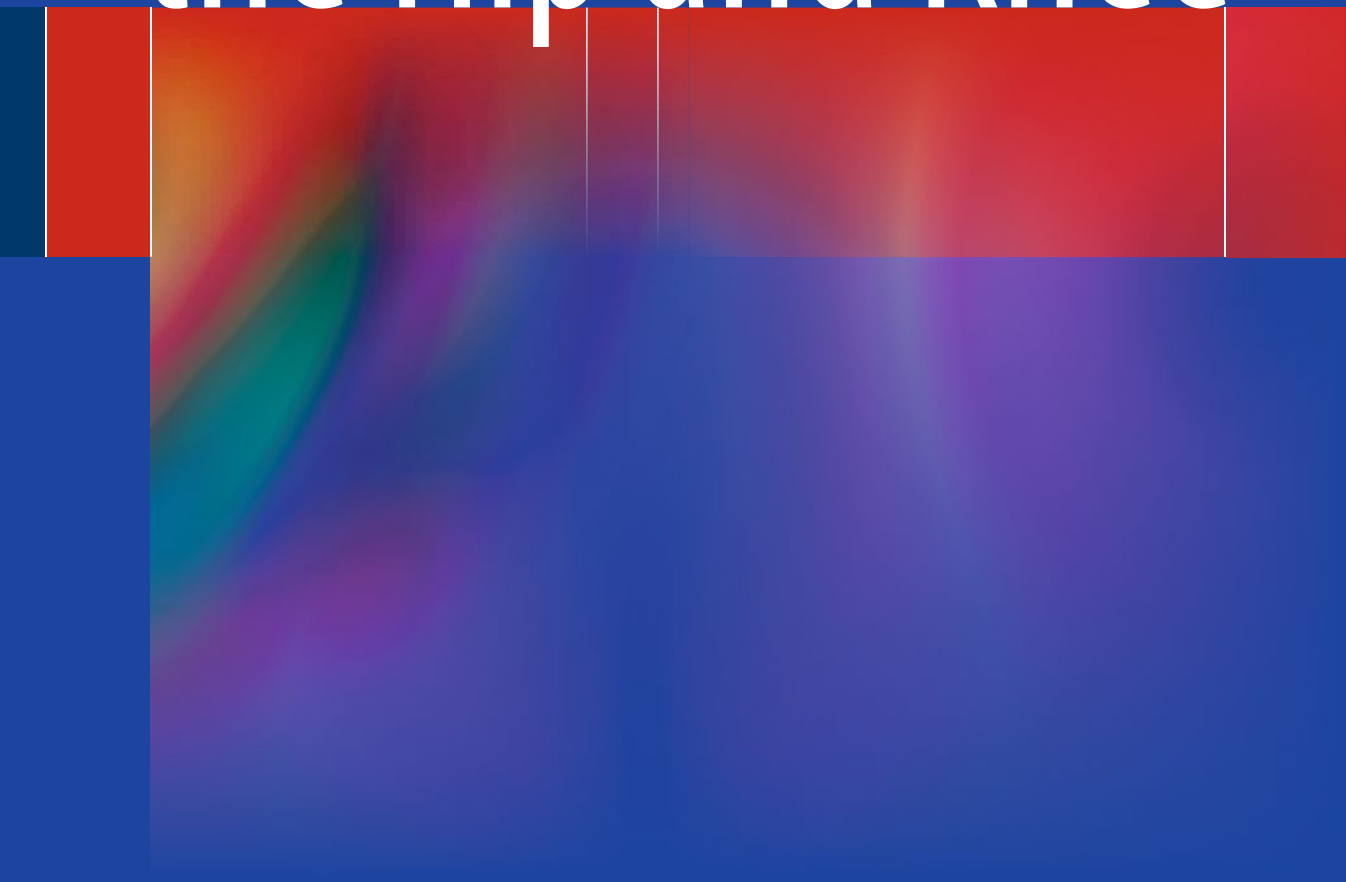
Bryan D. Springer · Javad Parvizi *Editors*

Periprosthetic Joint Infection of the Hip and Knee



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To those who have made my academic and personal life rewarding. To my wife, Fariba, who is the source of my inspiration. To my children Niosha and Cyrus who allow me to steal time from them for my selfish pursuits.

Javad Parvizi, M.D., F.R.C.S.

To my family, wife Summerson and children, Brycen, Finn, Bennett and Evie, whose true sacrifice allows me the time, energy, and effort to continue our work for the betterment of our patients.

Bryan D. Springer, M.D.

Foreword

The presence of periprosthetic total joint infection is frustrating for patient and surgeon alike. Patients who present for arthroplasty relying on a routine recovery are frequently devastated when on a rare occasion they incur a periprosthetic infection. These unexpected outcomes are costly and have significant socioeconomic implications. Therefore the clinician needs to be ever vigilant to correctly identify periprosthetic infection and treat such infections in an expeditious fashion.

