The use of antibiotic-loaded bone cement and systemic antibiotic prophylactic use in 2,971,357 primary total knee arthroplasties from 2010 to 2020: an international register-based observational study among countries in Africa, Europe, North America, and Oceania

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Background and purpose — Antibiotic-loaded bone cement (ALBC) and systemic antibiotic prophylaxis (SAP) have been used to reduce periprosthetic joint infection (PJI) rates. We investigated the use of ALBC and SAP in primary total knee arthroplasty (TKA).

Patients and methods — This observational study is based on 2,971,357 primary TKAs reported in 2010–2020 to national/regional joint arthroplasty registries in Australia, Denmark, Finland, Germany, Italy, the Netherlands, New Zealand, Norway, Romania, South Africa, Sweden, Switzerland, the

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UK, and the USA. Aggregate-level data on trends and types of bone cement, antibiotic agents, and doses and duration of SAP used was extracted from participating registries.

Results — ALBC was used in 77% of the TKAs with variation ranging from 100% in Norway to 31% in the USA. Palacos R+G was the most common (62%) ALBC type used. The primary antibiotic used in ALBC was gentamicin (94%). Use of ALBC in combination with SAP was common practice (77%). Cefazolin was the most common (32%) SAP agent. The doses and duration of SAP used varied from one single preoperative dosage as standard practice in Bolzano, Italy (98%) to 1-day 4 doses in Norway (83% of the 40,709 TKAs reported to the Norwegian arthroplasty register).

Conclusion — The proportion of ALBC usage in primary TKA varies internationally, with gentamicin being the most common antibiotic. ALBC in combination with SAP was common practice, with cefazolin the most common SAP agent. The type of ALBC and type, dose, and duration of SAP varied among participating countries.

Periprosthetic joint infection (PJI) is a serious complication following joint arthroplasty leading to longer hospital stay, increased risk of readmission, poor patient outcomes and increased cost burden [1,2]. It is a frequent cause of revision after total knee arthroplasty (TKA) and its incidence has increased over the last 2 decades [3,4].

In an attempt to reduce the risk of PJI, antibiotic-loaded bone cement (ALBC) has been used since it was introduced by Bucholz and Engelbrecht in 1970 [1,5,6]. Debate persists regarding the use of ALBC, its efficacy in reducing revision due to PJI, and whether the effect varies with cement type (brand) and viscosity [7,8].

Similarly, the use of systemic antibiotic prophylaxis (SAP) is acknowledged as an important part of mitigating PJI [9-11]. However, there is a lack of consensus in practice guidelines on the type of systemic antibiotic, dose (single dose or multiple doses) and duration (0–24, 24–48, or > 48 hours) of SAP internationally [10-12].

We aimed to investigate the use of ALBC and SAP use in primary TKA internationally. Specifically, we investigated the trends in use in the period between 2010 and 2020. The type (brand), viscosity of bone cement, and antibiotics in the cement were investigated for ALBC, and the type of antibiotic agent, dose, and duration for SAP.

Patients and methods

Participating registries

This is an international register-based observational descriptive study reported according to STROBE guidelines [13]. Primary cemented or hybrid TKAs for osteoarthritis (OA) reported to 16 national and regional arthroplasty registries in 14 countries across 4 continents between 2010 and 2020 were included (Table 1).

Brief history of participating registries

We invited all registry members of the International Society of Arthroplasty Registries (ISAR) to participate in this study and 16 regional/national arthroplasty registries were willing and able to participate. The majority of registries have high coverage and completeness (≥ 95%) of reporting primary TKAs and almost all publish annual reports on their websites providing extensive information on demographics, surgical techniques, and quality measures (Table 2).

Table 1. List of abbreviations used in the text, figures and tables

Abbreviation	Register	Website
AJRR	American Joint Replacement Registry	https://www.aaos.org/registries
AOANJRR	Australian Orthopaedic Association National Joint Replacement Registry	https://aoanjrr.sahmri.com/
DKR	Danish Knee Arthroplasty Registry	Dansk Knæalloplastikregister - Sundhed.dk
EPRD	German Arthroplasty Registry	https://www.eprd.de/
FAR	Finnish Arthroplasty Register	www.thl.fi/far
JointCare	JointCare Registry (South Africa)	https://www.joint-care.co.za
KP	Kaiser Permanente Total Joint Replacement Registry (USA)	https://national-implantregistries.kaiserpermanente.org/
LROI	Dutch Arthroplasty Register	www.lroi-report.nl
NAR	Norwegian Arthroplasty Register	https://helse-bergen.no/nrl
NJR	National Joint Registry (UK)	https://www.njrcentre.org.uk/
NZJR	New Zealand Joint Registry	https://www.nzoa.org.nz/nzoa-joint-registry
PABZ	Bolzano provincial register of knee prostheses (Italy)	www.provinz.bz.it/health-lifestyle/healthmonitoring/provincial-arthroplasty-register.asp
PATN	Trento provincial register of knee prostheses (Italy)	https://riap.iss.it/riap/it/il-progetto/chi-partecipa/provincia-autonoma-di-trento/
RAR	Romanian Arthroplasty Register	http://www.rne.ro/
SAR	The Swedish Arthroplasty Register	https://sar.registercentrum.se/
SIRIS	Swiss National Hip & Knee Joint Registry	https://www.siris-implant.ch/

Table 2. Chronology and completeness/coverage rate of 16 participating joint registries from 2010–2020

