

Staphylococcus aureus infections in German type 2 diabetes mellitus patients after orthopedic surgery: incidence, risk factors and clinical and health-economic outcomes

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Conflict of interest

The study was funded by Pfizer Inc. Holly Yu is an employee of Pfizer Inc.

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Background

- Orthopedic surgery is an effective surgical procedure that enhances quality of life by providing pain relief and restoring mobility in patients with various degenerative conditions or malfunction
- In Germany, a surgical site infection (SSI) rate of 0.98% after orthopedic surgeries has been reported, among all observed SSIs, 31% were due to *Staphylococcus aureus* (*S. aureus*)¹
 - *S. aureus* is the most common cause of surgical-site infections²
- Patient with diabetes are at increased risk for postoperative infection³⁻⁷
- SSIs caused by *S. aureus* can have been associated with worse clinical outcomes and a higher healthcare costs⁸⁻¹⁰

1. Langelotz et al, 2014

2. Herwaldt LA, 2003

3. Yang et al, 2014

4. Zhang et al., 2015

5. Meng et al, 2015

6. Pull ter Gunne & Cohen, 2009

7. Tsang & Gaston, 2013

8. Campbell et al, 2015

9. Noskin et al, 2005

10. Bedair et al, 2015

Objectives

- To assess incidence of *S. aureus* infections after orthopedic surgeries in type 2 diabetes mellitus (T2DM) patients in Germany
- To identify baseline characteristics associated with the risk of *S. aureus* infections
- To assess outcomes associated with *S. aureus* infections
 - Mortality
 - Healthcare resource use (HCRU)
 - Direct healthcare costs

Study design (I)

Retrospective, non-interventional study based on a German pseudonymized claims dataset for 2010-2012, including 596 349 patients with confirmed diagnosis of type 2 diabetes mellitus (T2DM)

Patients with at least one knee, hip or spine surgery

Index Date = First inpatient endoprosthetic hip, knee or a spine surgery between 07/01/2010 – 12/31/2011, conducted within 2 days after hospital admission

Exclusion criteria:

- Age < 18 at date of surgery
- Any surgery performed at the same part of the body (knee/hip/spine) as the index surgery in the 180 days before index date
- Any *S. aureus* infection within 90 days before index date

End of observational period

- First *S. aureus* infection OR death OR 12/31/2012 OR end of 1-year follow-up period

**3784 patients
with knee surgery**

**4111 patients
with hip surgery**

**1506 patients
with spine surgery**

Study design (II)

Identification of *S. aureus* infections

- *S. aureus* could have been diagnosed either inpatient or outpatient
- ICD-10 codes for *S. aureus* infections were the following:

A41.0	Sepsis due to <i>Staphylococcus aureus</i>
B95.6	<i>Staphylococcus aureus</i> as cause of disease that is classified
U80.0	<i>Staphylococcus aureus</i> with resistance to specific antibiotics

Outcomes

- Outcomes (mortality, HCRU and costs) were compared for the 365 days after index surgery, between the following patient groups:

***S. aureus* group**

Patients who experienced a *S. aureus* infection within 365 days after surgery

N = 239 patients

Non-*S. aureus* group

Patients who did not experience a *S. aureus* infection within 365 days after surgery

