ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ
ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ ΙΑΤΡΙΚΗ ΣΧΟΛΗ

ΔΙΕΥΘΥΝΤΗΣ:
Καθηγητής Ε. Ι. Γιαμαρέλλος - Μπουρμπούλης

ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ

«ΛΟΙΜΩΞΙΟΛΟΓΙΑ»

2022-23

Παρεντερική κατ΄οίκον αντιμικροβιακή Θεραπεία (ΟΡΑΤ)

Σ Τ Ε Λ Ι Ο Σ Α Σ Η Μ Α Κ Ο Π Ο Υ Λ Ο Σ

Αναπληρωτής Καθηγητής

Παθολογίας - Λοιμώξεων

Ιατρικού Τμήματος Πανεπιστημίου Πατρών

Υπεύθυνος Μονάδος Ειδικών Λοιμώξεων ΠΓΝΠ

ΠΑΝΕΠΙΣΤΗΜΙΟ ΠΑΤΡΩΝ
UNIVERSITY OF PATRAS

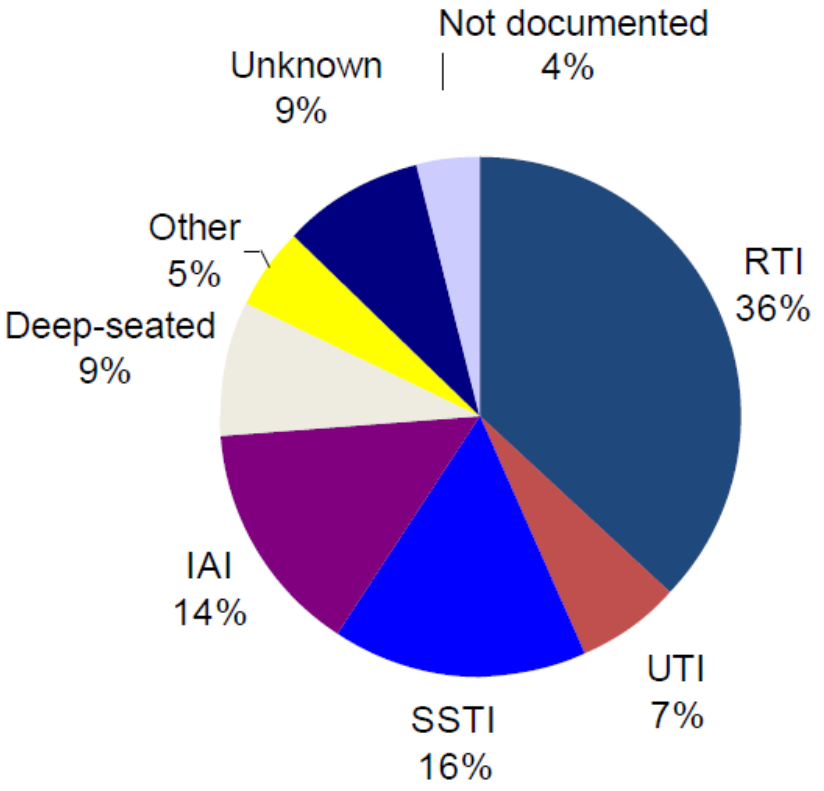
Σύγκρουση συμφερόντων

- Honoraria for presentations: *Pfizer, Gilead Sciences, MSD, Angelini*
- Consultant: *Pfizer, GSK, Angelini*
- Research Grants: *Pfizer, Gilead*

Intravenous antimicrobial therapy in hospitalized patients

- 1/3 hospital admissions receive antibiotic treatment[1]
- 1/10 receive i.v. antibiotics
  - ~24,000 per million population/yr
- All specialties
  - Integrated part of hospital care
  - Necessitate hospital admission
  - Prolong admission
  - **Some could be discharged if they do not require i.v. antibiotic therapy[2]**

Infection types in acute admissions receiving i.v. antibiotics (n=381)[1]



1. Seaton RA *et al. Int J Antimicrob Agents* 2007;29:693–699
2. McLaughlin C *et al. Q J Med* 2005;98:745–752

Outpatient parenteral antimicrobial therapy (OPAT)

Definition

- the administration of **parenteral antimicrobial therapy (IV or IM) in at least 2 doses** on different days **without intervening hospitalization**

Indications

- infections where requirement for IV antimicrobials is the only reason for admission to or barrier to discharge from hospital

- If no oral agent available or appropriate

IDSA 2018, Clinical Practice Guidelines
Clin Infect Dis 2004;38:1651–1672

Efficacy of OPAT

- The **first study** to show the efficacy of home IV antibiotic administration was published in the **paediatric literature in 1974**, demonstrating safe and effective treatment of chronic broncho-pulmonary infection associated with **cystic fibrosis**

- Since that time numerous studies have detailed the benefits of utilizing OPAT for various infections including
  - ✓ Cellulitis
  - ✓ Osteomyelitis
  - ✓ Septic arthritis
  - ✓ Infected prosthetic joints
  - ✓ Bacteremia
  - ✓ Endocarditis
  - ✓ Pyelonephritis

- OPAT has also been found to be **effective** in virtually all segments of the population, **from children to the elderly**

Pediatrics. 1974;54:358–360, *West J Med*. 1978;128(3):203-206, *Arch Intern Med*. 1979;139(4):413-415, *Ann Intern Med*. 1983;99(3):388-392, *JAMA*. 1982;248(3):336-339, *Am J Med*. 1989;87(3):301-305

Benefits for the patient

- **Quality of life**
  - Family and familiar surroundings
  - Sleep and privacy
  - Nutrition, clothing
  - Mental health
  - Special benefit for children (easily feel threatened in nosocomial environment)

- Reduced risk of **complicating infections** and antimicrobial **resistant** organisms

- Increased education and training in self-care
- Lower out-of-pocket costs
- Return to their daily activities (work, school)
- Treatment may be adjusted to each patient's lifestyle
- Most people prefer being treated at home rather than in the hospital has been repeatedly demonstrated

Int J Clin Pract Suppl 1998;95:4–8, *Antimicrob Chemother* 2002;49:149–154, *Arch Intern Med*. 2001;161(1):61-65, *Am J Med*. 2000;109(5):378-385, *Prof Nurse*. 1994;10(2):106-111, *Eur J Clin Microbiol Infect Dis*. 1999;18(5):330-334, *Can J Infect Dis*. 2000;11(suppl A):11a-14a

Benefits for the Health System

- Avoided admission
- Reduced length of stay
- More effective use of resources
- freeing up of hospital beds
- Impact on elective and acute work
- Lower rate of health care associated infections
- Specialists managing infection

has been used in many countries for over 30 years and evidence shows its clinical and cost effectiveness

Clin Infect Dis 2004;38:1651–1672, *Am J Med*. 1989;87(3):301-305

OPAT settings

Models for OPAT service

- ❑Ambulatory patient with attendance at health care facility (infusion center)
  - ❑Hospital clinic/day unit

Infusion Center
- live in reasonable proximity to the facility
- receiving once daily infusion
- Weekend access available

- ❑Self or caregiver administration

Treatment at Home
- most OPAT programs
- training
- infusions at home by themselves
- with the help of caregivers

- ❑Visiting nurse
  - ❑NHS
  - ❑private

Skilled Nursing Facility (SNF)
- discharging centres have the resources to provide additional oversight

OPAT settings

Hospital-based Infusion Operations (Nottingham)

OPAT settings

Office-based Infusion Operations

OPAT settings

OPAT at home

Self-administered

Visiting nurse

OPAT at home: which patient and how

I. Should patients (or their caregivers) be allowed to self-administer OPAT?
Recommendation
Patients (or their caregivers) should be allowed to self-administer OPAT
(***strong recommendation***, *low-quality evidence*)

II. Should patients (or their caregivers) be allowed to self-administer OPAT at home without visiting nurse support?
Recommendation
Patients (or their caregivers) may be allowed to self-administer OPAT at home without visiting nurse support as long as there is a system in place for effective monitoring for vascular access complications and antimicrobial adverse events
(weak recommendation, low-quality evidence)

III. Should elderly patients be allowed to be treated with OPAT at home?
Recommendation
Elderly patients should be allowed to be treated with OPAT at home
(***strong recommendation***, *low-quality evidence*)
- potential challenges to OPAT in the elderly, such as cognition, mobility, and dexterity, have been duly considered and that the patient or caregiver is able to communicate with the treatment team if necessary

IV. **III. Can persons who inject drugs (PWID) be treated with OPAT at home?**
No recommendation
V. **V. Should infants aged <1 month be treated with OPAT at home?**
No recommendation

IDSA 2018, Clinical Practice Guidelines

Comparison of OPAT settings

There is **no difference** in the rate of **readmissions** or **complications** between self-administered OPAT and Healthcare personnel-administered OPAT

Table 5. Evidence Table: Comparison of Outcomes in Self-Administration of Outpatient Parenteral Antimicrobial Therapy (OPAT) Medications Versus Healthcare Personnel Administration of OPAT Medications

Outcome	Conclusion	Summary of Findings	Quantity and Type of Evidence	Starting Level of Evidence	Factors That Alter the Strength of Evidence	Final Evidence Strength
Readmission	No increase	Lower hazard of readmission[a] for S-OPAT (HR 0.36,[b] 95% CI 0.24–0.53, $P < .001$) in 1 study [50] No difference in readmission rates (10.5% vs 12.6%, RR 0.83, 95% CI 0.59–1.14, $P = .30$) in 1 study [49]	2 cohort studies (n = 2059, 2229) [49, 50]	Low	Large effect (+1)	Moderate
Complications[c]	No increase	Similar overall complication rate (24% vs 23%, RR 1.03, 95% CI 0.86–1.24, $P = .80$) in 1 study [49] S-OPAT at home (vs administration by staff in OPAT clinic) was not associated with line infection (OR 0.84, 95% CI NR $P = .72$) or other line events (OR 1.32, 95% CI NR, $P = .22$) in 1 study [51]	2 cohort studies (n = 2059, 2766) [49, 51]	Low	…	Low

➢ **Patients (or their caregivers) should be allowed to self-administer OPAT (strong recommendation, low-quality evidence) – IDSA 2018**

J Antimicrob Chemother 2007;60:356–62, Int J Antimicrob Agents 2013;41:569–73, Eur J Clin Microbiol Infect Dis 2012; 31:2611–9, 2018 IDSA Clinical Practice Guideline for the Management of OPAT • CID 2019:68 (1 January)

Good practice recommendations for outpatient parenteral antimicrobial therapy (OPAT) in adults in the UK: a consensus statement

Journal of Antimicrobial Chemotherapy

J Antimicrob Chemother 2012; **67**: 1053–1062

Five key components of an OPAT service

1. OPAT team and service structure
2. Patient selection
3. Antimicrobial management and drug delivery
4. Monitoring of the patient during OPAT
5. Outcome monitoring and clinical governance

Good practise recommendations

1. OPAT team and service structure

- **Team** with **Medical Lead**
  - **Doctor (**eg Internal Medicine or Surgeon with ID interest**)**
  - **Infection specialist**
  - **Nurse**
  - **pharmacist**
- Identified **time for OPAT** members in the job plan
- **Inclusion/ exclusion criteria agreed (ID specialist)**
  - Infection-related and Patient suitability criteria
- Agreed **management plan** and clear **documentation**
- **Clinical responsibility** shared between **referring physician** and **OPAT physicians**
- Communication with patient's GP (written and clear)
- Out of hours/ **emergency plan** agreed

Good practise recommendations

2. Patient selection

- Agreed specific **infection-related inclusion and exclusion criteria** for OPAT (and severity criteria) – ID specialist
- Agreed and documented OPAT **patient suitability criteria** incorporating physical, social and logistic criteria (documented for each patient)
- **Initial assessment** for OPAT should be performed by a competent member of the OPAT team
- Patients and carers should be **fully informed** about the nature of OPAT and should be given the opportunity to decline or accept this mode of therapy
- All patients who have been assessed as being at risk of **venous thrombosis** as inpatients should be considered for further prophylaxis during OPAT if assessed as having ongoing risk.

Good practise recommendations

3. Antimicrobial management and drug delivery

- **Treatment plan** is **responsibility of the OPAT infection specialist**, following discussion with the referring clinician
- The **treatment**: Choice, Dose, Frequency, Duration, Flexibility based on clinical response
- Antimicrobial choice within OPAT should be subject to **review by the local antimicrobial stewardship programme**
- OPAT team to ensure **correct and continued prescription** of antimicrobials during OPAT
- **Storage, reconstitution and administration** of antimicrobials comply with published standards
- Choice of **intravascular access** for each patient (care of IV access)
- **Training of patients or carers** in the administration of intravenous medicines
- The **first dose** of a new antimicrobial should be administered in a **supervised setting**

Good practise recommendations

4. Monitoring of the patient during OPAT

- Pts with **SSTIs should be reviewed daily** by the OPAT team to optimize speed of intravenous to **oral switch**
- **weekly multidisciplinary meeting/virtual ward round** to discuss progress (including safety monitoring and outcome) of patients receiving OPAT
- Pts in excess of 1 week of antimicrobial therapy should be **regularly reviewed by the OPAT specialist nurse and physician**
- **Blood tests** at **least weekly if OPAT <1 month** or at least twice monthly if OPAT >1 month. (full blood count, renal and liver function, C-reactive protein (CRP) and therapeutic drug monitoring where appropriate)
- **Monitoring clinical response** to antimicrobial management and blood investigations, and for reviewing the treatment plan (communication with referring specialist)
- Mechanism in place for **urgent discussion and review** of **emergent clinical problems** during therapy according to clinical need (**clear pathway for 24 h immediate access** to advice/review/admission for OPAT patients)

Good practise recommendations

5. Outcome monitoring and clinical governance

- **Data on OPAT pts recorded prospectively** for service evaluation and quality assurance (database)
- Standard **outcome criteria** should be used on completion of intravenous therapy. (recorded adverse drug reactions, vascular access complications, *Clostridium difficile*-associated diarrhoea and *Staphylococcus aureus* bacteraemia)
- **Risk assessment** and audit of individual processes (particularly new processes) should be undertaken as part of the local clinical governance programme
- **Regular surveys of patient experience** should be undertaken (PROs)
- OPAT team members are responsible for personal **continuing professional development**

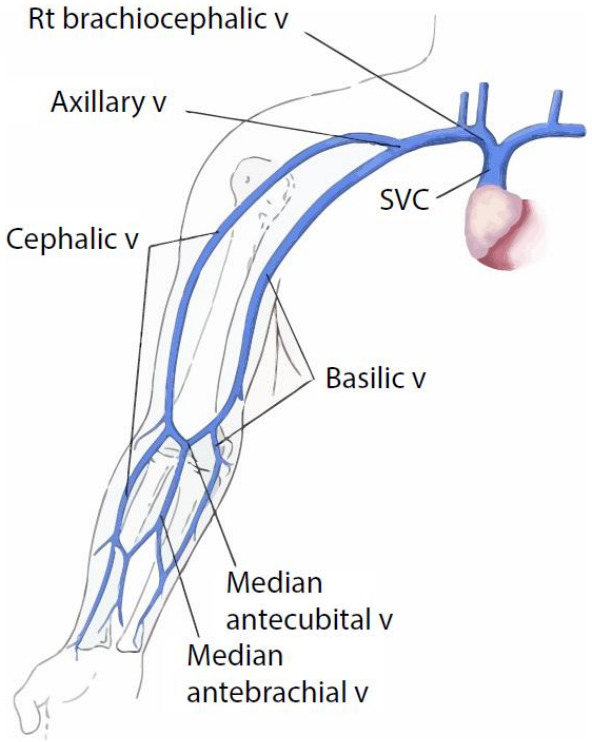
Vascular access

1. Peripheral lines

- **Short peripheral lines** for brief periods
- Brief periods **1 to 7 days**
  - frequent need to replace these lines makes them unwieldy for longer treatment courses

- **A midline catheter** is inserted in a manner similar to that of a PICC line but runs only 8 to 10 cm into the vein
  - this type of catheter is best reserved for shorter courses (**3 to 14 days**) of less irritating antibiotics.

