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RESEARCH ARTICLE

Antibiotics administered as continuous intravenous infusion over 24 hours by elastomeric devices to patients treated at home: a study of infusion efficiency

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Abstract

Background: Elastomeric infusion devices or 'Infusors' are commonly used to administer 24-h continuous intravenous infusions to hospital patients at home, a service which can increase hospital capacity.
Aim: This study sought to determine Infusor efficiency by measuring infusion lengths administered by Infusors to patients in the community setting and reviewing any impacting factors on varying infusion rates, if observed.
Method: Patients and nurses completed data collection forms daily over a 12-month period. The following information was recorded: time Infusor attached to patient, time Infusor emptied, Infusor 'empty' or 'not empty' when removed, volume of antibiotic solution remaining, Infusor storage details, antibiotic solution and dose, indication for treatment, and date (season). Statistical analyses was conducted using Stata. Data were analysed using descriptive statistics, including median and range for continuous variables, and frequency counts and percentages for categorical variables. Ethical approval was granted by Northern Sydney Local Health District (NSLHD) Research Office (Reference no: RESP/14/184), the Human Research Ethics Committee (HREC) (Reference no: LNR/14/HAWKE/265) and the study conforms to the *Australian National Statement on Ethical Conduct in Human Research*. Informed consent was obtained from all participants via a study information leaflet that was provided with the patient questionnaire and patients were informed that their participation in the study was optional. Patients indicated their consent by completing the data collection form for each day of treatment.
Results: A significant number of Infusors (27%) emptied outside the expected infusion duration of 24 h ± 10% (21.6–26.4 h) and Infusors were removed 'not empty' when the nurse visited >24 h on 35% of occasions. Infusors were more likely to empty >24 h if they contained piperacillin-tazobactam 13.5 g (predicted probability = 1.0), in winter (predicted probability = 0.83), and in cooler overnight storage locations (predicted probability = 0.64). Infusors were more likely to empty <24 h if they contained vancomycin (predicted probability = 0.12).
Conclusion: Infusors delivering 24-h continuous intravenous infusions in the home setting may empty at unpredictable times and may be affected by temperature or solutions with varying doses. Outpatient parenteral antimicrobial therapy clinicians should be aware of possible unfinished infusions from Infusors.

Keywords: hospital in the home, Infusor, emptying, ambulatory, infusion, pharmacy, antibiotic.

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INTRODUCTION

Since the 1990s, administration of intravenous antibiotics to patients outside the hospital setting (also called outpatient parenteral antimicrobial therapy [OPAT]) has increased;[1,2] a practice facilitated by the increasing availability of portable ambulatory intravenous infusion devices. The benefits of safely administering OPAT in settings such as hospital in the home (HITH), outpatient clinics, or patient self-administration models include reducing hospital costs, increasing hospital capacity, and providing treatment at home, a location most patients prefer.[3,4]

Portable ambulatory infusion devices such as electronic intravenous infusion devices and disposable restrictive flow devices[5,6] can administer intravenous antibiotics as continuous intravenous infusions over prolonged periods, such as 24 h. This allows a more practical once-a-day (approximately every 24 h) home or clinic visit by the nurse or patient. This is particularly important for intravenous antibiotics that would otherwise require more frequent dosing throughout the day. Patients who self-administer their intravenous antibiotic treatment at home may also benefit from fewer medication administrations to fit in with their daily activities.

Elastomeric infusion devices are an example of portable disposable restrictive flow devices used in many OPAT programs and are generally preferred by patients and healthcare staff since they are light, portable, disposable, quiet, and easy to use.[5–8] The use of elastomeric devices is widespread in patients requiring treatment with intravenous antibiotics, postoperative analgesia, and chemotherapy in the outpatient setting.[5,6,8–10]

The flow rate of elastomeric infusors depends on a restrictive flow mechanism. Like other elastomeric devices, the Baxter LV10 and LV5 Infusors (Infusors) used in this study contain a tiny glass tube (the 'flow restrictor') at the end of the intravenous tubing, which restricts the flow of solution. The hard outer shell of the Infusor encases a solution-filled balloon that is connected to the intravenous tubing. The deflating balloon provides the force to push the antibiotic solution through the tubing. When taped to the patient's skin and exposed to an approximate temperature of 31.3°C,[11] the flow restrictor causes the infusion to flow at approximately 10 mL per hour (for LV10) or 5 mL per hour (for LV5) over 24 h.

