Does Adding Antibiotics to Cement Reduce the Need for Early Revision in Total Knee Arthroplasty?

Eric Bohm MD, MSc, FRCSC, Naisu Zhu MD, DrPH, Jing Gu MD,
Nicole de Guia MHSc, Cassandra Linton MSc, Tammy Anderson MSc,
David Paton MSc, Michael Dunbar MD, FRCSC, PhD

Published online: 25 July 2013

© The Association of Bone and Joint Surgeons® 2013

Abstract

Background There is considerable debate about whether antibiotic-loaded bone cement should be used for fixation of TKAs. While antibiotics offer the theoretical benefit of lowering early revision due to infection, they may weaken the cement and thus increase the likelihood of aseptic loosening, perhaps resulting in a higher revision rate.

The institution of one or more of the authors (EB, MD) has received, during the study period, funding from Stryker Orthopaedics (Mahwah, NJ, USA), Zimmer, Inc (Warsaw, IN, USA), DePuy Orthopaedics, Inc (Warsaw, IN, USA), and Smith & Nephew, Inc (Memphis, TN, USA). One of the authors certifies that he (MD), or a member of his or her immediate family, has received or may receive payments or benefits, during the study period, an amount of USD 100,001 to USD 1,000,000 from Stryker. One or more authors (NZ, JG, NG, CL, TA) is an employee of the Canadian Institute of Health Information.

All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research* editors and board members are on file with the publication and can be viewed on request.

Each author certifies that his or her institution approved or waived approval for the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.

Data were obtained from the national Canadian Joint Replacement Registry and analysis was performed at Canadian Institute for Health Information (Toronto and Ottawa, Ontario, Canada), Concordia Joint Replacement Group (Winnipeg, Manitoba, Canada), and Dalhousie University (Halifax, Nova Scotia, Canada).

The opinions expressed in this article are those of the authors and do not necessarily represent the views of the Canadian Institute for Health Information.

Questions/purposes We (1) compared the frequency of early knee revision arthroplasty in patients treated with antibiotic-loaded or non-antibiotic-loaded cement for initial fixation, (2) determined effects of age, sex, comorbidities, and surgeons' antibiotic-loaded cement usage patterns on revision rate, and (3) compared causes of revision (aseptic or septic) between groups.

Methods Our study sample was taken from the Canadian Joint Replacement Registry and Canada's Hospital Morbidity Database and included cemented TKAs performed between April 1, 2003, and March 31, 2008, including 20,016 TKAs inserted with non-antibiotic-loaded cement and 16,665 inserted with antibiotic-loaded cement. Chi-square test was used to compare the frequency of early revisions between groups. Cox regression modeling was used to determine whether revision rate would change by age, sex, comorbidities, or use of antibiotic-loaded cement. Similar Cox regression modeling was used to compare cause of revision between groups.

Results Two-year revision rates were similar between the groups treated with non-antibiotic-loaded cement and antibiotic-loaded cement (1.40% versus 1.51%, $p = 0.41$). When controlling for age, sex, comorbidities, diabetes, and surgeons' antibiotic-loaded cement usage patterns, the revision risk likewise was similar between groups. Revision rates for infection were similar between groups; however, there were more revisions for aseptic loosening in the group treated with non-antibiotic-loaded cement ($p = 0.02$).

E. Bohm
Concordia Joint Replacement Group, University of Manitoba,
Winnipeg, MB, Canada

N. Zhu, J. Gu, N. de Guia, C. Linton, T. Anderson,
D. Paton Canadian Institute for Health Information,
Toronto, ON, Canada

M. Dunbar (✉)
QEII Health Sciences Centre, Dalhousie University,
1796 Summer Street, Halifax, NS, Canada
e-mail: michael.dunbar@dal.ca

Conclusions The use of antibiotic-loaded cement in TKAs performed for osteoarthritis has no clinically significant effect on reducing revision within 2 years in patients who received perioperative antibiotics. Longer followup and confirmation of these findings with other national registries are warranted.

Level of Evidence Level III, therapeutic study. See Instructions for Authors for a complete description of levels of evidence.

Introduction

Considerable debate exists about the putative benefits of using antibiotic-loaded bone cement in primary TKA [3, 11]. Antibiotic-loaded cement has been used extensively in THA, where Norwegian registry data suggest that its use reduces the risk of septic and aseptic revision [8, 9]. While the addition of antibiotics may potentially offer the benefit of fewer early revisions due to reduced infection in TKA [3], unintended negative consequences may also occur, perhaps related to the reduction in the mechanical properties of the cement [7] or the generation of antibiotic-resistant organisms [11, 14].

