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Complications - Infection

No Association Between Previous General Infection and Prosthetic Joint Infection After Total Hip Arthroplasty—A National Register-Based Cohort Study on 58,449 Patients Who Have Osteoarthritis

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ABSTRACT

Background: Prosthetic joint infection (PJI) following total hip arthroplasty (THA) is a complication associated with increased risk of death. There is limited knowledge about the association between infection before THA, and risk of revision due to PJI. We investigated the association between any previous hospital-diagnosed or community-treated infection 0 to 6 months before primary THA and the risk of revision.

Methods: We obtained data on 58,449 patients who were operated with primary unilateral THA between 2010 and 2018 from the Danish Hip Arthroplasty Register. Information on previous infection diagnoses, redeemed antibiotic prescriptions up to 1 year before primary THA, intraoperative biopsies, and co-habitations was retrieved from Danish health registers. All patients had a 1-year follow-up. Primary outcome was revision due to PJI. Secondary outcome was any revision. We calculated the adjusted relative risk with 95% confidence intervals (CI), treating death as competing risk.

Results: Among 1,507 revisions identified, 536 were due to PJI with a cumulative incidence of 1.0% ([CI] 0.9 to 1.2) and 0.9% ([CI] 0.8 to 1.0) for patients who did and did not have previous infection. For any revision, the cumulative incidence was 3.1% ([CI] 2.9 to 3.4) and 2.4% ([CI] 2.3 to 2.6) for patients who did and did not have previous infection. The adjusted relative risk for PJI revision was 1.1 ([CI] 0.9 to 1.4) and for any revision 1.3 ([CI] 1.1 to 1.4) for patients who did have previous infection compared to those who did not.

Conclusion: Previous hospital-diagnosed or community-treated infection 0 to 6 months before primary THA does not increase the risk of PJI revision. It may be associated with increased risk of any revision.

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Author Contributions: All authors conceptualized and designed the study and the analyses. RJ conducted the analyses and drafted the manuscript. All authors participated in interpretation of the results, critical revision and contribution in the discussion of the manuscript.

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Complications related to total hip arthroplasty (THA) can lead to extended hospitalizations, readmissions, and several revisions [1–3]. Prosthetic joint infection (PJI) is considered the most serious and can result in increased morbidity, reduced quality of life, higher healthcare and societal cost, and a greater risk of death [4,5]. Therefore, identifying risk factors that can help mitigate the risk of PJI is crucial [6].

Studies have shown that a Charlson Comorbidity Index [7] (CCI) ≥1 has been linked to an increased risk of revision due to PJI [8]. A study found that urinary tract infection (UTI) increased the risk of any revision, while inflammatory bowel disease increased the risk of PJI revision [9,10]. A recent study from Finland found that taking oral antibiotics during a 90-day period before primary total hip and knee arthroplasty was associated with lower risk of revision due to PJI [11]. However, little is known about the influence of previous hospital-diagnosed or community-treated infection before primary THA and the risk of revision.

We investigated the association between any previous hospital-diagnosed or community-treated infection up to 6 months before primary THA and the risk of revision. Primary outcome was risk of revision due to PJI and secondary outcomes were risk of any revision, and revision due to aseptic loosening.

Material and Methods

Study Design and Setting

We conducted a nation-wide population-based cohort study using prospectively collected data from national Danish health registers. Healthcare is tax-financed and free for all Danish citizens.

This study is reported according to the RECORD guidelines [12].

Data Sources

Danish citizens have a unique civil registration number, registered in the Civil Registration System (CRS), which allows for unambiguous linkage between registers with follow-up on all Danish inhabitants. This register holds information on sex, date of birth, emigration, and death [13].

The Danish Hip Arthroplasty Register (DHR) is a validated register and reporting is compulsory for all hospitals in Denmark, including private hospitals. It holds information on primary THA and revisions with a completeness of 95% for primary THA and 89% for revisions (2018) [14,15]. We obtained information on primary diagnosis, surgery side, surgery date, surgery type, fixation type, operation theater, surgery duration, antibiotic treatment duration, and reported indication for revision.

The Danish National Patient Register (DNPR) holds information on hospital discharges and outpatient clinic visit diagnoses with a completeness of up to 99% [16]. The registration is according to the International Classification of Diseases Tenth Revision (ICD-10) with validated Charlson Comorbidity Index (CCI) codes [17]. We obtained information on hospital discharge diagnoses of all patients up to 1 year before primary THA. The CCI is calculated using data from 10 years before THA and categorized into 3 levels of comorbidity: CCI score of 0 (low) in patients who have no comorbidities; CCI score of 1 to 2 (medium); and CCI score of ≥3 (high) [8].

Statistics Denmark is a national database with information on socioeconomic characteristics for all Danish citizens. We obtained information on cohabitation status from January 1st 2010 to December 31st 2018, which has been associated with increased risk of revision and mortality following THA [18]. Cohabitation was defined as living alone or cohabiting.

The Healthcare-Associated Infections Database (HAIBA) is an automated surveillance system in Denmark that monitors selected infections acquired at hospitals, for example bacteremia [19]. The HAIBA defines PJI based on microbiology findings in intraoperative biopsies from hip arthroplasty revisions registered in The Danish Microbiology Database (MiBa) and the data on surgery recorded in the Danish National Patient Register [20]. We obtained information on intraoperative biopsies collected at Danish orthopaedic departments and analyzed at departments of clinical microbiology from January 1st 2010 to December 31st 2019.

