

ADVERSE EVENTS DURING OPAT THERAPY

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WHY ADVERSE EVENTS?

Outpatient parenteral antimicrobial therapy (OPAT) is great *but* the administration of IV drugs is potentially complicated by:

- Drug-related adverse events (AEs)
- IV catheter-related AEs

A recent study (US cohort) has reported that up to 18% of patients receiving OPAT experience drug-related AEs (Keller *et al* 2017).

- 2.24 events per 1000 OPAT days

However, directly comparable data regarding IV catheter-related AEs from the same cohort were lacking.

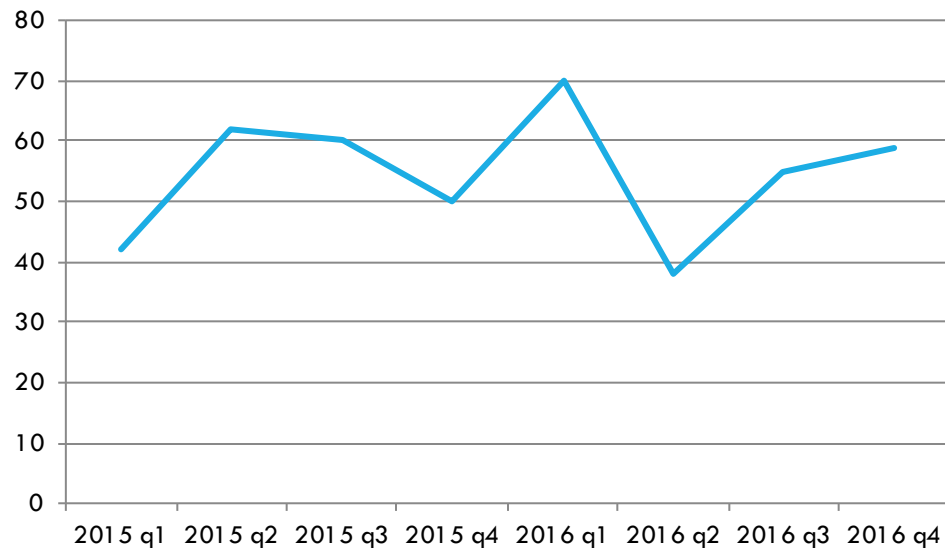
AIMS

1. To compare IV catheter and drug-related AE rates.
2. To determine if certain drugs or IV catheters were associated with higher AE rates.
3. To determine if different administration methods were associated with higher AE rates.



