Journal of Hospital Infection 103 (2019) 293–302

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin

Burden of surgical site infections in the Netherlands: cost analyses and disability-adjusted life years

M.B.G. Koek [a,*], T.I.I. van der Kooi [a], F.C.A. Stigter [a,b], P.T. de Boer [a], B. de Gier [a], T.E.M. Hopmans [a], S.C. de Greeff [a], on behalf of the Burden of SSI Study Group[†]

[a] *Department of Epidemiology and Surveillance, Centre for Infectious Disease Control, National Institute for Public Health and Environment (RIVM), Bilthoven, the Netherlands*
[b] *UWV, Utrecht, the Netherlands*

A R T I C L E I N F O

Article history:
Received 20 December 2018
Accepted 15 July 2019
Available online 19 July 2019

Keywords:
Surgical site infection
Costs
Burden
Economic burden
Disease burden
Disability-adjusted life years
Surveillance
Prevention
Infection prevention

S U M M A R Y

Background: Surgical site infections (SSIs) are associated with morbidity, mortality and costs.
Aim: To identify the burden of (deep) SSIs in costs and disability-adjusted life years (DALYs) following colectomy, mastectomy and total hip arthroplasty (THA) in the Netherlands.
Methods: A retrospective cost-analysis was performed using 2011 data from the national SSI surveillance network PREZIES. Sixty-two patients with an SSI (exposed) were matched to 122 patients without an SSI (unexposed, same type of surgery). Patient records were studied until 1 year after SSI diagnosis. Unexposed patients were followed for the same duration. Costs were calculated from the hospital perspective (2016 price level), and cost differences were tested using linear regression analyses. Disease burden was estimated using the Burden of Communicable Disease in Europe Toolkit of the European Centre for Disease Prevention and Control. The SSI model was specified by type of surgery, with country- and surgery-specific parameters where possible.
Findings: Attributable costs per SSI were €21,569 (THA), €14,084 (colectomy) and €1881 (mastectomy), mainly caused by prolonged length of hospital stay. National hospital costs were estimated at €10 million, €29 million and €0.6 million, respectively. National disease burden was greatest for SSIs following colectomy (3200 DALYs/year, 150 DALYs/100 SSIs), while individual disease burden was highest following THA (1200 DALYs/year, 250 DALYs/100 SSIs). For mastectomy, these DALYs were <1. The total cost of DALYs for the three types of surgery exceeded €88 million.
Conclusion: Depending on the type of surgery, SSIs cause a significant burden, both economically and in loss of years in full health. This underlines the importance of appropriate infection prevention and control measures.

* Corresponding author. Address: National Institute for Public Health and the Environment, RIVM, Centre for Infectious Disease Control, CIb, Dept. of Epidemiology and Surveillance, EPI/pb75, Postbus 1, 3720 BA Bilthoven, the Netherlands. Tel.: +31 30 2747055; fax: +31 30 2744409.
E-mail address: mayke.koek@rivm.nl (M.B.G. Koek).
† Members of the Burden of SSI Study Group: J. Entius, J.C.M. Diederen, E.H. Groenendijk, L. Nolles, K.P. Jalink-Olthof, B.J.H. den Broeder and H.G.M. Blaauwgeers.

https://doi.org/10.1016/j.jhin.2019.07.010

Introduction

Surgical site infections (SSIs) are frequently occurring nosocomial infections, accounting for approximately 25—30% of hospital-acquired infections (HAIs) [1]. In the Netherlands, 0.9—19.6% of all surgical patients will develop an SSI, depending on the type of surgery [2]. SSIs can have major implications for patients, hospitals and society; they increase morbidity as well as mortality [3], and as such may contribute to the burden on society in terms of healthcare costs (economic burden) and loss of years experienced in full health [disease burden, commonly measured in disability-adjusted life years (DALYs)]. As part of a larger European project on the disease burden of HAIs, a disease progression model was developed estimating that SSIs cause 58 DALYs per 100,000 European inhabitants, with 0.5 DALYs per SSI [4]. However, this estimate was based on SSIs in general, without distinction by type of surgery, while it is likely that the burden of disease varies between different types of surgery.

SSIs may also result in excess healthcare utilization and costs. With increasing overall healthcare costs, hospitals are encouraged to use their resources more efficiently and to avoid preventable costs. Currently, knowledge on the costs of SSIs in the Netherlands is limited. In 1996, a Dutch paper [5] estimated the attributable costs of an SSI following cardiothoracic surgery to be $16,878. A few years later, Geubbels estimated the cost of a superficial SSI to be between €900 and €2600, and that of a deep SSI to be between €3200 and €19,900 [6]. This study, however, based the costs of extra care on several assumptions and reported data on surgical specialty level instead of surgery level. Previous international studies have shown that costs can double, triple or even increase six-fold for patients with an SSI compared with patients without an SSI [7—9], depending on the type of surgery, setting and type of infection. The increased length of stay (LOS) is responsible for the majority of additional healthcare costs [10—13], followed by parenteral medication and additional surgical procedures [14,15]. However, due to different international healthcare systems and healthcare financial systems, costs calculated in these mostly UK- and US-based studies cannot be translated directly to the Dutch setting. Moreover, studies vary greatly in methodology, including evaluated cost components and unit costs [7]. Hence, to obtain useful estimates, country-specific data and surgery-type-specific data should be assessed for the Netherlands.

As such, this study determined the burden of disease in DALYs and the hospital costs for (deep) SSIs following three different, but commonly performed, types of surgery: colectomy, mastectomy and total hip arthroplasty (THA).

