Spinal Infection

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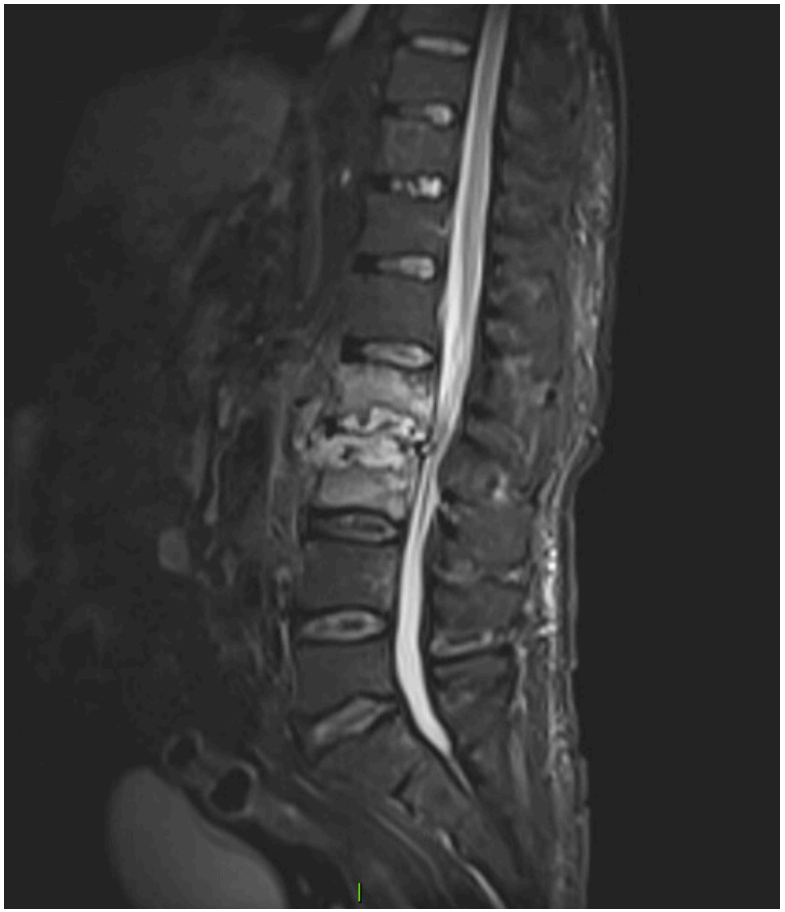
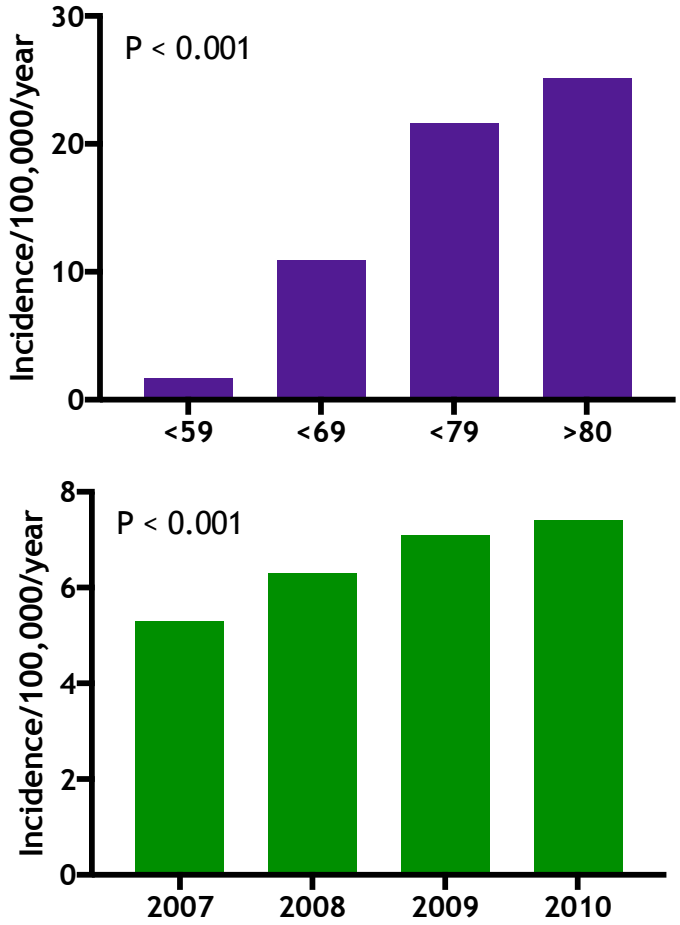
Overview