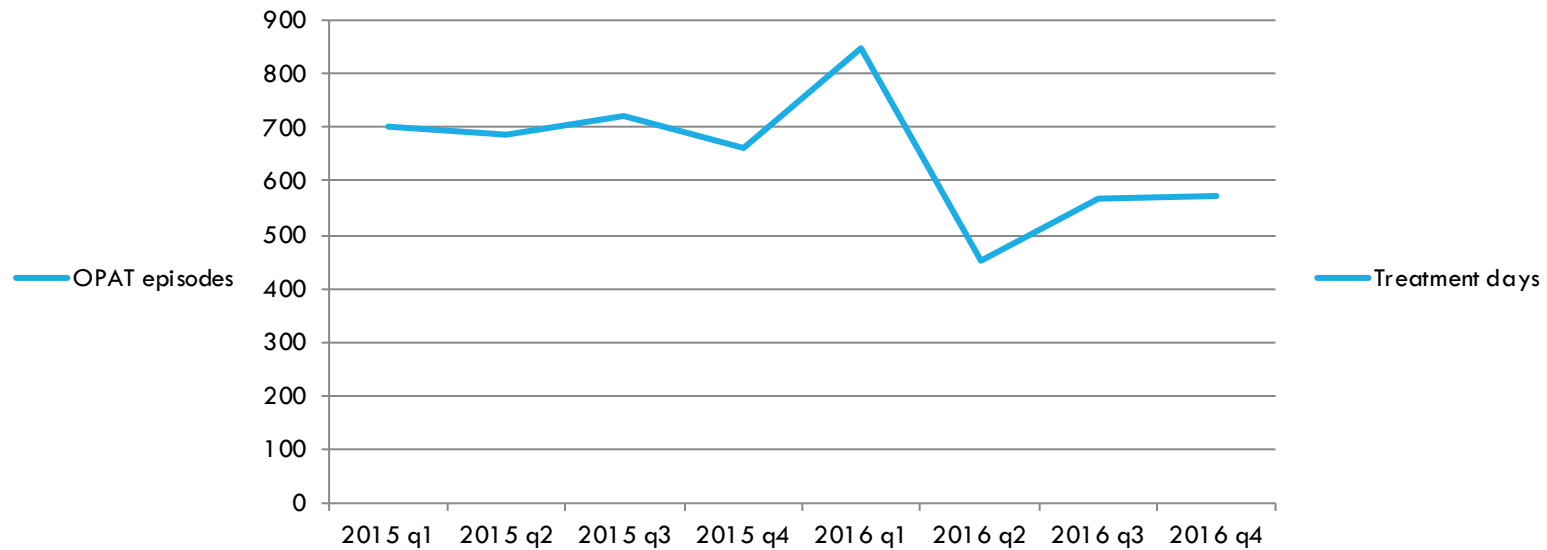
A BIT ABOUT OPAT AT UCLH/HTD

OPAT episodes



517 episodes in 2 years
423 patients

Treatment days



5212 treatment days in 2yrs
Mean days/episode= 10

METHODS

- Retrospective review of 544 OPAT episodes between January 2015 to September 2017 of prospectively collected OPAT electronic health record data.
- Administration was defined as either self-administered, nurse administered or mixed.
- OPAT outcomes were defined using the National Outcome Registry System (NORS) definitions.

METHODS CONT...

- **Clinically significant** drug-related AEs were defined as:
 - Hospital readmission related to drug complication
 - Change of OPAT antimicrobial drug related to drug toxicity
 - *Clostridioides (Clostridium) difficile* infection
- **Clinically significant** IV catheter-related AEs were defined as:
 - Hospital readmission related to a IV catheter complication
 - IV catheter blockage/displacement/extravasation/phlebitis requiring IV catheter change.

STATS

- Data was imputed as the OPAT start date -7 days or OPAT completion date respectively for missing line dates.
- Event rates were calculated as a percentage of OPAT episodes with an AE as well as per 1,000 IV catheter/drug days.
- Kaplan–Meier plots were used to assess differences:
 - IV catheter vs. drug AEs,
 - Different types of IV catheter
 - Method of administration.
- Poisson regression model to assess the risk of AEs controlling for both type of iv catheter and whether OPAT was administered by nursing staff or self-administered.

RESULTS

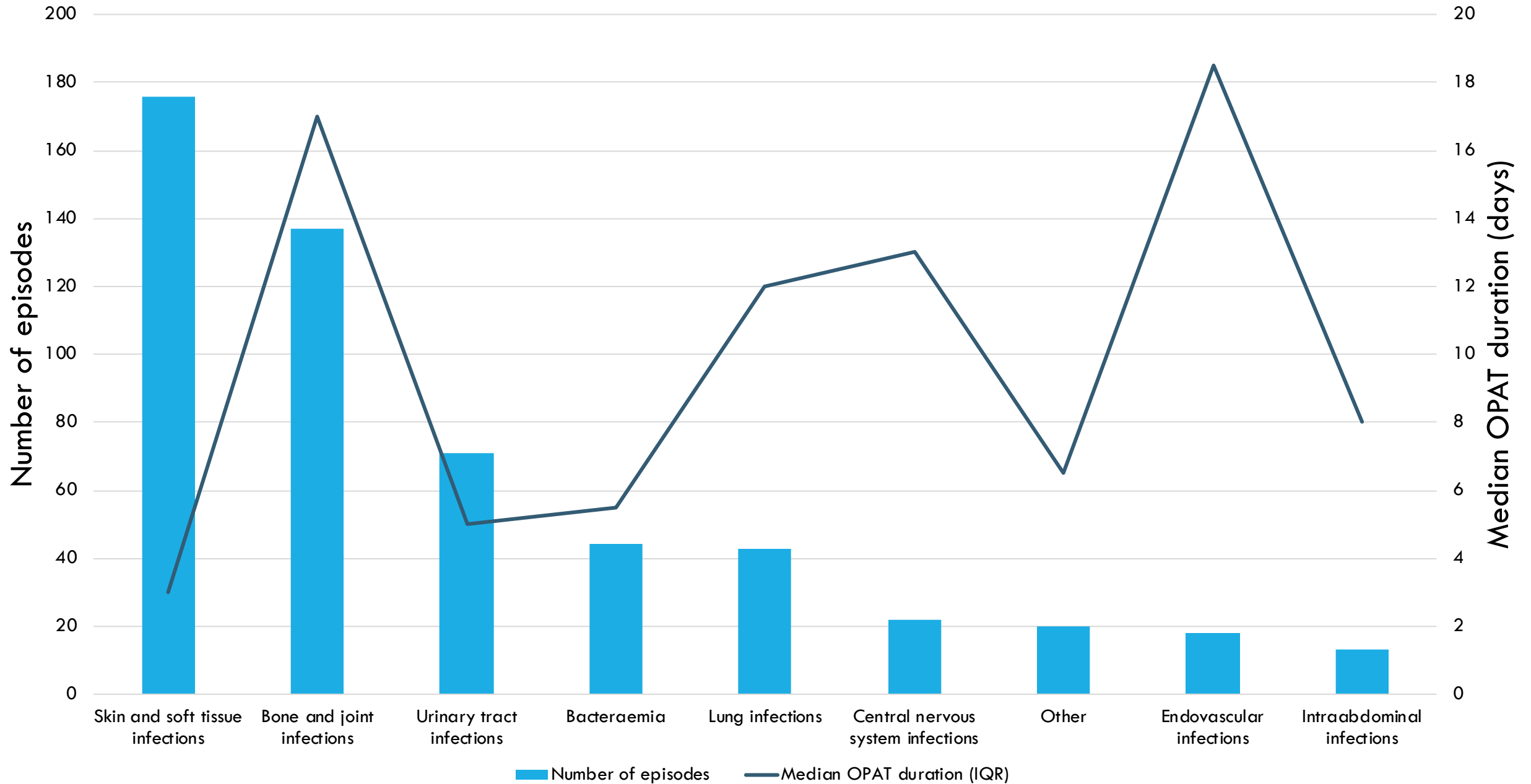
544 OPAT episodes (538 patients) – 781 referrals