Methods

Costs

Data source and study design

This study was performed using data available from the national surveillance system on hospital-associated infections (PREZIES). Almost all Dutch hospitals participate voluntarily in this network, and may undertake SSI incidence surveillance for one or more selected types of surgery. In this surveillance, hospitals collect data on patients, surgeries, risk factors and the presence of an SSI [16,17]. SSIs are diagnosed using information described in the patient files and meet the criteria of the (European) Centre of Disease Prevention and Control (CDC and ECDC) [18—22]. Superficial SSIs are distinguished from deep SSIs, which include deep incisional and organ space SSIs. By definition, SSIs in the surveillance and in this study occurred within 30 days after surgery, or within 1 year after implant surgery (deep SSIs alone). Detailed information on PREZIES has been published previously [16,23].

This study was designed as a retrospective cohort study. The focus was on deep SSIs because of the expected higher additional costs and LOS compared with superficial SSIs [13,24]. Colectomy, mastectomy and THA were selected as these types of surgery are performed frequently in many hospitals, and represent deep SSIs that differ in incidence, treatment options and adverse impact [24]. As distinguishing the type of SSI has been notoriously ambiguous for mastectomy without implants, both deep and superficial SSIs were included for this type of surgery. At the start of data collection, the most recent year with a complete database in PREZIES (including postdischarge surveillance of 1 year) was 2011. From 2011 PREZIES data, adults (≥18 years) undergoing one of the three types of surgery were selected. Hospitals were considered for the study if they had reported at least five (deep) SSIs for one of the studied types of surgery. Further selection was based on the size, type and geographic distribution of the hospitals, the possibility to include two or more of the studied types of surgery, and permission to obtain and use data. For each hospital, patients in the surveillance data with an SSI (exposed patients) were pairwise matched to two patients without an SSI (unexposed patients). Besides hospital, matching criteria consisted of type of surgery, age (±15 years), sex, American Society of Anesthesiologists physical status examination score (ASA score, ranging from 1 to 5) [25], duration of surgery (±25%), surgical wound class (ranging from 1 to 4) [20] and pre-operative hospital stay (categorized in 0, 1, 2—5 and >5 days) [26]. If more than two unexposed patients were available, two were selected at random. Patients exposed to an SSI were followed from the day of surgery up to 1 year after the diagnosis of the SSI. Follow-up for unexposed patients was the same number of days as their matched exposed patient (with an SSI). According to the Central Committee on Research Involving Human Subjects, ethical approval and informed consent were not necessary for this retrospective study. The boards of the participating hospitals approved the study.

Data collection

Patient records were studied to measure the use of health care by type of surgery and to compare comorbidity between groups. To assess resource use, data were collected on admissions, readmissions, admissions to the intensive care unit (ICU), inpatient physical therapy, inpatient dietician consultation, outpatient visits, emergency department visits, telephonic consultation, laboratory investigations, cultures, packed cells, and radiology or additional operative procedures possibly related to an SSI (see Appendix 1). As data on total parental nutrition and antibiotics could not be retrieved reliably from the different systems, these data were not collected.

To compare pre-operative comorbidity among the exposed and unexposed groups, comorbidity data needed to calculate the Charlson Comorbidity Index (range 0—33) were collected (see Appendix 1) [27,28].

Unit costs were based on the hospital's perspective, starting from the day of surgery, and retrieved from several sources (Appendix 1). All prices were converted to the 2016 price year using the Dutch consumer price index [29]. Discounting of costs was not needed because all costs were incurred within a single year.

Statistical analysis

Characteristics, including matching variables, of patients with and without an SSI were checked for significant differences. Values for laboratory investigations were missing for <5% of all patients, and were replaced using multiple imputation techniques. In two hospitals, reports on dietician and physiotherapy consultations were not available for research, resulting in missing values for all patients of these hospitals. Using the above-mentioned imputation technique, missing values were replaced for physiotherapy consultations (17% of all patients) in THA (38%, of which 31% were in one hospital) and colectomies (34%, all in one hospital). Missing values for dietician consultations (24% of all patients) were replaced for colectomies (42%, all in two hospitals). Differences in costs between patients with an SSI and the unexposed patients were analysed using linear regression methods. The covariates hospital, sex, age, ASA score, wound class, obesity, pre-operative stay, duration of surgery, previous surgery, surgery (not for SSI) during follow-up, Charlson Comorbidity Index and pairwise matching were tested for possible inclusion in the models in order to account for possible remaining differences in baseline characteristics. Models were fitted using the proportion explained variance (adjusted R^2) while taking into account a minimum number of subjects per variable [30]. In addition to linear regression models, generalized linear models (GLMs) with gamma distribution [31] were applied to the data. GLM results were comparable to those of linear regression (1–8% change) but were generally slightly less conservative. Due to the latter and because the GLM method did not always produce results for partial costs (caused by problems calculating the inverse of the identity link), the results of linear regression are presented as the main results. Scatterplots of the predicted values against the residuals and normal probability plots (Q-Q plots) are presented in Appendix 1. To correct for possible overestimation of bed-day costs, two sensitivity analyses were performed. In the first sensitivity analysis, the number of bed-days between surgery and SSI for patients with SSIs was maximized to the number of bed-days between surgery and discharge of the matched patients. In the second sensitivity analysis, in addition, the costs of bed-days during readmission were only included if the SSI was explicitly described as the reason for readmission. As such, all costs of bed-days during readmissions that were indirectly related to SSIs or related to possible other reasons were excluded from this sensitivity analyses. National hospital costs were calculated by multiplying the attributable costs at patient level with the estimated annual number of SSIs in 2011. Multiple imputation and data analyses were performed using SPSS Statistics Version 24.0.0.1 (IBM Corp., Armonk, NY, USA) and final models were checked in SAS Version 9.4 (SAS Institute, Cary, NC, USA).