Despite their widespread use, the accuracy of flow rates and infusion times from elastomeric devices has been questioned. Multiple studies in the laboratory setting observed significant differences in elastomeric device emptying rates caused by changes in temperature, dose/concentration, viscosity of the solution, and back pressure,[7,9,12–17] with only one of these studies conducted using antibiotic-filled elastomeric devices.[18] Whilst laboratory studies are helpful, impacts on Infusor flow rates are often measured in isolation. Few studies have reviewed flow rates or infusion times of antibiotic-filled elastomeric devices in the clinical setting. One study, in an Australian OPAT program, reviewed the number of unfinished antibiotic infusions delivered by elastomeric devices when the Infusor had been attached to the patient for at least 24 h. However, the factors influencing the emptying rate and the magnitude of emptying times were not reviewed.[19]

This study aimed to measure 24-h continuous infusion durations from antibiotic-filled elastomeric devices in an OPAT program over 12 months. The study also investigated possible contributing factors for any observed variations to expected infusion times.

METHOD

Ethics Statement

Ethical approval was granted by Northern Sydney Local Health District (NSLHD) Research Office (Reference no: RESP/14/184), the Human Research Ethics Committee (HREC) (Reference no: LNR/14/HAWKE/265) and the study conforms to the *Australian National Statement on Ethical Conduct in Human Research*. Informed consent was obtained from all participants via a study information leaflet that was provided with the patient questionnaire and patients were informed that their participation in the study was optional. Patients indicated their consent by completing the data collection form for each day of treatment.

Study Design

This prospective study was performed in an OPAT service in the Central Coast Local Health District, 123 km north of Sydney in New South Wales (NSW), Australia, servicing a population of approximately 330 000.[20] The study was conducted from 1 January 2015 to 31 December 2015 with a total of 294 patients administered continuous intravenous antibiotic infusions via an elastomeric device using a Baxter LV10 or LV5 Infusor during the 12 months of this study.

All consenting patients (>16 years old) treated with a 24-h continuous antibiotic infusion via an elastomeric device in the OPAT service during the study period were included in the study. Patients recorded the time the Infusor emptied (if emptying before the nurse

returned) and the storage location of the Infusor during the day and overnight ('under the blankets', 'under the pillow', 'on top of the blankets', 'off the bed', or 'other — somewhere else'). Overnight Infusor locations were recorded to assist with reviewing the possible impact of temperature on Infusor emptying rates, where a previous study showed substantial temperature differences for each overnight Infusor storage location.[21] The face and content validity of the data collection form/patient questionnaire was assessed by expert review of the questions and content by senior OPAT nurses, an infectious disease specialist, an OPAT pharmacist, and an academic pharmacist.[22]

The OPAT nurse visited once a day to change the Infusor, approximately 24 h after the previous visit, and recorded the date and time the Infusor was attached and detached, whether the Infusor was 'empty' or 'not empty', the estimated volume of antibiotic solution remaining in the Infusor (if any), and the patient's temperature. Pictures of an empty, half-full, and full Infusor were displayed on the data collection form to aid estimation of any remaining infusion fluid. The type and dose of antibiotic, indication for treatment, date (season), temperature from daily weather reports, type of infusion line, and infusion line issues were recorded for each patient.

To review the significance of variation in Infusor emptying times in this study, 'early', 'expected', and 'late' definitions were required. Infusors are generally expected to run to completion over a 24-h period. However, the manufacturer stipulates that a 10% variation rate can be expected when used in clinical practice.[15] Therefore, in this study, an Infusor was considered to empty in the 'expected' time range when it emptied inclusively between 21.6 and 26.4 h (24 h ± 10%), was considered to empty 'early' if emptied <21.6 h and was considered to empty 'late' if it emptied >26.4 h.

To mimic the expected and desired infusion lengths of 24 h in the clinical setting, the infusion emptying times were analysed for possible contributing factors as two groups: Infusors that emptied ≤24 h and Infusors that emptied >24 h (or were 'not empty' when removed after 24 h).

Statistical Analysis

All statistical analyses were conducted with Stata (version 18, StataCorp, College Station, TX, USA). Data were analysed using descriptive statistics, including median and range for continuous variables, and frequency counts and percentages for categorical variables. Bar charts were used to visualise the distribution of Infusor emptying times, whilst box plots were generated to compare the emptying times for prescribed intravenous antibiotics. Multivariable logistic regression was used to assess the association of antibiotic dosage, season, storage location and type of antibiotic, and the emptying of an Infusor. To aid the interpretation of odds ratios (ORs) generated by the modelling, predictive margins in the form of probabilities were computed and reported by bar charts. All variables were included in the modelling, and model fit was assessed using the Hosmer and Lemeshow goodness-of-fit test. All tests were two-sided, with a p-value <0.05 considered statistically significant.

