Healthcare ∎ (∎∎∎∎) ∎∎∎–∎∎∎

Contents lists available at ScienceDirect

Healthcare

journal homepage: www.elsevier.com/locate/hjdsi

Review article

Home infusion: Safe, clinically effective, patient preferred, and cost saving ☆

Jennifer M. Polinski *, Mary K. Kowal, Michael Gagnon, Troyen A. Brennan, William H. Shrank

CVS Health, 100 Scenic View Drive #121130, Cumberland, RI 02864, USA

ARTICLE INFO

Article history:
Received 13 October 2015
Received in revised form
8 March 2016
Accepted 16 April 2016

ABSTRACT

Background: As the U.S. healthcare payment system shifts from volume to value, identifying care approaches that improve outcomes while lowering costs are essential. We sought to understand the utility of home infusion versus medical-setting infusion as a mechanism to affect the three-part aim: better care, better health outcomes, and lower costs.

Study design: Systematic review.

Methods: We searched MEDLINE, EMBASE, and Science Citation Index for articles related to the safety, clinical effectiveness, quality of life and satisfaction, and/or costs of home infusion as compared with infusion in an outpatient medical facility or hospital.

Results: Of 253 potentially relevant articles, 13 met all inclusion criteria. Study design, disease state, and outcomes varied considerably. As compared to medical setting infusion patients, home infusion patients were no more likely to experience adverse drug events or side effects (all $p > 0.05$). Clinical outcomes were as good or better, e.g., for patients with hemophilia, a 40% (0.50–0.70) reduced likelihood of hospitalization for bleeding complications. Patients overwhelmingly preferred home infusion, reporting significantly better physical and mental well being and less disruption of family and personal responsibilities. Home infusion costs were significantly lower than medical setting infusion costs, with savings between $1928 and $2974 per treatment course.

Conclusions: Home infusion care can provide safe, clinically effective care improve patients' quality of life and reduce healthcare costs. As the overhaul of the healthcare payment system gains momentum, the home infusion care delivery model offers strong promise as one in a set of approaches that can improve care and lower costs.

Contents

1. Background

The transformation of the U. S. healthcare payment system from volume to value is well underway, with U. S. Department of Health and Human Services Secretary Burwell calling for tying 50%

☆Funding: CVS Health.

* Corresponding author.
E-mail address: jennifer.polinski@cvscaremark.com (J.M. Polinski).