While periprosthetic infection occurs infrequently, the number of arthroplasties performed continues to increase both nationally and internationally. Therefore the number of periprosthetic infections that occur even as a small percentage of the total number of implants in service results in a large infection burden. Therefore it behooves each and every arthroplasty surgeon to have an algorithmic approach to the recognition and treatment of such infections.

Dr. Springer and Dr. Parvizi have assimilated an international group of experts in periprosthetic infection to help guide the clinician through the diagnosis, treatment, and management of this difficult problem. The reader will find that if they apply the principles outlined in this book, satisfactory outcomes can be consistently obtained. While the diagnosis, management, and treatment of prosthetic infection will continue to evolve as more information becomes available, this book does an excellent job of synthesizing the current knowledge on this subject.

Charlotte, NC, USA — Thomas K. Fehring, M.D.

Preface

Very little in the care of total joint arthroplasty remains as devastating and vexing a problem as dealing with periprosthetic joint infection. There remain significant diagnostic and treatment hurdles in the prevention and cure of this entity. We are continually faced with more challenges, more resistant microbes, and less healthy host that require total joint arthroplasty. In addition, the economic impact of such treatment remains a tremendous burden to our healthcare system. All indicators point to an ever increasing burden of periprosthetic infection in our total joint arthroplasty population.

We are also at a time in the history of periprosthetic joint infection, where technology is offering us new insights into the prevention, diagnosis, and treatment of periprosthetic infection, where leading researchers and clinicians are working diligently to improve the outcomes of our patients faced with periprosthetic infection.

Despite these advances, there remains little consensus in many areas of periprosthetic infection. We hope that the work put forth in this book, by many of the thought leaders in periprosthetic infections, can serve as the reference for periprosthetic joint infection. The literature and data remain ever changing, but the foundation and principles of treatment remain the same.

Charlotte, NC, USA — Bryan D. Springer, M.D.
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Epidemiology of Total Hip and Knee Arthroplasty Infection

1

David J. Jaekel, Kevin L. Ong, Edmund C. Lau, Heather N. Watson, and Steven M. Kurtz

Introduction

Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are some of the most cost-successful surgical procedures and have allowed continued mobility and function for millions of patients with advanced degenerative joint disease. Continuous innovation and improvements of implants and surgical techniques have increased implant longevity and reduced implant wear and therefore negative patient outcomes [1–4]. However, the occurrence of infection has not reduced with advancement of implants and, in certain cases, has even increased [5–8]. Prosthetic joint infection (PJI) is a rare but devastating and sometimes life-threatening complication of total joint arthroplasty (TJA) that is associated with longer hospital stay, increased hospital cost, and higher morbidity. PJI is challenging to cure and is nonresponsive to systemic antibiotics because of how the infection develops on an implant surface. While short-term infection burden was originally reported as low as 0.2 % and 0.4 % for THA and TKA, respectively [9, 10], thousands of patients continue to present with painful complications and are an economic burden for hospitals because of inadequate reimbursement [11, 12]. To fully comprehend the societal burden of arthroplasty implant infection, the risk and incidence of this complication must be defined. Information on infection incidence in regard to THA and TKA from various sources ranging from single-center studies to large-scale multi-institution studies and national registries has been analyzed, but has not been synthesized for a broader view of the economic impact of PJI.

The later chapters of this book will discuss, in detail, the development and progression of PJI in THA and TKA, but the primary focus of this chapter is to catalogue the incidence of infection within populations across the globe and define what risk factors have the highest influence on infected revisions in the future. The first goal of this chapter is to collect and to compare infection

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rates from implant databases and national registries, which provide the largest sources for categorizing clinical utilization and device failure mechanisms. Next, this chapter identifies the influences of various risk factors such as age, sex, antibiotic cement use, and material type on the risk of PJI. Finally, the infection rates for revised components are discussed along with the overall economic impact of PJI in society.

Registries

International registries represent a vast and consistent source of data regarding the utilization of TJA in Australia and Europe. A registry is more than a data repository for basic clinical, patient, and implant data regarding the implantation and revision of TJAs. Where registries have been established, the information provides continuous feedback to clinicians in order to further the enhancement of surgical procedures. Sweden first established an orthopedic implant registry in the 1970s, with the rest of Europe and Australia following soon after.

National registries are significant in providing perspective on the current use and outcome of TJA across the globe; however, registries are not the only tool to measure the utilization of arthroplasty procedures. For example, neither the USA nor Germany currently has in place a national registry for joint replacements. These databases provide necessary information concerning the current use of TJA that is otherwise unavailable in these countries.