RESULTS

During the 12-month study period, 266 completed data collection forms were returned by 37 patients aged between 24–91 years (average 60.6 years). Incomplete data collection forms (such as missing attach/detach times) were excluded from the study. Patients that refrained from returning questionnaires, patients on half-filled Infusors (12-h infusions), and paediatric patients (<16 years) were also excluded from the study. Details of patient characteristics, time between nursing visits, antibiotics prescribed, indications, overnight storage conditions, seasons, Infusor emptying times, and volumes remaining in unemptied Infusors are summarised in Table 1. Storage of the Infusor during the day, patient temperature, daily ambient temperature (from weather reports), and central line types (such as peripherally inserted catheters [PICC lines]) and intravenous line issues were not well recorded and therefore not analysed in this study. All antibiotic infusion solutions were prepared using 0.9% w/v sodium chloride as the diluent.

The Central Coast is a temperate coastal region of NSW,[23] with average summer temperatures of 20–22°C and average winter temperatures of 12–14°C.[24]

Infusor Empty Time Known

The time to empty for 81 Infusors could be determined, and these times are shown in Figure 1. Infusors emptied over a time range of 18.59 to 28.35 h. On 17 occasions, the Infusor emptied earlier than 21.6 h ('early') and the time to empty was recorded by the patient and confirmed as empty by the nurse at the visit. On five occasions, the Infusor emptied later than 26.4 h ('late'). Infusors emptied within the 'expected' time range (21.4–26.4 h) on 59 occasions.

Assuming a 5% level of significance, it could be expected that 95% of the 81 Infusors would empty within the expected time range (i.e. 77 or more of the Infusors could be expected to empty between 21.6 h and

Table 1 Patient (n = 37) and study characteristics (n = 266)

Characteristic	Median (interquartile range)
Study participants: age (years)	63 (51–74.5)
Data collection form returned per patient	5 (2–9)
Time between nursing visits (h)	23.79 (22.42–25)

Characteristic	Frequency (%)
Study participants: sex: (n = 37)	
Male	20 (54)
Female	16 (43)
Not recorded	1 (3)
Antibiotic solution in Infusor (n = 266)	
Benzylpenicillin 7.2 g (buffered) LV10	11 (4.1)
Benzylpenicillin 10.8 g (buffered) LV10	2 (0.8)
Benzylpenicillin 14.4 g (buffered) LV10	11 (4.1)
Cefazolin 6 g LV10	60 (22.6)
Cefepime 3 g LV10	8 (3.0)
Flucloxacillin 8 g (buffered) LV10	100 (37.6)
Piperacillin/tazobactam 13.5 g LV10	38 (14.3)
Ticarcillin/clavulanic acid 12.1 g LV10	11 (4.1)
Vancomycin (varying doses) LV5 and LV10	25 (9.4)
Indication (n = 266)	
Prosthetic joint infection	58 (21.8)
Osteomyelitis	47 (17.7)
Spinal abscess	37 (13.9)
Septic arthritis	35 (13.2)
Bacteraemia	27 (10.2)
Bronchiectasis	18 (6.8)
Endocarditis	16 (6.0)
Sepsis	8 (3.0)
Epidural abscess	9 (3.4)
Cellulitis	5 (2.0)
Discitis	1 (0.3)
Diabetic foot infection	1 (0.3)
Exacerbation of chronic obstructive pulmonary disease	1 (0.3)
Not recorded	3 (1.1)
Seasons (n = 266)	
Spring	18 (6.8)
Summer	84 (31.6)
Autumn	95 (35.7)
Winter	69 (25.9)
Storage overnight (n = 266)	
Under the blankets	65 (24.4)
Under the pillow	6 (2.3)
On top of the blankets	140 (52.6)
Off the bed	45 (16.9)
Somewhere else	4 (1.5)
Not recorded	6 (2.3)
Infusor empty time status (n = 266)	
Infusor empty time known (n = 81)	81 (30.5)
Infusor empty time early (<21.6 h)	17 (21.0)
Infusor empty time expected (21.6–26.4 h)	59 (72.8)
Infusor empty time late (>26.4 h)	2 (2.5)
Infusor empty time late ('not empty' >26.4 h)	3 (3.7)
Empty time unknown (n = 185)	185 (69.5)
Infusor empty but patient did not record empty time	12 (6.5)
Infusor 'not empty' when removed <26.4 h	167 (90.3)
Infusor recorded as 'empty' and 'not empty'	2 (1.1)
Patient and nurse both did not record empty time	4 (2.1)
Time Infusor removed (n = 266)	
Infusor removed ≤24 h	154 (57.9)
Infusor removed >24 h	112 (42.1)
Infusor 'not empty' (n = 170)	
'Not empty' <26.4 h	167 (98.2)
'Not empty' >26.4 h	3 (1.8)
Infusor 'not empty' ≤24 h vs >24 h (n = 170)	
'Not empty' ≤24 h	131 (77.0)
'Not empty' >24 h	39 (22.9)
Infusor removed >24 h (n = 112)	
Infusor empty	69 (61.6)
Infusor 'not empty'	39 (34.8)
Infusor 'unknown empty'	4 (3.6)
Estimated volume remaining when Infusor removed 'not empty' by the nurse ≤24 h (n = 131)	
= 240 mL	1 (0.5)
>120 mL	3 (1.8)
= 120 mL	15 (10.0)
<120 mL	110 (85.9)
Not recorded	2 (1.8)
Estimated volume remaining when Infusor removed 'not empty' by the nurse >24 h (n = 39)	
= 240 mL	0
>120 mL	0
= 120 mL	2 (5.1)
<120 mL	36 (92.3)
Not recorded	1 (2.6)
Time attached where Infusor removed ≥half full (n = 21)	
13 h	1 (4.8)
17–21 h	12 (57.1)
23–24 h	8 (38.1)
Type of antibiotic and dose where Infusor removed ≥half full (n = 21)	
Cefazolin 6 g LV 10	5 (23.8)
Flucloxacillin 8 g LV10	9 (42.9)
Piperacillin/tazobactam 13.5 g LV10	4 (19.0)
Benzylpenicillin 14.4 g LV10	1 (4.8)
Ticarcillin/clavulanate 12.4 g LV10	2 (9.5)
Infusor analysed for impacting factors (n = 123)	
Number of Infusors emptied ≤24 h (n = 55)	
Benzylpenicillin 7.2 g LV10	4 (7.3)
Cefepime 3 g LV10	4 (7.3)
Cefazolin 6 g LV10	9 (16.3)
Flucloxacillin 8 g LV10	21(38.1)
Vancomycin 600 mg LV5	3 (5.5)
Vancomycin 750 mg LV5	4 (7.3)

