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Wound closure and follow-up after total knee arthroplasty — Do they affect the rate of antibiotic prescription?

Mark Zhu [a,c,*], Richard Rahardja [a], Jacob Munro [c], Brendan Coleman [d], Simon W. Young [a,b]

[a] University of Auckland, Auckland, New Zealand
[b] Department of Orthopaedic Surgery, North Shore Hospital, Auckland, New Zealand
[c] Department of Orthopaedic Surgery, Auckland Hospital, Auckland, New Zealand
[d] Department of Orthopaedic Surgery, Middlemore Hospital, Auckland, New Zealand

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ABSTRACT

Background: This study aimed to evaluate risk factors for oral antibiotic prescription in the first six weeks after primary TKA, particularly whether the wound closure method (staples or sutures) and two-week follow-up clinician (surgeon or general practitioner (GP)) altered antibiotic use.
Methods: Four thousand eight hundred forty-six TKAs from January 2013 to December 2016 at three tertiary hospitals in Auckland, New Zealand were analysed by manual review of patient electronic records and a national prescription database. Surgeon preference dictates the method of wound closure and whether wound review is followed up by the operating surgeon or by the patient's GP.
Univariate and multivariate analysis was carried out to identify significant patient and surgical risk factors for oral antibiotic prescribing.
Results: Oral antibiotics were prescribed in 24% of patients following primary TKA. Twenty-six percent of patients closed with staples were prescribed oral antibiotics versus 19% with sutures (adjusted OR = 1.4, $p < 0.004$). Excluding re-presentations and readmissions, GPs prescribed oral antibiotics in 22% of patients compared to seven percent of patients seen by surgeons (adjusted OR = 2.8, $p < 0.001$). Other risk factors for antibiotic prescription included increasing age, BMI and ASA score.
Conclusion: Oral antibiotic prescribing rates are higher if the wound was closed with staples and if a GP performed the two-week follow-up. Improved communication between surgeons and GPs are required to ensure adequate follow-up following TKA and appropriate oral antibiotic use.

1. Introduction

The management of the surgical wound is a critical aspect of aftercare following total knee arthroplasty (TKA) [1–4]. Follow-up of patients during the first six weeks post-operation is a common practice to assess the extent of wound healing and detect superficial surgical site infections (SSIs) [5–7]. Oral antibiotics are often prescribed to treat SSIs. However, misdiagnosis of SSI is common and often leads to inappropriate prescription of oral antibiotics [4,8]. Inappropriate oral antibiotic use may mask an underlying early prosthetic joint infection, delaying the patient's definitive management and preventing the identification of the

* Corresponding author at: 59 Wheturangi Road, Greenlane, Auckland 1051, New Zealand.
E-mail address: mzhu031@aucklanduni.ac.nz. (M. Zhu).

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causative microorganism [9–11]. Furthermore, in the absence of superficial infection, the use of oral antibiotics increases the risk of adverse events, healthcare costs and contributes to the emergence of resistant bacteria [12,13].

The use of oral antibiotics following primary TKA and its associated risk factors has not been previously studied. The method of wound closure (staples or absorbable subcuticular sutures) and the type of clinician performing the wound check (general practitioners (GPs) or surgeon/specialist) are two surgeon-controlled factors that may influence the prescription of oral antibiotics. Wound closure with staples rather than subcuticular sutures can cause inflammation around the staple sites, which may be misinterpreted as a superficial infection and increase the rate of antibiotic prescription [14]. The follow-up clinician may also affect antibiotic prescription, as GPs are less experienced in evaluating surgical wounds and face more hurdles in admitting patients to hospital or performing further tests to confirm either superficial and deep infections [1,2,9,15–19].

This study aims to identify the rate of early oral antibiotic prescription following primary TKA, and to identify associations between oral antibiotic prescription and patient, surgical and follow-up variables such as wound closure method and follow-up clinician.

