24)	0·27 (0·25–0·28)
Penicillin-resistant *Streptococcus pneumoniae*‡	125 (114–138)	1·5 (1·4–1·6)	342 (318–370)	4·1 (3·8–4·4)	8 (7–8)	0·09 (0·09–0·10)
Penicillin-resistant and macrolide-resistant *S pneumoniae*§	141 (127–158)	1·7 (1·5–1·9)	217 (202–236)	2·6 (2·4–2·8)	9 (8–9)	0·10 (0·10–0·11)
Vancomycin-resistant *Enterococcus faecalis* and *Enterococcus faecium*	39 (32–46)	0·5 (0·4–0·5)	127 (94–169)	1·5 (1·1–2·0)	2 (2–3)	0·03 (0·02–0·04)
Carbapenem-resistant *K pneumoniae*†	13 (11–15)	0·2 (0·1–0·2)	78 (55–108)	0·9 (0·7–1·3)	2 (1–2)	0·02 (0·01–0·03)
Multidrug-resistant *P aeruginosa**¶	47 (40–53)	0·6 (0·5–0·6)	77 (56–102)	0·9 (0·7–1·2)	3 (2–4)	0·04 (0·03–0·05)
Carbapenem-resistant *Acinetobacter* spp†	14 (12–15)	0·2 (0·1–0·2)	73 (49–101)	0·9 (0·6–1·2)	1 (1–2)	0·01 (0·01–0·02)
Carbapenem-resistant *E coli*†	12 (9–15)	0·1 (0·1–0·2)	17 (10–26)	0·2 (0·1–0·3)	1 (0–1)	0·01 (0·00–0·01)
Others (colistin-resistant *E coli*, *K pneumoniae*, *Acinetobacter* spp, *P aeruginosa*, and multidrug-resistant *Acinetobacter* spp*||)	0	0	0	0	0	0
Total (overall model)	7156 (6825–7488)	85·0 (81·1–88·9)	7400 (7073–7753)	87·8 (83·9–92·0)	276 (261–292)	3·28 (3·10–3·47)

Time discounting was not applied to the estimation. 95% UI=95% uncertainty interval. *Excluding isolates also resistant to colistin, carbapenems, or both. †Excluding isolates also resistant to colistin. ‡Excluding isolates also resistant to macrolides. §Excluding isolates resistant to penicillins alone. ¶Resistance to three or more antibiotic groups as marker of multidrug resistance. ||Aminoglycoside and fluoroquinolone resistance as marker of multidrug resistance.

Table: **Estimated annual burden of infections with selected antibiotic-resistant bacteria of public health importance, by decreasing number of disability-adjusted life-years (DALYs) per 100 000 people in Switzerland, 2015**

non-EU or EEA countries should be encouraged to apply this methodology for international comparability, and ultimately inform the development and implementation of prevention strategies.

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Michael Gasser, Walter Zingg, Alessandro Cassini, Andreas Kronenberg, and the Swiss Centre for Antibiotic Resistance
michael.gasser@ifik.unibe.ch

Institute for Infectious Diseases, University of Bern, 3001 Bern, Switzerland (MG, AK); Infection Control Programme and WHO Collaborating Centre, University of Geneva Hospitals, Geneva, Switzerland (WZ); and European Centre for Disease Prevention and Control, Solna, Sweden (AC)

1 European Centre for Disease Prevention and Control. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals. 2013. https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/healthcare-associated-infections-antimicrobial-use-PPS.pdf (accessed Oct 22, 2018).

2 Cassini A, Diaz Högberg L, Plachouras D, 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* 2018; published online Nov 5. http://dx.doi.org/10.1016/S1473-3099(18)30605-4.

3 Swissnoso. Point Prevalence Survey 2017 of healthcare-associated infections and antimicrobial use in Swiss acute care hospitals. 2018. www.swissnoso.ch/fileadmin/swissnoso/Dokumente/5_Forschung_und_Entwicklung/2_Punktpraevalenzstudie/ch_pps_2017_report_FINAL2.pdf (accessed Oct 19, 2018).

