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Swiss Point Prevalence Survey about Healthcare-associated Infections and Antibiotic Use in acute-care hospitals – Work package 2 (costs, mortality)

Report

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2. EXECUTIVE SUMMARY

Healthcare associated infections are an endemic patient safety problem of major concern. Estimating cost and attributable mortality due to healthcare-associated infections remains a challenging task, mainly because direct and indirect costs of individual patients are often not known, and there are no representative data on healthcare-associated infections on a national level. There is no estimation on cost for Switzerland, and the past estimation on annual cases dates back more than 10 years. The aim of this second work package of the Swiss Point Prevalence Survey 2017 (CH-PPS) was to estimate: 1) incidence and annual numbers of patients with healthcare-associated infections; 2) attributable cost; and 3) attributable mortality due to healthcare-associated infections in Swiss acute care hospitals.

The incidence of healthcare-associated infections was estimated from data of the CH-PPS 2017. Attributable length-of-stay was estimated by data imputation, weighting, and multistate modelling. Total cost was calculated by multiplying the estimated incidence of patients with healthcare-associated infections with the attributable length-of-stay and daily total cost per inpatient as published by the Swiss Office of Statistics in 2017.

Data on 12'931 patients from 96 acute care hospitals were collected in the CH-PPS in 2017. The pooled prevalence of patients with one or more healthcare-associated infections was 5.9% (95% confidence interval (CI): 5.5–6.3). The estimated incidence was 4.5 (95% CI: 3.7-5.2) patients per 100 hospitalisations. The extra length of stay due to healthcare-associated infections was estimated at 6.4 days (95% CI: 5.6-7.3). Taking into account incidence, attributable length of stay and daily cost per inpatient, the number of patients affected by healthcare-associated infections in Swiss acute care hospitals in 2017 was estimated at 59'091 (95%CI: 49'377-68'804) with a total cost of 751 Mio CHF (95%CI: 549-997). A total of 5'909 (95% CI: 1'975-11'009) fatal outcomes due to healthcare-associated infections were estimated for 2017.

This is the first study to estimate incidence, attributable length of stay and cost due to healthcare-associated infections in Switzerland. Although some limitations apply, particularly the fact that healthcare-associated infections at admission could not be modelled, the calculated estimations appear reasonable. Future studies must confirm the accuracy of these data. Combining the data from a prevalence survey with national statistical data in a multi-state modelling is a straightforward methodology in cost estimation for healthcare-associated infections.

3. BACKGROUND

Healthcare associated infections (HAIs) are an endemic patient safety problem of major concern.[1] [2] Up to 10% of patients in non-high-income countries and 6% in high-income countries suffer from an HAI on any day of hospitalization.[3] Their socio-economic burden is undeniably significant and impacts on quality of life and mortality.[4-8] Recent systematic reviews reported on the economic effect of different HAI-types on hospital costs and charges.[9-17] The financial impact of HAI on the US healthcare system between 1986 and 2013 was estimated at $10 billion.[18]

Estimating costs and attributable mortality from HAI remains a difficult task, mainly because direct and indirect costs of individual hospitals are often not known, and there are no representative data on HAI on a national level. Often, the latter focuses on specific HAI-types, different settings, or data are generated by point prevalence surveys (PPSs), which overestimate the burden of HAI for various reasons.[19-21] While the attributable net cost due to HAI on hospital level cannot be directly deducted even if direct and indirect costs are quantifiable,[22,23] from a society perspective, all attributable direct and indirect costs translate into real expenses for HAI.

The aim of this work package was to estimate the incidence of patients suffering from HAIs in acute care hospitals, the attributable direct and indirect costs, and the attributable mortality.

4. OBJECTIVES

- To estimate the incidence proportion of patients with one or more HAIs in acute care hospitals in Switzerland in 2017
- To estimate attributable length-of-stay (LOS) due to HAIs in Switzerland in 2017
- To estimate total (direct and indirect) cost of HAIs in Switzerland in 2017
- To estimate attributable mortality due to HAI in Switzerland in 2017

The data will help to inform future models on cost-effectiveness of HAI prevention in Switzerland, and to allow prioritizing activities within Swissnoso.

5. MATERIALS AND METHODS

The incidence of healthcare-associated infections was estimated from data of Swiss point prevalence survey in 2017.[24] Attributable length-of-stay was estimated by data imputation, weighting, and multistate modelling. Total cost was calculated by multiplying the estimated incidence of healthcare-associated infections with the attributable length-of-stay and daily total cost per inpatient as published by the Swiss Office of Statistics (FOS) for 2017 (https://www.bfs.admin.ch/asset/fr/je-f-14.04.01.01).[24,25] Outcomes were stratified by hospital provision type (basic, central, specialised) as per FOS definition (https://www.bfs.admin.ch/bfs/fr/home/statistiques/sante/systeme-sante/hopitaux.html). Figure 1 summarises the project methodology.

Figure 1. Outline of the project methodology for estimating total cost for healthcare-associated infections
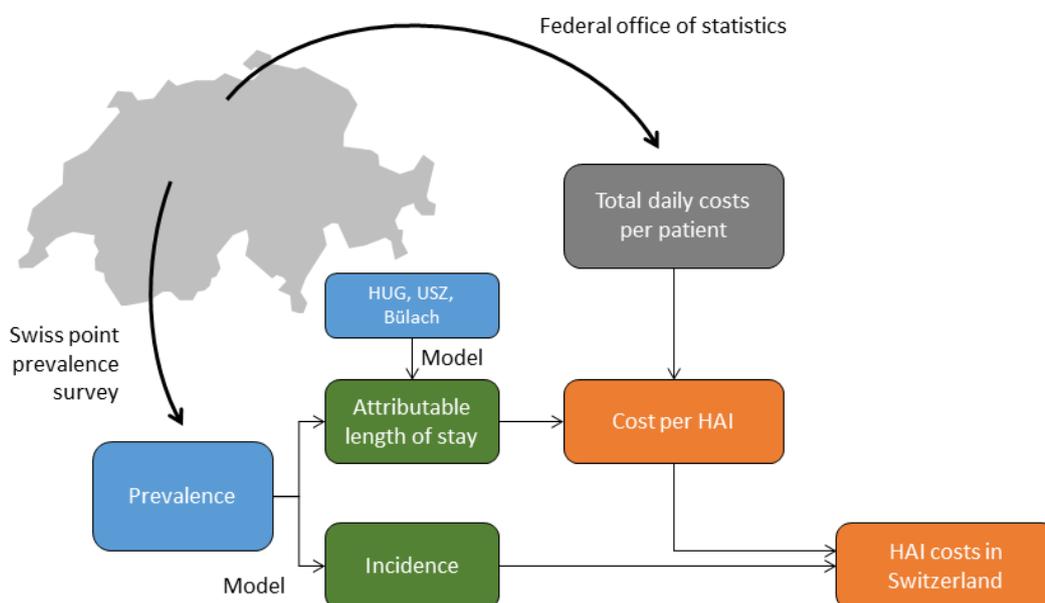
5.1. Prevalence survey – 2017

All acute care hospitals in Switzerland (177) were invited to participate in this cross-sectional survey during the second quarter of 2017. The protocol by the European Centre for Disease Prevention and Control was applied.[26] Patients of all ages, admitted before 8:00 on the day of

survey were included, except when admitted to outpatient clinics, or emergency and psychiatry wards. The detailed methodology is described elsewhere.[24,27]

5.2. Prevalence-incidence conversion, using the ECDC methodology

Estimates of the total number of patients per year with an HAI were calculated after conversion data prevalence to incidence data by applying the formula by Rhame and Sudderth:[28]

$$I_{estimated} = P \ \frac{LA}{(LN-INT)}$$

P   Prevalence, defined by the percentage of patients with at least one HAI on the survey day