N = 9162 patients

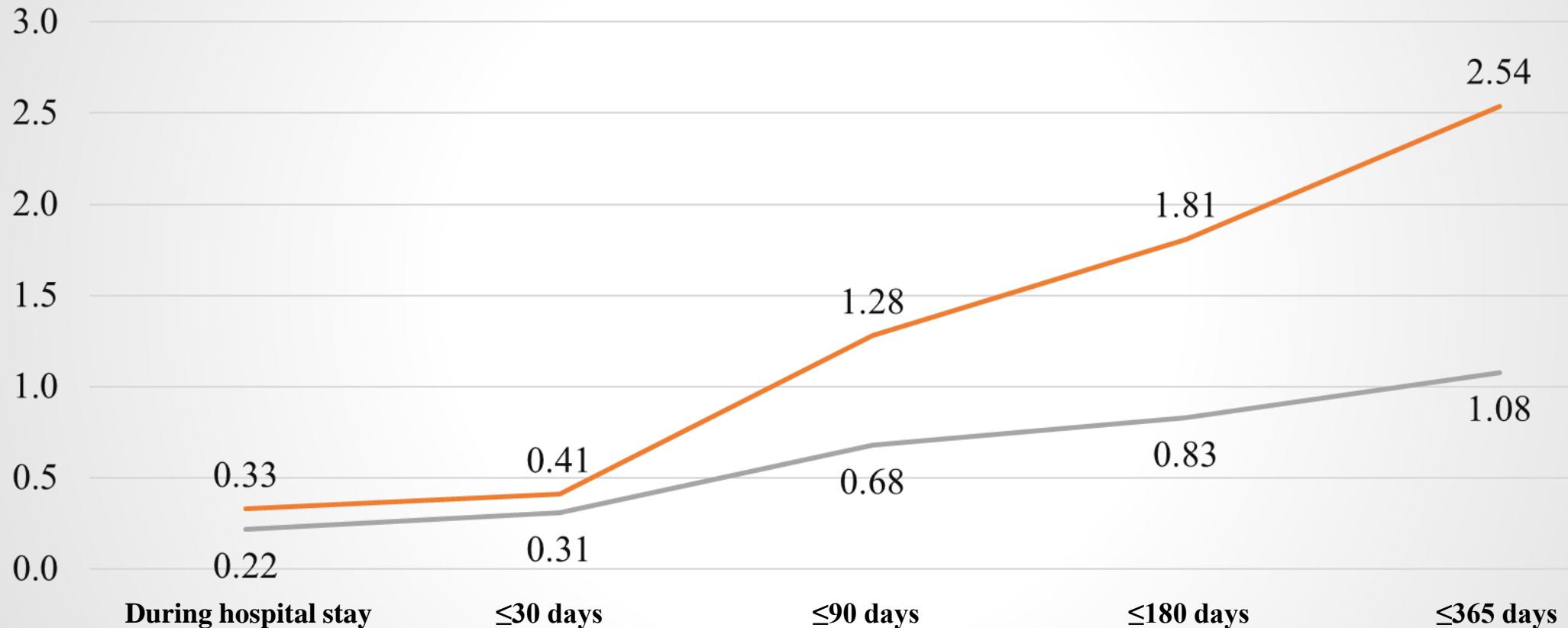
Results – Patient characteristics

Baseline characteristics	All T2DM patients (with elective surgery)	Knee surgery	Hip surgery	Spine surgery	p-value
N	9401	3784	4111	1506	
Mean age in years ¹ (SD)	72.6 (9.9)	71.5 (8.4)	75.5 (9.5)	67.5 (11.6)	< 0.001
Female sex, number (%)	5953 (63.3)	2468 (65.2)	2723 (66.2)	762 (50.6)	< 0.001
CCI ² (SD)	3.5 (2.3)	3.2 (2.0)	3.7 (2.4)	3.5 (2.5)	< 0.001
Length of index hospitalization in days (SD)	13.9 (7.9)	13.4 (4.7)	15.4 (8.4)	11.1 (11.3)	< 0.001
Number of previous prescriptions of antibiotics ² (SD)	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)	0.1 (0.3)	= 0.473

¹Age at date of the index surgery ²Based on 6-month baseline period before index
CCI, Charlson Comorbidity Index; SD, standard deviation; T2DM, type 2 diabetes mellitus