Registry	Established	Reported primary TKA with OA (2010–2020)	Coverage [a] (%)	Completeness [b] (%)	Completeness [b] Year	Publish annual report
SAR	1975	136,009	100	96–98	2010–2020	Yes
FAR	1980	94,803	100	98	2003–2020	Yes
NAR [c]	1987	47,584	100	97	2008–2020	Yes
DKR	1997	78,948	100	97	2020	Yes
NZJR	1998	77,305	100	> 95	2022	Yes
AOANJRR	1999	527,566	100	99	2022	Yes
KP	2001	145,078	100	> 90	2021	Yes
RAR	2001	33,105	99	98	2021	Biannual
NJR	2002	900,715	94	> 95	2022	Yes
LROI	2007	241,306	100	95–99	2021	Yes
AJRR [d]	2009	952,162	na	na	na	Yes
EPRD [e]	2010	269,968	na	na	na	Yes
PABZ	2010	5,901	100	100	2011–2020	Every 2–3 years
JointCare [f]	2012	1,308	12	16	2016–2020	No
SIRIS	2012	115,803	100	> 98	2020	Yes
PATN	2016	3,167	100	95	2016–2020	Every 2–3 years

na = not available.
[a] Coverage refers to the proportion (%) of hospitals/departments contributing to registration in the national/regional register out of the total number of hospitals/departments performing knee procedures in the country/region.
[b] Completeness refers to the proportion (%) of knee operations registered in the register out of the total number performed in the country/region.
[c] NAR established with registration of hip arthroplasty in 1987, but started registration of knee and other joint arthroplasties in 1994.
[d] AJRR does not have data on coverage or completeness due to the lack of centralized healthcare and market structure. NB: Data reported from AJRR (USA) does not include that of KP (USA) data.
[e] Registry was started in 2010 and enrolment started (November) 2012. Since 2019 national completeness is > 70 %.
[f] JointCare established as an organization in 2012, but the registry started in 2015. There is no mandatory reporting of arthroplasties in South Africa. Coverage and completeness are best estimates. JointCare comprises a network of surgeons in private practice and coverage is restricted to primary surgeries. The JointCare captures revisions only when reported by a patient in follow-up correspondence. The operative data pertaining to the revision surgery itself is not captured.

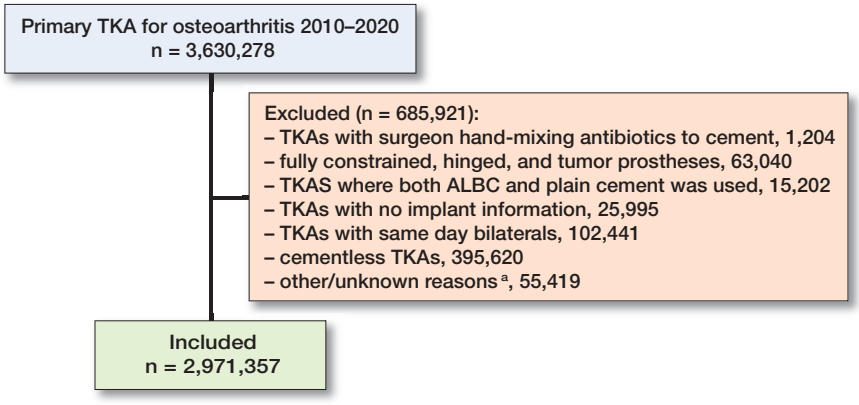

Figure 1. Inclusion and exclusion criteria. [a] Excluded TKAs with insufficient data to determine whether inclusion criteria are met.

Inclusion and exclusion criteria

To ensure a homogeneous study population, we included only cemented (both fully and hybrid) TKAs in patients with OA as the underlying diagnosis. Tumor prostheses (segmental), hinged, fully constrained prostheses, as well as same-day bilateral primary TKA procedures were excluded (Figure 1).

Data extraction

We used a distributed health data network that does not require centralized data storage of individual patient-level data [14]. The NAR was the coordinating center, and, in collaboration with KP, created and sent a data-sharing template to each participating registry for reporting of aggregate information for specifically defined data elements. Each participating registry identified the eligible study sample from their dataset and reported information on patient characteristics (age, sex, BMI, and ASA class), surgical and implant characteristics, ALBC attributes, and SAP using the data-sharing template provided, which was then sent back to the NAR to compile.

Statistics

Descriptive statistics, including frequencies and proportions, were used. Demographic and surgical data on sex, age, ASA classification, BMI, type of fixation, patella usage, type of bone cement brands, year of procedure, cement viscosity and type of antibiotics in the cement, and the choice of SAP agent, the dose (single dose vs. multiple doses) and the duration (0–24, 24–48, > 48 hours) of SAP were described.