2. Methods

We reviewed 4846 primary TKAs performed between January 2013 and December 2016 at three tertiary referral hospitals in Auckland, New Zealand. Ethical approval for the study was granted by the Health and Disability Ethics Committees (HDEC) and the University of Auckland Human Participants Ethics Committee (UAHPEC). Revision TKAs were excluded from the study. Data was obtained through manual review of individual patient electronic records and was supplemented with data from the New Zealand Joint Registry (NZJR). Patients were identified through a unique National Health Index (NHI) and were cross-referenced between both primary data sets to ensure a complete capture of all primary TKAs. Patient demographic data included age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score [20] and history of previous surgery. Surgical data included mean skin to skin time in minutes, the use of prophylactic antibiotics and theatre space suits.

Antibiotic dispensing data was accessed through electronic patient records for 42 days after the date of surgery, including information from a local database (TestSafe) containing prescribing and dispensing records from >95% of all Auckland Pharmacies since 2012. After consultation with an infectious disease specialist, the type of antibiotic prescribed and the frequency of prescription were carefully analysed before excluding oral antibiotics typically used for non-skin infections, such as nitrofurantoin, trimethoprim, mupirocin, norfloxacin and roxithromycin (Appendix A).

Wound closure and follow-up methods were individually identified using operation notes and discharge summaries. At all three institutions, the preference of each individual surgeon determined whether staples or absorbable sutures were used for wound closure, and whether the patient was reviewed by their GP or the surgeon at the two-week follow-up wound check. However, variations occurred such as when patients had prolonged inpatient stays, patients who were planned for GP follow-up but represented to hospital, or patients planned for surgeon follow-up but first presented to their GP instead. Therefore, these patients were excluded when the two-week follow-up analysis was performed. They were included in all other analysis including skin closure method. Prosthetic joint infection (PJIs) were identified from manual review of all patients notes, supplemented with re-operation data for infection from the NZJR. In all cases, the patient electronic notes were reviewed by the senior authors to confirm PJI using the Musculoskeletal Infection Society criteria [15]. Superficial infections that re-presented to hospital were identified from available Surgical Site Infection Improvement Program (SSIIP) files and review of all patient electronic notes. This was defined using the Centre for Disease Control criteria [21,22] which states that a superficial SSI is an infection of the skin or subcutaneous tissue occurring within 30 days post-operation, and involving one of the following:

a) Purulent drainage from the superficial incision
b) Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision
c) At least one of the following signs or symptoms: pain or tenderness, localised swelling, redness or heat, and the superficial incision is deliberately opened by surgeon unless the incision is culture-negative
d) Diagnosis of superficial incisional SSI by the surgeon or attending physician

2.1. Statistical analysis

Continuous data were assessed for normality through visual analysis of the normality plots (Q–Q plot and histogram). To assess differences between groups (receiving vs. not receiving antibiotics prescription), Student *t*-test was performed for continuous variables while Chi-square test of independence or Fisher exact test was used for categorical variables. Furthermore, a multivariable analysis using binary logistic regression model was performed to identify factors independently associated with antibiotics prescription. Patient demographic factors, surgical factors, the method of wound closure and clinician seen at follow-up were entered into the model. Results were considered significant at $p < 0.05$. All statistical analyses were performed using IBM SPSS Statistics version 24.

3. Results

Four thousand eight hundred fifty-two primary TKAs were identified in 4205 patients (647 patients underwent bilateral TKA) between January 2013 and December 2016. Six TKAs were excluded as the patient died within two weeks of the indexed procedure. Analysis was performed on 4846 TKAs (Appendix B). The mean age of patients was 68.3 years (range = 9–96 years). The mean BMI was 32.3 kg/m^2 (range = 16–58 kg/m^2). Fifty-six percent of the patients were female. Fifty-three of the TKAs were performed on the patient's right knee (Table 1).

Oral antibiotics were prescribed in the first six weeks in 1139 out of 4846 primary TKAs (23.5% of patients). Of 100 patients who had simultaneous bilateral primary TKA, 19 were prescribed antibiotics in the first six weeks. These cases were treated as a single event.

