A prospective cohort study of the use of domiciliary intravenous antibiotics in bronchiectasis

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BACKGROUND: We introduced domiciliary intravenous (IV) antibiotic therapy in patients with bronchiectasis to promote patient-centred domiciliary treatment instead of hospital inpatient treatment.

AIM: To assess the efficacy and safety of domiciliary IV antibiotic therapy in patients with non-cystic bronchiectasis.

METHODS: In this prospective study conducted over 5 years, we assessed patients’ eligibility for receiving domiciliary treatment. All patients received 14 days of IV antibiotic therapy and were monitored at baseline/day 7/day 14. We assessed the treatment outcome, morbidity, mortality and 30-day readmission rates.

RESULTS: A total of 116 patients received 196 courses of IV antibiotics. Eighty courses were delivered as inpatient treatment, 32 as early supported discharge (ESD) and 84 as domiciliary therapy. There was significant clinical and quality of life improvement in all groups, with resolution of infection in 76% in the inpatient group, 80% in the ESD group and 80% in the domiciliary group. Morbidity was recorded in 13.8% in the inpatient group, 9.4% in the ESD group and 14.2% in the domiciliary IV group. No mortality was recorded in either group. Thirty-day readmission rates were 13.8% in the inpatient group, 12.5% in the ESD group and 14.2% in the domiciliary group. Total bed days saved was 1443.

CONCLUSION: Domiciliary IV antibiotic therapy in bronchiectasis is clinically effective and was safe in our cohort of patients.

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INTRODUCTION

Bronchiectasis is a chronic debilitating respiratory condition. Patients suffer from daily cough, excess sputum production and recurrent chest infections because of inflamed and permanently damaged airways. It is a common condition, with an incidence of 1 in 1,000 in Scotland. Management of bronchiectasis consists of airway clearance and prompt treatment of infections with antibiotics, administered intravenously in more severe cases.

There is evidence that patients with bronchiectasis who have more frequent exacerbations have worse quality of life. The current British Thoracic Society (BTS) guidelines for non-cystic fibrosis bronchiectasis recommends antibiotic therapies for exacerbations that present with an acute deterioration (usually over several days) with worsening local symptoms (cough, increased sputum volume) or change of viscosity, increased sputum purulence with or without increasing wheeze, breathlessness, haemoptysis) and/or systemic upset.

Over 720 bronchiectasis patients in Edinburgh, UK, are monitored in secondary care. They frequently utilize primary and secondary care resources through consultations, A&E attendances and inpatient admissions. The economic burden is significant—inpatient admissions alone for bronchiectasis in NHS Lothian cost just over £1 million per year. There is a worldwide drive for the domiciliary management of chronic respiratory diseases like COPD. Outpatient intravenous (IV) therapy has gained widespread acceptance because of its advantages over inpatient hospitalizations, including fewer absences from school or work and less disruption of family life, decreased costs and high patient satisfaction. Outpatient and domiciliary parenteral antibiotic therapy programs are well-recognized and accepted modes of providing healthcare in the community worldwide, but the UK has been relatively slow to adopt this practice.

Although domiciliary IV antibiotic therapy has already been implemented in cystic fibrosis, this has not been done in non-cystic fibrosis bronchiectasis, where the cohort of patients are middle aged and elderly with comorbid conditions, compared to a relatively younger cohort in cystic fibrosis.

The aim of our study was to evaluate the efficacy and safety of domiciliary IV antibiotic therapy for treating exacerbations of non-cystic fibrosis bronchiectasis.

MATERIALS AND METHODS

Domiciliary IV antibiotic team

All cases were reviewed by the domiciliary team—comprising one respiratory physician leading the bronchiectasis service in NHS Lothian, one specialist registrar, one clinical nurse specialist, one physiotherapist and one respiratory pharmacist. Patients are referred to the bronchiectasis team by completing an outpatient IV antibiotic referral form specifying the antibiotic to be prescribed for 14 days. If the patient was unwell and required hospital admission he or she was taught how to self-administer IV antibiotics while an inpatient, and if competent was given early supported discharge (ESD). Patients were taught to self-administer IV antibiotics via a cannula, midline catheter or a totally implanted port— the midline catheter was the mode used in the majority of patients. A pall filter is attached to the cannula to aid self-administration. Clear instructions were given to patients on how to flush IV access, make up antibiotics and secure access.