Figure 7.1. Possible veins for midline catheter placement



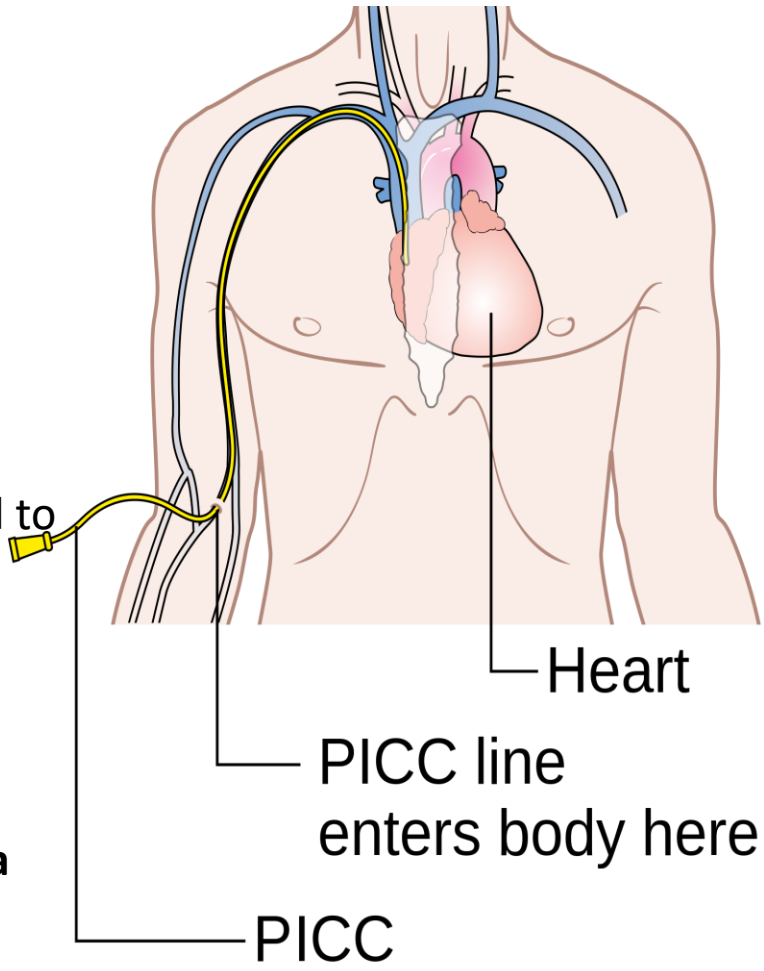
OpenStax College Circulatory Pathways. Version 1.3: June 19, 2013.

Vascular access

2. Central Vascular Access Devices

a. PICC

- ✓ The most common type of CVAD used in OPAT
- ✓ PICC lines are typically inserted into either the cephalic or basilic vein and terminate in the mid to distal superior vena cava (SVC)
- ✓ recommended for infusion therapies for **more than 2 weeks**
- ✓ **hyperosmolar solutions** and **medications with a pH of less than 5 or greater than 9**



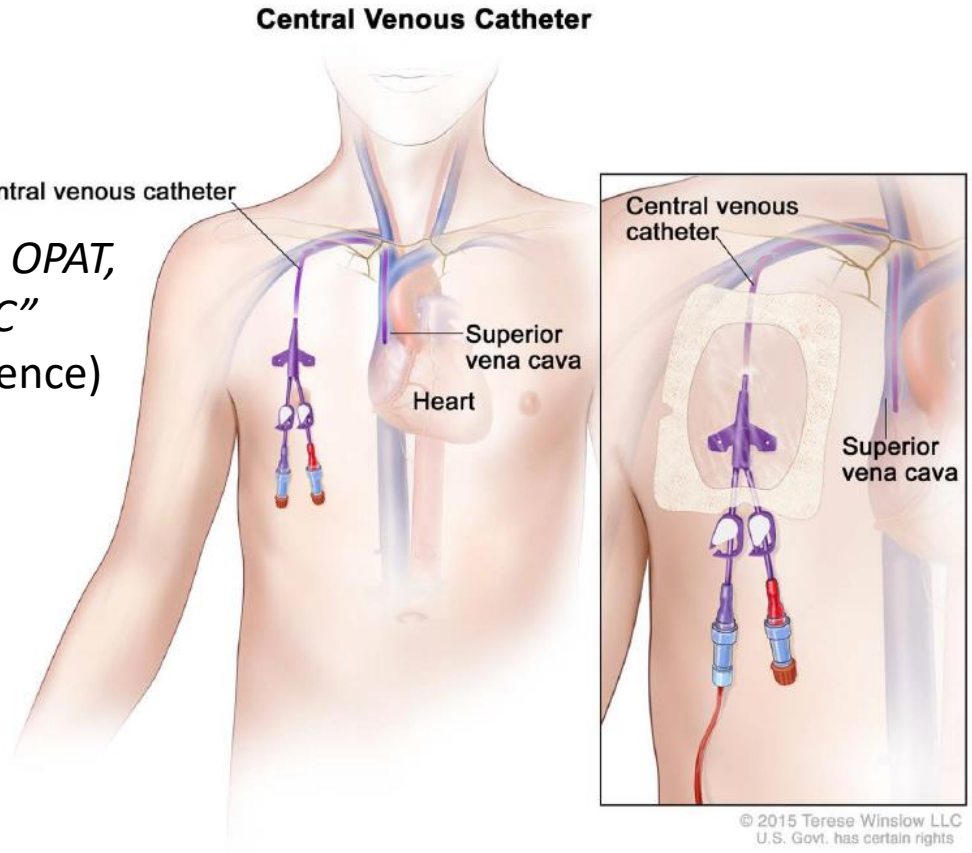
Vascular access

2. Central Vascular Access Devices

Figure 7.2. Typical placement of a Hickman catheter

b. Hickman catheter

"For patients with advanced CKD requiring OPAT, a t-CVC is recommended rather than a PICC"
(strong recommendation, low-quality evidence)

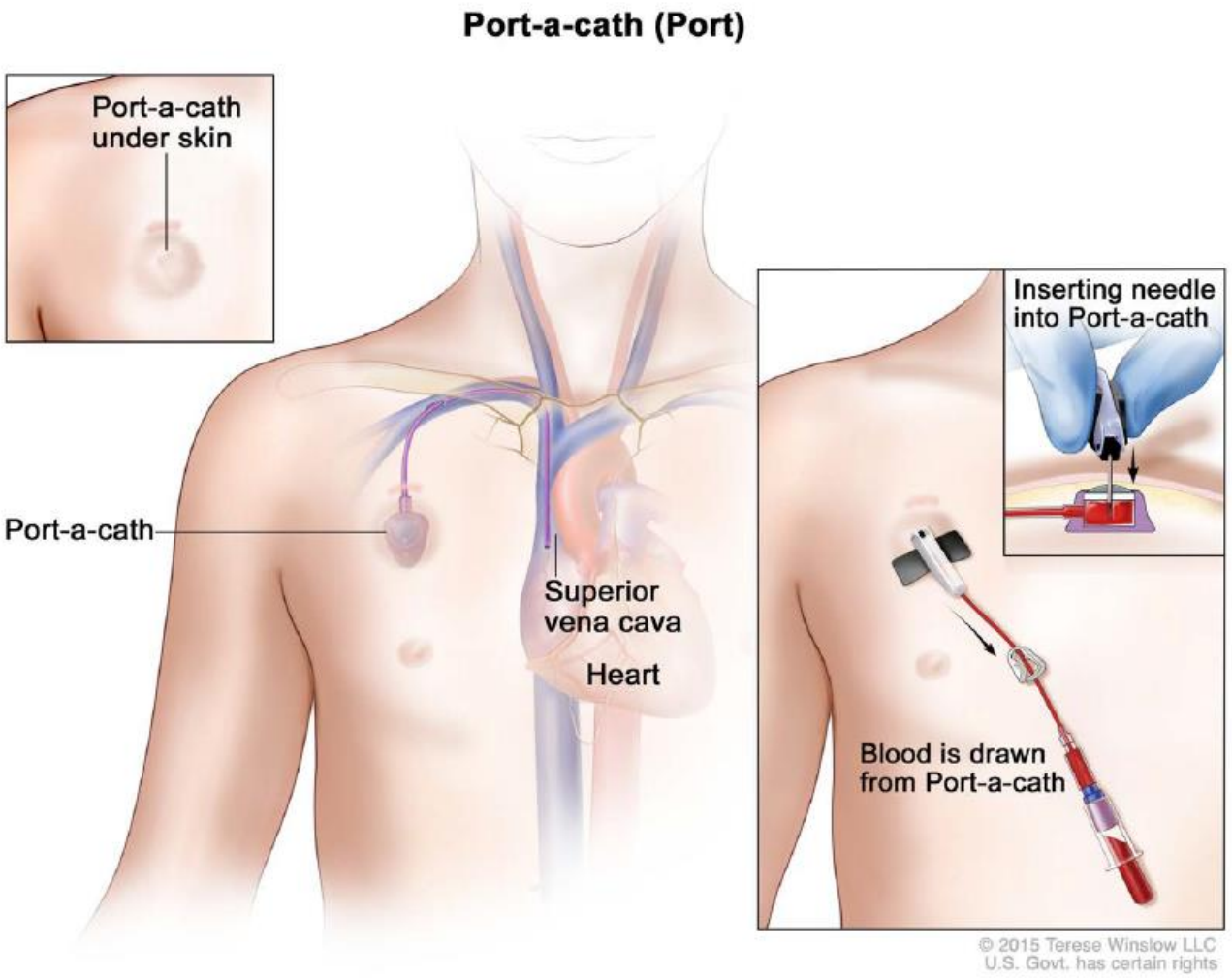


2018 IDSA Clinical Practice Guideline for the Management of OPAT • CID 2019:68 (1 January)

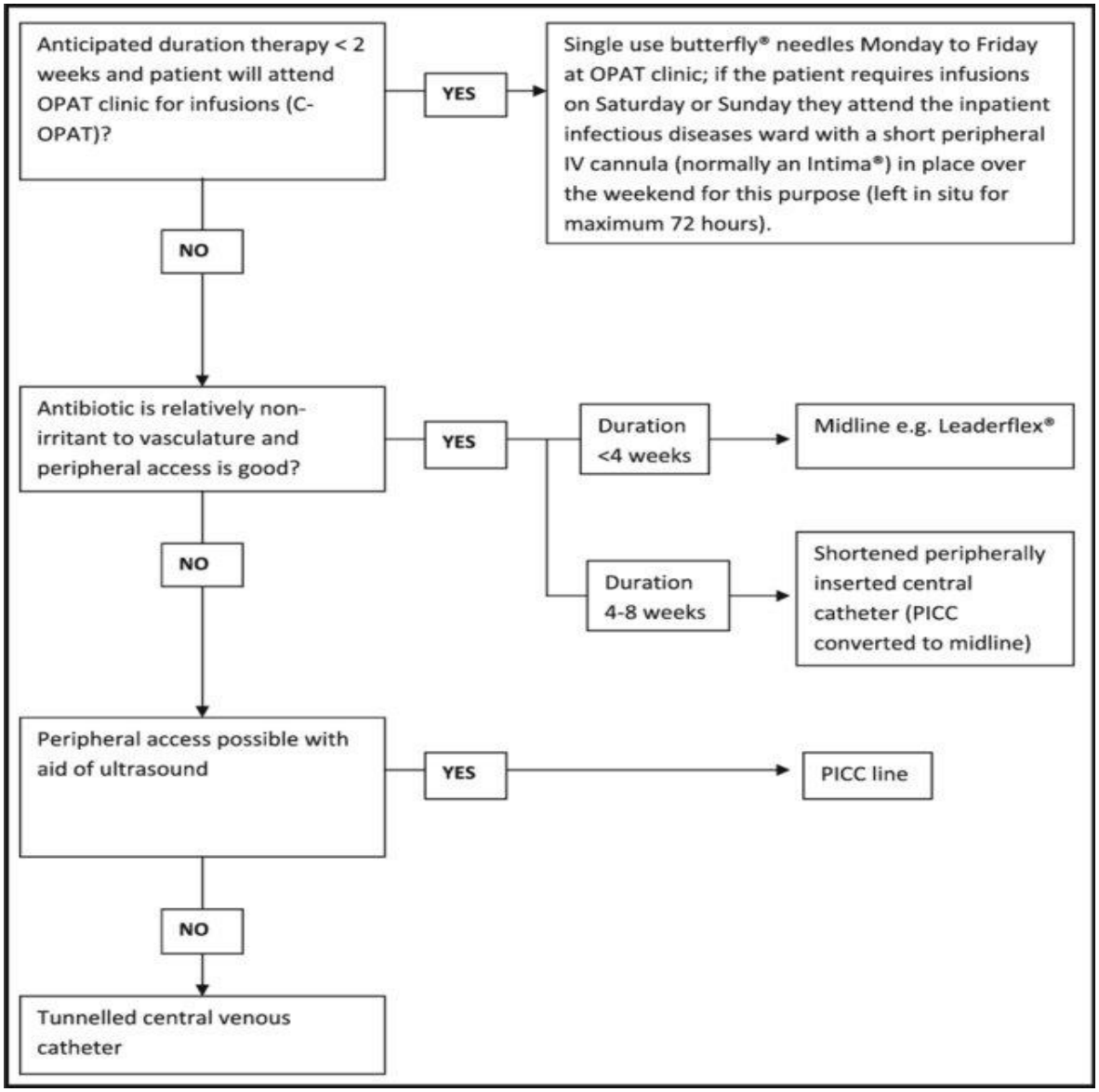
Vascular access

2. Central Vascular Access Devices

c. Port-a-cath



Vascular access



European Journal of Clinical Microbiology 2012;31(10):2611-9

Vascular access

Complications

- It is **not necessary to remove a vascular access** device if CA-VTE develops during OPAT, as long as the catheter remains well positioned and arm pain and swelling decrease with anticoagulation
  (**weak recommendation**, very low-quality evidence) IDSA Guidelines 2018

- No recommendation can be made regarding the need to treat patients with a history of prior CA-VTE with prophylactic oral anticoagulation while on OPAT
  (**no recommendation**, no evidence).