LA   Average length of hospital stay, derived from the number of patient-days and the number of cases for 2017 (Federal Office of Statistics)

LN   Average length of hospital stay of infected patients (admission to discharge date); since the discharge date was not known at the time of the PPS, the length of stay of infected patients was calculated as up to the survey date

INT   Average length between date of admission and date of onset of HAI; if a patient had multiple infections on the day of the survey, the date of onset of the first infection was considered

Table 1. Values used for the Rhame and Sudderth formula

	All hospitals	**Basic**	**Central**	**Special**
P, %	5.92	3.93	6.18	6.74
LA, days*	6.17	5.15	6.45	6.09
LN-INT, days				
median	7	7	7	6
mean	9.75	10.14	9.56	12.50

*Values from the Swiss Office of Statistics

Because of the uncertainty inherent to the Rhame and Sudderth formula, two estimates were calculated, one using the mean number of days from HAI onset until PPS date (LN-INT) and one using the median time from HAI onset until PPS date. The latter approach was chosen because the median time from admission to PPS date for all patients in the PPS was much more similar to the overall length of stay. However, since this relationship is not necessarily true for patients with HAIs, we also used the mean time from HAI onset until PPS date to obtain a lower estimate of the incidence. The point estimate was calculated as the mean of the two estimates.[26,29]

5.3. Estimating attributable length of stay

There were three important analysis steps: data imputation/augmentation, weighting, and multistate modelling.

Imputation

Imputation refers to the "guessing" of missing data. The PPS dataset was missing patients' prospective follow-up information on infections and discharge after the date of PPS. However, we were able to obtain this information for a subset of patients from the university hospitals of Geneva (HUG) and Zürich (USZ) and the regional hospital of Bülach. From this subset, we developed an imputation model that could "predict" patients' discharge date and whether they would develop an infection, thereby augmenting the dataset to fill in the missing information. Note that it is sufficient to be accurate *on average* rather than be accurate for every individual patient since we infer only average quantities from the augmented data. Figures 1 and 2 show visualise the imputation process and the augmented dataset.

Figure 2. Illustration of the imputation strategy
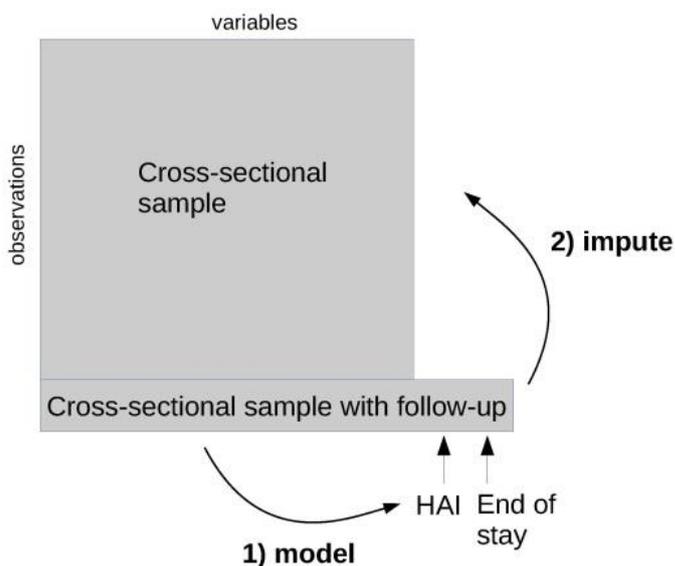
Figure 3. Visualization of augmented dataset
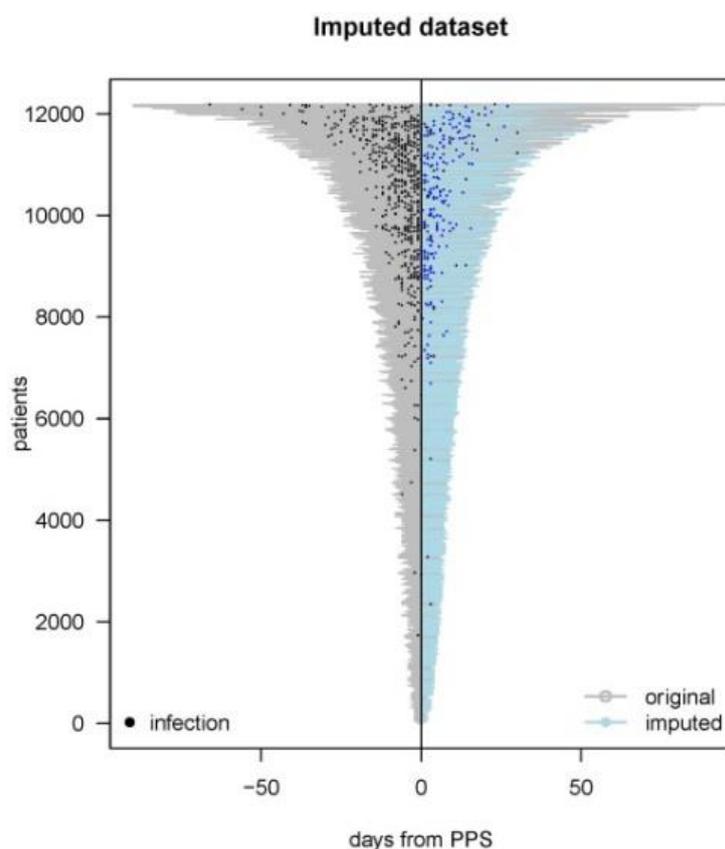
Weighting

Applying our imputation model we can create an augmented dataset where the discharge time is known for every patient. However, data sampled from PPSs are length-biased with regard to patients' length of stay. Patients with a length of stay of 10 days will have double the probability of being sampled compared to patients with a stay of 5 days, thus sampled patients will have longer hospitalization times compared to the true underlying hospital population. In other words long-stayers are overrepresented and short-stayers are underrepresented in a PPS sample. This is particularly relevant since HAIs are associated with longer hospitalisation. We therefore used weighted analyses to correct for the length of hospital stay (LOS). Each patient is assigned a LOS-weight inversely proportional to their LOS, thereby down-weighting the long-stayers and up-weighting the short-stayers.

Multi-state modelling

These weights were used in a multivariable regression model to estimate incidence proportions. The regression model allowed estimating the incidence proportion while adjusting for patient and hospital characteristics. For example, it is known that a fatal McCabe score will increase the

risk of acquiring an HAI,[1,24,30-32] and a regression model allows to quantify that risk. To estimate the attributable length of stay, a naïve approach would be to compare average LOS between patients who acquire an infection and patients who do not. However, this would be flawed because patients only acquire infection some time after hospital admission, therefore infected patients would be expected to have longer hospitalisation times even if infection had no prolonging effect at all.[21] To analyse the attributable LOS more accurately, if a patient acquires an infection on the 5th day of their hospital stay, their LOS beyond the infection should be compared to an infection-free patient with at least 5 days of hospitalisation (infection-free patient from day 5). This is done by estimating the composite transitions of patients from hospital admission to infection and discharge in a multistate model.

Simulations

We also implemented simulation studies to test our methods and verify that they work before applying them to the real data.

5.4. Systematic review

The systematic review on attributable mortality followed the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) guidelines.[33] The data sources used for the systematic search of English and non-English publications were: Ovid Medline, Pub Med and EMBASE. Medical Subject Headings (MeSH terms) were included in the search terms and sought in the OVID Medline and PubMed databases. Emtree terms were sought in the EMBASE database. Only quantitative original studies on humans, and published between 1 January 2000 and 15 December 2017, and written in English, French, German, or Spanish were eligible. Case series, case reports, review articles, editorials, other systematic reviews, data from conference proceedings, abstracts, books, manufacturers or experts, government agency reports, white papers, theses and dissertations, or any other type of reports not published in a peer-reviewed journal were excluded. Study population included all patients hospitalized in acute-care hospital settings in high-income countries, regardless of age. High-income countries were defined based on the World Bank definition, as those countries with a gross national income (GNI) per capita of $12,236 or more in 2017 (http://datatopics.worldbank.org/sdgatlas/archive/2017/the-world-by-income.html).

