Risk factors differ for Gram-negative surgical site infection following hip and knee arthroplasty: an observational study from a national surveillance system

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ABSTRACT

AIM: To describe risk factors for surgical site infection (SSI) caused by aerobic Gram-negative organisms after hip and knee arthroplasty.

METHOD: Publicly funded hip and knee arthroplasties (performed between 1 July 2013 and 31 December 2017) that developed SSIs were compared to those that did not. SSIs were grouped by causative organism: Gram-negative (*Pseudomonas* spp. or enteric Gram-negative bacilli) or staphylococcal (pure or mixed growth of *Staphylococcus* spp.). Independent risk factors in each group were identified.

RESULTS: 24,842 (54%) hip and 20,993 (46%) knee arthroplasties were performed. There were 497 (1.1%) SSIs. Staphylococci were responsible for 233 SSIs (47%) and Gram-negatives were responsible for 73 (15%). Age, sex, body mass index ≥35kg/m^2, smoking status, socioeconomic deprivation, American Society of Anesthesiologists classification, revision surgery and prophylactic antibiotic dose were all independent predictors of all-cause SSI. On subgroup analysis, socioeconomic deprivation and Pasifika ethnicity were independent risk factors for Gram-negative SSI, but not staphylococcal SSI.

DISCUSSION: In this study, socioeconomic deprivation and ethnicity were independent and novel risk factors for Gram-negative SSI following arthroplasty. Some of the SSI risk factors can be modified before arthroplasty (e.g., appropriate timing of prophylactic antibiotics, smoking cessation, weight loss). Non-modifiable risk factors can help identify high-risk procedures where additional pre- and post-operative interventions may be warranted.

Surgical site infection (SSI) following orthopaedic surgery is associated with significant morbidity.[1,2] The issue will become increasingly important with the projected increases in hip and knee arthroplasty.[3] In New Zealand, 9,169 total hip joint replacements and 8,321 total knee joint replacements were performed in 2018.[4] Deep infection is the leading cause and second highest cause of revision surgery within one year of primary knee and hip arthroplasty respectively and the leading indication for re-revision.[4]

Since 2013, the New Zealand Health Quality & Safety Commission Orthopaedic Surgical Site Infection Improvement Programme (SSIIP) has conducted national SSI surveillance for selected hip and knee procedures. The SSIIP, using a quality improvement approach, observed an association between increased adherence to key process measures (appropriate prophylactic antibiotic selection, dose and timing and use of an alcohol-based skin preparation) and a decrease in the SSI rate from 1.36% to 0.91%.[5] The most commonly isolated pathogen was *Staphylococcus aureus*, and strategies to target this pathogen are being introduced through the implementation of a preoperative anti-staphylococcal intervention bundle.[6]

Despite causing a moderate proportion of SSI, Gram-negative SSI are less well described and not specifically targeted in preventative measures like staphylococcal SSIs.[7–12] This study examined the SSIIP database to find predictors of SSI, particularly those caused by aerobic Gram-negatives, to identify modifiable risk factors amenable to quality improvement interventions.

Method

Data collection

Since 2013, the SSIIP has collected data on all publicly funded routine elective hip and knee arthroplasties through New Zealand's 20 district health boards (DHBs). Procedures between 1 July 2013 and 31 December 2017 were included in the analysis. Additional information was available through the Ministry of Health National Minimum Dataset (NMDS) (i.e., socioeconomic deprivation (New Zealand Index of Deprivation[13]), diagnosis of diabetes mellitus (type 1 and type 2), smoking status and ethnicity). Data collection methodology has been published previously.[5,14,15] Pasifika ethnicity was defined as one category. However, Pasifika contains many culturally distinct groups, with Samoan (48%), Tongan (22%) and Cook Island Māori (21%) being the most common.[16]

Regular training is provided by the SSIIP in surveillance methods and application of the SSI definitions to ensure high-quality data are recorded. Data not gathered by the surveillance system includes: antimicrobial use in the pre-admission period, presence of other comorbidities other than diabetes and smoking (such as inflammatory arthropathies, glycaemic control, anticoagulation or immunosuppression) or clinical information such as perioperative bacteraemia or bacteriuria. Of note, arthroplasties performed for fractured neck of femur are excluded.