Table 14. Evidence Table: Outcomes for Vascular Access Retention in the Setting of Catheter-Associated Venous Thromboembolism

Outcome	Conclusion	Summary of Findings	Quantity and Type of Evidence	Starting Level of Evidence	Factors That Alter the Strength of Evidence	Overall Evidence Strength
Preservation of line function	Line function can be preserved	42/42[a] (100%) [101] and 70/70 (100%) [102] of patients had a functional catheter at 3 months	2 clinical trials (N = 74, 70) [101, 102]	Low	Large effect (+1) Indirectness (–1)	Low
Recurrent symptomatic thromboembolism	Insufficient evidence	0/74 (0%) [101] and 1 (1.43%) [102] had recurrent thromboembolism	2 clinical trials (N = 74, 70) [101, 102]	Low	Risk of bias (–1) Indirectness (–1)	Very low
Major bleeding	Insufficient evidence	3 (4%) and 7 (10%) had major bleeding [101, 102]	2 clinical trials (N = 74, 70) [101, 102]	Low	Indirectness (–1)	Very low

Delivery devices

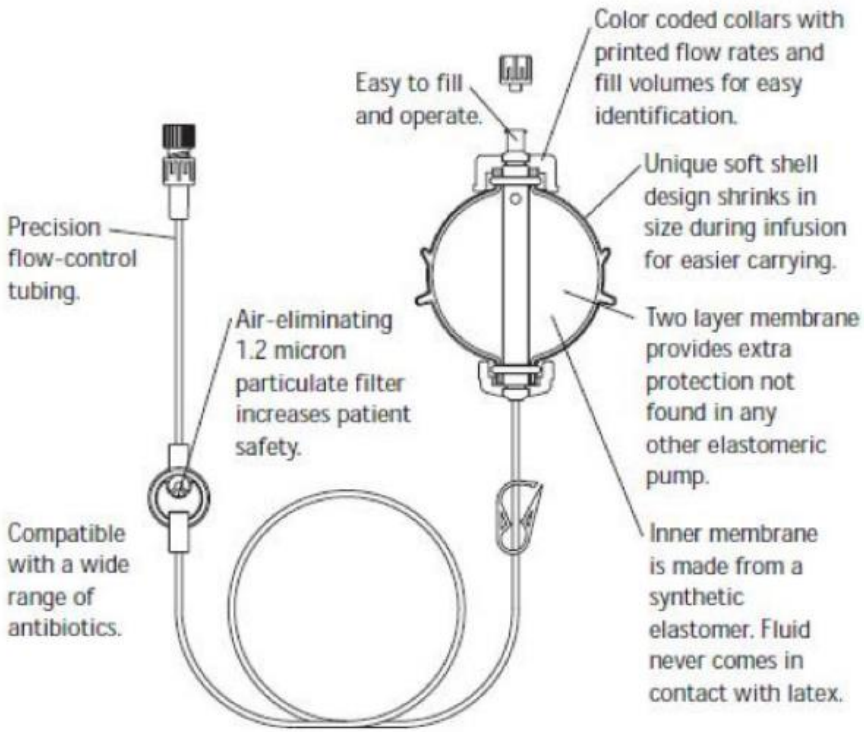
Syringe pump

Figure 7.4. A syringe pump with advanced delivery features that offer safety and accuracy may be required for adult and pediatric care areas where safe delivery of controlled substances are critical

Delivery devices

Elastomeric pump (non-electrical)

Figure 7.5. An elastomeric pump allows mobility for the homecare patient while they're receiving IV infusions. A wide range of flow rates and sizes covers most OPAT infusion protocols.



Delivery devices

Electronic infusion pump

Figure 7.6. Ambulatory electronic infusion pumps are able to deliver medication while allowing the patient to be mobile.

Delivery devices

Comparison of delivery devices

Drug Delivery Method	Description	Advantages	Disadvantages
Bolus or 'Push' [19, 49]	- Slow administration of a drug (usually over 3 to 5 minutes). - Through an IV access device using a syringe only.	- Low tech. - Most commonly used (hospital and community). - Least expensive (supply and administration costs).	- Not all antibiotic regimens can be delivered; some drugs require longer infusion times to avoid infusion related-toxicity or mitigate irritant properties
Non-electrical Pump (elastomeric devices are the most commonly used) [6, 18, 24, 49, 62]	- Controlled rate low pressure self-infusing devices. - Flow rate relies upon mechanical restriction through a narrow-bore tube.	- Disposable. - Portable. - Lightweight. - Relatively inexpensive (costs dependent on medication regimen). - Closed prefilled system resulting in less handling of the drug. - Fixed rates so programming errors are eliminated.	- Device size and relative rates are fixed. - Pharmacy input is required to fill each device. - Antimicrobial selection is limited due to drug stability; for example a drug selected for a 24 hour infusion must be stable at room temperature for 24 hours.
Electrical Pump [18, 19, 49]	- Programmable high pressure electrical devices.	- Controlled delivery - Flexible rates extending the range of drugs that can be used.	- Comparatively expensive. - Patient activity restricted due to battery life and transportability of the pump. - Reliant on trained users to programme the pumps. - Device supply and maintenance can be an issue.

Antimicrobial selection for OPAT

- ✓ **Pharmacokinetics and pharmacodynamics**
- ✓ **Spectrum of activity**
- ✓ **Stability**
- ✓ **Safety**
- ✓ **Laboratory monitoring**

Antimicrobial selection for OPAT

Practical considerations

- some **methods of administration** enhance practicality
  - IV push delivery over 1-2 minutes can be utilized for many antimicrobials, in particular, the cephalosporins (ready-to-use syringes)
- **less frequent administration** schedules enhance convenience and promote compliance
  - reduce catheter-associated complications (eg, hematoma, catheter migration, infections, thromboses)
- **drug stability** is of significant importance
  - Ideally, a reconstituted antimicrobial should be stable in the recommended storage conditions for up to 1 week after mixing
- **shorter courses** of therapy is another strategy to simplify OPAT and reduce antibiotic consumption and complications

Antimicrobial selection for OPAT

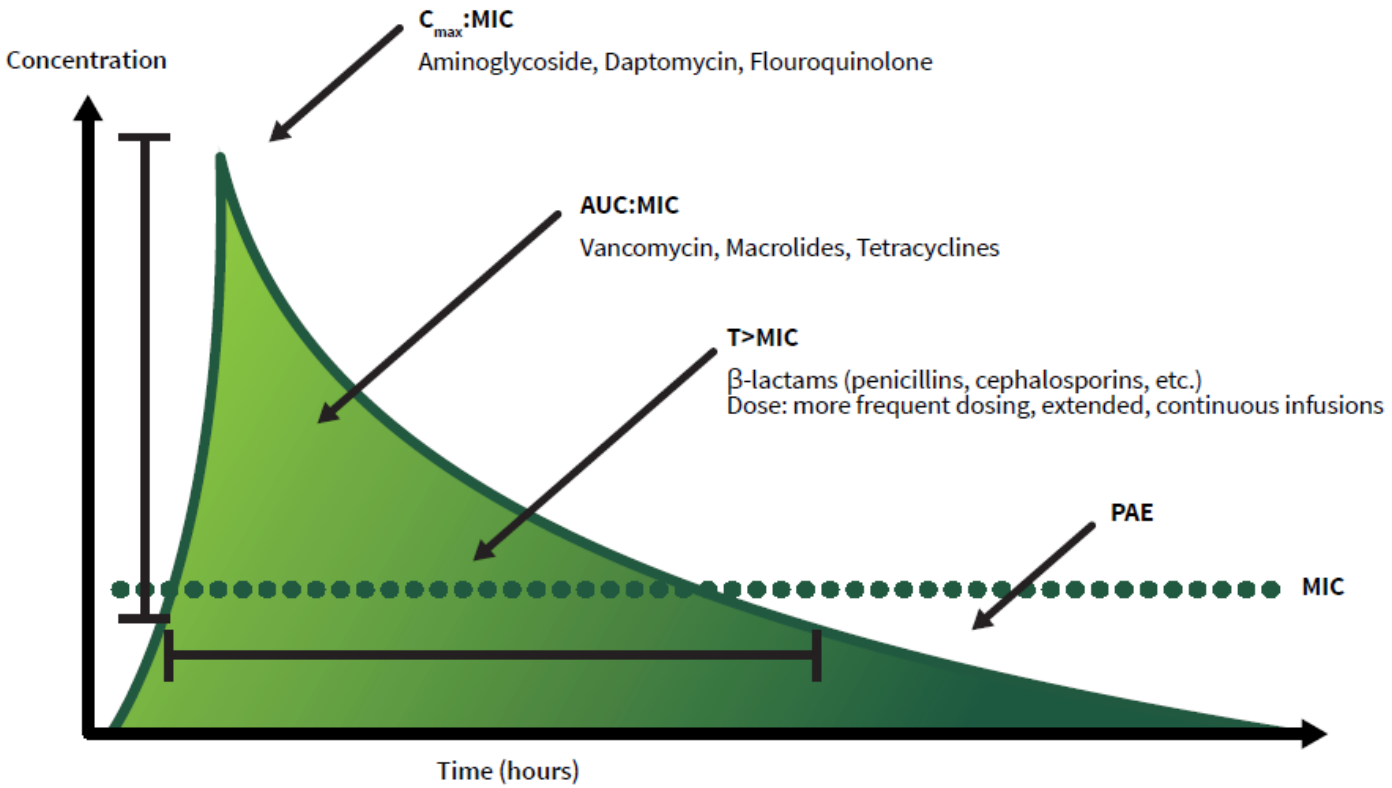
Frequency of administration and stability

Once daily
ceftriaxone
Teicoplanin (or 3/week)
ertapenem
daptomycin
aminoglycosides
levofloxacin
antifungals

Stable for more than 24 hours at room temperature or if refrigerated and can be used in syringe pumps or electronic infusion pumps
Aztreonam Cefazolin Cefepime Ceftazidime Clindamycin Nafcillin Oxacillin Penicillin Piperacillin ± tazobactam Ticarcillin ± clavulanate

Antimicrobial selection for OPAT

PK / PD targets



OPAT outcomes

Outpatient parenteral antimicrobial therapy (OPAT) in a teaching hospital-based practice: a retrospective cohort study describing experience and evolution over 10 years

International Journal of Antimicrobial Agents 39 (2012) 407– 413

The 10-y experience 2001-2010 of the Glasgow OPAT service (Scotland)

Outpatient parenteral antimicrobial therapy (OPAT) modalities for all OPAT episodes during 10-year study period.

	n (%)
Site of delivery (*n* = 2638)	
OPAT clinic	2024 (76.7)
Self or carer administered at home	493 (18.7)
OPAT home visits	103 (3.9)
Community nurse administered at home	3 (0.1)
Not recorded	15 (0.6)
Intravenous (i.v.) device used (*n* = 2848)[a]	
Butterfly needle	1321 (50.1)
Temporary short peripheral i.v. device (e.g. Venflon®)	732 (27.7)
Peripherally inserted i.v. catheter (midline)	375 (14.2)
Leaderflex® (midline)	247 (9.4)
Peripherally inserted central venous catheter	33 (1.3)
Hickman®	140 (5.3)

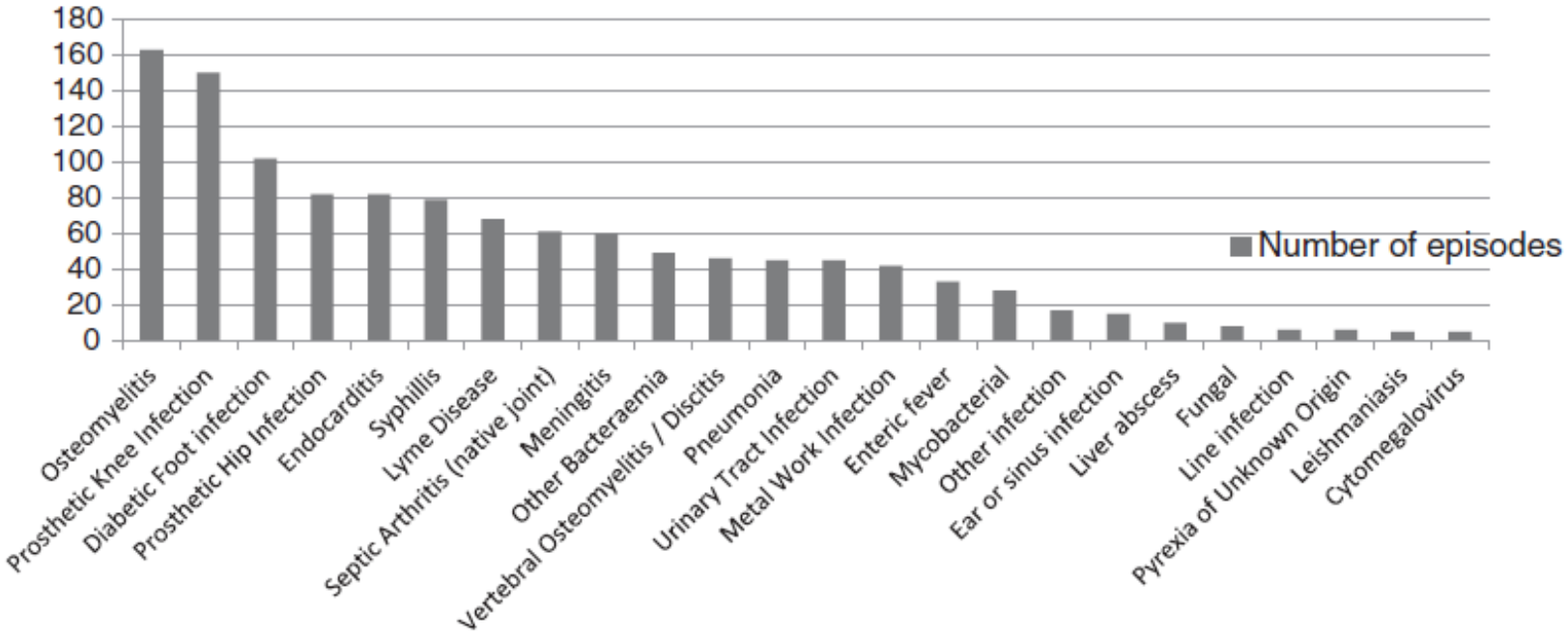
OPAT outcomes

Outpatient parenteral antibiotic therapy: Principles and practice

R.A. Seaton *, D.A. Barr [1]

European Journal of Internal Medicine 24 (2013) 617–623

The 10-y experience 2001-2010 of the Glasgow OPAT service (Scotland)