Ethics, data sharing, funding, and disclosures

NAR was the initiator and coordinating center for this study. Thus, ethical approval of the study was obtained primarily from the Regional Committee for Research Ethics in Western Norway (REK Vest) (registration number 2021/319783/REK Vest, dated November 24, 2021). In addition, ethical approval was obtained through the ethical approval process of each registry. During this study, the corresponding author (THL) received a postdoctoral grant from the Western Norway Regional Health Authority. No external funding was received in support of this work. Thus, each participating reg-

Table 3. Summary of the number and types of bone cement (ALBC vs. plain) used in primary TKA recorded in each registry (2010–2020)

Register	Number of primary TKA	Type of cement ALBC n (row %)	Type of cement Plain n (row %)
Group 1 (ALBC used in > 50% of TKAs)			
NJR	815,768	810,644 (99)	5,124 (0.6)
AOANJRR	414,534	393,897 (95)	20,637 (5.0)
LROI	198,764	195,155 (98)	3,609 (1.8)
EPRD	141,936	139,673 (98)	2,263 (1.6)
SAR	123,129	123,088 (100)	41 (0.04)
SIRIS	93,463	91,784 (98)	1,679 (1.8)
FAR	83,469	83,395 (100)	74 (0.1)
NZJR	73,744	60,173 (82)	13,571 (18)
DKR	49,377	37,442 (76)	11,935 (24)
NAR	40,709	40,709 (100)	0 (0)
RAR	30,816	17,818 (58)	12,998 (42)
PABZ	4,544	4,540 (100)	4 (0.1)
PANT	1,150	970 (84)	180 (16)
JointCare	839	829 (99)	10 (1.2)
Group 2 (ALBC used in ≤ 50% of TKAs)			
AJRR	775,697	241,866 (31)	533,831 (69)
KP	123,418	51,463 (42)	71,955 (58)
Total	2,971,357	2,293,446 (77)	677,911 (23)

istry used its own resource. All authors declare no conflicts of interest. Completed disclosure forms for this article following the ICMJE template are available on the article page, doi: 10.2340/17453674.2023.17737

Results

We included 2,971,357 cemented or hybrid primary TKAs (Figure 1). 77% (n = 2,293,446) of TKAs were performed with ALBC (Table 3). There was wide variation in ALBC usage among participating countries ranging from 100% use in NAR (Norway) to 31% in AJRR (USA) (Table 3). Most of the TKAs with ALBC were performed on female patients, aged 65–74 years, and were fully cemented. The majority of participating registries reported information on ASA class (11 of 16 registries) and BMI (12 of 16 registries), and they reported that most of the TKAs with ALBC were performed on pre-obese or obese class I patients and on those with ASA class II (Table 4, see Appendix). Detailed demographic and surgical-related characteristics are presented in Tables 5–7 (see Supplementary data).

Trends in ALBC usage

ALBC usage in primary TKA increased slightly over time internationally with pooled data from 14 of the 16 registries with ALBC use in > 50% of primary TKAs (Figure 2 left panel), but a declining trend was observed since 2016 with pooled data from registries with ALBC use in < 50% of primary TKAs (Table 3) (Figure 2 right panel). Country-wise, we also observed an increased proportion of ALBC use in primary TKA in most countries over time, particularly in DKR (Denmark), NZJR (New Zealand), RAR (Romania), and KP (USA) except for the year 2020, while a decline was observed in PATN (Italy) and AJRR (USA) (Figure 3).

Type of ALBC used

15 of the16 registries, excepting the AJRR (n = 241,866), provided detailed information on the type of ALBC used in TKAs. Various types of bone cement were used in the different countries. Palacos R+G (Heraeus Medical, Wehrheim, Germany) was the most common (62%) ALBC type reported followed by Refobacin Bone Cement R (Zimmer Biomet, Warsaw, IN, USA) (18%), Simplex with Tobramycin (Stryker, Kalamazoo, MI, USA) (5%), CMW 2 G (DePuy, Warsaw, IN, USA) (4%), Palacos MV+G (Heraeus Medical) (3%), and SmartSet GHV (DePuy) (3%). The majority of ALBC used was high viscosity (92%) and contained gentamicin (94%) or tobramycin (5%) (Table 8, see Appendix).

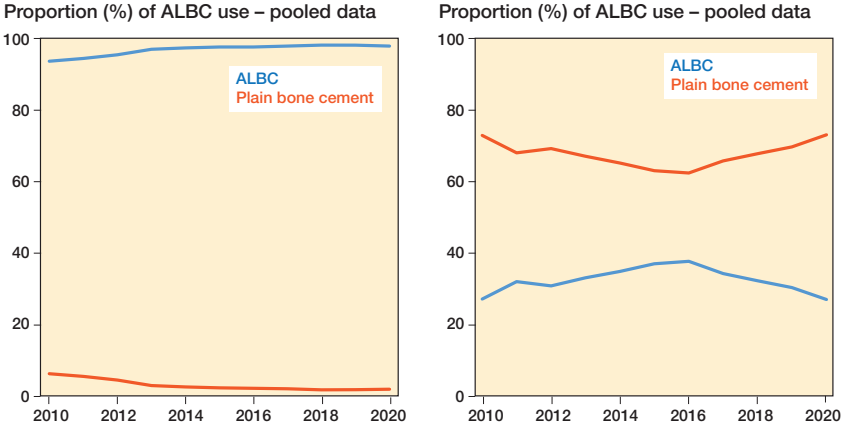

Figure 2. Trends in ALBC vs. plain bone cement used from 2010–2020. Left panel: pooled data from 14 of 16 participating registries with > 50% ALBC use in primary TKAs (2010–2020), see Table 3. Right panel: pooled data from 2 of 16 participating registries with < 50% ALBC use in primary TKAs (2010–2020)

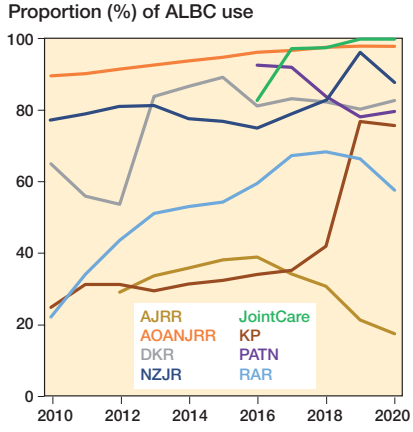

Figure 3. Trends in ALBC usage in primary TKA among 8 of 16 registries that reported ≤ 90% usage of ALBC in primary TKA for at least 1 year in the period 2010–2020.

