26° Congresso Nazionale della Società Italiana di Chemioterapia
Salerno 1-3 dicembre 2011

Epidemiology and microbiology of prosthetic joint infections

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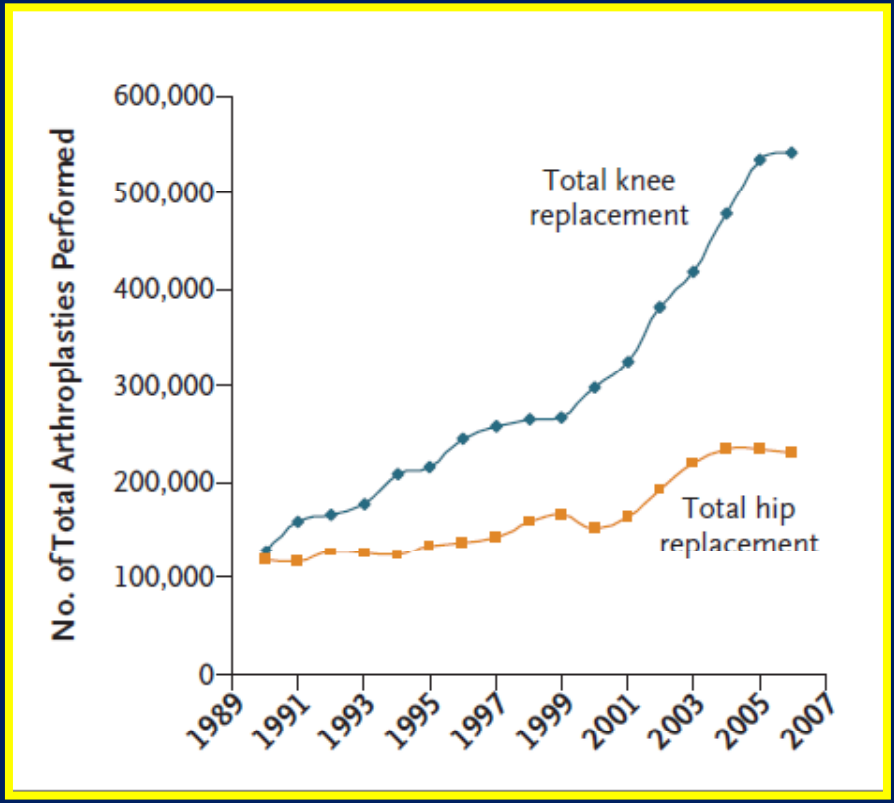
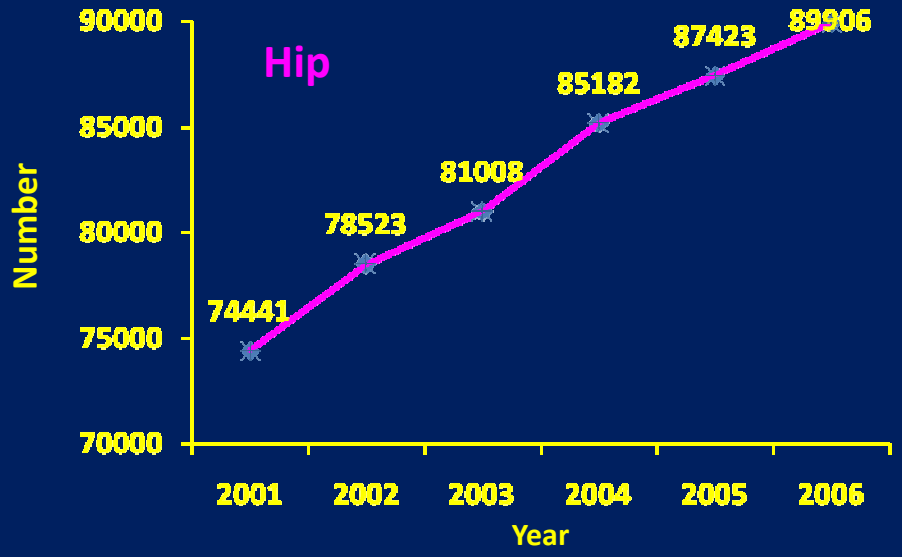
Total arthroplasties performed in the United States*

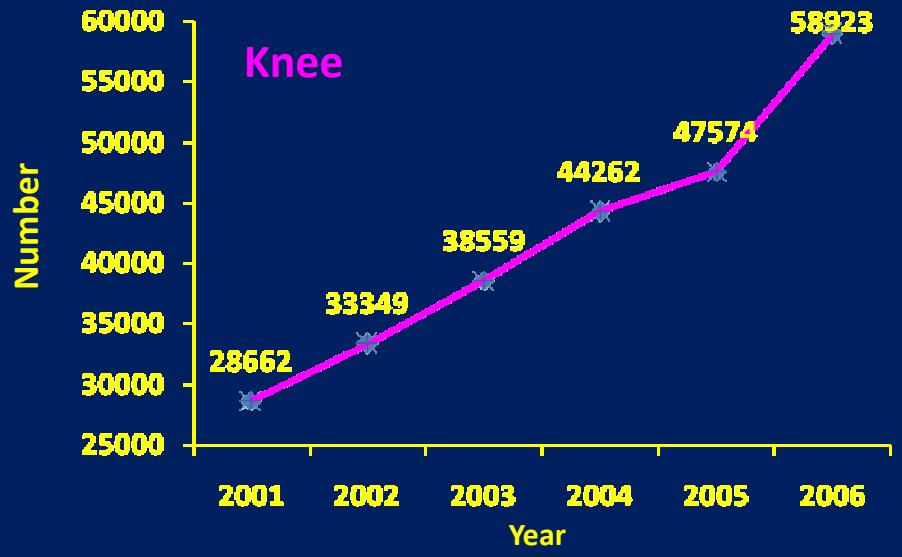


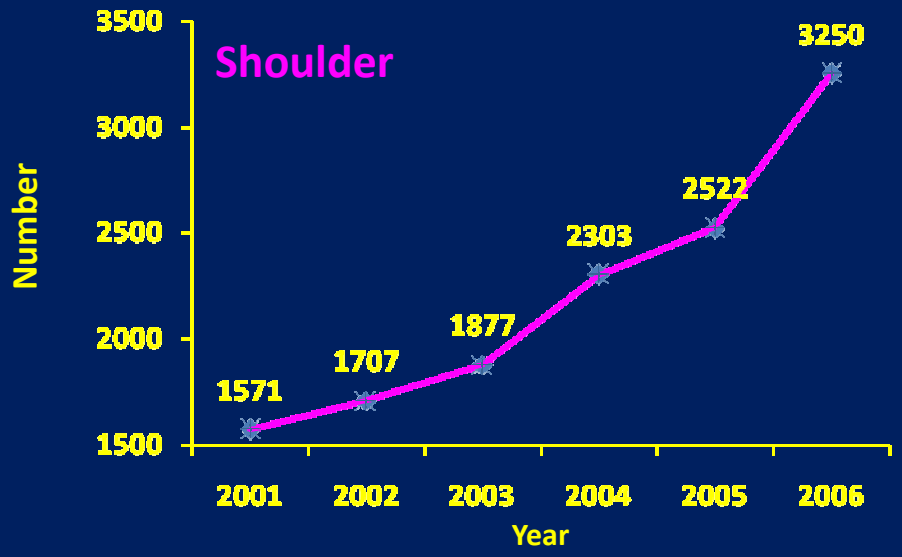
***Only primary THA and TKA**

Del Pozo JL, N Engl J Med 2009;361:787-94

Procedures performed in Italy (2001-2006)







Torre M, ISS 2009
Boggio L, Assobiomedica 2010

Total procedures performed in Italy in 2010

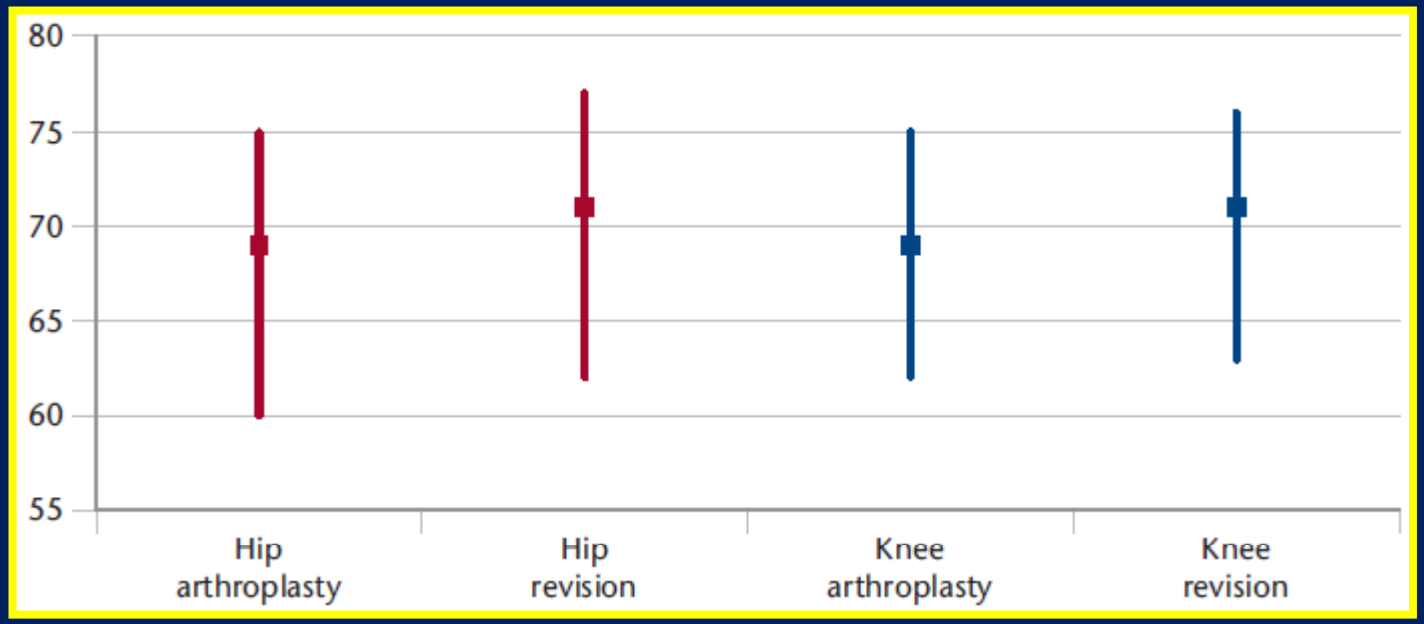
Anca	95.500	Cementate 30.000
Endoprotesi	16.000	Revisioni 4.500
Ginocchio pt	57.000	Revisioni 4.600
Ginocchio mono	6.500	
Spalla	4.000	
Caviglia	200	
Gomito	100	

