Review Article

Comparing Patient Preference Between At-home and In-hospital Settings: Systematic Review and Meta-Analysis on Injectable Medications

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Abstract

Out-of-hospital self-care in patients receiving injectable antibiotics or biologically derived medicines (biologics) is reported to significantly improve quality of life and reduce hospitalizations, but unexpected complications produce some negative outcomes and patient experience. This study aimed to compare patients' experience with long-term injectable therapies, in and out of the hospital setting. Two systematic reviews and meta-analyses were carried out using the most common out-of-hospital self-administered long-term injectable antibiotic and biologic therapies for patients diagnosed with infections or IBD, RA, or psoriasis. The first review investigated patient preference for self-administering subcutaneous injections at home (intervention) vs. intravenous injections in a hospital inpatient or outpatient setting. There was a statistically significant difference between the homecare (intervention) and hospital (control) group (p = 0.05) favoring the intervention. The second review was on injectable antibiotics. The results demonstrated that the use of injectable antibiotics, at home (intervention) or in hospital (control) produced similar benefits (p = 0.30 cure and p = 0.90 treatment failure) and harm (hospital admission after and during treatment p = 0.64, p = 0.99 respectively, disease complications p = 0.77 and medications side effects p = 0.15). This research found no substantial differences in patient outcomes based on the setting. Home care is an important option to support patient autonomy and well-being. The recent global COVID-19 pandemic further highlighted the importance of an option to continue long-term disease management without hospitalization.

Keywords: Antibiotics, Biologics, Self-management, Home care, Out-of-hospital care

Introduction

Self-care is an important component of chronic disease management [1, 2]. The number of years lived with a disability is increasing in the UK due to the increase in chronic diseases and the aging population [3, 4]. Patients capable of self-care or self-management of their conditions have been found to have significantly improved medical outcomes, with fewer hospitalizations, improved quality of life, and higher survival rates [5, 6]. Self-management of chronic conditions has been described as maintaining health through practicing health-promoting habits [7, 8]. It encompasses diverse behaviors in which an individual with chronic illness engages to maintain emotional and physical stability such as sufficient sleep, adherence to prescribed medication, stress management, and physical alertness [9]. Some patients are not capable of managing their conditions due to personal, health, and social barriers that led to the development of self-management support programs over the past years, however, these encountered challenges, mainly due to the diversity of those barriers especially in patients with challenging physical limitations or cognitive function impairment [10-13]. The continuation of therapy for long-term conditions is the greatest priority, and health practitioners should appreciate the significance of patient participation and the importance of them being able to understand their conditions and what is being asked of them [14]. To be successful, practitioners, patients, caregivers, and healthcare organizations must be proactive in their engagement with one another. With a coordinated approach and suitably enabled patients, a range of chronic conditions can be treated more efficiently [15]. To reach this conclusion, Dineen-Griffin *et al.* [15] conducted a systematic review of 58 studies from 18 different nations, the majority from the United Kingdom (UK) and the United States of America

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(USA). Type 2 Diabetes Mellites (T2DM) (37.9%, n = 22), Chronic Obstructive Pulmonary Disease (COPD) (20.7%, n = 12), and depression (13.8%, n = 8) were the most frequently reported conditions. Most of the interventions were provided by nurses or general practitioners (GPs)and only in 14 studies telephone reminders were given in primary care with healthcare professionals from various disciplines (24%, n = 14).

With increasing demand for healthcare services patient involvement in their care has increasingly gained prominence and is typically regarded as a critical component of contemporary models of healthcare delivery [16]. Home parenteral therapy (HPT) was initially developed in response to increasing healthcare costs, constraints on hospital beds, and the need to control the spread of hospital-acquired infection [17]. HPT is better suited for low-dependency patients where a nursing service is not required and the patient or carer wishes to move to the home setting, e.g., in palliative care [18]. Therapies that are commonly administered at home include antibiotics (for infection), desferrioxamine (for thalassemia), morphine (for pain), total parenteral nutrition (for malabsorption diseases or short gut), and chemotherapy (for cancers). Education-based out-of-hospital care can be used to improve the health outcomes of individuals when delivered by a qualified specialized healthcare professional [19]. Grady and Gough [20] suggested that the development of generic skills has proven effective in allowing patients to manage their illnesses and effectively improve their overall outcomes regardless of the type of their chronic condition. Gobeil-Lavoie *et al*. [21] advised that patients with complex health needs present challenges which are often related to the ability to prioritize self-care activities, increasing the risk of psychological distress due to the impact of their conditions, further complicated by possible poor self-efficacy and receiving conflicting information from multiple healthcare practitioners. Addressing the psychosocial outcomes of sickness significantly improves patients' self-adequacy [22].

Review Question

Do patients self-administering injectable therapies out-of-hospital achieve the same health outcomes as those receiving therapy in-hospital?

Rationale

Homecare offers a familiar environment, with reduced traveling and reduced cross-infection risk. It is considered more convenient for the patient and costs may be comparable to, or cheaper than, hospital provision. Conversely, patients often need to be trained to do unfamiliar things such as self-administration of injections and they will not have equivalent support if any adverse event occurred. The rationale of this study was to compare the health outcomes, and complications, of long-term therapy with injectable biologics or antibiotics in various settings for a range of diseases. By conducting meta-analyses and systematic reviews, the researchers aimed to provide evidence-based information to inform decisions for clinicians and patients about the advantages and disadvantages of treatment in both settings. The University of Wolverhampton ethics in human research committee approved the study.

Materials and Methods

The Cochrane© Handbook for systematic reviews of interventions was used to conduct this systematic review [23] and reported using the preferred reporting items for systematic review and meta-analysis (PRISMA statement) [24]. This systematic review included people treated with injectable biologics or antibiotics at home. Review Manager (RevMan®) software by the Cochrane Collaboration Group was used for the conduct of the meta-analyses [25]. In addition, RevMan® Software was used for calculating risk ratio (RR), odds ratio (OR), the ratio of means (RoM), as well as hazard ratio (HR), which are expressed on a log scale, and measure differences in mean, risk difference, which are illustrated on their natural scale. The software also conducted a heterogeneity analysis of the included studies [25]. The random-effect (RE) model and fixed-effect (FE) model were utilized as applicable.

The population (P), intervention (I), comparison (C), outcome (O), and site (S) framework [26] was used for framing identifying predetermined measurable outcomes, and the literature search words and eligibility criteria.