Table 9. Number and percentage of SAP used as reported by 9 of 16 participating registries. Values are count and row %

Registry	TKAs	SAP and ALBC	No SAP but ALBC	SAP and plain cement	No SAP and plain cement
KP [a]	123,418	43,226 (35)	8,237 (6.7)	63,824 (52)	8,131 (6.6)
SAR	123,129	123,082 (100)	6 (0.0)	41(0.0)	
FAR	83,469	83,281 (100)	114 (0.1)	74 (0.1)	
NZJR	73,744	57,794 (78)	2,379 (3.2)	12,568 (17)	1,003 (1.4)
DKR	49,377	37,422 (76)	20 (0.0)	11,915 (24)	20 (0.0)
NAR	40,709	40,709 (100)			
RAR	30,816	17,499 (57)	319 (1.0)	12,833 (42)	165 (0.5)
PABZ	4,544	4,429 (98)	111 (2.4)	4 (0.1)	
JointCare	839	734 (88)	95 (11)	9 (1.1)	1 (0.1)
Total	530,045	408,170 (77)	11,281 (2.1)	101,268 (19)	9,320 (1.8)

[a] KP does not prospectively capture the specific information on SAP that was needed for the study. Instead, KP retrospectively retrieved the information from its integrated electronic health record specifically for this study.

Table 11. Duration/dose of SAP used in primary TKA as reported by 5 of 16 participating registries (n = 341,177 TKAs). Values are count (%)

Factor	DKR	KP	NAR	PABZ	SAR
Primary TKAs	49,377	123,418	40,709	4,544	123,129
TKAs with no SAP	40 (0.1)	16,368 (13)	0	111 (2.4)	6 (0.0)
Duration/dose					
1 day 1 dose [a]	3,858 (7.8)	30,971 (25)	1,831 (4.3)	4,433 (98)	788 (0.6)
1 day 2 doses		60,877 (50)	1,412 (3.5)		3,681 (3.0)
1 day 3 doses		7,098 (5.8)	2,060 (5.1)		97,251(79)
1 day 4 doses		2,065 (1.7)	33,597 (83)		17,874 (15)
1 day > 1 dose	29,961 (62)				
2 days		5,386 (4.4)			959 (0.8)
2 days or more	544 (1.1)				
3 days		223 (0.2)			354 (0.3)
Others [b]		416 (0.3)			391 (0.3)
Unknown	14,974 (30)	14 (0.0)	1,809 (4.4)		1,825 (1.6)

[a] Preoperatively
[b] Includes 1-day ≥ 5 doses; SAP administered over ≥ 4 days.

SAP usage

9 of 16 registries reported information on SAP use, representing 18% (530,045 of 2,971,357) of the total number of TKAs included in this study. The other registries reported that SAP use is mandatory in their respective country, but they did not record data on SAP use. 98% (517,890 of 530,045) of primary TKAs recorded in these 9 registries used SAP although there was a slight variation among reporting countries with 100% usage in NAR (Norway) to 87% in KP (USA). 2% (9,320 of 530,045) of TKA procedures were reported with plain cement and no SAP (Table 9).

The use of ALBC in combination with SAP was a common practice in all countries recording SAP data. Of all reported primary TKA procedures performed in these countries, 77% used ALBC in combination with SAP, but the proportion varied from 100% in NAR (Norway) to 35% in the KP (USA) (Table 9).

Type, dose, and duration of SAP used

Over 50 different single SAP agents were reported. Cefazolin was the most common (32%) SAP agent used in primary TKA procedures followed by cefuroxime (27%), cloxacillin (22%), cefalotin (5%), clindamycin (4%), and vancomycin (3%) (Table 10, see Appendix). Country-wise, cefazolin was the most commonly used SAP in NZJR (New Zealand) (84%) and KP (USA) (77%), whereas cefuroxime was common in DKR (Denmark) (61%) and PABZ (Italy) (40%), cloxacillin in SAR (Sweden) (91%) and cefalotin in NAR (Norway) (70%). 5 of the 9 registries recording information on SAP use included detailed information on the dose and duration of SAP used (Table 11).

Discussion

ALBC

ALBC use is standard practice in the Scandinavian countries [1] but in other European countries and North America, the use of ALBC in primary joint arthroplasty is still variable [1,15].

In the present study, we observed that the trend for ALBC use in primary TKA is increasing over a 10-year span, with the exception of AJRR (USA). The proportion and type of ALBC used varies among countries, e.g., the AJRR (USA) (31%), had the lowest use of ALBC compared with NAR (Norway), which reported 100% use. Similar to the present study, 1 earlier study on primary TKA also reported lower utilization rates (27%) of ALBC in the USA in the period 2006–2016 [15]. The potential explanations for such variation in practice could be the lack of international consensus and the absence of high-quality evidence supporting prophylactic use of ALBC in primary TKA [7,8].

