

# Guidelines to practice in hospitals at home: safe and effective continuous infusion pumps substantially increased penicillin use in erysipelas treatment

Niina Metsä-Simola <sup>1,2</sup>, Jenni Saarenketo<sup>3</sup>, Henri Lehtonen<sup>3,4</sup>, Niklas Broman<sup>3,4</sup>, Tony Häggblom<sup>5</sup>, Pia Björklöf<sup>3</sup>, Salla Sariola<sup>6</sup>, Maija P. Valta <sup>3,4,7,\*</sup>

<sup>1</sup>Helsinki Institute for Demography and Population Health, University of Helsinki, Helsinki, Finland

<sup>2</sup>Max Planck, University of Helsinki Center for Social Inequalities in Population Health, Helsinki, Finland

<sup>3</sup>Turku City Hospital OPAT Clinic, The Wellbeing Services County of Southwest Finland, Turku, Finland

<sup>4</sup>Department of Medicine, University of Turku, Turku, Finland

<sup>5</sup>Turku City Hospital Department of Infectious Diseases, The Wellbeing Services County of Southwest Finland, Turku, Finland

<sup>6</sup>Faculty of Social Sciences, University of Helsinki, Helsinki, Finland

<sup>7</sup>Department of Hematology and Stem Cell Transplantation, Turku University Hospital, The Wellbeing Services County of Southwest Finland, Turku, Finland

\*Corresponding author. Department of Hematology and Stem Cell Transplantation, Turku University Hospital, The Wellbeing Services County of Southwest Finland, Hämeenkatu 11, 20540 Turku, Finland. E-mail [maija.valta@utu.fi](mailto:maija.valta@utu.fi)

## Abstract

Hospitals at home are increasingly offering outpatient parenteral antimicrobial therapy (OPAT) in an attempt to reduce costly inpatient care, but these settings favour broad-spectrum antibiotics that require less frequent dosing than penicillin. Benzyl penicillin could be delivered via continuous infusion pumps (eCIPs), but studies on their safety and efficacy in OPAT are scarce, and it remains unclear how much the availability of eCIPs increases penicillin use in real-life settings. We examined 462 electronic healthcare records of erysipelas patients treated between January 2018 and January 2022 in a large Finnish OPAT clinic. Average marginal effects from logistic models were estimated to assess how the introduction of eCIPs in December 2020 affected penicillin use and to compare clinical outcomes between patients with and without eCIPs. Introduction of eCIPs increased the predicted probability of penicillin treatment by 36.0 percentage points (95% confidence interval 25.5–46.5). During eCIP implementation, patients who received an eCIP had 73.1 (58.0–88.2) percentage points higher probability than patients without an eCIP to receive penicillin treatment. They also had about 20 percentage points higher probability to be cured at the time of discharge and 3 months after it. Patient and nurse satisfaction regarding eCIPs was very high. Benzyl penicillin eCIP treatment is effective and safe, and substantially increases the use of penicillin instead of broad-spectrum antibiotics. To reduce the risk of antimicrobial resistance, eCIPs could increasingly be promoted for use in OPAT clinics, and there should be adequate education and support in their implementation.

## Introduction

The healthcare workforce shortage and increasing healthcare costs are major public health challenges exacerbated by population aging [1, 2]. In an attempt to control costs and to cope with scarce resources, many European countries have reduced the number of hospital beds and focused more on delivering primary and community care [3]. An attractive alternative for patients who do not require constant monitoring is to treat patients at home [4]. For adult patients in need of intravenous (iv) antibiotics, the hospital at home may offer outpatient parenteral antimicrobial therapy (OPAT), which is defined as the administration of at least two doses of parenteral antimicrobials on different days without interim observation [5]. OPAT has revolutionized the treatment of infections requiring prolonged durations of therapy [6]. It is clinically feasible and cost effective for a range of infections, patient-preferred, and allows optimization of hospital bed capacity and patient flow [7, 8].

A major downside of OPAT is that it may favour the use of broad-spectrum antibiotics that require less frequent dosing than narrow-spectrum penicillin. Indiscriminate use of broad-spectrum antibiotics drives the evolution of antimicrobial resistance (AMR), a major global threat to public health [9–11]. It can also negatively

impact treatment outcomes and costs, treatment-related infections, such as *Clostridium difficile*, and even mortality [12, 13].