Inclusion criteria were:

- Randomized controlled trials (RCT), randomized cohorts, and randomized case-control
- A study outlining self-management at homecare focuses on injectable antibiotics.
- Studies with a focus on home service for defined health conditions
- Published from the year 2000 up to 2021
- Studies focusing on populations who are living independently in the community
- Published in credible and verifiable journals which are full papers
- No limitations based on location, gender, race, career, ethnicity, culture, or country of origin
- Comprehensive and extensive data analysis
- Both quantitative and qualitative research design

Literature Searches

Based on the research question and objectives, two searches were made from 2000 till the 31st of April 2022:

1. Keywords: "autoimmune disorder" OR "self-management" OR "home care" OR "homecare" OR "self-care" OR "self-administered" OR "self inject") and ("injectable biologics" OR "outpatient injectable biologics therapy" OR "biologics") and ("inflammatory bowel disease" OR "Crohn's" OR "ulcerative colitis" OR "IBD" OR "UC" OR "autoimmune disease".
2. Keywords: "self-management" OR "home care" OR "homecare" OR "self-care" OR "self-administered" OR "self-inject") AND ("injectable antibiotics" OR

"outpatient injectable antibiotics therapy") AND ("respiratory disease" OR "respiratory disorders" OR "pneumonia" OR "urinary tract infection" OR "UTI" OR "osteomyelitis" OR "bone infection" OR "skin infection" OR "infection".

The preliminary search was primarily conducted through Google® Scholar™ to test the suitability of the search words and explore the volume of available studies. All the articles related to the research question were noted. Multiple search engines and databases were then used; PubMed®, Social Care Online and EMBASE©, Wiley Online Library©, and Science Direct® and the Cochrane Library©. An additional search was conducted on various credible, leading websites such as NICE, NHS, America's Centres for Disease Control and Prevention (CDC), and Clinical Trials Registers. The identified publications were extracted and listed then all duplicates were deleted. Furthermore, a manual search was also carried out through the reference lists of selected articles to recognize any useful articles that may have been missed from the original search. The full-text versions of all selected studies were obtained through the university library through inter-loan services.

Data Extraction and Missing Analysis

Data extraction was conducted using a Microsoft® Excel™ spreadsheet. Additional information extracted includes the author, year of publication, as well as other baseline characteristics. When data presented in a particular study was unclear or missing or presented in a form that is non-extractable, the authors or publishers were contacted to provide the missing data. Where it was not possible to obtain data, the study was removed from the meta-analysis.

The RevMan© v.5.4.1 software was utilized to assess the RoB for all studies. The reviewers judged the domains based on Higgins *et al*. [23] criteria:

- Low risk of bias – green: the field measured is considered to be present, clear, and, complete.
- High risk of bias – red: absence of the field measured, or the field measured does not meet the selection criteria.
- Unclear reporting – yellow: the field measured is incomplete or reported in a way that does not allow for precise decisions to be made.

In this study, the RoB was assessed by two independent reviewers for all the included studies. In scenarios where there was a disagreement, a compromise was reached through a consensus or a third reviewer.

When the observed item scores are dichotomous (correct–incorrect), the Cochrane Mantel-Haenszel statistic (CMH) was used to compare two groups, and the sum score is used as a proxy for the latent variable. Heterogeneity was measured based on the value of the I^2 where.

- 0% to 40%: might not be important - low.
- 30% to 60%: may represent moderate heterogeneity.
- 50% to 90%: may represent substantial heterogeneity.
- 75% to 100%: considerable heterogeneity.

The fixed effect (FE) model has a stringent assumption regarding the population sample size whereas the random effects model has a hierarchical linear model in which the data being analyzed comes from a hierarchy of different populations whose differences are related to the hierarchy [27]. The random-effects technique assumes that separate studies estimate different but related, intervention effects [28].

Results and Discussion

Comparison Between Injectable Biologics Use at Home and in Hospital

The literature search retrieved 3438 articles from all databases after excluding duplicates. After the abstract, title, and full-text screening of the selected studies, 45 studies were eligible to be included in this systematic review. One study published outside the focus date range was included due to its high relevance. 8941 participants were included in this analysis. The mean minimum age included in this systematic review was 11 years, and the highest mean age was 60 years. The funnel plot analysis was asymmetric indicating possible high variance in effect size produced from the included studies which can be due to smaller studies having sampling errors in their effect estimates. The includes studies are: Allen *et al*. [29], Boeri *et al*. [30], Bolge *et al*. [31], Bolge *et al*. [32], Bolt *et al*. [33], Borruel *et al*. [34]. Capelusnik *et al*. [35], Cha *et al*. [36], Chapel *et al*. [37], Chilton *et al*. [38], Dashiell-Aje *et al*. [39], Desplats *et al*. [40], Edel *et al*. [41], Eftimov *et al*. [42], Emadi *et al*. [43], Espanol *et al*. [44], Falanga *et al*. [45], Fernandes *et al*. [46], Gardulf *et al*. [47], Gelhorn *et al*. [48], Gladiator *et al*. [49], Grisanti *et al*. [50], Hadden *et al*. [51], Harbo *et al*. [52], Hoffmann *et al*. [53], Husni *et al*. [54], Huynh *et al*. [55], Kariburyo *et al*. [56], Louder *et al*. [57], Mohamed *et al*. [58], Nagahori *et al*. [59], Nicolay *et al*. [60], Perez-Ordóñez *et al*. [61], Permin *et al*. [62], Reid *et al*. [63], Runken *et al*. [64], Samaan *et al*. [65], Santus *et al*. [66], Scarpato *et al*. [67], Sylwestrzak *et al*. [68], Tłustochowicz *et al*. [69], Van Deen *et al*. [70], van Schaik *et al*. [71], Willeke *et al*. [72], Wu *et al*. [73]. The included studies showed a low RoB **(Figure 1)**.