3.1. Method of surgical wound closure

Three thousand one hundred forty-one (64.8%) TKA wounds were closed with staples and 1705 (35.2%) TKAs with absorbable subcuticular sutures (Table 2). Of patients closed with staples, 26.1% were prescribed oral antibiotics while only 18.8% of patients closed with sutures were prescribed oral antibiotics. This was a significant difference in both univariate (OR = 1.5, $p < 0.001$) and multivariate analysis (OR = 1.4, $p = 0.004$).

3.2. Clinician performing the two-week wound check

For the two-week wound check, 3856 patients (79.6%) were seen by their GP, 740 (15.3%) by their surgeons, and 250 (5.2%) were seen on re-presenting to orthopaedics after referral by either a GP or an emergency department physician, or remained in a hospital facility for greater than two weeks post-surgery (Table 2). Excluding re-presentations and readmissions, GPs prescribed oral antibiotics in 21.7% of patients compared to 7.3% of patients seen by surgeons ($p < 0.001$). Multivariate analysis revealed that a patient's odds of being prescribed antibiotics was almost three times higher if they saw their GP rather than their surgeon for follow-up (OR = 2.78, $p < 0.001$).

3.3. Combination of wound closure and follow-up

GPs were more likely to prescribe antibiotics regardless of whether the wound was closed by staples or sutures. In patients where staples were used for wound closure, the antibiotic prescription rate was 23.3% when they were seen by GPs compared to 10.5% when a surgeon conducted the two-week follow-up. If the wound was closed with absorbable sutures, 17.5% of patients were prescribed antibiotics by their GPs and 5.8% by their surgeons.

Table 1
Patient baseline demographics.

Demographic	Primary TKA
Number of TKA	*n = 4852*
Excluded	*n = 6*
n = 4846	
Hospital	
1. Hospital A	2203 (45%)
2. Hospital B	1100 (23%)
3. Hospital C	1543 (32%)
Age at surgery	
Mean (years)	68.3
Side	
1. Right	2548 (53%)
2. Left	2298 (47%)
Sex	
1. Male	2147 (44%)
2. Female	2699 (56%)
BMI	
Mean (kg/m^2)	32.3
1. Underweight (<18.50)	11 (0.2%)
2. Normal (18.5–24.99)	429 (9%)
3. Overweight (25–29.99)	1304 (27%)
4. Obese (30–39.99)	2340 (48%)
5. Morbidly obese (>39.99)	492 (10%)
NR	270 (6%)
ASA	
1	293 (6%)
2	3012 (62%)
3	1477 (30%)
4	24 (0.5%)
NR	40 (0.8%)
Patients who had previous surgery on same joint	
1. Yes	248 (5%)
2. No	4598 (95%)

Table 2
Surgeon risk factors.

Risk factor	Primary TKA
	$n = 4846$
Skin closure method	
1. Staples	3141 (65%)
2. Absorbable sutures	1705 (35%)
2 week follow-up	
1. GP	3856 (80%)
2. Surgeon	740 (15%)
3. Readmission/representation	250 (5%)
Skin to skin time	
Mean minutes	90.8
Space suit use	
1. Yes	2972 (61%)
2. No	1874 (39%)
Antibiotic prophylaxis	
1. Yes	4338 (90%)
2. No	11 (0.2%)
NR	497 (10%)
Time prophylaxis given	
1. More than one hour prior to incision	43 (0.9%)
2. Within one hour prior to incision	4041 (83%)
3. After incision	66 (1%)
4. On induction	64 (1%)
NR	632 (13%)

3.4. PJIs

Review of patient electronic notes found a total of 19 PJIs (0.4%). Nine occurred in patients closed with staples (0.3%) while the remaining 10 PJIs occurred in patients closed with sutures (0.6%). Eleven PJIs occurred in patients who were reviewed by their GP (0.3%), three occurred in patients reviewed by their surgeon (0.4%) and five in patients reviewed by both their GP and surgeon (two percent). These differences were not statistically significant. Due to the small event size of PJIs, multivariate analysis was not possible.