The exposure of interest was the presence of one or more HAIs; cases with HAIs were compared with unexposed, matched controls (without HAIs). Studies where cases with a specific HAI were compared to controls with the same infection of community onset were excluded. Only clinical HAI surveillance definitions were eligible, either issued by the ECDC or the US National Healthcare Safety Network (NHSN).[26,34] Healthcare-associated infections were

further classified to the following categories: bloodstream infection (BSI), lower-respiratory tract infection (LRTI), urinary tract infection (UTI), surgical site infection (SSI), and other infection. The outcome was in-hospital mortality.

All retrieved studies were merged into an Endnote database and duplicates were removed. Two independent experts independently reviewed all abstracts and eligible full text articles by applying the PICO criteria. To ensure reproducibility and transparency in that stage of the review, articles from each EndNote database were uploaded on the Rayyan QCRI platform (rayyan.qcri.org). Reviewers worked independently, blinded to each other. Discrepancies were resolved by consensus or by discussion with a third reviewer where necessary. The content of every article was assessed by using the PRISMA checklist. The Integrated quality Criteria for the Review Of Multiple Study designs (ICROMS) was applied to assess risk of bias and internal validity.[35]

6. RESULTS

6.1. Point prevalence survey in acute care hospitals in Switzerland, 2017

Ninety-six acute care hospitals (79% of all hospitals ≥ 100 beds) provided data on 12,931 patients. The HAI-prevalence was 5.9% (95% confidence interval (CI): 5.5–6.3). The HAI prevalence of hospitals with basic provision, central provision and specialized care were 3.9% (95% CI: 3.0-4.9), 6.2% (95% CI: 5.7-6.6), and 6.7% (95% CI: 4.7-8.8). The most common type of HAI was surgical site infection (29.0%), followed by lower respiratory tract (18.2%), urinary tract (14.9%) and bloodstream (12.8%) infections. The highest prevalence was identified in intensive care (20.6%), in large hospitals > 650 beds (7.8%), among elderly patients (7.4%), male patients (7.2%) and patients with an ultimately (9.3%) or rapidly (10.6%) fatal McCabe score. More detailed information is published elsewhere.[24]

6.2. Estimation of incidence proportions

The estimated incidence of patients with one or more HAI in 2017 was 4.48 (95% CI: 3.74-5.22). Table 2 summarises prevalence, incidence and number of cases, stratified for all-HAI, HAI occurring during hospitalization, and the four major HAI-types occurring during hospitalization.

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Table 2. Prevalence and incidence of healthcare-associated infections, stratified by type and time of occurrence

	All hospitals	**Basic**	**Central**	**Special**
Cases in CH 2017	1'319'187	250'562	947'937	120'688
All HAI				
Prevalence	5.92	3.93	6.18	6.74
	(5.51-6.32)	(2.99-4.86)	(5.72-6.64)	(4.66-8.81)
Incidence	4.48	2.44	4.93	5.06
	(3.74-5.22)	(1.99-2.89)	(4.17-5.70)	(3.28-6.84)
Cases	59'100	6'114	46'733	6'107
	(49'338-68'862)	(4'986-7'241)	(39'529-54'032)	(3'959-8'255)
HAI during hospitalisation				
Prevalence	4.23	2.48	4.42	5.85
	(3.88-4.58)	(1.73-3.23)	(4.03-4.81)	(3.91-7.79)
Incidence	3.62	1.70	3.97	4.38
	(2.88-4.35)	(1.59-1.82)	(3.2-4.75)	(2.83-5.94)
Cases	47'755	4'260	37'633	5'286
	(37'993-57'385)	(3'984-4'560)	(30'334-45'027)	(3'415-7'169)
BSI, LRTI, UTI, SSI during hospitalisation				
Prevalence	3.09	2.23	3.13	4.79
	(2.79-3.38)	(1.52-2.95)	(2.8-3.46)	(3.02-6.55)
Incidence	2.65	1.78	2.83	3.55
	(2.13-3.17)	(1.64-1.92)	(2.29-3.36)	(2.25-4.86)
Cases	34'958	4'460	26'827	4'284
	(28'099-41'818)	(4'109-4'811)	(21'708-31'851)	(2'715-5'865)

BSI: bloodstream infection; HAI: healthcare-associated infection; LRTI: lower-respiratory tract infection; SSI: surgical site infection; UTI: urinary tract infection.

6.3. Estimating attributable length of stay

Calculating the transition rates in the multi-state model allowed determining the length of stay with HAI versus the length of stay without HAI (in parentheses: 95% confidence intervals).

Table 3. Estimated attributable length of stay, stratified by age, gender, McCabe score, and provision type

	HAI (N = 548)	BSI (N = 79)	LRI (N = 134)	Other (N = 152)	SSI (N = 83)	UTI (N = 100)
Average	6.4	6.6	6.0	5.9	7.1	5.2
	(5.6-7.3)	(4.5-8.7)	(4.7-7.3)	(4.3-7.5)	(5.2-9.0)	(3.4-7.0)
Age group						
0-17	4.6	6.2	5.9	3.5	4.5	3.7
	(0.8-8.4)	(0.6-11.9)	(1.2-10.6)	(0.1-6.9)	(-0.4-9.4)	(1.7-5.7)
18-44	9.0	12.2	11.6	6.4	10.4	9.6
	(5.4-12.6)	(0.6-23.8)	(2.8-20.4)	(2.5-10.3)	(3.3-17.5)	(2.5-16.7)
45-64	7.9	8.2	7.4	7.4	8.6	7.9
	(6.2-9.6)	(4.7-11.7)	(2.9-11.9)	(4.6-10.2)	(6.2-11.0)	(3.3-12.5)
65-84	6.0	5.5	5.7	5.7	6.4	4.0
	(4.9-7.2)	(-0.5-11.5)	(3.9-7.5)	(2.8-8.6)	(2.6-10.2)	(1.8-6.2)
85+	4.1	4.9	5.3	5.3	6.2	4.4
	(2.4-5.8)	(0.5-9.4)	(3.0-7.6)	(1.7-8.9)	(0.3-12.1)	(1.2-7.6)
Gender						
male	7.1	8.0	6.9	6.9	7.9	5.4
	(5.9-8.3)	(4.7-11.3)	(5.1-8.7)	(4.4-9.4)	(5.4-10.4)	(2.1-8.7)
female	5.8	5.3	5.0	6.3	6.5	5.0
	(4.5-7.0)	(1.8-8.7)	(3.0-7.0)	(3.7-8.8)	(3.5-9.5)	(2.5-7.5)
McCabe score						
nonfatal	7.4	7.2	6.6	6.6	8.0	6.5
	(6.3-8.4)	(4.4-10.0)	(5.1-8.1)	(3.8-9.4)	(5.4-10.6)	(4.4-8.6)
ultimately fatal	2.7	3.4	2.1	2.9	3.2	-0.6
	(1.3-4.1)	(-0.2-7.0)	(-3.1-7.1)	(0.4-5.4)	(0.8-5.4)	(-2.2-1.0)
rapidly fatal	5.2	6.1	8.3	-0.4	7.2	7.8
	(2.6-7.8)	(1.8-10.4)	(4.1-12.5)	(-3.4-2.6)	(3.8-10.6)	(-1.3-16.9)
Provision type						
central	6.2	6.3	5.8	5.1	6.8	4.9
	(5.4-7.1)	(4.3-8.3)	(4.5-7.1)	(3.4-6.7)	(4.5-9.1)	(3.3-6.5)
basic	8.2	9.0	7.0	5.3	9.2	8.7
	(5.7-10.8)	(3.3-14.7)	(3.5-10.5)	(-4.4-14.9)	(4.2-14.2)	(3.7-13.7)
special	6.6	10.4	10.5	3.0	11.9	5.2
	(-0.4-13.6)	(6.8-14.0)	(5.7-14.3)	(-1.3-7.3)	(1.7-22.1)	(2.4-8.0)

BSI: bloodstream infection; HAI: healthcare-associated infection; LRTI: lower-respiratory tract infection; SSI: surgical site infection; UTI: urinary tract infection.