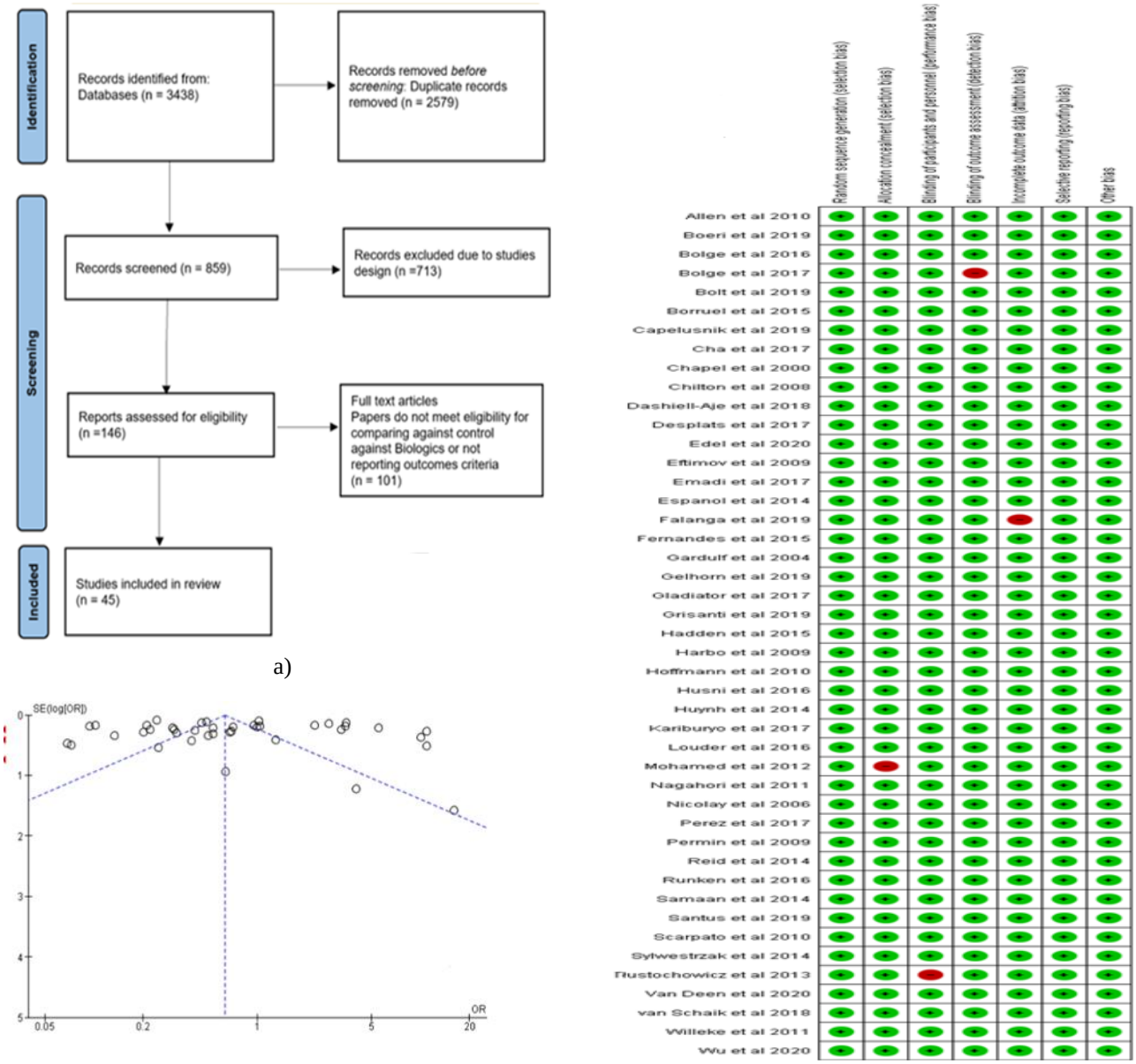


Figure 1. a) PRISMA chart for home vs. hospital injectable biologics studies, b) Funnel plot for injectable biologics studies, c) Risk of bias traffic light for injectable biologics studies

The selected 45 studies were pooled for this analysis. The RE model **(Figure 2)** presents a statistically significant difference ($p = 0.05$) between the home, SC injectable group and the in-hospital, IV injection, or infusion. Based on the relative ratio calculation for SC and IV groups, the IV route remained the preferred route. Included studies showed considerable heterogeneity ($p < 0.001$, $I^2 = 98\%$).

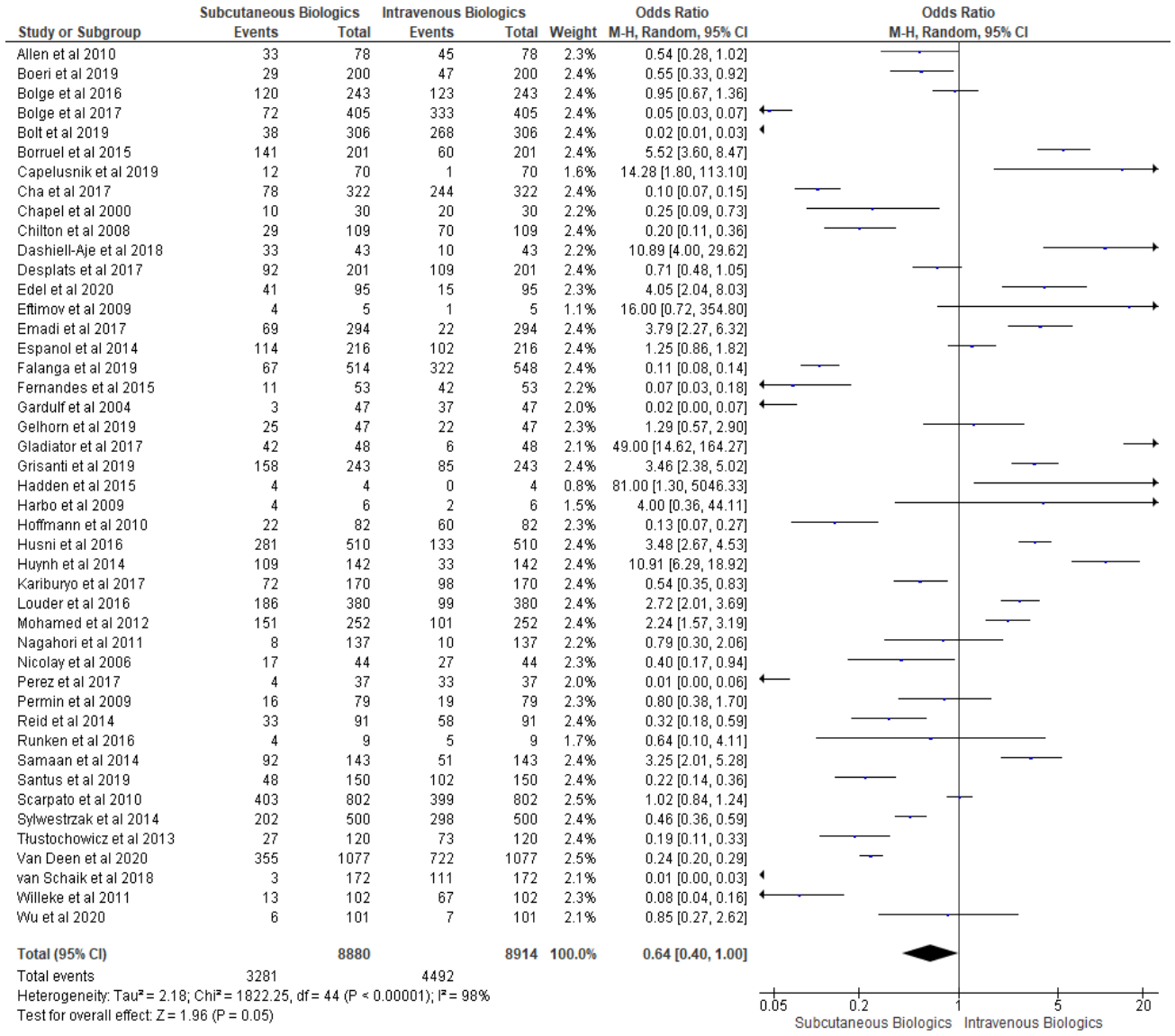
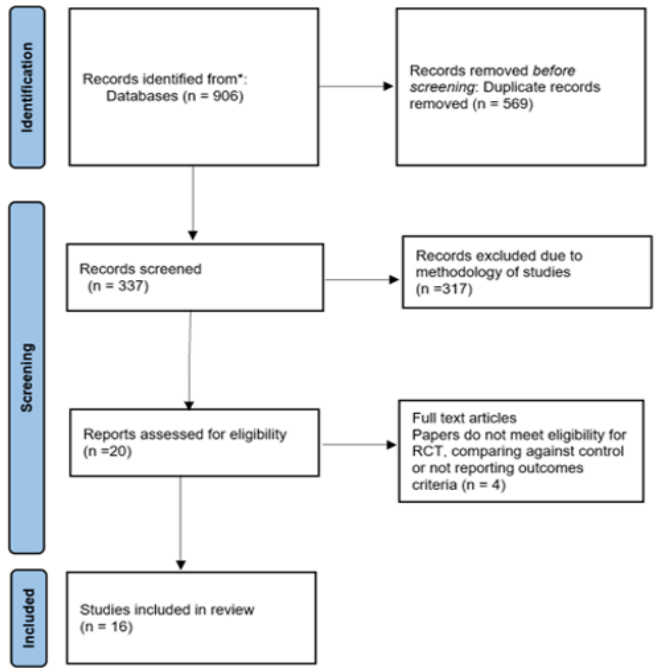