The Danish National Database of Reimbursed Prescriptions Prescription holds information on prescriptions redeemed at public pharmacies in Denmark [21]. We extracted data on prescriptions of systemic antibacterial drugs with the drug identifier "J01" (Anatomical Chemical classification system [ATC]) redeemed up to 1 year before the date of the primary THA. Indication for prescriptions is not recorded in the national prescription registry.

Study Population

From the DHR, we retrieved information on patients aged ≥45 years who underwent primary THA due to osteoarthritis from January 1st 2010 to December 31st 2018. In case of bilateral THA, only the first was included, and only the right hip in case of bilateral THA on the same date.

We identified 69,759 THAs from the DHR, of which 11,310 were excluded due to bilateral THA, registration error in the DHR, or missing values. The study population comprised 58,449 THA patients eligible for analysis (Figure 1).

Among the 58,449 patients included from DHR, 13,663 (23%) were identified with infection diagnosis following hospitalization discharge or redeemed prescription of antibiotic treatment 0 to 6 months before primary THA (Figure 1). The most prevalent infection diagnoses were pneumonia and urinary tract infection (Supplementary Table 1). The median age for the "previous infection group" was 71 years (interquartile range [IQR] 65 to 77) and 70 years (IQR 63 to 76) for the no previous infection group. There was a higher percentage of females and more cases with medium to high CCI in the "previous infection group." The distribution of cohabitation status, fixation type, duration of surgery, type of operation theater, and duration of antibiotics were similar for both groups (Table 1).

Previous Infection

The exposure was any infection 0 to 6 months before primary THA, defined as any infection diagnosis documented following hospitalization (eg, pneumonia) or any redeemed prescription of systemic antibiotic treatment 0 to 6 months before primary THA, ensuring that all community-treated infections were included. Previous infection earlier than 6 months before primary THA was not believed to be associated with revision risk. Sensitivity analyses (Supplementary Table 4) for previous infection earlier than 6 months was planned. We extracted data from 1 year before primary THA on both documented infection diagnosis following hospital discharge and redeemed prescription of systemic antibiotic treatment. The hospitalization discharge diagnoses included are presented in Supplementary Table 1.

Revision

Revision was defined as any subsequent surgical procedure after primary THA registered in DHR, including debridement, antibiotics, and implant retention (DAIR), partial or complete removal or exchange of components. Outcomes were evaluated at 1 year after primary THA. Infection before primary THA was not believed to influence revisions performed after this lapse of time.

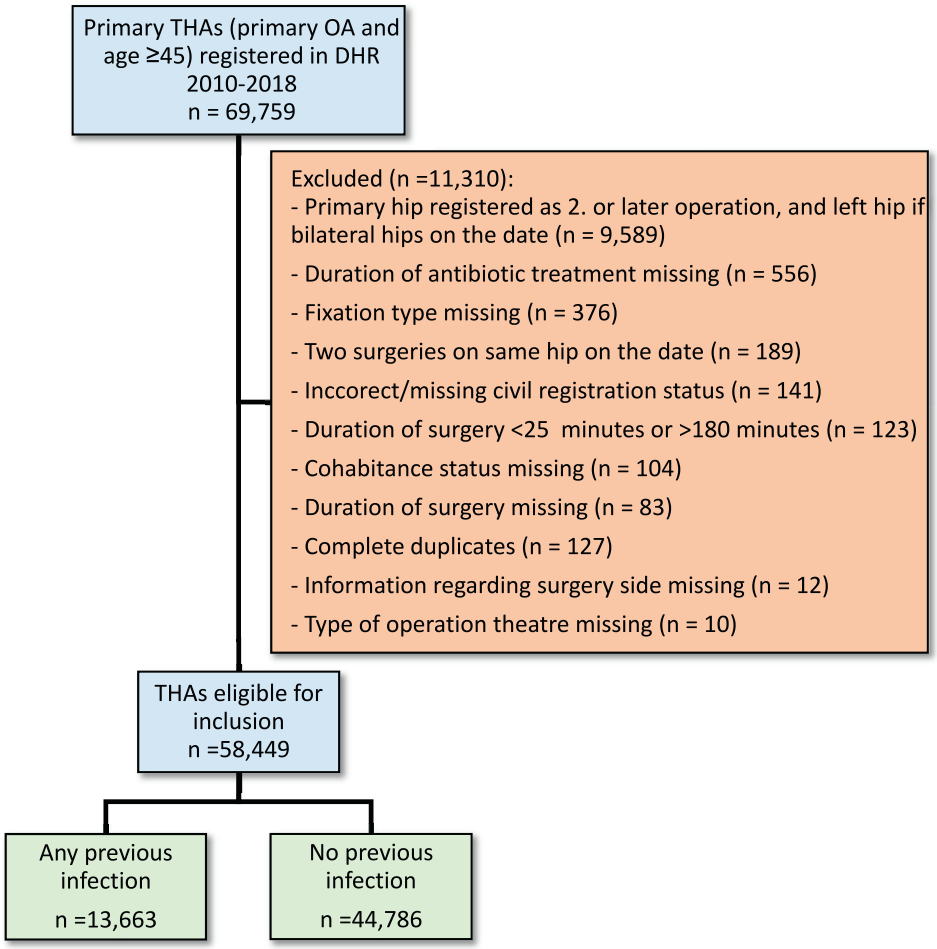

Fig. 1. Flowchart of inclusion, exclusion, and 1-year follow-up of the study population. OA, osteoarthritis; THA, total hip arthroplasty; DHR, Danish Hip Arthroplasty Register.