6.4. Estimation of cost

Tables 4 to 9 summarise the costs for HAI and different HAI-types (BSI, LRTI, UTI, SSI, other HAI-types), stratified by the different provision types.

Table 4. Estimated costs for healthcare-associated infections

	All hospitals	Basic	Central	Special
Cases in CH 2017	1'319'187	250'562	947'937	120'688
Total costs per patient-day (CHF)	1'985.86	1'907.42	1'975.27	2'211.76
Attributable LOS (days)	6.4	8.2	6.2	6.6
	(5.6-7.3)	(5.7-10.8)	(5.4-7.1)	(0.0-13.6)
Costs per HAI (CHF)	12'709	15'641	12'247	14'598
	(11'121-14'497)	(10'872-20'600)	(10'666-14'024)	(0-30'080)
All HAI				
Incidence	4.48	2.44	4.93	5.06
	(3.74-5.22)	(1.99-2.89)	(4.17-5.70)	(3.28-6.84)
Cases	59'100	6'114	46'733	6'107
	(49'338-68'862)	(4'986-7'241)	(39'529-54'032)	(3'959-8'255)
Total costs, Mio CHF	751.13	95.62	572.33	89.15
	(548.67-998.27)	(54.21-149.17)	(421.63-757.77)	(0.00-248.31)
HAI during hospitalisation				
Incidence	3.62	1.70	3.97	4.38
	(2.88-4.35)	(1.59-1.82)	(3.2-4.75)	(2.83-5.94)
HAI cases	47'755	4'260	37'633	5'286
	(37'993-57'385)	(3'984-4'560)	(30'334-45'027)	(3'415-7'169)
Total costs, Mio CHF	606.94	66.62	460.88	77.17
	(422.51-831.89)	(43.31-93.94)	(323.56-631.48)	(0.00-215.64)
BSI, LRTI, UTI, SSI during hospitalisation				
Incidence	2.65	1.78	2.83	3.55
	(2.13-3.17)	(1.64-1.92)	(2.29-3.36)	(2.25-4.86)
Cases	34'958	4'460	26'827	4'284
	(28'099-41'818)	(4'109-4'811)	(21'708-31'851)	(2'715-5'865)
Total costs, Mio CHF	444.30	69.76	328.54	62.54
	(312.48-606.23)	(44.68-99.10)	(231.54-446.69)	(0.00-176.43)

BSI: bloodstream infection; CHF: Swiss francs; HAI: healthcare-associated infection; LRTI: lower-respiratory tract infection; SSI: surgical site infection; UTI: urinary tract infection.

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Table 5. Estimated costs for healthcare-associated bloodstream infections

	All hospitals	Basic	Central	Special
Cases in CH 2017	1'319'187	250'562	947'937	120'688
Prevalence	0.82	0.30	0.87	1.42
	(0.66-0.98)	(0.04-0.57)	(0.69-1.04)	(0.44-2.40)
Incidence	0.62	0.17	0.54	0.82
	(0.52-0.72)	(0.14-0.19)	(0.46-0.62)	(0.32-1.33)
Cases in 2017	179	426	5'119	990
	(6'860-9'498)	(351-476)	(4'361-5'877)	(386-1'605)
Costs per patient-day	1'985.86	1'907.42	1'975.27	2'211.76
Attributable LOS	6.6	9.0	6.3	10.4
	(4.5-8.7)	(3.3-14.7)	(4.3-8.3)	(6.8-14.0)
Costs per HAI	13'107	17'167	12'444	23'002
	(8'936-17'277)	(6'294-28'039)	(8'494-16'395)	(15'040-30'965)
Total costs, Mio CHF	107.20	7.31	63.70	22.76
	(61.30-164.10)	(2.21-13'35)	(37.02-96.36)	(5.81-49.70)

HAI: healthcare-associated infection; LOS: length-of-stay

Table 6. Estimated costs for healthcare-associated lower-respiratory tract infections

	All hospitals	Basic	Central	Special
Cases in CH 2017	1'319'187	250'562	947'937	120'688
Prevalence	1.18	1.15	1.17	1.42
	(0.99-1.36)	(0.63-1.66)	(0.96-1.37)	(0.44-2.40)
Incidence	1.12	0.93	1.29	1.08
	(1.02-1.21)	(0.87-0.99)	(1.07-1.51)	(0.93-1.23)
Cases in 2017	14'775	2'330	12'228	1'303
	(13'456-15'962)	(2'004-2'481)	(10'143-14'313)	(1'122-1'484)
Costs per patient-day	1'985.86	1'907.42	1'975.27	2'211.76
Attributable LOS	6.0	7.0	5.8	10.5
	(4.7-7.3)	(3.5-10.5)	(4.5-7.1)	(5.7-14.3)
Costs per HAI	11'915	13'352	11'457	23'224
	(9'334-14'497)	(6'676-20'028)	(8'889-14'024)	(12'607-31'628)
Total costs, Mio CHF	176.04	31.11	140.10	30.27
	(125.59-231.40)	(13.38-49.68)	(90.16-200.74)	(14.15-46.95)

HAI: healthcare-associated infection; LOS: length-of-stay

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Table 7. Estimated costs for healthcare-associated urinary tract infections

	All hospitals	**Basic**	**Central**	**Special**
Cases in CH 2017	1'319'187	250'562	947'937	120'688
Prevalence	0.96	0.66	0.92	2.48
	(0.79-1.13)	(0.27-1.06)	(0.74-1.11)	(1.19-3.77)
Incidence	0.98	0.56	1.08	2.63
	(0.97-0.99)	(0.55-0.57)	(0.96-1.19)	(2.52-2.75)
Cases in 2017	12'928	1'403	10'238	3'174
	(12'796-13'060)	(1'378-1'428)	(9'100-11'280)	(3'041-3'319)
Costs per patient-day	1'985.86	1'907.42	1'975.27	2'211.76
Attributable LOS	5.2	8.7	4.9	5.2
	(3.4-7.0)	(3.7-13.7)	(3.3-6.5)	(2.4-8.0)
Costs per HAI	10'326	16'595	9'679	11'501
	(6'752-13'901)	(7'057-26'132)	(6'518-12'839)	(5'308-17'694)
Total costs, Mio CHF	133.50	23.28	99.09	36.51
	(86.40-181.55)	(9.73-37.32)	(59.32-144.83)	(16.14-58.73)

HAI: healthcare-associated infection; LOS: length-of-stay

Table 8. Estimated costs for surgical site infections

	All hospitals	**Basic**	**Central**	**Special**
Cases in CH 2017	1'319'187	250'562	947'937	120'688
Prevalence	1.87	1.75	1.96	0.53
	(1.64-2.11)	(1.12-2.38)	(1.7-2.22)	(0.00-1.13)
Incidence	1.2	0.97	1.4	0.08
	(0.95-1.44)	(0.81-1.13)	(1.11-1.69)	(0.04-0.12)
Cases in 2017	15'830	2'430	13'271	97
	(12'532-18'996)	(2'034-2'831)	(10'522-16'020)	(48-145)
Costs per patient-day	1'985.86	1'907.42	1'975.27	2'211.76
Attributable LOS	7.1	9.2	6.8	11.9
	(5.2-9.0)	(4.2-14.2)	(4.5-9.1)	(1.7-22.1)
Costs per HAI	14'100	17'548	13'432	26'320
	(10'326-17'873)	(8'011-27'085)	(8'889-17'975)	(3'760-48'880)
Total costs, Mio CHF	223.20	42.65	178.26	2.54
	(129.41-339.52)	(16.26-76.69)	(93.53-287.96)	(0.18-7.08)