Figure 2. Random model, patient preference of injectable biologics by self-administration
Intervention: Injectable biologics at home, Control: Injectable biologics at the hospital, Event: patient preference for injectable biologics by self-administration at home or in the hospital.

Comparison Between Injectable Antibiotics Use at Home and in Hospital

The literature search retrieved 906 articles from all databases after excluding duplicates. After the abstract and full-text screening of the selected studies, 16 studies were eligible to be included in this systematic review. Only one study was accepted due to its high relevant value which was published in 1994. 1751 participants were included in this analysis. The minimum age included in this systematic review was seven years in the hospital and home group, and the oldest age of participants was 45 years in the hospital group. The funnel plot analysis was asymmetric indicating possible high variance in effect size produced from the included studies which can be due to smaller studies having sampling error in their effect estimates. There were 16 studies pooled for this analysis: Aimonino-Ricauda *et al*. [74], Biondo *et al*. [75], Fishman *et al*. [76], Hensey *et al*. [77], Hensey *et al*. [78], Hernandez *et al*. [79], Ibrahim *et al*. [80], Ibrahim *et al*. [81], Ibrahim *et al*. [82], Orme *et al*. [83], Proesmans *et al*. [84], Raisch *et al*. [85], Rehm *et al*. [86], Stovroff *et al*. [87], Termoz *et al*. [88], Vianello *et al*. [89]. Included studies showed a low RoB.



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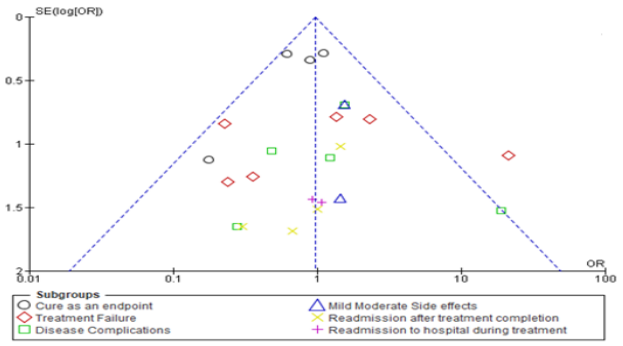

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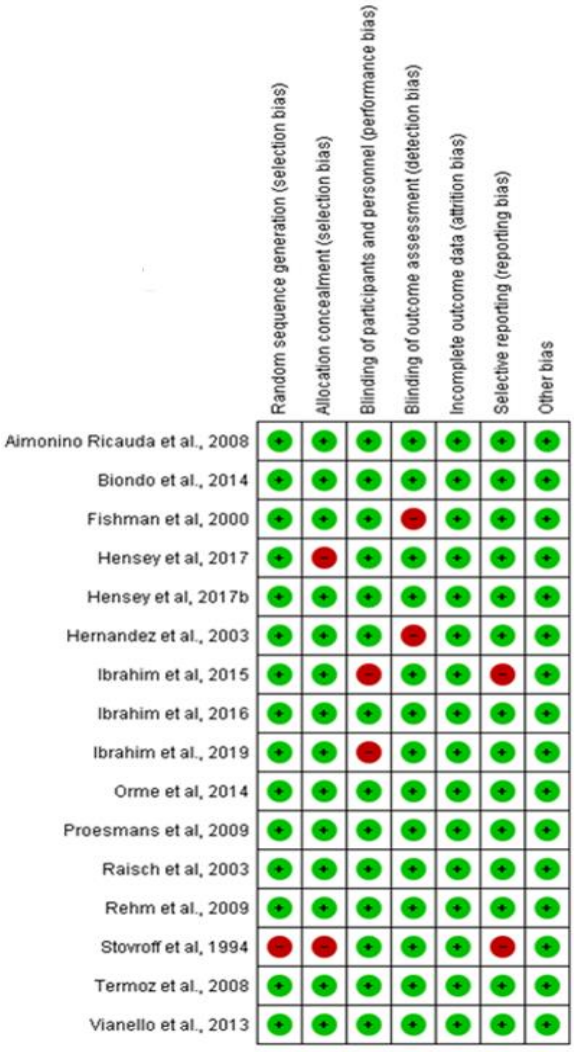


c)

Figure 3. a) Funnel plot for injectable antibiotics studies, b) PRISMA flow diagram for injectable antibiotics studies, c) Risk of bias summary for injectable antibiotics studies

Cure as an Endpoint

Four studies were pooled for this analysis [75, 82, 86, 88] and showed a low heterogeneity ($p < 0.27$, $I^2 = 21\%$). There was no statistically significant difference **(Figure 4a)** between at-home and in-hospital groups ($p = 0.21$) but based on the relative ratio calculation for SC and IV groups, the IV route remained the preferred route where more patients achieved cure. The number needed to treat (NNT) for the clinical endpoint (cure) as an outcome was calculated as: at home: 161/333 = 0.483, in hospital: 148/278 = 0.532, ARR = 0.483 – 0.532 = -0.049, NNT = 1/0.049 = 20.4 Therefore for every 21 patients treated at home, one additional patient will be cured compared to patients treated in hospital.