Courtesy of Dr. Silvio Borrè - Infectious Diseases Division - Vercelli

Scottish arthroplasty project annual report 2010

arthroplasty procedures and their outcomes for patients operated on during 2009

Median age of arthroplasty patients

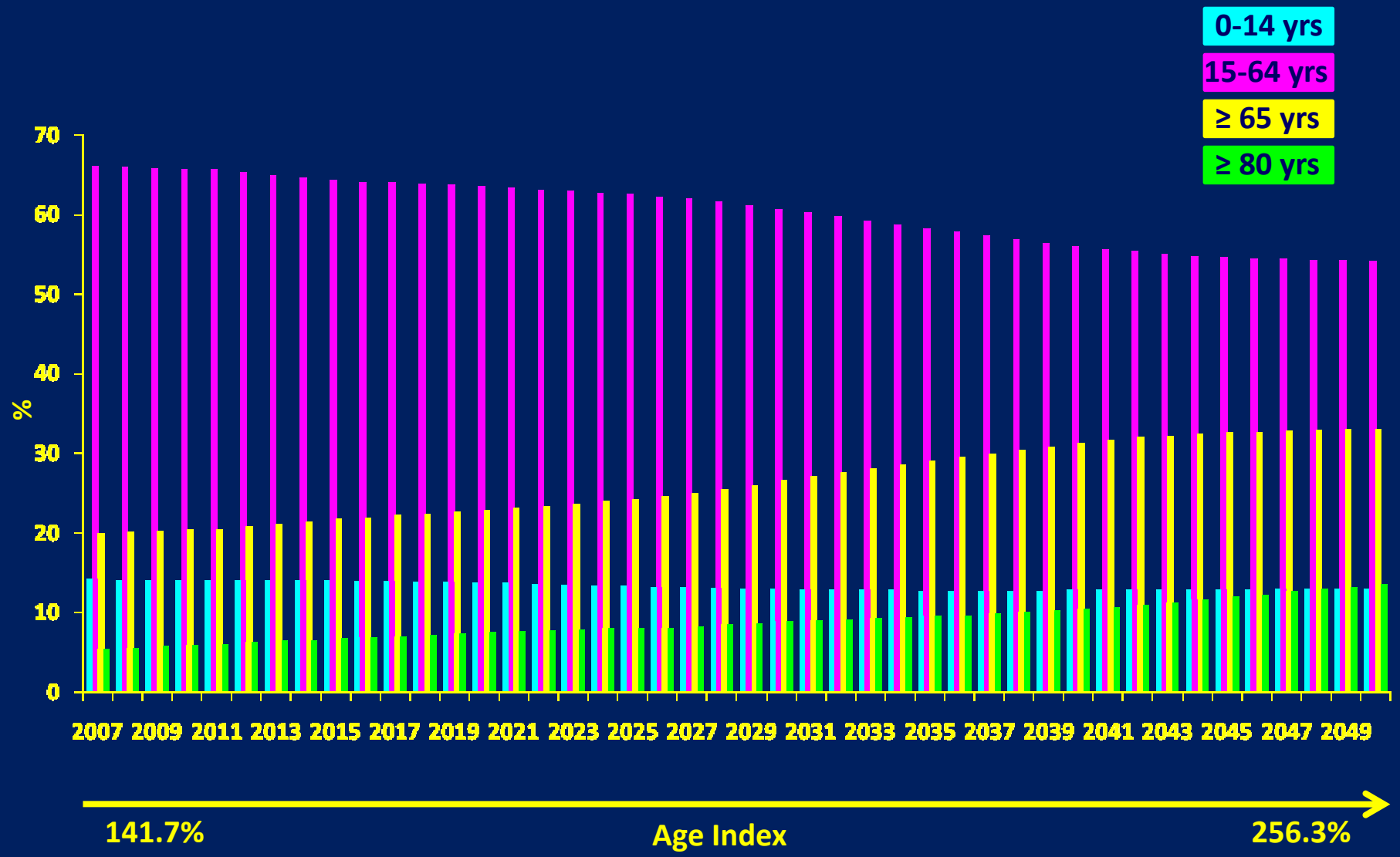


Elective patients only; bilateral operations included once; lines extend to show the IQR

In Italy for hip replacement only [mean]: total 68.8 yr, partial 81.8 yr, revision 70.8 yr.

www.arthro.scot.nhs.uk
Torre M, ISS 2009

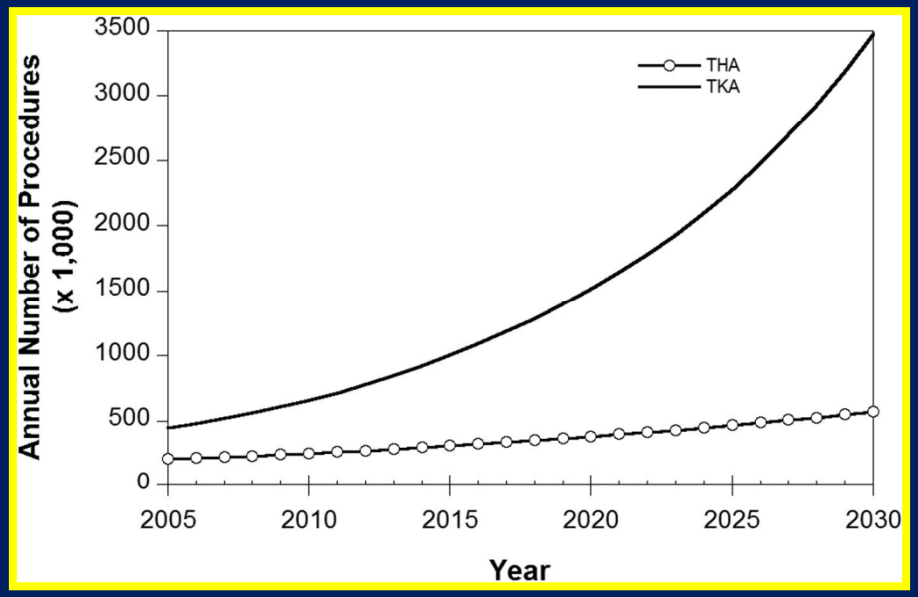
Projections of Age in Italy from 2007 to 2050



www.ISTAT.it

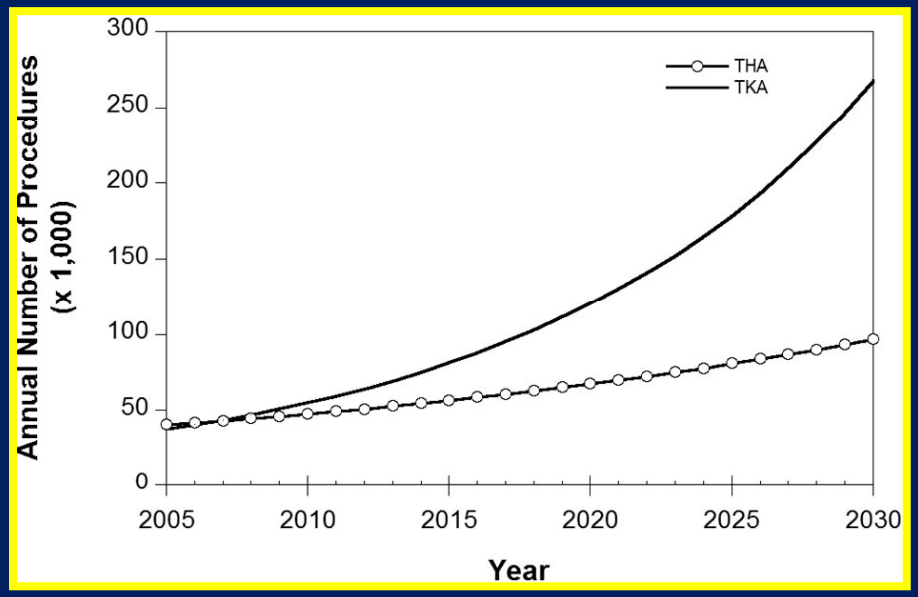
Projections of Primary and Revision Hip and Knee Arthroplasty in the US from 2005 to 2030

Primary THA and TKA



Overall, primary THA and TKA are projected to grow by 174% and 673%, respectively, between 2005 and 2030.