Revision due to PJI was defined as a revision with ≥2 culture-positive biopsies for the same bacteria out of ≥3 taken biopsies or revisions reported as deep infection (PJI) in the DHR by the reporting surgeon postoperatively, based on visual assessment preoperatively and clinical data, including results of blood samples, joint aspiration, and radiological examinations of the hip. This definition has been validated and has a predictive value of over 90% [22].

The most prevalent bacterial species in culture-positive biopsies was included and likely concomitant contaminants omitted. In case of more pathogens identified in equal prevalence, the culture-positive biopsy was classified as polymicrobial.

Reported revision causes in the DHR other than PJI were corrected to PJI if ≥2 biopsies were culture-positive for the same bacteria out of ≥3 taken biopsies, as this is a major criterion for diagnosing PJI [23,24]. In 84 cases (6% of all revisions), causes where corrected from causes other than PJI to PJI.

Outcomes

The primary outcome was revision due to PJI. Secondary outcomes were: any revision, and revision due to aseptic loosening.

Statistics

Patient characteristics, revision causes, and microbiological overviews were presented as counts and percentages. Age and duration of primary surgery were presented as medians with IQRs.

We calculated and plotted the cumulative incidence curves with 95% confidence intervals (CI), treating death as competing risk, stratified by any previous infection at 1 year [25]. We calculated relative risk (RR) of revision with 95% CI for previous infection with the pseudo-observation method and analyzed using generalized linear regressions [26]. The group with no previous infections was used as control group. The RR calculations were adjusted for the potential confounders. Patient-related confounders were sex, age groups (<65, 65 to 74, ≥75 years); CCI (low, medium, high); cohabitation status (living alone or cohabiting). Surgery-related confounders were fixation (cementless, cemented or hybrid); duration of THA surgery (minutes); operation theater (laminar or conventional flow); duration of antibiotic treatment in relation to primary THA (only preoperatively, maximum of 24 hours and longer than 24 hours). For every 10 events, we allowed 1 degree of freedom of the covariates in the regression model to prevent overfitting.

Sensitivity analyses were performed for the primary outcome to investigate the significance of timing of infection before primary THA, and the adjusted RR of revision due to PJI for previous infection within 0 to 1, 0 to 3, and 7 to 12 months before primary THA were calculated. Furthermore, we stratified previous infection into “Inpatient infection” and “Outpatient infection” within 0 to 6 months before primary THA. The “inpatient infection” was infection diagnosis following hospitalization discharge and the “outpatient infection” was defined as redeemed prescription of antibiotic treatment. The adjusted RR of the primary outcome and that of any revision was calculated accordingly. We calculated the adjusted RR of revision due to PJI and

Table 1
Patient Characteristics by Group With and Without Any Previous Infection 0 to 6 mo Before Total Hip Arthroplasty (THA).

Characteristic	Previous infection (N = 13,663)	No Previous infection (N = 44,786)
Age groups (y)		
≤64	3,285 (24)	13,141 (29)
65 to 74	5,472 (40)	18,226 (41)
≥75	4,906 (36)	13,419 (30)
Sex		
Women	8,879 (65)	23,950 (53)
Men	4,784 (35)	20,836 (47)
Charlson Comorbidity Score		
Low 0	9,303 (68)	35,363 (79)
Medium 1 to 2	3,452 (25)	8,035 (18)
High ≥3	908 (7)	1,388 (3)
Cohabitation status		
Alone	5,440 (40)	15,871 (35)
Cohabitant	8,223 (60)	28,915(65)
Prostheses fixation type		
Cemented	1,771 (13)	4,358 (10)
Uncemented	9,406 (69)	33,223 (74)
Hybrid A + B	2,486 (18)	7,205 (16)
Duration of THA (min, IQR)	55 (45:68)	55 (45:65)
Operation Theater		
Laminar flow	12,261 (90)	39,934 (89)
Conventional	1,402 (10)	4,852 (11)
Duration of antibiotic treatment in relation to THA		
Only preoperatively	1,276 (9)	3,933 (9)
MAX 24 h	12,143 (89)	40,363 (90)
>24 h	244 (2)	490 (1)

Values are count (% Column wise). Duration of surgery is given as median with interquartile range (IQR).

any revision for any previous infection stratified by sex (women and men), age (<65 or ≥65 years), comorbidity (CCI 0 or CCI ≥1).

All statistical analyses were performed using STATA version 17 (STATACorp, TX).

Results

Revision Risk

At 1-year follow-up, 1,507 revisions (3% of the study population) were identified (Table 2). For the revision due to PJI, there were 536 revisions (1% of the study population) with a cumulative incidence of 1.0% (0.9 to 1.2) and 0.9% ([CI] 0.8 to 1.0) for patients who had previous infection and those who did not, respectively (Figure 2).

There was a higher risk of any revision (3.2% [{CI} 2.9 to 3.4] and 2.4% [{CI} 2.3 to 2.6]) for patients who had previous infection versus no previous infection, respectively (Figure 3A). We found no difference in revision due to aseptic loosening (0.2% [{CI} 0.2 to 0.3] and 0.2% [{CI} 0.1 to 0.2]) for patients who had previous infection versus no previous infection, respectively (Figure 3B).

The adjusted RR for revision due to PJI was 1.1 ([CI] 0.9 to 1.4). The adjusted RR for the risk of any revision was higher (1.3 [{CI} 1.1 to 1.4]) in the any previous infection group compared to the no previous infection group. No difference was found for the risk of revision due to aseptic loosening (Table 3).

Among the 1,507 revisions, 1,129 (75%) had biopsies taken. For revisions reported as PJI in DHR, 91% had biopsies taken (Supplementary Table 2). Of the 1,129 revisions with biopsies taken, 1,084 (96%) had 5 or more biopsies obtained intraoperatively (Supplementary Table 3).