Treatment Failure as an Endpoint

Six studies were pooled for this analysis [75, 80, 81, 83, 85, 87] and showed a moderate heterogeneity ($p = 0.01$, $I^2 = 65\%$). The RE model **(Figure 4b)** shows no statistically significant difference between at-home and in-hospital groups ($p = 0.90$) but based on the relative ratio calculation for SC and IV groups, the IV route remained the preferred route where fewer events of treatment failure were reported. NNT for treatment failure as an outcome was calculated as: at home: 21/211 = 0.100, in hospital: 19/260 = 0.073, ARR = 0.100 - 0.073 = 0.027, NNT would be 1/0.05 = 20. Therefore, for every 20 patients treated with the intervention, one additional patient would experience treatment failure as compared to the control group.

Readmission to Hospital after Treatment Completion

The pooled effect estimate of 6 studies [76-78, 80-81, 83, 87], showed low heterogeneity ($p = 0.29$, $I^2 = 20\%$). There was no statistically significant difference **(Figure 4c)** between the at-

home and in-hospital groups (p = 0.35) but based on the relative ratio calculation for SC and IV groups, the IV route remained the preferred route where fewer events of readmission were reported. NNT for readmission to hospital after treatment completion as an outcome was calculated as: at home: 10/183 = 0.055, in hospital: 16/374 = 0.043, ARR = 0.055 - 0.043 = 0.012, NNT would be 1/0.012 = 83. Therefore, for every 83 patients treated with the intervention, one additional patient would be admitted to the hospital after the completion of the antibiotic course as compared to the control group.

Readmission to Hospital During Treatment

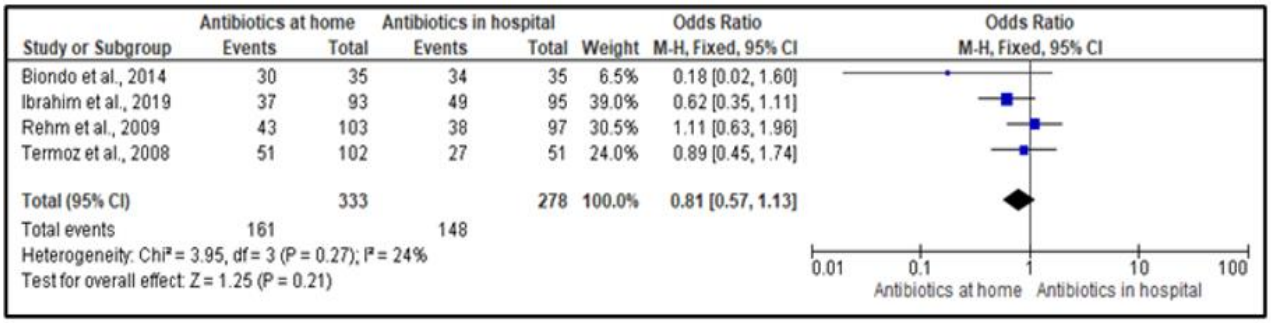
The pooled effect estimate of 2 studies [80, 83], showed low heterogeneity (p = 0.95, I^2 = 0%). There was no statistically significant difference **(Figure 4d)** between at-home and in-hospital groups (p = 0.99) but based on the relative ratio calculation for SC and IV groups, the SC route remained the preferred route where fewer events of readmission to hospital during treatment were reported. NNT for readmission to hospital during treatment as an outcome was calculated as: at home: 5/58 = 0.034, in hospital: 2/56 = 0.036, ARR = 0.034 - 0.036 = -0.002, ARR would be 1/0.002 = 500. For every 500 patients treated with the intervention, one additional patient would be admitted to the hospital during the treatment with an antibiotic course as compared to the control group.

Disease Complications During Treatment

The pooled effect estimate of 6 studies [74, 76, 79, 84, 87, 89], showed low heterogeneity (p = 0.79, I^2 = 0%). There was no statistically significant difference **(Figure 4e)** between at-home and in-hospital groups (p = 0.76), but based on the relative ratio calculation for SC and IV groups, the IV route remained the preferred route with fewer events of complications reported. NNT for disease-related complication during treatment as an outcome was calculated as: at home: 17/192 = 0.088, in hospital: 22/262 = 0.084, ARR = 0.088 - 0.084 = 0.004, ARR would be 1/0.004 = 250. For every 250 patients treated with the intervention, one additional patient would experience disease-related complications during the treatment as compared to the control group.

Mild-moderate Side Effects Due to Injectable Antibiotics Administration

The pooled effect estimate of 9 studies [74, 75, 79-81, 83, 84, 87-89], showed low heterogeneity (p = 0.92, I^2 = 0%). There was no statistically significant difference **(Figure 4f)** between at-home and in-hospital groups (p = 0.15) but based on the relative ratio calculation for SC and IV groups, the SC route remained the preferred route with less mild-moderate side effects reported. The number needed to treat to cause harm (NNH) for mild-moderate side effects due to injectable antibiotics administration as an outcome was calculated as: at home: 38/364 = 0.104, in hospital: 48/427 = 0.112, ARR = 0.104 - 0.112 = -0.008, ARR would be 1/0.008 = 125. For every 125 patients treated with the intervention, one additional patient would be harmed as compared to the control group.