3.5. Superficial infections

One hundred sixty-one superficial infections were identified in our cohort using the Centre for Disease Control (CDC) criteria, giving an overall rate of 3.3%. One hundred thirteen patients who were seen by both the GP and surgeon were diagnosed with a superficial infection (45.2%). Thirty in the GP follow-up group (0.8%) were diagnosed with a superficial infection, of these, 23 (76.7%) were given antibiotics and seven were not prescribed antibiotics. Eighteen in the surgeon follow-up group (2.4%) were also diagnosed with a superficial infection, of these, 16 patients (88.9%) were prescribed antibiotics.

One hundred eleven superficial infections were identified in patients closed with staples (3.5%) and 50 in patients closed with sutures (2.9%). This difference was again not statistically significant ($p = 0.30$). No other risk factors were identified for superficial SSI.

3.6. Other factors

On univariate analysis, increasing age ($p = 0.045$), BMI ($p < 0.001$), ASA score ($p < 0.001$) and hospital C ($p < 0.001$) were associated with increased antibiotic prescription (Table 3). Sex, operative duration, history of previous surgery on same joint, theatre space suit use, use and timing of antibiotic prophylaxis did not affect antibiotic prescription rates. On multivariate analysis, only hospital C ($OR = 1.4$, $p = 0.016$) and an increasing ASA score ($OR = 5.7$, $p < 0.001$) were associated with antibiotic prescription (Table 4).

4. Discussion

In this study of 4846 patients undergoing TKA, method of wound closure and follow-up were two surgeon-controlled risk factors for a high rate of oral antibiotic prescription (23.5%). A similar rate was reported by Shantz et al., who in a randomised trial of 190 patients comparing staples to suture closure, found that 22% of patients “reported the use of antibiotics related to their index procedure” [23].

We found that patients closed with staples are more likely to be prescribed oral antibiotics compared to absorbable sutures ($OR = 1.35$, $p = 0.004$). However, a meta-analysis carried out by Krishnan et al. identified no differences in infection, inflammation, dehiscence or discharge in 13 studies comparing staples to sutures in wound closure following orthopaedic procedures [24]. Despite identifying an associated increase in oral antibiotic prescription, our study found no evidence that the use of staples

Table 3
Univariate analysis of patients' characteristics and antibiotic prescription.