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once antibiotics were administered. All procedures were done aseptically. Patients were taught by the clinical nurse specialist and had to demonstrate the technique of administration of antibiotics to the nurse specialist and were deemed eligible for domiciliary therapy only once the domiciliary team were satisfied with the technique and safety measures. Patients were provided with antibiotics, an epipen in case of anaphylaxis, flushes, syringes, needles, sharps bin, bandages and a patient information booklet. The patients returned at 1 week to be reviewed by the clinical nurse specialist and were provided with a fresh supply of equipment and antibiotics to complete the course of antibiotic therapy. All patients returned for a final visit on day 14 to return left-over equipment and to finish treatment assessment. Patients were given the contact details of the domiciliary team, for them to contact if they had any problems with IV access, adverse reactions or worsening of symptoms. If there were occasions out of clinic hours when a patient presented with problems, the patient would phone the respiratory ward, at Royal Infirmary of Edinburgh, and then would be reviewed by the on-call team. The clinical nurse undertook routine management of outpatients on IV antibiotics and monitored their blood, lines/access devices, sputum, spirometry, incremental shuttle walking test and progress/condition. The medication aspects were supported by the ward pharmacist.

There had to be a unified consensus from the domiciliary team that the patient was suitable for domiciliary IV antibiotic therapy, for safety reasons. Patients were refused by the domiciliary team if they had any of the following features: unable to cope at home; development of cyanosis or confusion; breathlessness, with a respiratory rate $\geq 25$/min; circulatory failure; respiratory failure; temperature $\geq 38$ °C unable to take oral therapy.

If requiring initial hospital admission, patients were considered for ESD if they had none of the above adverse features for 24 h or longer.

Choice of antimicrobial and drug delivery
All patients received 14 days of IV antibiotic therapy using antibiotics as per sensitivity testing, and the respiratory physician decided this. Antibiotics were administered by inserting an antecubital peripheral long line catheter.

Study design
Patients were recruited prospectively over 5 years from December 2006 to December 2011, from the Royal Infirmary of Edinburgh, UK. All patients requiring IV therapy for an acute exacerbation were assessed by the domiciliary IV team for consideration of 14-day domiciliary IV therapy or ESD with domiciliary IV therapy.

Outcome measures—at the start and end of exacerbation
Outcome measures recorded were treatment outcome (by measuring forced expiratory volume in 1 s (FEV$_1$), forced vital capacity (FVC), incremental shuttle walk test, 24-h sputum volume, sputum microbiology with IV markers of inflammation—white cell count, C-reactive protein and erythrocyte sedimentation rate, health status questionnaires—Leicester Cough Questionnaire and St George’s Respiratory Questionnaire$_{11}$), morbidity, mortality and 30-day readmission rates.

Patients
Inclusion criteria. Patients were included if they satisfied any of the following criteria: (1) had an established radiological diagnosis of bronchiectasis (high resolution CT scan of the chest); (2) had an exacerbation defined by acute deterioration (usually over several days) with worsening local symptoms (cough, increased sputum volume or change of viscosity, increased sputum purulence with or without increasing wheeze, breathlessness, haemoptysis) and/or systemic upset; (3) needed IV antibiotics because of failure to respond to oral antibiotics, having a pathogen requiring IV antibiotic therapy or severe exacerbations necessitating inpatient admission.

Patients who were considered to be suitable for domiciliary IV treatment or ESD had to meet the following requirements: (1) were committed and able to attend the hospital for assessments; (2) were able to demonstrate that they can safely administer IV antibiotics; (3) had home circumstances appropriate for treatment; and (4) had no evidence of potential IV drug abuse.
Patient selection
A total of 196 patients were referred and thereby assessed for domiciliary IV antibiotic therapy.

Baseline characteristics
Of the total 80 episodes admitted to hospital for 14 days, there were a total of 36 patients who received IV therapy on one or more occasions. For the ESD group, of the 32 episodes, 23 patients received IV therapy on one or more occasions. For the domiciliary group, of the 84 episodes, 52 patients received IV therapy on one or more occasions. The characteristics of the individual patients in the cohort are shown in Table 1. The three groups differed at start of IV therapy by age, gender, smoking status, comorbidities, pre-therapy FVC and exercise capacity. The group receiving inpatient IV therapy was older, had more patients who had coexistent COPD, and had less number of patients with coexistent asthma and previous malignancy. In addition, this group had lower baseline spirometry and exercise capacity compared to the ESD or domiciliary group.