Public Data Sources

Administrative claims databases are an important source of data for TJA, even in countries with an established registry. These databases collect a sampling of electronic hospital discharge records, or as with the Medicare database in the USA, the complete insurance claim history for individual patients. Specific hip and knee replacement procedures are classified in these databases by hospitals in accordance with the codes from the International Classification of Diseases, Clinical Modification, 9th Revision (ICD-CM-9). Claims filed by surgeons and clinics often use current procedural terminology (CPT) codes. In the USA, three public sources of administration claims data are available and are summarized in the following subsections.

The National Hospital Discharge Survey (NHDS, http://www.cdc.gov/nchs/nhds/about_nhds.htm2009) is conducted annually by the National Center for Health Statistics (NCHS). The program was started in 1965 and has continuously recorded a statistically representative sample of hospitalizations from nonfederal and nonmilitary short-stay community hospitals across the USA. It is currently the oldest and most well-established inpatient discharge database available in the USA. The NHDS acquires inpatient records from 239 hospitals and samples ~300,000 discharge records each year. The NHDS database includes patient demographics (e.g., age and sex), disease diagnosis, procedures performed, resource utilization, and institutional characteristics.

The Nationwide Inpatient Sample (NIS, http://www.hcup-us.ahrq.gov/nisoverview.jsp) was established in 1988 by the Healthcare Cost and Utilization Project (HCUP) of the Agency of Healthcare Quality and Research (AHRQ). It has a far larger sample size than the NHDS in terms of both discharge records and number of hospitals. The NIS includes twice the number of hospitals and collects 25 times more records with an average of 5–8 million records per year. The NIS annually samples 20 % of US inpatient hospital stays. The NIS is able to capture patient, payer, and hospitalization factors, including charges, cost, and reimbursement information during hospitalization, which facilitates the evaluation of the economic impact of specific diagnoses and procedures.

Made available by the Center for Medicare and Medicaid Services (CMS), the 5 % Medicare Limited Data Set (LDS) consists of seven components: hospital inpatient, hospital outpatient, home health agency, skilled nursing facility, hospice care, physician carrier (Part B), and durable medical equipment. LDS also tracks the date of death or the rare withdrawal of a patient from the program with a denominator file. Medicare

beneficiaries in the LDS are identified with an encrypted identification number that is linked through all aspects of the database as well as time. For this reason, utilization of healthcare resources by a patient can be traced through different systems such as inpatient, outpatient, or home hospice care. Medicare data is also available in the 100 % format, i.e., for all Medicare beneficiaries. Of the seven file components, the inpatient, outpatient, home health agency, skilled nursing facility, and hospice care data are available in the 100 % format, but not the physician carrier and durable medical equipment data.

Infection and Reinfection Incidence in Primary and Revision TJA

In the modern history of arthroplasty surgery, the number of TKA procedures has been greater than the number of THA performed internationally; and therefore, in 2008, when one of the largest studies of a US medical database analyzed data collected by the NIS between 1990 and 2004, it was expected that the number of infections would follow similar trends. By 2004, approximately 5,838 knee arthroplasties were revised because of infection while only an estimated 3,352 hip arthroplasties were revised because of infection, yet both yielded similar infection rates of 1.04 % (Table 1.1) [13]. The data were collected using the ICD-9-CM procedure codes for primary or revision THA (81.51 and 81.53, 00.70–00.73, respectively) and TKA (81.54 and 81.55, 00.80–00.84, respectively). However, this method excluded infected arthroplasty devices that were removed as the first stage of a two-stage infection treatment protocol. Upon revisiting the NIS database in 2012, the analysis of the 2001–2010 datasets included ICD-9-CM procedural codes for arthrotomy or removal of a hip (80.05) or knee (80.06) prosthesis with PJI (ICD-9-CM 996.66), and the number of infected prostheses nearly doubled. In the updated analysis of the 2004 dataset, the number of infections increased for THA from 3,352 to 5,933 and for TKA from 5,838 to 10,677 (Tables 1.1 and 1.2).

The revision burden for infections as a proportion of the total number of primary and revision arthroplasties was additionally calculated; and in 2001, the infection burden rates for THA and TKA were 1.99 % and 2.05 %, respectively.

Table 1.1 Number of infections and infection rates from patients with both primary and revision hip or knee replacement surgery from the Kurtz et al. 2008 analysis of the NIS [13]