Of the 1,129 revisions with taken biopsies, 529 (47%) were culture positive. Among these, 424 had ≥2 culture-positive biopsies. The overall most prevalent bacteria were *Staphylococcus aureus* (32%), coagulase-negative Staphylococci (23%), and *Streptococcus* species (11%) (Table 4).

Table 2
Revision Causes at 1 Year After Primary Total Hip Arthroplasty.

Revision Cause	Previous Infection (N = 426)	No Previous Infection (N = 1,081)
PJI[a]	137 (1.0)	397 (0.9)
Dislocation	121 (0.9)	251 (0.6)
Femoral fracture	93 (0.7)	224 (0.5)
Aseptic loosening	39 (0.3)	97 (0.2)
Pain without loosening	11 (0.1)	28 (0.1)
Other	25 (0.2)	84 (0.2)

Values are count (% of Total study population in previous infection and no previous infection group) unless otherwise specified.
PJI, prosthetic joint infection.
[a] ≥2 Culture-positive biopsies for the same bacteria of ≥3 taken biopsies or reported PJI to the DHR.

Stratified Analysis

When analyzing for previous infection at 0 to 1, 0 to 3, and 7 to 12 months before primary THA, the adjusted RRs of revision due to PJI were similar compared to previous infection 0 to 6 months before primary THA and with no statistical difference between the groups (Supplementary Table 4).

When stratifying previous infection into “inpatient infection” and “outpatient infection” 0 to 6 months before primary THA, the adjusted RR of revision due to PJI was similar in both groups. However, we found a higher risk of any revision, but only in the “inpatient infection” group, with a RR of 1.2 ([CI] 1.1 to 1.4) (Supplementary Table 5).

The stratification for patient characteristics with adjusted RR of revision due to PJI did not show any difference in the subgroups of sex or comorbidity level, but a higher RR for patients aged <65 years. When stratifying the adjusted RR of any revision, we found an increased risk for women, patients aged <65 years, and patients who had no comorbidities (Supplementary Table 6).

Discussion

We found no statistically significant association between infection diagnoses following hospitalization discharge or redeemed prescriptions of antibiotics treatment 0 to 6 months before primary THA and the risk of revision due to PJI. However,

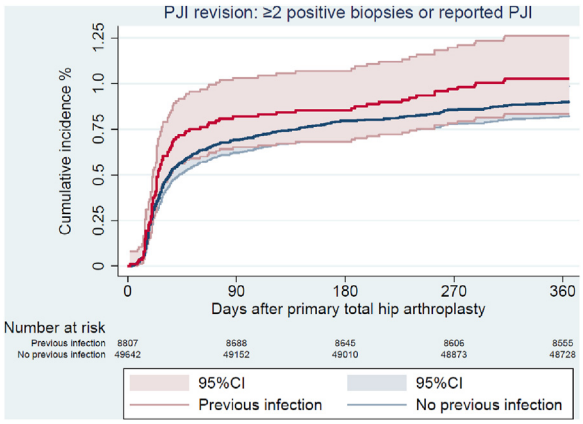

Fig. 2. Cumulative incidence for prosthetic joint infection revision after 1 year for patients who did and did not have previous infections (0 to 6 months before primary total hip arthroplasty).

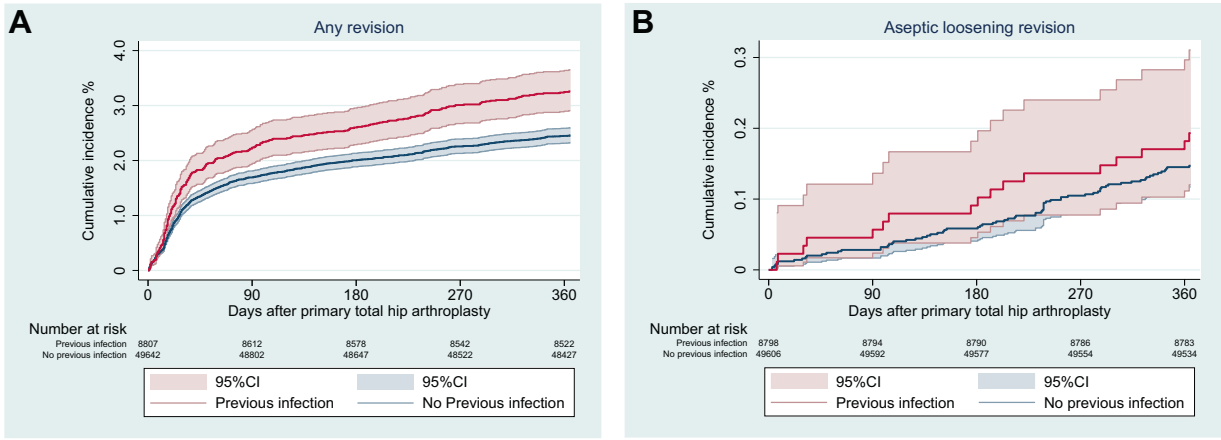

Fig. 3. A and B: Cumulative incidence for aseptic loosening revision and any revision after 1 year for patients who did and did not have previous infections (0 to 6 months before primary total hip arthroplasty).

previous infection may be associated with significantly increased risk of any revision.