The 2006 annual report of the Australian joint replacement registry (AJRR) [1] found a higher risk of mid-term (2- to 5-year) revision in cemented TKAs (hazard ratio [HR] = 1.198), but this was not controlled for medical comorbidities, diabetes, implant type, or perioperative antibiotics. We found few relevant publications in the peer-reviewed literature. In a small randomized controlled trial of 340 knees, Chiu et al. [5] found a significant reduction in deep infection rates from 3.1% to 0% through the use of cefuroxime-impregnated cement. Conversely, using a community-based total joint registry involving nearly 23,000 TKAs, Namba et al. [16] found a higher rate of infection at 1 year in the group treated with antibiotic-loaded cement (1.4% versus 0.7%) when controlling for confounding factors. In a retrospective adjusted analysis involving 1625 consecutive patients, Ghandi et al. [10] could not detect a beneficial effect of antibiotic-loaded cement on infection rates at 1-year followup. There is disagreement among published studies on whether or not the addition of antibiotics to bone cement during primary TKA reduces the early revision rate.

Using data from the Canadian Institute for Health Information (CIHI), we (1) compared the frequency of early knee revision arthroplasty in a group of patients treated with antibiotic-loaded cement for initial fixation with a group treated with cement without antibiotics, (2) determined whether the revision rate would change based on patients' age, sex, and comorbidities or by habitual antibiotic-loaded cement usage patterns among surgeons,

and (3) compared the causes of revision (aseptic or septic) between groups of patients managed with antibiotic-loaded cement or non-antibiotic-loaded cement.

Patients and Methods

We performed a retrospective cohort study using two databases maintained by the CIHI: the Canadian Joint Replacement Registry (CJRR) and the Hospital Morbidity Database (HMDb). The CJRR began data collection in 2001 initially as a voluntary registry and, for the duration of this study, captured detailed operative information on approximately 43% of all hip and knee arthroplasties performed yearly in Canada. The HMDb is a mandatory administrative database that captures patient-level information on all inpatient hospitalizations in Canada; this information includes primary and revision joint arthroplasties (regardless of CJRR form completion) and medical comorbidities. The two databases were linked by requiring exact matches on encrypted health card number, province of health card authority, and arthroplasty side, as well as surgery dates that differed by no more than 1 day. Linkages were not possible for surgeries that occurred in Manitoba or Quebec, as both provinces encrypt health card numbers before data submission to the HMDb, but not CJRR, making a standard linkable identifier impossible. Patients with invalid or missing health card number, province of health card authority, sex, and age were also excluded from this study. Also not captured in this study were revisions where the index primary procedure took place in a different province or territory. With these criteria, the overall linkage rate between the two datasets for the current study was 77%, which is similar to that found in other national registries [17]. Institutional review board approval was not needed for this study, as some of the authors who conducted analyses were staff at the CIHI, which manages the CJRR. CIHI's role is to collect and analyze information on health and health care in Canada. CIHI is a secondary user of personal health information, specifically for the planning and management of the health system, including statistical analysis and reporting. CIHI adheres to its privacy policy [4] and to any applicable privacy legislation and/or agreements.

Age, sex, medical comorbidities, and diabetes can affect the risk of revision [2, 6, 15, 16]. To allow for control of these possible confounding factors, patients were stratified into four age groups: 54 years or younger, 55 to 64 years, 65 to 74 years, and 75 years or older. A modified Charlson Comorbidity Index score that excluded diabetes was used to measure the extent of a patient's medical comorbidities and was adapted from the methodology of Quan et al. [18]. Patients' modified Charlson Comorbidity Index scores

ranged from 0 to 7, but this was dichotomized into presence/absence of comorbidities due to skewed frequency distribution with a low median and few high scores. The presence of diabetes was also based on the methodology of Quan et al. [18] and was dichotomized into no diabetes or diabetes with/without complications. The use of perioperative prophylactic antibiotics was not included in the model as it is the standard of care in Canada, and nearly 100% of the patients in this sample were recorded as receiving prophylactic antibiotics. We restricted our sample to only those patients with degenerative arthritis to reduce the possibility of bias of antibiotic-loaded cement being used selectively in patients known to be at higher risk of infection, such as those with rheumatoid arthritis or other inflammatory conditions.