4 Colzani E, Cassini A, Lewandowski D, 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:** e0170662.

The threat of bioterrorism

Manfred S Green and colleagues[1] reviewed the modern aspects of bioterrorism threats, using the US Centers for Disease Control and Prevention (CDC) classification for their analysis of biological agents with potential for bioterrorism. The CDC categorised these agents into three distinct groups, depending on public health impact (severity of illness and mortality), dissemination potential, public perception, and the easiness of preparation.[2]

Classification for disease prioritisation is a complex decision process.[3] At a state level, disease prioritisation is mainly motivated by the need to allocate limited financial and human resources to achieve the greatest benefit in safeguarding human health. In the broad perspective of public health, the prioritisation of infectious diseases had long been discussed.[4] Although the analytical criteria should be transparent and reproducible, these tasks are daunting because of their interdependence, impairing a separate assessment. The variety of potential bioterrorism pathogens is, by far, greater than the resources that could be allocated to tackle them all at the same time. The case-fatality rate of a provoked infectious event has both social and economic impacts. Therefore, the economic cost might be much higher than the number of human casualties, as was observed in 2001, in the anthrax letter attacks (five deaths *vs* millions of US dollars in the decontamination process expenses).[5]

The European Centre for Disease Prevention and Control reviewed the disease prioritisation methodology in 2015,[6] in a report examining the best practices for ranking infectious disease threats. They compared five methods to prioritise the communicable disease risks with use of bibliometric index, Delphi panels, multi-criteria decision analysis, qualitative algorithms, and questionnaires. Finally, they proposed a tool for disease prioritisation that includes a weighing criterion.[7] For us, this weighing criterion is decisive and should be implemented when a decision is made at a political level. The bioterrorist threat assessment should be regularly re-assessed, because threats can evolve swiftly with viral disease eradications and emergence of new pathogens, including those related to synthetic biology. Moreover, our modern societies are now much more sensitive to unexpected events, with a high media exposure, reflecting the emerging role of social networks. Any low-cost bioterrorist attack, even with a minor clinical impact due to a poorly pathogenic agent, can provoke a global deflagration with an immediate and long-lasting fear cost at the social level. From this standpoint, ever-changing public opinion might be the most important criterion and must be much more taken into account in the bioterrorist risk assessment, preparedness, and response, including an updated ready-to-use communication tool.

Finally, although probably provoking a severe health and societal crisis, bioterrorism is a variation of the natural emergence of infectious diseases. The medical counter-measures against a bioterrorist occurrence or a natural emergence are frequently overlapping, as exemplified by the use of polyclonal serum during an outbreak of anthrax in drug users, or the Ebola vaccine in the outbreaks in Africa this decade.[8,9] Nationally and transnationally, interfacing and strengthening the research, development, and implementation of these counter-measures is clearly beneficial for global health and security. Building efficient communications is a big part of the challenge.

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Jean-Nicolas Tournier, Christophe N Peyrefitte, Fabrice Biot, Audrey Merens, Fabrice Simon
jean-nicolas.tournier@intradef.gouv.fr

Microbiology and Infectious Diseases Department, Institut de Recherche Biomédicale des Armées, 91220 Brétigny-sur-Orge, France (J-NT, CNP, FB); Viral Genomics and Vaccination Unit, CNRS UMR-3569, Institut Pasteur, Paris, France (J-NT); French National Reference Center for Anthrax, Brétigny sur Orge, France (J-NT, FB); Unité Mixte de Recherche, Unité des Virus Emergent, IRD-190, French National Institute of Health and Medical Research–1207, Marseille, France (CNP); French National Reference Center for Orthopoxviruses, Brétigny sur Orge, France (CNP); Biology Laboratory, Hôpital d'Instruction des Armées Bégin,