- The problem
- Diagnosis
- Management
  - Recent trial data
  - IDSA Clinical Practice Guidelines
- Local experience in OPAT



The problem



Akiyama et al, 2013

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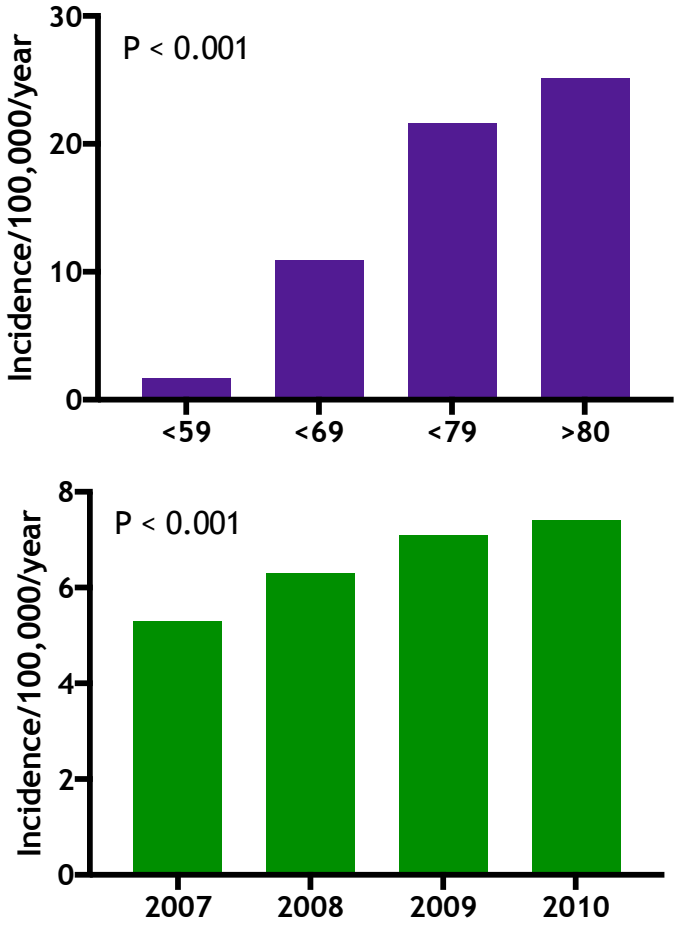