Table 1. Characteristics of the study population

|                        | Inpatient group for 14 days (N = 36) | Early supported discharge (N = 23) | Domiciliary IV group (N = 52) | P value* |
|------------------------|--------------------------------------|-----------------------------------|-------------------------------|----------|
| Age                    | 71 (62–76)                           | 65 (56–69)                        | 61 (63–69)                    | 0.0008   |
| Gender (% female)      | 63.9%                                | 65.2%                             | 41.7%                         | 0.001    |
| Smoking status         | 73.8%/25%/1.2%                       | 65.2%/30.5%/4.3%                 | 51.9%/44.2%/3.9%             | 0.005/0.01/0.4 |
| BMI                    | 25.5 (21.5–30.5)                     | 24.5 (22–33)                      | 25 (22–28)                   | 0.8      |
| High BMI > 30 kg/m²    | 5.6%                                 | 4.3%                              | 11.5%                         | 0.1      |
| IHD                    | 16.7%                                | 17.4%                             | 11.5%                         | 0.5      |
| Asthma                 | 25%                                  | 47.8%                             | 28.8%                         | 0.001    |
| COPD                   | 41.7%                                | 13%                               | 11.5%                         | <0.0001  |
| Previous malignancy    | 5%                                   | 8.7%                              | 13.5%                         | 0.09     |
| ABPA on long term steroids | 5.6%                              | 8.7%                              | 5.8%                          | 0.6      |
| Diabetes mellitus      | 11.1%                                | 8.7%                              | 2%                            | 0.03     |
| % DM requiring insulin | 0%                                   | 0%                                | 0%                            | —       |
| Pre therapy FEV₁ (L)   | 1.1 (0.9–1.4)                        | 1.4 (1–1.8)                       | 1.4 (1–1.9)                   | 0.06     |
| FEV₁ (% predicted)     | 54.7%                                | 2.3 (1.7–2.8)                     | 2.4 (2–2.9)                   | 0.906    |
| Pre therapy FVC (L)    | 1.9 (1.5–2.3)                        | 2.3 (1.7–2.8)                     | 2.4 (2–2.9)                   | 0.007    |
| FVC (% predicted)      | 66.5%                                | 81.3%                             | 82.7%                         | 0.004    |
| Pre therapy ISWT (m)   | 45 (15–125)                          | 130 (40–270)                      | 250 (190–420)                 | 0.02     |
| Dose of ICS (micrograms) | 500 (250–500)                       | 500 (250–500)                     | 500 (250–500)                 | 0.2      |
| Dose of oral steroid (mg) | 5 (2.5–5)                          | 5 (2.5–5)                        | 5 (2.5–5)                    | 1        |
| Long term antibiotic for chest | 10%                                 | 4.3%                              | 7.7%                          | 0.2      |
| % Colomicin (neb)      | 25%                                  | 0%                                | 50%                           | <0.0001  |
| % Gentamicin (neb)     | 0%                                   | 100%                              | 0%                            | <0.0001  |
| % Clarithromycin (oral) | 75%                                | 0%                                | 50%                           | <0.0001  |
| % Coamoxiclav (oral)   | 0%                                   | 0%                                | 0%                            | —       |

Abbreviations: ABPA, allergic bronchopulmonary aspergillosis; BMI, body mass index; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; ICS, inhaled corticosteroid; IHD, ischaemic heart disease; ISWT, incremental shuttle walk test; neb, nebulized.

*P values comparing baseline and pre-therapy characteristics of the groups.
Sputum microbiology
Sputum was sent for qualitative microbiology in all patients prior to starting IV antibiotic therapy (see Table 2). In all groups, the most common microorganism identified was *Pseudomonas aeruginosa*. The groups add up to more than 100% as some patients had more than 1 pathogen isolated.

Treatment used
Ten different types of IV antibiotics (Table 3) were used alone or in combination.