Definition of PJI

A universally accepted definition of PJI diagnosis is lacking. The International Consensus Meeting on Periprosthetic Joint Infection and the European Bone and Joint Infection Society (EBJIS) have presented generally accepted definitions that with major and minor criteria [23,24]. We have attempted to cover this by including all revisions with the major criterion for confirmed PJI of ≥2 culture-positive biopsies for the same bacteria of ≥3 taken biopsies. We do not have the clinical assessment of the surgeon, which is a major criterion in confirming PJI and to address this, we account reported PJI in DHR as a proxy for visual evidence of infection, which has been validated [24]. However, this was a small portion, since 91% had biopsies taken intraoperatively (Supplementary Table 2).

Comparison With Other Studies

A recent paper investigating previous UTI found a significantly increased risk of revision due to PJI within 2 years of follow-up for patients who had UTI 1 and 2 weeks before THA [10]. However, they excluded infections more than 6 weeks before THA. Aslam et. al looked at bacteremia up to 1 year before THA and found increased risk of revision due PJI, but they did not describe the causes of the bacteremia [27]. Honkanen et al. [11] concluded that the use of antibiotics before surgery reduced the risk of revision due to PJI, maybe due to a decolonization effect, but the study was conducted at a single center with a small cohort compared to our study. Furthermore, they investigated both total hip and knee arthroplasty and with a limit of 90 days before surgery. In our study, we have been able to expand the definition of previous infection by including both infections diagnosed at hospitals and infections treated in the community by redeemed prescription of antibiotics, but our data has not confirmed the increased risk of revision due to PJI.

However, our findings suggest that patients with previous infection have a significantly increased risk of any revision, agreeing to some extend with Moran et al., showing that inflammatory bowel disease increases the risk of any revision [9]. The stratification analyses showed an increased risk for women, people aged <65 years, and patients who had no comorbidities. This was surprising, as most studies have reported men and comorbidities as risk factors revision following primary THA.

Methodological Considerations

The strength of this study is a complete national cohort including a large sample size and the ability to merge registers with high completeness of prospectively collected national data and no loss of follow-up, which reduced the risk of selection bias. However, it has been demonstrated that completeness of registration of revision due to PJI in DHR is only 67% [28], and therefore in risk of underestimation relying on DHR data only. Microbiology data contribute markedly to identifying previously unknown PJIs [22]. By utilizing all national microbiology data, we are able to identify more precisely the PJIs in both the exposed (any infection 0 to 6

Table 3
Relative Risk (RR) for Revision at 1 Year After Total Hip Arthroplasty With 95% Confidence Interval (CI).

Revision Cause	Revisions	Previous Infection (N = 13,663)		No Previous Infection (N = 44,786)
	n	Crude RR (95% CI)	Adjusted RR (95% CI)	
PJI Revision[a]	536	1.1 (0.9 to 1.4)	1.1 (0.9 to 1.4)[b]	1.0 (ref)
Aseptic loosening revision	135	1.3 (0.9 to 1.9)	1.3 (0.8 to 2.1)[c]	1.0 (ref)
Any revision	1,507	1.3 (1.2 to 1.4)	1.3 (1.1 to 1.4)[b]	1.0 (ref)

PJI, prosthetic joint infection.
[a] Revision with ≥2 culture-positive biopsies of ≥3 taken biopsies or reported PJI in the DHR.
[b] Adjusted for age groups, sex, Charlson Comorbidity Index, cohabitation status, prosthesis fixation type, and duration of antibiotic treatment in relation to primary total hip arthroplasty.
[c] Adjusted for age groups, sex, Charlson Comorbidity Index, and cohabitation status.

Table 4
Microbiological Overview of First-Time Revisions After Total Hip Arthroplasty.

Culture	≥2 Positive Biopsies (N = 424)
Staphylococcus aureus	165 (39)
Coagulase negative staphylococci	68 (16)
Streptococcus species	51 (12)
Enterococcus species	23 (5)
Escherichia coli	14 (3)
Propionibacterium species	15 (4)
Corynebacterium species	8 (2)
Micrococcus species	1 (0)
Polymicrobial	38 (9)
Other	37 (9)

The most prevalent bacterial species in culture-positives biopsies are included. In case of more species identified in equal prevalence, the culture-positive biopsy/biopsies are classified as polymicrobial. Values are count (% column wise).

months before primary THA) and the nonexposed group. It is a limitation though, that biopsies were only taken in 75% of the revisions, which might lead to an underestimation of PJIs. However, the relative risk estimation should not be affected, biopsies being expected consistently taken in both exposed and nonexposed groups. Regarding revision causes that are reported as PJI in DHR, the rate of registered taken biopsies was over 90%, which is similar to a previous Danish study investigating the incidence of PJI [22]. The positive predictive value of a revision due to PJI registered in DHR has been estimated to be 77%, which may lead to misclassification of the revision cause [28]. However, since infection before primary THA in our study is not related to the registration of data in DHR, we assume that it results in nondifferential misclassification that does not bias toward the null.

We adjusted for several patient-related and surgery-related confounders, of which cohabitation or living alone are relevant for the prediction of the implant failure following primary THA [29]. They are a crude proxy for their ability to deal with their life's physiological and physical stress [18,30]. However, we do not have information on alcohol consumption, smoking status, BMI, and diabetes, which are known risk factors for infection. Developing infections and undergoing PJI revision are related to those factors and therefore unmeasured confounding could bias the results. Moreover, our finding of increased risk of any revision for patients who had any infection 0 to 6 months before THA cannot be well explained and may be influenced by unmeasured confounding such as the above mentioned factors.

Conclusions

In conclusion, we found that infection diagnosis following hospitalization discharge or redeemed prescription of antibiotic treatment 0 to 6 months before primary THA is not associated with increased risk of revision due to PJI. However, it may be associated with increased risk of any revision. In perspective, there is no evidence to postpone THA after recovery from any infection before planned THA due to osteoarthritis.