Participants Characteristics	n	Antibiotics Prescription Given?		p value[a]	*Deep Infection*	p value[b]
		Yes	No			
All participants	4846	1139 (23.5%)	3707 (76.5%)	–	19 (0.4%)	–
Hospital						
Hospital A	2203	559 (25.4%)	1644 (74.6%)	<0.001**	4 (0.2%)	0.006
Hospital B	1100	176 (16%)	924 (84%)		10 (0.6%)	
Hospital C	1543	404 (26.1%)	1139 (73.8%)		5 (0.5%)	
Sex						
Female	2699	656 (24.3%)	2043 (75.7%)	0.140	8	0.254
Male	2147	483 (22.5%)	1664 (77.5%)		11	
Age (years)						
Mean ± SD	68.3 ± 9.5	68.8 ± 9.5	68.2 ± 9.6	0.045**	–	
BMI (kg/m^2)						
Mean ± SD	32.3 ± 6.0	32.9 ± 6.3	32.1 ± 5.9	<0.001**		
Underweight (<18.50)	11	1 (9.1%)	10 (90.9%)	0.0018	0	0.683
Normal (18.5–24.99)	429	99 (23.1%)	330 (76.9%)		2	
Overweight (25–29.99)	1304	277 (21.2%)	1027 (78.8%)		5	
Obese (30–39.99)	2340	571 (24.4%)	1769 (75.6%)		8	
Morbidly Obese (>39.99)	492	148 (30.1%)	344 (69.9%)		4	
Skin to skin time (minutes)						
Mean ± SD	91.0 ± 29.9	90.8 ± 31.4	91.1 ± 29.4	0.751	–	
ASA score						
1	293	37 (12.6%)	256 (87.4%)	<0.001**	1	0.046
2	3012	698 (23.2%)	2314 (76.8%)		6	
3	1477	387 (26.2%)	1090 (73.8%)		11	
4	24	11 (45.8%)	13 (54.2%)		0	
Previous surgery on same joint?						
Yes	248	61 (24.6%)	187 (75.4%)	0.677	1	>0.99
No	4598	1078 (23.4%)	3520 (76.6%)		18	
Space suit use						
Yes	2972	679 (23%)	2293 (77%)	0.174	9 (0.3%)	0.241
No	1874	460 (24.5%)	1414 (75.5%)		10 (0.6%)	
Antibiotic prophylaxis given?						
Yes	4338	1025 (23.6%)	3313 (76.4%)	0.728	19 (0.4%)	>0.99
No	11	3 (27%)	8 (73%)		0 (0%)	
Time prophylaxis given						
More than one hour prior to incision	43	13 (30.2%)	30 (69.8%)	0.225	2 (5%)	0.0002
Within one hour prior to incision	4041	954 (23.6%)	3087 (76.4%)		15 (0.4%)	
After incision	66	12 (18.1%)	54 (81.8%)		0 (0%)	
On induction	64	10 (15.6%)	54 (84.4%)		0 (0%)	
Skin closure method						
Staples	3141	819 (26.1%)	2322 (73.9%)	<0.001**	9 (0.3%)	0.147
Monocryl sutures	1705	320 (18.8%)	1385 (81.2%)		10 (0.6%)	
Clinician performing the wound check						
GP	3856	835 (21.7%)	3021 (78.3%)	<0.001**	11 (0.3%)	0.0001
Surgeon	740	54 (7.3%)	686 (92.7%)		3 (0.4%)	
Both	250	250			5 (2%)	
90 day deep infection						
Yes	19	7 (36.8%)	12 (63.2%)	0.169		
No	4827	1132 (23.5%)	3695 (76.5%)			
90 day superficial infection						
Yes	161	152 (94.4%)	9 (5.6%)	<0.001		
No	4685	987 (21.1%)	3698 (78.9%)			

ASA, American Society of Anesthesiologists; BMI, body mass index; SD, standard deviation.
[a] p value for antibiotic prescription given.
[b] p value for prosthetic joint infection.
** Association statistically significant: $p < 0.05$ Chi-square test of independence for categorical variables or Student *t*-tests for continuous data.

caused an increase in the incidence of superficial wound infections (OR = 1.21, p = 0.30). The main advantage for wound closure with staples is speed — multiple studies report staples shorten wound closure times [25–27], saving up to seven minutes per TKA case [23]. However, Singh et al., in an RCT comparing wound closure methods following hip arthroplasty, reported staple use costs the NHS £1,000,000 more than sutures after the cost of application, staple removal and increased number of dressing changes are taken into consideration [28]. Similarly, Eggers et al. reported that when taking into consideration a longer length of stay, staples result in a 33% increase in total costs due to greater post-operative care [25]. Staples are known to cause inflammation around the insertion points and more pain upon removal if they are not taken out at an appropriate time [29]. This may create doubt in the mind of clinicians and lead to an increased incidence of antibiotic prescription. As a result, it seems that the operative time saved with staple closure comes at the cost of poor antibiotic stewardship.

Table 4
Multivariate analysis: Independent predictors of antibiotic prescription.

	OR (95% C.I.)[a]	p value[a]
HospitalAA		
Hospital A	1.33 (1.00–1.78)	0.052
Hospital C	1.40 (1.07–1.83)	0.016**
Hospital B	Reference	
Age (years)	1.00 (0.99–1.01)	0.465
Sex		
Female	1.12 (0.96–1.31)	0.153
Male	Reference	
BMI (kg/m^2)	1.01 (0.99–1.02)	0.390
Skin closure method		
Staples	1.35 (1.10–1.67)	0.004**
Monocryl sutures	Reference	
ASA score		
1	Reference	
2	1.92 (1.28–2.88)	0.002**
3	2.10 (1.38–3.22)	0.001**
4	5.70 (2.05–15.82)	<0.001**
Clinician performing the wound check		
GP	2.78 (2.02–3.82)	<0.001**
Surgeon	Reference	

Multivariable analysis: All factors reported in the table were entered into the model.
Age and BMI added to the model as continuous variables.
[a] *p* value obtained from binary logistics regression; **statistically significant at $p < 0.05$.