Definitions

The Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) SSI definitions were used. Patients were followed for 90 days after surgery.[17] Briefly, superficial incisional SSIs involve only skin and subcutaneous tissue of incision and must occur within 30 days of operative procedure. Deep incisional SSI must occur within 90 days of operative procedure and involve deep soft tissues of the incision (e.g., fascia and muscle layers), and even deeper infections are considered organ/space SSI. Superficial SSIs managed outside hospital were not part of surveillance.

All-cause SSIs were analysed. This included all culture positive and culture negative SSIs. For subgroup analysis, SSIs were categorised by the pathogen(s) isolated from microbiological samples. "Staphylococcal SSI" had either pure growth of a *Staphylococcus* sp. or mixed *Staphylococcus* spp.. Partly informed by previous literature,[10] the "Gram-negative SSIs" were defined as due to either *Pseudomonas* spp. or organisms from the order Enterobacterales, commonly called "enteric" Gram-negatives (e.g., *Escherichia coli*, *Klebsiella* spp., *Proteus* spp.) either isolated pure or mixed with each other. SSIs with other Gram-negative organisms or other Gram-positive organisms isolated were excluded from subgroup analysis. Examples of organisms isolated from microbiological samples of SSIs that were not included in subgroup analysis were: *Candida* spp., *Acinetobacter* spp., *Streptococcus* spp., *Enterococcus* spp. and *Corynebacterium* spp..

Appropriate dose of cefazolin prophylaxis was defined as 1g for patients <80kg, 2g if 80–120kg and 3g if >120kg. Lower doses were defined as underdosed. Antibiotic surgical prophylaxis administered within 60 minutes before incision was considered "on time," and prophylaxis given >60 minutes before or after incision was defined as "not on time."

Statistical analysis

All statistical analyses were conducted using STATA version 13.0 (StataCorp, College Station, TX, USA). Each stratum had the same statistical methodology.

For univariate analysis, age, sex, BMI (kg/m$^{2)}$, weight, duration of surgery, ethnicity, smoking status, diabetes, socioeconomic status (New Zealand Index of Deprivation), whether the procedure was a revision procedure, the use of alcohol containing skin antiseptic, American Society of Anesthesiologists classification (ASA class), perioperative exposure to various antibiotics (gentamicin, cefazolin, cefuroxime) and timing and dose of standard cefazolin prophylaxis were cross tabulated against procedures that developed SSI and those that did not at 90-day follow-up. Categories with fewer than five events in any single cell were reviewed before proceeding to analytical statistics.

A time-to-failure (SSI) Cox regression analysis was performed, where entry into the analysis occurred on the day of surgery and exit from analysis occurred at day of SSI, or end of 90-day follow-up, or date of death (if available), whichever occurred first. Univariate Cox analysis was performed, and variables that had p-value <0.2 on univariate analysis entered the reverse stepwise multivariate Cox regression. Then one at a time, the variable with the highest p-value was removed and the model re-run. This was repeated until all variables remaining within the model had a p-value less than 0.05. At this stage, because

of its clinical importance, age was re-entered into the model to verify no statistically significant effect on the final model.

Robustness of relationships was checked by sorting all variables by Likelihood Ratio (LR) chi-square test values (from univariate analysis) and then consecutively entry (one at a time) into a forward stepwise Cox regression and with variables exiting the model if at any iteration the p-value was >0.05. At this stage age was re-entered into the model for the reasons described above.

Ethical considerations

Under New Zealand Health and Disability Ethics Committee guidelines, formal Ethical Committee review was not needed for this type of quality-improvement-related audit.

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This work is self-funded. The authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Over the study period, there were 45,835 arthroplasties comprised by 24,842 (54%) hip and 20,993 (46%) knee procedures. There were 497 SSIs (1.1%): 233 staphylococcal SSIs (47%) and 73 Gram-negative SSI (15%). Enterobacterales contributed a majority of the Gram-negative SSI (n=54, 74%), and *Pseudomonas* spp. (all *P. aeruginosa*, except one) contributed (n=19, 26%). SSIs that were excluded from sub-analyses either had no specimen for microbiology taken (n=31, 6%) or were cultured negative (n=61, 12%) or had other positive culture results that did not meet study definitions (n=99, 20%). There were 301 (61%) and 196 (39%) hip and knee SSIs, respectively. Hip procedures had an SSI rate of 1.2% and knee procedures an SSI rate of 0.9%. Deep SSI accounted for majority of SSI (n=206, 41%) and the remainder were either organ space (n=129, 26%) or superficial (n=162, 33%). There was no significant relationship between the depth of infection and SSI organism group (data not shown). Perioperative exposure to different prophylactic antibiotics (gentamicin, cefazolin, cefuroxime) had no association with SSI on univariate or multivariate analysis (data not shown). Rates of early (<30 days) and late (30–90 days) SSI were not different when comparing Gram-negative and staphylococcal SSI (p=0.13, data not shown).