HAI: healthcare-associated infection; LOS: length-of-stay

**Table 9.** Estimated costs for other healthcare-associated infections

	All hospitals	Basic	Central	Special
Cases in CH 2017	1'319'187	250'562	947'937	120'688
Prevalence	1.57	0.42	1.76	1.24
	(1.36-1.78)	(0.11-0.74)	(1.52-2.01)	(0.32-2.16)
Incidence	1.14	0.11	1.36	0.9
	(0.89-1.38)	(0.09-0.12)	(1.08-1.63)	(0.72-1.08)
Cases in 2017	15'039	276	12'892	1'086
	(11'741-18'258)	(226-301)	(10'238-15'451)	(869-1'303)
Costs per patient-day	1985.86	1907.42	1975.27	2211.76
Attributable LOS	5.9	5.3	5.1	3.0
	(4.3-7.5)	(0.0-14.9)	(3.4-6.7)	(0.0-7.3)
Costs per HAI	11'717	10'109	10'074	6'635
	(8'539-14'894)	(0-28'421)	(6'716-13'234)	(0-16'146)
Total costs	176.20	2.79	129.87	7.21
	(100.26-271.14)	(0.00-8.55)	(68.76-204.49)	(0.00-21.05)

HAI: healthcare-associated infection; LOS: length-of-stay

6.5. Estimated mortality

From 1967 titles and abstracts, a total of 257 articles were eligible for full text analysis and data collection (Figure 3). Of these only 32 studies were matched case control studies.[36-67]