This methodology provided a sample of 36,681 TKAs performed between April 1, 2003, and March 31, 2008. Of these, 20,016 TKAs were inserted using non-antibiotic-loaded cement, while the remaining 16,665 were inserted using antibiotic-loaded cement. The two groups were clinically similar in age (70 years in both groups, $p = 0.58$) and sex distribution (62% female in both groups, $p = 0.17$). The presence of comorbidities (4% versus 5%, $p < 0.001$) and rates of diabetes (2% versus 3%, $p < 0.001$), while clinically similar, were statistically different between groups (Table 1).

The most commonly used cement was Simplex® (Stryker Orthopaedics, Mahwah, NJ, USA) (79%), followed by Palacos® (Heraeus Medical, Hanau, Germany) (12%), CMW® (DePuy Orthopaedics, Inc, Warsaw, IN, USA) (6%), and a mixture of others (3%). The three main cement types were fairly evenly split in terms of antibiotic

status: 46% of the Simplex®, 53% of the Palacos®, and 38% of the CMW® cement contained antibiotics. There does not appear to be a regional bias in Canada as to type of cement used. The majority of surgeons using antibiotic-loaded cement used it on a routine basis.

Statistical Methods

The 2-year crude revision rates were compared using the chi-square test, and Cox regression modeling was used to determine HRs for revision while controlling for the effects of age, sex, comorbidities, and diabetes. Statistical significance was set at 5% and differences were reported with 95% CIs. To assess for the possible confounding effect of surgeons selecting antibiotic-loaded cement for patients that they perceived to be at high risk of infection, the analysis was repeated after stratifying surgeons into two categories: alternating and consistent. The alternating surgeon group included those surgeons who regularly switched back and forth between antibiotic-loaded and non-antibiotic-loaded cement types, presumably based on perceived high-risk patients, while the consistent surgeon group included those surgeons who consistently used either antibiotic-loaded or non-antibiotic-loaded cement types for their patients.

Results

There were no differences in revision rates between patients who received antibiotic-loaded cement and those who received non-antibiotic-loaded cement. Revision within 2 years occurred in 532 knees, representing an overall 2-year revision rate of 1.45%. This reflected a revision rate of 1.40% (95% CI, 1.24%–1.57%) in the non-antibiotic-loaded cement group and 1.51% (95% CI, 1.32%–1.69%) in the antibiotic-loaded cement group; this absolute increase of 0.11% (95% CI, –0.14% to +0.35%) was not significant ($p = 0.41$).

When controlling for age, sex, comorbidities, and diabetes, there still was no difference between groups. The HR of revision in the antibiotic-loaded cement group was 1.066 (95% CI, 0.90–1.27) compared to the non-antibiotic-loaded cement group (Table 2); this difference was not significant ($p = 0.46$). The cumulative revision rates of the two groups are presented (Fig. 1). When the analysis was stratified by surgeon ($n = 411$) according to their pattern of cement type usage, the HR rose to 1.04 (95% CI, 0.86–1.44) for surgeons who consistently used one cement type ($n = 375$) and to 1.19 (95% CI, 0.75–1.90) for surgeons who alternated between cement types ($n = 36$); again, these differences were not significant ($p = 0.71$ and $p = 0.46$).

Table 1. Results of demographic descriptive analysis of dataset

Variable	Antibiotic-loaded cement group	Non-antibiotic-loaded cement group	χ^2 or t value	p value
Number of patients	16,665	20,016		
Age (years)*	69.5 $\pm$ 9.5	69.5 $\pm$ 9.5	0.55	0.58
Sex (number of patients)			1.90	0.17
Female	10,278 (61.7%)	12,485 (62.4%)		
Male	6387 (38.3%)	7531 (37.6%)		
Comorbidity (number of patients)			20.40	< 0.001
No	15,878 (95.3%)	19,261 (96.2%)		
Yes	787 (4.7%)	755 (3.8%)		
Diabetes (number of patients)			15.87	< 0.001
No	16,128 (96.8%)	19,510 (97.5%)		
Yes	537 (3.2%)	506 (2.5%)		
Revision in 2 years (number of patients)			0.67	0.41
No	16,414 (98.5%)	19,735 (98.6%)		
Yes	251 (1.5%)	281 (1.4%)		

* Values are expressed as mean $\pm$ SD.