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References

[1] Vanhegan IS, Malik AK, Jayakumar P, Ul Islam S, Haddad FS. A financial analysis of revision hip arthroplasty: the economic burden in relation to the national tariff. J Bone Joint Surg Br 2012;94:619–23.
[2] Schairer WW, Sing DC, Vail TP, Bozic KJ. Causes and frequency of unplanned hospital readmission after total hip arthroplasty. Clin Orthop Relat Res 2014;472:464–70.
[3] Danish hip arthroplasty register: annual report 2022. http://danskhoftealloplastikregister.dk/wp-content/uploads/2022/07/DHR-aarsrapport-2021_Udgivet-2022_offentliggjort-version.pdf. [Accessed 25 May 2023].
[4] Kunutsor SK, Whitehouse MR, Blom AW, Beswick AD, INFORM Team. Re-infection outcomes following one- and two-stage surgical revision of infected hip prosthesis: a systematic review and meta-analysis. PLoS One 2015;10:e0139166.
[5] Gundtoft PH, Pedersen AB, Varnum C, Overgaard S. Increased mortality after prosthetic joint infection in primary THA. Clin Orthop Relat Res 2017;475:2623–31.
[6] Kurtz SM, Ong KL, Lau E, Bozic KJ, Berry D, Parvizi J. Prosthetic joint infection risk after TKA in the Medicare population. Clin Orthop Relat Res 2010;468:52–6.
[7] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.
[8] Pedersen AB, Svendsson JE, Johnsen SP, Riis A, Overgaard S. Risk factors for revision due to infection after primary total hip arthroplasty. A population-based study of 80,756 primary procedures in the Danish Hip Arthroplasty Registry. Acta Orthop 2010;81:542–7.
[9] Moran MM, Wessman P, Rolfson O, Bohl DD, Kärrholm J, Keshavarzian A, et al. The risk of revision following total hip arthroplasty in patients with inflammatory bowel disease, a registry based study. PLoS One 2021;16:e0257310.
[10] Blanchard NP, Browne JA, Werner BC. The timing of preoperative urinary tract infection influences the risk of prosthetic joint infection following primary total hip and knee arthroplasty. J Arthroplasty 2022;37:2251–6.
[11] Honkanen M, Jämsen E, Karppelin M, Huttunen R, Syrjänen J. The effect of preoperative oral antibiotic use on the risk of periprosthetic joint infection after primary knee or hip replacement: a retrospective study with a 1-year follow-up. Clin Microbiol Infect 2019;25:1021–5.
[12] Benchimol EI, Smeeth L, Guttmann A, Harron K, Hemkens LG, Moher D, et al. [The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement]. Z Evid Fortbild Qual Gesundhwes 2016;115-116:33–48.
[13] Schmidt M, Pedersen L, Sørensen HT. The Danish civil registration system as a tool in epidemiology. Eur J Epidemiol 2014;29:541–9.
[14] Danish hip arthroplasty register: annual report. 2019. http://danskhoftealloplastikregister.dk/wp-content/uploads/2019/09/DHR-%C3%A5rsrapport-2019_til-offentligg%C3%B8relse.pdf. [Accessed 25 May 2023].
[15] Gundtoft PH, Varnum C, Pedersen AB, Overgaard S. The Danish hip arthroplasty register. Clin Epidemiol 2016;8:509–14.
[16] Schmidt M, Schmidt SA, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish National Patient Registry: a review of content, data quality, and research potential. Clin Epidemiol 2015;7:449–90.
[17] Thygesen SK, Christiansen CF, Christensen S, Lash TL, Sørensen HT. The predictive value of ICD-10 diagnostic coding used to assess Charlson comorbidity index conditions in the population-based Danish National Registry of Patients. BMC Med Res Methodol 2011;11:83.
[18] Edwards NM, Varnum C, Overgaard S, Pedersen AB. Impact of socioeconomic status on the 90- and 365-day rate of revision and mortality after primary total hip arthroplasty: a cohort study based on 103,901 patients with osteoarthritis from national databases in Denmark. Acta Orthop 2021;92:581–8.
[19] Gubbels S, Nielsen J, Voldstedlund M, Kristensen B, Schønheyder HC, Ellermann-Eriksen S, et al. National automated surveillance of hospital-acquired bacteremia in Denmark using a computer algorithm. Infect Control Hosp Epidemiol 2017;38:559–66.
[20] Voldstedlund M, Haarh M, Mølbak K, MiBa Board of Representatives. The Danish microbiology database (MiBa) 2010 to 2013. Euro Surveill 2014;19:20667.
[21] Pottegård A, Schmidt SAJ, Wallach-Kildemoes H, Sørensen HT, Hallas J, Schmidt M. Data resource profile: the Danish national prescription registry. Int J Epidemiol 2017;46:798.
[22] Gundtoft PH, Overgaard S, Schønheyder HC, Møller JK, Kjærsgaard-Andersen P, et al. The "true" incidence of surgically treated deep prosthetic joint infection after 32,896 primary total hip arthroplasties: a prospective cohort study. Acta Orthop 2015;86:326–34.
[23] Parvizi J, Gehrke T, International Consensus Group on Periprosthetic Joint Infection. Definition of periprosthetic joint infection. J Arthroplasty 2014;29:1331.
[24] McNally M, Sousa R, Wouthuyzen-Bakker M, Chen AF, Soriano A, Vogely HC, et al. The EBJIS definition of periprosthetic joint infection. Bone Joint J 2021;103-B:18–25.
[25] Sayers A, Evans JT, Whitehouse MR, Blom AW. Are competing risks models appropriate to describe implant failure? Acta Orthop 2018;89:256–8.
[26] Klein JP, Logan B, Harhoff M, Andersen PK. Analyzing survival curves at a fixed point in time. Stat Med 2007;26:4505–19.
[27] Aslam S, Reitman C, Darouiche RO. Risk factors for subsequent diagnosis of prosthetic joint infection. Infect Control Hosp Epidemiol 2010;31:298–301.
[28] Gundtoft PH, Pedersen AB, Schønheyder HC, Overgaard S. Validation of the diagnosis 'prosthetic joint infection' in the Danish Hip Arthroplasty Register. Bone Joint J 2016;98-b:320–5.
[29] Johnsen SP, Sørensen HT, Lucht U, Søballe K, Overgaard S, Pedersen AB. Patient-related predictors of implant failure after primary total hip replacement in the initial, short- and long-terms. A nationwide Danish follow-up study including 36,984 patients. J Bone Joint Surg Br 2006;88:1303–8.
[30] Brembo EA, Kapstad H, Van Dulmen S, Eide H. Role of self-efficacy and social support in short-term recovery after total hip replacement: a prospective cohort study. Health Qual Life Outcomes 2017;15:68.