One potential way to reduce broad-spectrum antibiotic use in OPAT units is to deliver benzyl penicillin via elastomeric continuous infusion pumps (eCIPs). eCIPs are small nonelectric portable devices that infuse antibiotic solution continuously and steadily for 24 hours and thus provide an alternative for intermittent dosing [5, 14, 15], with only one daily visit by a trained nurse to exchange the eCIP. While eCIPs are increasingly used in OPAT clinics [14, 16], studies on their safety and efficacy are few in number [17–20]. Studies on benzyl penicillin delivery via eCIPs are even more scarce, with previous findings limited by small sample size and lack of a comparison group [21, 22], as well as the use of benzyl penicillin in combination with a broad-spectrum antibiotic [21]. To our knowledge, no previous study has investigated whether the availability of eCIPs in OPAT affects patients' probability of receiving treatment with narrow-spectrum penicillin instead of broad-spectrum alternatives.

We used electronic health record data between January 2018 and January 2022 from one large Finnish OPAT clinic to investigate how the introduction of eCIPs from December 2020 onwards affected the probability of narrow-spectrum penicillin use in the treatment of

erysipelas, which is one of the most common infections in OPAT clinics [23–25]. We also compare clinical outcomes between patients with and without eCIPs and examine satisfaction regarding eCIPs among patients and OPAT nurses. In developed countries, skin and soft tissue infections significantly contribute to morbidity and healthcare costs [26], and the most common reason for hospital admission in patients with these infections is the need for iv antibiotics [27]. Our study provides new evidence on whether these patients can be safely and effectively treated with eCIPs without the need for inpatient hospitalization, and how much potential this has in reducing the use of broad-spectrum antibiotics. The practical value of our findings is highlighted by the real-life study setting. Finland is a welfare state with universal healthcare available to all permanent residents, and the Turku city hospital OPAT clinic treats all adult erysipelas patients within the region if they need parenteral antibiotics but not inpatient care. Our results are thus directly generalizable to the general adult population.

## Methods

The study uses data from the Turku City Hospital OPAT clinic, which serves an urban population of approximately 200 000 inhabitants, operates 7 days a week, and treats around 1200 patients annually. Patients are referred to the clinic from all healthcare providers within the region (Turku University Hospital, Turku City Hospital, and Turku City primary healthcare centres). Patients discharged with erysipelas diagnosis (International Classification of Diseases 10th Revision code A46) from Turku City Hospital OPAT clinic (referred to herein as OPAT clinic) between January 2018 and January 2022 were included in the study (for eligibility criteria, see [Supplementary Appendix S1](#)). Data on patient and care characteristics were retrieved through the Consultants to Government and Industry (CGI) database that collects structured electronic health record data of Turku City Hospital (herein referred to as CGI data). The use of Finnish registry data for the purposes of scientific research carried out in the public interest does not require informed consent from participants. Research approval was granted by the Institutional Research Committee of Turku City Health Authorities (No 1262-2021).

The great majority of erysipelas cases are due to *Streptococcus pyogenes* (group A *Streptococcus*) or *Streptococci* from Lancefield groups C and G for which guidelines recommend penicillin as the first-line antibiotic [28]. If parenteral antibiotics are needed, the use of iv benzyl penicillin requires 4–6 intermittent daily doses (8–16 MIU/day) for a duration of 3–6 days, or the use of benzyl penicillin eCIPs. Benzyl penicillin eCIPs (Baxter, Deerfield, IL, USA) were introduced to the Turku OPAT clinic in December 2020. During the introduction, lectures of the new treatment were given, and the benefits of using benzyl penicillin were highlighted to the referring physicians and nurses in their local clinic meetings (Turku University Hospital, Turku City Hospital, Turku City primary healthcare centres), and furthermore, pamphlets containing information about the eCIPs were delivered to all referring clinics.

After the introduction of eCIPs in December 2020, more comprehensive electronic patient and care episode data could be collected from semi-structured discharge summaries (herein referred to as discharge data, see [Supplementary Appendix S2](#) for more details). There were some inconsistencies between the structured CGI data and the semi-structured discharge data on whether patients met the eligibility criteria (shown in [Supplementary Appendix S1](#)), which led to the exclusion of 33 patients from the CGI data (because they were not considered eligible based on discharge data) and 30 patients from the discharge data (because they were not considered eligible based on CGI data). After these exclusions, we identified the start and end dates of OPAT treatment periods for each patient. For some patients, antibiotic treatment had been started before admission to OPAT. Treatment periods were combined if there was a maximum gap of 6 days between them. The combined periods were then linked

to information on prescribed antibiotics and patient characteristics to create complete care episodes.

From the CGI data, four care episodes had to be removed because information on antibiotic use was missing, five episodes because the first antibiotic prescription began after the end of the OPAT treatment, and five episodes because there was no prescription for parenteral antibiotics. Due to an obvious error in coding, one care episode of 80 days was removed. From the more comprehensive discharge data, 10 care episodes were removed because the first antibiotic prescription was coded to begin more than 1 week before the start of OPAT treatment, and one episode because it was missing from the CGI data. Finally, eight care episodes in the CGI data were recorded to begin after the introduction of eCIPs but were missing from the more detailed discharge data. After excluding these episodes from the CGI data, the dataset included 462 care episodes among 412 patients. Of these episodes, 108 were observed after the introduction of eCIPs. The final discharge dataset included 108 care episodes among 103 patients. eCIPs were used in 64 episodes among 62 patients.