- Median (IQR) 7 (2-18) days duration of OPAT
- Median (IQR) age 57 (39-71)
- 2 (0.4%) died during OPAT

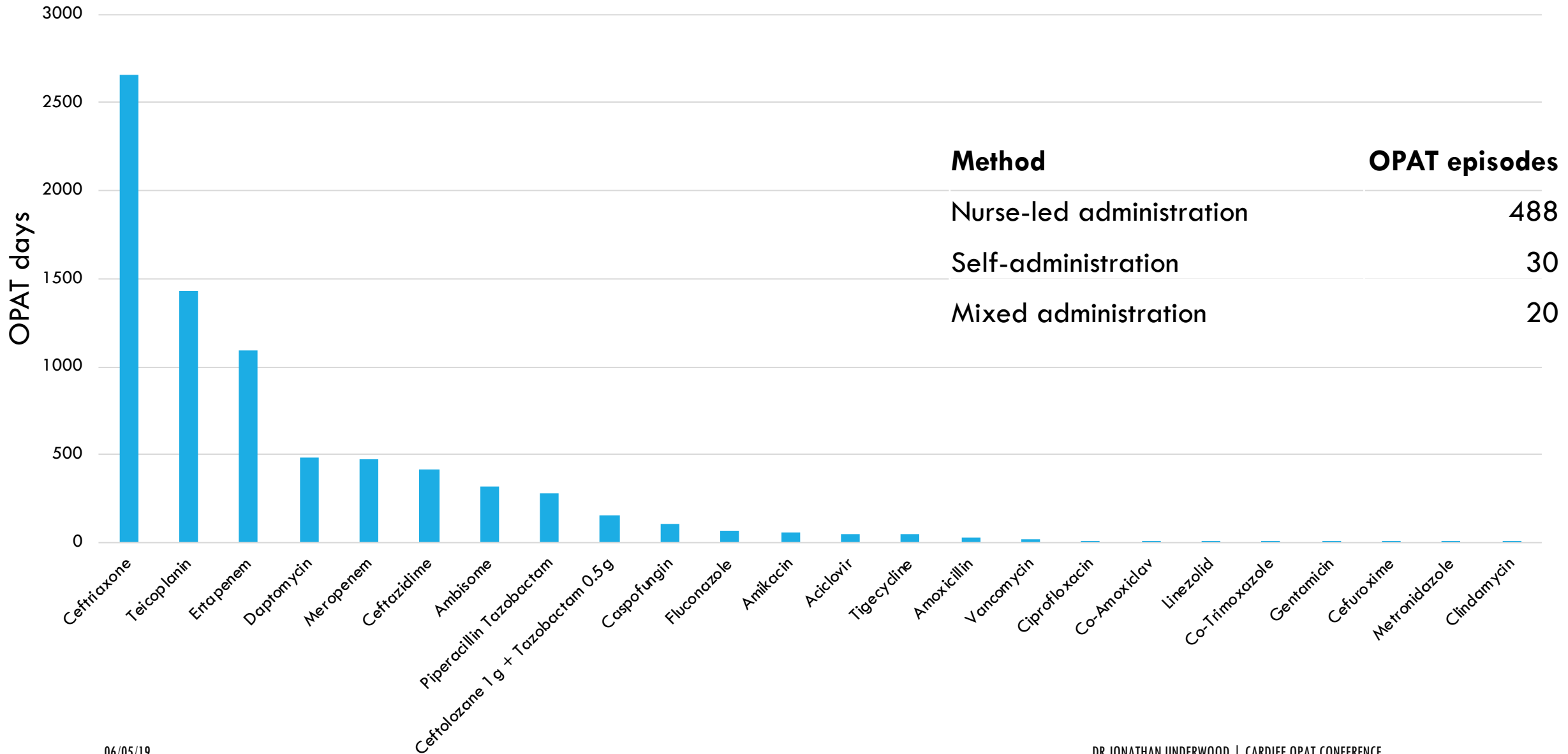
The commonest indications were:

- Skin and soft tissue infections (32.0%)
- Urinary tract infections (12.7%)
- Osteomyelitis/discitis (8.5%)

Demographic		n	%
Gender	Male	325	59.7
	Female	219	40.3
Diabetes	Yes	70	12.9
OPAT Outcome	Failure	35	6.4
	Intermediate	2	0.4
	Partial Success	12	2.2
	Success	491	90.3
Readmitted		35	6.4
Cause for readmission	<i>C. difficile</i> infection	1	2.9
	New Infection	1	2.9
	Rash	1	2.9
	IV catheter AE	3	8.8
	Drug AE	4	11.8
	Unrelated	8	23.5
	Worsening index infection	16	47.1

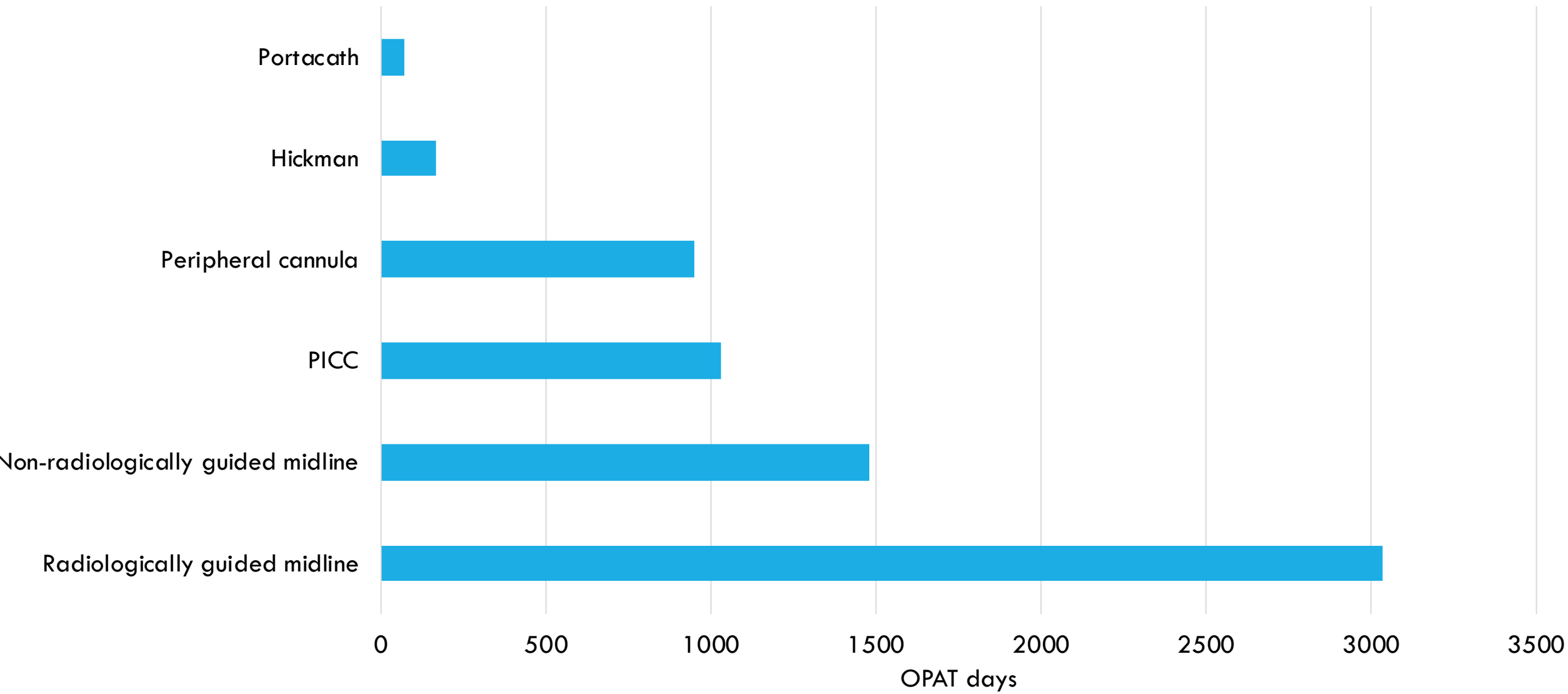


Drugs used



Method	OPAT episodes
Nurse-led administration	488
Self-administration	30
Mixed administration	20

Lines Used



ADVERSE EVENTS

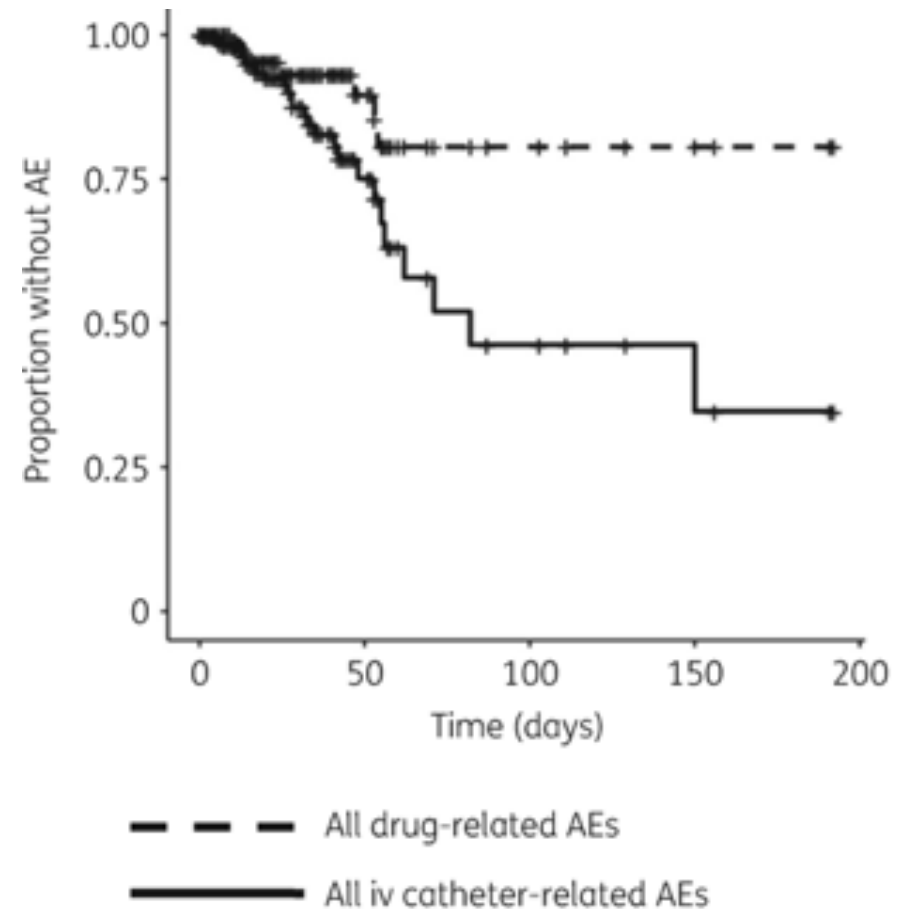
Drug-related AEs:

- 13 (2.3%) of OPAT episodes at 1.7 (0.9-2.9) per 1,000 days.

IV-catheter related AEs:

- 32 (5.9%) of OPAT episodes at 5.7 (4.2-7.9) per 1,000 days.