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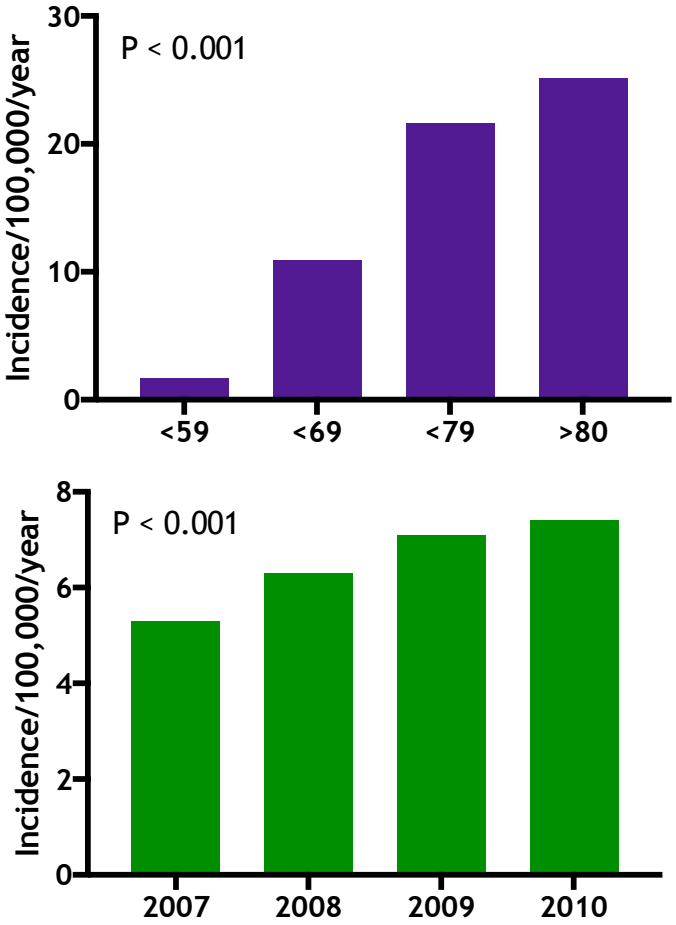

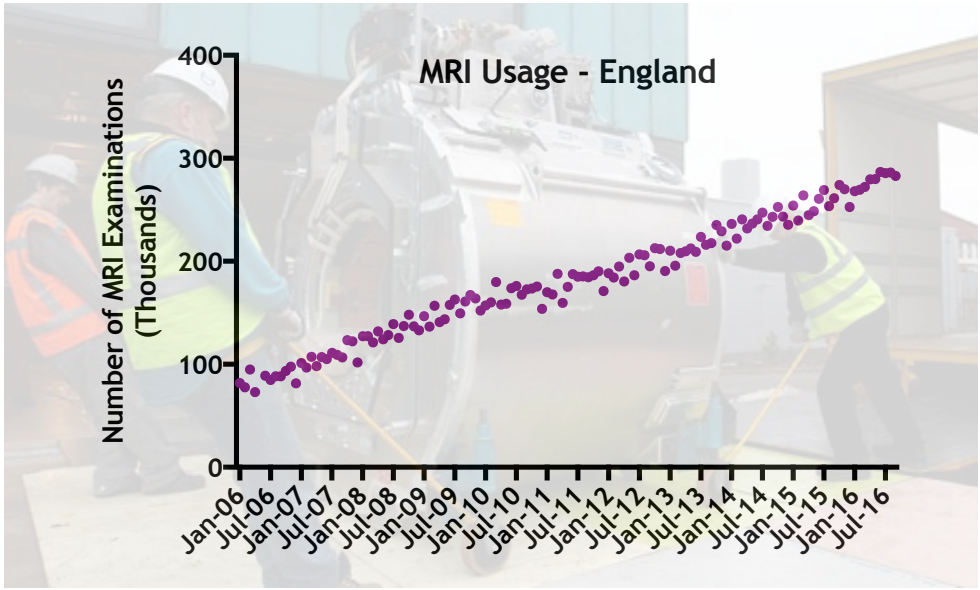

Akiyama et al, 2013

NHS England

The problem - classification

Primary Infection

- Spinal infection as presenting issue
- Presumed haematogenous spread
- No preceding severe illness
- Usually middle aged and mild-moderate comorbidity

Secondary Infection

- Spinal infection complicating severe systemic illness
- Usually haematogenous but sometimes direct spread
- Often frail or with significant comorbidity

Post-surgical

- Post-surgical infection
- Occasionally following other kinds of spinal instrumentation
- May involve patients with metalwork