Results – Cumulative incidence of *S. aureus* infections

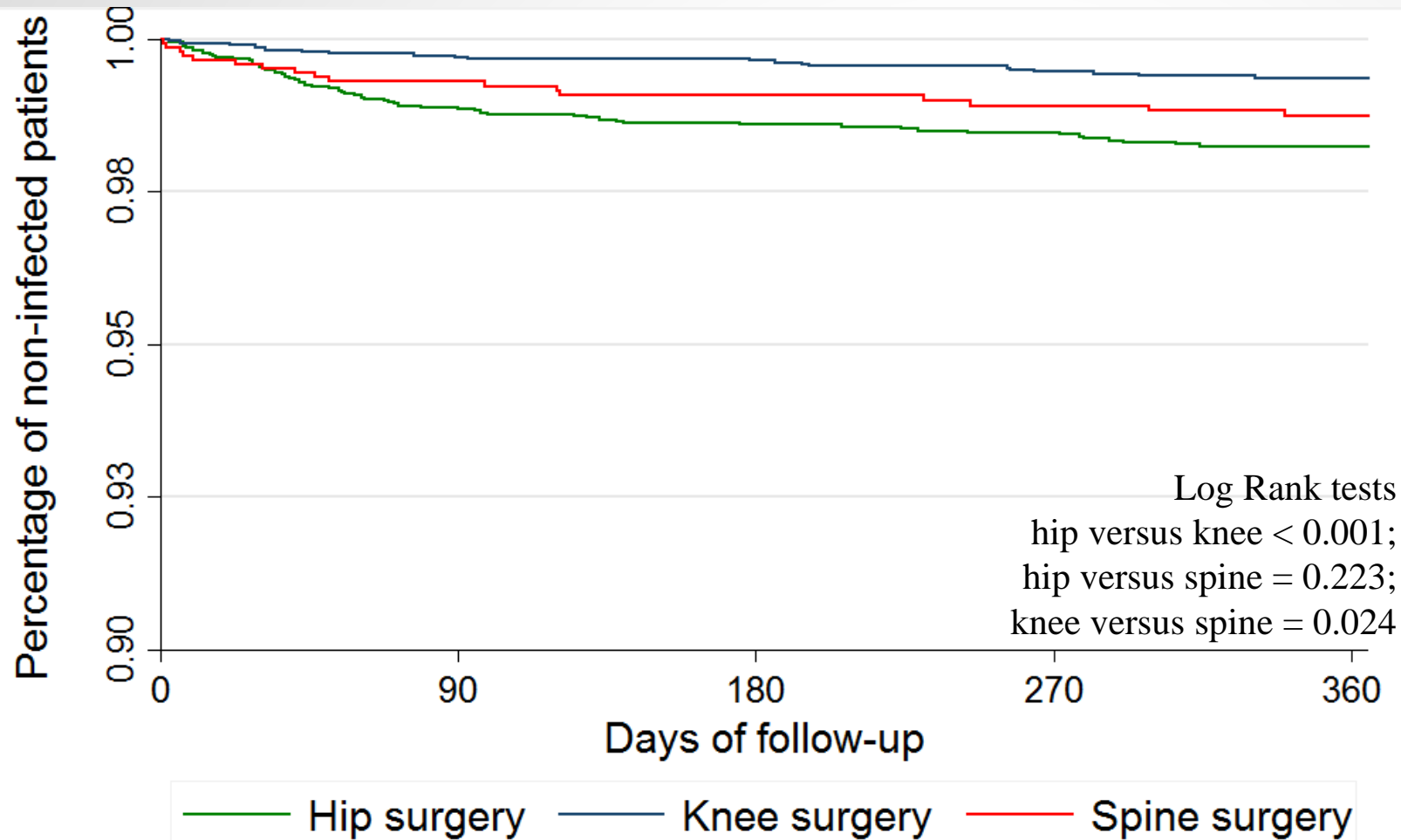
% of patients who developed *S. aureus* infections during different time intervals after orthopedic surgery



— Analysis **without censoring** for follow-up surgeries performed on a different part of the body from the index surgery
— Analysis **with censoring** for follow-up surgeries performed on a different part of the body from the index surgery

➤ In total, 2.54% (1.08% with censoring) of the patients experienced a *S. aureus* infection within 365 days

Results – Kaplan Meier curves for time until first *S. aureus* infection



Incidence rates (per 100 patient years) for 365 days follow-up

(censored)

Knee: 1.80 (0.65)

Spine: 2.22 (1.35)

Hip: 3.73 (1.90)

Mean time until *S. aureus* infection (days)