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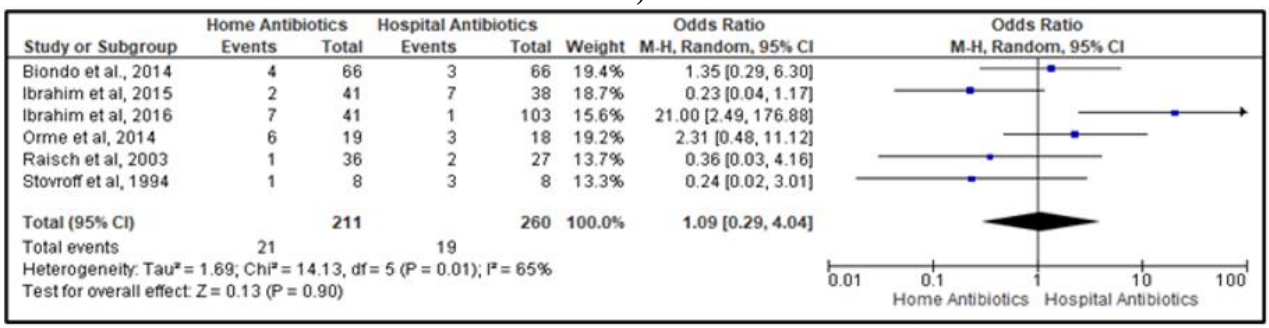

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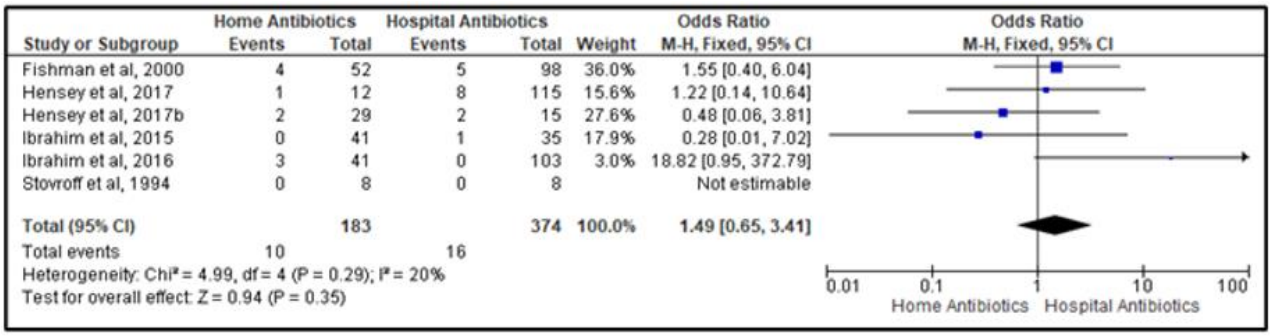

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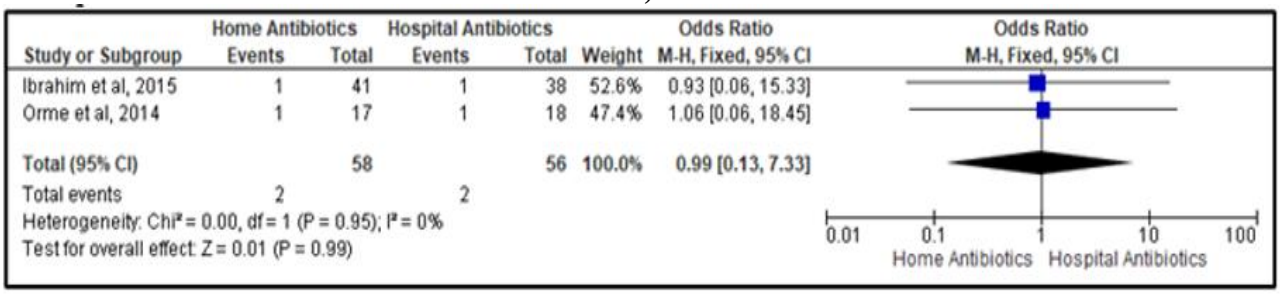

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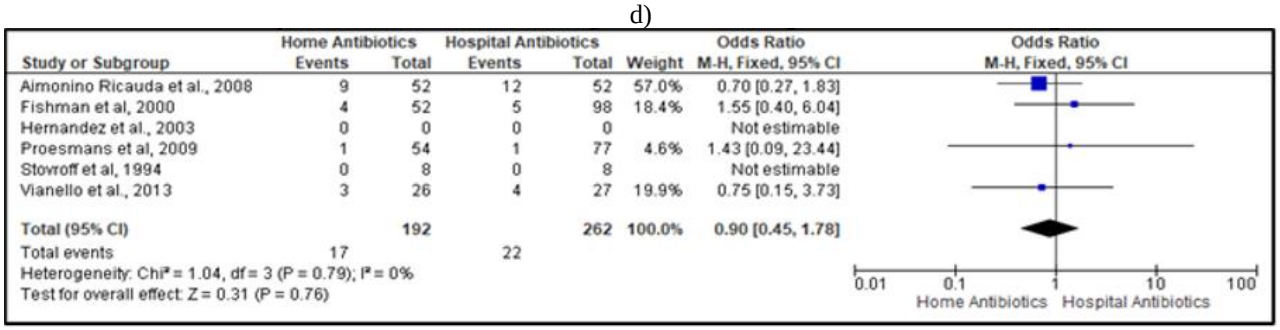

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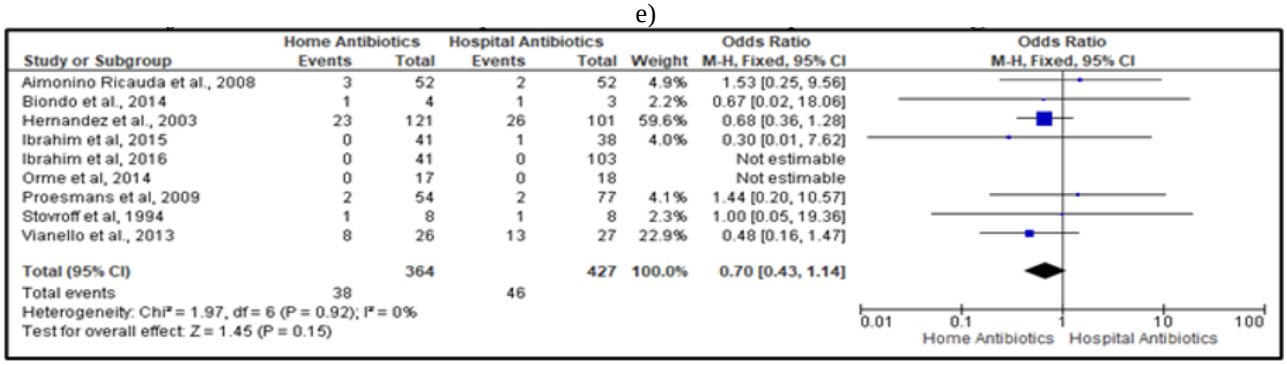

f)

Figure 4. a) Fixed model, successful treatment (cure) after injectable antibiotics. Intervention: Injectable antibiotics at home, Control: Injectable antibiotics at hospital, Event: Clinical endpoint achieved (cure); b) Random model, treatment failure after injectable antibiotics. Intervention: Injectable antibiotics at home, Control: Injectable antibiotics at hospital, Event: Clinical endpoint not achieved (treatment failure); c) Fixed model, hospital admission after injectable antibiotics. Intervention: Injectable antibiotics at home, Control: Injectable antibiotics at hospital, Event: hospital admission after treatment completion; d) Fixed model, hospital admission after injectable antibiotics. Intervention: Injectable antibiotics at home, Control: Injectable antibiotics at hospital, Event: hospital admission during treatment; e) Fixed model, disease complication during treatment. Intervention: Injectable antibiotics at home, Control: Injectable antibiotics at hospital, Event: Disease complication treatment; f) Fixed model, mild-moderate side effects due to injectable antibiotics administration. Intervention: Injectable antibiotics at home, Control: Injectable antibiotics at hospital, Event: Mild-Moderate side effects due to injectable antibiotics administration.