χ^2 test for difference: $P < 0.001$



ADVERSE EVENTS

Drug-related AEs

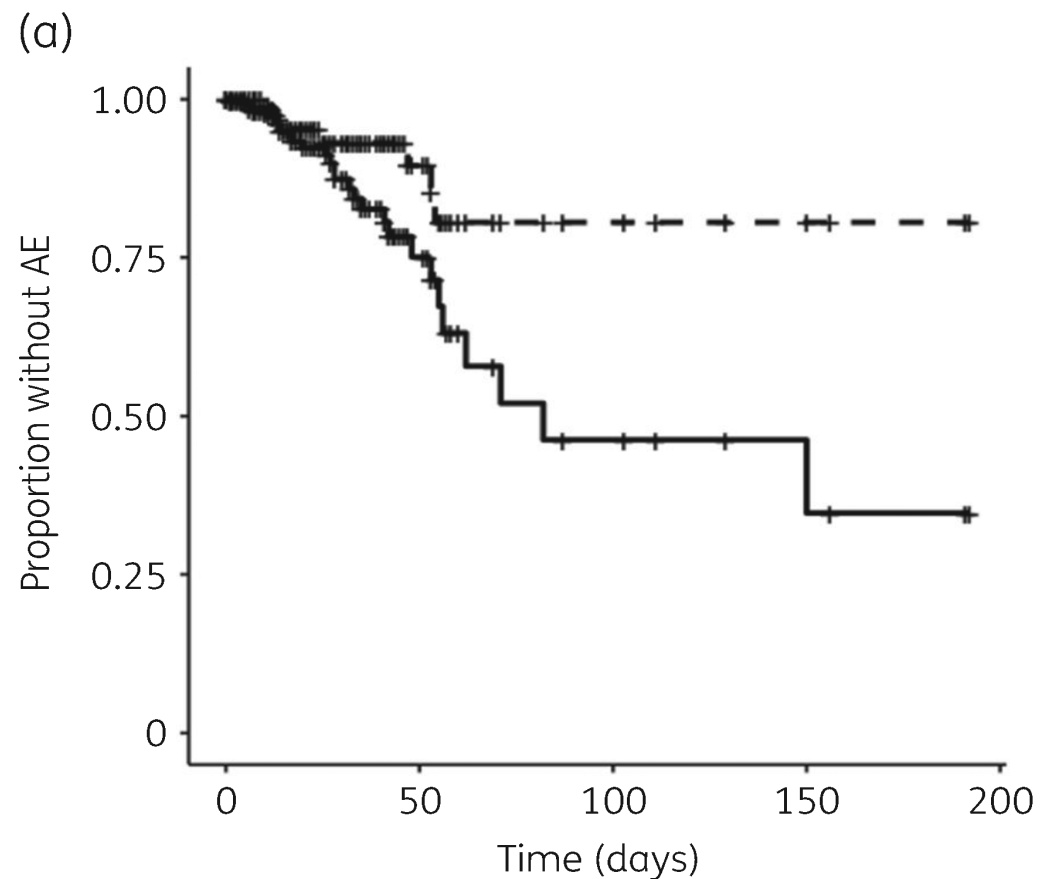
Adverse Event	Frequency (n)
Rash	8
Other	2
Nausea / Vomiting	1
Renal Dysfunction	1
Catheter-related sepsis	1