Table 1 (*continued*)

Characteristic	Frequency (%)
Vancomycin 900 mg LV5	3 (5.5)
Vancomycin 1.2 g LV5	3 (5.5)
Vancomycin 1.5 g LV5	1 (1.8)
Vancomycin 1.5 g LV10	1 (1.8)
Vancomycin 2.5 g LV10	1 (1.8)
Vancomycin 3.5 g LV10	1 (1.8)
Number of Infusors emptied >24 h (n = 68)	
Benzylpenicillin 7.2 g LV10	2 (3)
Benzylpenicillin 14.4 g LV10	4 (5.8)
Cefepime 3 g LV10	1 (1.5)
Cefazolin 6 g LV10	19 (28.0)
Flucloxacillin 8 g LV10	22 (32.4)
Piperacillin/tazobactam 13.5 g LV10	16 (23.5)
Ticarcillin/clavulanic acid 12.4 g LV10	2 (2.9)
Vancomycin 2 g LV10	2 (2.9)

Patient and study characteristics where 37 patients returned 266 data collection forms. LV 10 describes the large volume (LV) Infusor administering the antibiotic solution at 10 mL/h and LV5 describes the large volume (LV) Infusor administering the antibiotic solution at 5 mL/h.

26.4 h). However, only 73% of this group's Infusors (n = 59) emptied within this time. Furthermore, a single-sample test for proportions indicated that this proportion was statistically significant from the expected proportion ($p < 0.01$).

Where an exact time to empty was recorded (n = 78), the time taken to empty was analysed based on the type of antibiotic and this is shown in Figure 2. Note that for the three occasions where Infusors were removed 'not empty' after 26.4 h, an actual time to empty was not recorded and therefore not analysed, despite being classified as 'late emptying Infusors' in Figure 1.

Infusor Empty Time Unknown

It was not possible to determine the emptying time of Infusors on 185 occasions, as outlined in Table 1.

Infusors were removed 'not empty' on 170 occasions (64% of the time). The nurse removed the Infusor ≤24 h 58% of the time (n = 156), which could account for the large number of unemptied Infusors removed. However, on 42% of occasions when a nurse visited >24 h after the Infusor was connected (n = 112), where it would be expected that the Infusor would be empty, an unemptied Infusor was removed 35% of the time (n = 39). The estimated volume remaining in these Infusors is shown in Table 1.