Disease burden

The disease burden was estimated using the healthcare-associated SSI model of the Burden of Communicable Disease in Europe Toolkit Version 1.4 [32]. The national number of SSIs was applied, stratified by type of surgery and by ASA score, derived from 2011 PREZIES data. PREZIES data were extrapolated to country level using the national estimated number of surgeries in 2010 (final year of registration available, Statistics Netherlands [33]), and multiplication factors were 4.98 (colectomy), 1.97 (mastectomy) and 1.88 (THA). ASA class 4 (N=1 for mastectomy and N=1 for THA) was grouped with ASA class 3. SSIs with unknown ASA class (3.4% for colectomy and <1% for mastectomy and THA) were added to the ASA class 1 and class 2 stratum. Case fatality was specified as 8.4%, 0% and 16.8%, respectively, based on Astagneau *et al.* [34]. Duration of infection was specified as the differences in total LOS between SSI patients and unexposed patients in this paper, and disability weights of 0.125 for general hospitalization and 0.655 for ICU admission were applied [35]. For remaining life expectancy, general population life expectancies (as in the Global Burden of Disease study 2010) for patients with ASA class 1 or 2 were applied [36]. For ASA class 3 and 4, remaining life expectancies of 5 and 0.5 years were applied, in analogy to the life expectancies per McCabe score used by Cassini *et al.* [4]. Remaining disability or loss of quality of life after treatment of the SSI was not taken into account.

Models were run with 10,000 iterations. In line with the methodology used in the Global Burden of Disease Study, future DALYs were not discounted [37]. Results are presented as the disease burden at national level (total estimated number of DALYs due to SSIs occurring in 2011) and at individual level (number of DALYs per 100 SSI cases in 2011). To prevent false precision, the results are rounded to one significant digit for numbers under 10, and to two significant digits for numbers between 10 and 10,000. National costs of disease burden were calculated by multiplying the number of DALYs at national level by a €20,000 threshold. This threshold is conventionally used in cost-effectiveness analysis of preventive interventions using quality-adjusted life years in the Netherlands, and is the lowest Dutch threshold published [38].

Results

Costs

Eight Dutch hospitals (four general teaching and four non-teaching hospitals), situated in different parts of the country and varying from 280 to 675 beds, were selected for the study. Six hospitals (three teaching/three non-teaching) provided data for colectomy, five (3/2) for mastectomy and four (2/2) for THA. One hundred and eighty-six patients were selected and included using the matching procedure. Numbers of patients with SSIs (exposed) vs without SSIs (unexposed) were 26/52, 20/40 and 16/32, respectively. For colectomy, the patient file was not available for data collection for two unexposed patients, resulting in data for only 50 unexposed patients. In Table I, characteristics of exposed (SSI) and unexposed (non-SSI) patients are shown, including matching variables and tests for difference.

The use of resources is shown in Table II. Using the unit costs from Appendix 1, the costs of treatment and hospital costs attributable to SSIs were calculated (Table III). The total attributable hospital costs per SSI were €21,569 [95% confidence interval (CI) 15,169–27,970] for THA, €14,084 (95% CI

Table I
Patient characteristics

		Colectomy			Mastectomy			Total hip arthroplasty		
		Deep SSI (N=26)	No SSI (N=50)	P-value[a]	SSI (N=20)	No SSI (N=40)	P-value[a]	Deep SSI (N=16)	No SSI (N=32)	P-value[a]
Age, years[b]		69.7 (13.1)	70.9 (11.7)	0.664	64.6 (13.0)	63.3 (11.0)	0.681	69.6 (8.8)	71.1 (7.7)	0.548
Female		42% (11)	40% (20)	0.846	100% (20)	100% (40)	NA	75% (12)	75% (24)	1.000
ASA score	1	19% (5)	14% (7)	0.690	35% (7)	30% (12)	0.792	19% (3)	19% (6)	1.000
	2	50% (13)	58% (29)		50% (10)	55% (22)		50% (8)	50% (16)	
	3	31% (8)	26% (13)		15% (3)	13% (5)		31% (5)	31% (10)	
	4	-	2% (1)		-	3% (1)		-	-	
Wound class	1	-	-	0.642	100% (20)	100% (40)	NA	100% (16)	100% (32)	NA
	2	96% (25)	98% (49)		-	-		-	-	
	3	4% (1)	2% (1)		-	-		-	-	
Obesity	Yes	4% (1)	2% (1)	0.738	45% (9)	45% (18)	0.456	31% (5)	22% (7)	0.748
	No	19% (5)	26% (13)		30% (6)	18% (7)		38% (6)	47% (15)	
	UNK	77% (20)	72% (36)		25% (5)	38% (15)		31% (5)	31% (10)	
Pre-operative stay, days[b]		1.5 (3.1)	0.8 (1.0)	0.235	0.5 (0.5)	0.3 (0.5)	0.346	0.4 (0.5)	0.4 (0.5)	1.000
Duration of surgery, min[b]		145.2 (94.9)	139.3 (81.7)	0.774	137.9 (96.1)	129.6 (87.0)	0.734	81.8 (25.9)	81.3 (26.0)	0.942
Previous surgery[c]	Yes	4% (1)	4% (2)	0.993	20% (4)	20% (8)	1.000	-	-	0.619
	No	31% (8)	32% (16)		60% (12)	60% (24)		25% (4)	19% (6)	
	UNK	65% (17)	64% (32)		20% (4)	20% (8)		75% (12)	81% (26)	
Surgery (not for SSI) during follow-up	Yes	-	-	0.871	5% (1)	3% (1)	0.884	6% (1)	-	0.325
	No	15% (4)	14% (7)		25% (5)	25% (10)		19% (3)	19% (6)	
	UNK	85% (22)	86% (43)		70% (14)	73% (29)		75% (12)	81% (26)	
Elective procedure		4% (1)	4% (2)	0.974	100% (20)	100% (40)	NA	100% (16)	100% (32)	NA
Charlson Comorbidity Index[b]		3.1 (1.3)	2.8 (1.6)	0.383	2.8 (1.2)	2.4 (0.6)	0.198	1.2 (1.3)	0.9 (1.2)	0.398
Death during follow-up		19% (5)	12% (6)	0.403	5% (1)	5% (2)	1.000	-	-	NA

ASA, American Society of Anesthesiologists; SSI, surgical site infection; UNK, unknown, NA, not available.
Values presented are percentages (N of cases) unless stated otherwise.
[a] P-values were calculated using logistic regression and Chi-squared analyses.
[b] Values presented for continuous variables are mean (standard deviation).
[c] Previous surgery on same organ or area.