Diagnosis

- Sometimes straightforward:
  - Fever
  - Back pain
  - Typical pathogen

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  - Known second focus
  - Equivocal MRI findings
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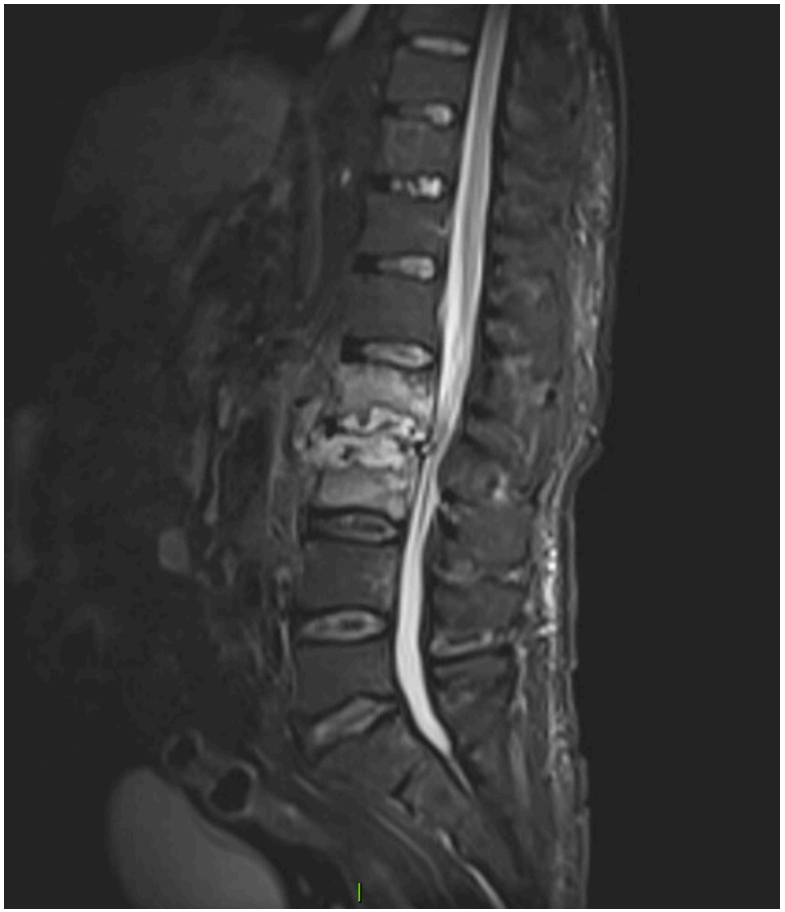


Diagnosis – tissue sampling

- IDSA:
  - CT guided biopsy should be performed in those where a microbiological diagnosis cannot be obtained by other methods
  - Antibiotics should be withheld until sampling is obtained unless:
    - Sepsis
    - Neurological signs

Factor	Adjusted OR	P
Paravertebral abscess	5.91 (1.5-23.1)	0.01
No antibiotics	1.00	
1-3 days	0.09 (0.01-1.5)	0.09
4+ days	0.05 (0.01-0.24)	<0.01

Kim et al, 2012

Management – Duration

- Duration of Treatment for Spondylodiscitis Study
- Randomised 359 patients with vertebral osteomyelitis to 6 or 12 weeks of antibiotic therapy
- Multicentre, open label study with antibiotic therapy decisions at discretion of local investigator
  - Median duration of IV antibiotic therapy was 14 days
  - Most common oral therapy with rifampicin/ fluoroquinoline
- Primary end point was microbiological cure on ETT analysis

Bernard et al, Lancet (2015)

Management - Duration

- All patients had microbiologically confirmed infection
- 19% of patients had abscesses at baseline
- 4% had drainage of abscesses

	6 week	12 week	Difference (95% CI)
Number of patients	176	175	
Cured	160 (90.9%)	159 (90.9%)	+0.1 (-6.2 – 6.3)
Cured and alive	156 (88.6%)	150 (85.7%)	+2.9 (-4.2 – 10.1)
Cured per protocol	142 (80.7%)	141 (80.6%)	+0.1 (-8.3 – 8.5)