	Total hip arthroplasty				Total knee arthroplasty			
Year	Infected procedures	Percent surgery with infection (%)	Lower 95 % confidence interval (%)	Upper 95 % confidence interval (%)	Infected procedures	Percent surgery with infection	Lower 95 % confidence interval (%)	Upper 95 % confidence interval (%)
1990	1,104	0.66	0.51	0.80	1,090	0.63	0.52	0.74
1991	922	0.54	0.43	0.65	1,197	0.61	0.49	0.74
1992	1,192	0.66	0.56	0.77	1,629	0.71	0.59	0.84
1993	1,154	0.67	0.54	0.81	1,470	0.65	0.53	0.76
1994	1,207	0.66	0.51	0.82	1,577	0.63	0.54	0.73
1995	1,092	0.61	0.50	0.73	1,793	0.69	0.58	0.81
1996	1,350	0.71	0.60	0.83	2,105	0.74	0.63	0.85
1997	1,534	0.79	0.68	0.90	2,479	0.82	0.71	0.92
1998	1,797	0.92	0.75	1.10	2,771	0.98	0.85	1.11
1999	1,844	0.94	0.79	1.10	2,984	1.00	0.87	1.12
2000	1,989	0.96	0.82	1.11	3,051	0.97	0.86	1.08
2001	2,398	1.04	0.91	1.18	3,644	1.04	0.93	1.15
2002	2,879	1.17	1.01	1.32	4,273	1.09	0.96	1.22
2003	2,878	1.17	1.03	1.32	5,324	1.26	1.11	1.40
2004	3,352	1.23	1.07	1.40	5,838	1.21	1.07	1.36

Table 1.2 Number of infections, infection rates, and resource utilization from patients with both primary and revision hip or knee replacement surgery between 2001 and 2010

	Total hip arthroplasty in the USA				Total knee arthroplasty in the USA			
Year	Number of infected procedures [95 % CI]	Percentage of infected procedures [95 % CI]	Mean cost per case of infected (thousands 2011 US$) [95 % CI]	Mean length of stay per infected [95 % CI]	Number of infected procedures [95 % CI]	Percentage of infected procedures [95 % CI]	Mean cost per case of infected (thousands 2011 US$) [95 % CI]	Mean LOS per infected [95 % CI]
2001	4,545 [3,757–5,333]	1.99 % [1.78–2.21]	33.0 [29.8–36.2]	11.5 [10.3–12.7]	7,113 [6,038–8,187]	2.05 % [1.86–2.23]	26.7 [23.7–29.6]	9.3 [8.2–10.4]
2002	5,219 [4,346–6,092]	2.15 % [1.93–2.36]	33.4 [30.5–36.4]	12.1 [11.2–13.1]	8,532 [7,246–9,819]	2.20 % [1.99–2.41]	25.6 [23.7–27.4]	9.0 [8.4–9.7]
2003	5,271 [4,389–6,154]	2.20 % [1.97—2.43]	34.9 [31.2–38.5]	12.5 [11.4–13.5]	9,936 [8,377–11,495]	2.38 % [2.13-2.63]	27.9 [24.1–31.7]	9.0 [8.0–10.0]
2004	5,933 [4,965–6,901]	2.23 % [2.00–2.46]	31.2 [28.6–33.8]	10.5 [9.7–11.3]	10,677 [9,101–12,253]	2.26 % [2.06–2.47]	25.6 [23.7–27.5]	8.4 [7.8–8.9]
2005	5,634 [4,726-6,541]	2.03 % [1.83–2.22]	31.6 [28.8–34.5]	10.8 [10.0–11.6]	12,113 [10,341–13,884]	2.23 % [2.05–2.41]	25.6 [23.7–27.4]	7.9 [7.5–8.3]
2006	6,213 [5,167-7,268]	2.32 % [2.06–2.58]	31.9 [29.2–34.6]	11.1 [10.2–12.1]	12,488 [10,748–14,227]	2.30 % [2.12–2.49]	25.7 [24.6–26.8]	8.1 [7.8–8.5]
2007	6,926 [5,809-8,052]	2.36 % [2.16–2.56]	33.2 [30.3–36.1]	10.5 [9.7–11.4]	13,424 [11,551–15,298]	2.23 % [2.07—2.40]	25.7 [24.1–27.3]	7.8 [7.4–8.2]
2008	7,380 [6,195–8,564]	2.29 % [2.06-2.53]	31.5 [29.2–33.8]	9.5 [8.9–10.0]	15,983 [13,837–18,129]	2.37 % [2.17–2.56]	26.3 [24.9–27.7]	7.4 [7.1–7.7]
2009	7,162 [6,005–8,319]	2.18 % [1.97–2.39]	31.9 [29.1–34.7]	9.5 [8.8–10.2]	14,802 [12,681–16,924]	2.18 % [1.99–2.37]	25.5 [24.0–26.9]	7.2 [6.9–7.5]
2010	7,761 [6,518–9,005]	2.21 % [1.98–2.44]	31.7 [29.9–33.6]	9.3 [8.7–9.8]	16,798 [14,437–19,159]	2.32 % [2.14–2.50]	26.2 [24.6–27.8]	7.1 [6.8–7.4]

Source: Extracted from the Kurtz et al. 2012 NIS analysis [14]