Factors Affecting Infusor Empty Times: Season, Antibiotic, and Overnight Infusor Storage

To review the impact of factors such as temperature, season, and overnight Infusor storage and antibiotic type on Infusor emptying times, the emptying times of Infusors were grouped into Infusors that emptied ≤24 h (n = 55) and Infusors that emptied >24 h or were 'not empty' >24 h (n = 68). This mimics the expected time between nursing visits of approximately 24 h.

To determine the effect of antibiotic solution, overnight Infusor storage location, and season on Infusor emptying times, data were analysed using multivariable binary

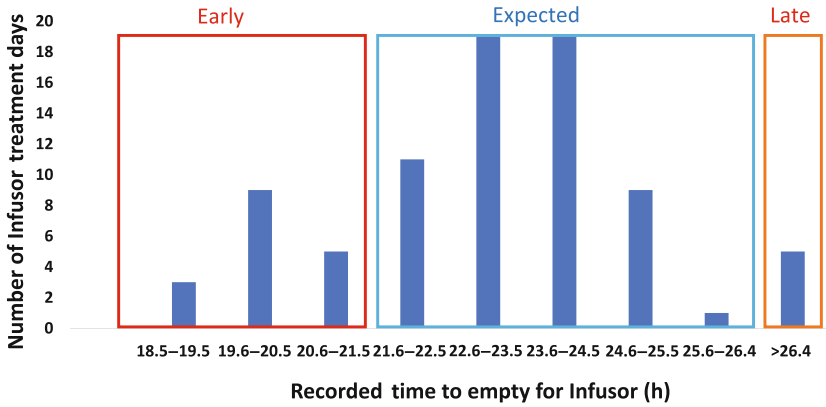

Figure 1 Range of emptying times for Infusors where the empty time was known (n = 81) where 78 Infusors had a recorded emptying time and three Infusors were 'not empty' >26.4 h (therefore the Infusor would have emptied 'late' on these three occasions). For late-emptying Infusors with a recorded 'time to empty' >26.4 h, two Infusors had a known emptying time (flucloxacillin 8 g LV10 [emptying time = 28.35 h] and piperacillin/tazobactam 13.5 g [emptying time = 28.35 h]) and three Infusors had an unknown emptying time (piperacillin/tazobactam 13.5 g ['not-empty' when removed at 26.67 h], cefazolin 6 g ['not-empty' when removed at 28.67 h], and flucloxacillin 8 g ['not-empty' when removed at 27.5 h]).

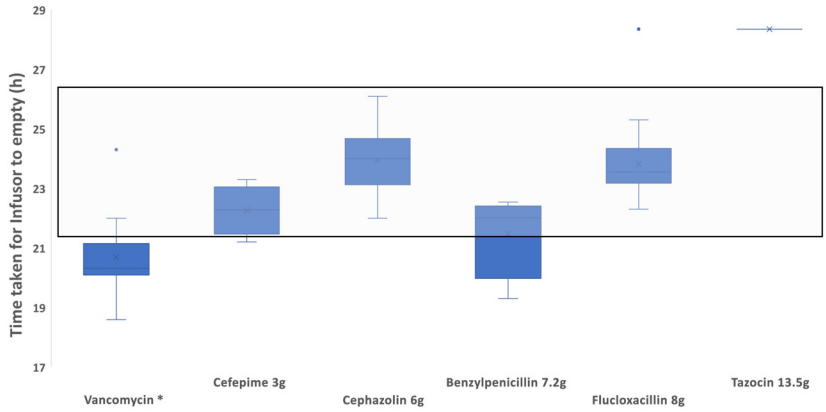

Figure 2 Time to empty for each antibiotic if Infusor emptying time was known (n = 78). *Due to varying strengths and low numbers, all vancomycin strengths are grouped together in Figure 3. Vancomycin 600 mg/120 mL LV5 (n = 3), vancomycin 750 mg/120 mL LV5 (n = 4), vancomycin 900 mg/120 mL LV5 (n = 3), vancomycin 1.2 g/120 mL LV5 (n = 3), vancomycin 1.5 g/120 mL LV5 (n = 1), vancomycin 1.5 g/240 mL LV10 (n = 1), vancomycin 2 g/240 mL (n = 1), vancomycin 2.5 g/240 mL (n = 1), and vancomycin 3.5 g/240 mL (n = 2). The shaded area shows the range for the expected emptying time of 24 h ± 10% (21.6–26.4 h). Emptying times for cefazolin and flucloxacillin LV10 Infusors were within the manufacturer listed expected emptying time range with 50% of cefazolin 6 g Infusors emptying between 23.13–24.68 h (with emptying range 22.00–26.09 h) and 50% of flucloxacillin 8 g Infusors emptying between 23.18–24.34 h (with emptying time range 22.3–25.3 h). Outliers included a vancomycin 2 g LV10 emptying at 24.3 h, a flucloxacillin 8 g LV10 emptying at 28.35 h, and a piperacillin/tazobactam (Tazocin) 13.5 g LV10 emptying at 28.35 h.