OPAT outcomes

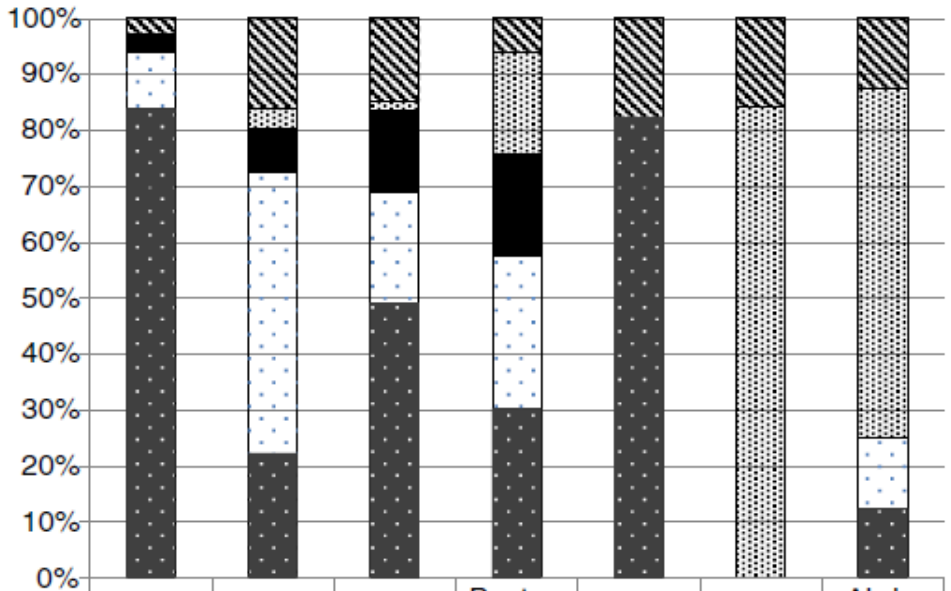
Outpatient parenteral antibiotic therapy: Principles and practice

R.A. Seaton *, D.A. Barr [1]

European Journal of Internal Medicine 24 (2013) 617–623

The 10-y experience 2001-2010 of the Glasgow OPAT service (Scotland)

First line antimicrobial agent use for common OPAT treated conditions in Glasgow OPAT service



Once daily

	SSTI	BJI	CVS	Bacteraemia	CNS	UTI	Abdo. Abscess
other	17	72	9	2	6	7	2
ertapenem	1	15	1	6	0	37	10
daptomycin	20	35	9	6	0	0	0
teicoplanin	62	223	12	9	0	0	2
ceftriaxone	521	99	30	10	28	0	2

OPAT outcomes

Outpatient parenteral antimicrobial therapy (OPAT) in a teaching hospital-based practice: a retrospective cohort study describing experience and evolution over 10 years

International Journal of Antimicrobial Agents 39 (2012) 407– 413

The 10-y experience 2001-2010 of the Glasgow OPAT service (Scotland)

Outcome	N (%)
Cure	1501 (67.2)
Improvement	562 (25.2)
No change	52 (2.3)
Deterioration	91 (4.1)
Death	8 (0.4)
Not recorded	19 (0.9)

92.4% success

Outpatient parenteral antibiotic therapy (OPAT) in different countries: a comparison

INTERNATIONAL JOURNAL OF Antimicrobial Agents

S. Esposito[a,*], S. Noviello[a], S. Leone[a], A. Tice[b], G. Seibold[b], D. Nathwani[c], F. Scaglione[d]

International OPAT Registry

The analysis of data concerned 9826 patients in the USA, 981 in the UK and 620 in Italy

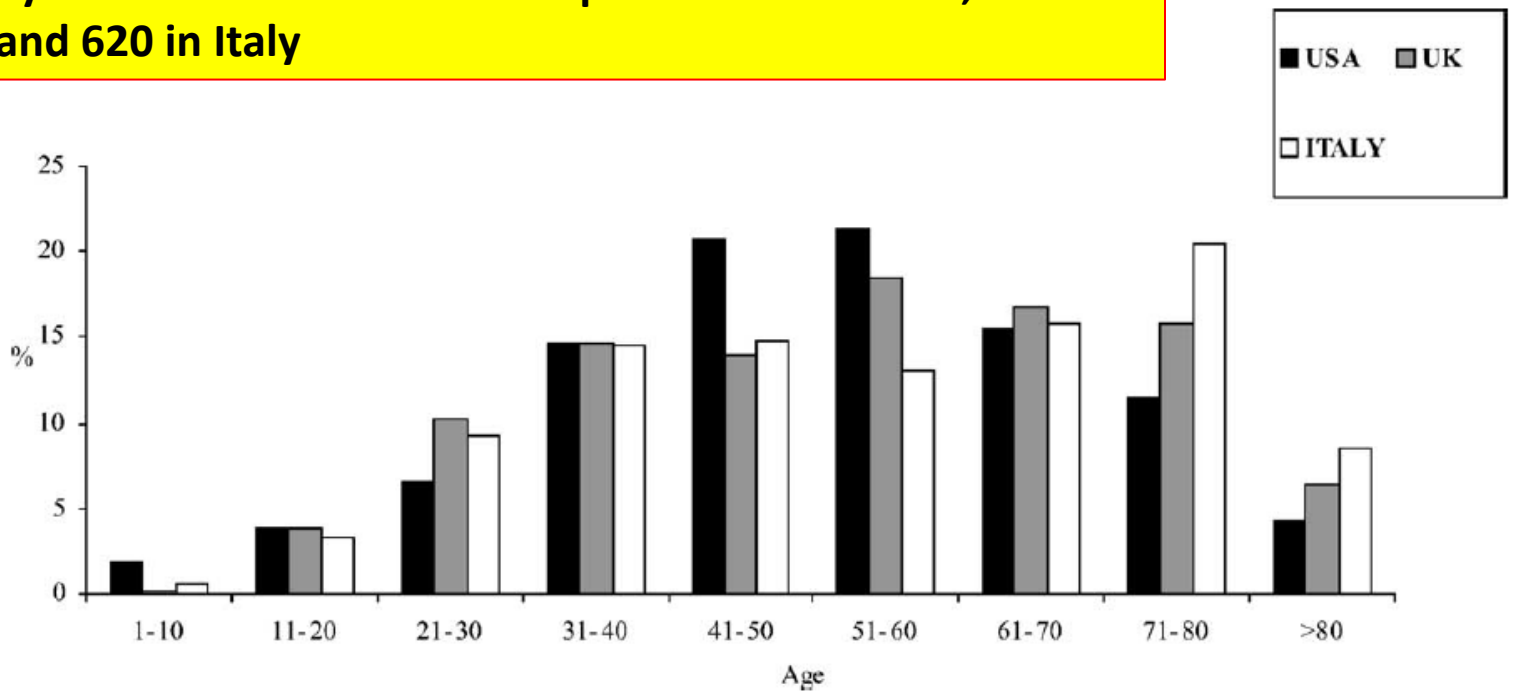


Fig. 1. Patients' age distribution (years).

Outpatient parenteral antibiotic therapy (OPAT) in different countries: a comparison

S. Esposito[a,*], S. Noviello[a], S. Leone[a], A. Tice[b], G. Seibold[b], D. Nathwani[c], F. Scaglione[d]

INTERNATIONAL JOURNAL OF Antimicrobial Agents

International OPAT Registry

Delivery model

	USA		UK		Italy	
	N	%	*N*	%	*N*	%
Administration by self or family members	6063	55.5	140	14.3	159	25.6
Infusion centre – clinic/MD office	3866	35.5	2	0.2	27	4.4
In home – visiting nurse or doctor	792	7.3	277	28.2	104	16.8
Infusion centre – hospital	8	0.1	390	39.8	307	49.5
Emergency room/urgent care	–	–	169	17.2	–	–
Other	190	1.7	3	0.3	23	3.7
Total	10919	100	981	100	620	100

Note: The total number of delivery models used in the USA is higher than the number of patients because many were treated with different administration models.

- In the USA OPAT is mainly performed according to the administration by the patient him/herself or by family members at the patients' home, the hospital infusion centre is preferred in Italy and the UK (Table 1);

- a **large percentage of antibiotic courses is carried out by i.m. route in Italy (39%),** which is rarely used in other countries (0.2% in the USA; never in the UK)

Outpatient parenteral antibiotic therapy (OPAT) in different countries: a comparison

INTERNATIONAL JOURNAL OF Antimicrobial Agents

S. Esposito[a,*], S. Noviello[a], S. Leone[a], A. Tice[b], G. Seibold[b], D. Nathwani[c], F. Scaglione[d]

International OPAT Registry

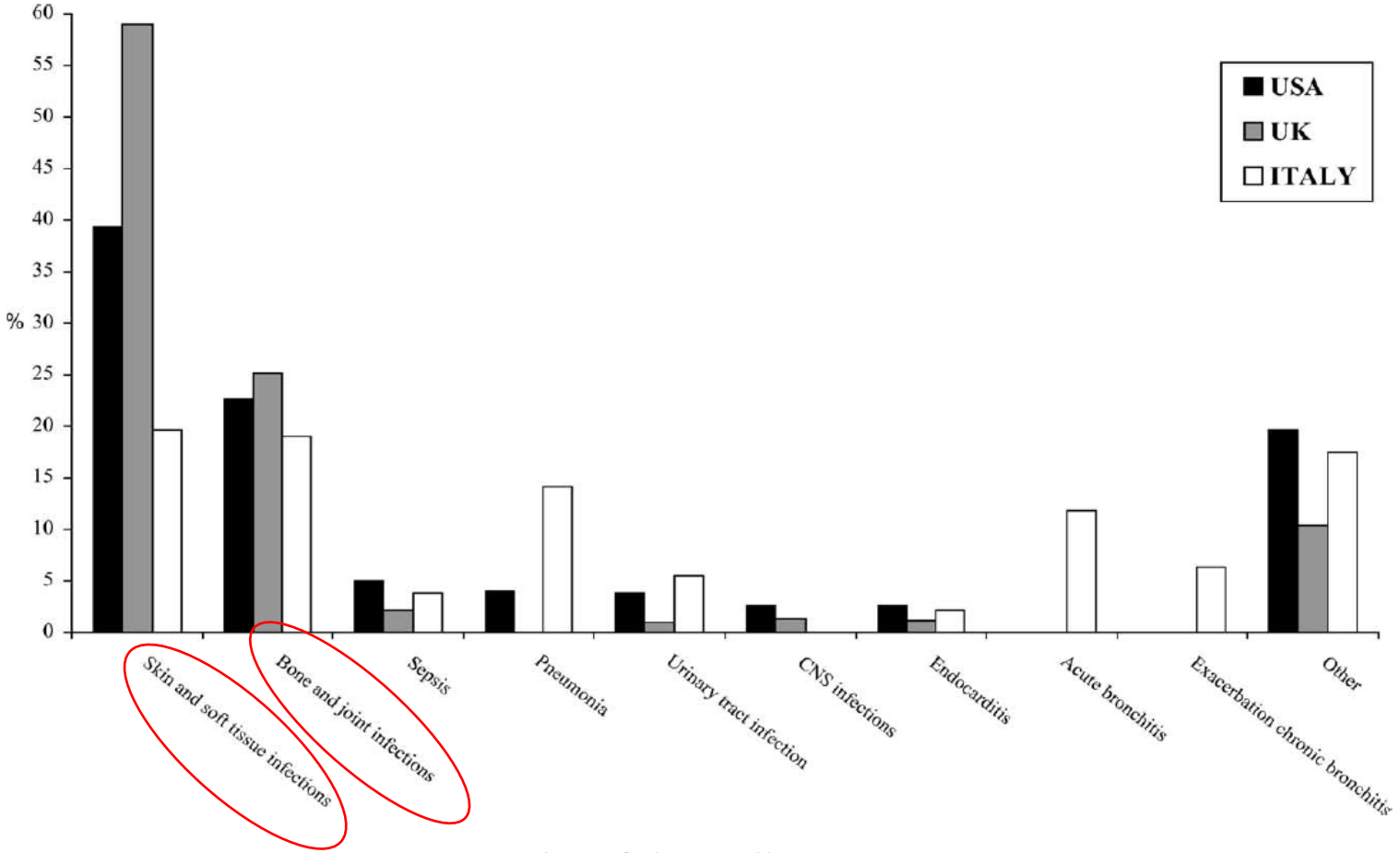


Fig. 2. Infections treated by country.

Outpatient parenteral antibiotic therapy (OPAT) in different countries: a comparison

INTERNATIONAL JOURNAL OF Antimicrobial Agents

S. Esposito[a,*], S. Noviello[a], S. Leone[a], A. Tice[b], G. Seibold[b], D. Nathwani[c], F. Scaglione[d]

International OPAT Registry

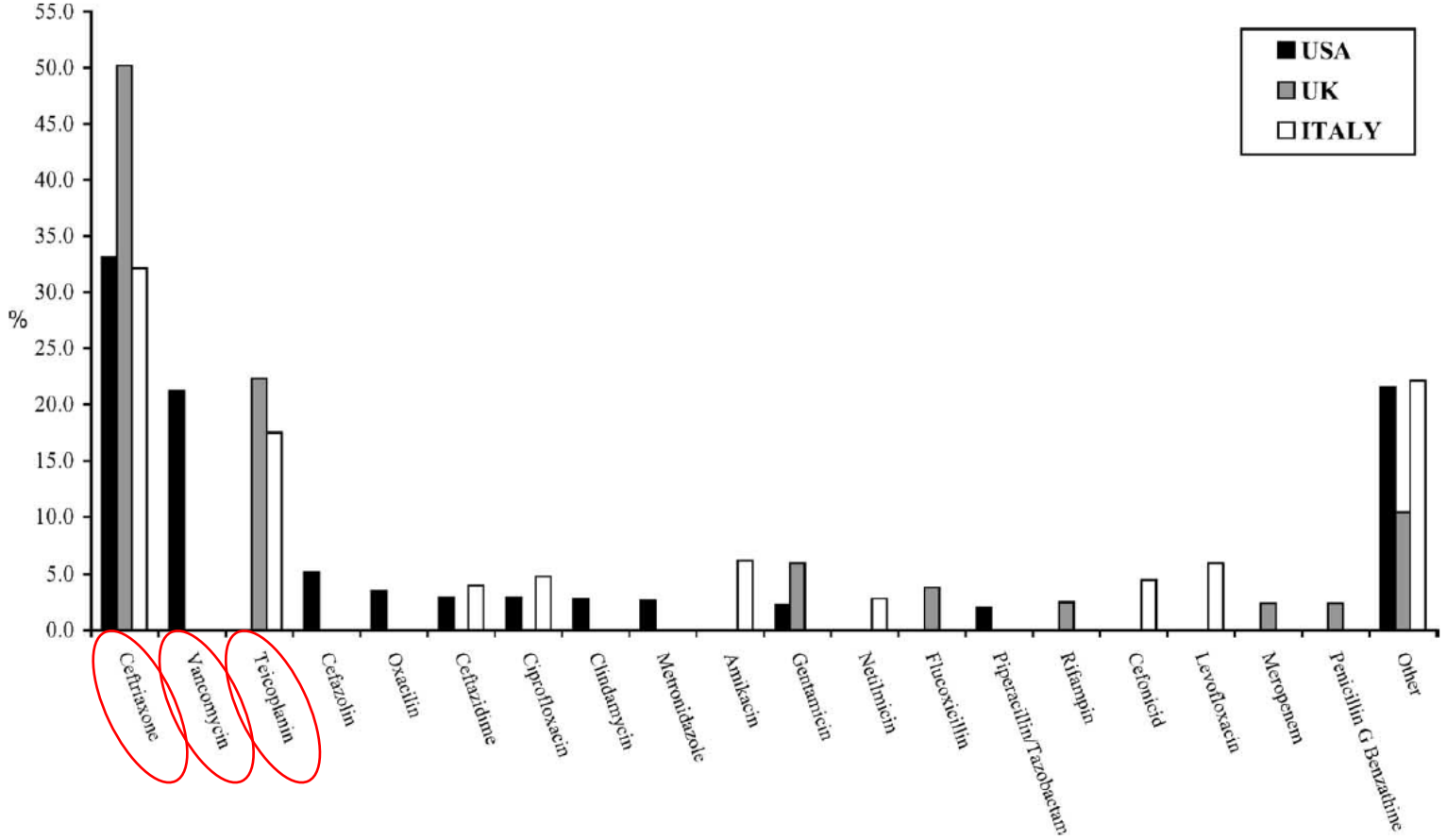


Fig. 3. Top antibiotics utilised.