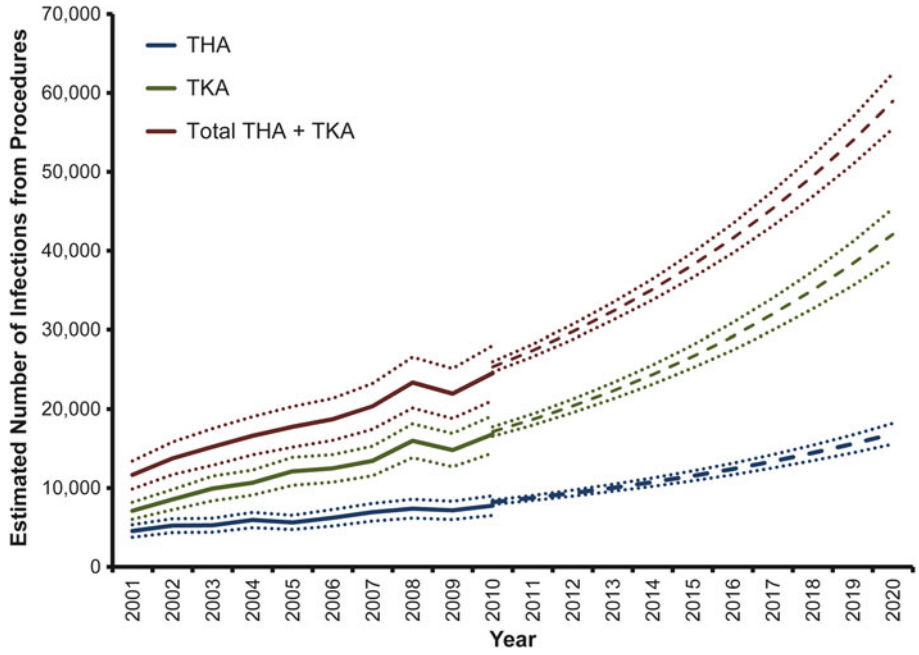

Fig. 1.1 Historical and projected number of infections with THA, TKA, and combined THA and TKA procedures within the USA between 2001 and 2020. *Dashed lines* represent the projected values per procedure, whereas the *dotted lines* represent the 95 % CIs of the NIS estimates from 2001 to 2010 and the statistical projections. The total cost was adjusted to 2012 using the Consumer Price Index [14]

These rates were also almost twice the previous calculations (1.04 % and 1.04 %, respectively). By 2010 (the most recent dataset available from NIS), the infection burden for both THA and TKA increased to 2.21 and 2.32 %; however, this increase was only significant for TKA. A more dramatic increase was observed in the raw numbers of infected arthroplasties, which grew from 4,545 and 7,113 in 2001 to 7,761 and 16,798 in 2010 for THA and TKA, respectively. The average infection burden across the sampled years remained similar at 2.20 % for THA and 2.25 % for TKA. Using a Poisson model coupled with population projections from the US Census Bureau, the NIS data were used to predict that the number of infected TKAs will increase from 16,798 in 2010 to 42,079 by 2020 (Fig. 1.1) [14]. The analysis of the NIS data also showed a steep decline in length of hospital stay for patients, which could influence the chance of discovering an early infection during the initial hospital stay and delay infection from a revision procedure [13].

Single-institution studies in the USA indicated similar incidence of infection in their patient groups. Pulido et al. monitored 9,245 patients and measured an overall incidence of 0.7 % with joint-specific incidence of 1.1 % for TKA and 0.3 % for THA (Tables 1.3 and 1.4) [15]. Malinzak et al. reported infection rates of 0.52 % and 0.47 % for TKA and THA, respectively, after monitoring 8,494 cases from 1991 to 2004 [16]. When concentrating on the Medicare LDS, which thus limited the population to ages over 65, infection occurred in 2.01 % of TKA [17] and 2.22 % for THA [18]. This study followed similar trends that were observed nationally in the USA.

Internationally, hospitals and clinics also experienced an infection incidence of nearly 1 % (Tables 1.3 and 1.4) [19–22]. For TKA procedures, infection occurred in 0.8–0.9 % of cases in Finland when observed from single-institution studies or analysis of data from the Finnish Arthroplasty Register from 1997 to 2006 [20, 21]. Similarly, a single-institution study in Japan

Table 1.3 Infection rates for total hip arthroplasty (THA)

Country	Infection rate (%)	Time period analyzed	Literature source	Data source
USA	1.99–2.20	2001–2010	Kurtz et al. [14]	NIS
USA	0.3	2001–2006	Pulido et al. [15]	Single institution
USA	0.47	1991–2004	Malinzak et al. [16]	Single institution
USA	2.22	1997–2006	Ong et al. [18]	Medicare 5 %
Norway	0.7	2005–2006	Dale at al. [19]	Norwegian Registry

Table 1.4 Infection rates for total knee arthroplasty (TKA)