Knee: 165.96

Spine: 104.41

Hip: 112.14

Overall: 126.19

- The *S. aureus* incidence rate was highest among hip surgery patients
- The average time to *S. aureus* infection onset was about 4 months post surgery

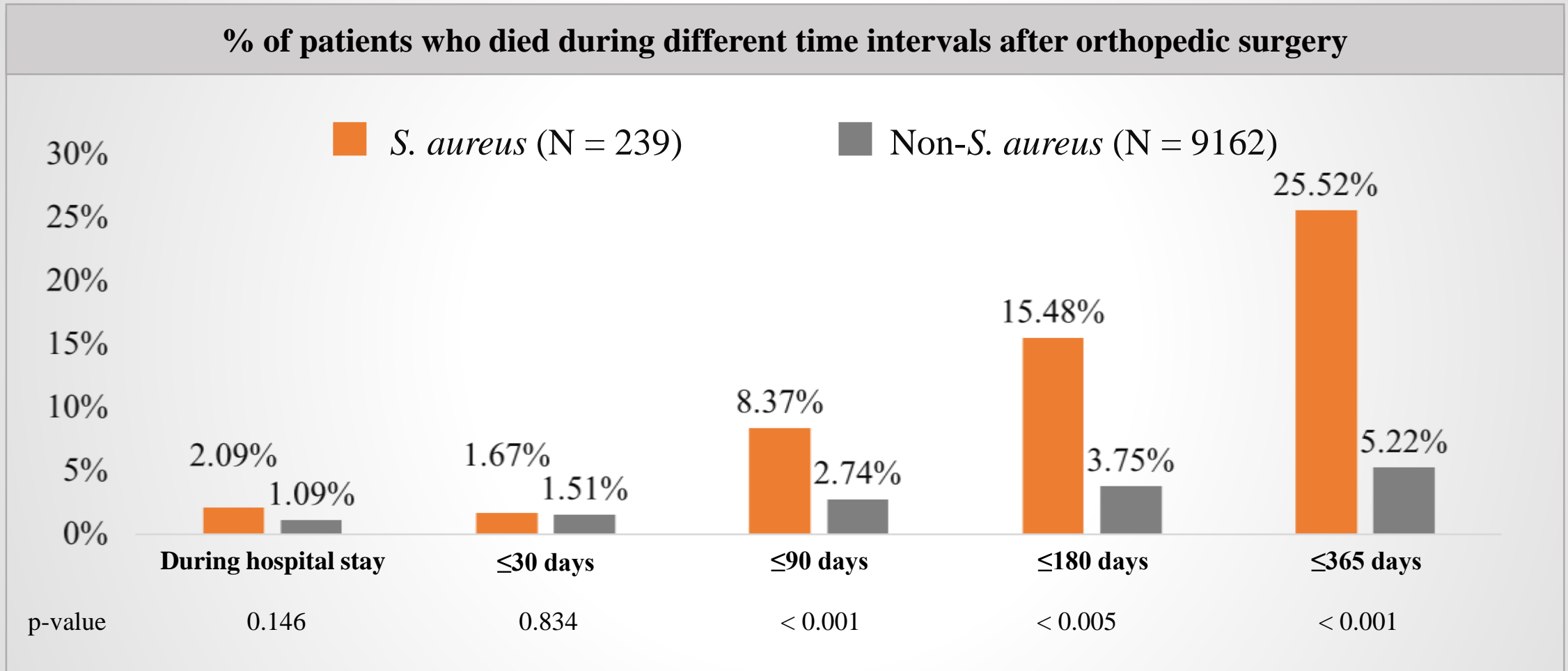
Results - Risk factors of *S. aureus* infections - Cox regression model