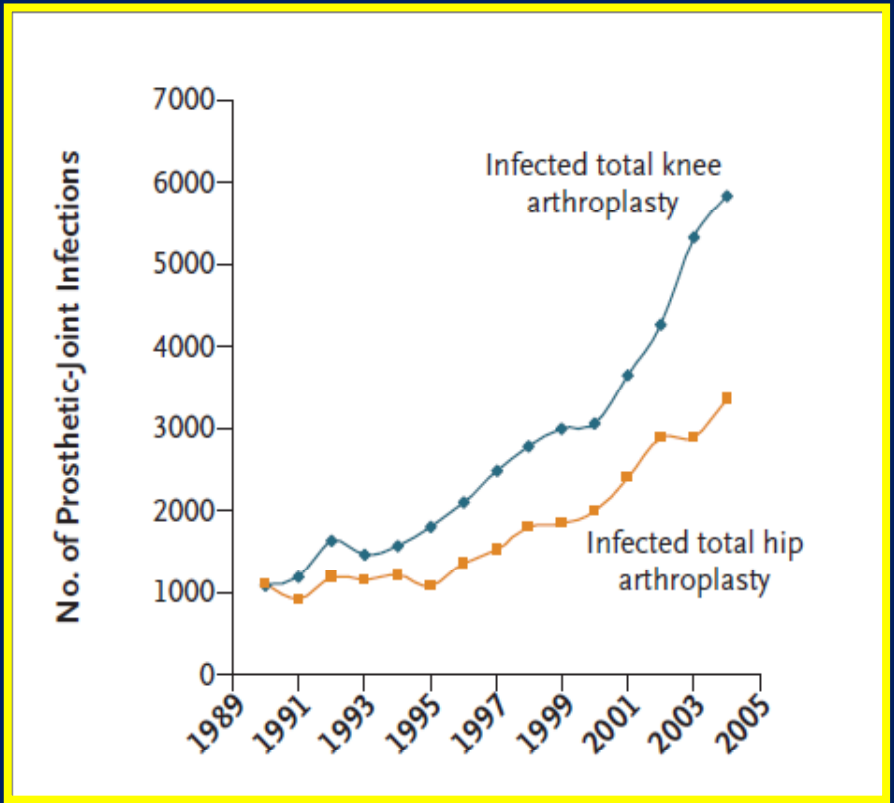
Revision THA and TKA



Overall, THA and TKA revisions are projected to grow by 137% and 601%, respectively, between 2005 and 2030.

Kurtz S et al., J Bone Joint Surg Am. 2007;89:780-5

Prosthetic infections according to procedure in the United States



- Between 1990 and 2004, a nearly 2-fold increase was observed in the incidence of infection for both hip (0.66 to 1.23) and knee (0.63 to 1.21).
- The increasing trend between infection burden and year was highly significant (*P<0.0001*) with the odds of infection increasing annually at a rate of close to 5% (OR, 1.05; 95% CI, 1.04-1.06).

Kurtz S et al., J Arthroplasty. 2008;23: 984-91
Del Pozo JL, N Engl J Med 2009;361:787-94

Rates of infection after first implantation and revision procedures

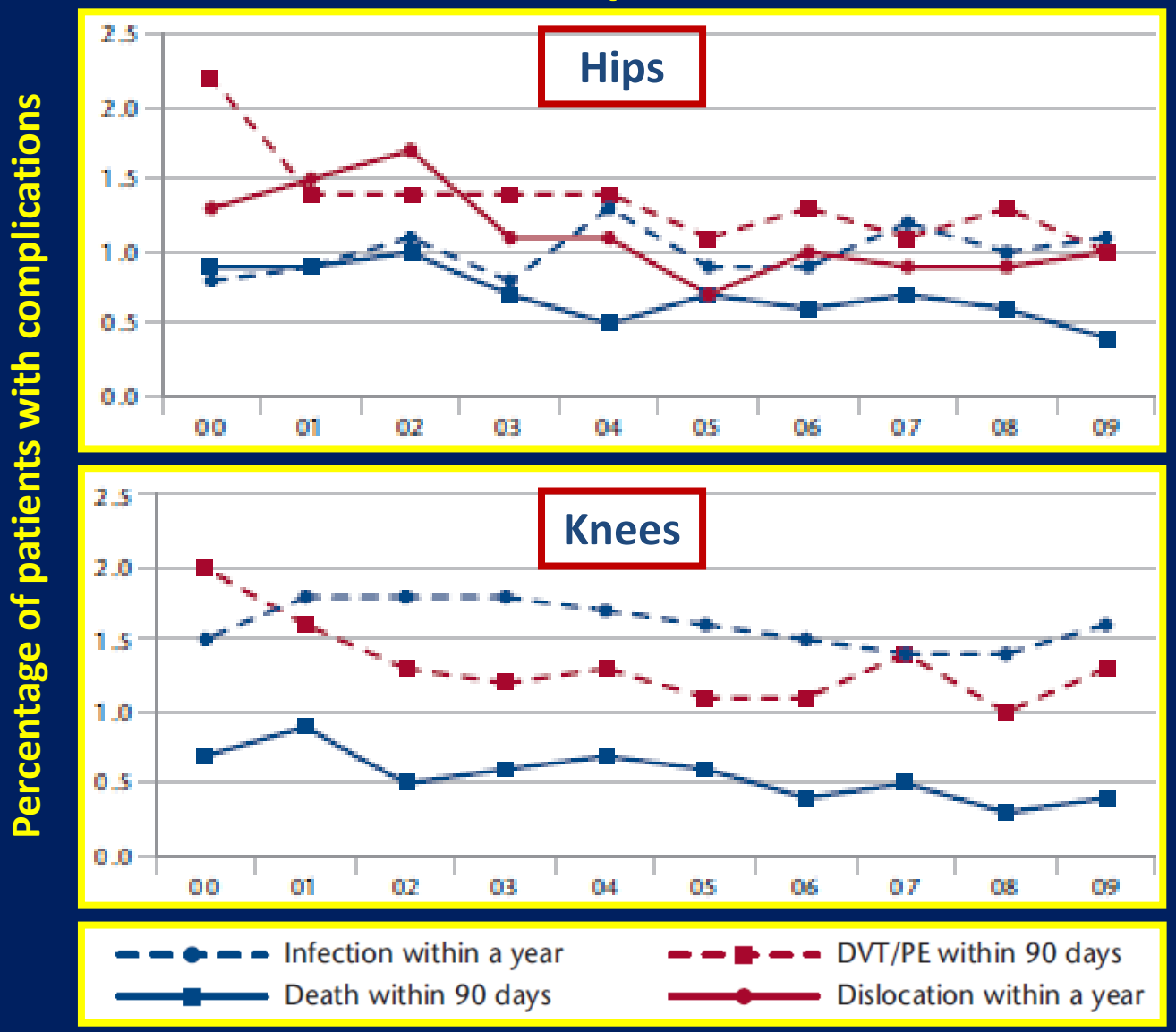
	Primary	Revision
hip arthroplasty	<1%	3%
knee arthroplasty	<2%	6%
shoulder arthroplasty	<2%	4%

The reported infection rates are probably underestimated, since many cases of presumed aseptic failure may be due to unrecognized infections.

Coste JS, J Bone Joint Surg Br 2004;86:65-69.
Zimmerli W, N Engl J Med 2004;351:1645-54.
Del Pozo JL, N Engl J Med 2009;361:787-94
Sampedro MF, Infect Dis Clin N Am 2007;21:785-819

Scottish arthroplasty project annual report 2010

National rates for complications, 2000 to 2009



www.arthro.scot.nhs.uk

Epidemiology of revision THA and TKA in the US

Causes of failure and specific types of revision THA & TKA procedures performed in the US using ICD-9-CM codes were analyzed (October 1, 2005 - December 31, 2006).