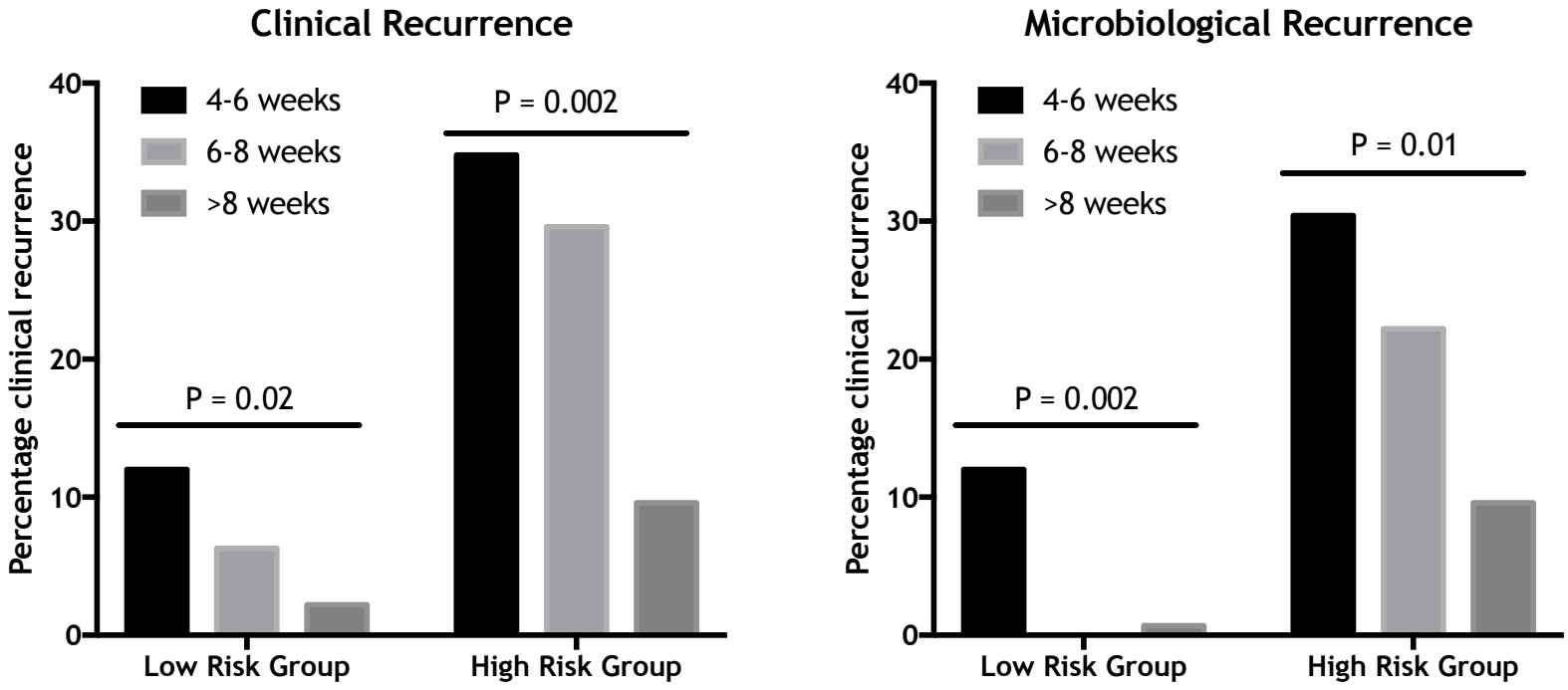
Bernard et al, Lancet (2015)

Management - Duration

- Retrospective review of 345 cases of vertebral osteomyelitis; compared to RCT patients had:
  - More comorbidity (i.e. diabetes 30% v 15%)
  - More extensive disease (paravert abscess 70% v 19%)
  - More resistant bacteria (MRSA 25% v 2%)
- Risk stratified cases based on presence of risk factors for failure:
  - End stage renal failure
  - Undrained paravertebral/psoas abscess
  - Presence of MRSA

Park et al, CID, 2016

Management - Duration



- Relatively infrequent use of rifampicin (22% in SA)
- Low vancomycin trough conc (74% <15 μg/ml)