Outpatient parenteral antibiotic therapy (OPAT) in different countries: a comparison

S. Esposito[a,*], S. Noviello[a], S. Leone[a], A. Tice[b], G. Seibold[b], D. Nathwani[c], F. Scaglione[d]

International OPAT Registry

INTERNATIONAL JOURNAL OF Antimicrobial Agents

- **Ceftriaxone** was the most frequently utilized antibiotic in OPAT, the second and third being **teicoplanin** and an aminoglycoside in the UK and Italy, and vancomycin and cefazolin in the USA
- Ceftriaxone is the top antimicrobial agent, probably not only due to its **long half-life**, but also its **wide antibacterial** spectrum (gram + and gram -)

- **Teicoplanin** has become the **top antimicrobial agent in the Italian OPAT** registry. Firstly, its pharmacokinetic and pharmacodynamic properties **permit once daily dosing**
- long elimination half-life, **teicoplanin can be successfully used three-times weekly** for the treatment of chronic infections.
- **mainstay for the treatment of SSTIs and BJIs** that are the infections most suitable for OPAT in several countries
- spectrum of activity, including **methicillin-resistant staphylococcal species** (frequent need to prescribe **antimicrobial therapy on an empirical basis)**

Outpatient parenteral antibiotic therapy (OPAT) in different countries: a comparison

INTERNATIONAL JOURNAL OF Antimicrobial Agents

S. Esposito[a,*], S. Noviello[a], S. Leone[a], A. Tice[b], G. Seibold[b], D. Nathwani[c], F. Scaglione[d]

International OPAT Registry

Clinical outcome

	USA		UK		Italy	
	N	%	*N*	%	*N*	%
Improved	9089	92.5	950	96.8	590	95.1
No change	226	2.3	9	0.9	8	1.4
Failed	128	1.3	13	1.3	15	2.4
Other	392	3.9	9	1.0	7	1.1
Total	9826	100	981	100	620	100

Infections amenable to OPAT

Infective Endocarditis and Cardiac Device infections

- annual incidence of about 3 to 9 cases per 100,000 persons in developed countries
- Staphylococci (aureus increasing), streptococci, and enterococci
- The traditional course of treatment for infective endocarditis is 4 to 6 weeks of IV antibiotic(s)

✓ Several studies have shown that selected patients with infective endocarditis can be safely treated via OPAT

✓ accepted practice for patients to be initially treated in the hospital and then discharged on OPAT once clinically stable
  - ✓ **stable and responding well**
  - ✓ **without signs of heart failure**
  - ✓ **without indications for surgery**
  - ✓ **without uncontrolled extra-cardiac foci**

✓ patients with uncomplicated infective endocarditis caused by viridans group streptococci could be discharged on OPAT after 2 weeks of hospitalization (ceftriaxone once daily)
✓ MRSA endocarditis → daptomycin (once daily)
✓ Enterococcal endocarditis (VRE) → daptomycin or linezolid

Clin Infect Dis. 2001;33(2):203–209, *Postgrad Med J*. 2012;88(1041):377-381

Infective Endocarditis and Cardiac Device infections

Table 3. European Society of Cardiology recommendations on suitability of patients for OPAT treatment of endocarditis 2009.[19]

Phase of treatment	Guidelines for use of OPAT
Critical phase (weeks 0–2)	• Complications occur during this phase • Preferred inpatient treatment during this phase • Consider OPAT if patient has oral streptococci, patient is stable and/or there are no complications
Continuation phase (beyond week 2)	• Consider OPAT if medically stable. • Do not consider OPAT if patient has or has had heart failure, concerning echocardiographic features, neurological signs or renal impairment
Essential for OPAT	• Educate patient and staff • Regular post discharge evaluation (nurses 1/day, physician 1–2/week) • Prefer physician directed program, not home infusion model

OPAT = outpatient parenteral antimicrobial therapy.

J Infect 2009;59:387–93, *Postgrad Med J* 2012;88:377–81, *J Antimicrob Chemother* 2013;68:1650–4, *Eur Heart J* 2009;30:2369–413

Infective Endocarditis and Cardiac Device infections

- **recent cohort reports that OPAT services are successfully treating *S. aureus* and prosthetic valve endocarditis (negative blood cultures, no cardiac failure, no embolic events)**

Table 1. Characteristics of recently published UK OPAT service cohorts.

Cohort	Number of OPAT episodes	Example conditions treated (% OPAT episodes)	Antibiotics used (% OPAT episodes)	IV access device*	Site of delivery
Glasgow[1]	2,638	SSTI (52.7)	Ceftriaxone (58.8)	Butterfly needle (50.1)	C-OPAT (76.6)
		BJI (24.5)	Teicoplanin (26.4)	Short peripheral device (27.7)	S-OPAT (18.7)
		Endocarditis (3.1)	Daptomycin (2.0)	Midline (23.6)	OPAT nurse H-OPAT (3.9)
		Meningitis (2.3)	Ertapenem (1.8)	PICC (1.3)	Primary care nurse H-OPAT (0.1)
		UTI (1.7)	Flucloxacillin (1.1)	Tunnelled central line (5.3)	

Int J Antimicrob Agents 2012;39:407–413.

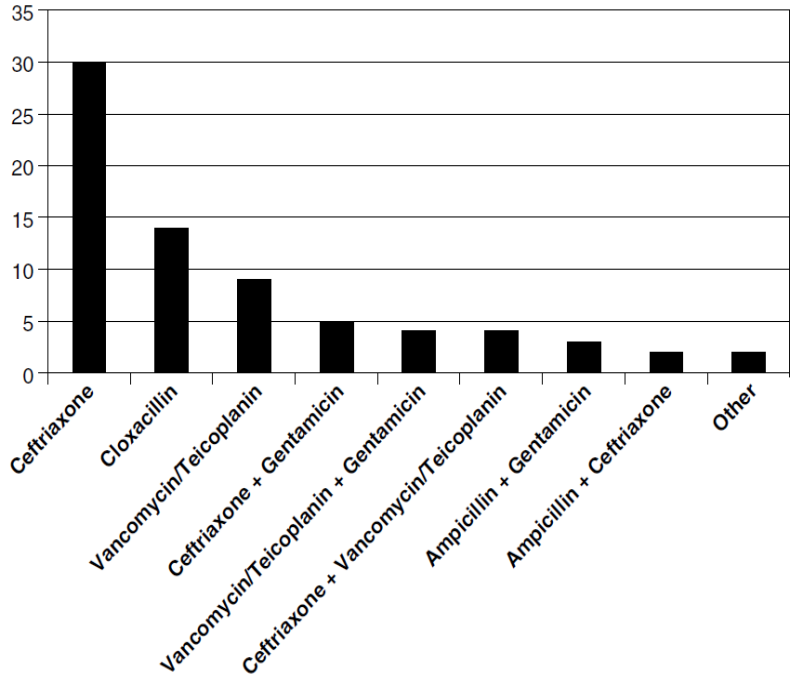
Infective Endocarditis and Cardiac Device infections

Efficacy and safety of outpatient parenteral antibiotic therapy for infective endocarditis: a ten-year prospective study☆

Enferm Infecc Microbiol Clin. 2011;29(8):587–592

- Prospective single center study of a cohort including all patients with IE admitted to the Hospital of Barcelona entering the OPAT program from January 1997 to December 2006
- 392 consecutive episodes of IE
  - 42 native-valve
  - 23 prosthetic-valve
  - 8 pacemaker-lead

outcome	All cases	VGS or S. bovis	S. aureus or CoNS	P
Readmission	16%	13%	27%	0.285
Death	4%	0%	9%	0.161



Outpatient Parenteral Antibiotic Treatment for Infective Endocarditis: A Prospective Cohort Study From the GAMES Cohort

Clinical Infectious Diseases 2019

- **2000 consecutive IE** patients in 25 Spanish hospitals (2008–2012)
- **429 patients (21.5%) received OPAT**
- only **21.7% fulfilled IDSA criteria**
- Failing to fulfill IDSA criteria was not a risk factor for mortality or readmission
- OPAT provided **excellent results** despite the use of **broader criteria**

Table 2. Criteria Used to Indicate Outpatient Parenteral Antibiotic Treatment in Infective Endocarditis Patients by GAMES Investigators in the Present Cohort

Type of IE	Recommendation	Indications	Requirements
Native valve	Rapid transfer to OPAT (as of 10 days after admission/surgery)	• IE by any causative agent, except HDTTM[a] • Patients not presenting severe clinical complications • Patients undergoing or not undergoing cardiac surgery	• Negative blood cultures at 72 hours • No severe clinical complications o post-surgical complications • No anticoagulation issues • TEE ruling out severe aortic regurgitation and prosthetic dysfunctior
	Postponed transfer (at least 3 weeks after admission/surgery)	• Patients presenting with severe complications at onset • Very fragile patients or patients with severe comorbidities undergoing cardiac surgery or other treatment	• Identical criteria plus: • No severe sequelae or clinical complications • Need for frequent and/or complex cures
Prosthetic valve	Rapid transfer to OPAT (as of 10 days after admission)	• All cases caused by viridans or bovis group streptococci or *Enterococcus faecalis* and • Not undergoing cardiac surgery	• Same as for rapid transfer in NVIE
	Postponed transfer (at least 3 weeks after admission/surgery)	• Cases of IE undergoing cardiac surgery and • Not caused by HDTTM or • Presenting severe complications	• Same as for postponed transfer in NVIE

Osteoarticular infections

- **prolonged 4- to 6-week course** of treatment is necessary
- common bacteria that cause osteomyelitis are *S. aureus*, coagulase-negative **staphylococci**, and gram-negative bacilli
- Treatment of infections associated with **prosthetic implants** includes **removing** the prosthetic material whenever possible
- Osteoarticular infections with *S. aureus* and coagulase-negative staphylococci are best treated with parenteral antibiotics. Oxacillin or nafcillin are the best antibiotics for methicillin-susceptible strains
- **MRSA options?** (IV) Daptomycin, Teicoplanin, Vancomycin, linezolid, Dalbavancin and (p.o) Linezolid, Minocycline, TMP/SXT, RIF
- Many gram-negative osteoarticular infections can be treated with an oral quinolone
- **Diskitis/vertebral osteomyelitis** in the adult, on the other hand, is a deep, serious, and difficult-to-treat infection: **standard recommendations are IV infusion of antimicrobial agents for at least 2 weeks**

Osteoarticular infections

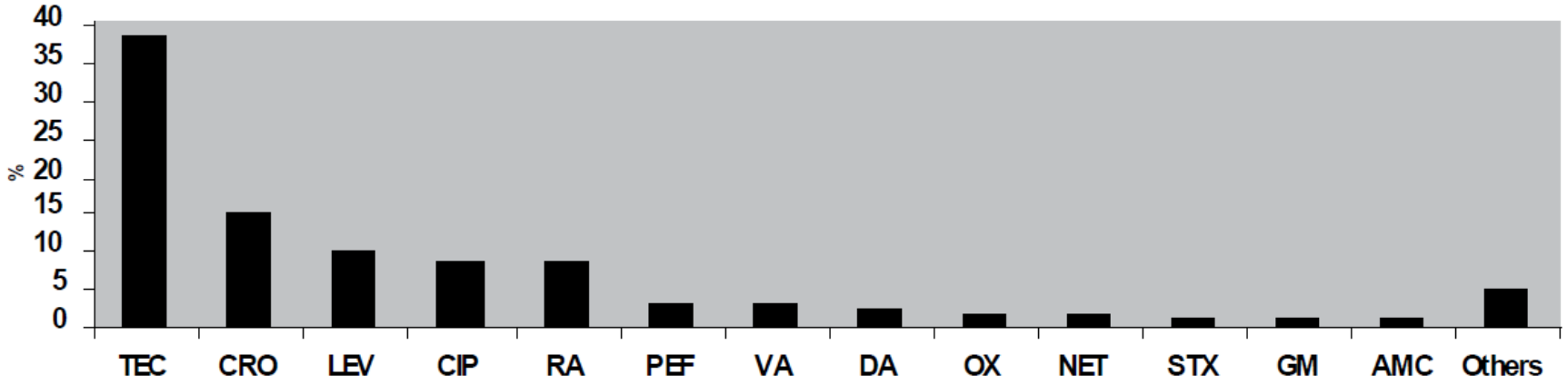
- **Retrospective analysis** of patients with acute osteomyelitis who received OPAT has demonstrated good success, with **cure rates between 70% and 95%.**
- Safety is less of an issue in patients with osteomyelitis than in patients with some other types of infection
- most of these patients are stable, and osteomyelitis is almost never a fulminant infection
- However, clinical failures are associated with severe local devastating consequences

Infect Dis Clin North Am. 1998;12:903-919, J Clin Pharm Ther. 2001; 26:445-451.

Osteoarticular infections

Outpatient Parenteral Antibiotic Therapy for Bone and Joint Infections: An Italian Multicenter Study

Journal of Chemotherapy *Vol. 19 - n. 4 (417-422) - 2007*



TEC: Teicoplanin; CRO: Ceftriaxone; LEV: Levofloxacin; RA: Rifampicin; CIP: Ciprofloxacin; PEF: Pefloxacin; DA: Clindamycin; OX: Oxacillin; NET: Netilmicin; SXT: Cotrimoxazole; GM: Gentamicin; AMC; Coamoxiclav

Osteoarticular infections

Outpatient Parenteral Antibiotic Therapy for Bone and Joint Infections: An Italian Multicenter Study

Journal of Chemotherapy *Vol. 19 - n. 4 (417-422) - 2007*

TABLE 3 - *Clinical outcome at follow-up (30 days after the end of therapy).*

	Septic arthritis		Osteomyelitis		Prosthetic joint infection		Spondylodiskitis		Total	
	N.	%	N.	%	N.	(%)	N.	%	N.	%
Improvement	4	18.2	13	23.2	14	43.7	4	40	35	29.2
Cure	18	81.8	36	64.3	13	40.6	5	50	72	60
Relapse	–	–	1	1.8	1	3.1	1	10	3	2.5
No variation	–	–	1	1.8	–	–	–	–	1	0.8
Impairment	–	–	5	8.9	4	12.6	–	–	9	7.5
Total	22	100	56	100	32	100	10	100	120	100

Outpatient parenteral antimicrobial therapy for orthopedic infections – a successful public healthcare experience in Brazil

The Brazilian Journal of
INFECTIOUS DISEASES
www.elsevier.com/locate/bjid

Table 2 – Distribution of patients on outpatient parenteral antimicrobial therapy according to diagnosis.