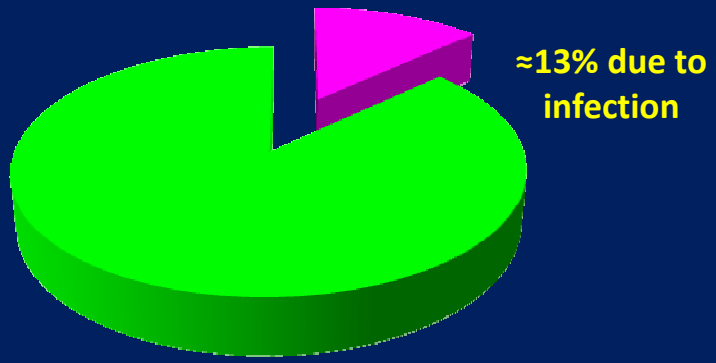
Diagnosis codes	revision THA procedures (N. 51.345 - mean age of 67.1 yrs)	revision TKA procedures (N. 60.355 - mean age of 65.8 yrs)
Mechanical loosening	19.7%	16.1%
Dislocation	22.5%	7.1%
Implant failure/breakage	9.9%	9.7%
Periprosthetic fracture	6.2%	1.5%
Periprosthetic osteolysis	6.6%	3.2%
Bearing surface wear	5.0%	4.9%
Other complication	14.1%	15,4%
Infection	14.8%	25.2%

Bozic KJ, J Bone Joint Surg Am 2009;91:128-33
Bozic KJ, Clin Orthop Relat Res 2010;468:45-51

National joint registry for England and Wales annual report 2011

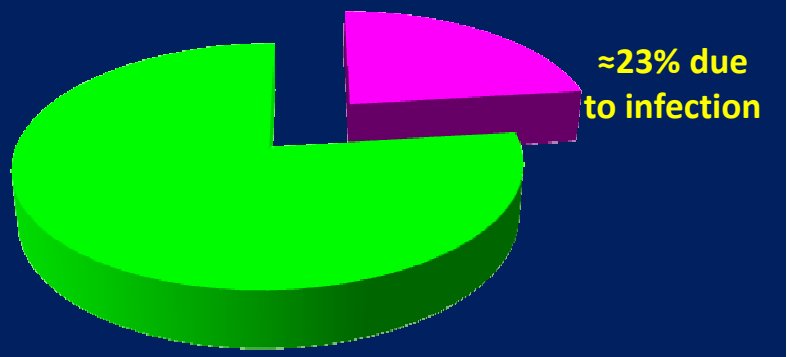
Hip (2010)

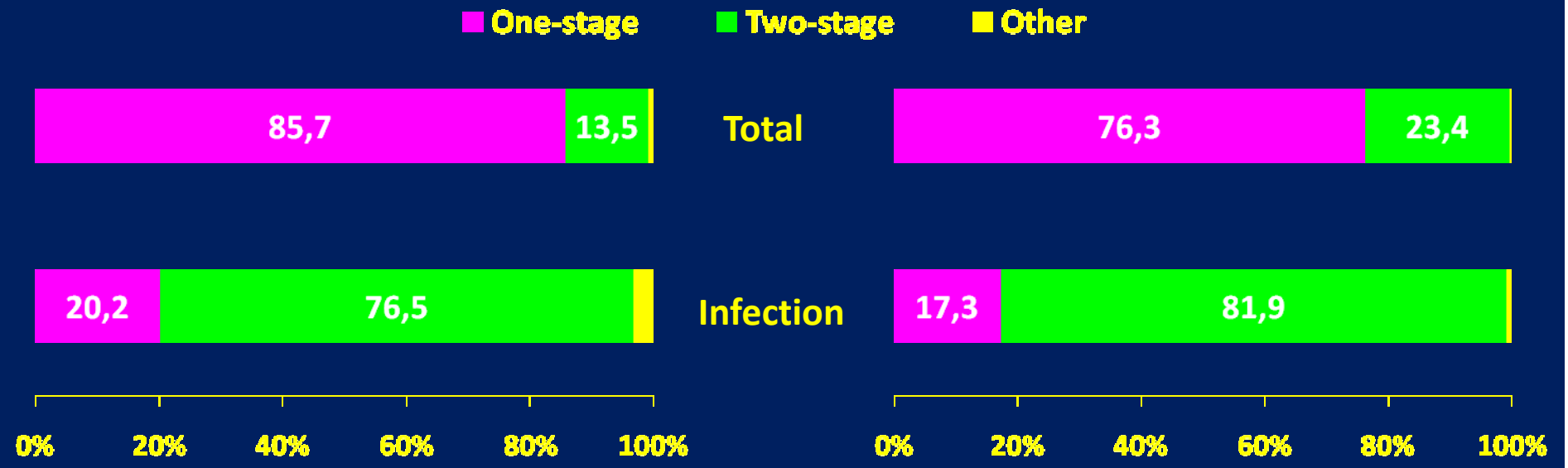
- 76.759 hip replacement procedures (+6%)
- 7.852 (10%) were revision surgeries



Knee (2010)

- 81.979 knee replacement procedures (+5.7%)
- 5.109 (6%) were revision surgeries





www.njrcentre.org.uk

Socio-economic burden of PJIs

- Higher costs (direct & indirect costs)
- Greater physical limitation
- Greater reduction in health-related quality of life

	Infected	Uninfected	*P value*
Length of stay	hip (9.7 days) knee (7.6 days)	hip (4.3 days) knee (3.9 days)	*<0.0001*
Hospitalization charges	hips 1.76 (95%CI, 1.74-1.77) times knee 1.52 (95%CI, 1.51-1.54) times		*<0.0001*

Kurtz S et al., J Arthroplasty. 2008;23: 984-91

Risk factors of prosthetic joint infection

- Rheumatoid arthritis
- Psoriasis
- Diabetes mellitus
- Malignancy
- Joint malignancy
- Obesity
- Poor nutritional status
- Extremely advanced age
- Tobacco abuse
- Immunosuppression
- Steroid therapy
- SSI
- Delayed healing
- ASA score ≥2
- Wound dehiscence
- Wound hematoma
- Wound drainage
- Longer surgical drain
- NNIS 1 or 2
- Prior joint arthroplasty
- Bacteraemia
- Postoperative UTI
- HIV
- Simultaneous bilateral arthroplasty
- Prolonged hospital stay
- Long operative time
- Allogeneic blood transfusion
- Prior native joint septic arthritis

Berbari EF, Clin Infect Dis 1998;27:1247-54; Choong PF, Acta Orthop 2007;78:755-65; Del Pozo JL, N Engl J Med 2009;361:787-94; Esposito S, Infection 2009;37:478-96; Putido L, Clin Orthop Relat Res 2008; 466:1710-15; Jamsen E, J Bone Joint Surg Am 2009;91:38-47; Zimmerli W, N Engl J Med 2004;351:1645-54.

Risk factors of PJI: case-control study at Mayo Clinic (Rochester, MN)

Significant risk factors in a multivariate analysis of risk factor for PJI in 462 cases with PJI and their matched controls.

Risk factor	Matched OR (95% CI)	*P* value
Postoperative surgical site infection	35.9 (8.3–154.6)	≤.01
NNIS System surgical patient risk index score		
1 vs. 0	1.7 (1.2–2.3)	≤.05
2 vs. 0	3.9 (2.0–7.5)	≤.01
Systemic malignancy	3.1 (1.3–7.2)	≤.01
Prior joint arthroplasty	2.0 (1.4–3.0)	≤.01

Berbari EF, Clin Infect Dis 1998;27:1247-1254

Risk factors for prosthetic hip and knee infections according to arthroplasty site

Between 1 January 2000 and 31 January 2007 at a single hospital in Australia, 63 patients developed a PJI (36 hips & 27 knees). Cases of prosthetic hip or knee joint infection were matched 1:2 to controls.

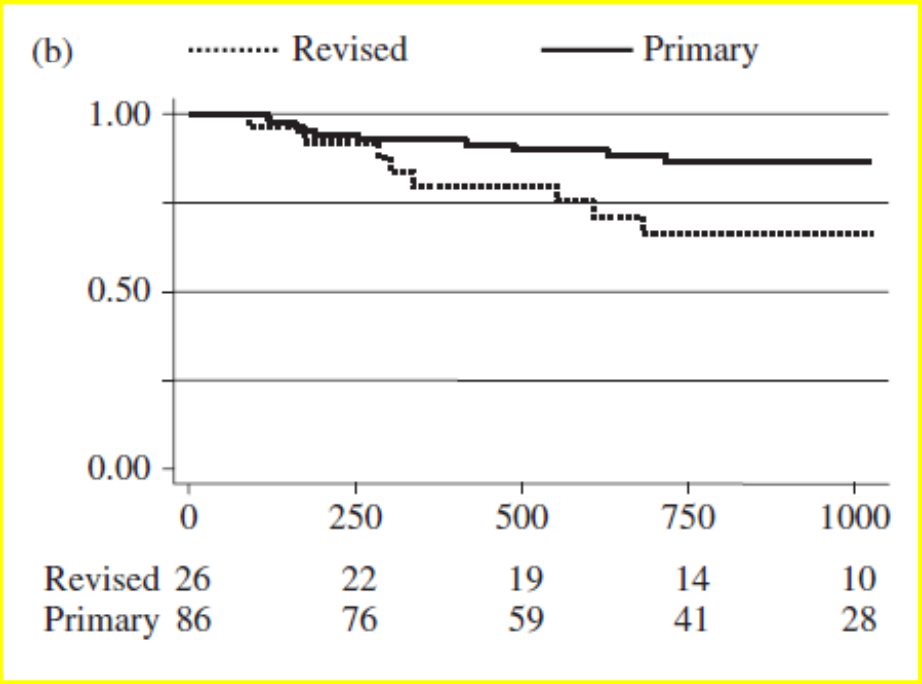
Variable	Cases ($N=63$)	Controls ($N=126$)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
ASA score[a]	2.7 (0.6)	2.4 (0.5)	2.2 (1.3–4.0)	0.006		
Skin–skin time (min)[b]	115 (95–130)	105 (95–120)	1.0 (0.9–1.0)	0.1		
BMI[a]	32.4 (7.2)	30.4 (6.2)	1.0 (0.9–1.1)	0.05		
Blood transfusion	25 (39.7%)	29 (23.0%)	2.1 (1.0–4.2)	0.04		
Drain tube	51 (81.0%)	110 (87.5%)	0.6 (0.2–1.4)	0.2		
Loss via drain tube (mL)[b]	450 (270–700)	292.5 (120–575)	1.001 (1.00003–1.002)	0.05	1.001 (1.00005–1.002)	0.04
IDC days[a]	2 (2–2)	2 (2–2)	0.9 (0.6–1.2)	0.4		
Superficial incisional SSI	22 (34.9%)	15 (11.9%)	4.3 (1.9–9.9)	0.001	3.9 (1.5–10.3)	0.006
Wound discharge	24 (38.1%)	13 (10.3%)	5.7 (2.4–13.3)	<0.001	2.7 (1.1–6.8)	0.03
Diabetes mellitus	19 (30.0%)	23 (18.3%)	1.4 (0.9–2.1)	0.06		
Rheumatoid arthritis	5 (7.9%)	3 (2.4%)	3.3 (0.8–13.9)	0.09		
Systemic steroid therapy	5 (7.9%)	3 (2.4%)	3.3 (0.8–13.9)	0.09	16.3 (1.2–227.7)	0.04
Renal function (mL/min)[b]	67.5 (50–86)	62.5 (50–76)	1.0 (0.9–1.0)	0.1		

OR, odds ratio; CI, confidence interval; ASA, American Society of Anesthesiologists; BMI, body mass index; IDC, indwelling urinary catheter; SSI, surgical site infection.
[a] Mean (standard deviation).
[b] Median (interquartile range).