Park et al, J Infect, 2013
Park et al, CID, 2016

Management - Duration

- "We recommend a total duration of 6 weeks of parenteral or highly bioavailable oral antimicrobial therapy for most patients with bacterial NVO"
- "Selected panel members advocate the use of longer treatment duration for >6 weeks followed by a course of oral therapy for 3 months or longer in patients perceived to be at high risk for failure"

- Risk factors for failure:
  - MRSA
  - Extensive infection/abscess
  - No surgical intervention

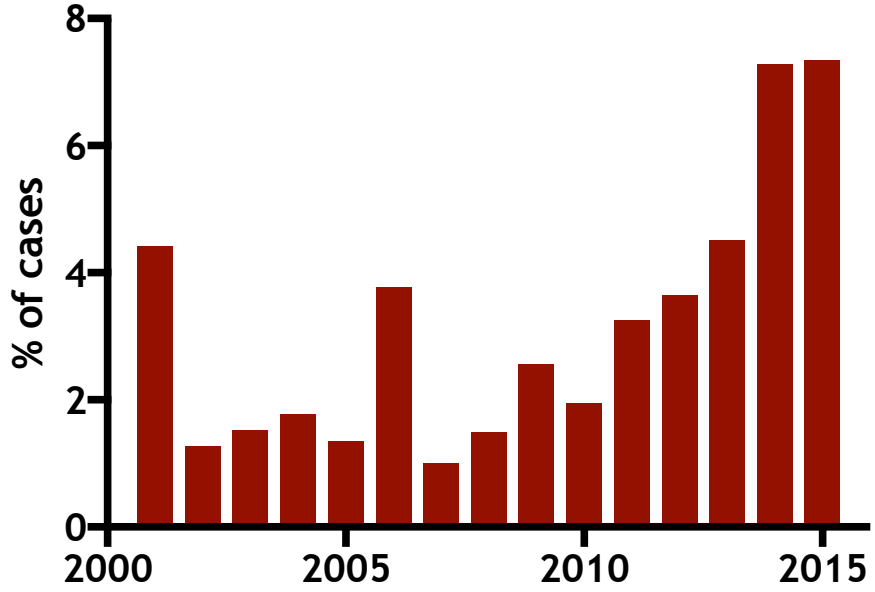
Agents recommended for oral therapy	
Metronidazole	TMP-SMX
Moxifloxacin	Clindamycin
Linezolid	Doxycycline
Levofloxacin	Rifampicin
Ciprofloxacin	

Glasgow OPAT Experience

- Review of prospectively collected database
  - November 2000 – February 2016
  - Patients recruited into RCTs were excluded
  - Patients with a diagnosis of vertebral osteomyelitis or epidural collection
  - Additional review of follow up and imaging
- Surgical – a history of spinal surgery
- Secondary – a history of severe systemic illness without the preceding 6 months or subsequent identification of a clear primary focus
- Primary – all other cases

Glasgow OPAT Experience

- 154 Patients met the inclusion criteria
  - 80 primary infection (52%)
  - 38 secondary infection (25%)
  - 35 post-surgical infection (23%)