The cohort demographics are included in Table 1. Male sex, BMI, weight, surgery duration ≥2 hours, smoking status, deprivation, revision arthroplasty, ASA class, cefazolin timing and dosing of prophylaxis were associated with an increase in risk of all-cause SSI on univariate analysis. After adjustments for confounders, independent risk factors for all-cause SSI were age (as continuous variable), male sex, BMI, revision arthroplasty and deprivation in the fifth quintile, ASA class ≥3, cefazolin underdosing and smoking status (Table 2).

On univariate analysis of staphylococcal SSI, male sex, BMI, weight, surgery duration ≥2 hours, diabetes, revision arthroplasty, ASA class, antibiotic timing and cefazolin underdosing were risk factors of statistical significance (Table 1). On multivariate analysis male sex, BMI, revision arthroplasty, ASA class, prophylaxis timing and duration of surgery remained significant (Table 2).

On univariate analysis Gram-negative SSI risk factors were BMI, weight, surgery duration ≥2 hours, ethnicity, deprivation, revision arthroplasty, ASA class and cefazolin underdosing (Table 1). A low number of Gram-negative SSI events were not administered prophylaxis on time (n=2), from New Zealand Index of Deprivation quintile 1 (n=3) and ASA class 1 (n=3). However, these were retained acknowledging this as a limitation of further analyses. On multivariate analysis BMI, revision arthroplasty, deprivation and ethnicity remained as independent risk factors. The risk factors identified conferred higher hazard ratios for Gram-negative infection, with New Zealand Index of Deprivation quintiles 4 and 5 having eight times the SSI risk, BMI of ≥40kg/m^2 four times the SSI risk, and Pasifika ethnicity (not associated with other SSI groups) more than doubled the risk of SSI (Table 2).

Maori and Pasifika people with a BMI of ≥40kg/m^2 are more frequently underdosed than non-Māori non-Pasifika of similar BMI (Table 3). Underdosing was not associated with deprivation quintile (data not shown).

Those with higher BMI have longer procedures. However, within each BMI category, Pasifika people were more likely to have longer procedures, as were Maori with BMI of ≥40kg/m^2 (Table 4).

Prevalence of SSI risk factors within the entire cohort by ethnic group is presented Table 5. Māori had a statistically significant higher crude rate of SSI when compared directly to non-Māori non-Pasifika (1.4% and 1.0% respectively, p-value 0.049), while Pasifika did not (1.1%, p-value 0.923). Māori

Table 1: Univariate Analysis of 45,835 hip and knee arthroplasties performed between 2013 and 2017.