Diagnosis	Number of patients	%
Soft tissue infection	13	11.20
Chronic osteomyelitis	51	43.96
Acute osteomyelitis	51	43.96

- **116 patients**
- In one year save of **11,698 bed-days** at the orthopaedics ward to be redirected to patients really needing to be hospitalized
- The duration of treatment varied from 10 to 180 days
- **98.3% used PICC lines**
- **Only three patients presented adverse effects**
- **All pts favourable outcome**

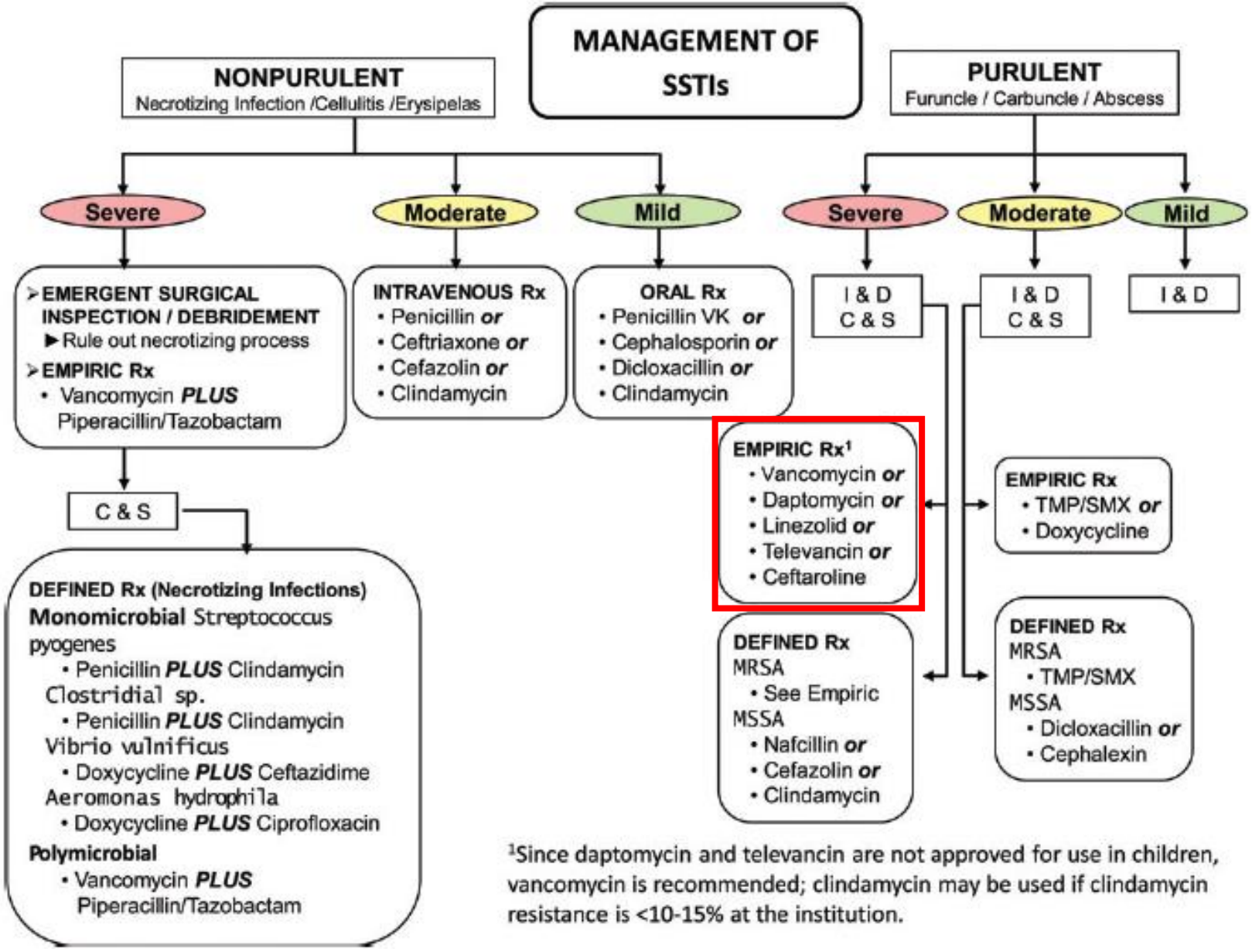
Table 3 – Antimicrobials used for treating orthopedic infections in outpatient parenteral antimicrobial therapy.

Antimicrobial	Number of patients	%
Teicoplanin	53	39.55
Ertapenem	22	16.42
Tigecycline	13	9.70
Vancomycin	12	8.96
Meropenem	10	7.46
Ceftazidime	9	6.72
Linezolid	5	3.73
Ceftriaxone	3	2.24
Colistin	3	2.24
Amycacin	2	1.49
Streptomycin	1	0.75
Gentamycin	1	0.75

Skin and Soft tissue infections

- Traditionally, patients with severe skin and soft tissue infections were hospitalized, treated with IV antibiotics in the hospital, discharged on oral antibiotics once improved
- The development of OPAT has allowed for discharge from the hospital sooner, on IV antibiotic therapy
- When parenteral antimicrobial therapy is required, **ceftriaxone is appropriate for streptococcal infections**
- **Oxacillin and nafcillin are appropriate for methicillin-susceptible *S. aureus* infections**
  - QDS dosing regimen makes it **uncomfortable for OPAT use** unless administered as a 24-hour infusion using an elastomeric device. Stable for 24 hours at room temperature and 7 days if refrigerated (2-8°)
- If a **mixed infection** is to be treated, ampicillin-sulbactam, piperacillin-tazobactam, or ertapenem may be used
- Vancomycin, teicoplanin, daptomycin, ceftaroline, linezolid, tedizolid are effective options for treatment of methicillin-resistant *S. aureus* **(MRSA) infections**
- Another option is **dalbavancin**, a long-lasting agent that has recently been approved as a single-dose (30 min IV infusion) for the treatment of acute bacterial skin and skin structure infections, including MRSA.

Skin and Soft tissue infections



[1]Since daptomycin and televancin are not approved for use in children, vancomycin is recommended; clindamycin may be used if clindamycin resistance is <10-15% at the institution.

Skin and Soft tissue infections

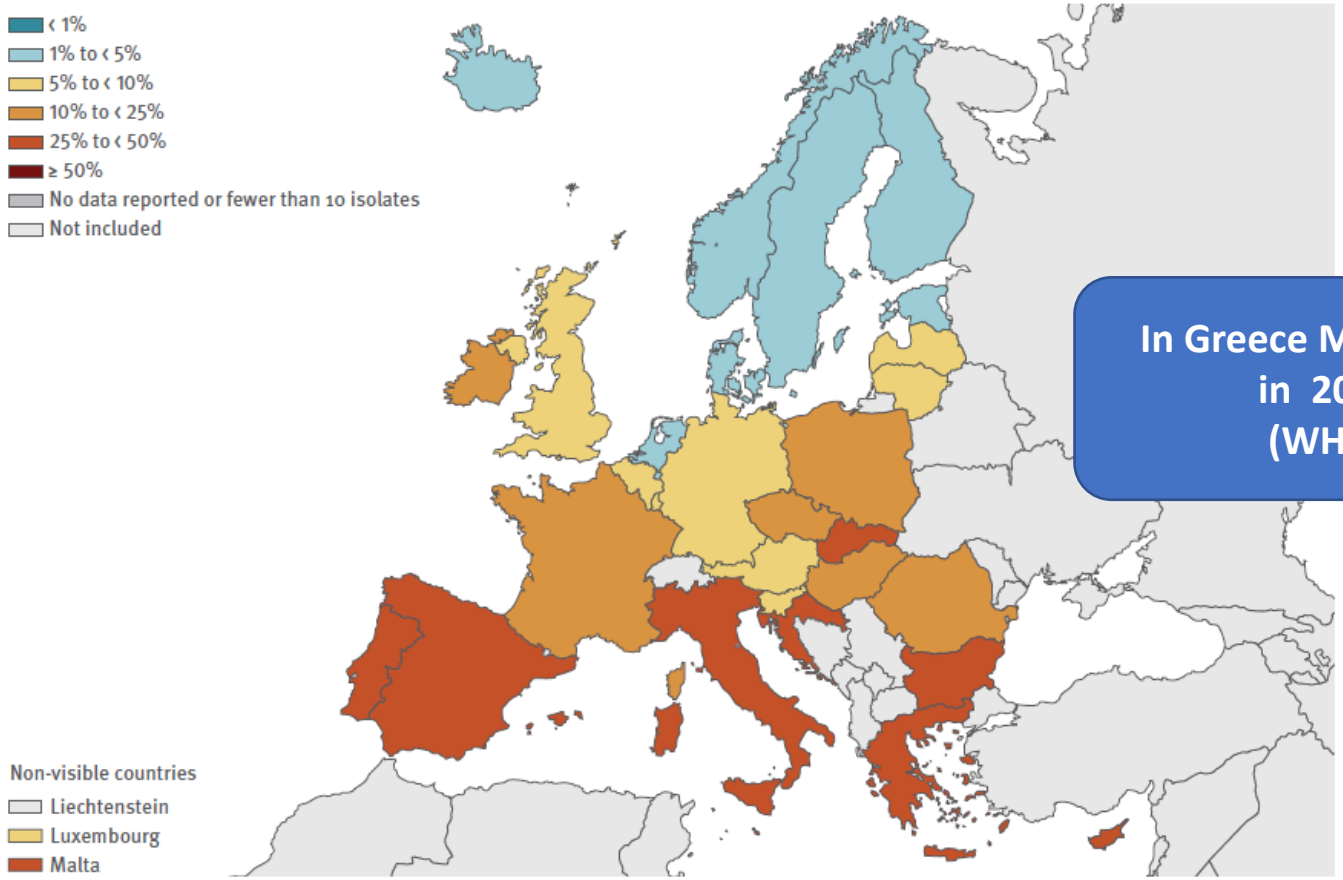
Table 1. Characteristics of recently published UK OPAT service cohorts.

Cohort	Number of OPAT episodes	Example conditions treated (% OPAT episodes)	Antibiotics used (% OPAT episodes)	IV access device*	Site of delivery
Glasgow[1]	2,638	SSTI (52.7)	Ceftriaxone (58.8)	Butterfly needle (50.1)	C-OPAT (76.6)
		BJI (24.5)	Teicoplanin (26.4)	Short peripheral device (27.7)	S-OPAT (18.7)
		Endocarditis (3.1)	Daptomycin (2.0)	Midline (23.6)	OPAT nurse H-OPAT (3.9)
		Meningitis (2.3)	Ertapenem (1.8)	PICC (1.3)	Primary care nurse H-OPAT (0.1)
		UTI (1.7)	Flucloxacillin (1.1)	Tunnelled central line (5.3)	
Oxford[4]	2,059	BJI (73.3)	Ceftriaxone (43.0)	PICC (65.6)	H-OPAT (76.0)
		SSTI (5.6)	Teicoplanin (36.8)	Tunnelled central line (31.4)	S-OPAT (24.0)
		Bacteraemia (5.7)	Meropenem (6.2)	Midline (1.6)	
		Endovascular (3.5)	Vancomycin (5.9)	Non-tunnelled central line (1.1)	
			Ertapenem (1.6)		
Sheffield[2]	334	SSTI (59)	Ceftriaxone (80.5)	Peripheral cannula (77.0)	Predominantly C-OPAT and S-OPAT
		CNSI (10)	Vancomycin (3.6)	PICC (14.7)	
		Endovascular (7)	Amphotericin B (3.3)	Tunnelled central line (7.5)	
		Intra-abdominal (5)	Teicoplanin (3.0)		
		BJI (4)	Ertapenem (3.0)		

C-OPAT = OPAT delivery in OPAT clinic/infusion centre
H-OPAT = delivery of OPAT in patient's home by OPAT nurses
S-OPAT = OPAT delivery by self (patient or carer) in patient's home

Prevalence of MRSA (ECDC 2017)

Figure 3.25. *Staphylococcus aureus*. Percentage (%) of invasive isolates with resistance to meticillin (MRSA), by country, EU/EEA countries, 2017



In Greece MRSA invasive isolates in 2017 was 35,3 % (WHONET Greece)

1. ECDC. http://ecdc.europa.eu/en/publications/Publications/antimicrobial-resistance-europe-2017.pdf (Last accessed 13 May 2019), 2.Garau J, Ostermann H, Medina J, et al. Clin Microbiol Infect 2013; 19:E377–85., 3. Dryden MS. J Antimicrob Chemother 2010; 65(Suppl. 3):iii35–iii44. . Souli M et al. Infectious Diseases, 2016; 48: (4): 287–292 3.