All patients who received an eCIP were given a satisfaction questionnaire on their last follow-up visit to the OPAT clinic. OPAT nurses were also given questionnaires, and informed consent was obtained from them as well as from the patients completing questionnaires. Both patient and nurse versions consisted of ordinal scale and open-ended questions ([Supplementary Appendix S3](#)). For the ordinal scale questions, there were 4–10 possible answers. The patient response rate was 95% and nurse response rate 100%.

## Variables

Our main outcome of interest was treatment following care guidelines. CGI data and discharge data both included the Anatomical Therapeutic Chemical Classification code and the start and end date of each prescribed antibiotic. Treatment was classified as following care guidelines (herein referred to as penicillin treatment) if the patient was treated in OPAT with iv or intramuscular (im) benzyl penicillin. Of the patients not receiving penicillin, the vast majority were treated with either cefuroxime or ceftriaxone ([Supplementary Appendix S4](#)). Either the referring physician or the OPAT physician selected the agent, dose, and frequency of iv or im antibiotic, and all patients received the antibiotic via the local OPAT team. eCIPs were prepared containing 10 or 20 million IU benzyl penicillin/infusor under laminar flow by the staff of a single pharmacy (Yliopiston Apteekki, Helsinki, Finland). Twenty million IU were used only if the patient had a blood culture-positive erysipelas.

In Finland, all antibiotics require a prescription, and parenteral antibiotics are always administered by trained medical practitioners. Patients were visited by a nurse 1–3 times daily and had laboratory parameters monitored at least once or twice during the care episode. A nurse and a physician were on call at all times to deal with any urgent problems. A medical doctor specialized in internal medicine physically met the patients and followed their treatment at the OPAT clinic. In Finland, the specialization in internal medicine takes 6 years (after becoming a certified medical physician), and this training comprises a considerable amount of practice in treating infectious diseases (e.g. in the infectious diseases unit of a university hospital). The consultant was responsible for determining if further iv therapy or a switch to another iv treatment was warranted, or if the treatment could be stepped down to oral medication.

For patients treated after the introduction of eCIPs, we could also determine the clinical outcomes of treatment from the discharge data. These were evaluated at the time of discharge and 3 months after the discharge by calling the patient. At discharge, a patient was considered cured if local signs of infection had resolved and there was no fever, and at 3 months if there had been no unplanned readmission to hospital for the same cause. The patient was considered cured with unplanned changes in the antimicrobial treatment if the iv antibiotic had to be changed during OPAT or before the 3-

month evaluation due to relapse of infection, adverse event, or other causes. Unplanned readmissions to hospital during or after OPAT or deaths during or after OPAT were considered treatment failures.

Adverse events were classified according to the Safety Reporting Requirements for INDs and BA/BE Studies FDA Guidance [29]. Grade classification (grades 1–5) was used as recommended by the Common Terminology Criteria for Adverse Events [30]. We recorded adverse events during care episodes and for the following 3 months.

Both datasets included information on a patient's sex, age (in years), comorbidities (hypertension, diabetes, venous insufficiency, arteriosclerosis obliterans; yes/no for each), and highest measured C-reactive protein (CRP, missing for 21 care episodes in the CGI data). The discharge data also included information on antibiotic allergies (yes/no), previous erysipelas infections (yes/no), use of prophylactic antibiotic (yes/no), blood culture positivity for sepsis (yes/no), and site of infection (lower extremity, upper extremity, other).

### Statistical analyses

First, we used CGI data to assess how the introduction of eCIPs affected the predicted probability of penicillin treatment. To take into account differences in patient and care-episode characteristics between the two time periods, we estimated average marginal effects (AMEs) from a logistic model [31] that was controlled for sex, age, comorbidities, and CRP. Second, we used discharge data after the introduction of eCIPs to assess how receiving an eCIP affected the predicted probability of (1) receiving penicillin, (2) being cured at the time of discharge without any unplanned changes in treatment, and (3) being cured at 3 months after discharge without any unplanned changes in treatment. The logistic model for receiving penicillin was controlled for sex, age, comorbidities, antibiotic allergy, previous erysipelas infection, prophylactic antibiotic use, CRP, blood culture positivity, and site of infection. The models for clinical outcomes were otherwise similar, but blood culture positivity and site of infection had to be omitted because there were too few cases.