	No SSI	All-cause SSI	Staphylococcal SSI	Gram-negative SSI
	(n=45,835)	(n=497)	(n=233)	(n=73)
Age category	*Reference*	*p=0.926*	*p=0.324*	*p=0.982*
< 65 years	15,127 (98.9%)	165 (1.1%)	84 (0.6%)	24 (0.2%)
≥65 years	30,708 (98.9%)	332 (1.1%)	149 (0.5%)	49 (0.2%)
Sex	*Reference*	*p=0.001*	*P<0.001*	*p=0.793*
Female	25,035 (99.1%)	235 (0.9%)	90 (0.4%)	41 (0.2%)
Male	20,788 (98.8%)	262 (1.2%)	143 (0.7%)	32 (0.2%)
BMI category, kg/m²	*Reference*	*p<0.001*	*p<0.001*	*p<0.001*
BMI<30	20,555 (99.2%)	157 (0.8%)	78 (0.4%)	19 (0.1%)
30≤BMI<35	10,608 (99.1%)	100 (0.9%)	53 (0.5%)	9 (0.1%)
35≤BMI<40	6,526 (98.6%)	94 (1.4%)	45 (0.7%)	9 (0.1%)
BMI≥40	3,695 (97.8%)	84 (2.2%)	33 (0.9%)	20 (0.5%)
Weight	*Reference*	*p<0.001*	*p<0.001*	*p<0.001*
<80kg	16,239 (99.2%)	132 (0.8%)	63 (0.4%)	18 (0.1%)
80-120kg	22,952 (98.9%)	247 (1.1%)	118 (0.5%)	33 (0.1%)
>120kg	1,876 (97%)	58 (3%)	25 (1.3%)	11 (0.6%)
Duration of surgery	*Reference*	*p<0.001*	*p<0.001*	*p=0.004*
≥2hours	6,507 (98.1%)	123 (1.9%)	65 (1%)	19 (0.3%)
<2hours	39,328 (99.1%)	374 (0.9%)	168 (0.4%)	54 (0.1%)
Ethnicity	*Reference*	*p=0.143*	*p=0.198*	*p=0.001*
Non-Māori non-Pasifika	39,470 (99%)	416 (1%)	193 (0.5%)	54 (0.1%)
Māori	4,655 (98.6%)	64 (1.4%)	32 (0.7%)	12 (0.3%)
Pasifika	1,481 (98.9%)	16 (1.1%)	7 (0.5%)	7 (0.5%)
Smoking status	*Reference*	*p=0.017*	*p=0.376*	*p=0.198*
Non-smoker	42,585 (99%)	448 (1%)	213 (0.5%)	65 (0.2%)
Smoker	3,250 (98.5%)	49 (1.5%)	20 (0.6%)	8 (0.2%)

Table 1 (continued): Univariate Analysis of 45,835 hip and knee arthroplasties performed between 2013 and 2017.

	No SSI	All-cause SSI	Staphylococcal SSI	Gram-negative SSI
	(n=45,835)	(n=497)	(n=233)	(n=73)
Diabetes	*Reference*	*p=0.098*	*p=0.028*	*p=0.924*
No	40,649 (99%)	429 (1%)	196 (0.5%)	65 (0.2%)
Yes	5,186 (98.7%)	68 (1.3%)	37 (0.7%)	8 (0.2%)
NZ Deprivation Quintiles	*Reference*	*p=0.017*	*p=0.073*	*p=0.032*
1 (least deprived)	6,521 (99.1%)	58 (0.9%)	22 (0.3%)	3 (0%)
2	8,366 (99.1%)	75 (0.9%)	44 (0.5%)	10 (0.1%)
3	9,418 (98.9%)	100 (1.1%)	41 (0.4%)	14 (0.1%)
4	11,343 (98.9%)	125 (1.1%)	60 (0.5%)	26 (0.2%)
5 (most deprived)	10,072 (98.7%)	137 (1.3%)	65 (0.6%)	20 (0.2%)
Revision arthroplasty	*Reference*	*p<0.001*	*p<0.001*	*p<0.001*
No	42,241 (99.1%)	402 (0.9%)	188 (0.4%)	55 (0.1%)
Yes	3,594 (97.4%)	95 (2.6%)	45 (1.2%)	18 (0.5%)
Alcohol containing skin preparation	*Reference*	*p=0.375*	*p=0.747*	*p=0.476*
No	313 (98.4%)	5 (1.6%)	2 (0.6%)	0 (0%)
Yes	45,074 (98.9%)	483 (1.1%)	229 (0.5%)	73 (0.2%)
ASA class	*Reference*	*p<0.001*	*p<0.001*	*p=0.001*
1	3,848 (99.5%)	20 (0.5%)	11 (0.3%)	3 (0.1%)
2	26,845 (99.2%)	219 (0.8%)	99 (0.4%)	31 (0.1%)
≥3	14,446 (98.3%)	245 (1.7%)	116 (0.8%)	38 (0.3%)
Antibiotic prophylaxis timing	*Reference*	*p=0.002*	*p=0.001*	*p=0.884*
On time	43,726 (99%)	463 (1%)	214 (0.5%)	69 (0.2%)
Not on time	1,141 (98%)	23 (2%)	14 (1.2%)	2 (0.2%)
Dose of cefazolin prophylaxis	*Reference*	*p<0.001*	*p<0.001*	*p<0.001*
Appropriate	36,018 (99%)	356 (1%)	169 (0.5%)	48 (0.1%)
Under dosed	1,905 (97.4%)	51 (2.6%)	23 (1.2%)	10 (0.5%)

Shown p-values are for chi-square tests comparing No SSI vs SSI subgroups.