Table 2. Risk of first revision by antibiotics usage in cement

Antibiotics in cement	HR (95% CI)			
	Model 0 Antibiotics in cement	Model 1 Antibiotics in cement + diabetes + comorbidity	Model 2 Antibiotics in cement + diabetes + comorbidity + age	Model 3 Antibiotics in cement + diabetes + comorbidity + age + sex
Yes	1.074 (0.91–1.27)	1.070 (0.90–1.27)	1.068 (0.90–1.27)	1.066 (0.90–1.27)
No	1.00	1.00	1.00	1.00
p value for antibiotics in cement	0.41	0.44	0.45	0.46
p value for the survival modelling; testing global null hypothesis: $\beta = 0$	0.41	0.42	< 0.001	< 0.001

HR = hazard ratio.

Fig. 1 A graph shows the cumulative revision rates of TKA implants with non-antibiotic-loaded cement and antibiotic-loaded cement. LCL = lower confidence limit; UCL = upper confidence limit.

Twice as many patients were recorded as being revised for aseptic loosening in the non-antibiotic-loaded cement group as in the antibiotic-loaded cement group ($p = 0.02$); however, reported rates of revision for infection or pain of unknown origin did not appear to differ between groups (Table 3). Data on this question were available through CJRR for 202 of the 532 patients (39%).

Discussion

Considerable debate exists regarding the benefits of using antibiotic-loaded bone cement in primary TKA [3, 11]. The 2006 annual report of the AJRR [1] found a higher risk of mid-term (2- to 5-year) revision in cemented TKAs (HR = 1.198), but this was not controlled for medical

comorbidities, diabetes, implant type, or perioperative antibiotics. Peer-reviewed, published data from a small randomized controlled trial [5], a retrospective study [10], and a regional registry [16] have produced contradictory findings on its effectiveness at reducing infection rates. Using a large dataset containing nearly 37,000 patients who underwent primary TKA for osteoarthritis from two Canadian registries, we (1) compared the frequency of early knee revision arthroplasty in patients treated with antibiotic-loaded or non-antibiotic-loaded cement for initial fixation, (2) determined effects of age, sex, and comorbidities or surgeons' antibiotic-loaded cement usage patterns on revision rate, and (3) compared causes of revision (aseptic or septic) between groups.

This study had a number of limitations. First, the outcome metric we used was that of revision and not infection.

Table 3. Revision rate and reasons for revision by cement antibiotic status

Variable	Non-antibiotic-loaded cement group (n = 20,016)	Antibiotic-loaded cement group (n = 16,665)	p value
Number of patients with 1 st revision within 2 years of primary procedure	281	251	
Revision rate (%)	1.40	1.51	0.41
Number of patients with CJRR data on reasons for revision*	96	106	
Single-stage infection	5	8	0.49
Two-stage infection	9	14	0.39
Aseptic loosening	22	11	0.02
Unknown pain	12	18	0.37

* Reasons for revision were suppressed due to small cell sizes in many categories; CJRR = Canadian Joint Replacement Registry.

It is conceivable that the use of antibiotic-loaded cement reduced the incidence of superficial infections that required only antibiotics for treatment or deep infections that only required a washout as treatment. However, given the relationship between infection and eventual need for revision [2, 19], one would expect that a reduction in infection would result in a reduced revision rate. We believed including revision for any reason and not just revision for infection is appropriate for several reasons: it facilitates comparison of our results to other registries, it reflects any unintended negative effects of antibiotics on the mechanical properties of the cement [20] that could lead to early loosening, it captures revisions for both diagnosed and undiagnosed infection, and the majority of early TKA revisions are done for either aseptic loosening or infection [2]. Second, we recognize that loss to followup due to patients undergoing revision TKA in a province different from that of their primary TKA is possible; however, we have no reason to believe that loss would differ between the cement types and thus should not bias the results. Third, the overall rates of medical comorbidities (4.2%) and diabetes (2.8%) were quite low in our sample. This is likely due to the fact that they are coded positive only if they affect hospitalizations costs or length of stay and thus likely provide a better reflection of disease severity. Because the rates of diabetes and comorbidities were low, with few high comorbidity scores, the Charlson Comorbidity Index was dichotomized. This has a granulizing effect on the analyses and reduces the power to comment on the relationship between increasing comorbidity and risk of infection. Fourth, the rates of comorbidities and diabetes were clinically similar but statistically different between the two groups, which could introduce a bias into the results. We have attempted to account for this by treating comorbidities and diabetes as separate variables in the Cox regression analysis. Fifth, there was some heterogeneity in the types of cement used in this study. As this

was not a randomized trial, it is possible that there was a selection bias in the type of cement used, although it appears there was no regional bias within Canada. Sixth, although we believe we have done all we can with the data to reduce selection bias, it is possible that there was a selection bias to use antibiotic-loaded cement in higher-risk patients, which could skew the results. We restricted our sample to only those patients with degenerative arthritis to remove the possible bias of antibiotic-loaded cement being used selectively in patients at higher risk of infection, such as those with rheumatoid arthritis or other inflammatory conditions. Finally, to maintain the power to make comments regarding infection rates when using antibiotic-loaded cement, we have not accounted for factors such as previous surgery to the index knee, specific additional steps to reduce infection intraoperatively, or specifics of the surgical procedure such as handling of the PCL or the patella.