## Results

During the 3-year follow-up period, we could retrieve structured data for 354 care episodes before and 108 after the introduction of eCIPs from the CGI database (Table 1). There were no major differences in sex and age distributions between study groups. The most

**Table 1.** Erysipelas care episodes ( $n = 462$ ) in Turku OPAT clinic; structured electronic health record data, January 2018–January 2022

	Study period before eCIPs ( $n = 354$ )	Study period after eCIPs ( $n = 108$ )
Patient characteristics		
Male, %	55.6	52.8
Age at care episode (years), median (range)	67 (23–101)	69 (23–95)
Comorbidities		
Hypertension, %	58.1	65.7
Diabetes, %	31.9	38.0
Venous insufficiency, %	10.7	17.6
Arteriosclerosis obliterans <sup>a</sup> , %	6.8	4.6
Care episode characteristics		
CRP <sup>b</sup> (mg/l), median (range)	56 (2–346)	81 (2–435)
Treated with penicillin, %		
Yes	30.8	63.9
No	69.2	36.1

Data retrieved from the structured CGI database.

a: Peripheral artery disease.

b: CRP: C-reactive protein.

common patient comorbidity was hypertension, followed by diabetes. The proportion of patients with comorbidities increased slightly over time, and there was also a minor increase in median CRP (a sensitive biomarker of infection) level. After the introduction of eCIPs, the proportion of patients treated with penicillin more than doubled, from 30.8% to 63.9%. When patient and care-episode characteristics were controlled for, patients treated after the introduction of eCIPs had 36.0 percentage points (95% confidence interval 25.5–46.5) higher probability of being treated with penicillin following care guidelines compared to patients treated before eCIPs (Table 2).

Comprehensive data from semi-structured discharge summaries were obtained for the care episodes following the introduction of eCIPs, with 64 episodes implementing the eCIP (Table 3). Patients with eCIPs were more often male and had fewer comorbidities than patients without eCIPs. The most striking difference between patients with and without eCIPs was the prevalence of antibiotic allergies, with 38.6% of patients without an eCIP reporting an allergy to at least one antibiotic. Blood culture-positive infections were rare, and patients with and without eCIPs had similar CRP levels, with a lower extremity being the most common site of infection in both groups. Nevertheless, only 15.9% of patients without an eCIP were treated with benzyl penicillin, compared to 90.6% of patients with eCIPs. Treatment failures were rare with and without eCIPs, but more patients without eCIPs experienced unplanned changes in treatment. Compared to three patients without eCIPs, only one patient with an eCIP experienced an adverse event (Supplementary Appendix S5). One patient died, but the cause of death was not related to erysipelas or its treatment.

When all patient and care-episode characteristics were controlled for, patients who received an eCIP had 73.1 (58.0–88.2) percentage points higher probability than patients without an eCIP to receive penicillin treatment (Table 4). The association remained similar when only patients without antibiotic allergies were included (Supplementary Appendix S6). Compared to patients without eCIPs, patients with eCIPs had 21.4 (5.5–37.8) percentage points higher predicted probability to be cured without any unplanned changes in treatment at the time discharge. The difference remained similar 3 months after discharge.

Patients who received an eCIP and nurses working in Turku OPAT were very satisfied with eCIPs (Supplementary Appendix S7). All nurses and 85% of patients gave the highest possible rating for general satisfaction. Similar proportions of patients would choose eCIP again and recommend it to others. Patients were especially happy that they could 'continue their active lifestyle' and 'did not have to stick to the restrictive timetable of infusions three times a day' with eCIPs. The most often mentioned downside of eCIPs was

**Table 2.** AME of eCIP introduction on penicillin use; CGI data on erysipelas care episodes in Turku OPAT, January 2018–January 2022

	AME	95% CI <sup>a</sup>	
Study period after eCIP introduction	0.360	0.255	0.465
Male patient	−0.058	−0.145	0.029
Patient age at care episode	0.002	−0.001	0.005
Patient comorbidities			
Hypertension	−0.120	−0.228	−0.011
Diabetes	0.007	−0.098	0.112
Venous insufficiency	0.066	−0.072	0.205
Arteriosclerosis obliterans <sup>b</sup>	−0.069	−0.235	0.096
CRP <sup>c</sup>	−0.001	−0.001	0.000

Table excluded 21 care episodes with missing information on CRP. Results from logistic models adjusted for within-patient clustering.

a: CI: confidence interval.

b: Peripheral artery disease.

c: CRP: C-reactive protein.