		Hazard ratio	p-value	95% confidence interval
Age at index surgery (years)		1.05	0.001	1.02 – 1.07
Surgery type	Knee	Reference		
	Hip	1.96	0.009	1.18 – 3.23
	Spine	2.16	0.019	1.14 – 4.09
Length of index hospitalization (days)		1.03	< 0.001	1.02 – 1.04
Charlson Comorbidity Index (CCI)*		1.21	< 0.001	1.13 – 1.29

log likelihood: -875.71; LR chi² = 92.18; (Prob > chi²) < 0.001

- Non-significant variables were gender and number of antibiotic prescriptions in the pre-index period
- Older age, higher CCI and length of index hospitalization were associated with higher infection risk
- Patients undergoing an endoprosthetic hip or spine surgery faced a significantly higher risk for a *S. aureus* infection compared to patients undergoing a knee surgery

Results – Mortality associated with *S. aureus* infections



➤ Mortality was higher among patients who experienced a *S. aureus* infection after endoprosthetic surgery than those who did not

Results – Risk factors associated with 365-day mortality – Cox regression model

		Hazard ratio	p-value	95% confidence interval
<i>S. aureus</i> infection within 365 days after surgery	No	Reference		
	Yes	2.94	< 0.001	2.24 – 3.86
Age at index surgery (years)		1.11	< 0.001	1.10 – 1.12
Gender	Female	0.71	< 0.001	0.59 – 0.85
Surgery type	Knee	Reference		
	Hip	3.15	< 0.001	2.41 – 4.12
	Spine	2.43	< 0.001	1.72 – 3.43
Length of index hospitalization (days)		1.01	< 0.001	1.01 – 1.02
Charlson Comorbidity Index (CCI)*†		1.21	< 0.001	1.18 – 1.24
Number of antibiotic prescriptions*		1.21	0.017	1.03 – 1.41

Patients included: 9401; events (deaths): 539; log likelihood: –4438.94; LR $\chi^2 = 952.99$; (Prob > χ^2) < 0.001; analysis included censoring for follow-up surgeries not carried out in the same part of the body as the index surgery

* Based on 6-month baseline period before index; † Age was excluded from CCI

➤ Patients with a *S. aureus* infection had a 2.9 times risk of death

Results – Health care resource use (HCRU) and costs

1-year follow up per patient per year	<i>S. aureus</i> N=239	Non- <i>S. aureus</i> N=9163	p-value
HCRU			
No. of outpatient general practitioners (GPs) visits	5.84	5.29	0.574
No. of outpatient specialist visits	8.49	9.56	< 0.001
No. of all-cause hospitalizations*	3.15	0.84	< 0.001
No. of hospital days*	50.42	7.90	< 0.001
Sum of defined daily dosages of antibiotics	7.97	1.61	< 0.001
Direct medical costs (€)			
Outpatient (GPs) costs	412.98	281.74	< 0.001
Outpatient (specialists) costs	376.52	379.67	0.036
Hospitalization costs	21,422.16	3,226.72	< 0.001
Outpatient medication costs	540.63	371.62	< 0.001
Total medical costs	22,752.29	4,259.75	< 0.001

* Index hospitalization not included

➤ HCRU and all-cause medical costs per patient per year were significantly higher for patients who experienced a *S. aureus* infection

Limitations

- Results were subject to accurate use of the ICD-10 diagnosis code of *S. aureus* and data compilation since microbiological and clinical information were not available in the database
- With no pathogen-specific surgical site infection in ICD-10, misclassification and under-reporting of postsurgical *S. aureus* infection could happen
- Severity of diabetic condition was not able to be defined and controlled in the analysis

Conclusions

- The *S. aureus* infection risk in T2DM patients, undergoing a knee, hip, or a spine surgery in Germany is about 2.54% in the first year after surgery (1.08% if censored for any follow-up surgery at a different location)
- The incidence risk is influenced by the type of surgical procedure and patient's age
- Within 1 year, *S. aureus* infected patients, compared to non *S. aureus* infected patients, experienced substantially higher:
 - Mortality (25.52% vs. 5.22%, p-value: <0.001),
 - Healthcare resource use (50.4 vs. 7.9 hospital days, p-value: <0.001), and
 - Direct medical costs (€22,752 vs. €4,259, p-value: >0.001)
- Effective infection control measures should be considered to target this population, with the aim to reduce the risk of *S. aureus* infections after orthopedic surgeries

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