Injectable Biologics Analysis

890 patients preferred oral route in eight studies (Edel *et al.* [41] n=39, Capelusnik *et al.* [35] n=15, Nagahori *et al*. [59] n=119, Emadi *et al.* [43] n=203, Wu *et al.* [73] n=88, Boeri *et al.* [30] n=124, Willeke *et al*. [72] n=22 and Husni *et al.* [54] n=280). Additionally, 217 patients did not have præference to the administration route or the setting in 10 studies (van Schaik *et al.* [71] n=3, Tłustochowicz *et al.* [69] n=27, Permin *et al.* [62] n=16, Gardulf *et al.* [47] n=3, Falanga *et al.* [45] (n=67), Chilton *et al.* [38] (n=29), Cha *et al.* [36] (n=56), Kariburyo *et al.* [56] (n=8), Espanol *et al*. [44] n=4, Chapel *et al*. [37] n=4). The preference for oral therapy was not considered in this study as it was out of its scope (parenteral therapy) and it is not an option formulation for most of the current UK-marketed biologic agents.

The individual-reviewed studies did not show a consistent preference for one route over the other, while this systematic review showed a statistical significance difference ($p = 0.05$) but similarly did not favor the SC route over the IV route. In the reviewed studies, patients reported more autonomy, flexibility with involvement with social activities, and better patient engagement with their treatment and conditions when using SC biologics at home compared to IV in the clinic. However, more research is required on home-based care for patients receiving injectable biologics, which is currently much less than published research on IV administration in hospitals. Given the duration of treatment, it will be interesting to see future research analyzing out-of-pocket costs due to travel from home to hospitals and whether it influences patients' preferences.

Overton *et al.* [90] completed a systematic review (n=18 studies) on patient preferences for SC vs. IV administration of injectables biologics and its impact on adherence to therapy. Among the 85 patients on SCI treatment who completed their survey, 61 (72%) preferred SC injections, 3 (4%) had no preference, and 21 (25%) preferred IVIg. Three randomized crossover studies were discovered. In two of the studies, many of the patients (56% and 91%) who had used SCIg and IV immunoglobulins (Ig) during the study reported preferring SCIg. In the third study, 11 of 20 and 5 of 10 patients in cohorts in the Sweden and UK, respectively, preferred IVIg therapy. This aligned with the current study of overall preference for IV injection in hospitals. Stoner *et al.* [91] in their systematic review on biologics IV vs. SC, demonstrated unclear patient preference for SC or IV injections (ranging between 44% to 91 %). Only one study reported that patients preferred IV drug delivery, and another found that there was no difference in patient preference for either method. The patients' reasons for preferring SC injection were that treatment could be given at home and aided in avoiding difficulties with IV access. However, patients reported that the increased number of days for treatment was a disadvantage for SC injections. This aligned with this study's findings.

Abolhassani *et al.* [92] studied Immunoglobulin replacement by the SC route as an alternative to conventional IV administration (total of 47 studies, 1484 participants). The authors reported that patients on SC injections achieved acceptable IgG trough levels ($p < 0.01$), low incidence of side effects ($p < 0.001$), efficacy similar to IV infusions, treatment satisfaction, and better health-related quality of life, and faster functional recovery with less time off work.

Injectable Antibiotics Analysis

Hernandez *et al*. [79] reported that when compared to hospital care, hospital-at-home care allowed for significant cost savings when compared to standard treatment. The hospital-at-home intervention produced better clinical service and also provided a similar cure rate for both hospital and homecare settings. Vianello *et al*. [89] reported that for neuromuscular disorders patients, with respiratory tract infections, homecare treatment was found to be a good alternative to hospital-based treatment. It was found that instead of receiving standard hospital treatment, substitutive hospital-at-home services increased physical activity while reducing expenses for patients and hospital bed utilization. Aimonino-Ricauda *et al*. [74] and Hernandez *et al*. [79] agreed that the overall sample's patient mortality has no discernible difference between the two contexts of care and is even slightly reduced in-home care because hospital patients sometimes experienced failures in standards of care.

A study conducted by Termoz *et al*. [88] on all patients with cystic fibrosis between 1996 and 2005 to evaluate the difference between IV antibiotic treatment mainly in the home versus hospital, and they found that treatment in the hospital was slightly better than a home for patients with cystic fibrosis in the following variables: FEV1 (10.2% vs. 9.5%), FVC (7.3% vs. 6.8%) and body weight, and this explained the importance of hospital management for cystic fibrosis.

Another RCT study by Rehm *et al*. [86] found that patients diagnosed with bacteremia with or without infective endocarditis managed in an outpatient setting had longer therapy courses (mean 25.4 vs. 13.5 days, $p < 0.001$), high rates of completing management (90.3% vs. 45.4%, $p < 0.001$) and success rate (86.4% vs. 55.7%, $p < 0.001$). Also, less relapse of S. aureus (3.9% vs. 15.5%, $p = 0.007$) and fewer deaths (3.9% vs. 18.6%, $p < 0.001$) were found in patients managed at outpatient, favoring outpatient management over hospital management.

Ibrahim *et al*. [82] also found that managing as an outpatient had longer therapy courses (mean 25.4 vs. 13.5 days, $p < 0.001$), high rates of completing management (90.3% vs. 45.4%, $p<0.001$), and success rate (86.4% vs. 55.7%, $p < 0.001$). Also, less relapsing of S. aureus (3.9% vs. 15.5%, $p < 0.007$) and fewer deaths (3.9% vs. 18.6%, $p < 0.001$) were found in patients managed at outpatient.