### Table 2. Microorganisms isolated at the beginning of intravenous therapy

| Microorganisms isolated | Inpatient group for 14 days (N = 80 episodes) | Early supported discharge group (N = 32 episodes) | Domiciliary IV group (N = 84 episodes) |
|-------------------------|---------------------------------------------|-----------------------------------------------|----------------------------------------|
|                         | Inpatient for 14 days (N = 80 episodes) | Early supported discharge (N = 32 episodes) | Domiciliary group (N = 84 episodes) |
| *Pseudomonas aeruginosa* | 48.8%                                      | 28.1%                                         | 34.5%                                  |
| Coliforms               | 11.3%                                      | 15.6%                                         | 17.9%                                  |
| MRSA (methicillin-resistant) | 7.5%                          | 3.1%                                          | 1.2%                                   |
| Staphylococcus aureus   | 3.8%                                      | 6.3%                                          | 9.5%                                   |
| MSSA (methicillin-sensitive) | 8.8%                       | 15.6%                                         | 32.1%                                  |
| Haemophilus influenzae  | 8.8%                                      | 15.6%                                         | 32.1%                                  |
| Streptococcus pneumoniae| 3.8%                                      | 6.3%                                          | 14.3%                                  |
| Moraxella catarrhalis   | 5%                                        | 6.3%                                          | 13.1%                                  |
| Mixed normal flora      | 13.8%                                     | 21.9%                                         | 28.6%                                  |

### Table 3. Intravenous antibiotic used

| Antibiotic used | % |
|-----------------|---|
| Cefazidime      | 48.9 |
| Gentamicin      | 14.8 |
| Ceftriaxone     | 12.7 |
| Tazocin         | 9.7 |
| Amoxicillin with clavulanic acid | 5.1 |
| Meropenem       | 4 |
| Vancomycin      | 2.6 |
| Colymycin       | 2 |
| Flucloxacillin  | 2 |
| Cefuroxime      | 1.5 |

### Table 4. Clinical outcomes measured on day 1 and day 14

|                     | Inpatient group for 14 days (N = 80), median (interquartile range) | Early supported discharge group (N = 32), median (interquartile range) | Domiciliary IV group (N = 84), median (interquartile range) |
|---------------------|-------------------------------------------------------------------|----------------------------------------------------------------------------|--------------------------------------------------------------------------------|
|                     | Day 1                                                                 | Day 14                                                                   | Day 1                                                                 | Day 14                                                                   | Day 1                                                                 | Day 14                                                                   |
|                     | P value*                                                          |                                                                            | P value*                                                          |                                                                            | P value*                                                          |                                                                            |
| ISWT (m)            | 45 (15–125)                                                       | 120 (30–190)                                                              | < 0.0001                                                          | 130 (40–270)                                                              | 230 (80–340)                                                              | 0.0009                                                                   |
| FEV1 (L)            | 1.2 (0.9–1.3)                                                     | 1.2 (1–1.3)                                                               | 0.02                                                              | 1.3 (1–1.8)                                                               | 1.5 (1–1.9)                                                               | 0.03                                                                     |
| PVC (L)             | 1.9 (1.5–2.2)                                                     | 2 (1.6–2.4)                                                               | 0.0009                                                          | 2.3 (1.7–2.8)                                                             | 2.3 (2.1–2.9)                                                             | 0.02                                                                     |
| LCO (Units)         | 11.7 (7.7–14.7)                                                  | 14.2 (11.2–17.8)                                                         | < 0.0001                                                        | 12.5 (10.2–15.3)                                                         | 16.8 (13.1–19)                                                            | < 0.0001                                                               |
| SGRQ (Units)        | 69.8 (62.3–80)                                                   | 62.6 (49–70.8)                                                            | < 0.0001                                                        | 52.2 (39.6–69.9)                                                         | 42.8 (31.5–64)                                                            | < 0.0001                                                               |
| Sputum volume (ml)  | 20 (10–50)                                                        | 10 (5–20)                                                                | < 0.0001                                                        | 17.5 (10.5–25)                                                           | 10 (2.5–15)                                                               | 0.01                                                                     |
| % PPM               | 95%                                                               | 53.8%                                                                    | < 0.0001                                                         | 17.5 (10.5–25)                                                           | 10 (2.5–15)                                                               | 0.01                                                                     |
| WCC (10³/l)         | 10.7 (8.7–13.3)                                                  | 8.9 (7.1–11.1)                                                            | < 0.0001                                                         | 9.1 (7.4–13)                                                              | 7.5 (5.8–10.3)                                                            | 0.05                                                                     |
| CRP (mg/l)          | 31 (14–125)                                                       | 9.5 (5–15.5)                                                              | < 0.0001                                                         | 19 (5–127)                                                                | 5.5 (1–10.5)                                                              | 0.0004                                                                  |
| ESR (mm/h)          | 41 (21–63)                                                       | 21 (13–36)                                                               | < 0.0001                                                         | 33 (19–52)                                                                | 23.5 (11.5–37.5)                                                         | 0.02                                                                     |