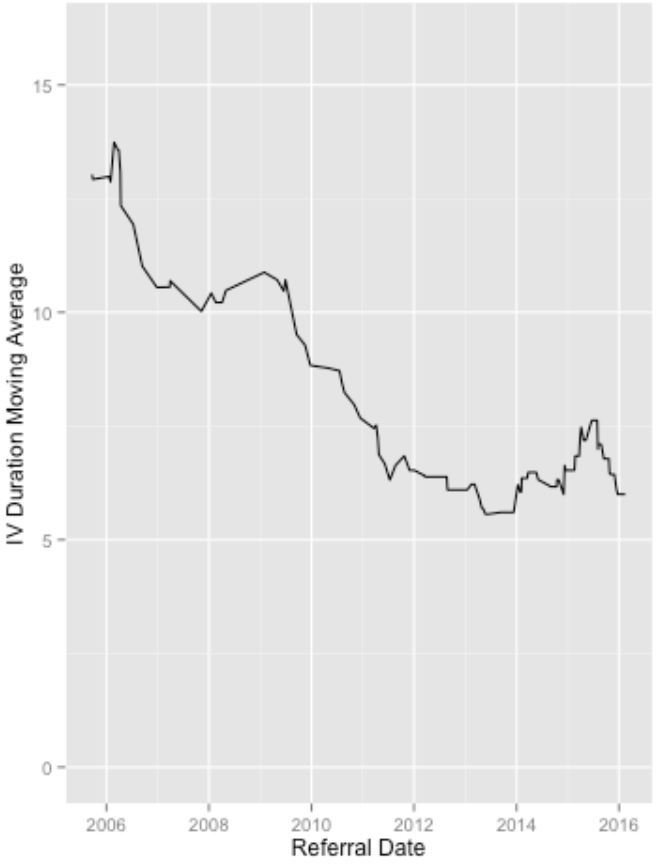
Baseline Characteristics

	Primary	Secondary	Post-surgical	P value
Male (%)	49 (61%)	23 (61%)	22 (62%)	0.97
Age (IQR)	57.6 (50 – 69)	**64.9 (55 – 73)**	52.7 (38 – 67)	0.02
Comorbidity (IQR)	0 (0 – 1)	**2 (0 – 4)**	0 (0 – 1)	<0.001
Bacteraemia	35 (44%)	**23 (61%)**	5 (14%)	0.001
S. aureus	35 (44%)	20 (52%)	11 (30%)	
β haemolytic strep.	3 (3%)	0 (0%)	3 (9%)	0.006
Gram negative bacilli	4 (5%)	**8 (21%)**	0 (0%)	

- 25% had invasive investigation/management
  - 14% had radiological/surgical biopsy
  - 11% had radiological/surgical intervention

Treatment

- IV agent
  - Ceftriaxone: 68 (44%)
  - Teicoplanin: 43 (28%)
  - Daptomycin: 30 (20%)
  - Ertapenem: 11 (7%)
  - Pip/taz: 1 (0.6%)
- 84% received 2nd agent:
  - Rifampicin 43%
  - Ciprofloxacin 15%



Outcome

- 7 episodes of treatment failure/relapse (4.5%)
  - 2 patients at end of IV therapy
  - 2 patients while on oral stepdown therapy
  - 3 late relapses (5, 7 and 11 months)
- 1 patient subsequently empirically treated for TB
- 20 patients readmitted while on IV therapy:
  - 8 had OPAT related reason for readmission
  - 2 PICC line infections
  - 1 Clostridium difficile
  - 5 drug toxicity
- 28 patients experienced significant drug toxicity not requiring admission

Outcome – failure/relapse

- Infection type:
  - Primary – 0/80 (0%)
  - Secondary – 1/38 (2.6%) P < 0.001
  - Post-surgical – 6/35 (17%)
- CRP response at end of IV therapy useful for prediction of relapse, particularly early relapse.
  - CRP < 10: 3/116 (2.6%)
  - CRP > 10: 4/34 (11.8%) P = 0.04
- No association between choice of IV therapy or duration of therapy and failure.

Outcome - Imaging

- Most patients had follow up imaging conducted:
  - 84% of patients had at least 1 follow up MRI conducted
  - 32% of patients had multiple follow up MRI scans
- Follow up imaging was often misleading:

CRP <10	Imaging	N°	Outcome
Yes	Improved	39	1 late relapse (2.5%)
	Static	22	1 late relapse (4.5%)
	Worsening	16	No relapses/failures (0%)
No	Improved	5	1 late relapse (20%)
	Static	6	1 early failure (17%)
	Worsening	7	3 early failures (43%)

Summary

- Discitis is increasingly common and can be effectively managed in OPAT.
- 6 weeks of antibiotic therapy with early oral switch is appropriate for the majority of patients.
- Longer courses of treatment and surgical therapy should be considered for those at higher risk.
- Routine follow up imaging may be misleading and should not be used routinely.