High rates of community-acquired, Panton-Valentine leukocidin (PVL)- positive methicillin-resistant *S. aureus* (MRSA) infections in adult outpatients in Greece

S Vourli[1], H Vagiakou[2], G Ganteris[2], M Orfanidou[2], M Polemis[1], A Vatopoulos (avatopou@nsph.gr)[1], H Malamou-Ladas[2]
1. Department of Microbiology., National School of Public Health, Athens, Greece
2. Department of Microbiology, "G Gennimatas" General Hospital, Athens, Greece

- In Greek adult pts with cSSTI ***S. aureus was isolated in* 30,8%**
- In 27/88 **(30,7%) MRSA**
- **All strains were SCC*mec* type IV, και PVL (+)**
- Clone ST80

TABLE

Main characteristics of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) strains* isolated in a tertiary-care hospital in Athens, Greece, January 2006 - December 2007 (n=27)

No	Sex**	Age	Disease	PFGE type	*spa* type	Resistance Phenotype***
1	M	45	Furuncle	A1	t044	Oxa Tet Km FA
2	M	43	Abscess (skin)	A	t044	Oxa Tet Km FA
3	F	45	Abscess (skin)	A	t044	Oxa Tet Km FA
4	M	34	Furuncle	A1	t044	Oxa Tet Km FA
5	F	43	Abscess (soft tissue)	A	t044	Oxa Tet Km FA
6	F	46	Folliculitis	A	t131	Oxa Tet Km FA
7	M	51	Furuncle	A2	t044	Oxa Tet Km FA
8	F	32	Abscess (soft tissue)	A	t044	Oxa Tet Km FA
9	M	45	Abscess (soft tissue)	A	t044	Oxa Tet Km FA
10	M	32	Abscess (soft tissue)	A	t044	Oxa Tet Km FA
11	F	38	Abscess (skin)	A	t044	Oxa Tet Km FA
12	F	31	Wound infection	A1	t044	Oxa Tet Km FA
13	F	29	Abscess (skin)	A	t044	Oxa Tet Km FA
14	M	35	Wound infection	A	t044	Oxa Tet Km FA
15	F	48	Furuncle	A	t044	Oxa Tet Km FA
16	M	39	Abscess (skin)	A3	t044	Oxa Tet Km FA
17	F	46	Abscess (skin)	A	t044	Oxa Tet Km FA
18	M	51	Abscess (soft tissue)	A2	t044	Oxa Tet Km FA
19	M	56	Abscess (soft tissue)	A1	t044	Oxa Tet Km FA
20	F	51	Furuncle	A	t044	Oxa Tet Km FA
21	M	45	Abscess (soft tissue)	A	t044	Oxa Tet Km FA
22	M	47	Abscess (soft tissue)	A	t044	Oxa Tet Km FA
23	M	43	Wound infection	A	t044	Oxa Tet Km FA
24	F	46	Abscess (soft tissue)	A	t044	Oxa Tet Km FA
25	F	51	Wound infection	A4	t044	Oxa Tet Km FA
26	M	34	Furuncle	A	t044	Oxa Tet Km FA
27	F	51	Abscess (skin)	A1	t044	Oxa Tet Km FA

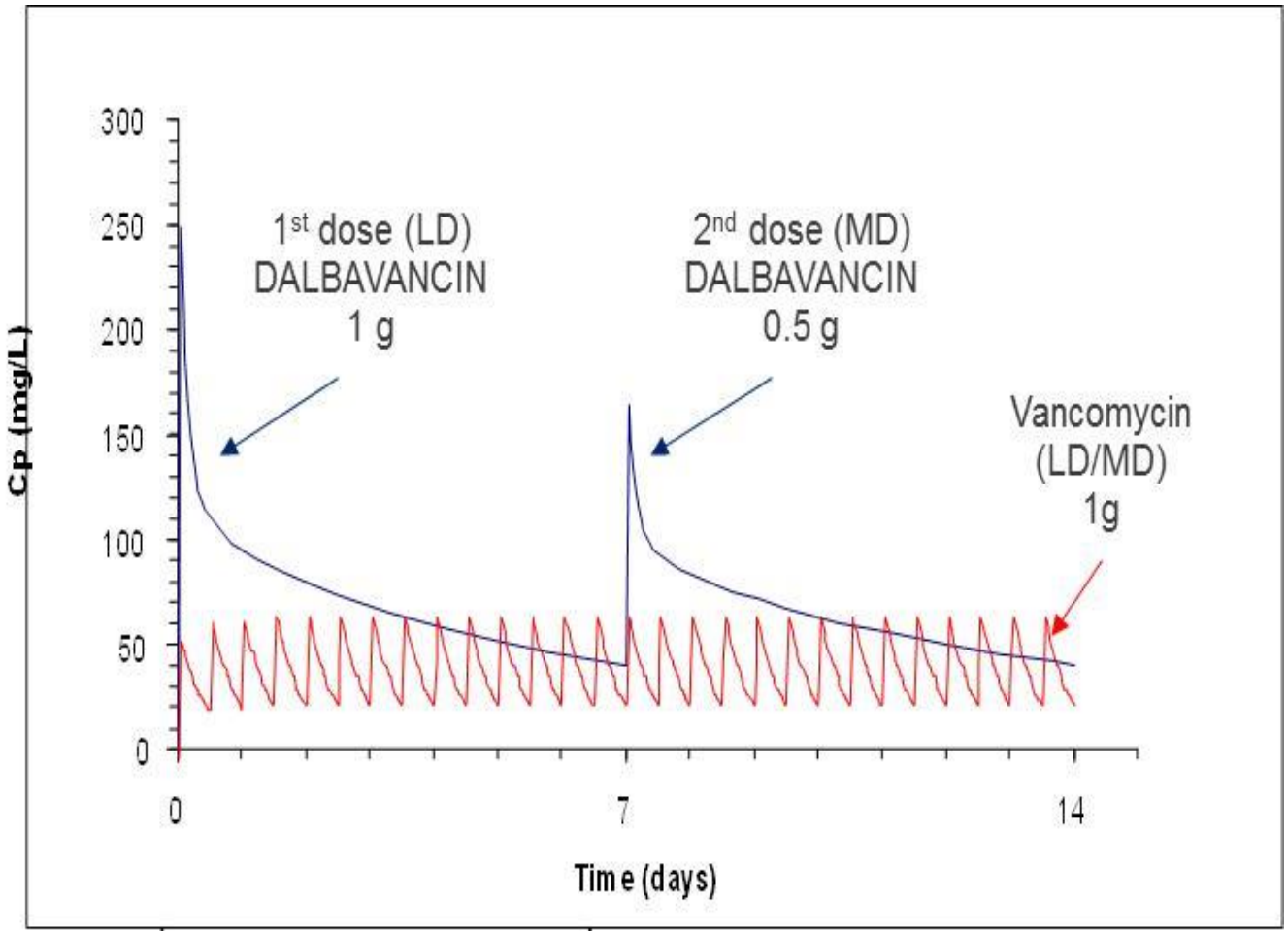
* Note: All stains were sensitive to tobramycin and gentamicin, cotrimoxazole, chloramphenicol, quinolones, clindamycin, erythromycin.
** M=male; F=female
*** Oxa=Oxacyclin; Tet=Tetracyclin; Km=Kanamycin; FA=Fucidic acid

PK Data for Glycopeptides

Parameter	Vancomycin	Teicoplanin	Dalbavancin
Standard dose	15 mg/kg q12h	6 mg/kg q24 h	1 g on day 1, 500 mg on day 8
C_{max} (mg/l)	20–50	68–155	312
AUC (mg*h/l)	260	420–621	27103
Vd (L/kg)	0.3	0.9–1.6	0.11
Protein-binding (%)	10–55	88–94	93–98
Blister fluid:plasma concentration	NA	NA	0.60–1.11
Terminal $t_{1/2}$ (h)	4–8	70–100	147–258
Renal excretion (%)	>80–90	48–61	42

Henson KER et al, Expert Rev Anti Infect Ther 2015

Dalbavancin - Pharmacokinetics



Curr Opin Infect Dis 2018, 31:141–147
Dorr, JAC 2005;55 Supp S2:ii25; data on file

A Randomized Clinical Trial of Single Dose vs Weekly Dalbavancin for Treatment of Acute Bacterial Skin and Skin Structure Infection

A randomized, double-blind trial in patients > 18 years with ABSSSI. Patients were randomized to **dalbavancin 1500 mg either as a single IV infusion** or 1000 mg IV on Day 1 followed one week later by 500 mg IV. The primary endpoint was a ≥20% reduction in the area of erythema at 48-72 hours in the Intent to Treat (ITT) population.
Clinical outcome was also assessed at Days 14 and 28.

Results
698 patients.
more patients with a methicillin-resistant *Staphylococcus aureus* (MRSA) at baseline on the two-dose regimen [36/210 (17.1%) vs 61/220 (27.7%)].
Dalbavancin delivered as a single dose was non-inferior to a two dose regimen (81.4% vs 84.2%; difference -2.9%; 95%CI: -8.5, 2.8).
Clinical outcomes were also similar at Day 14 (84.0% vs 84.8%), Day 28 (84.5% vs 85.1%) and at Day 14 in clinically evaluable patients with MRSA in a baseline culture (92.9% vs.95.3%) in the single and two dose regimens, respectively.
Treatment emergent adverse events (TEAE) occurred in 20.1% of the single dose patients and 19.9% on the two dose regimen.

A single 1500 mg infusion of dalbavancin is non-inferior to a two-dose regimen, has a similar safety profile and removes logistical constraints related to delivery of the second dose

Dunne et al CID 2016

CNS infections

- Success rates for CNS infections treated with OPAT are good
- These infections are similar to endocarditis in that patients are at high risk for complications and rehospitalization
- **Complications of meningitis occur most frequently by day 2-3 and are very rare after day 3-4** (→ candidates for OPAT in clinical responders)
- **Patients need to be monitored closely**, and the clinician should have a low threshold for readmission
- **Ceftriaxone** the main antibiotic used
  - Completion of 10 d of parenteral therapy for bacterial meningitis
  - Longer courses for brain abscess (CT guided duration)

Clin Infect Dis. 1999;29:1394-1399

Urinary tract infections

- When a patient has a urinary tract infection, the first treatment decision is whether the patient can be treated with an oral antibiotic

- When IV treatment is necessary, many treatment options are amenable to once-daily dosing:

  - Ceftriaxone (non-ESBL)
  - Ertapenem (ESBL)
  - Aminoglycosides

RESEARCH ARTICLE

Shortening duration of ertapenem in outpatient parenteral antimicrobial therapy for complicated urinary tract infections: A retrospective study

- **76% episodes related to pyelonephritis or urosepsis** diagnoses
- **45% of patients presented renal tract abnormalities** or prior urological surgery
- The median duration of appropriate parenteral antibiotic therapy in our study was 6 days

- **Clinical cure** was achieved with short-course parenteral treatment **alone in 81%** of patients
- Clinical cure increased to **96% when adjunctive fosfomycin** was used

Table 1. Clinical and microbiological characteristics of patients.

Age in years (Mean and Range)		49 (22–91)
Male		13 (43%)
Indication	Pyelonephritis	19 (57.6%)
	Urosepsis	6 (18.2%)
	Urinary Tract Infection	5 (15.2%)
	Prostatitis	3 (9.0%)
Microbiology	ESBL *E.coli*	20 (60.6%)
	Other ESBL	2 (6.1%)
	AmpC Producer	2 (6.1%)
	Other	2 (6.1%)
	No positive sample*	7 (21.1%)
Microbiology for patients receiving OPAT ertapenem	ESBL/AmpC Producer	31 (93%)
	Drug Allergy	2 (7%)

Abdominal infections

- Before OPAT → source control!!
- Polymicrobial infections
- Empiric antibiotic treatment should include broad-spectrum coverage for enteric gram-negative bacteria, anaerobic bacteria, and enteric streptococci
- Ertapenem once daily (ESBL coverage but no pseudomonas)

Abdominal infections

Safety and Efficacy of Long-Term Outpatient Ertapenem Therapy

Antimicrobial Agents and Chemotherapy 2014;58: p. 3437–3440

- Of the 46 patients **with intra-abdominal infections**
  - 38 had an **intra-abdominal abscess**,
  - 6 had an infected pancreatic pseudocyst
  - 2 had an infected biloma
- Fifteen patients had polymicrobial infection

Type of infection	No. of patients
Intra-abdominal	46
Osteomyelitis	12
Skin and soft tissue	5
Empyema	2
Vascular graft infection	1
Mediastinitis	1
Pyelonephritis	1
Total	68

- **96% completed the planned course** of ertapenem
- **91% had cure** with resolution of signs and symptoms of infection and evidence of improvement on CT

Before initiating OPAT think again oral options

Updated good practice recommendations for outpatient parenteral antimicrobial therapy (OPAT) in adults and children in the UK

JAC-Antimicrobial Resistance

Table 1. Evidence for oral versus intravenous antimicrobial therapy in selected infections

Infection type (population)	Evidence
Bone and joint infections (adults)[131]	Multicentre UK-wide randomized study of oral versus intravenous antibiotic treatment for bone and joint infections (OVIVA). In a heterogeneous group of patients with device-related and non-device-related bone and joint infection who had received <7 days of initial intravenous therapy, randomization to carefully selected oral antibiotic therapy was found to be non-inferior to continuation of intravenous therapy, with 86% success observed in both groups at 1 year. In addition, significantly lower rates of line-related complications and lower treatment costs were observed in the oral treatment group.
Bone and joint infections (children)[132,133]	Increasing evidence that pOPAT is only indicated for a minority of children with bone and joint infections. The majority of patients should be managed with an early intravenous-to-oral switch.
Endocarditis[134]	Clinically improved patients with endocarditis were randomized to early intravenous-to-oral switch or standard therapy with exclusively intravenous antibiotics. Early transition to oral therapy was found to be non-inferior to intravenous therapy. This study population would be typical of the group usually managed via OPAT; therefore, appropriate oral therapy may be a suitable alternative to OPAT for selected low-risk patients.
Intra-abdominal infection[135]	Oral antibiotics had equivalent outcomes and incurred lower costs than intravenous antibiotics following appendicectomy.
Lower urinary tract infections (adults)[136]	Non-inferiority of oral fosfomycin compared with intravenous ertapenem for the treatment of lower urinary tract infections caused by ESBL-producing Enterobacteriaceae.
Pyelonephritis (children)[137]	No difference between oral antibiotics (10–14 days) and intravenous antibiotics (3 days) followed by oral antibiotics (10 days) with respect to duration of fever or subsequent renal damage.
Pleural empyema (children)[138]	Discharge on intravenous antibiotics offers no benefit over discharging children with empyema on oral antibiotics.