Table II

Use of resources by patients undergoing colectomy, mastectomy and total hip arthroplasty

Resource	Colectomy					Mastectomy					Total hip arthroplasty			
	Deep SSI (*N*=26)		No SSI (*N*=50)			SSI (*N*=20)		No SSI (*N*=40)			Deep SSI (*N*=16)		No SSI (*N*=32)	
Bed-days inpatient (24 h)[a]	34.7	(27.4)	9.0	(7.6)		7.9	(7.5)	6.9	(7.7)		49.8	(31.4)	6.6	(4.9)
Ambulatory care (<24 h)	—		—			0.1	(0.2)	—			0.1	(0.3)	—	
ICU-days (24 h)	2.0	(3.4)	0.4	(1.8)		0.1	(0.2)	0.2	(1.3)		—		—	
(<24 h)	0.1	(0.3)	0.04	(0.2)		—		—			0.1	(0.3)	—	
Visit hospital physiotherapist[b]	3.6	(4.6)	2.1	(1.6)		0.8	(1.2)	0.7	(2.1)		18.0	(8.0)	11.1	(7.8)
Visit hospital dietician[c]	5.0	(3.9)	2.6	(2.9)		1.1	(2.6)	0.3	(1.1)		1.1	(3.5)	0.2	(0.9)
Visit emergency department	0.3	(0.7)	0.1	(0.5)		0.7	(0.9)	0.4	(0.7)		1.1	(1.0)	0.1	(0.3)
Visit outpatient department	11.7	(9.2)	10.4	(7.4)		22.0	(9.8)	16.1	(9.1)		13.2	(7.8)	6.2	(3.8)
Telephonic consultation	2.9	(4.5)	2.0	(2.5)		2.4	(2.6)	1.7	(2.0)		0.7	(1.3)	0.4	(0.8)
Laboratory investigation (sample)[d]	64.5	(81.8)	18.9	(16.4)		15.6	(12.6)	10.1	(9.3)		52.0	(52.2)	11.5	(13.4)
Culture	6.1	(5.0)	1.3	(2.8)		2.0	(1.4)	0.9	(1.6)		9.9	(5.1)	0.8	(1.2)
Blood culture	2.9	(3.7)	0.4	(0.8)		0.4	(1.0)	0.2	(0.5)		2.8	(4.7)	0.03	(0.2)
Packed cells	0.6	(0.9)	0.2	(0.5)		0.1	(0.4)	0.03	(0.2)		1.0	(1.3)	0.3	(1.0)
Radiology														
Abdominal ultrasound	0.8	(1.0)	0.7	(0.8)	Breast ultrasound	0.4	(0.7)	0.4	(0.6)	Hip ultrasound	0.3	(0.4)	—	
Abdominal X-ray	0.5	(0.9)	0.1	(0.3)	Chest X-ray	0.8	(1.4)	0.6	(1.1)	Hip/pelvis X-ray	5.6	(2.6)	3.6	(1.4)
Abdominal CT scan	2.2	(1.5)	0.5	(0.8)	Chest CT scan	0.1	(0.3)	0.1	(0.2)	Lumbal spine X-ray	0.1	(0.3)	0.2	(0.4)
					Mammography	0.7	(0.7)	0.8	(0.5)	Hip/pelvis MRI scan	0.1	(0.3)	—	
Surgery during follow-up														
Relaparotomy	0.9	(0.7)	0.1	(0.4)	Incision and drainage	0.6	(0.8)	0.1	(0.3)	Debridement	1.9	(1.9)	—	
Drainage abscess	0.2	(0.6)	—		Drainage and ultrasound	0.1	(0.3)	0.03	(0.2)	Removal prosthesis/spacer	0.1	(0.3)	—	
										Revision one stage	0.3	(0.7)	0.03	(0.2)
										Girdle stone	0.1	(0.3)	—	

SSI, surgical site infection; ICU, intensive care unit; CT, computed tomography.

Values are mean (standard deviation, SD). Radiology and surgery during follow-up are restricted to procedures possibly related to an SSI.

[a] Bed-day >24 h while admitted to ICU was calculated as ICU-days.

[b] Missing values of physiotherapy consultations for colectomy and total hip arthroplasty were imputed. The original values [mean (SD)/*N* observations] for colectomy were 4.3 (3.9)/*N*=15 and 2.0 (1.8)/*N*=29 for patients with and without SSI, respectively. For total hip arthroplasty, the original values were 15.9 (9.7)/*N*=10 and 5.6 (2.8)/*N*=20, respectively.

[c] Missing values of dietician consultations for colectomy were imputed. The original values [mean (SD)/*N* observations] were 5.3 (4.8)/*N*=15 and 2.4 (3.5)/*N*=29 for patients with and without SSI, respectively.

[d] Missing values of laboratory investigations were imputed. The original values [mean (SD)/*N* observations] for colectomy were 59.6 (77.6)/*N*=24 and 19.3 (16.5)/*N*=48 for patients with and without SSI, respectively. For mastectomy, these values were 14.7 (12.7)/*N*=18 and 8.7 (8.1)/*N*=37, respectively, and for total hip arthroplasty, they were 52.0 (52.2)/*N*=10 and 11.3 (13.5)/*N*=20, respectively.