logistic regression with clustering of observations by patient being adjusted for by Stata's vice (cluster) option.

Of the 123 Infusors where an empty time before ≤24 h (n = 55) or >24 h (n = 68) was known, the predicted probabilities of each Infusor type emptying later than 24 h are shown in Figure 3.

Effect of Overnight Storage

Predicted probabilities of storage location and Infusor emptying time showed a higher probability of Infusors emptying late when stored in the coolest location, off the bed (with only one patient recording a storage location of 'other'), and a lower probability of emptying late when stored in a warmer overnight storage location, under the blankets, as shown in Figure 3a.

Effect of Season

Unlike other factors in the analysis, the overall effect of season was found to be significantly associated with emptying status (p = 0.016), with Infusors more likely to empty earlier in summer when compared to winter (p = 0.039). Other pairwise comparisons were not found to be statistically significant. As seen in Figure 3b, Infusors were more likely to empty >24 h in winter and least likely to empty late in summer.

Effect of Antibiotic Type in Infusor

Of the five antibiotics, and as shown in Figure 3c, piperacillin/tazobactam Infusors were predicted to empty after 24 h with near certainty, followed by cefazolin (predicted probability = 0.65). Conversely, vancomycin was least likely to empty after 24 h (predicted probability = 0.15).

DISCUSSION

To the authors' knowledge, this is the only published study to review antibiotic-filled elastomeric device emptying rates in an OPAT program in the patients' home setting, which also examined the impact of possible contributing factors causing variations to expected infusion times. This study demonstrated that elastomeric devices may empty unpredictably when used in the clinical setting and may commonly deviate from the expected 24-h duration, as well as vary outside the expected time range stipulated by the manufacturer (21.6–26.4 h), which is noteworthy. Only 73% of Infusors (when the emptying time was known) emptied between 21.6 h and 26.4 h in this study, with the remaining 27% either emptying earlier than 21.6 h or later than 26.4 h, which is substantially different from the emptying times stated by the manufacturer.

Importantly, this study also showed that the nurse commonly removed unfinished Infusors in the clinical setting. Infusors were 'not empty' when the nurse visited >24 h 35% of the time. This is problematic for HITH nurses who plan their home visits approximately 24 h apart since it is not practical for them to wait for an infusion to finish or return later.