Table 2: Multivariate Cox regression of risk factors for SSI following hip and knee arthroplasty.

	All-cause SSI			Staphylococcal SSI*			Gram-negative SSI*		
	Hazard Ratio	**95% CI**	**p-value**	**Hazard Ratio**	**95% CI**	**p-value**	**Hazard Ratio**	**95% CI**	**p-value**
Age (continuous)	1.01	1.00–1.03	0.012	-	-	-	-	-	-
Sex									
Female	1	1.00–1.00	ref	1	1.00–1.00	ref	-	-	-
Male	1.42	1.15–1.75	0.001	2.02	1.52–2.70	<0.001	-	-	-
BMI category, kg/m^2									
BMI<30	1	1.00–1.00	ref	1	1.00–1.00	ref	1	1.00–1.00	ref.
30≤BMI<35	1.16	0.88–1.53	0.298	1.26	0.89–1.80	0.197	0.85	0.38–1.88	0.682
35≤BMI<40	1.77	1.32–2.36	<0.001	1.7	1.16–2.48	0.006	1.24	0.56–2.79	0.596
BMI≥40	2.62	1.86–3.69	<0.001	2.05	1.34–3.14	0.001	4.28	2.18–8.40	<0.001
Revision arthroplasty									
No	1	1.00–1.00	ref	1	1.00–1.00	ref	1	1.00–1.00	ref
Yes	2.55	1.92–3.37	<0.001	2.29	1.52–3.46	<0.001	2.99	1.46–6.10	0.003
NZ Index of Deprivation									
1 (least deprived)	1	1.00–1.00	ref	-	-	-	1	1.00–1.00	ref
2	1.11	0.74–1.66	0.619	-	-	-	6.64	0.84–52.47	0.073
3	1.29	0.88–1.89	0.199	-	-	-	5.84	0.74–46.17	0.094
4	1.23	0.85–1.79	0.268	-	-	-	8.65	1.15–65.03	0.036
5 (most deprived)	1.55	1.08–2.24	0.019	-	-	-	8.48	1.12–64.10	0.038

Table 2 (continued): Multivariate Cox regression of risk factors for SSI following hip and knee arthroplasty.

	All-cause SSI			Staphylococcal SSI*			Gram-negative SSI*		
	Hazard Ratio	**95% CI**	**p-value**	**Hazard Ratio**	**95% CI**	**p-value**	**Hazard Ratio**	**95% CI**	**p-value**
Ethnicity									
Non-Māori non-Pasifika	-	-	-	-	-	-	1	1.00–1.00	ref
Māori	-	-	-	-	-	-	1.65	0.83–3.29	0.15
Pasifika	-	-	-	-	-	-	2.52	1.06–5.97	0.036
ASA class									
1	1	1.00–1.00	ref	1	1.00–1.00	ref	-	-	-
2	1.5	0.85–2.66	0.165	1.04	0.56–1.96	0.892	-	-	-
≥3	2.38	1.32–4.28	0.004	2.05	1.09–3.86	0.026	-	-	-
Antibiotic dose									
Appropriate	1	1.00–1.00	ref	-	-	-	-	-	-
Under dosed	1.47	1.03–2.10	0.035	-	-	-	-	-	-
Prophylaxis timing									
On time	-	-	-	1	1.00–1.00	ref.	-	-	-
Not on time	-	-	-	1.83	1.02–3.28	0.042	-	-	-

Table 2 (continued): Multivariate Cox regression of risk factors for SSI following hip and knee arthroplasty.

	All-cause SSI			Staphylococcal SSI*			Gram-negative SSI*		
	Hazard Ratio	**95% CI**	**p-value**	**Hazard Ratio**	**95% CI**	**p-value**	**Hazard Ratio**	**95% CI**	**p-value**
Duration of surgery									
<2 hours	-	-	-	1	1.00–1.00	ref	-	-	-
≥2 hours	-	-	-	1.48	1.03–2.11	0.032	-	-	-
Smoking status									
Non-smoker	1	1.00–1.00	ref	-	-	-	-	-	-
Smoker	1.61	1.14–2.27	0.007	-	-	-	-	-	-

*Forcing age into this model did not change these relationships.
- not statistically significant on multivariate analysis.
ref = reference group for comparison.
Shown p-values are for multivariate Cox regression within respective SSI subgroup. For example, only for all-cause SSI, procedures that had antibiotics under dosed had HR 1.47 (p value = 0.035) of SSI compared to appropriately dosed procedures.