Country	Infection rate (%)	Time period analyzed	Literature source	Data source
USA	1.21	2001–2010	Kurtz et al. [13]	NIS
USA	1.1	2001–2006	Pulido et al. [15]	Single institution
USA	0.52	1991–2004	Malinzak et al. [16]	Single institution
USA	2.01	1997–2006	Kurtz et al. 2010 [17]	Medicare 5 %
Finland	0.8	2002–2006	Jamsen et al. [21]	Single institution
Finland	0.9	1997–2006	Jamsen et al. [20]	Finnish Arthroplasty Register
Japan	0.8	1995–2006	Susuki et al. [22]	Single institution

observed that infections occurred in 0.8 % of TKA procedures performed between 1995 and 2006 [22]. For THA, an analysis of the Norwegian Arthroplasty Register data from 2005 and 2006 revealed an infection incidence of 0.7 % [19]. Studies in the USA and abroad suggest that infection rates for the general population are similar and are estimated to range from approximately 0.7 to 2.25 % [13–16, 18–23]. It is unknown how many of these studies adjusted the numbers to include patients treated with a two-stage revision procedure. Generally, periprosthetic infections occur rarely but have a significant impact on morbidity and resource utilization. As the number of revisions continues to meet or exceed projected increases, infections will have an increased impact on the population of arthroplasty patients [13].

Infection can develop at various moments over the course of the lifetime of primary joint replacement implants and is not confined to the short period after surgery. Typically, time to infection diagnosis can range from 2 weeks postoperatively to over 3 years [15, 18, 19, 22, 24]. Nevertheless, understanding which periods most infections occur in is crucial to accurately enhancing future preventative measures. In a study of 9,245 patients in the USA, Pulido et al. reported that 27 % of infected TJA occurred within the first 30 days postoperatively while 65 % developed an infection within the first year postoperatively. The average time to diagnosis of infection was approximately 1.2 years [15]. In a retrospective analysis by Malinzak, 83.7 % of infections were diagnosed within 2 years with an average time to infection of 9.6 months [16]. For patients over 65 years of age in the US Medicare population, 73–77 % of all THA and TKA were diagnosed with infection within 2 years of primary surgery [17, 18]. Specifically for TKA, the incidence of infection was 1.55 % within 2 years, but dropped to 0.46 % between 2 and 10 years postoperatively [17]. In congruence with US data on TKA, the Finnish Arthroplasty Register reported that 68 % of patients operated on between 1997 and 2004 were diagnosed with PJI within the first year postoperatively [20, 21]. Suzuki et al. found that infection developed within 3 months in 65 % of primary TKA cases at a single institution in Japan [22]. The Norwegian Arthroplasty Register noted a median time to revision for infection with primary THA of 47 days (range 4–1,782 days) [19]. The incidence of revision due to infection increased rapidly in the first year after surgery but declined beyond 1 year in the patient population captured by the Australian Joint Replacement Registry [25]. Even though the sources of the data range in region and scope, the consensus shows that greater than 60 % of infections are detected within 1 year

Table 1.5 Incidence of infection within revisions

Country	Hip/knee	% of revisions	Time period	Source	Data source
USA	Hip	8.4	1990–2004	Kurtz et al. 2007 [53]	NIS
USA	Hip	14.8	2005–2006	Bozic et al. [27]	NIS
Australia	Hip	8.2	2010	National Arthroplasty Registry [25]	Registry
Norway	Hip	15–20	2009	National Arthroplasty Registry [28]	Registry
Sweden	Hip	10.8	2008	National Arthroplasty Registry [30]	Registry
USA	Knee	16.7	1990–2004	Kurtz et al. 2007 [53]	NIS
USA	Knee	25.2	2005–2006	Bozic et al. [26]	NIS
Australia	Knee	15.4	2010	National Arthroplasty Registry [25]	Registry
Sweden	Knee	~20	2011	National Arthroplasty Registry [30]	Registry

of surgery and an overwhelming majority is diagnosed by 2 years post-primary THA or TKA.

A recent analysis of NIS data from 2005 and 2006 revealed that infection is the third most frequent reason for revision of THA, accounting for 14.8 % of revisions and the most frequent for TKA with 25.2 % of revisions (Table 1.5) [26, 27]. Infection was also the most common indication for arthrotomy and removal of prosthesis for either THA (74.3 %) or TKA (79.1 %). Following similar trends, the Australian National Joint Replacement Registry 2010 annual report indicated infection as the third most prevalent reason for revision of THA (15.4 %) and the second most for TKA (17.1 %) [25]. Similarly, 15–20 % of THA revisions in Norway from 2007 to 2010 were due to infection [28] and 17 % of THA in Sweden in 2008 were due to infection [29]. An estimated 20 % of TKA revisions were caused by infection in the Swedish population in 2001 [30]. However, compared to other reasons for revision in Sweden, the frequency of infection reduced from 25.9 % during the first 2 years postoperatively to 2.9 % within10 years.