### Table 5. Comparison of mortality, morbidity and safety between the three groups

| Complications                  | Inpatient group for 14 days (N = 80 episodes) | Early supported discharge group (N = 32 episodes) | Domiciliary IV group (N = 84 episodes) |
|-------------------------------|-----------------------------------------------|--------------------------------------------------|----------------------------------------|
|                               | Day 1                                         | Day 14                                          | Day 1                                 | Day 14                                 |
| 14-day mortality              | 0%                                            | 0%                                              | 0%                                    | 0%                                    |
| 14-day morbidity              | 11 (13.8%)                                    | 3 (9.4%)                                        | 12 (14.2%)                           |
| Readmission within 30 days    | 11 (13.8%)                                    | 4 (12.5%)                                      | 12 (14.2%)                           |
| Allergy to antibiotic         | 1 (1.2%)                                      | 0%                                              | 1 (1.2%)                             |
| Side effects with antibiotic  | 4 (5%)                                        | 2 (6.3%)                                       | 4 (4.7%)                              |
| Anaphylaxis                   | 0%                                            | 0%                                              | 0%                                    |
| Clostridium difficile         | 0%                                            | 0%                                              | 0%                                    |
| Intravenous access-related    | 0%                                            | 2 (6.3%)                                       | 3 (3.6%)                             |
| complications (including line sepsis, line blockage, line fell out) | | | |
| Norovirus                     | 1 (1.25%)                                     | 0%                                              | 0%                                    |

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; ISWT, incremental shuttle walk test; LCO, Leicester Cough Questionnaire (range 3–21; minimal clinical important difference (MCID) 1.3 Units); PPM, potentially pathogenic microorganisms; SGRQ, St George’s Respiratory Questionnaire (0–100; MCID 4 Units); WCC, white cell count. *P* values within group comparison comparing beginning and end of treatment.
stroke). No mortality was recorded in the groups. Thirty-day readmission rates were similar in all groups and the reason for readmission was further exacerbation of bronchiectasis, in all episodes recorded. Side effects with antibiotics, including allergies, developed in 5% in the inpatient group as compared to 6.3% and 4.7% in the ESD group and the domiciliary IV group, respectively. There was no IV access-related complications in the inpatient group in comparison to 6.3% in the ESD group and 3.6% in the domiciliary IV group.

Bed days saved
Together, the domiciliary IV therapy and the ESD group saved a total of 1,443 bed days. This allowed freeing up inpatient beds, which could be reallocated.

Subgroup analysis of individual patients
Of the total 196 episodes of IV antibiotics, a total of 111 patients received treatment. There were 36 individual patients who were admitted as inpatients, of whom 16 required more than one course of IV antibiotics. In the ESD group, 23 individual patients received IV antibiotics, of whom 6 had more than one course of antibiotics. In the domiciliary group, 52 individual patients received IV antibiotics, of whom 19 had more than one course of antibiotics. The first event of individual patients was used. There were similar results in individual patient outcomes (Table 6) as compared to outcomes of all episodes (Table 3), in all groups.

**DISCUSSION**
Main findings
We have introduced domiciliary IV antibiotic therapy in patients with bronchiectasis in a tertiary centre in the UK, by using a team to promote patient-centred domiciliary therapy instead of inpatient treatment. Although domiciliary IV antibiotic therapy is common in cystic fibrosis and other infectious diseases, this is the first large study reporting IV antibiotic therapy in bronchiectasis. This prospective study found that in the patients assessed as suitable by the home IV team, domiciliary IV antibiotic therapy in bronchiectasis is clinically effective and safe.