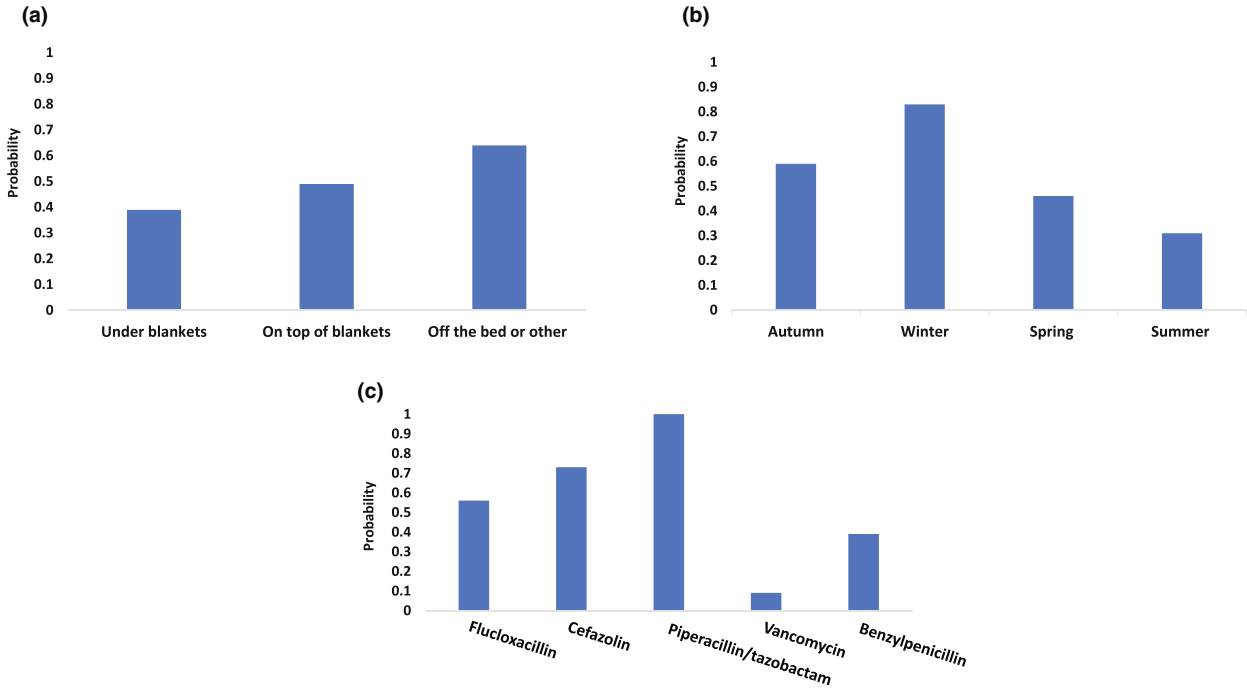

Figure 3 Predicted probabilities of Infusors emptying >24 h. (a) Predicted probabilities of emptying after 24 h for different overnight storage locations where Infusors were stored 'under the blankets' (predicted probability = 0.39), 'on top of the blankets' (predicted probability = 0.49), or 'off the bed or other', where patients stored their Infusor 'off the bed' and on one occasion in an undescribed location (predicted probability = 0.64). (b) Predicted probabilities of emptying after 24 h for different seasons. Autumn (predicted probability = 0.59), winter (predicted probability = 0.83), spring (predicted probability = 0.46), and summer (predicted probability = 0.31). (c) Predicted probabilities of Infusors emptying after 24 h for different antibiotic solutions: flucloxacillin 8 g (predicted probability = 0.57), cefazolin 6 g (predicted probability = 0.72), piperacillin/tazobactam 13.5 g (predicted probability = 1.0), vancomycin varying doses as outlined in Table 1 (predicted probability = 0.12), and benzylpenicillin 7.2 g/14.4 g (predicted probability = 0.45).

Small volumes remaining in an Infusor when removed by nurses may not pose significant clinical issues. However, some of the incomplete antibiotic volumes in Infusors recorded in this study were substantial, with 20 Infusors containing ≥50% of the initial volume of prescribed antibiotic solution (≥120 mL) when removed, after the infusion had been running for at least 17 h (as outlined in Table 1). On these occasions, patients were potentially administered antibiotic doses significantly lower than the prescribed standard doses, which could impact therapeutic success. Lower doses consistently administered by Infusors could also encourage antimicrobial resistance.

This study observed that Infusors containing different antibiotic solutions may empty at different rates. The higher-dosed piperacillin/tazobactam 13.5 g Infusors were more likely to empty after 24 h, and the lower-dosed vancomycin Infusors were more likely to empty before 24 h. However, where infusion times were known, a good proportion of cefazolin 6 g and flucloxacillin 8 g Infusors consistently emptied within the 24 h ± 10% range. Interestingly, a study conducted in the laboratory by Perks et al.[18] demonstrated that antibiotic dose was inversely related to Infusor flow rate, with antibiotic doses >12.02 g resulting in infusions emptying later than 24 h, supporting our study's findings.

Our findings of early- or late-finishing antibiotic infusions administered via Infusors in the clinical setting may not be surprising. The manufacturer stipulates in their *HealthCare Professional Guide: Elastomeric Products*[11] that further deviations in infusion length (outside their stated 21.6–26.4 h) can occur if Infusors are used outside their calibrated conditions, such as using diluents other than glucose 5%, storing Infusors other than at the same height as the flow restrictor, and exposing the flow restrictor to temperatures other than 31.3°C (skin temperature).[11] Controlling such parameters in a community setting is challenging, especially when normal saline is the common diluent used in OPAT programs, temperatures in the home will likely fluctuate, and consistent storage of the Infusor at the same height as the flow restrictor may be challenging in practice.

Varying temperatures, such as those experienced in different seasons and overnight Infusor storage

locations, impacted the emptying rates of Infusors in this study. Infusions administered in winter were more likely to empty later than 24 h, when compared to summer. Infusors stored in the coolest location 'off the bed or other' were also more likely to empty later than 24 h than Infusors stored in the warmest location 'under the blankets'. These results suggest that skin temperature and ambient temperatures can affect the flow rate of Infusors. A warmer ambient temperature may result in a warmer antibiotic solution temperature, reducing the viscosity of the solution, resulting in a faster flow rate. Conversely, cooler solutions are generally more viscous and may result in slower flow rates.