**Figure 3.** Systematic review profile for in-hospital mortality
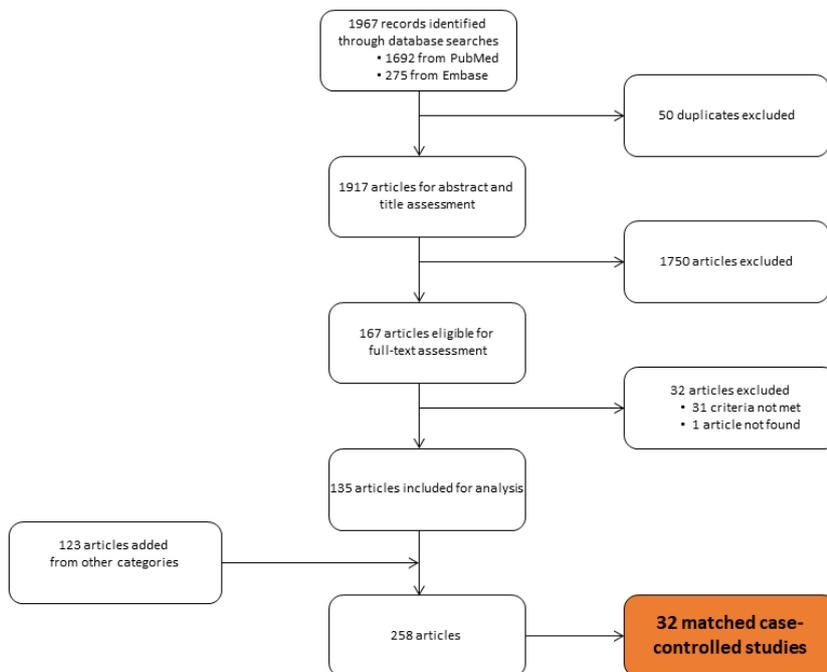
Figures 3 to 8 summarize the meta-analyses of matched case-control studies on healthcare-associated infections, all-cause bloodstream infections, central line-associated bloodstream infections, and surgical site infections. No sufficient numbers of studies on ventilator-associated pneumonia (VAP) (2), [60,64] hospital-acquired pneumonia (HAP) (1),[40] UTI (1) [47] and *Clostridioides difficile* infection (CDI) (2) [52,59] were identified by the systematic review.
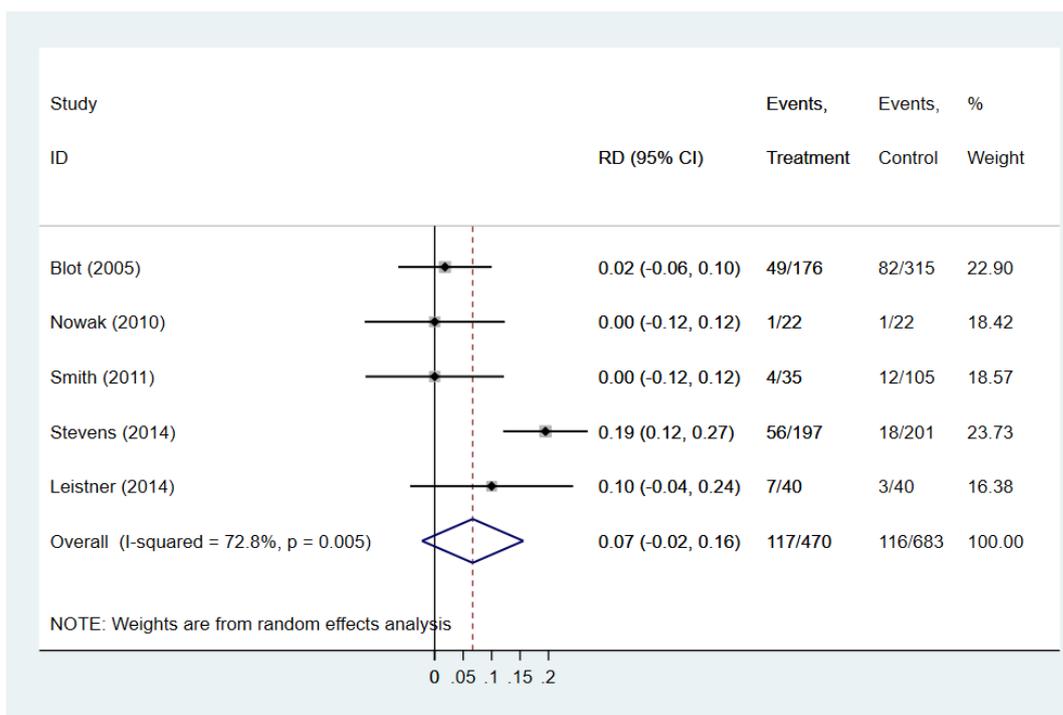
Figure 3. In-hospital mortality from healthcare-associated infections, meta-analysis
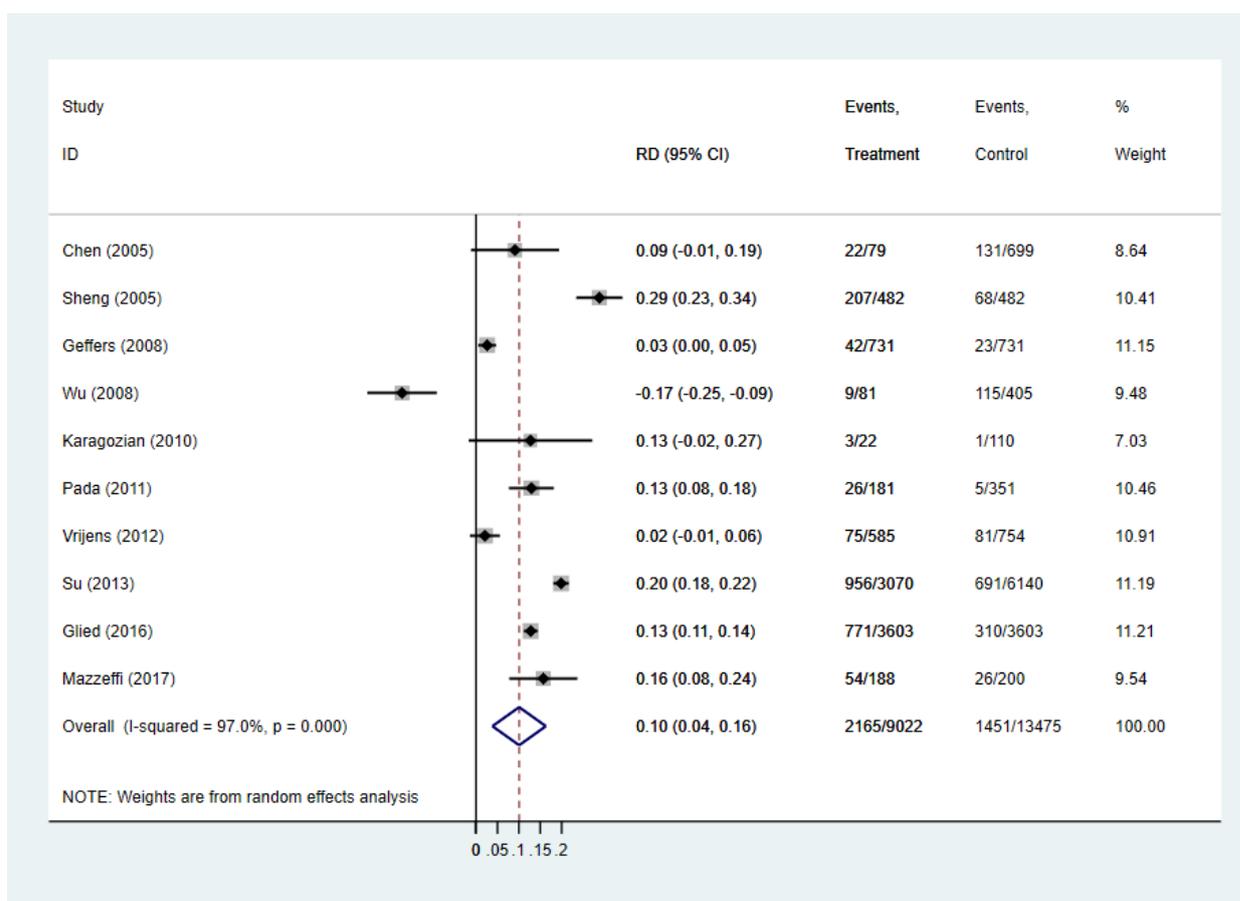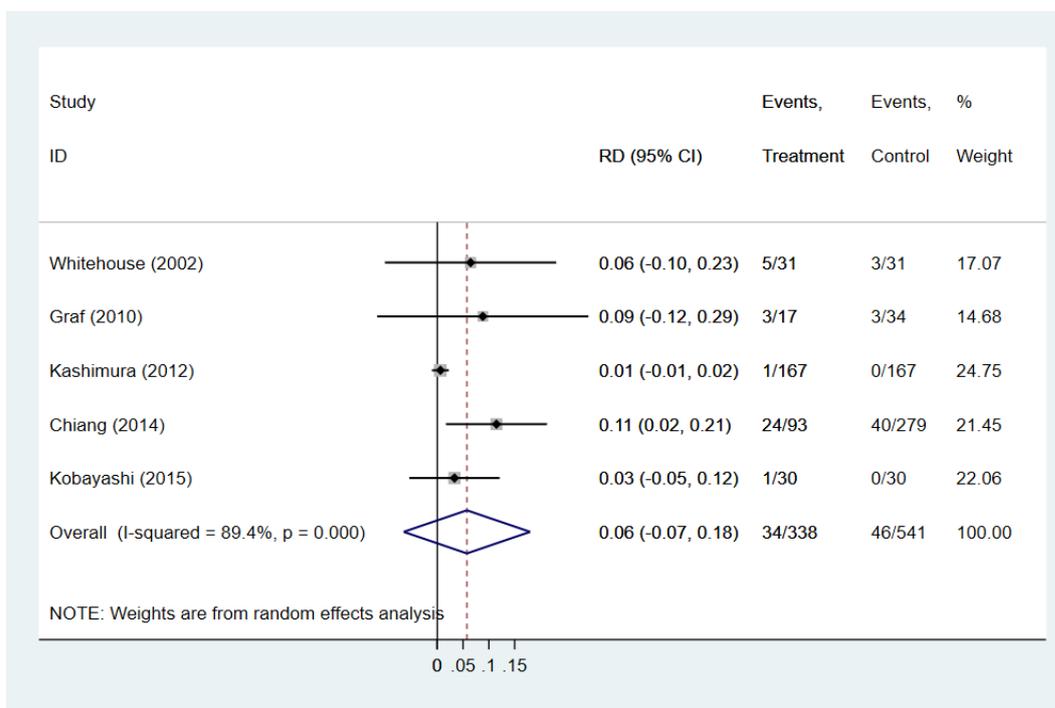
Figure 4. In-hospital mortality from healthcare-associated all-cause bloodstream infections, meta-analysis
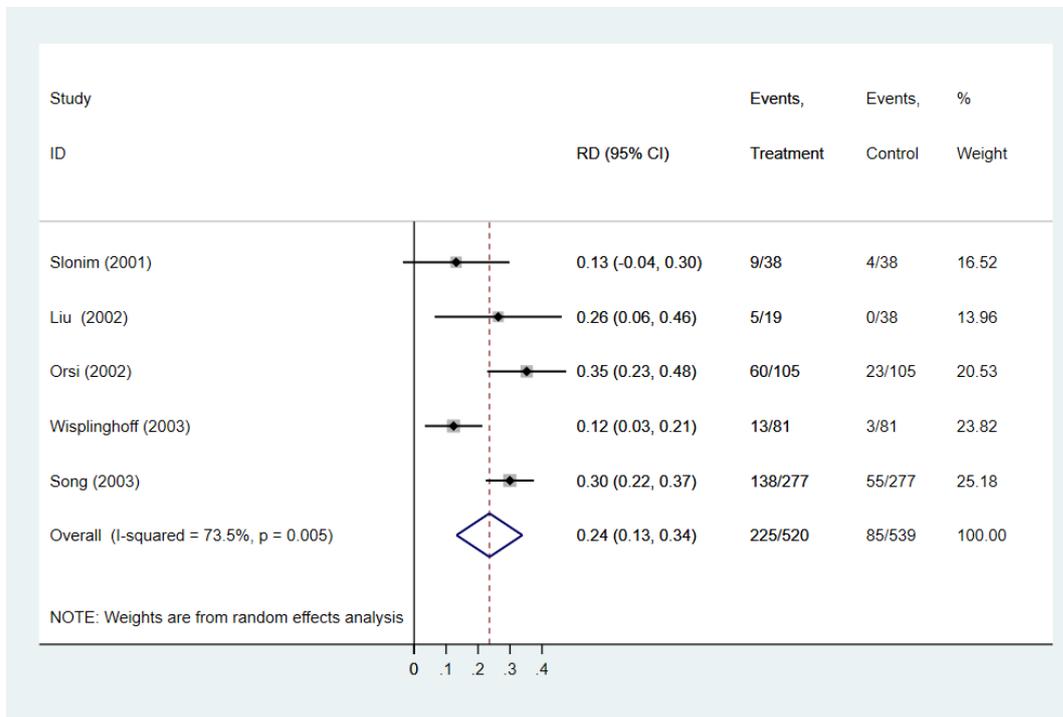
Figure 5. In-hospital mortality from healthcare-associated central line-associated bloodstream infections, meta-analysis