**Table 3.** Erysipelas care episodes ( $n = 108$ ) in Turku OPAT clinic; semi-structured electronic health record data, December 2020–January 2022

	Without eCIP ( $n = 44$ )	With eCIP ( $n = 64$ )
Patient characteristics		
Male, %	47.7	56.3
Age at care episode (years), median (range)	72 (23–94)	68 (30–95)
Comorbidities		
Hypertension, %	75.0	60.9
Diabetes, %	43.2	35.9
Venous insufficiency, %	25.0	21.9
Arteriosclerosis obliterans <sup>a</sup> , %	4.6	3.1
Antibiotic allergy, %	38.6	4.7
Previous erysipelas infection, %	45.5	48.4
Prophylactic antibiotic, %	9.1	7.8
Care episode characteristics		
CRP <sup>b</sup> (mg/l), median (range)	117 (13–299)	142 (8–435)
Blood culture positive infection (sepsis), %	4.6	6.3
Site of infection, %		
lower extremity	88.6	89.1
upper extremity	2.3	7.8
other	9.1	3.1
Treated with penicillin, %	15.9	90.6
Clinical end result, %		
Cured	72.7	90.6
Cured but unplanned changes in treatment <sup>c</sup>	22.7	6.3
Treatment failure	4.6	3.1
Clinical end result at 3 months, %		
Cured	68.2	85.9
Cured but unplanned changes in treatment <sup>c</sup>	5.6	1.6
Treatment failure	25.0	12.5
Missing	2.3	–
Adverse event, %		
Yes	6.8	1.6
No	93.2	98.4

Data retrieved from semi-structured discharge summaries available since December 2020.

a: Peripheral artery disease.

b: CRP: C-reactive protein.

c: The patient was considered cured with unplanned changes in the antimicrobial treatment if the iv antibiotic had to be changed during OPAT or before the 3-month evaluation due to relapse of infection, adverse event, or other causes. There were only 4 patients with adverse events ([Supplementary Appendix S5](#)). One patient died, but the cause of death was not related to erysipelas or its treatment. No other causes or eCIP malfunctions were recorded. Therefore, most cases of unplanned changes represent relapses of infection.

that bathing or dressing was somewhat difficult with the eCIP lines (open answers).

## Discussion

In this real-life observational longitudinal study, we showed that the introduction of eCIPs to a large urban OPAT clinic led to a major shift towards enhanced antimicrobial stewardship in the treatment of erysipelas. The proportion of patients treated with narrow-spectrum benzyl penicillin following care guidelines [28] more than doubled compared to the time period when eCIPs were not yet available, resulting in a considerable reduction in the use of broad-spectrum antibiotics (mainly cefuroxime or ceftriaxone). The observed change highlights that the feasibility of different treatment options is a key element in putting guidelines into practice.

The major increase in penicillin treatment following the introduction of eCIPs occurred even though less than two-thirds of patients received the eCIP. The choice of antibiotic treatment—including the decision to implement an eCIP—was left to the discretion of the referring or OPAT physician, and it reflects the feasibility of different treatment options within the OPAT clinic, the prescribing physician's knowledge of eCIPs, and the patient's characteristics. If a patient had a previous antibiotic allergy, their treatment was very unlikely to start with a penicillin eCIP. In Western countries, approximately 10% of the population report allergies to penicillin [32], but clinically significant penicillin hypersensitivity is uncommon (<5%) [33]. It is well acknowledged that overdiagnosis of penicillin allergy leads to costly and inappropriate treatment [34]. The Infectious Diseases Society of America (IDSA) recommends that individuals with an unconfirmed penicillin allergy should have their penicillin allergy evaluated and, if appropriate, tested to confirm current hypersensitivity or tolerance [33]. Nevertheless, even when patients with antibiotic allergies were excluded, patients who received an eCIP had about 70 percentage points higher probability to receive penicillin treatment compared to patients without eCIPs.

Patients with eCIPs had also better clinical outcomes (percentage of cured patients) at the end of their care episodes and 3 months after discharge than those without eCIPs. Except for 1 patient who developed a probable penicillin hypersensitivity reaction, all patients tolerated eCIPs well. These findings are in line with limited prior evidence. Previously, a small study of 31 patients found the use of benzyl penicillin eCIPs in OPAT feasible and efficient in the treatment of severe deep-seated microbiologically proven infections (e.g. endocarditis, intracranial abscesses) [22], and another study of 43 patients concluded that benzyl penicillin combined with a broad-spectrum iv antibiotic was effective in treating endocarditis [21].

In our study, the number of comorbid conditions was slightly lower among eCIP patients than those without them, but a considerable proportion of eCIP patients still had at least one comorbid condition. Their positive clinical outcomes and low probability of adverse effects suggest that eCIPs are a feasible option even for patients with multiple health conditions. Furthermore, the oldest patient treated with an eCIP was 95 years old. The suitability of eCIPs to elderly patients is of particular importance given the increasing pressure that population ageing is causing on healthcare systems. The prerequisites for the use of eCIPs include a close collaboration between the pharmacist, infectious disease centre, and the OPAT unit. Written local guidelines, training of staff, and logistical planning of eCIP storage are mandatory.