The majority of patients in our study (79.6%) were instructed to see their GP for a two-week wound check, presumably aiming to limit demand on outpatient resources in the public hospital system. This seemed to be a major contributor to the high rate of oral antibiotic prescriptions in our study; GP's were three times more likely to prescribe oral antibiotics compared to surgeons (OR = 2.78, $p < 0.001$) in multivariate analysis. This difference persisted regardless of the method of skin closure. There are a number of potential reasons for this including the different practicing pressures faced by GPs and surgeons [17,19]. As they are less familiar with surgical wound assessment, GPs may be more likely to interpret expected wound 'inflammation' as infection [26]. They are also less confident in excluding the presence of superficial infection, and therefore more likely to practice defensively and prescribe antibiotics [30,31]. GPs also face more hurdles in admitting patients to hospital for IV antibiotics if superficial infection is diagnosed [9,19]. In a public health system, the lower antibiotic prescription rate with surgeon follow-up clinics will be balanced against the cost of lost clinic time and new patient assessments. Potential options may include improving communication avenues between GPs and surgeons in the event of any wound concerns or conducting patient follow-up in specialised nurse-led clinics with surgeon supervision.

Our study found that five percent of our patient cohort were prescribed antibiotics after either being readmitted to hospital or seen by both the GP and the surgeon. These are likely to be patients with persistent wound problems or high-risk patients who required multiple reviews. The incidence of both superficial infection (45.2%) and PJIs (2%) were high in this group. In a study by Schairer et al. who investigated the rates and causes of readmission following TKA, the 30-day readmission rate was 3.4% and the 90-day readmission rate was 6% following primary TKA, comparable to our series [32].

A number of patient factors were linked to the prescription of oral antibiotics. These include increasing age, BMI, and ASA score. These are known risk factors for superficial wound infection and PJI, therefore an increased antibiotic prescription may be expected [33–37]. Interestingly, patients of hospital C were also more likely to be prescribed oral antibiotics compared to hospitals A and B (OR = 1.4, p = 0.016). Hospital C's catchment region includes a large number of lower socioeconomic areas and the higher prescription rate here may be influenced by differing population characteristics, patient co-morbidities and clinician expectations.

In our study, 3.3% of patients were diagnosed with a superficial SSI as defined by the CDC criteria. This is comparable to a study by Carroll et al. who also used CDC criteria to identify a superficial SSI rate of 4.4% in 964 patients following knee or hip arthroplasty [6]. Regardless, the superficial SSI rate is considerably lower than the rate of antibiotic prescription (23.5%). This is likely due to two main reasons. Firstly, it is well known that superficial SSIs are notoriously difficult to diagnose [4,33], [38–40]. In our study, this was diagnosed and recorded with a combination of prospective SSIIP data and retrospective review of hospital electronic notes. This method may cause inaccuracies and is a limitation of the study. Secondly, the prescription of oral antibiotics should only occur when a superficial SSI is diagnosed. The large discrepancy (>20%) between the rate of antibiotic prescription and superficial infection as determined by the CDC criteria indicates that a large number of patients were prescribed antibiotics unnecessarily.

In the presence of PJI, premature use of oral antibiotics may cause delays in identification of the causative organism and correct treatment [4]. Inappropriate antibiotic prescription also contributes to the development of antibiotic resistant organisms. Anderson et al. reported a doubling in the prevalence of Methicillin-resistant Staphylococcus aureus (MRSA) infections from 2000 to 2005 [41]. Similarly, Gorwitz et al. reported an increase in MRSA colonisation from 0.8% to 1.5% in the period 2001–2004 [42], and Siddiqui et al. reported that 44% of their early infections in 2013 were caused by MRSA [43]. Multiple studies have reported similar trends [40,44–49]. Furthermore, treatment cost of PJIs due to resistant organisms is over $30,000 more per case when compared to those caused by sensitive pathogens [50]. Overall, it is increasingly important to reduce the unnecessary use of oral antibiotics following TKA.