Peel TN, J Hosp Infect 2011;79:129-133

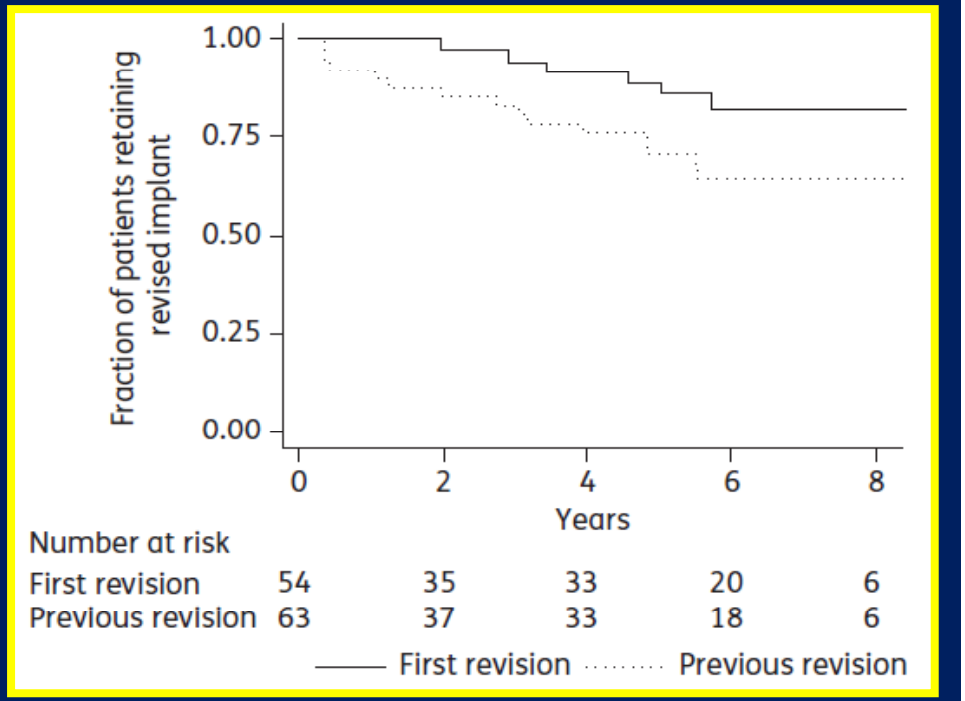
Kaplan-Meier plots for time to failure by primary versus previously revised implant

Cases managed with DAIR



Previously revised joints were associated with a significant risk of treatment failure (HR=3.1, 95% CI=1.2-8.3, *P=0.008*).

Cases managed with two-stage revision



Previously revised joints were associated with a significant risk of treatment failure (HR=2.9, 95% CI=1.2-7.4, *P=0.023*).

Byren I, J Antimicrob Chemother 2009;63:1264-71
Bejon P, J Antimicrob Chemother 2010;65:569-75

Dental procedures as risk factors for PJI: a case-control study

Analysis of dental procedures performed within 6 months and within 2 years of hospital admission and risk of PJI among case patients and control subjects

Variable	Case patients (n = 303)[a]	Control subjects (n = 318)[a]	Odds ratio (95% confidence interval)[b] 6 Months	P	2 Years	P
Low-risk dental procedure[c]						
Any	192 (57)	161 (47)	1.0 (Reference)		1.0 (Reference)	
Edentulous	47 (14)	26 (8)	1.8 (0.9–3.7)	.10	1.7 (0.8–3.4)	.16
Low-risk procedure without antibiotic prophylaxis	41 (12)	65 (19)	1.1 (0.6–2.1)	.77	0.6 (0.4–1.1)	.11
Low-risk procedure with antibiotic prophylaxis	59 (17)	87 (26)	0.7 (0.3–1.5)	.33	0.8 (0.5–1.2)	.29
High-risk dental procedure[d]	164 (48)	116 (34)	1.0 (Reference)		1.0 (Reference)	
Edentulous	47 (14)	26 (8)	1.7 (0.9–3.5)	.13	1.7 (0.8–3.4)	.16
High-risk procedure, without antibiotic prophylaxis	33 (10)	49 (14)	0.8 (0.4–1.7)	.60	0.8 (0.4–1.6)	.56
High-risk procedure, with antibiotic prophylaxis	95 (28)	148 (44)	0.5 (0.3–0.9	.01	0.7 (0.5–1.1)	.14

Low-risk dental procedures include restorative dentistry, dental filing, endodontic treatment, and fluoride treatment. High-risk dental procedures include dental hygiene, mouth surgery, periodontal treatment, dental extraction, and therapy for dental abscess.

Berbari EF, Clin Infect Dis 2010;50:8-16

Classification of prosthetic joint infections

Category	Early	Delayed	Late
Presenting after surgery	<3 months	3 to 24 months	>24 months
Acquisition	During implantation	During implantation	Haematogenous*
Aetiology	Virulent microorganisms *eg.: S. aureus*, GNB, *Streptococcus* spp	Less virulent microorganisms: CoNS and *P. acnes*	*S. aureus*, CoNS, GNB, *Streptococcus* spp, other bacteria and fungi

*The most frequent sources of bacteremia are skin, respiratory tract, and urinary tract infections.

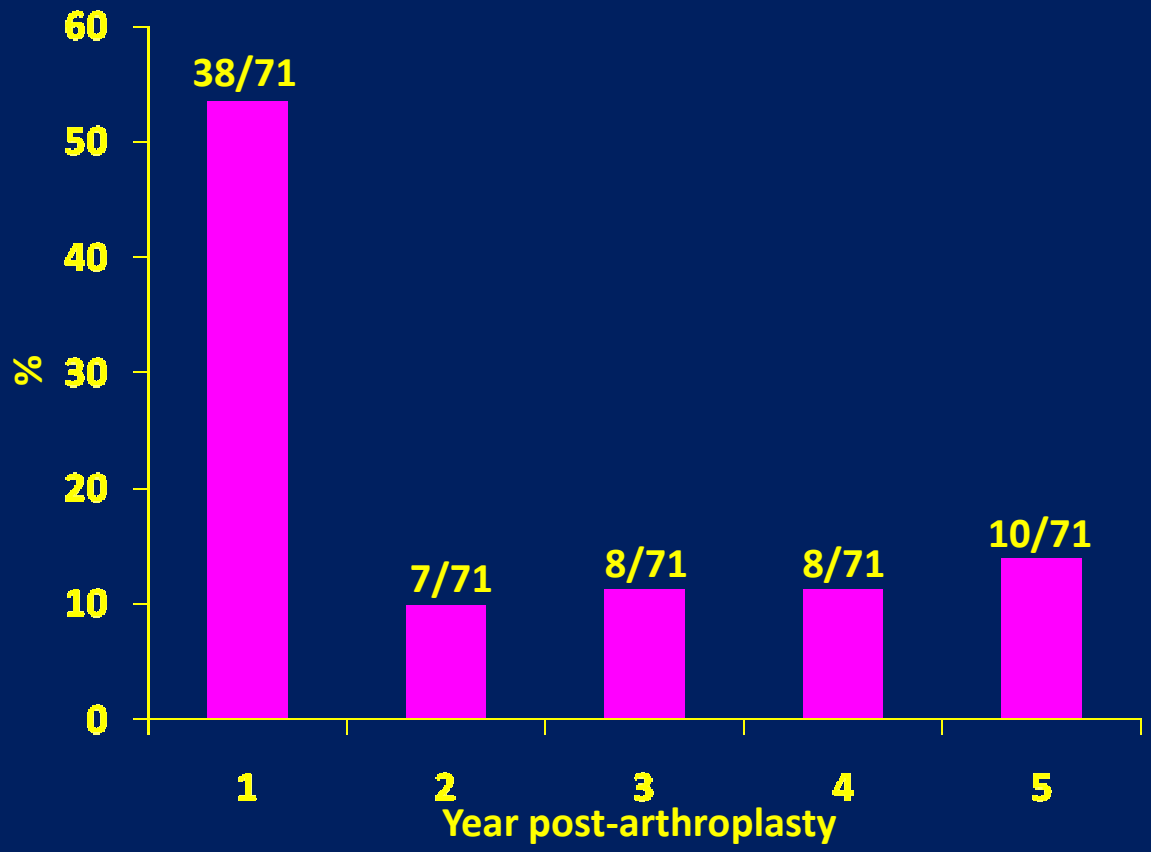
Zimmerli W et al., N Engl J Med 2004;351:1645-54