Using our dataset of nearly 37,000 TKAs, the use of antibiotic-loaded cement was not associated with a relevant reduction in early revision risk. The 2-year revision rate was 1.40% in the non-antibiotic-loaded cement group and 1.51% in the antibiotic-loaded cement group. Our overall revision rate of 1.45% at 2 years is consistent with that found in other large national registries [6] and provides confirmation of our methodology used to identify revisions. Contrary to our findings with TKA, recent results from the Norwegian hip registry have demonstrated a beneficial effect of antibiotic-loaded cement in lowering THA revision rates at 10 years for any cause, including both aseptic loosening and infection [8, 9]. There are several possible explanations for this observation. It is possible that the addition of antibiotics to the cement in fact has some beneficial effects on its mechanical properties. This effect may be more clinically apparent in THA, where the stresses in the cement consist of both tension and compression, whereas in the knee it is primarily compression. It is also

conceivable that both the duration and magnitude of locally elevated antibiotic levels after surgery are smaller in TKA than THA due to the smaller amount of cement used in TKA and the superficial nature of the knee resulting in faster and more complete drainage of postoperative bleeding. The 2-year revision rate was chosen as the end point since aseptic loosening and infection are the leading causes of early TKA revision [20] and should therefore provide adequate time for the effect of antibiotics on both infection rate and mechanical cement properties to become apparent [20].

When adjusting for the possible confounding factors of age, sex, comorbidities, and diabetes, the HR of revision risk in the antibiotic-loaded cement group was 1.066 (95% CI, 0.90–1.27) compared to the non-antibiotic-loaded cement group. These observations remained even after stratifying into surgeons who consistently used one cement type and those who alternated cemented types on a case-by-case basis, presumably selecting antibiotic-loaded cement for perceived higher-risk patients. Our findings are consistent with the survivorship curves (antibiotic-loaded cement versus non-antibiotic-loaded cement) at 2 years contained in the 2006 annual report of the AJRR [1].

A higher proportion of patients had revision for aseptic loosening in the non-antibiotic-loaded cement group compared to the antibiotic-loaded cement group. This is similar to results initially reported by Havelin et al. [12] from the Norwegian Hip Registry, where they found a nonsignificant trend toward a higher revision rate for aseptic loosening in THA in the non-antibiotic-loaded cement group compared to the antibiotic-loaded cement group at 5.5 years. Those authors believed this might be due to subclinical infections that are diagnosed as aseptic loosening. We believe this underscores the importance of using revision for any cause as the primary end point. The Finnish Arthroplasty Register reported in 2009 on 43,149 primary and, importantly, revision knee arthroplasties implanted over the period of 1997 to 2004 [13]. They reported lower rates of septic failures with antibiotic-loaded cement, but this was seen mostly in patients undergoing revision and when parenteral antibiotics were considered as a factor. The inclusion of revision arthroplasty and all diagnoses, such as inflammatory conditions, make direct comparison to our findings difficult.

We found that use of antibiotic-loaded bone cement in TKAs performed for osteoarthritis has no clinically significant effect on reducing the risk of revision within 2 years in patients who receive perioperative antibiotics. Longer followup with adjustment for the effect of implant type on longer-term revision risk and confirmation of these findings with other registries are warranted.

Acknowledgments The authors thank the orthopaedic surgeons, nurses, and secretaries who have contributed to the CJRR.