The main limitation of our study is the lack of access to GP records. As a result, we were unable to definitively identify the reasoning behind each antibiotic prescription. To mitigate this, we reviewed the laboratory records of all patients with an antibiotic prescription in the post-operative period to exclude all who were suspected of having a different focus of infection. Furthermore, an infectious disease specialist analysed all antibiotic prescriptions and after careful consideration of the type and frequency of each antibiotic, five oral antibiotics were excluded (nitrofurantoin, trimethoprim, mupirocin, norfloxacin and roxithromycin) (Appendix A). These antibiotics are rarely used for skin infections and only accounted for five percent of the total antibiotic prescriptions identified. Overall, the antibiotic prescription rate in our study is similar to those found by Shantz, where only wound related antibiotic use was recorded [23].

5. Conclusion

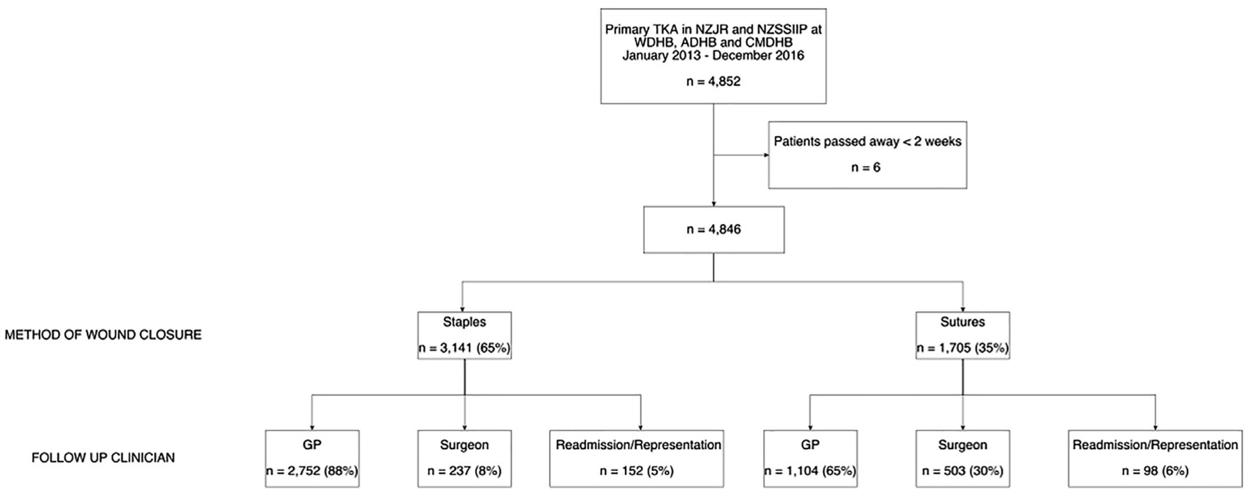
Almost one quarter of patients were prescribed oral antibiotics in the first six weeks following primary TKA. Wound closure method did not influence the rate of superficial SSI but was a risk factor for inappropriate antibiotic prescription. GPs were associated with higher rates of prescribing. Wound checks should be performed by the operating surgeon.

Appendix A. List of antibiotics

Type of antibiotic	Total number of Rx	Percent
Amoxicillin/Augmentin	437	37%
Flucloxacillin	412	35%
Cefaclor	99	8%
Cephalexin	81	7%
Erythromycin Ethylsuccinate	44	4%
Co-Trimoxazole	25	2%
Doxycycline	20	2%
Ciprofloxacin	10	1%
Clindamycin	6	1%
Phenoxymethylpenicillin	5	<1%
Norfloxacin[a]	14	1%
Trimethoprim[a]	13	1%
Roxithromycin[a]	9	1%
Nitrofurantoin[a]	6	1%
Mupirocin[a]	*1*	<1%
	1182	

[a] Bolded antibiotics were excluded from analysis.

Appendix B. Method flow chart



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