Furthermore, we observed a variation in viscosity and type of antibiotic in the ALBC used in primary TKA among countries. This could be attributed to lack of clear evidence on the impact on revision rates of bone cement brand, level of viscosity, and dose and type of antibiotics in cement. A previous study from the NAR (Norway) on hip arthroplasty has reported that the low viscosity CMW3 (DePuy) as well as the high viscosity CMW1 (DePuy) [16] were associated with higher failure rates in hip replacement. In contrast, a study on knee arthroplasty from KP (USA) reported a lower risk for all causes of revision with the use of Simplex medium-viscosity cement compared

with Palacos high-viscosity cement, although no difference was observed in revision for aseptic loosening [17].

In our study, over 90% of bone cements reported contained gentamicin, although no large randomized controlled trial (RCT) on the prophylactic effect of gentamicin-loaded bone cement is available. Zhang et al. [18] in their meta-analysis found that ALBC containing gentamicin reduced deep infection rates, but no difference was found between cefuroxime-loaded cement and bone cement without antibiotics. Further, a large RCT (n = 2,948) from Spain reported that the use of ALBC with erythromycin and colistin-loaded Simplex cement in TKA did not reduce the incidence of infection [19].

SAP

9 of 16 participating registries reported the use of ALBC in combination with SAP as common practice, representing 13% of total TKAs included in our study. However, the type of antibiotic agent used, duration, and doses varied among countries. A possible explanation could be attributed to lack of consensus guidelines and/or a disparate range of recommendations for SAP use in total joint arthroplasties [20]. Further, the observed variation in choice of SAP could also be attributed to regional differences in the most prevalent pathogens, including risk of Clostridium difficile infection and resistance patterns and thereby different SAP is recommended [21]. In our study, the first-generation cephalosporin cefazolin was the most common (32%) SAP agent used in primary TKA followed by the second-generation cephalosporin cefuroxime (27%). In line with our findings, a recent international survey study on guidelines for SAP use reported that 10 of 17 (59%) guidelines from arthroplasty societies suggested first-generation cephalosporin as the SAP agent of choice [20].

In our study, we observed a variation regarding the dose/duration of SAP used among participating countries ranging from 1-day 1 dose (preoperative) as standard practice in Bolzano, Italy to 1-day 4 doses in Norway. In 2017, however, the Centers for Disease Control and Prevention released a guideline for the prevention of surgical site infection and recommended a single dose of perioperative antibiotic prophylactic without subsequent postoperative dosing [22] and this recommendation was based on first- and second-generation cephalosporins [22]. An earlier register-based study on hip arthroplasty from Norway reported that patients who received a 1-day 1, 2, or 3 doses SAP had a 3–7 times higher rate of revision due to infection than those with 1-day 4 doses SAP [23]. Thus, a multiple-dose (4 times in a single day) regime is currently standard practice in Norway. Conversely, a recent cohort study from the Dutch Arthroplasty Register found a similar risk of revision for infection following primary hip and knee arthroplasty with single- versus multiple-dose of SAP [12]. Similarly, a systematic review and meta-analysis was also unable to demonstrate the efficacy of postoperative SAP in reducing the rate of PJI [9].

Strengths and limitations

The strength of this study is that it is the first large international multi-register-based observational study describing current practice in the use of ALBC and SAP in primary TKA incorporating 16 national/regional registries over 4 continents. Collaborations among national/regional registries provide added opportunities to increase/improve generalizability of the findings and to examine variation in clinical practices and outcomes between countries [24]. Due to privacy, security, and data ownership regulation, many registries cannot share even de-identified patient-level data, although pooled analysis of individual patient data is an ideal approach [25]. However, our study managed challenges in data sharing among multiple registries with a decentralized data warehouse where each participating register shared aggregate-level data, leading to an unprecedented collaboration among 16 arthroplasty registries located in 14 different countries.

Our study has some limitations. Conclusions regarding international trends in ALBC and SAP use are limited, as the data obtained is restricted to registries that are members of ISAR. These registries may not be representative of global trends given geographical regions' over-representation of registries from Europe and no/under-representation of registries from North America, Africa, Asia, and Latin America. Nevertheless, we believe that the data from these participating registries offers a relevant description of ALBC and/or SAP utilization trends globally. Second, the data presented herein relies on accurate coding of implants' information and is subject to reporting error. The majority of participating registries reported high completeness (> 95%) for primary joint arthroplasty, which shows that they undergo a rigorous process of internal auditing to ensure the accuracy of the collected data. Third, there may be variation in how data regarding bone cements is recorded; registries use either barcode notes, scanning of implants' product numbers, or just text from the surgeons. Standardization of the collection of cement information from the adhesive labels with product numbers should be recommended for all registries. Fourth, only 9 of 16 participated registries recorded information on the use of SAP and type of antibiotic, and of these, only 5 recorded further information on dosage and duration of SAP. Lack of guidelines for SAP for total joint arthroplasty or consistency in their advice among arthroplasty societies was also reported [20]. Thus, recording data on the use, type of antibiotic, dosage, and duration of SAP used is recommended. We think that by doing this, registries can easily determine whether guidelines/recommendations (if existing) are actually being followed.

Conclusion

The proportion of ALBC usage in primary TKA is increasing, but varies internationally over time, with gentamicin being the most commonly included antibiotic. Use of ALBC in combination with SAP was common practice in those registries that collected these data with the 1st generation cephalospo-

rin cefazolin being the most common SAP agent. The type of ALBC and type and dose/duration of SAP used also varies internationally and needs national/regional consensus in practice guidelines based on high-quality evidence. As this is a descriptive study, caution needs to be taken when generalizing the findings beyond the participating countries.