Probability of infection as a function of the time that the prosthesis was in situ

6101 elective total joint arthroplasties (hip 4002 [66%] & knee 2099 [34%])

Mean FU, 70 months (range, 3-154)

71 (1.2%) PJIs (hip 46 & knee 25)



Uckay I, J Infect 2009;59:337-345

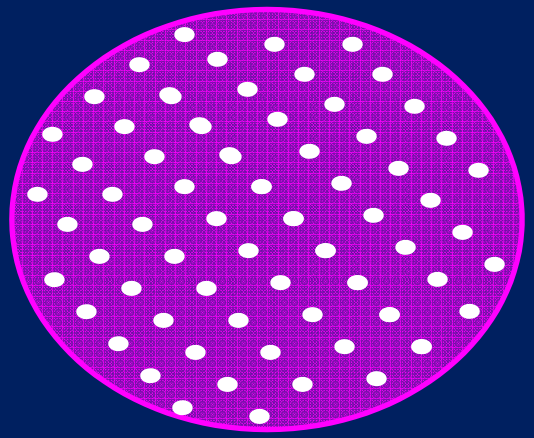
Haematogenous origin of PJIs among patients with remote infections

Author	N. of arthroplasties	% of infection	Method	Most important origin
Ainscow	1112	0.3% (3 of 1112)	Prospective	Skin
Schmalzried	3051	0.6% (19 of 3051)	Retrospective	Urinary tract
Cook	3013	0.5% (15 of 3013)	Retrospective	Lung
Uckay	6101	0.1% (7 of 6101)	Retrospective	Gastrointestinal

Ainscow DA, J Bone Joint Surg Br 1984;66:580-2.
Cook JL, J Knee Surg 2007;20:27-33.
Schmalzried TP, Clin Orthop Relat Res 1992;280:200-7.
Uckay I, J Infect 2009;59:337-345.

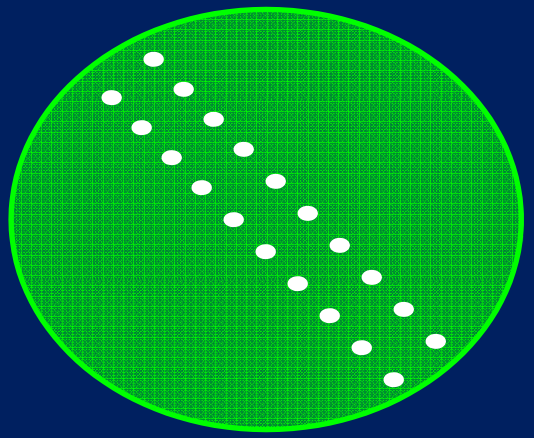
Pathogenesis of foreign body infection

Absence of implant



>100.000 colony-forming units of *S. aureus*

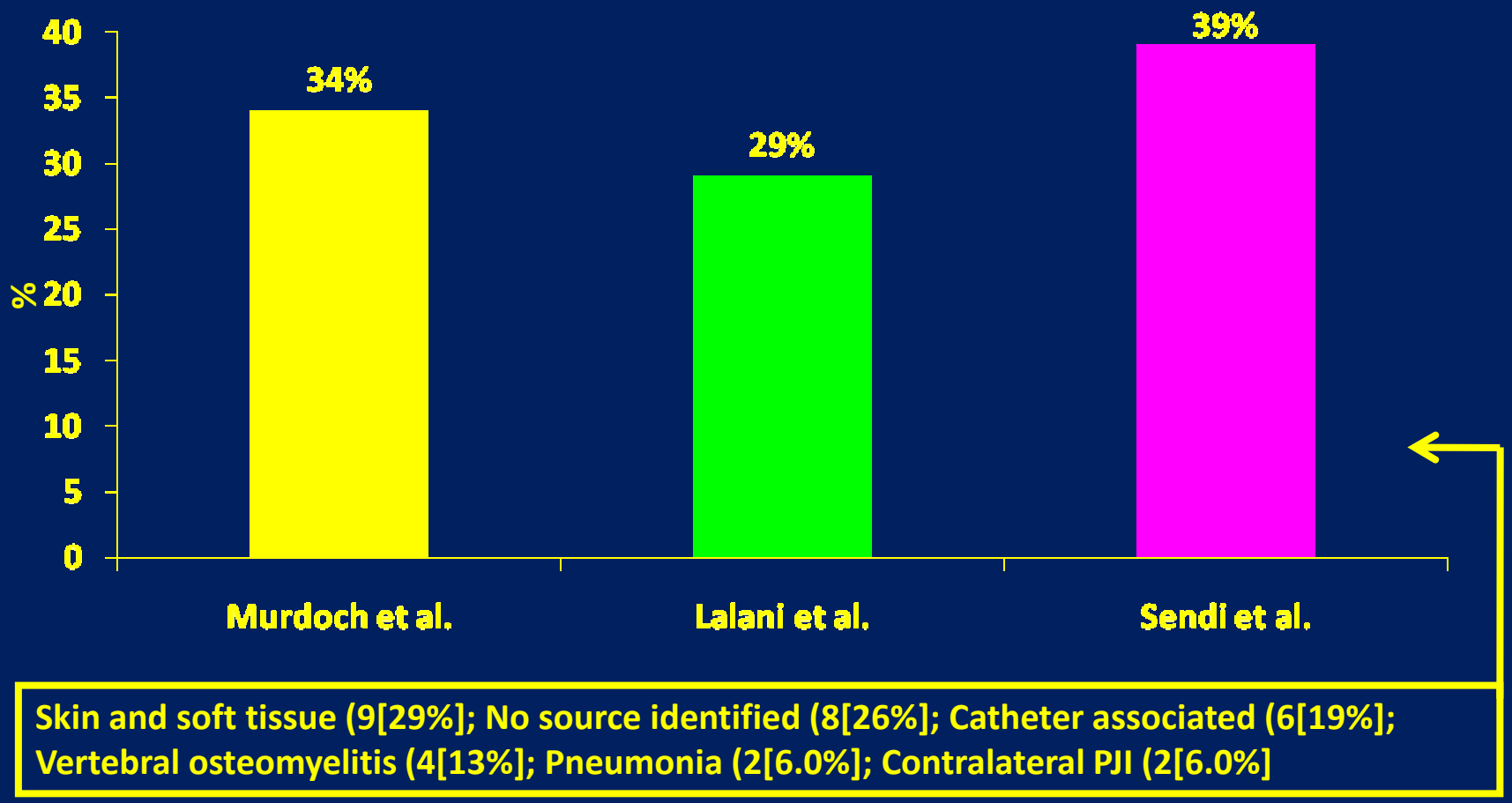
Presence of implant



100 colony-forming units of *S. aureus*

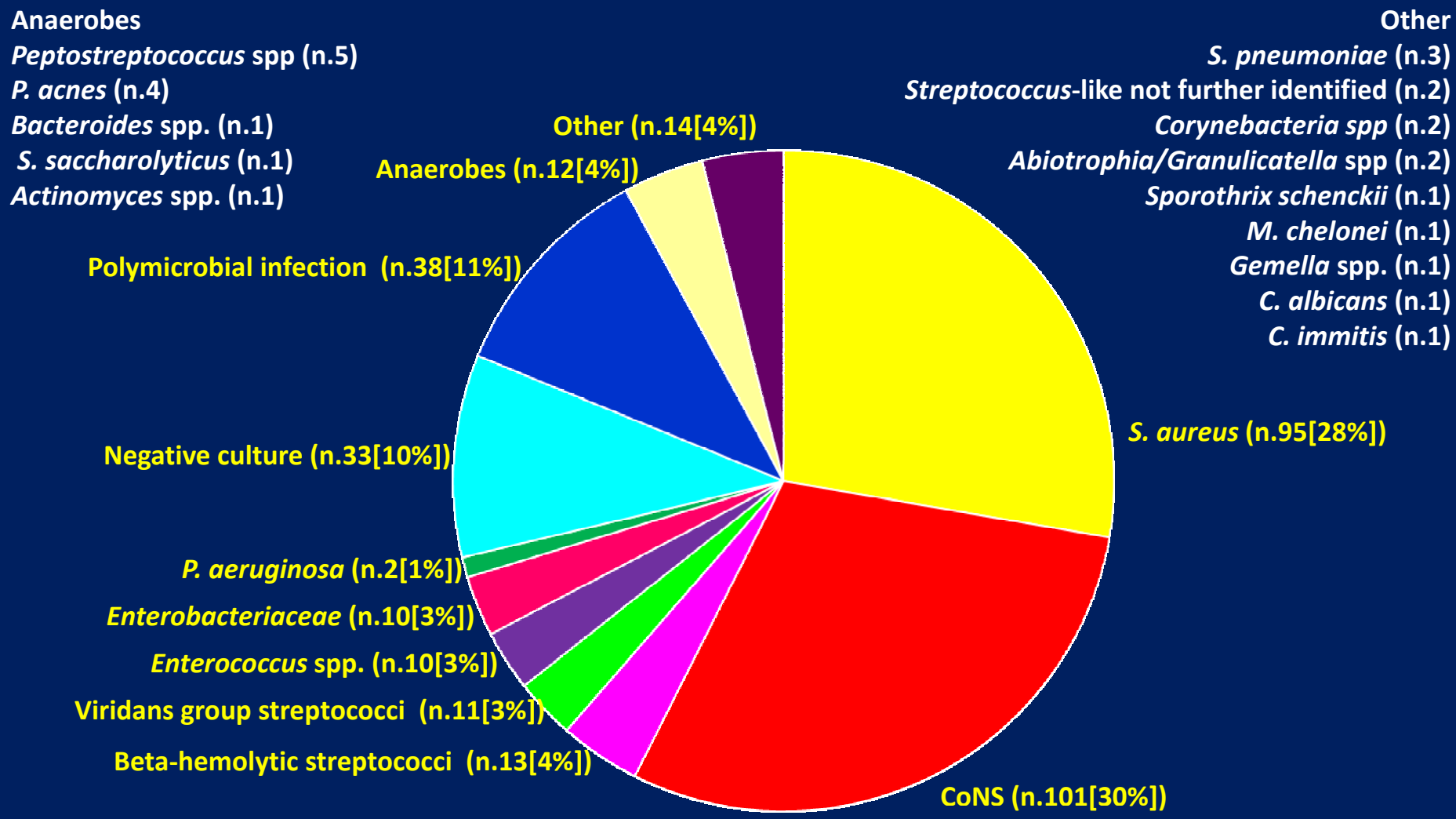
Zimmerli W et al., J Infect Dis 1982;146:487-97