Table III

Mean costs of treatment, mean costs of surgical site infections (SSIs), and the economic and disease burden of SSIs following colectomy, mastectomy and total hip arthroplasty

	Colectomy				Mastectomy				Total hip arthroplasty			
Costs per patient (2016 Euros)	Deep SSI	No SSI	Diff.	Adjusted diff. (95% CI)[a]	SSI	No SSI	Diff.	Adjusted diff. (95% CI)[a]	Deep SSI	No SSI	Diff.	Adjusted diff. (95% CI)[a]
Bed-days	16,662	4303	12,359	9472 (6503–12,440)	3786	3310	476	1375 (-858–3607)	23,943	3167	20,776	17,520 (12,148–22,893)
ICU-days	3338	707	2631	2549 (316–4781)	83	373	-290	-374 (-1177–429)	133	0	133	125 (-15–265)
Inpatient physiotherapist	118	70	48	43 (-30–116)	25	22	3	3 (-30–36)	598	369	229	172 (-23–366)
Hospital dietician	150	78	73	45 (-114–203)	31	9	22	24 (-11–60)	34	5	29	-5 (-19–10)
Emergency department visits	90	37	54	64 (-16–145)	183	105	78	32 (-76–140)	278	25	253	213 (128–298)
Outpatient department visits	1074	957	117	-17 (-395–361)	2020	1474	546	451 (-78–980)	1211	571	640	506 (240–772)
Telephonic consultations	132	90	42	12 (-55–80)	108	77	31	25 (-26–76)	32	17	14	8 (-18 – 33)
Laboratory investigation	858	252	606	480 (143–817)	208	134	74	85 (-17–187)	692	153	539	417 (194–639)
Culture	115	24	91	90 (54–126)	38	16	21	22 (9–36)	185	15	171	141 (111–171)
Blood culture	84	12	72	68 (35–100)	10	5	5	3 (-11–18)	79	1	78	71 (16–126)
Packed cells	134	44	91	106 (30–182)	22	5	16	20 (-16–56)	218	75	143	53 (-103–209)
Radiology	499	160	339	337 (222–451)	151	141	10	-7 (-72–59)	291	170	121	80 (30–129)
Surgery during follow-up	943	121	821	836 (597–1074)	203	30	173	221 (107–335)	2599	47	2552	2268 (1404–3132)
Total	24,198	6854	17,344	14,084 (9474–18,694)	6868	5701	1167	1881 (-946–4709)	30,293	4613	25,680	21,569 (15,169–27,970)
Burden of disease (95% CI)												
Number of surgeries/year[b]	14,012				7475				33,339			
Number of SSIs/year[c,d]	2100 (2000–2100)				330 (330–330)				480 (480–480)			
National burden (DALYs/year)[d]	3200 (3200–3200)				0.10 (0.1–0.1)				1200 (1200–1200)			
Individual burden (DALYs/100 SSIs)[d]	150 (150–160)				0.03 (0.03–0.03)				250 (250–250)			
Costs at national level (2016 Euros, per year) (uncertainty range)												
Hospital costs[e,d]	29,580,000 (18,950,000–39,260,000)				621,000 (-312,000 to 1,550,000)				10,350,000 (7,280,000–13,430,000)			
Costs of DALYs[f]	64,000,000 (64,000,000–64,000,000)				2000 (2000–2000)				24,000,000 (24,000,000–24,000,000)			
Total[d]	93,580,000 (82,950,000–103,260,000)				623,000 (-310,000–1,550,000)				34,350,000 (31,280,000–37,430,000)			

ICU, intensive care unit; DALY, disability-adjusted life year; CI, confidence interval.

[a] The adjusted differences and 95% CIs were calculated using linear regression techniques while taking into account matching of the cohorts and possible remaining differences in baseline characteristics and comorbidity. Adjusted attributable total costs calculated using generalized linear models with gamma distribution and identity link were 15,266 (10,728–19,804) for colectomy, 1855 (-101 to 3610) for mastectomy and 22,340 (16,301–28,380) for total hip arthroplasty. The costs per SSI of the two sensitivity analyses were 12,691 vs 11,738 for colectomy, 1852 vs 1690 for mastectomy, and 21,070 vs 20,925 for total hip arthroplasty.

[b] Derived from Statistics Netherlands (CBS) [33].

[c] Estimated using PREZIES data and CBS data [33]. Deep SSIs for colectomy and total hip arthroplasty, all SSIs for mastectomy.

[d] Rounded to one significant digit for numbers <10, to two significant digits for numbers between 10 and 10,000, to three significant digits for numbers between 10,000 and 1,000,000, and to nearest 10,000 for numbers $>1,000,000$.

[e] Number of SSIs (national/year) x adjusted difference in costs per SSI. To calculate uncertainty around the estimate, the lower limits of the 95% CI of number of SSIs and of the 95% CI of hospital costs were multiplied, and similarly the upper limits of the 95% CIs were multiplied.

[f] Number of DALYs at national level x 20,000 Euro threshold for prevention (willingness-to-pay).

9474–18,694) for colectomy and €1881 (95% CI -946–4709) for mastectomy (2016 price level). LOS on non-ICU wards was the main driver for hospital costs in general. Attributable costs for THA were mainly driven by the extra bed-days during readmission, with a mean of 44.7 days for patients with an SSI vs 1.8 days for patients without an SSI. For colectomy, the additional LOS was partially caused by readmission (12.1 vs 2.0 days) and partially caused by prolonged LOS during the initial admission (24.6 vs 7.4 days). For mastectomy, the additional LOS for patients with an SSI was 1 day. The results of the sensitivity analyses adjusting for possible overestimation of the attributable costs of bed-days before and after diagnosis of the SSI are described in Table III (footnote a).

Disease burden

The disease burden at patient level was highest for SSIs following THA (250 DALYs per 100 SSIs), while the disease burden at national level was highest for colectomy (3200 DALYs/year; see Table III). For mastectomy, these numbers were close to zero: 0.1 DALYs/year and 0.03 DALYs per 100 SSIs.