Perspective

We believe that the present study contributes important knowledge on the debate concerning antibiotic use and could be a basis for future international studies, such as RCTs, to answer the question regarding the effectiveness of ALBC or different SAP treatments. Thus, further clinical studies to investigate and compare the efficacy of routine use of ALBC and SAP in primary TKA in preventing PJI are recommended.

Supplementary data

Tables 5–7 are available on the article page, doi: 10.2340/17453674.2023.17737

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Appendix

Table 4. Demographic characteristics of primary TKA with ALBC by registry

Variable	AJRR	AOANJRR	DKR	EPRD	FAR	JointCare	KP	LROI	NAR
TKA with ALBC	241,866	393,897	37,442	139,673	83,395	829	51,463	195,155	40,709
Female sex [a]	145,418 (60)	226,436 (58)	23,259 (62)	92,275 (66)	54,187 (65)	551 (67)	31,270 (61)	125,841 (65)	25,242 (62)
Age group [b]									
< 55	21,259 (8.8)	23,406 (5.9)	2565 (6.8)	10,013 (7.2)	5,318 (6.4)	67 (8.1)	3,323 (6.5)	12,502 (6.4)	5,599 (14)
55–64	70,351 (29)	100,317 (26)	7,940 (21)	33,797 (24)	20,946 (25)	249 (30)	15,160 (30)	48,770 (25)	8,038 (20
65–74	96,199 (40)	160,880 (41)	15,235 (41)	46,879 (34)	31,885 (38)	327 (39)	21,323 (41)	79,073 (41)	15,194 (37)
≥ 75	54,057 (22)	109,294 (28)	11,702 (31)	48,984 (35)	25,246 (30)	186 (22)	11,658 (23)	54,649 (28)	11,878 (29)
ASA class	na		na			na			
I		15,606 (4.0)		2,056 (1.5)	3,370 (4.0)		655 (1.3)	28,422 (15)	3,737 (9.2)
II		162,375 (41)		7,898 (5.6)	25,392 (30)		30,790 (60)	131,168 (67)	27,457 (67)
III		121,261 (31)		4,493 (3.2)	19,704 (24)		18,677 (36)	34,310 (18)	8,539 (21)
IV–V		3,493 (1.0)		75 (0.1)	473 (0.6)		305 (0.6)	449 (0.2)	71 (0.2)
Missing		91,162 (23)		125,208 (90)	34456 (41)		1,036 (2.0)	806 (0.4)	905 (2.2)
BMI category [c]									na
Underweight	270 (0.3)	441 (0.2)	105 (0.3)	175 (0.1)	48 (0.1)	4 (0.5)	77 (0.1)	195 (0.1)	
Normal	8,871 (9.8)	24,479 (10)	6,374 (17)	12,610 (9.0)	6,317 (7.6)	95 (12)	5,736 (11.1)	22,222 (11.4)	
Pre-obese	24,250 (27)	72,070 (31)	12,691 (34)	31,072 (22)	17,444 (21)	219 (26)	16,039 (31)	57,431 (29)	
Obese class 1	26,212 (29)	71,974 (31)	8,309 (22)	26,413 (19)	14,740 (18)	253(31)	16,319 (32)	40,270 (21)	
Obese class 2	18,603 (21)	40,592 (17)	3,532 (9.4)	12,885 (9.2)	6,312 (7.6)	150 (18)	9,742 (18.9)	15,388 (7.9)	
Obese class 3	12,107 (13)	25,550 (11)	1,577 (4.2)	7,216 (5.2)	1,650 (2.0)	108 (13)	3,517 (6.8)	5,494 (2.8)	
Missing	151,553 (63)	158,791 (40)	4,853 (13)	49,302 (35)	36,884 (44)		33 (0.1)	54,155 (28)	

Variable	NJR	NZJR	PABZ	PATN	RAR	SAR	SIRIS	Total
TKA with ALBC	810,644	60,173	4,540	970	17,818	123,088	91,784	2,293,446
Female sex	463,557 (57)	31,032 (52)	2,925 (64.4)	561 (58)	13,822 (78)	70,452 (57)	55,210 (60)	1,361,082 (59)
Age group [b]								
< 55	46,596 (5.7)	4,365 (7.3)	120 (2.6)	42 (4.3)	809 (4.5)	6,287 (5.1)	6,055 (6.6)	148,326 (6.5)
55–64	181,159 (22)	17,054 (28)	659 (15)	178 (18)	5,211 (29)	28,738 (23)	21,925 (24)	560,492 (24)
65–74	325,568 (40)	24,098 (40)	1,934 (43)	413 (43)	8,836 (50)	49,937 (41)	34,089 (37)	911,870 (40)
≥ 75	257,321 (32)	14,656 (24)	1,827 (40)	337 (35)	2,313 (17)	38,123 (31)	29,649 (32)	906,910 (40)
ASA class					na			
I	68,137 (8.4)	6,151 (10)	397 (8.7)	8 (0.8)		20,918 (17)	6,312 (6.9)	155,769 (6.8)
II	595,982 (74)	38,104 (63)	2,285 (50)	180 (19)		80,930 (66)	43,391 (47)	1,145,952 (50)
III	144,145 (18)	15,101 (25)	288 (6.3)	27 (2.8)		20,832 (16.9)	19,611 (21.4)	406,988 (18)
IV–V	2,380(0.3)	102 (0.3)	2 (0.0)			235 (0.2)	264 (0.3)	7,953 (0.3)
Missing		611 (1.0)	1,568 (35)	755 (78)		173 (0.1)	22,206 (24)	278,886 (12)
BMI category [c]			na	na	na			
Underweight	950(0.1)	67 (0.1)				181 (0.1)	298 (0.3)	2,811 (0.1)
Normal	58,700 (7.2)	4,343 (7.2)				22,203 (18.0)	13,150 (14.3)	185,100 (8.1)
Pre-obese	207,996 (26)	13,628 (23)				53,221 (43.2)	24,457 (26.6)	530,518 (23)
Obese class 1	201,963 (25)	12,639 (21)				34,747 (28.2)	15,778 (17.2)	469,617 (21)
Obese class 2	104,287 (13)	7,100 (12)				10,440 (8.5)	6,596 (7.2)	235,627 (10)
Obese class 3	44,072 (5.4)	4,051 (6.7)				2,113 (1.7)	2,946 (3.2)	110,401 (4.8)
Missing	192,676 (24)	18,345 (31)				183 (0.1)	28,559 (31.1)	684,628 (30)