When the focus of the analysis is narrowed to revised ultra-high molecular weight polyethylene hip cup liners, similar trends are observed. In a study of 212 revised acetabular liners, the most frequent reason for revision was loosening (35 %), followed by instability (28 %) and infection (21 %) [24]. Infection was preceded by aseptic loosening as a more frequent cause of revision in almost all studies and data sources sampled. The one exception in the literature was a study by Bozic et al. which reported infection as an overwhelmingly more frequent reason for revision of TKA (25.2 %) than loosening (16.1 %) [26]. Recently, many experts suggest that the infection rates are masked by various clinical circumstances and in some cases of aseptic loosening and poor fixation, subclinical infections are the real cause [31–33]. Septic loosening was suspected when bacteria were recovered from aseptically loose implants by more vigorous methods for detecting surface bacteria, such as polymerase chain reaction assays and implant sonication [31–33]. If antibiotics are administered before the retrieval of diagnostic samples, there is also an increased probability of missing the infection [34]. With improved diagnostic techniques for detecting infected arthroplasty components, infection could become the primary cause of revision surgery. However, even without new diagnostic methods, PJI has the potential to become the most prevalent implant failure mode for TJA procedures in the USA and abroad within the next 2 decades.

Infection following a primary arthroplasty procedure is already a taxing ordeal because of pain, increased hospital stay, and the two-stage exchange process. Nevertheless, infection is additionally associated with higher reinfection rates [20, 35–37]. Revised TKA, regardless of revision reasons, is linked to lower infection-free survival rates than primary procedures and has an infection rate of approximately 8.25 % [20]. TKA devices specifically revised for infection have increased infection rates ranging from 10 to 33 % [35–37]. Many studies on reinfection suffer from small cohort sizes, which may explain the variability in infection rates. The largest study thus far was conducted at the Mayo clinic and focused on 368 patients who had TKA revised for infection between 1998 and 2006 [35]. 15.8 % of

the patients developed reinfection and 86 % of cases were categorized as late chronic infections. The median time to reinfection was 3.6 years (range: 0.01–7.82 years) and the only significant risk factor associated with reinfection was chronic lymphedema [35]. The findings fall in the ranges previously reported for reinfection and highlight the long-term effects of developing device-related infections.

Risk Factors Associated with PJI

In the literature, numerous patient, social, and surgery-related risk factors have been associated with PJI, ranging from sex to allogenic blood transfusion (Table 1.6) [9, 11, 15–22, 38–40]. Earlier in this chapter TKA was shown to be associated with minor but significantly higher infection rates than THA [13, 15, 16]; and for both procedures, the most commonly reported risk factor was gender. In eight studies reviewing risk factors for infection in multiple international registries and individual institutions, males were at higher risk than their female counterparts [9, 17–22, 29, 30, 41]. A 2010 report from the Australian Hip and Knee Registry found that at 9 years postoperatively, the cumulative incidence of infection was 1.3 % for males and only 0.6 % for females [25]. After a retrospective review of 2,022 primary TKAs, Suzuki et al. suggested the difference in infection rates could be due to differences between sexes in the pH level of the skin, sebum induction, and skin thickness [22]. In contrast, Dale et al. proposed that the disparities between sexes could be caused by differences in referral thresholds or bacterial flora [19]. However, definitive reasons for the differing infection rates remain unknown.

Elevated body mass index (BMI) is frequently reported as a risk factor for PJI [15, 16, 18, 22, 38, 39]. In a retrospective study of 6,108 THA and TKA patients by Malinzak et al., BMI greater than 50 was associated with an infection rate of 7.0 %, BMI greater than 40 but less than 50 was 1.1 %, and less than 40 was 0.47 %. When limited to TKA patients, BMI over 40 was 3.3 times more likely to lead to an infection when compared to BMI less than 40. In a similar analysis, Jämsen et al. reviewed 8,775 primary THA and TKA procedures recorded in the Finnish Joint Register that were performed between 2002 and 2008 [40]. Overall infection rates increased from 0.37 % in patients with normal BMI to 4.66 % in the morbidly obese. Obesity, however, was not a predictor of PJI if the BMI of the patient was below 40 kg/m^2 [40]. The underlying mechanisms for the increased infection rate may be linked to greater technical difficulty, longer duration of the procedure, poorly vascularized fatty tissue, and associated comorbidities in this elevated-BMI population [40].