Economic burden

The economic burden in terms of total national hospital costs for SSIs following colectomy were almost €30 million per year (Table III). For THA and mastectomy, the national hospital costs were approximately €10 million and €0.6 million per year, respectively. In the two sensitivity analyses, the national hospital costs for colectomy decreased slightly to €27 million vs €25 million per year (sensitivity analysis 1 and 2), while the totals for mastectomy and THA remained approximately the same. National costs of DALYs were an estimated €64 million for colectomy and €24 million for THA. Total costs at national level (hospital costs and costs of DALYs) for SSIs following these three types of surgery combined were over €128 million, with an uncertainty range from €113 million to €140 million.

Discussion

This study demonstrated that SSIs have a substantial impact on disease burden and economic burden. For colectomy and THA, the adjusted attributable costs were more than €14,000 and 21,000 per SSI, causing a national economic burden of SSIs for these two types of surgery of €40 million per year. The combined national disease burden was also considerable: 4400 DALYs annually. The total costs for patients with an SSI were at least three-fold and at least six-fold higher for colectomy and THA, respectively, than the costs of patients without an SSI. These additional costs were mainly (>80%) caused by prolonged LOS, especially during readmission for THA, and during readmission as well as during initial admission for colectomy. The performed sensitivity analyses showed similar results for THA and mastectomy, but slightly lower costs for colectomy. The latter is most likely an underestimation, as the attributable LOS before diagnoses of the SSI was minimized while in reality it may take time (and additional bed-days) to distinguish leakage and other complaints from an abdominal SSI. These findings are considerably higher than the €9900 and €7700 increase in university hospital costs calculated by a previous Dutch study [6], probably because the present data are much more detailed and specified due to collecting inpatient data. The present results are comparable with the almost U$18,000 (€21,600 in 2016) increase in US hospital costs for orthopaedic SSIs found in 2002 by Whitehouse. The latter study had a similar study design with similar follow-up durations, but found an excess total LOS for orthopaedic surgeries of only 14 days. In addition to the costs, they demonstrated that orthopaedic patients with SSIs experience substantially greater physical limitations and reductions in their health-related quality of life [12]. The combined disease burden found for colectomy and THA (4400 DALYs/year) is comparable to that of hepatitis C or human immunodeficiency virus (HIV) infection in the Netherlands (4600 and 5200 DALYs/year, respectively) [39]. Burden at patient level was higher for both types of surgery compared with the results of Cassini *et al.* (0.5 DALYs/SSI), which might be explained by the fact that Cassini *et al.* aggregated all types of surgery and both deep and superficial SSIs [4]. The present study did not find significantly increased costs, LOS or disease burden for mastectomy, in contrast to colectomy and THA. However, there is literature describing increased costs and LOS for SSIs following mastectomy [40,41]. As for mastectomy, superficial SSIs were included (11 out of 20 SSIs) and given that superficial SSIs are mostly treated at home, this may have decreased the difference in LOS between both cohorts and thereby reduced the cost difference found in this study. It is also possible that the standard of care is different between the studies or countries.

Strengths and weaknesses

This paper contributes to the literature in that it provides evidence for the Dutch situation alongside largely US- and UK-based studies for the economic burden as well as the disease burden of SSIs. For the cost study, it was possible to match all except two SSI patients to two unexposed (no SSI) patients. Although comorbidity data were not reported to PREZIES, it was possible to calculate a proxy for comorbidity (i.e. the Charlson Comorbidity Index) using data from the patient files. Comparison of this index between both groups suggested that both cohorts were comparable. Possible remaining differences in comorbidity and risk factors were taken into account by including comorbidity and risk factor covariates in the analyses. Being a multi-centre study increases generalizability of the results. As this study included costs with a follow-up period of 1 year after SSI diagnosis, cost differences were captured as much as possible [42]. Finally, to calculate disease burden, country- and surgery-specific estimates were applied where possible in order to base the results on Dutch data and to differentiate disease burden between the types of surgery.

However, this study had some limitations. First, although the combined approach of the analyses reveals that the estimated cost differences are probably close to the true value, it is acknowledged that the sample sizes of this study were quite small and hence may have influenced the width of the CIs (being too wide or too small). Secondly, due to the selections made for the cost study, the calculated costs may not be optimally representative for patients with SSIs in general. For instance, by matching patients with an SSI to unexposed patients, cohorts with more underlying comorbidities were selected, which may have caused either underestimation or overestimation of the costs caused by SSIs: underestimation as the costs of SSIs were compared with the presumably relatively high treatment costs of comorbid unexposed patients; or overestimation because costs of SSIs in comorbid patients are probably higher than costs of SSIs in healthier patients. The inclusion of non-university hospitals alone may also have influenced the representativeness of the results, as patients in university hospitals generally have more severe comorbidities and cost prices for university hospitals are generally higher [43]. The latter was partly solved using bed-day costs that were weighted averages for university and non-university hospitals. Secondly, some cost components (medication, antibiotics, total parental nutrition, and treatment or readmissions in other hospitals) were not included, or were only partially included, because information collected about these components was too difficult to retrieve or even absent. Fourth, there are several limitations to the use of standard cost prices. For instance, it is known that short hospital stays are associated with higher average bed-day costs than longer hospital stays [44]. This dependency on LOS might not be captured adequately in the use of a standard average bed-day cost. Finally, data on resource use were from 2011. There is no indication for a major change in standard of care since then, but PREZIES SSI incidence surveillance data show that the difference in LOS of the primary admission (between patients with and without an SSI) has decreased slightly since 2011. This change varies for the three types of surgery in this study between -2 days (THA) and +1.5 days (colectomy). As recent PREZIES prevalence data show no relevant change over time in LOS of readmissions due to SSIs (from 2014 onwards, no data available before 2014), the use of 2011 data is unlikely to have a large impact on the implications for current practice.