Our study has some limitations. First, there were some inconsistencies between the structured CGI data and the semi-structured discharge data. While structured data have been suggested to increase accuracy, it is often less complete than semi-structured data, and minor inconsistencies are common [35–37]. Importantly, both data sources showed that after the introduction of eCIPs, the proportion of patients treated with penicillin was over 60% ([Supplementary Appendix S4](#)). Second, the healthcare personnel in the uptake area of the Turku OPAT clinic were vigorously educated about current guidelines recommending the use of narrow-spectrum antibiotics for the treatment of erysipelas and the availability of eCIPs. The education concerning guidelines might have increased the use of penicillin even without the availability of eCIPs, although this is unlikely given the impracticality of frequent intermittent dosing. Third, as none of the patients were treated with intermittent-dose penicillin, we could not assess the efficacy of eCIP penicillin as compared to it. Fourth, after eCIPs became available, they were not randomly assigned to patients. It is thus possible that the better clinical outcomes of eCIP patients partly reflect selection. However, in contrast to previous studies without any comparison group [21, 22], we were able to assess differences in clinical

**Table 4.** AMEs of eCIP use on different care outcomes; discharge summary data on erysipelas care episodes in Turku OPAT after the introduction of eCIPs, December 2020–January 2022

	Treatment with penicillin			Cured at discharge without unplanned changes in treatment			Cured at 3 months after discharge without unplanned changes in treatment		
	AME	95% CI <sup>a</sup>	OR	AME	95% CI <sup>a</sup>	OR	AME	95% CI <sup>a</sup>	OR
eCIP used	0.731	0.580	0.882	0.214	0.055	0.378	0.205	0.017	0.394
Patient characteristics									
Male	–0.020	–0.120	0.079	0.058	–0.083	0.181	–0.031	–0.185	0.123
Age at care episode	0.000	–0.004	0.005	–0.003	–0.008	0.001	–0.004	–0.009	0.002
Comorbidities									
Hypertension	–0.063	–0.219	0.093	0.034	–0.175	0.225	0.102	–0.098	0.302
Diabetes	–0.041	–0.171	0.088	–0.136	–0.279	0.055	–0.028	–0.202	0.146
Venous insufficiency	0.080	–0.048	0.209	0.050	–0.106	0.173	–0.071	–0.289	0.147
Arteriosclerosis obliterans <sup>b</sup>	0.018	–0.148	0.185	–0.135	–0.504	0.235	0.003	–0.356	0.362
Antibiotic allergy	–0.028	–0.172	0.117	0.041	–0.160	0.199	0.060	–0.137	0.257
Previous erysipelas infection	–0.076	–0.221	0.069	–0.038	–0.203	0.122	–0.035	–0.202	0.132
Prophylactic antibiotic	0.039	–0.121	0.199	–0.212	–0.513	0.100	–0.018	–0.302	0.267
Care episode characteristics									
CRP <sup>c</sup>	0.000	–0.001	0.001	–0.001	–0.002	0.000	–0.001	–0.002	0.000
Blood culture positive infection (sepsis)	–0.166	–0.488	0.157	–	–	–	–	–	–
Site of infection (ref. lower extremity)									
Upper extremity	0.126	–0.126	0.377	–	–	–	–	–	–
Other	0.053	–0.172	0.277	–	–	–	–	–	–

Data retrieved from semi-structured discharge summaries available since December 2020. Results from logistic models adjusted for within-patient clustering.

Model for treatment with penicillin includes patient's sex, age, comorbidities, antibiotic allergy, previous erysipelas infection, prophylactic antibiotic use, CRP, positive blood culture, and site of infection. Models for clinical outcomes include patient's sex, age, comorbidities, antibiotic allergy, previous erysipelas infection, prophylactic antibiotic use, and CRP.

a: CI: confidence interval.

b: Peripheral artery disease.

c: CRP: C-reactive protein.

outcomes after accounting for various characteristics that might have affected the choice of treatment. Our data also include patient populations typically missing from trial-based studies, which is important when assessing the safety and efficacy of treatment in a real-world setting.

## Conclusions

After the introduction of eCIPs to a large OPAT clinic, a dramatically larger proportion of erysipelas patients were treated with guideline-suggested narrow-spectrum benzyl penicillin instead of the previously common broader-spectrum antibiotics. The use of eCIPs was also safe, effective, and preferred by both patients and healthcare workers. The increasing use of benzyl penicillin eCIPs in OPAT may thus reduce selective pressure for AMR—a major global public health concern—while maintaining low treatment costs and high patient satisfaction [10, 11]. Further studies are warranted to confirm our findings and to examine whether eCIPs can also help to avoid *C. difficile* infections and other problems related to the use of broad-spectrum antibiotics [12, 13].