Prosthetic joint infection following *S. aureus* bacteremia



Murdoch DR et al., Clin Infect Dis 2001;32:647-9
Lalani T et al., Scand J Infect Dis 2008;40:973-7
Sendi P et al., J Infect 2011;63:17-22

Microbiological findings for 339 case patients with prosthetic hip or knee infection at the Mayo Clinic (Rochester, MN), 2001-2006



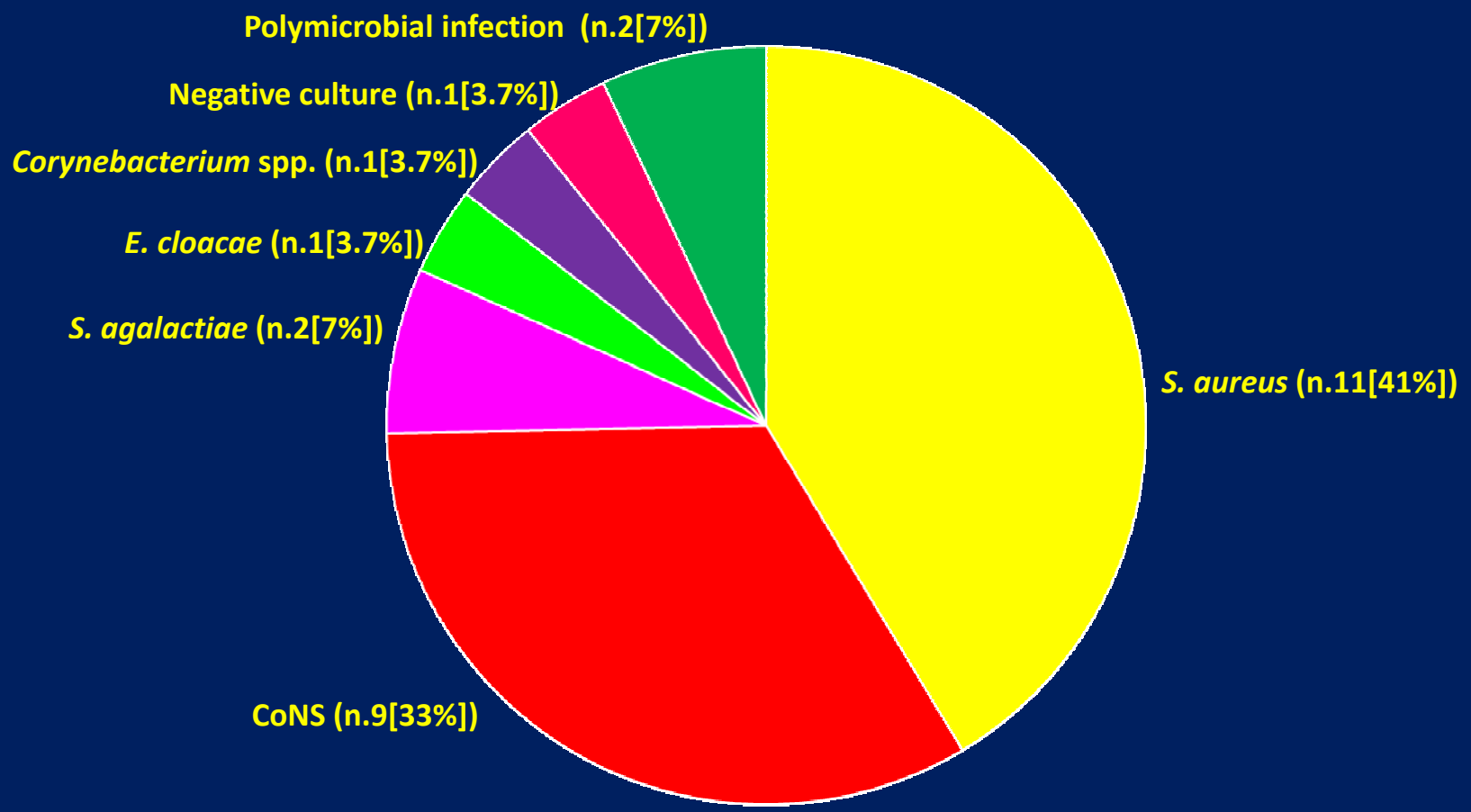
Berbari EF, Clin Infect Dis 2010;50:8-16

Microbiological characteristics of PJI in three hospitals in Switzerland

	Betsch *et al.* Hip & Knee (N.68) *(Bern)*	Giulieri, *et al.* Hip (N.63) *(Liestal)*	Laffer *et al.* Knee (N.40) *(Basel)*
Coagulase-negative staphylococci	9 (13.2%)	11 (17.5%)	9 (21.4%)
Staphylococcus aureus	26 (38.2%)	27 (42.8%)	14 (33.3%)
Streptococcus species	11 (16.2)	7 (11.1%)	6 (15.0%)
Enterococcus species	2 (2.9%)	2 (3.2%)	3 (7.1%)
Gram-negative bacilli	2 (2.9%)	3 (4.8%)	6 (15.0%)
Anaerobes	2 (2.9%)	1 (1.6%)	2 (4.8%)
Polymicrobial	15 (22.0%)	8 (12.7%)	2 (5.0)%
Culture negative	1 (1.5%)	4 (6.3%)	2 (4.8%)

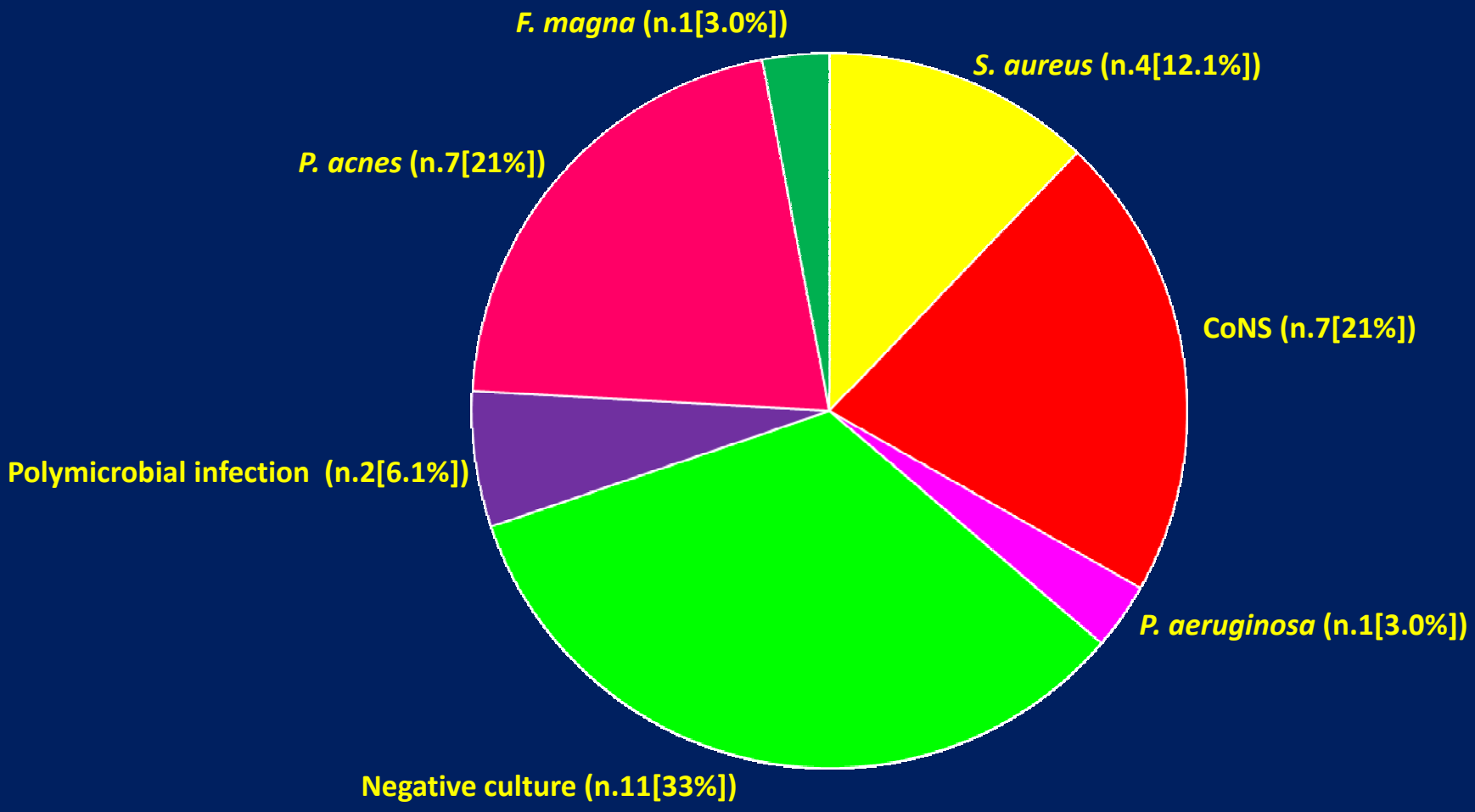
Betsch BY, Clin Infect Dis 2008;46:1221-1226;
Giulieri SG, Infection 2004;32:222-228;
Laffer RR, Clin Microbiol Infect 2006;12:433–439