There are also limitations to the estimation of disease burden. First, it was not estimated using patient-based data or questionnaires, but using a mathematical tool. In this tool, no long-term sequelae of SSIs besides mortality were included, such as invalidity due to implant removal surgery. Co-morbidity was taken into account by adjusting life expectancies to ASA scores, but the assumed life expectancies are uncertain and not evidence-based. To the best of the authors' knowledge, actual mortality rates from SSIs in the Netherlands remain unknown. Therefore, case fatalities were derived from a 2001 article from France, representing a different decade and a different health system. It is plausible that mortality from SSIs had decreased by 2011. Also, mortality due to SSIs in the French paper is different from the (unspecified) mortality seen in the small cohorts in this study. However, the SSI incidence rates of both studies were fairly comparable.

Future implications

Despite assumptions and uncertainties, this study gives detailed information on costs of SSIs and provides first estimates of the SSI disease burden for the Netherlands. It gives insight into variability between types of surgery and into evidence that is still lacking. Moreover, by combining costs and burden of disease, an order of magnitude of the economic burden of SSIs is provided. The SSI disease burden of the three studied types of surgery alone is comparable to that of hepatitis C or HIV in the Netherlands. In addition, for these three types of surgery, the economic burden of SSIs exceeds €128 million per year (€40 million hospital costs and €88 million on DALY costs). Societal impact could have been even greater than demonstrated in this study if production losses of SSIs occurring after discharge had been included. By doing so, the total costs of an SSI can double [45].

The costs and burden in this study account for only a small part of all types of surgery but they warrant vigorous prevention efforts. For instance, in aiming to reduce the incidence of SSIs by 50%, the breakeven point to invest in interventions would be €20 million from the hospital's perspective, €44 million from the cost of DALYs perspective, and €64 million when seen from the total cost perspective. Hence, interventions reducing the incidence of SSIs are very likely to be cost-effective.

In conclusion, in light of the emergence of highly resistant micro-organisms and an aging population, SSIs are of concern. The considerable disease and economic burden of SSIs found in this study underline the importance of infection prevention and control strategies. Surveillance of SSIs to gain insight into the disease burden and trends over time, in combination with knowledge about the financial consequences, will help to target interventions.

Acknowledgements

The authors wish to thank all hospitals and hospital staff who were involved in data collection. The authors also thank their PREZIES colleagues Anouk Meijs and Janneke van Heereveld for their help in data collection.

Conflict of interest statement
None declared.

Funding sources
None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2019.07.010.

References

[1] PREZIES Team. PREZIES prevalence survey, national results 2017. Bilthoven: RIVM. 2018. Available at: https://www.rivm.nl/sites/default/files/2018-11/Jaarcijfers%20Prevalentie%202017%20ziekenhuizen%20algemeen.pdf [last accessed December 2018].

[2] PREZIES Team. Incidence of surgical site infections in hospitals, 2012–2015. Bilthoven: RIVM; 2018. Available at: https://www.volksgezondheidenzorg.info/onderwerp/zorginfecties/cijfers-context/huidige-situatie#node-incidentie-postoperatieve-wondinfecties-ziekenhuizen [last accessed December 2018].

[3] de Lissovoy G, Fraeman K, Hutchins V, Murphy D, Song D, Vaughn BB. Surgical site infection: incidence and impact on hospital utilization and treatment costs. Am J Infect Control 2009;37:387–97.

[4] Cassini A, Plachouras D, Eckmanns T, Abu Sin M, Blank HP, 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 Med 2016;13:e1002150.

[5] VandenBergh MF, Kluytmans JA, van Hout BA, Maat AP, Seerden RJ, McDonnel J, et al. Cost-effectiveness of perioperative mupirocin nasal ointment in cardiothoracic surgery. Infect Control Hosp Epidemiol 1996;17:786–92.

[6] Geubbels ELPE. Prevention of surgical site infections through surveillance. Dissertation. Amersfoort: UMC Utrecht, RIVM; 2002.

[7] Broex EC, van Asselt AD, Bruggeman CA, van Tiel FH. Surgical site infections: how high are the costs? J Hosp Infect 2009;72:193–201.

[8] Kusachi S, Kashimura N, Konishi T, Shimizu J, Kusunoki M, Oka M, et al. Length of stay and cost for surgical site infection after abdominal and cardiac surgery in Japanese hospitals: multi-center surveillance. Surg Infect (Larchmt) 2012;13:257–65.

[9] Graf K, Ott E, Vonberg RP, Kuehn C, Schilling T, Haverich A, et al. Surgical site infections – economic consequences for the health care system. Langenbecks Arch Surg 2011;396:453–9.

[10] Tanner J, Khan D, Aplin C, Ball J, Thomas M, Bankart J. Post-discharge surveillance to identify colorectal surgical site infection rates and related costs. J Hosp Infect 2009;72:243–50.

[11] Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ. The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. Infect Control Hosp Epidemiol 1999;20:725–30.

[12] Whitehouse JD, Friedman ND, Kirkland KB, Richardson WJ, Sexton DJ. The impact of surgical-site infections following orthopedic surgery at a community hospital and a university hospital: adverse quality of life, excess length of stay, and extra cost. Infect Control Hosp Epidemiol 2002;23:183–9.

[13] Monge Jodra V, Sainz de Los Terreros Soler L, Diaz-Agero Perez C, Saa Requejo CM, Plana Farras N. Excess length of stay attributable to surgical site infection following hip replacement: a nested case–control study. Infect Control Hosp Epidemiol 2006;27:1299–303.

[14] Edwards C, Counsell A, Boulton C, Moran CG. Early infection after hip fracture surgery: risk factors, costs and outcome. J Bone Joint Surg Br 2008;90:770–7.

[15] Kashimura N, Kusachi S, Konishi T, Shimizu J, Kusunoki M, Oka M, et al. Impact of surgical site infection after colorectal surgery on hospital stay and medical expenditure in Japan. Surg Today 2012;42:639–45.