IV catheter-related AEs

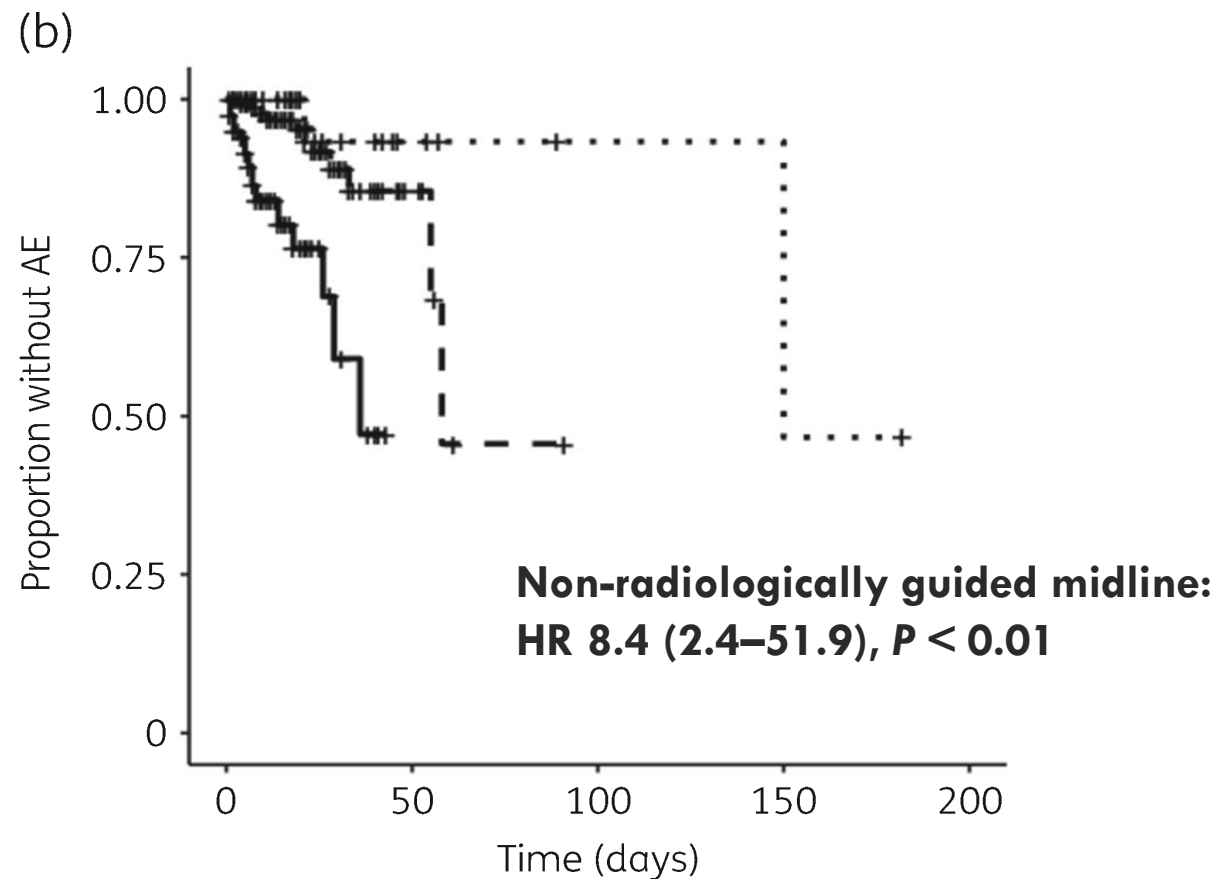
Adverse Event	Frequency (n)
Extravasation	13
Blocked	8
Displaced	8
Phlebitis	6
Thromboembolism	3
Leaking	1

IV catheter type	Usage n (%)	Adverse event n(%)	Adverse event rate per 100 days (95% CIs)
Hickman	5 (0.8%)	0 (0%)	NA*
Portacath	5 (0.8%)	0 (0%)	NA*
PICC	32 (5.6%)	2 (6.3%)	1.9 (0.5-7.8)
Non-radiologically guided midline	118 (20.5%)	29 (19.5%)	15.6 (10.3-23.4)
Radiologically guided midline	155 (26.9%)	11 (7.1%)	3.6 (2.0-6.5)
Peripheral cannula	261 (45.3%)	3 (1.1%)	3.2 (1.0-9.8)
Antimicrobial			
	Usage n (%)	Adverse event n (%)	Adverse event rate per 100 days (95% CIs)
Aminoglycoside	6 (0.9%)	0 (0%)	NA
Daptomycin	17 (2.5%)	0 (0%)	NA
Glycopeptide	110 (16.4%)	2 (0.2%)	1.4 (0.3-5.5)
Non-Beta-Lactam (other)	38 (5.5%)	1 (2.6%)	1.3 (0.6-2.9)
Non-Beta-Lactam (all)	171 (24.9%)	3 (1.8%)	1.2 (0.4-3.6)
Beta-Lactam	517 (75.1%)	10 (1.9%)	1.7 (0.2-12.3)