This study has shown that domiciliary therapy with IV antibiotics results in similar clinical outcomes compared to inpatient therapy. There was significant improvement in exercise capacity, spirometry, sputum volume reduction, markers of systemic inflammation, microbial clearance and health-related quality of life at the end of therapy, in both groups. A subgroup analysis of individual patients, in all three groups, showed similar outcomes to the analysis of all episodes.

Morbidity was recorded in 13.8% in the inpatient group as compared to 9.4% in the ESD group and 14.2% in the domiciliary IV group. No mortality was recorded in any of the three groups. Readmission rates at 30 days were <15% in all groups. Side effects with antibiotics, including allergies, were similar (<7%) in all groups. There was no IV access-related complications in the inpatient group in comparison to 6.3% in the ESD group and 3.6% in the domiciliary IV group. No cases of *Clostridium difficile* were recorded in the groups. This study shows that in our centre, domiciliary IV (both ESD and domiciliary *de novo*) antibiotic therapy is a safe and efficient model of health-care delivery in the treatment of exacerbations in non-cystic fibrosis bronchiectasis.

Over the past 5 years, 116 episodes of inpatient admissions were avoided by this service, which meant releasing 1,443 bed days, which could be reallocated. It is known that the acquisition costs of antibiotics for domiciliary IV therapy can sometimes exceed inpatient alternatives. However, in our centre, antibiotic regimen was the same for both groups. Hence, directs costs including antibiotics, saline flushes and equipment did not come at any higher costs than that needed for inpatient therapy.

Interpretation of findings in relation to previously published work
Owing to lack of research in non-cystic fibrosis bronchiectasis, data are often extrapolated from studies done in cystic fibrosis, to guide therapy. To date, there has been only one blinded, randomized control trial investigating the role of domiciliary IV antibiotics versus hospital treatment in cystic fibrosis-related bronchiectasis. This was done in 19 patients and all patients had at least 2–3 days treatment in hospital before being started on domiciliary IV antibiotic treatment. We accept that our study was not a randomized trial, but this is a large study done in a tertiary centre in the UK, where we have been able to demonstrate that domiciliary IV antibiotics for acute exacerbations can be done safely and effectively.
Ideally, domiciliary treatment should be as effective as inpatient treatment and clinical improvement not sacrificed on the basis of economic considerations and convenience. Domiciliary treatment allows patients to be treated at home, which should translate into better quality of life and decreased risks of inpatient errors and nosocomial complications. In addition, domiciliary IV antibiotics provide the opportunity to deliver more patient-centred care than in the traditional inpatient setting. All these benefits support the aim of the UK healthcare quality strategy, with emphasis on patient-centred and ambulatory care. We have been able to establish this service with careful risk assessment and management, and have been able to demonstrate that this service is safe and clinically effective. This is of significant importance in bronchiectasis, where prompt treatment of exacerbations with appropriate antibiotics is one of the key aims in managing this chronic condition.

Strengths and limitations of this study

To the best of the authors’ knowledge, this is the first large prospective cohort study assessing the safety and efficacy of domiciliary IV antibiotic therapy in non-cystic fibrosis bronchiectasis in the UK, where patients are middle aged and elderly and have pre-existing comorbid conditions. This study provides data that will help both primary and secondary care teams consider domiciliary therapy for bronchiectasis, if a service is available in their centre.

We accept that this study is not a randomized control trial. Inpatient or domiciliary treatment was up to the discretion of the patient and domiciliary team. Also, we did not assess the cost effectiveness that domiciliary treatment would have to the NHS. However, the main aim of this study was to establish a domiciliary IV antibiotic service for exacerbations in bronchiectasis and demonstrate the safety and efficacy of this service in our centre.

Implications for future research, policy and practice

A prospective randomized trial would consolidate our research findings. In patients deemed suitable for domiciliary treatment, domiciliary treatment either fully or as ESD is safe and efficacious.

Conclusion

In patients assessed as suitable by the home IV team, domiciliary IV antibiotics in bronchiectasis is clinically effective and was safe in our cohort of patients.

COMPETING INTERESTS

The authors declare no conflict of interest.

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