[16] Koek MB, Wille JC, Isken MR, Voss A, van Benthem BH. Post-discharge surveillance (PDS) for surgical site infections: a good method is more important than a long duration. Euro Surveill 2015;20. Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES2015.20.8.21042 [last accessed September 2019].

[17] Verberk JDM, Meijs AP, Vos MC, Schreurs LMA, Geerlings SE, de Greeff SC, et al. Contribution of prior, multiple-, and repetitive surgeries to the risk of surgical site infections in the Netherlands. Infect Control Hosp Epidemiol 2017;38:1298–305.

[18] Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 2008;36:309–32.

[19] European Centre for Disease Prevention and Control. Surveillance of surgical site infections in European hospitals – HAISSI protocol. Version 1.02. Stockholm: ECDC; 2012.

[20] Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. Am J Infect Control 1999;27:97–132, quiz 3–4; discussion 96.

[21] Horan TC, Gaynes RP. Surveillance of nosocomial infections. 3rd ed. Philadelphia: Lippincott Williams and Wilkins; 2004.

[22] Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. Am J Infect Control 1988;16:128–40.

[23] PREZIES Team. SSI surveillance protocol 2018. Bilthoven: RIVM; 2017. Available at: https://www.rivm.nl/documenten/protocol-en-ds-powi-2018 [last accessed December 2018].

[24] Coello R, Charlett A, Wilson J, Ward V, Pearson A, Borriello P. Adverse impact of surgical site infections in English hospitals. J Hosp Infect 2005;60:93–103.

[25] Owens WD, Felts JA, Spitznagel Jr EL. ASA physical status classifications: a study of consistency of ratings. Anesthesiology 1978;49:239–43.

[26] Vogel TR, Dombrovskiy VY, Lowry SF. In-hospital delay of elective surgery for high volume procedures: the impact on infectious complications. J Am Coll Surg 2010;211:784–90.

[27] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.

[28] Moses S. Charlson comorbidity index. Family Practice Notebook; 2019. https://fpnotebook.com/prevent/Exam/ChrlsnCmrbdtyIndx.htm [last accessed March 2019].

[29] Statistics Netherlands. Consumer prices; price index 2015=100. Updated 6 December 2018. Available at: http://statline.cbs.nl/Statweb/publication/?DM=SLEN&PA=83131ENG&D1=0&D2=0&D3=64,77,90,103,116,129,142,155,168,181,194,207,220,233,246,259,272,285&LA=EN&HDR=T&STB=G1,G2&VW=T [last accessed December 2018].

[30] Austin PC, Steyerberg EW. The number of subjects per variable required in linear regression analyses. J Clin Epidemiol 2015;68:627–36.

[31] Gregori D, Petrinco M, Bo S, Desideri A, Merletti F, Pagano E. Regression models for analyzing costs and their determinants in health care: an introductory review. Int J Qual Health Care 2011;23:331–41.

[32] Colzani E, Cassini A, Lewandowski D, Mangen MJ, Plass D, McDonald SA, 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.

[33] Statistics Netherlands. Surgeries, type of hospitalisation, age and gender, 1995–2010. 2014. Updated 5 February 2014. Available at: http://statline.cbs.nl/Statweb/publication/?DM=SLNL&PA=80386NED&D1=0&D2=0&D3=0&D4=a&D5=l&VW=T [last accessed December 2018].

[34] Astagneau P, Rioux C, Golliot F, Brucker G, Group INS. Morbidity and mortality associated with surgical site infections: results from the 1997–1999 INCISO surveillance. J Hosp Infect 2001;48:267–74.

[35] 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. Popul Health Metr 2015;13:10.

[36] Murray CJ, Ezzati M, Flaxman AD, Lim S, Lozano R, Michaud C, et al. GBD 2010: design, definitions, and metrics. Lancet 2012;380:2063–6.

[37] World Health Organization. WHO methods and data sources for global burden of disease estimates 2000–2011. Geneva: WHO, Department of Health Statistics and Information Systems; 2013. Available at: https://www.who.int/healthinfo/statistics/GlobalDALYmethods_2000_2011.pdf [last accessed March 2019].

[38] National Health Care Institute. Cost-effectiveness in practice. 2015. Available at: https://www.zorginstituutnederland.nl/publicaties/rapport/2015/06/26/kosteneffectiviteit-in-de-praktijk [last accessed December 2018].

[39] de Gier B, Mooi SH, Hahné SJM. State of infectious diseases in The Netherlands, 2017. Bilthoven: RIVM; 2018. Rapport 2018-0032.

[40] Olsen MA, Chu-Ongsakul S, Brandt KE, Dietz JR, Mayfield J, Fraser VJ. Hospital-associated costs due to surgical site infection after breast surgery. Arch Surg 2008;143:53–60, discussion 1.

[41] Reilly J, Twaddle S, McIntosh J, Kean L. An economic analysis of surgical wound infection. J Hosp Infect 2001;49:245–9.

[42] Perencevich EN, Sands KE, Cosgrove SE, Guadagnoli E, Meara E, Platt R. Health and economic impact of surgical site infections diagnosed after hospital discharge. Emerg Infect Dis 2003;9:196–203.

[43] Hakkaart-van Roijen L, Tan SS, Bouwmans CAM. Manual for costing research. Methods and standardized prices for economic evaluations in health care. Amstelveen: College voor zorgverzekeringen; 2010.

[44] Ishak KJ, Stolar M, Hu MY, Alvarez P, Wang Y, Getsios D, et al. Accounting for the relationship between per diem cost and LOS when estimating hospitalization costs. BMC Health Serv Res 2012;12:439.

[45] Graves N, Halton K, Doidge S, Clements A, Lairson D, Whitby M. Who bears the cost of healthcare-acquired surgical site infection? J Hosp Infect 2008;69:274—82.