## Supplementary data

Supplementary data are available at *EURPUB* online.

## Conflict of interest

M.P.V. and P.B. have received a lecture fee from Yliopiston Apteekki (A pharmacy company owned by the University of Helsinki). All other authors declare that they have no conflicts of interest.

## Funding

J.S. has received research funding from the Research Council of Finland (grant number 324322), the Finnish Medical Foundation, and Kone Foundation Finland (grant number 201802186). S.S. has

received funding from the Research Council of Finland (grant number 316941). M.P.V. has received State Research Funding to the responsibility area of Turku University Hospital.

## Data availability

The data used in this study were collected by N.M.-S. and M.P.V. and are not publicly available. Those interested may apply for permission to use these data for scientific research from M.P.V. (e-mail [majja.valta@utu.fi](mailto:majja.valta@utu.fi)).

## Key points

- Outpatient parenteral antibiotic therapy in hospital-at-home settings can reduce the need for inpatient hospital care but may favour the use of broad-spectrum antibiotics.
- Continuous infusion of benzyl penicillin via elastomeric infusers substantially decreases broad-spectrum antibiotic use among erysipelas patients treated at home.
- When erysipelas patients can be treated with outpatient parenteral antibiotic therapy, the use of elastomeric benzyl penicillin infusers is safe and effective and should thus be increasingly promoted.

## References

- 1 Aaltonen M, Forma L, Pulkki J *et al*. Changes in older people's care profiles during the last 2 years of life, 1996–1998 and 2011–2013: a retrospective nationwide study in Finland. *BMJ Open* 2017;7:e015130.
- 2 Martikainen P, Murphy M, Metsä-Simola N *et al*. Seven-year hospital and nursing home care use according to age and proximity to death: variations by cause of death and socio-demographic position. *J Epidemiol Community Health* 2012;66:1152–8.