Missing cases: [a] AJRR (n = 333); LROI (n = 228). [b] LROI (n = 161); SAR (n = 3); SIRIS (n = 490). [c] BMI categories are based on WHO classification: underweight (<18.5), normal (18.5–< 25), pre-obese (25–< 30), obese class 1 (30–< 35), obese class 2 (35–< 40), and obese class 3 (≥ 40.00). na = not available.

Table 8. Overview of ALBC used in primary TKA with OA (N = 2,053,128) as reported by 15 of the 16 participating registries (except AJRR) from 2010–2020

Type/name of ALBC	Company	Viscosity	Antibiotics used	Used in TKA n (% of N) [a]
Palacos R + G	Heraeus	High	Gentamicin	1,265,765 (62)
Refobacin Bonecemet R	Zimmer Biomet	High	Gentamicin	362,845 (18)
Simplex with Tobramycin	»	Medium/high	Tobramycin	101,001 (5.0)
CMW 2 G	»	Medium	Gentamicin	90,927 (4.4)
Palacos MV+G	»	Medium	Gentamicin	55,624 (2.7)
SmartSet GHV	»	High	Gentamicin	58,331 (2.8)
CMW 1 G	DePuy	High	Gentamicin	24,703 (1.2)
Copal G+ V or C+V	»	High	Gentamicin and vancomycin or Clindamycin and vancomycin	10,116 (0.5)
Simplex HV	»	High	Gentamicin	33,463 (1.6)
Cemex with Gentamicin	Alere	High	Gentamicin	8,028 (0.4)
Palamed G	»	Medium	Gentamicin	7,980 (0.4)
Refobacin Bonecemet R-3	»	High	Gentamicin	7,133 (0.4)
SmartSet GMV	»	Medium	Gentamicin	5,015 (0.2)
Simplex EC	Styrker	Medium/high	Erythromycin and colistin	4,419 (0.2)
Palacos (other than R + G)	»	Low/medium/high	Vancomycin and gentamicin	4,477 (0.2)
Aminofix 1	Lépine	Medium	Gentamicin	2,796 (0.1)
Gentafix 1	Teknimed	High	Gentamicin	1,997 (0.1)
Hi-Fatigue G Bone Cement	Zimmer	High	Gentamicin	1,073 (0.1)
Subiton G	Subiton	High	Gentamicin	736 (0.0)
Versabond	Smith & Nephew	Medium	Gentamicin	498 (0.0)
Smartset GMV Endurance	»	Medium	Gentamicin	376 (0.0)
CMW 3 G	»	Low	Gentamicin	352 (0.0)
Orthocem 1G	»	Standard/high	Gentamicin	356 (0.0)
Synicem 1G	MedicalExpo	Standard	Gentamicin	331 (0.0)
Rally HV	»	High	Gentamicin	293 (0.0)
Refobacin Revision (Refobacin Revision-3)	»	High	Gentamicin and clindamycin	274 (0.0)
Palacos LV+G	»	Low	Gentamicin	164 (0.0)
Aminofix 3	»	Low	Gentamicin	103 (0.0)
Gentafix 3	»	Low	Gentamicin	94 (0.0)
Amplifix 1	Amplitude	Medium	Gentamicin	89 (0.0)
Genta C~ment 1 Bone Cement	Biomedical	High	Gentamicin	85 (0.0)
Subiton Quirurgico G	»	Low	Gentamicin	42 (0.0)
Biogent I	»	Standard	Gentamicin	31 (0.0)
VancoGenx	»	High	Vancomycin and gentamicin	19 (0.0)
MectaCem III	Medacta	Low/standard	Gentamicin	14 (0.0)
Cemex Gent LV	»	Low	Gentamicin	1 (0.0)
BonOs R Genta	Osartis	High	Gentamicin	1 (0.0)
Other (not specified) [b]				1,216 (0.1)
Unknown [c]				2,360 (0.1)

[a] FAR and KP reported a greater number of ALBC than the number of TKAs included. This was because patients may have had more than 1 type of cement, as explained by the KP. Thus, the total denominator of ALBC (n = 2,022,371) was greater than the number of TKA with ALBC included (n = 2,020,823) (see Table 2).
[b] Procedure using a mixture of different types of cement or others. Difficult to differentiate antibiotics used because it is mixed-use and will contain cement with different antibiotics. Most of the antibiotics used are gentamicin (though a small number are mixed with erythromycin, tobramycin and/or vancomycin) but insufficient information in most procedures.
[c] TKA with ALBC, but missing information on name of ALBC, antibiotic loaded, and /or company/manufacturer.