This study provides some clinically useful information when using Infusors in the clinical setting, including: the importance of monitoring and documenting the volume of remaining solution in unemptied Infusors, especially for patients responding slowly to treatment or those on piperacillin/tazobactam 13.5 g Infusors, which we showed were more likely to empty late; carefully interpreting vancomycin levels, where a consistent and accurate vancomycin infusion rate over 24 h is assumed, although our findings indicate the infusion may finish early; avoiding temperature extremes (e.g. air-conditioned or controlled environments may be preferred in hot or cold climates or seasons); reviewing and amending overnight Infusor storage locations for Infusors with slower or faster than expected infusion times (although caution is advised for antibiotics with poor stability, since warming solutions to encourage a faster flow rate may also accelerate antibiotic degradation in solution); or considering alternative methods of administration if Infusor flow rates are problematic. Battery-operated infusion pumps may be an option because some studies conducted in the laboratory suggest more uniform flow rates from battery-operated infusion pumps where the viscosity of the solution, temperature, and device storage may have less impact,[13,25] but further research is warranted.

There were limitations to this study. First, due to missing data relating to recording of infusion emptying times, our study may be underpowered for detecting all but the strongest effects on emptying status, as well as potentially limiting the generalisability of our findings. Second, patient outcomes, treatment duration, and hospital readmissions were not recorded, therefore the impact of unpredictable emptying times on clinical outcomes could not be reviewed, but there were no obvious treatment failures reported during this study. Third, estimating fluid remaining in the Infusor was based on reviewing pictures of Infusors, which could cause variations due to personal interpretation, and exact volumes of fluid remaining were not measured. Lastly, some information was not well recorded and therefore not analysed in this study, such as the type of vascular access devices used and storage of the Infusor during the day. However, to the authors' knowledge, there were no reported concerns with the PICC lines used during this study.

Elastomeric Infusors may have unpredictable emptying rates in the outpatient setting, and clinicians should be aware of possible unfinished infusions from these devices or infusions that finish earlier than expected. Temperature and type of antibiotic solution can cause variations in Infusor emptying rates. Further research is required to review actual volumes remaining in unemptied elastomeric devices and to compare alternative OPAT intravenous infusion administration methods such as battery-operated/electronic pumps in the clinical setting.

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CONFLICT OF INTEREST STATEMENT

JS has received personal payment for royalties from Oxford University Press for work on *The Syringe Driver*, unrelated to this research and payment from BD for participation in Delphi Panel reviewing literature on drug compatibility with IV bags. MD holds voluntary membership of the Data and Safety Monitoring Committee (DSMC) and is an investigator of DSMC Preventing InfusAte injuries: throughout a child's hospitalisation (PATCH): a type 1 hybrid randomised controlled trial.The remaining authors declare that they have no conflicts of interest.

AUTHORSHIP STATEMENT

Toni Docherty: Conceptualisation; investigation; writing – original draft; methodology; validation; visualisation; writing – review and editing; project administration; formal analysis; data curation. **Michael David:** Methodology; writing – review and editing; formal analysis; supervision; software; data curation; visualisation.

Jennifer Schneider: Writing – review and editing; formal analysis; supervision; data curation; visualisation. **Gabrielle O'Kane:** Conceptualisation; investigation; methodology; writing – review and editing; validation. **Joni Morris:** Conceptualisation; writing – review and editing; investigation. **Catherine Paavola:** Conceptualisation; investigation; writing – review and editing; methodology; validation. **Janelle Sawers:** Methodology; writing – review and editing; conceptualisation; investigation; validation. **Deirdre O'Mahony:** Conceptualisation; investigation; writing – review and editing; methodology; validation. **Joyce Cooper:** Conceptualisation; investigation; methodology; validation; writing – review and editing; formal analysis; supervision; project administration; visualisation.

ETHICS STATEMENT

Ethical approval was granted by Northern Sydney Local Health District (NSLHD) Research Office (Reference no: RESP/14/184), the Human Research Ethics Committee (HREC) (Reference no: LNR/14/HAWKE/265) and the study conforms to the *Australian National Statement on Ethical Conduct in Human Research*. Informed consent was obtained from all participants via a study information leaflet that was provided with the patient questionnaire and patients were informed that their participation in the study was optional. Patients indicated their consent by completing the data collection form for each day of treatment.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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