- 3 Kroneman M, Siegers JJ. The effect of hospital bed reduction on the use of beds: a comparative study of 10 European countries. *Soc Sci Med* 2004;**59**:1731–40.
- 4 Shepperd S, Iliffe S. Hospital at home versus in-patient hospital care. *Cochrane Database Syst Rev* 2005;**3**:CD000356.
- 5 Norris AH, Shrestha NK, Allison GM *et al.* 2018 Infectious Diseases Society of America clinical practice guideline for the management of outpatient parenteral antimicrobial therapy. *Clin Infect Dis* 2019;**68**:e1–35.
- 6 Farmer ECW, Seaton RA. Recent innovations and new applications of outpatient parenteral antimicrobial therapy. *Expert Rev Anti Infect Ther* 2021;**19**:55–64.
- 7 Gilchrist M, Barr D, Drummond F *et al.* Outpatient parenteral antimicrobial therapy (OPAT) in the UK: findings from the BSAC National Outcomes Registry (2015–19). *J Antimicrob Chemother* 2022;**77**:1481–90.
- 8 Saillen L, Arensdorff L, Moulin E *et al.* Patient satisfaction in an outpatient parenteral antimicrobial therapy (OPAT) unit practising predominantly self-administration of antibiotics with elastomeric pumps. *Eur J Clin Microbiol Infect Dis* 2017;**36**:1387–92.
- 9 Byrne MK, Miellet S, McGlinn A *et al.* The drivers of antibiotic use and misuse: the development and investigation of a theory driven community measure. *BMC Public Health* 2019;**19**:1425.
- 10 Dadgostar P. Antimicrobial resistance: implications and costs. *Infect Drug Resist* 2019;**12**:3903–10.
- 11 Meyer E, Gastmeier P, Deja M *et al.* Antibiotic consumption and resistance: data from Europe and Germany. *Int J Med Microbiol* 2013;**303**:388–95.
- 12 Brown KA, Langford B, Schwartz KL *et al.* Antibiotic prescribing choices and their comparative C. difficile infection risks: a longitudinal case-cohort study. *Clin Infect Dis* 2021;**72**:836–44.
- 13 World Health Organization. *Global Action Plan on Antimicrobial Resistance*. Geneva, Switzerland: World Health Organization, 2015.
- 14 Chapman ALN, Patel S, Horner C *et al.* Outpatient parenteral antimicrobial therapy: updated recommendations from the UK. *J Antimicrob Chemother* 2019;**74**:3125–7.
- 15 Roberts JA, Abdul-Aziz M-H, Davis JS *et al.* Continuous versus intermittent  $\beta$ -lactam infusion in severe sepsis. A meta-analysis of individual patient data from randomized trials. *Am J Respir Crit Care Med* 2016;**194**:681–91.
- 16 Van Abel AL, Childs-Kean LM, Jensen KL *et al.* A review of evidence, antimicrobial stability, and feasibility considerations for OPAT continuous infusion. *Ther Adv Infect Dis* 2023;**10**:20499361231191877.
- 17 Diamantis S, Dawudi Y, Cassard B *et al.* Home intravenous antibiotherapy and the proper use of elastomeric pumps: systematic review of the literature and proposals for improved use. *Infect Dis Now* 2021;**51**:39–49.
- 18 García-Queiruga M, Cortizas BF, Alfonsín FL *et al.* Continuous infusion of antibiotics using elastomeric pumps in the hospital at home setting. *Rev Esp Quimioter* 2021;**34**:200–6.
- 19 Thijs L, Quintens C, Vander Elst L *et al.* Clinical efficacy and safety of vancomycin continuous infusion in patients treated at home in an outpatient parenteral antimicrobial therapy program. *Antibiot Basel Switz* 2022;**11**:702.
- 20 Van Anglen LJ, Schroeder CP, Couch KA. A real-world multicenter outpatient experience of ceftolozane/tazobactam. *Open Forum Infect Dis* 2023;**10**:ofad173.
- 21 Briggs S, Broom M, Duffy E *et al.* Outpatient continuous-infusion benzylpenicillin combined with either gentamicin or ceftriaxone for enterococcal endocarditis. *J Antimicrob Chemother* 2021;**76**:2168–71.
- 22 Walton AL, Howden BP, Grayson LM *et al.* Continuous-infusion penicillin home-based therapy for serious infections due to penicillin-susceptible pathogens. *Int J Antimicrob Agents* 2007;**29**:544–8.
- 23 Gardiol C, Voumard R, Cochet C *et al.* Setting up an outpatient parenteral antimicrobial therapy (OPAT) unit in Switzerland: review of the first 18 months of activity. *Eur J Clin Microbiol Infect Dis* 2016;**35**:839–45.
- 24 Hase R, Yokoyama Y, Suzuki H *et al.* Review of the first comprehensive outpatient parenteral antimicrobial therapy program in a tertiary care hospital in Japan. *Int J Infect Dis* 2020;**95**:210–5.
- 25 Yadav K, Suh KN, Eagles D *et al.* Evaluation of an emergency department to outpatient parenteral antibiotic therapy program for cellulitis. *Am J Emerg Med* 2019;**37**:2008–14.
- 26 Poulakou G, Lagou S, Tsiodras S. What's new in the epidemiology of skin and soft tissue infections in 2018? *Curr Opin Infect Dis* 2019;**32**:77–86.
- 27 Talan DA, Salhi BA, Moran GJ *et al.* Factors associated with decision to hospitalize emergency department patients with skin and soft tissue infection. *West J Emerg Med* 2015;**16**:89–97.
- 28 Stevens DL, Bisno AL, Chambers HF *et al.* Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2014;**59**:147–59.
- 29 Food and Drug Administration. *Guidance for Industry and Investigators: Safety Reporting Requirements for INDs and BA/BE Studies*. Silver Spring, MD: Food and Drug Administration, 2012.
- 30 Colevas AD, Setser A. The NCI Common Terminology Criteria for Adverse Events (CTCAE) v 3.0 is the new standard for oncology clinical trials. *JCO* 2004;**22**:6098.
- 31 Norton EC, Dowd BE, Maciejewski ML. Marginal effects-quantifying the effect of changes in risk factors in logistic regression models. *JAMA* 2019;**321**:1304–5.
- 32 Phillips CJ, Gilchrist M, Cooke FJ *et al.* Adherence to antibiotic guidelines and reported penicillin allergy: pooled cohort data on prescribing and allergy documentation from two English National Health Service (NHS) trusts. *BMJ Open* 2019;**9**:e026624.
- 33 Shenoy ES, Macy E, Rowe T *et al.* Evaluation and management of penicillin allergy: a review. *JAMA* 2019;**321**:188–99.
- 34 Rubin R. Overdiagnosis of penicillin allergy leads to costly, inappropriate treatment. *JAMA* 2018;**320**:1846–8.
- 35 Häyrynen K, Saranto K, Nykänen P. Definition, structure, content, use and impacts of electronic health records: a review of the research literature. *Int J Med Inform* 2008;**177**:291–304.
- 36 Poulos J, Zhu L, Shah AD. Data gaps in electronic health record (EHR) systems: an audit of problem list completeness during the COVID-19 pandemic. *Int J Med Inform* 2021;**150**:104452.
- 37 Mikkelsen G, Aasly J. Concordance of information in parallel electronic and paper based patient records. *Int J Med Inform* 2001;**63**:123–31.