Table 3: Relationship between BMI, ethnicity and cefazolin dosing.

BMI (kg/m²)	Ethnicity	Cefazolin underdosed	Total	
BMI ≥40	Non-Māori non-Pasifika	570 (26.3%)	2,171	*reference*
	Māori	244 (30.9%)	789	p-value 0.012
	Pasifika	133 (32.7%)	407	p-value 0.008
All	Non-Māori non-Pasifika	1394 (4.3%)	32,641	*reference*
	Māori	374 (9.1%)	4,122	p-value <0.001
	Pasifika	183 (13.2%)	1,382	p-value <0.001

BMI data available for 41,823 procedures (91%).
Procedures missing ethnicity data, n=230.
Procedures not administered cefazolin, n=3,347.
Procedures with weight unavailable for dose calculation, n=4,655.
Shown p-values are for chi-square tests comparing ethnicity head to head (with non-Māori non-Pasifika as the reference group) within each respective BMI category. For example, for BMI ≥40, Pasifika, compared to non-Māori non-Pasifika, had a significantly greater proportion of procedures that had cefazolin underdosed (p=0.008).

Table 4: Relationship between BMI, ethnicity and duration of surgery.

	Ethnicity	Non-Māori non-Pasifika		Māori		Pasifika	
BMI (kg/m²)	Duration of Surgery	n (%)	p-value	n (%)	p-value	n (%)	p-value
BMI<30	2 or more hours	2,279 (11.9%)	ref	153 (12.1%)	0.87	38 (16.4%)	**0.038**
	<2 hours	16,830 (88.1%)		1,113 (87.9%)		194 (83.6%)	
30≤BMI<35	2 or more hours	1,092 (12%)	ref	173 (13.9%)	0.053	66 (20.4%)	**<0.001**
	<2 hours	7,993 (88%)		1,068 (86.1%)		258 (79.6%)	
35≤BMI<40	2 or more hours	792 (15.4%)	ref	182 (17.2%)	0.15	82 (20.6%)	**0.007**
	<2 hours	4,347 (84.6%)		876 (82.8%)		317 (79.4%)	
BMI≥40	2 or more hours	448 (18%)	ref	195 (22.8%)	**0.002**	118 (27.8%)	**<0.001**
	<2 hours	2,045 (82%)		659 (77.2%)		307 (72.2%)	

Shown p-values are for chi-square tests comparing ethnicity head to head (with non-Māori non-Pasifika as the reference group) within each respective BMI category. For example, for BMI ≥40, Pasifika, compared to non-Māori non-Pasifika, had a significantly higher proportion of surgeries lasting greater than 2 or more hours (p <0.001).

and Pasifika ethnicities are consistently overrepresented in the higher risk groups (Table 5).

Discussion

Overall, in our cohort, Gram-negative SSI contributed significant morbidity accounting for 15% of all SSIs. In other studies Gram-negatives contribute between 9% and 43% of SSIs.[8–12] *Pseudomonas* spp. contributed 26% of Gram-negative infections, agreeing with previous literature (between 10% and 40%).[8–11]

New Zealand Index of Deprivation confers a modest but significant increase in risk for all-cause SSI (Table 2). However, the most deprived are at an eight-fold increase in risk of Gram-negative SSI. There is a paucity of high-quality evidence to accurately describe the effect of poverty on risk of SSI following orthopaedic infection, with conflicting studies that often use proxy measurements such as health insurance type.[18–21] Unfortunately, SSI has not been an outcome of interest in orthopaedic studies that purposefully measure income and poverty levels.[22,23] Although the New Zealand Index of Deprivation does not measure an individual's poverty level, it is a well-established and comprehensive measure of socioeconomic deprivation of the area in which people reside[13] and is considered a more meaningful representation of a person's socioeconomic environment than any single parameter, such as income.