Appendix

Supplementary Table 1
Table of Included Infection Diagnoses.

Infection Type	ICD-10 Codes	Number of Events (%)
Abscess	A541, B43, D733, E060A, E236A, E321, H000A, H050A, H440A, H600, H600A, J340, J340A, J36, J383D, J387G, J390, J391, J398A, J851, J852, J853, K046, K047, K113, K122, K130A, K140A, K209A, K353A, K353B, K570, K572, K574, K578, K61, K630, K750, K810A, K858A, L02, L050, M508A, M608A1, M686A, M869A, N151, N320, N412, N450, N492A, N619A, N619B, N700A, N700B, N710A, N730A, N730B, N732A, N732B, N733A, N735A, N738A, N738C, N751, N764, N768A	<10
Bacteremia	A394, A499A	<10
Candidiasis and other fungal infections	B35, B36, B37, B38, B39, B40, B41, B42, B43, B44, B45, B46, B47, B48, B49	11 (1)
Female pelvic infection	N70, N71, N72, N73, N74, N75, N76, N77	<10
Heart infections (acute rheumatic fever, infectious peri- or myocarditis, endocarditis)	I00, I01, I02, I301, I320, I33, I38, I398, I400, I376	<10
Human immunodeficiency virus (HIV) disease	B20, B21, B22, B23, B24	<10
Infection of CNS	A022C, A170, A203A321, A390, A584D, A80, A81, A82, A83, A84, A85, A86, A87, A88, A89	<10
Meningitis	G00, G01, G02, G03, G04, G05, G06, G07, A321, A390, A170, A203, A87, A548, A022, B375, B003, B010, B021, B051, B261, B384	<10
Infectious complications of procedures, catheters etc.	T802, T814, T826, T827, T835, T836, T857, T880, T880A, T89, T899	27 (3)
Influenza	J10, J11	<10
Intra-abdominal infections	K35, K37, K570, K572, K574, K578, K61, K630, K650, K659, K67, K750, K751, K800, K803, K804, K810, K819, K830, K858A, K859	82 (8)
Gastrointestinal infections	A00, A01, A02, A03, A04, A05, A06, A07, A08, A09	54 (5)
Male genital infection	N41, N45, N481, N482, N49, N511, N512	18 (2)
Miscellaneous bacterial infections	A20, A21, A22, A23, A24, A25, A26, A27, A28, A30, A31, A32, A33, A34, A35, A36, A37, A38, A42, A43, A44, A48, A49, A65, A66, A67, A68, A69, A70, A71, A74, A75, A77, A78, A79, N510	37 (4)
Miscellaneous viral infections	A90, A91, A92, A94, A95, A96, A97, A98, A99, B03, B04, B05, B06, B07, B08, b09, B25, B36, B27, B28, B29, B30, B31, B32, B33, B34	11 (1)
Obstetrical infections	O23, O264, O411, O740, O753, O85, O86, O883, O91, O98	<10
Other lower-respiratory tract infections	J20, J21, J22, J340, J350, J383C, J383D, J387B, J387F, J387G, J440, J851, J86	28 (2)
Other or sequelae	B90, B91, B92, B94, B95, B96, B97, B98, B99, K040, K052, L04, L05, N481, N482, N49, N510, N511, N512, N619E	25 (2)
Eye infections	H00, H030, H031, H043, H050, H061, H10, H130, H131, H150, H191, H192, H220, H320, H440, H441	18 (2)
Ear infections	H60, H609, H610, H620, H621, H622, H623, H650, H660, H661, H662, H663, H664, H669, H67, H681, H701, H708, H830, H940	12 (1)
Parasitic infections	B50, B51, B52, B53, B54, B55, B56, B57, B58, B60, B614, B65, B66, B67, B68, B69, B70, B71, B72, B73, B74, B75, B76, B77, B78, B79, B80, B81, B82, B83, B85, B86, B87, B88, B89	<10
Prosthetic infections	T845, T846, T847	28 (2)
Pneumonia	J12, J13, J14, J15, J16, J17, J18	208 (20)
Sepsis	A021, A227, A282B, A327, A40, A41, A427, A548G	52 (5)
Sexually transmitted diseases	A50, A51, 52, A53, A54, A55, A56, A57, A58, A59, A60, A63, A64	<10
Skin infections	A46, H010, H03, H601, H602, H603, H62, K122, K130A, K61, L00, L01, L02, L03, L08, L303, L738, M726	171 (17)
Septic arthritis, osteomyelitis, myositis	M00, M01, M630, M631, M632, M86	12 (1)
Tuberculosis	A15, A16, A17, A18, A19	<10
Upper respiratory tract infections	J00, J01, J02, J03, J04, J05, J06, J36, J390, J391	29 (3)
Urinary tract infections	N080, N10, N11, N12, N136, N151, N159, N160, N288D, N288E, N288F, N290, N291, N30, N340, N341, N390	174 (17)
Viral hepatitis	B15, B16, B17, B18, B19	<10

Supplementary Table 2
Overview of Revision Causes and the Distribution of Taken Biopsies During First-Time Revisions. Values are Count (% Row Wise).