Table 10. Type of SAP used as reported by 9 of 16 participating registries: DKR, FAR, JointCare, KP, NZJR, NAR, PABZ, RAR, and SAR (n = 530,495 TKAs)

Generic name	ATC code	Registry reporting SAP	Used in TKA n (% of 517,890) [a]
Cefazolin	J01DB04	JointCare, KP, NAR, NZJR, PABZ, RAR	165,915 (32)
Cefuroxime	J01DC02	DKR, FAR, JointCare, KP, NAR, NZJR, PABZ, RAR, SAR	139,306 (27)
Cloxacillin	J01CF02	FAR, NAR, SAR	114,240 (22)
Cefalotin	J01DB03	FAR, NAR	23,404 (4.5)
Clindamycin	J01FF01	FAR, JointCare, KP, NAR, NZJR, RAR, SAR	18,716 (3.6)
Vancomycin	J01XA01	DKR, FAR, JointCare, KP, NAR, NZJR, PABZ, RAR, SAR	13,963 (2.7)
Cefpirome	J01DE02	FAR, RAR	8,652 (1.7)
Gentamicin	J01GB03	JointCare, KP, NAR, NZJR, RAR	8,620 (1.7)
Ceftriaxone	J01DD04	FAR, JointCare, KP, NZJR, PABZ, RAR	6,106 (1.2)
Cefotaxime	J01DD01	NAR, PABZ, RAR, SAR	2,475 (0.5)
Dicloxacillin	J01CF01	DKR, NAR	1,396 (0.3)
Cefoperazone	J01DD12	RAR	1,337 (0.3)
Cefalosporine	J01D	RAR	1,086 (0.2)
Ceftazidime	FJ01DD02	FAR, KP, PABZ, RAR	1,056 (0.2)
Amoxicillin-clavulanic acid	AJ01CR02	JointCare, RAR	273 (0.1)
Oxacillin	J01CF04	RAR	751 (0.1)
Ciprofloxacin	J01MA02	FAR, JointCare, KP, NAR, RAR, SAR	336 (0.1)
Teicoplanin	J01XA02	JointCare, PABZ, RAR	271 (0.1)
Polymyxin	J01XB02	KP	104 (0.0)
Tobramycin	J01GB01	KP	84 (0.0)
Levofloxacin	J01MA12	JointCare, KP, PABZ, RAR	63 (0.0)
Piperacillin	J01CA12	KP, RAR	58 (0.0)
Cefamandole	J01DC03	NZJR, PABZ	54 (0.0)
Cefadroxil	J01DB05	RAR	34 (0.0)
Aztreonam	J01DF01	KP	33 (0.0)
Cefalexin	J01DB01	NAR, RAR	25 (0.0)
Ampicillin/sulbactam	J01CR01	RAR,	22 (0.0)
Metronidazole	J01XD01	KP, NAR	16 (0.0)
Azithromycin	J01FA10	KP	13 (0.0)
Amoxicillin	J01CA04	NZJR, RAR	12 (0.0)
Ampicillin	J01CA01	KP, NAR, PABZ, RAR	10 (0.0)
Amikacin	J01GB06	RAR	10 (0.0)
Combination of 2 or more SAP used			
Cefuroxime and vancomycin		FAR	47 (0.0)
Clindamycin and other (unspecified)		FAR	19 (0.0)
Cefuroxime and other (unspecified)		FAR	18 (0.0)
Cefuroxime and clindamycin		FAR	14 (0.0)
Vancomycin and other (unspecified)		FAR	3 (0.0)
Clindamycin and vancomycin		FAR	2 (0.0)
Others (n < 10) [b]			78 (0.0)
Unknown [c]			9,268 (1.8)

ATC = Anatomical Therapeutic Chemical Classification System.

[a] 4% (20,627) of TKAs reported by the 9 registries did not use SAP. Besides, some registries reported use of 2 or more types of SAP per procedure. These could explain the reason why the number of SAP agents used presented here differs from the total number of TKAs from the 9 registries presented in Table 9.

[b] Penicillin G (J01CE01) (n = 3), cefepime (J01DE01) (n = 7), cefotetan (J01DC05) (n = 3), cefoxitin (J01DC01) (n = 7), piperacillin/tazobactam (J01CG02) (n = 7), flucloxacillin (J01CF05) (n = 8), meronem (J01DH02) (n = 4), ertapenem (J01DH03) (n = 6), imipenem/cilastatin (J01DH51) (n = 2), imipenem (J01DH56) (n = 2), sulfamethoxazole-trimethoprim (J01EE01) (n = 9), erythromycin (J01FA01) (n = 3), clarithromycin (J01FA09) (n = 1), norfloxacin (J01MA06) (n = 1), moxifloxacin (J01MA14) (n = 1), doxycycline (J01AA02) (n = 8), linezolid (J01XX08) (n = 5), daptomycin (J01XX09) (n = 1).

[c] Others, but not specified or reported as unknown.