Before initiating OPAT think again oral options

Antibiotics with >90% oral bioavailability

- Cephalexin
- Clindamycin
- Doxycycline
- Fluconazole
- Levofloxacin
- Linezolid
- Minocycline
- Trimethoprim-sulfamethoxazole
- Voriconazole

Example: for an ABSSTI caused by MRSA, if the severity of the infection is only mild to moderate, oral doxycycline, trimethoprim-sulfamethoxazole, levofloxacin, or clindamycin may be reasonable alternatives

Early switch to oral – Early discharge (cSSTI)

Early switch to oral

- Intravenous antibiotics for more than 24h
- Stable clinical infection or clinical improvement
- Afebrile/temperature of less than 38 C for more than 24h
- WBC count not less than 4.000/ml or more than 12.000/ml

- Absence of unexplained tachycardia
- SBP of at least 100mmHg

- Patient tolerates p.o. fluids/diet (able for p.o. treatment)
- Bacteria susceptible to p.o. treatment (if microbiological cultures available)

Early discharge

(3 – 5 days)

- ➢ All key early switch eligibility criteria listed above
- ➢ No other reason to stay in hospital except for infection management

- ➢ Stable mental status
- ➢ Stable comorbid illness
- ➢ Stable social situation

Bassetti et al, Curr Opin Infect Dis 2018, 31:163–169

Barriers for OPAT implementation (The Greek paradigm)

Barrier	Hospitals who use OPAT (N=53)		Hospitals who do not use OPAT (N=14)	
	n	%	n	%
Absence of outpatient reimbursement of certain antimicrobials (e.g. ceftarolin and tigecyclin)	40	75%	9	64%
Complexity for the patient of purchasing and reimbursement of antimicrobials in community pharmacies (no unit-dose, delayed approval of the certificate for reimbursement, …)	39	74%	5	36%
High cost of outpatient therapy for the patient	30	57%	5	36%
Lack of guidelines in the hospital for good practice of OPAT	27	51%	10	71%
Insufficient knowledge of the health care practitioners (home nurse, general practitioner, …) about the procedures of home treatment	26	49%	8	57%
Legal prohibition of delivery of certain medicines and medical devices by the hospital pharmacy	26	49%	3	21%
Lack of experience with OPAT	25	47%	7	50%
Concerns about the safety of home parenteral administration (hygiene, preparation …)	24	45%	7	50%
Difficulty of monitoring at home (eg. kidney function, blood level of the medicine, complications, adverse events, …)	19	36%	5	36%
Insufficient transition care with the general practitioner and home nurse	7	13%	4	29%
Refusal of the patient for outpatient therapy	4	8%	3	21%

OPAT with once daily schemes

Agent	Antimicrobial activity	Dose and administration	Adverse drug reactions (ADRs)	Other comments
Ceftriaxone	Gram-positive (excluding MRSA, Enterococci), Gram-negative (including Salmonellae)	1–2 g OD	Allergy, cholestasis, leucopenia, *Clostridium difficile*	*Clostridium difficile* risk low in OPAT
Teicoplanin	Gram-positive (including MRSA, coagulase negative Staphylococci and Enterococci)	6–10 mg/kg OD or 15–20 mg/kg 3× s/wk*	Fatigue, allergy, myelotoxicity	Prior loading dose for 3 days. TDM required*
Daptomycin	Gram-positive (including MRSA, coagulase-negative Staphylococci and Enterococci)	4–6 mg/kg OD 6–10 mg/kg OD	Myositis (monitor CPK weekly) Eosinophilic pneumonitis (rare)	"Round dose up" to full vial Alternate day dosing when Creat clearance <30 ml/min Interference with some prothrombin time assays
Ertapenem	Gram-positive and resistant Gram negatives	1 g OD	Allergy	No activity against Enterococci or Pseudomonads

Outpatient parenteral antimicrobial therapy with ceftriaxone, a review

Int J Clin Pharm (2012) 34:410–417

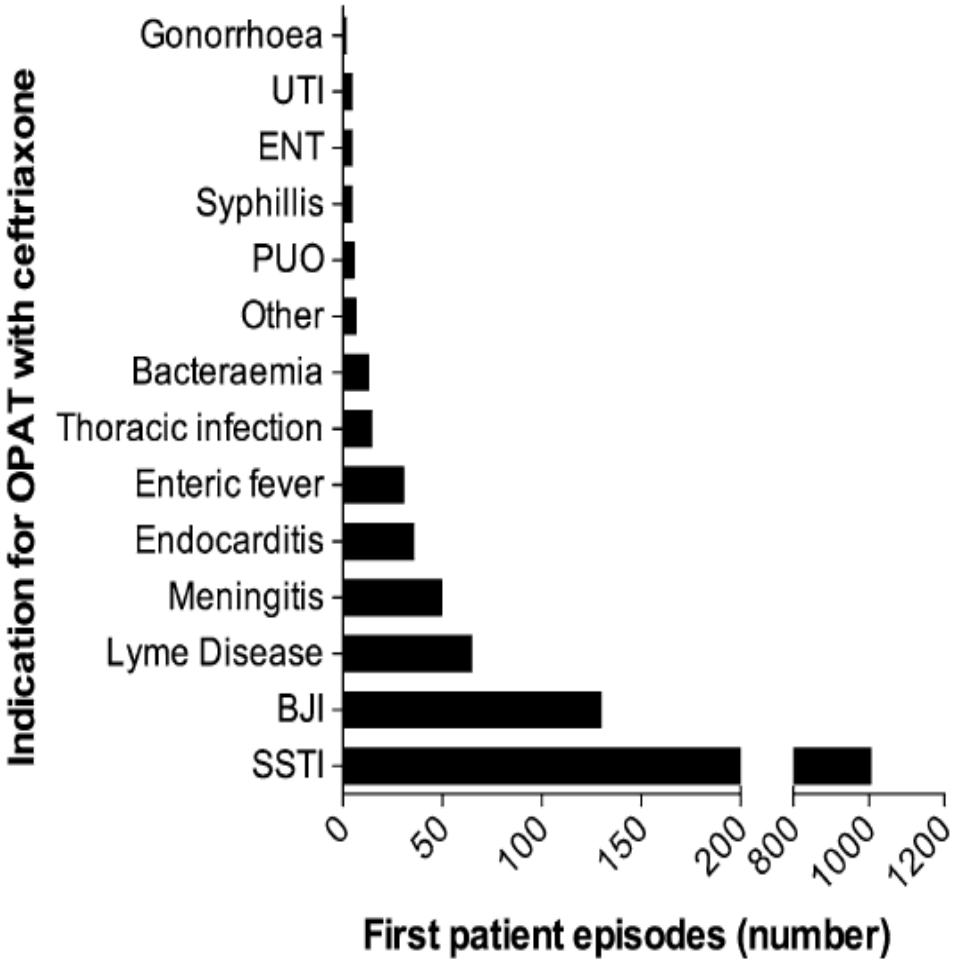


Table 1 Microbiologically-confirmed infections treated with ceftriaxone in the Glasgow OPAT service

Organism	Frequency	%
S. aureus	102	37.1
Beta-haemolytic streptococcus	66	24.0
Streptococcus viridans	25	9.1
Streptococcus pneumoniae	17	6.2
Coliforms (unspecified)	15	5.5
Neisseria meningitidis	9	3.3
Salmonella typhi	9	3.3
Salmonella paratyphi	8	2.9
Other gram negative	5	1.8
Other gram positive	5	1.8
Non-invasive salmonella	4	1.5
Proteus spp.	4	1.5
Serratia spp.	3	1.1
Streptococcus bovis	3	1.1
Total	275	100.0

Included are all first attendances over a 10-year period from 2001 to 2010

Journal of Antimicrobial Chemotherapy (2009) **64**, 181–187
doi:10.1093/jac/dkp147
Advance Access publication 2 May 2009

JAC

Development of teicoplanin dosage guidelines for patients treated within an outpatient parenteral antibiotic therapy (OPAT) programme

Table 4. Teicoplanin loading dose guidelines for thrice-weekly administration

	Ideal body weight (kg) (or total body weight if lower)		
Target	40–59	60–79	>80
10–20 mg/L			
CL_{CR} <60 mL/min	600 mg	800 mg	1000 mg
CL_{CR} ≥60 mL/min	800 mg	800 mg	1000 mg
20–30 mg/L			
CL_{CR} <60 mL/min	1000 mg	1200 mg	1400 mg
CL_{CR} ≥60 mL/min	1200 mg	1400 mg	1600 mg

Doses should be given 24 hourly for the first 3 days.

Table 5. Teicoplanin maintenance dose guidelines for thrice-weekly administration (Monday, Wednesday and Friday)

	CL_{CR}[a] (mL/min)							
Target	<25	25–40	41–54	55–74	75–89	90–104	105–120	>120
10–20 mg/L	200 mg	400 mg	600 mg	800 mg	800 mg	1000 mg	1000 mg	1000 mg
20–30 mg/L	400 mg	600 mg	800 mg	1000 mg	1200 mg	1400 mg	1600 mg	1800 mg

If renal function changes during treatment, doses should be modified according to renal function and, ideally, teicoplanin concentration measurements.
[a]Where CL_{CR} is estimated using the Cockcroft–Gault equation[12] with total body weight.

INFECTIOUS DISEASES, 2017
VOL. 49, NO. 3, 200–207
http://dx.doi.org/10.1080/23744235.2016.1247292

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Safety and efficacy of daptomycin in outpatient parenteral antimicrobial therapy: a prospective and multicenter cohort study (DAPTODOM trial)

Daptomycin is safe and efficacious in outpatients with Gram-positive bacterial infections and can be administered in 2-minute bolus infusion

Table 4. Comparison of patients receiving daptomycin in 30-minute infusion *versus* 2-minute bolus infusion.

	30-minute infusion, $N = 36$	2-minute bolus, $N = 18$	p
Mean age (SD)	67.3 (16.5)	67.0 (13.5)	.953
Male sex	24 (67%)	12 (67%)	1.000
Median dose of daptomycin, mg/kg (IQR)	5.86 (5–10)	4.67 (4.1–5.4)	.013
Venous access:			.528
• Short peripheral catheter	25 (69%)	13 (72%)	
• Peripherally inserted CVC	4 (11%)	0	
• CVC	5 (14%)	4 (22%)	
• Port-a-cath	2 (6%)	1 (6%)	
Reason for OPAT			.077
• Bacteremia or endocarditis	17 (47%)	3 (17%)	
• Uncomplicated SSTi	16 (44%)	12 (67%)	
• Other	3 (8%)	3 (17%)	
Bacterial isolation*			.192
• *S. aureus*	17 (53%)	7 (44%)	
• *Enterococcus* spp.	2 (6%)	2 (13%)	
• CoNS	3 (9%)	5 (31%)	
• Other	10 (31%)	2 (13%)	
Median (IQR) days of daptomycin treatment during OPAT	11.5 (6.5–16.5)	17.5 (10.0–25.0)	.208
Complications during OPAT**	8 (23%)	2 (11%)	.464
Catheter-related adverse events			1.000
• Phlebitis	1	0	
• Catheter-related bacteremia	0	0	
Adverse effects related to daptomycin			1.000
• Increase in serum creatine kinase levels	1	0	
Readmission due to complications	1	1	1.000

CURRENT OPINION

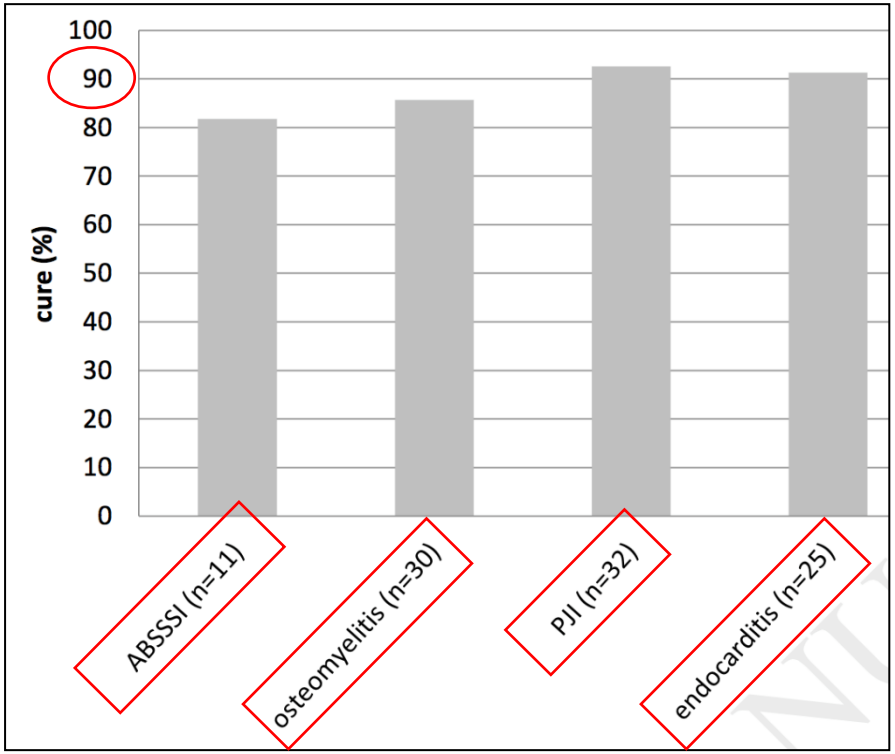
The role of dalbavancin in skin and soft tissue infections

Matteo Bassetti[a,b], *Maddalena Peghin*[a], *Alessia Carnelutti*[a], *and Elda Righi*[a]

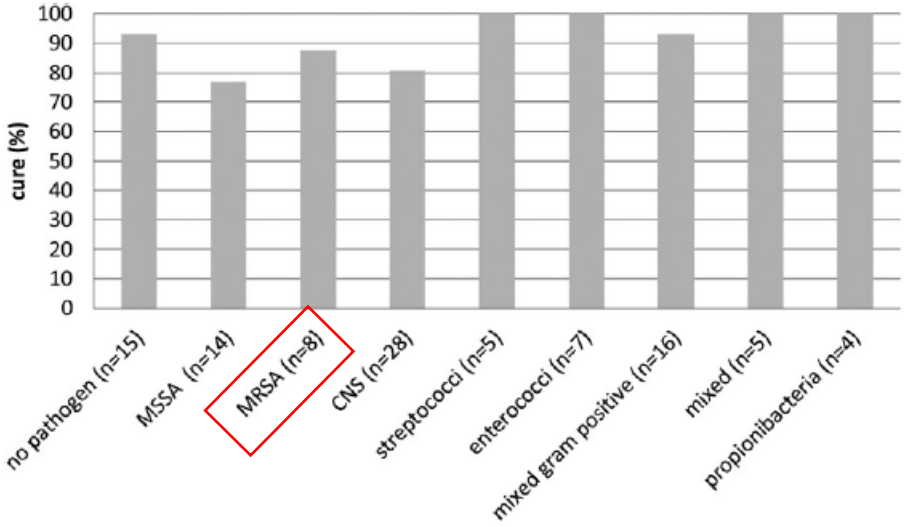
Clinical use of Dalbavancin

Type of Infection	Use	Dalbavancin dose
Approved		
Acute bacterial skin and skin structure infections (ABSSSIs)	Empiric or targeted treatment when MRSA in suspected or confirmed	1000 mg on day 1 followed by 500 mg on day 8 OR 1500 mg single dose
Off-label		
Bone and joint infections	Empiric or targeted treatment	1500 mg on day 1 followed by 1500 mg on day 8
Complicated bacteremia or endocarditis	Targeted treatment in infections due to Gram-positive pathogens (option for early discharge in MRSA infections)	1500 mg on day 1 followed by 1500 mg on day 8 OR 1500 mg single dose
Catheter-related bloodstream infections	Empiric or targeted treatment	1500 mg single dose
Mediastinitis	Targeted treatment in infections due to Gram-positive pathogens (option for early discharge in MRSA infections)	1500 mg on day 1 followed by 1500 mg on day 8 OR 1500 mg single dose

Clinical use of Dalbavancin
Real-life data 2019



Wunsch S et al. Int J Infect Dis 2019



Success rate was high (89%), tolerability and safety were excellent in this setting

An antibiotic that fits Greek NHS for OPAT in a hospital-based setting?

OPAT with once daily schemes and easy mode of administration - candidates for a Greek OPAT?

Antibiotic	Mode of administration / stability
Ceftriaxone	Short infusion via syringe. Stable for 7 days if refrigerated (2-8°) up to concentration of 50mg/ml
Daptomycin	Bolus over 2 minutes or infusion over 30 minutes. Unstable once reconstituted, not suitable for pre-compounding
Ertapenem	Short infusion via syringe. Stable for 5 days if refrigerated (2-8°) when diluted between 10-20 mg/ml
Gentamycin	Once daily short infusion over 30 minutes via syringe. Stable for 7 days if refrigerated (2-8°)
Teicoplanin	Once daily short infusion over 30 minutes via syringe. Stable if refrigerated (2-8°) for 7 days in a silicone-free syringe (degrades in standard syringe)
Dalbavancin	Once weekly (different dosing schemes) over 30 min

Comfortable mode of administration

J Antimicrob Chemother 2015; 70: 360–373

Conclusions