References

1. Australian Orthopaedic Association. National Joint Replacement Registry Report 2006. Available at: <https://aoanjrr.dmac.adelaide.edu.au/documents/10180/75132/Annual%20Report%202006?version=1.1&t=1349406762263>. Accessed March 28, 2013.
2. Bohm ER, Dunbar MJ, Frood JJ, Johnson TM, Morris KA. Rehospitalizations, early revisions, infections, and hospital resource use in the first year after hip and knee arthroplasties. *J Arthroplasty*. 2011;27:232–237.
3. Bourne RB. Prophylactic use of antibiotic bone cement: an emerging standard—in the affirmative. *J Arthroplasty*. 2004;19:69–72.
4. Canadian Institute for Health Information. Privacy policy on the collection, use, disclosure and retention of personal health information and de-identified data. Available at: https://secure.cihi.ca/free_products/Privacy%20Policy2013_EN_Web.pdf. Accessed March 28, 2013.
5. Chiu FY, Chen CM, Lin CF, Lo WH. Cefuroxime-impregnated cement in primary total knee arthroplasty: a prospective, randomized study of three hundred and forty knees. *J Bone Joint Surg Am*. 2002;84:759–762.
6. Department of Orthopedics, Lund University Hospital. The Swedish Knee Arthroplasty Register Annual Report 2010. Available at: http://www.knee.nko.se/english/online/uploadedFiles/114_SKAR2010_Engl1.0.pdf. Accessed March 28, 2013.
7. Dunne N, Hill J, McAfee P, Todd K, Kirkpatrick R, Tunney M, Patrick S. In vitro study of the efficacy of acrylic bone cement loaded with supplementary amounts of gentamicin: effect on mechanical properties, antibiotic release, and biofilm formation. *Acta Orthop*. 2007;78:774–785.
8. Engesaeter LB, Espehaug B, Lie SA, Furnes O, Havelin LI. Does cement increase the risk of infection in primary total hip arthroplasty? Revision rates in 56,275 cemented and uncemented primary THAs followed for 0–16 years in the Norwegian Arthroplasty Register. *Acta Orthop*. 2006;77:351–358.
9. Engesaeter LB, Lie SA, Espehaug B, Furnes O, Vollset SE, Havelin LI. Antibiotic prophylaxis in total hip arthroplasty: effects of antibiotic prophylaxis systemically and in bone cement on the revision rate of 22,170 primary hip replacements followed 0–14 years in the Norwegian Arthroplasty Register. *Acta Orthop Scand*. 2003;74:644–651.
10. Gandhi R, Razak F, Pathy R, Davey JR, Syed K, Mahomed NN. Antibiotic bone cement and the incidence of deep infection after total knee arthroplasty. *J Arthroplasty*. 2009;24:1015–1018.
11. Hanssen AD. Prophylactic use of antibiotic bone cement: an emerging standard—in opposition. *J Arthroplasty*. 2004;19:73–77.
12. Havelin LI, Espehaug B, Vollset SE, Engesaeter LB. The effect of the type of cement on early revision of Charnley total hip prostheses: a review of eight thousand five hundred and seventy-nine primary arthroplasties from the Norwegian Arthroplasty Register. *J Bone Joint Surg Am*. 1995;77:1543–1550.
13. Jansen E, Huhtala H, Puolakkka T, Moilanen T. Risk factors for infection after knee arthroplasty: a register-based analysis of 43,149 cases. *J Bone Joint Surg Am*. 2009;91:38–47.
14. Jiranek WA, Hanssen AD, Greenwald AS. Antibiotic-loaded bone cement for infection prophylaxis in total joint replacement. *J Bone Joint Surg Am*. 2006;88:2487–2500.
15. Lai K, Bohm ER, Burnell C, Hedden DR. Presence of medical comorbidities in patients with infected primary hip or knee arthroplasties. *J Arthroplasty*. 2007;22:651–656.
16. Namba RS, Chen Y, Paxton EW, Slipchenko T, Fithian DC. Outcomes of routine use of antibiotic-loaded cement in primary total knee arthroplasty. *J Arthroplasty*. 2009;24:44–47.

17. National Joint Registry for England and Wales. 7th Annual Report 2010. Available at: http://www.njrcentre.org.uk/njrcentre/portals/0/njr_7th_annual_report_2010.pdf. Accessed March 28, 2013.
18. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, Saunders LD, Beck CA, Feasby TE, Ghali WA. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005;43:1130–1139.
19. Saleh K, Olson M, Resig S, Bershadsky B, Kuskowski M, Gioe T, Robinson H, Schmidt R, McElfresh E. Predictors of wound infection in hip and knee joint replacement: results from a 20 year surveillance program. *J Orthop Res*. 2002;20:506–515.
20. van de Belt H, Neut D, Schenk W, van Horn JR, van der Mei HC, Busscher HJ. Gentamicin release from polymethylmethacrylate bone cements and *Staphylococcus aureus* biofilm formation. *Acta Orthop Scand*. 2000;71:625–629.