Stovroff *et al*. [87] found that home-based antimicrobial therapy was satisfactory and cost-effective for both patients and their families. The efficacy and safety of home-based OPAT were similar to that of hospital-based treatment. During their hospitalization, the patients receiving treatment in the hospital required the placement of more than five IV catheters. In contrast, the peripheral IV central catheter (PICC) lines were successfully placed in patients receiving treatment at home, and no further IV access was necessary ($p = 0.001$). There were no complications reported from the PICC lines. Neither group experienced recurrent infections nor required hospital readmission. The patients' and families' acceptance of the PICC line concept was unanimously favorable. Rehm *et al*. [86] found that patients managed at outpatient had longer therapy courses (mean 25.4 vs. 13.5 days, $p < 0.001$), high rates of completing management (90.3% vs. 45.4%, $p < 0.001$), and success rate (86.4% vs. 55.7%, $p < 0.001$). The authors also found that patients had less relapse of S. aureus (3.9% vs. 15.5%, $p < 0.007$) and fewer deaths (3.9% vs. 18.6%, $p < 0.001$) in patients managed in outpatient settings. These findings were in line with Raisch *et al*. [85] and Orme *et al*. [83] finding that febrile neutropenia patients were better managed in an outpatient setting than hospitalization.

The management of cellulitis in hospital and homecare settings was studied by Ibrahim *et al*. [80] and 2016). The authors used retrospective data to compare the outcome of a homecare setting against a hospital looking at treatment failure, cure rate, hospital readmission after treatment completion, and complications. The authors found that these outcomes were not different between the two settings.

Fishman *et al*. [76] studied appendicitis patients and Hensey *et al*. [77, 78] studied pyelonephritis and meningitis patients, comparing homecare patients vs. hospital patients measuring disease complications. The authors found that patients in the homecare settings had fewer disease-related complications compared to patients managed within the hospital settings. Proesmans *et al*. [84] studied 131 treatment observations (TOs) and analyzed 47 patients, 54 (41%) TOs were home treatment and 77 (59%) were hospital treatments. Percent change in weight gain and FEV1 was comparable in the 2 settings. Complications were rare in both groups and when compared to the hospital setting, the outcome of IV-AB therapy for a lung infection in children with CF was not inferior in the home setting. Therefore, home antibiotics treatment was considered a valuable treatment option for children with CF.

Biondo *et al*. [75] studied outpatient vs. hospitalization management for uncomplicated diverticulitis: a prospective, multicentre randomized clinical trial (DIVER Trial) measuring cure rate and readmission after completion of therapy. 132 patients were randomized: 4 patients in the hospital setting and 3 patients in the homecare setting presented failure of treatment without differences between the groups ($p = 0.619$). The overall healthcare cost per episode was 3 times lower in a homecare setting, with savings of €1124.70 per patient. No differences were observed between the groups in terms of quality of life.

This systematic review compared homecare and hospital care infection management with injectable antibiotics. The preference of hospital management versus home management for injectable antibiotics depended on the case presentation for the patients. Cystic fibrosis is a disease involving different body organs that produce mucous such as the lung, which is considered the most affected organ [93]. This disease happens due to CFTR gene mutation, which leads to this disease's development [94]. From the quality review of the primary data literature, it was found that management with injectable antibiotics for cystic fibrosis is reported to be more suited to homecare management due to improved FEV1 (10.2% vs. 9.5%) and FVC (7.3% vs. 6.8%) and reduced exposure to infection. FEV1 and FVC were considered the indicators that showed improvement for cystic fibrosis [88]. This review found no significant difference in the efficacy of antibiotics (cure as an endpoint) ($p = 0.30$).

Regarding cellulitis, Raff and Kroshinsky [95] found no difference in treatment failure between hospital and home treatment with injectable antibiotics ($p = 0.90$). However, adverse events were found less in a home group than in a hospital (two cases [2%] vs. 10 cases [11%]; $p = 0.048$). Also, other secondary outcomes such as length of stay in the emergency department, Ibrahim *et al*. [80-82] found that cellulitis stopped spreading within 24 hours, cost-effectiveness, and quality of life outcomes were favorable for management at home.

Rehm *et al*. [86] showed that patients being managed as outpatients had longer therapy courses (mean 25.4 vs. 13.5 days, $p < 0.001$), high rates of completing management (90.3% vs. 45.4%, $p < 0.001$), and success rate (86.4% vs. 55.7%, $p < 0.001$) compared with hospital management. In addition to low relapsing for S. aureus and death from bacteremia. These findings favored the treatment in outpatients due to its several benefits over hospital inpatient management with injectable antibiotics. This systematic review found that hospital admission after completion of therapy ($p = 0.64$) or during the treatment ($p = 0.99$), was not significantly different between the two settings. However, fewer people were admitted to the hospital from a home setting.

Sriskandarajah *et al*. [96] found more than 88% of the studies reported fewer hospital admissions in the hospital-in-home group (5% of patients) than in the hospital group (25% of patients). This review found that hospital admission after completion of treatment was 5.5% for home and 4.5% for hospital and during treatment was 3.5% for home and 3.6% had their hospital stay prolonged which showed no significant difference between the two settings compared to Sriskandarajah *et al*. [96] favoring home setting. Complications due to condition were also reported by the

authors as 2% for home and 21% for hospital, in this review it was found that 8.9% for home and 8.4% demonstrating less difference between the two settings compared to Sriskandarajah *et al*. [96] favoring home setting. Side effects due to the injectable antibiotics were reported by the authors as 2% for home and 21% for hospital, in this review it was found that the events were 10.5% for home and 11.3% for hospital. Sriskandarajah *et al*. [96] reported mortality as being 4% for home and 12% for hospital favoring home setting, however, this review could not measure this outcome as it was not reported in the selected studies.

Study Limitations

There was a preponderance of studies from the USA compared to the UK and Europe. This can be due to two factors; the different health funding model between the USA (private health insurance) and UK (NHS) which has driven strong cost-effectiveness research and consequently hospital in the home principles developed in the USA earlier and more rapidly than in the UK or Europe. Despite efforts to reduce variability by selecting studies with specified intervention components, some heterogeneity was identified. The inability to translate studies that are not published in English was another limitation, as the study did not attract any external funding.

Conclusion

1. Home-based self-care and self-administration of injectables is a viable option for a wide range of patients who would previously have been treated in a hospital setting, as long as they are trained on the injection technique and have access to suitable support for when and if complications arise.
2. Disease-related complications and medication-related complications are possible for both settings, however the immediate access to medical and nursing support in a hospital setting makes their physical and emotional impact less for the patient, this can be mitigated by improving the support provided for patients self-administering at home, which warrants further research.
3. Standardized research protocols and definitions for the measured outcomes, will allow better future systematic reviews which investigate patients' preferences between home and hospital settings and reduce the heterogeneity of the included studies.
4. Future studies should report outcomes separately, not grouped, to allow the identification of the actual cause of harm and the actual enablers of successful therapy, which will in turn enable better future systematic reviews.

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