The link between ethnicity and SSI risk could foreseeably be confounded by BMI, deprivation and co-morbidity. However, we found Pasifika ethnicity was an independent risk factor for Gram-negative SSI after controlling for these. Again, there is a paucity of high-quality evidence to link ethnicity to SSI, with past studies having conflicting outcomes in different settings.[18,21] DeKeyser et al have discussed the role of education level and genetics in SSI risk in an ethnically homogenous Utah study population.[20] Although genetic predisposition is possible, we consider modifiable factors to also be implicated, either at an environmental or systems level, and that health literacy may be a confounder not measured in the present study. Māori have a significantly higher crude rate of SSI compared to non-Māori and non-Pasifika (Table 1). However, Māori ethnicity was not an independent risk factor on multivariate analysis, suggesting that this is mediated through other known risk factors in the model. For example, 17% of Māori patients were smokers compared to 11% of Pasifika and 6% of non-Māori non-Pasifika (Table 5). Importantly, Māori and Pasifika are over-represented in the most deprived areas of New Zealand.[24] Social, cultural and economic factors are well established determinants of overall health in New Zealand,[25] but until now this has not been associated with SSI directly, which raises concern regarding equitable health outcomes following hip and knee arthroplasty. Duration of surgery has been acknowledged as an important SSI risk factor for orthopaedic surgery previously.[8,26,27] On sub-analysis (Table 4), it became clear that ethnicity and BMI were intertwined into procedure duration. Further research is needed to explain why, within a BMI group, certain ethnicities have longer surgeries.

Although large-scale health system reform and altering social deprivation are beyond the scope of quality improvement programmes, ensuring key performance measures are attained equally for all ethnicities is important from an equity perspective. This current study showed that, even after being controlled for BMI, a known confounder,[28,29] Māori and Pasifika were still more frequently underdosed cefazolin prophylaxis (a key process measure of the SSIIP).

Cefazolin prophylaxis is more frequently underdosed in obese patients.[29,30] A majority of Pasifika ethnicity (31%) in this cohort studied had a BMI of 40kg/m^2 or more. Targeting this highest BMI category for intervention, in which Pasifika and Māori are over-represented, could correct this modifiable risk factor.

Knowledge of the sites of staphylococcal colonization informs interventions such as intra-nasal decolonization and antiseptic skin washes in pre-operative and intensive care settings.[6,31] Gram-negative bacteria inhabit the lower gastrointestinal tract and occasionally the urinary system and the risk of inpatient colonization increases with disease severity and longer hospitalisation.[32,33] Aboltins et al suggested Gram-negative colonization or contamination of the skin around the hip and groin area cause Gram-negative SSI.[34] If this is true, antiseptic wipes included in interventions to reduce perioperative carriage of *S. aureus* may be helpful to reduce the risk of Gram-negative SSI.

Patients with multiple risk factors could be targeted for intensive care pathways[35] that include pre-operative conditioning for weight reduction, smoking cessation, medical optimisation, skin decolonization, rigid adherence to antibiotic surgical prophylaxis guidelines and culturally appropriate wound care instructions before and after the procedure.

Table 5: Risk factors for SSI by ethnicity.

		Non-Māori non-Pasifika	Māori	Pasifika
Meets criteria for SSI	No SSI	39,472 (99%)	4,657 (98.6%)	1,481 (98.9%)
	SSI	416 (1%)	64 (1.4%)	16 (1.1%)
	p-value	ref	**0.049**	**0.923**
BMI category (kg/m^2)	BMI<30	19,109 (53.3%)	1,266 (28.6%)	232 (16.8%)
	30≤BMI<35	9,085 (25.4%)	1,241 (28.1%)	324 (23.5%)
	35≤BMI<40	5,139 (14.3%)	1,058 (23.9%)	399 (28.9%)
	BMI≥40	2,493 (7%)	854 (19.3%)	425 (30.8%)
	p-value	ref	**<0.001**	**<0.001**
Duration of surgery	2 or more hours	5,469 (13.7%)	785 (16.6%)	339 (22.6%)
	<2hours	34,419 (86.3%)	3,936 (83.4%)	1,158 (77.4%)
	p-value	ref	**<0.001**	**<0.001**
Smoking status	Non-smoker	37,573 (94.2%)	3,918 (83%)	1,339 (89.4%)
	Smoker	2,315 (5.8%)	803 (17%)	158 (10.6%)
	p-value	ref	**<0.001**	**<0.001**
Diabetes	No	35,891 (90%)	3,875 (82.1%)	1,108 (74%)
	Yes	3,997 (10%)	846 (17.9%)	389 (26%)
	p-value	ref	**<0.001**	**<0.001**
NZ Index of Deprivation	1 (least deprived)	62,32 (15.7%)	246 (5.2%)	73 (4.9%)
	2	7,784 (19.6%)	455 (9.6%)	158 (10.6%)
	3	8,606 (21.6%)	694 (14.7%)	173 (11.6%)
	4	9,866 (24.8%)	1,216 (25.8%)	343 (23.1%)
	5 (most deprived)	7,326 (18.4%)	2,108 (44.7%)	741 (49.8%)
	p-value	ref	**<0.001**	**<0.001**

Table 5 (continued): Risk factors for SSI by ethnicity.