Revision Cause	Biopsies Taken (N = 1,129)	NO Biopsies Taken (N = 378)
PJI[a]	411 (91)	41 (9)
Dislocation	257 (65)	137 (35)
Femoral fracture	227 (67)	111 (33)
Aseptic loosening	111 (74)	39 (26)
Pain without loosening	37 (82)	8 (18)
Other	86 (67)	42 (33)

PJI, prosthetic joint infection.
[a] Reported PJI to the DHR.

Supplementary Table 3
Overview of Numbers of Biopsies Taken Per Case During Revision.

Biopsies Taken (n)	Cases
<5	45 (4)
5	985 (87)
>5	99 (9)

Values are count (%). A adjusted for age groups, sex, charlson comorbidity index, cohabitation status, prosthesis fixation type and duration of antibiotic treatment in relation to primary total hip arthroplasty.

Supplementary Table 4
Relative Risk (RR) for Prosthetic Joint Infection (PJI) Revision At 1 Year After Total Hip Arthroplasty (THA) With 95% Confidence Interval (CI).

Previous Infection, Months Before THA	Previous Infection		No Previous Infection
	Crude RR (95% CI)	Adjusted RR (95% CI)[a]	
0 to 1	1.1 (0.8 to 1.5)	1.1 (0.8 to 1.5)	1.0 (ref)
0 to 3	1.2 (0.9 to 1.4)	1.1 (0.9 to 1.5)	1.0 (ref)
7 to 12	1.2 (1.0 to 1.5)	1.3 (1.0 to 1.5)	1.0 (ref)

[a] Adjusted for age groups, sex, Charlson Comorbidity Index, cohabitation status, prosthesis fixation type and duration of antibiotic treatment in relation to primary total hip arthroplasty.

Supplementary Table 5
Relative Risk (RR) for Prosthetic Joint Infection (PJI) Revision and Any Revision At 1 Year After Total Hip Arthroplasty With 95% Confidence Interval (CI).

Previous Infection	PJI Revision			Any Revision			
	Revisions	Crude RR (95% CI)	Adjusted RR (95% CI)	No Previous Infection	Revisions	Crude RR (95% CI)	Adjusted RR (95% CI)[a]	No Previous Infection
Only previous hospital infection diagnosis (inpatient infection)	536	1.8 (0.8 to 4.3)	1.4 (0.5 to 4.0)	1.0 (ref)	1,507	1.5 (0.8 to 2.8)	1.1 (0.6 to 2.2)	1.0 (ref)
Only previous redeemed prescription antibiotic treatment (outpatient infection)	536	1.1 (0.9 to 1.3)	1.1 (0.9 to 1.3)	1.0 (ref)	1,507	1.2 (1.1 to 1.4)	1.2 (1.1 to 1.4)	1.0 (ref)

[a] Adjusted for age groups, sex, charlson comorbidity index, cohabitation status, prosthesis fixation type, and duration of antibiotic treatment in relation to primary total hip arthroplasty.

Supplementary Table 6
Relative Risk (RR) for Prosthetic Joint Infection (PJI) Revision and Any Revision At 1 Year After Total Hip Arthroplasty (THA) With 95% Confidence Interval (CI) Stratified by Patient Characteristics.

Characteristic	PJI Revision			Any Revision			No Previous Infection
	Any Previous Infection			Any Previous Infection			
	Cases	Crude RR (95% CI)	Adjusted RR (95% CI)[a]	Cases	Crude RR (95% CI)	Adjusted RR (95%)[a]	
Sex							
Women	262	1.2 (1.0 to 1.6)	1.3 (0.9 to 1.8)	821	1.3 (1.1 to 1.5)	1.3 (1.1 to 1.5)	1 (ref)
Men	274	1.1 (0.9 to 1.5)	1.1 (0.8 to 1.5)	686	1.3 (1.1 to 1.5)	1.2 (1.0 to 1.5)	1 (ref)
Age (years)							
≥65	396	1.0 (0.8 to 1.2)	1.0 (0.8 to 1.3)	1,115	1.2 (1.1 to 1.4)	1.2 (1.0 to 1.4)	1 (ref)
<65	140	1.6 (1.2 to 2.3)	1.8 (1.1 to 3.0)	392	1.5 (1.2 to 1.9)	1.6 (1.2 to 2.0)	1 (ref)
Comorbidity							
No comorbidity	376	1.1 (0.9 to 1.4)	1.1 (0.9 to 1.5)	1,047	1.2 (1.1 to 1.4)	1.3 (1.1 to 1.5)	1 (ref)
Any comorbidity	160	1.1 (0.8 to 1.5)	1.2 (0.8 to 1.9)	460	1.2 (1.0 to 1.5)	1.3 (1.0 to 1.5)	1 (ref)

[a] Adjusted for age groups, sex, charlson comorbidity index, prosthesis fixation type, and duration of antibiotic treatment in relation to primary total hip arthroplasty.