Kaplan–Meier plots of OPAT-related AEs

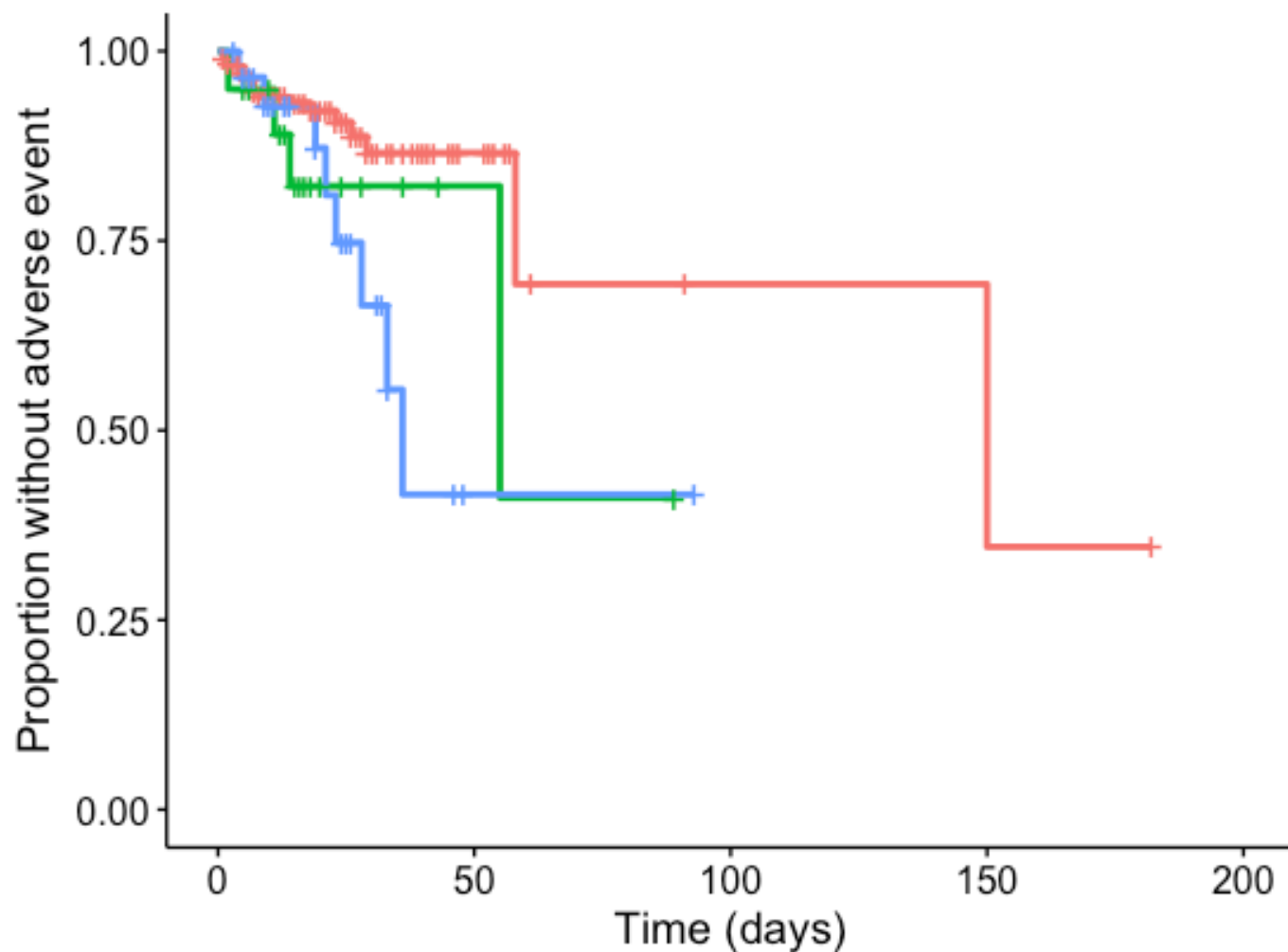


--- All drug-related AEs
— All iv catheter-related AEs



..... PICC-related AEs
--- Radiologically guided midline-related AEs
— Non-radiologically guided midline-related AEs

Adverse event rate by administration



HR 4.15 (1.7–9.1), $P < 0.01$

Strata + Nurse + Nurse & Self Administration + Self-Administration

DISCUSSION

Drug-related AE rate (1.7 per 1000 OPAT days) was lower than in a recent US-based case series (2.24 per 1000 OPAT days)

- Driven by vancomycin vs teicoplanin
- Infrequent use of aminoglycosides
- Majority of OPAT episodes initiated after in-patient care – may lead to reduced AEs and improved clinical outcomes

IV catheter-related AEs mainly driven by midlines – particularly non-radiologically guided midlines

- Inserted in the outpatient setting
- Unsecured and smaller bore

Self-administration associated with higher AEs

- Not accounting for indication and antibiotic which may confound

LIMITATIONS

1. Cohort study at risk of unrecognized confounding bias despite the prospective and systematic data collection.
2. Small n for each OPAT indication limited detailed multivariable analyses.
3. Possible reporting bias over time, although this should not have differed between drug- and catheter-related AEs.
4. Expertise of OPAT staff inserting non-radiologically guided midline catheters may have improved over time.

CONCLUSIONS

1. IV catheter-related AEs exceed those associated with parenteral antimicrobial drugs.
2. Regular and efficient stewardship of IV antimicrobials, both at referral to and during OPAT care is needed to minimize the duration of iv catheter use and the consequent harm to patients.
3. Line selection and route of administration likely to be important factors in determining IV catheter-related AEs.



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