		Non-Māori non-Pasifika	Māori	Pasifika
ASA class	1	3,382 (8.6%)	362 (7.8%)	105 (7%)
	2	23,487 (59.8%)	2,625 (56.5%)	814 (54.6%)
	3 or more	12,391 (31.6%)	1,663 (35.8%)	571 (38.3%)
	p-value	ref	**<0.001**	**<0.001**
Type of SSI	Deep	175 (42.1%)	25 (39.1%)	6 (37.5%)
	Organ/space	98 (23.6%)	26 (40.6%)	4 (25.0%)
	Superficial	143 (34.4%)	13 (20.3%)	6 (37.5%)
	p-value	ref	**0.001**	**0.986**
Timing of antibiotic prophylaxis	On time	38,089 (97.5%)	4,480 (96.9%)	1,402 (96.6%)
	Not on time	970 (2.5%)	142 (3.1%)	49 (3.4%)
	p-value	ref	**0.016**	**0.033**
Dose of cefazolin prophylaxis	Appropriate	31,247 (95.7%)	3,748 (90.9%)	1,199 (86.8%)
	Under-dosed	1,394 (4.3%)	374 (9.1%)	183 (13.2%)
	p-value	ref	**<0.001**	**<0.001**

ref = reference.
Shown p-values are for chi-square tests comparing ethnicity head to head (with non-Māori non-Pasifika as the reference group) within each respective category. For example, Māori, compared to non-Māori non-Pasifika, had a significantly higher proportion of procedures performed on those with a diagnosis of diabetes ($p < 0.001$).

This study has a number of limitations. *Pseudomonas* SSI events were low in number and had to be grouped with the Enterobacterales. Glycaemic control, particularly in the post-operative period, may be more important than a mere diagnosis of diabetes alone.[36,37] We had not collected information on some well-described risk factors for SSI, preventing their inclusion for analysis (e.g., history of inflammatory arthropathy, malnutrition, choice of anticoagulation, intraoperative wound irrigation).[36] To the best of our knowledge, no study has analysed all known SSI risk factors. Future work needs to focus on systematic data collection of all known risk factors for SSI to accurately describe risk and measure impacts of interventions. Ideally this information needs to be collected prospectively and stored electronically to allow its extraction. While the dataset used in the current study is unique to New Zealand, particularly the relationship between ethnicity and socioeconomic status, the impact health inequity on risk of SSI is of relevance to other high-income countries. Temporal changes in data across the study period were outside the scope of this study, and indeed previous stewardship efforts by the SSIIP may already be addressing the risks identified (e.g., antibiotic timing and dose).[14,15] SSIs that did not require hospitalisation were not captured by the surveillance system, and therefore incidence, distribution and burden caused by Gram-negative organisms are all unknown. Additionally, individual surgeon procedure volume data were not available, and therefore its impact on SSI risk is unable to be quantified.

This study set out to understand current risk factors for SSI, particularly those modifiable by quality improvement interventions, with a novel focus on Gram-negative SSI. We found a number of risk factors for SSI following arthroplasty. However, not all of the risk factors identified are modifiable (e.g., age, male sex, revision arthroplasty, ASA class, social deprivation, duration of surgery). Smoking, BMI, time and dose of antibiotic prophylaxis were identified as modifiable risk factors. SSI improvement programmes must incentivise equitable health outcomes when monitoring adherence to key process measurements. Prevalence of risk factors is not uniform across all ethnicities. Therefore, modifiable risk factors (e.g., correct prophylaxis dosing in overweight patients) may be of increased importance to specific ethnicities. Lastly, SSIs of different etiologies also appear to have unique risk factors, and the usual pooled analysis approach may fail to recognise subtle relationships, therefore hampering the development of appropriate interventions that can be implemented within quality improvement programmes.

COMPETING INTERESTS
Nil.

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