Figure 6. In-hospital mortality from surgical-site infections, meta-analysis

Study ID	RD (95% CI)	Events, Treatment	Events, Control	% Weight
Whitehouse (2002)	0.06 (-0.10, 0.23)	5/31	3/31	17.07
Graf (2010)	0.09 (-0.12, 0.29)	3/17	3/34	14.68
Kashimura (2012)	0.01 (-0.01, 0.02)	1/167	0/167	24.75
Chiang (2014)	0.11 (0.02, 0.21)	24/93	40/279	21.45
Kobayashi (2015)	0.03 (-0.05, 0.12)	1/30	0/30	22.06
Overall (I-squared = 89.4%, p = 0.000)	0.06 (-0.07, 0.18)	34/338	46/541	100.00

NOTE: Weights are from random effects analysis

Mortality was based on estimated incidence (from prevalence) data and data from the literature. Table 10 summarises the estimated mortality for HAI-types where sufficient numbers of studies were identified to perform a meta-analysis (HAI, BSI, CLABSI, SSI).

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Table 10. Estimated attributable in-hospital mortality from healthcare-associated infections –
Acute care hospitals in Switzerland, 2017

	All hospitals
Hospital cases, N	1'319'187
HAI [36,39,41,46,48,53,58,62,63,66]	
Prevalence	5.92 (5.51-6.32)
Incidence	4.48 (3.74-5.22)
Cases in 2017	59'091 (49'377-68'804)
*Attributable mortality	0.1 (0.04-0.16)
Total attributable mortality	5'909 (1'975-11'009)
BSI [37,43,49,54]	
Prevalence	0.82 (0.66-0.98)
Incidence	0.62 (0.52-0.72)
Cases in 2017	8'188 (6'842-9'534)
*Attributable mortality	0.24 (0.13-0.34)
Total attributable mortality	1'965 (889-3'242)
CLABSI [42,44,51,55,67]	
Prevalence	0.23 (0.15-0.31)
Incidence	0.13 (0.11-0.16)
Cases in 2017	1'714 (1'451-2'111)
*Attributable mortality	0.07 (0.00-0.16)
Total attributable mortality	120 (0-338)
SSI [38,56,57,61,65]	
Prevalence	1.87 (1.64-2.11)
Incidence	1.2 (0.95-1.44)
Cases in 2017	15'819 (12'593-19'045)
*Attributable mortality	0.06 (0.00-0.18)
Total attributable mortality	949 (0-3'428)

BSI: bloodstream infection; CLABSI: central line-associated bloodstream infection; HAI: healthcare-associated infection; SSI: surgical site infection

*Results based on meta-analyses

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7. DISCUSSION

7.1. Prevalence of healthcare-associated infections in Switzerland, 2017

The CH-PPS 2017 was the first, and by the number of participating hospitals and patients, the largest national HAI-prevalence survey in Switzerland.[24] Past national surveys, in 2004 for the last time, used the period prevalence methodology.[19] Almost 80% of the acute care hospitals with 100 beds or more submitted data, which makes the survey representative for Switzerland. The HAI-prevalence (5.9%) was similar to the average European HAI-prevalence of the first ECDC-PPS in 2011 and 2012 (6.0%),[29] but higher than prevalence in the second ECDC-PPS in 2016 and 2017 (5.5%; 95% CI: 4.6–6.7).[32] Similar ratios were measured in France (5.8%; 95% CI: 4.9–7.0), Ireland (6.1%; 95% CI: 5.0–7.6), Poland (5.8%; 95% CI: 4.8–6.9), England (6.4%; 95% CI: 5.4–7.6), Northern Ireland (6.1%; 95% CI: 4.8–7.9) and Wales (5.7%; 95% CI: 4.7–6.7) in 2016 and 2017. Ratios in Austria (4.0%; 95% CI: 3.4–4.7) and Germany (3.6%; 95% CI: 2.8–4.7) were statistically significantly lower than Switzerland; the ratio in Italy (8.0%; 95% CI: 6.8–9.5) was statistically significantly higher.

7.2. Incidence of healthcare-associated infections in Switzerland, 2017

Incidence from prevalence calculation using the Rhame Sudderth formula has limitations.[21,28,68] This is due to the fact that the Rhame and Sudderth formula was applied on a full dataset of patient information while in a prevalence survey, only data up to the day of survey are known. This is particularly relevant for estimating the time between infection and discharge. Thus, some uncertainty about the correct incidence estimation applying the Rhame and Sudderth formula cannot be ruled out. The model of attributable LOS-estimation also used prevalence-incidence estimations. However, this model only took into account HAI occurring during hospital stay. Neither HAI at admission nor HAI other than the first during hospitalisation were taken into account. Thus, the calculated HAI incidence proportion of 2.3 (95% CI: 2.1-2.6) of this model is an underestimation of the overall HAI incidence.

Applying the ECDC methodology with its limitations on the other hand allowed us to compare the CH-PPS data with ECDC-PPS data. The estimated HAI-incidence proportion of the 2016/2017 ECDC-PPS was 3.7 (95% CI: 2.4-5.3). Thus, the Swiss HAI-incidence of 4.5 (95% CI: 3.7-5.2) was non-significantly higher.[32] Table 11 compares data from Switzerland with neighbouring countries.

Table 11. Comparison of prevalence, incidence, and annual cases with healthcare-associated infections in Switzerland and neighbouring countries [32]

Country	Prevalence % (CI95%)	Incidence % (CI95%)	Cases N (CI95%)
Switzerland	5.9 (5.5–6.3)	4.5 (3.7–5.2)	59'100 (49'338–68'862)
Austria	4.0 (3.4–4.7)	2.3 (1.5–3.3)	62'306 (40'978–89'762)
Germany	3.6 (2.8–4.7)	3.1 (1.9–4.8)	604'495 (373'766–938'383)
France	5.8 (4.9–7.0)	4.1 (2.7–5.9)	467'961 (311'830–671'498)
Italy	8.0 (6.8–9.59	6.0 (4.2–8.3)	534'709 (373'705–740'544)

CI95%: 95% confidence interval

Despite a significantly lower HAI incidence, Austria (population of 8.8 Mio) had more estimated annual HAI cases in 2017 than Switzerland (population of 8.6 Mio). This is due to the fact that the number of annual cases in Austria was much higher (2'707'753) than Switzerland (1'319'187).

7.3. Attributable length of stay due to healthcare-associated infections

The largest source of uncertainty of our results are in connection with the imputation process. Essentially, follow-up information was extrapolated for 10'369 patients from the 1'714 acute care patients from Bülach, HUG and USZ for whom information for the entire hospitalisation was available. Although the patients from Bülach, HUG and USZ provided a case mix of patients that was representative for all other Swiss hospitals, we could only impute follow-up from basic patient (age, gender, McCabe score, surgery since admission) and hospital characteristics (ward specialty, provision type), while other predictive indicators, such as reason for hospitalization and treatment, were not available. As mentioned, HAI at admission could not be integrated to the model because no information was available if HAI present at admission was the reason for hospitalisation. We imposed the assumption that time to infection and time to discharge follow the distribution dictated by our model. While imputation is a recommended procedure for missing information, we apply it generously because the missing information (what happens after the survey) was our outcome of interest for the model.

Healthcare-associated infections generally have a prolonging effect on LOS. However, they can shorten LOS if a patient dies because of HAI-related complications. Consequently, in-hospital mortality should be analysed separately. In our multi-state model we did not distinguish between discharge and death. Our results highlight the importance of follow-up information on

HAI and discharge, which are readily available in hospital registries, but are cumbersome to retrieve.