Microbiological findings for 27 case patients with prosthetic elbow infection at the Schulthess Clinic in Zurich (Switzerland), 1994-2007



Achermann Y, Clin Microbiol Infect 2011;17:432-38

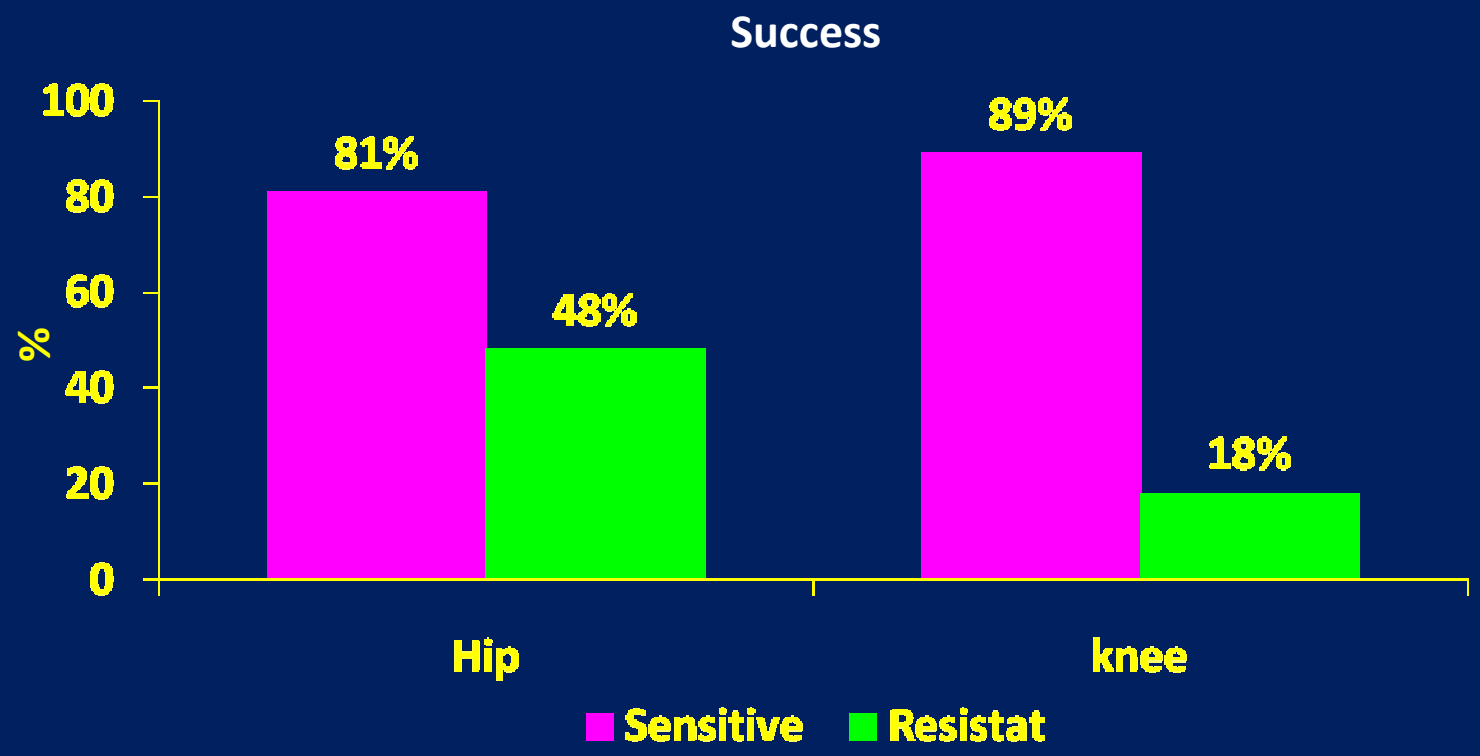
Microbiological findings for 33 case patients with prosthetic shoulder infection at the Mayo Clinic (Rochester, MN), 2004-2008



Piper KE, J Clin Microbiol 2009;47:1878-84

Results of periprosthetic Hip and Knee Infections caused by resistant bacteria

Seventy pts with PJIs were treated between 1997 and 2001. 35 pts had infections of their THA and 35 pts had infections of their TKA. The pts were subdivided into 2 subgroups: pts who had infections with Staphylococcal bacterial strains that were sensitive to methicillin and pts who had infections with bacteria that were resistant to methicillin (both MRSA and MRSE).



Kilgus DJ, Clin Orthop Relat Res 2002;404:116-24

Higher risk of failure of MRSA PJIs

Retrospective cohort study (1998-2004) to identify risk factors for treatment failure in THA or TKA PJI due to *S. aureus*

- **33% (45 of 137) episodes of PJIs were the result of *S. aureus***
- **24% (33 of 137) episodes were MSSA**
- **9.0% (12 of 137) episodes were MRSA**

Multivariate analysis of treatment failure in *S. aureus* PJIs

Variable	Hazard Ratio	p Value (95% confidence interval)
MRSA	9.2	0.0012 (2.40–35.46)
TKA PJI	5.8	0.0100 (1.52–22.19)
Retention of joint hardware	4.2	0.014 (1.33–12.97)

Patients with MRSA PJI had longer hospital durations than MSSA (median days [range]: 15 [4-40] *vs*. 10 [5-33]; *P = 0.01*; respectively)

Salgado CD, Clin Orthop Relat Res 2007;461:48-53

Unusual causes of prosthetic joint infection

- Aerobic gram +ve bacteria
  - *Staphylococcus caprae*
  - *Staphylococcus simulans*
  - *Staphylococcus lugdunensis*
- Aerobic catalase-negative gram +ve cocci
  - *Streptococcus bovis*
  - Gemella morbillorum
  - Abiotrophia spp
  - *Streptococcus pneumoniae*
- Aerobic nonspore-forming gram +ve bacilli
  - *Corynebacterium jeikeium*
  - *Listeria monocytogenes*
  - *Actinomyces* spp
  - *Nocardia* spp
  - *Dietizia maris*
  - *Tsukamurella paurometabolum*
  - *Oerskovia xanthineolytica*
- Aerobic spore-forming gram +ve bacilli
  - non-anthrax *Bacillus* spp
- Aerobic gram -ve bacteria
  - *Achromobacter xylosoxidans*
  - *Pseudomonas oryzihabitans*
  - *Pseudomonas luteola*
  - *Salmonella* spp
- Aerobic gram -ve cocci and coccobacilli
  - *Neisseria meningitides*
  - *Haemophilus influenzae*
  - *Moraxella catarrhalis*
- Anaerobic bacteria
  - *Clostridium difficile*
  - *Veillonella dispar*
  - *Veillonella parvula*
  - *Prevotella melanonogenica*
  - *Clostridium perfringens*
- Zoonotic bacteria
  - *Brucella spp*
  - *Francisella tularensis*
  - *Yersinia enterocolitica*
  - *Pasteurella multocida*
  - *Campylobacter jejuni*
- Fungi
  - *Aspergillus fumigatus*
  - *Rhodotorula minuta*
  - *Histoplasma capstulatum*
  - *Sporothrix schenckii*
- Mycobacteria
  - *Mycobacterium tuberculosis*
  - Rapidly growing mycobacteria
  - *Mycobacterium avium complex*
- Other
  - *Mycoplasma hominis*
  - *Echinococcus*
  - *Tropheryma whipplei*

Marculescu CE et al., Clin Orthop Relat Res 2006;451:55-63
Marculescu CE et al., Clin Orthop Relat Res 2006;451:64-72

Conclusions

- The incidence of periprosthetic infection after joint arthroplasty (both primary and revision) are on the rise.
- Infections associated with prosthetic joints cause significant morbidity and account for a substantial proportion of health care expenditures.
- As the number of primary procedures performed in the next two decades is expected to rise exponentially, increased resources should be devoted to research investigation and product development focused on prevention, early diagnosis, and treatment of PJIs.