Increased BMI could be compounded by diabetes, which has long been known as another risk factor for PJI [16, 18, 42, 43]. Diabetes has been shown to have a high correlation with PJI, in addition to elevating glucose levels postoperatively [16]. Jämsen et al. discovered that infection occurred in 1.59 % of THA and 2.19 % of TKA patients previously diagnosed with diabetes, while infection rates in nondiabetic patients were 0.66 % and 0.48 %, respectively [40]. Jamsen et al. found a correlation between elevated preoperative glucose levels and increased infection rate in obese patients. Patients with uncontrolled diabetes are potentially the population of arthroplasty patients with the poorest glycemic control, which directly influences their risk of infection [42]. However, a review of 751,340 primary and revision THA and TKA by Bolognesi et al. revealed no increase in the rate of infections in

Table 1.6 Risk factors commonly associated with PJI summarized from the literature [15, 16, 18, 22, 38, 39]

Patient-related risk factors	Social and surgery-related risk factors
Male gender	Larger, urban nonteaching hospitals
Higher BMI/obesity	Patients receive public assistance
Age	Longer-duration procedures
Preexisting comorbidities	Increased blood loss
Urinary tract infection	Allogenic blood transfusion
Rheumatoid arthritis	Lack of antibiotic cement
Diabetes	Revision TKA
Preoperative nutritional status	Emergency vs. planned surgery
ASA risk score > 2	Previous open reduction/ internal fixation
	Postoperative complications

the diabetic patient population [16, 18, 42, 43]. Patient management of the disease may also explain the discrepancy between the findings of these studies. Marchant et al. retrospectively compared hospitalizations from 1998 to 2005 from the NIS database with controlled and uncontrolled diabetes mellitus and found that there is a much higher chance of developing a wound infection when diabetes is inadequately controlled (odds ratio: 2.28) [42].

Other comorbidities amplify a patient's risk for PJI after TJA. The American Society of Anesthesiologists (ASA) physical status classification system assesses the physical state of a patient prior to surgery. In the literature, ASA scores greater than two have been identified as a risk factor for PJI, which signifies that the incidence of infection increases with even minor comorbidities [15, 19, 21]. Preexisting comorbidities have been previously connected to poor functional outcomes and other complications postoperatively. Ong et al. and Kurtz et al. identified several comorbidities as one of the primary risk factors for increased incidence of PJI as measured by the modified Charlson Index [17, 18]. Additionally, postoperative complications, previously linked to patient comorbidities prior to surgery, were also a risk factor for PJI [11, 20].

Rheumatoid arthritis (RA), as compared to osteoarthritis (OA), was also found to be a significant risk factor for infection by both the Norwegian and the Finnish Arthroplasty Registers [20, 21, 28]. A study of 2,647 patients reported an incidence of infection of 2.45 % for RA and 0.82 % for OA from 2002 to 2006 [21]. Other noted, but less prominent, risk factors for PJI mentioned in the literature were increased blood loss [11], elderly patients [19], emergency vs. planned surgery [19], revision TKA [20], race [9], previous open reduction or fixation surgery [22], nutritional status [44], urinary tract infection [15], and allogenic blood transfusion (Table 1.6) [15].

Multiple studies utilized the Charlson Comorbidity Index (CCI) to identify the presence of patient comorbidities in various databases and institutions, including the Medicare administrative claims database [9, 11, 15–22, 38, 39]. Studies by Kurtz et al. and Ong et al. identified preexisting comorbidities, longer-duration procedure, receiving public assistance for premiums, and male sex as risk factors for PJI in the Medicare population [17, 18]. The CCI evaluated preexisting conditions based on one composite score for 19 comorbid conditions; thus, patients with different combinations of preexisting conditions may still have the same CCI score.

Bozic et al. proposed that the CCI does not have the specificity to define the impact of individual diseases on patient outcomes, especially in elderly populations [45, 46]. Bozic et al. used the 5 % national sample of the Medicare database to detect associations between infection and specific preexisting medical comorbid conditions for either THA or TKA patients. A multivariate Cox regression was used to evaluate the link between infection and 29 distinct comorbidities. After adjusting for the effects of all 29 comorbidities, 13 conditions showed a significant effect on risk of infection following TKA. In order of significance for their impact on the outcome of TKA, the conditions with the highest risk of PJI were congestive heart failure, chronic pulmonary disease, preoperative anemia, and diabetes (Table 1.7) [45]. For THA, the highest attributable risk was associated with rheumatologic disease, obesity, coagulopathy, preoperative anemia, congestive heart failure, and diabetes (Table 1.7) [46]. The 5 % Medicare sample, compared to other databases, allowed for the identification of specific disorders as risk factors for infection. The focus of this research was to provide a basis for superior clinical decision-making in populations of patients aged 65 and above [45].

There are also several social and surgical risk factors for PJI. Public assistance is also associated with higher risk of infection [13, 17, 18, 47]. Ong et al. suggest that public assistance is an indication of socioeconomic status, which could indicate nutritional level, obesity, and existence of comorbidities that would predispose patients for higher risk of PJI [18]. Revision infection rates of primary TKA were also higher at large nonteaching urban hospitals as opposed to rural and teaching institutions [13, 26]. It is more likely a reflection of treatment patterns for revision surgery where urban nonteaching hospitals are often referral centers for revision (including