Our results show that while the HAI incidence increases with age, attributable LOS decrease with age. Similarly, fatal McCabe scores increase the risk of HAI, but have a less pronounced effect on attributable LOS. This is consistent when taking into account that patients are hospitalised for reasons other than HAI, and that HAI is a complication occurring on top of other health problems. Similarly, attributable LOS is longer in hospitals with basic provision where average LOS is shorter (5.2 versus 6.5 days in central hospitals), and patients are less ill.[24]Thus, the effect of HAI on LOS is lower in sicker patients even if they have a higher risk for HAI. These findings support the coherence of our model on estimating attributable LOS. While the data are reliable for all HAI, the confidence intervals for individual HAI-types are large. This is due to the fact that the numbers of HAI-types occurring during hospital stay were rather low.

Compared to the published matched case-control studies we identified in a systematic review, our estimated attributable LOS are lower. Table 12 summarises our findings with the range identified in the literature.

Table 12. Attributable lengths of stay for the different types of healthcare-associated infections, estimated in Switzerland and compared to published matched case-control trials

HAI-type	CH-PPS days (CI95%)	Studies N	Range N
All HAI	6.6 (4.5-8.7)	NA	NA
BSI	6.6 (4.5-8.7)	9	6.0-25.7
HAP	6.0 (4.7-7.3)	3	5.7-15.1
UTI	5.2 (3.4-7.0)	2	3, 29
SSI	7.1 (5.2-9.0)	17	2.3-49.1

BSI: bloodstream infection; CI95%: 95% confidence interval; HAI: healthcare-associated infection; HAP: hospital-acquired pneumonia; NA: not available; SSI: surgical site infection; UTI: urinary tract infection

7.4. Cost of healthcare-associated infections in Switzerland, 2017

Attributable LOS-estimations allowed to calculate costs for HAI and the different HAI-types for acute care hospitals in Switzerland in 2017. Based on the data of FOS total costs (direct and indirect costs combined) were calculated to reflect the financial burden for the Swiss society. Estimating a preventable proportion of 32% of HAIs,[69] significant cost-savings could be hypothesised. However, the effect of HAI-reduction on direct and indirect cost is different, and thus, the hospital and the societal perspectives are different as well.[70] Table 13 summarises the

estimated cost of the different HAI-types in Switzerland and data from published matched case-control studies.

Table 13. Attributable cost for the different types of healthcare-associated infections, estimated in Switzerland and compared to published matched case-control trials

| HAI-type	CH-PPS CHF (CI95%)	Studies References	Range (year-adjusted CHF)
BSI	13'107 (8'936-17'277)	37,41,45,49,71-73	3'357-70'958
HAP	11'915 (9'334-14'497)	74	21'522
UTI	10'326 (6'752-13'901)	75,76	2'553-3'810
SSI	14'100 (10'326-17'873)	56,57,77-87	3'576-62'964

BSI: bloodstream infection; CI95%: 95% confidence interval; HAP: hospital-acquired pneumonia; NA: not available; SSI: surgical site infection; UTI: urinary tract infection

Except for UTI, taking into account only two studies,[75,76] our calculated costs are in the lower range of published figures.

7.5. Attributable mortality due to healthcare-associated infections

Estimating mortality based on estimated incidence from prevalence and identified matched-case control studies from the systematic review is the weakest part of this work package. Mortality of 10% due to HAI seems to be an overestimation; however, good data on mortality due to HAI are still lacking. Of interest is the difference between mortality from all-cause BSI (24%; 13-34%) and CLABSI (7%; 0-16%). What appears to be counter-intuitive is coherent, because all-cause BSI also includes secondary BSI, which have a higher mortality compared to catheter-associated BSI.[88] Indeed, in our database the difference can be explained by a larger proportion of secondary BSI (59.2%) compared to CLABSI (17.3%) (Figure 7). Secondary BSI occurred predominantly in UTI (17.3%), SSI (17.3%) and GI (11.1%). No estimations were possible for LRTI and UTI due to lack of studies. For PN, VAP and UTI only one, two and one matched case-control-studies were identified.

Figure 7. Distribution of bloodstream infections in the CH-PPS in 2017
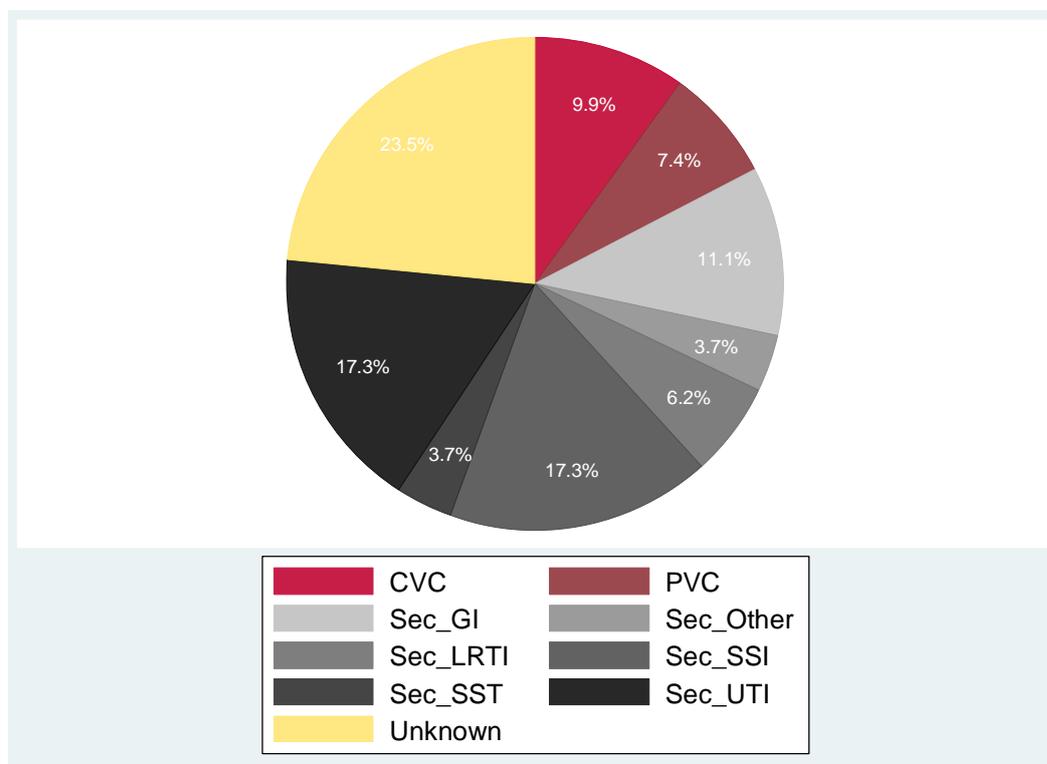
7.6. Attributable mortality due to healthcare-associated infections

This is the first study to estimate incidence, attributable length of stay and cost due to healthcare-associated infections in Switzerland. The calculated estimations appear reasonable; however, some limitations must be mentioned:

1. The imputation step used data from three hospitals only, of which two are University-affiliated and one of which only provided data on BSI, LRTI and SSI. Although representability of the patients from HUG, USZ and Bülach was unexpectedly aligned with the entire CH-PPS database, some bias, particularly on LOS and case-mix cannot be ruled out.

2. We used an incidence estimate based on the Rhame and Sudderth formula because the more accurate methodology based on multi-state modelling was not applicable to the ensemble of HAI. This model only took into account the first HAI during hospitalisation and excluded HAI present on admission. To take into account HAI at admission in the model, future surveys should provide such information.

Although some limitations apply, the calculated estimations appear reasonable. Future studies must confirm the accuracy of our data. Combining the data from a prevalence survey with

national statistical data in a multi-state modelling is a straightforward methodology in cost estimation for healthcare-associated infections.

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