http://dx.doi.org/10.1016/j.hjdsi.2016.04.004
2213-0764/

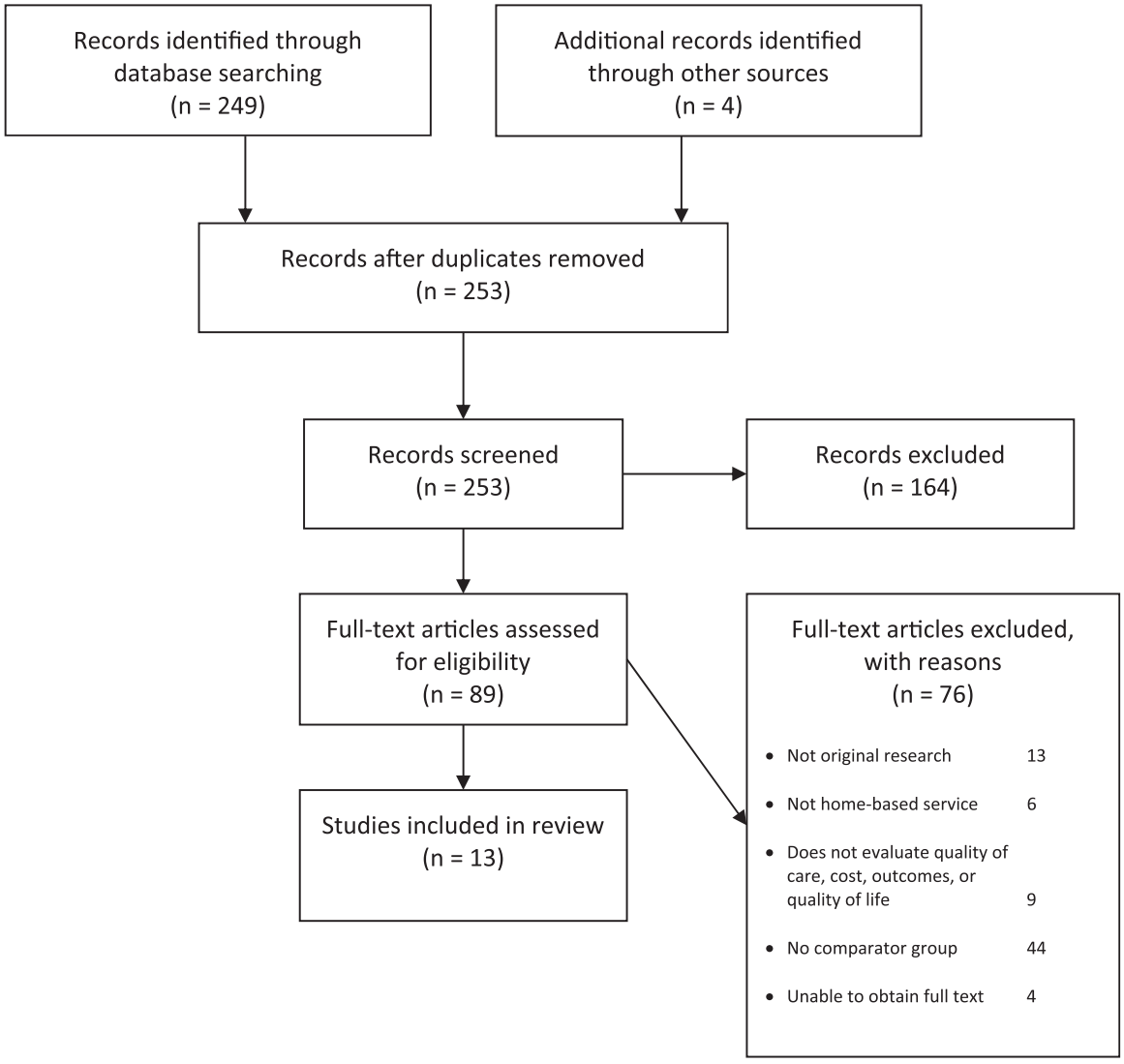

Fig. 1. Article selection process.

of Medicare payments to alternative payment models that provide better care at lower costs by 2018.[1] As providers participate in these models, there is an urgency to identifying approaches that deliver better care at lower cost. A wide variety of well-intentioned strategies have been implemented to improve quality and reduce costs, but savings are difficult to achieve.[2–7] For example, in the first year of the Medicare Shared Savings Program, 53 Accountable Care Organizations (ACOs) earned shared savings, 52 saved money but not enough to meet required "minimum savings rates," and 115 did not accrue any savings.[8,9].

One model that has potential to deliver cost-effective, quality care receiving increasing attention is home infusion therapy. Efforts to support patients who can receive infused care in a lower-cost setting seem appealing, particular if that lower-cost setting is the patient's home. Commercial health plans have long provided comprehensive coverage for home infusion services,[10] and Congress is considering whether or not Medicare should expand home infusion therapy coverage to all patients rather than just homebound or inpatient beneficiaries.[11,12] One study suggests that Medicare would save $8.5 million per year by allowing home infusion care for anti-infective therapies, with savings largely attributable to shorter inpatient lengths of stay and dramatically reduced hospital and skilled nursing facility overhead costs.[13] Similarly, home infusion may improve patients' care experiences, as many patients would prefer to be in their own homes rather than in the hospital.

Despite the growing prevalence of home infusion as a care delivery model – in 2008, an estimated 829,000 patients received 1.24 million home infusions[14] – the quality of care delivered when medications are infused at home has not been systematically evaluated, nor has the safety of care, clinical outcomes, patients' satisfaction, and costs.

In this study, we systematically reviewed the literature to better understand the utility of home infusion as a mechanism to affect the three-part aim: better care, better health outcomes, and lower costs. We aimed to better understand whether the use of home infusion could be an important part of the arsenal for risk-bearing entities who aim to improve care and reduce costs.

2. Methods

We searched MEDLINE, EMBASE, and Science Citation Index for articles published on or before November 1, 2014. Our search strategy focused on terms related to home infusion, safety, clinical effectiveness, quality of life and satisfaction, and costs (e.g., in Medline: [infusion AND (home-based OR home-infusion) AND drug AND (quality of life OR patient-centered outcomes OR satisfaction)].

Final articles were included if they reported original data regarding home infusion's safety, effectiveness, costs and length of stay (LOS), and/or impact on patients' quality of life. Articles had to compare home infusion of medications

Please cite this article as: Polinski JM, et al. Home infusion: Safe, clinically effective, patient preferred, and cost saving. *Healthcare* (2016), http://dx.doi.org/10.1016/j.hjdsi.2016.04.004

with infusion of medications in at least one other setting (e. g., inpatient or ambulatory visit). Case series (< 15 patients studied) and case reports were excluded. Three reviewers (J.P., M.K., M.G.) participated in the article selection process, with > 2 reviewers evaluating each title and abstract and then assessing complete manuscripts, noting one or more reasons for exclusion when articles were removed from consideration. Disagreement at both review stages was resolved by the judgment of a third reviewer (J.P., M.K., or M.G.) All three reviewers assessed the final group of selected articles to verify inclusion. Two authors (J.P. and M.K.) reviewed and extracted data from the final group of selected articles, including the key objectives, data sources, the study population's characteristics, study design and analytic approach, outcomes measured, key results, and conclusions. J.P. used the Newcastle-Ottawa Quality Assessment Scale, a scale that ranges from 0 to 9, with 9 being the highest, to assess each article's methodological rigor.[15].

3. Results

Of 253 potentially relevant titles and abstracts screened, 89 were evaluated in full, and 13 met all inclusion criteria (Fig. 1). Many articles addressed multiple themes: 4 articles assessed the quality and safety of home infusion,[16–19] 7, clinical outcomes,[18–24] 5, quality of life,[19,20,23,25,26] and 4, costs and length of stay.[19,24,27,28] Among them, the articles presented a range of study designs, disease states, patient samples, and outcomes measured. The presence of comparator groups within each study made assessment easier, yet synthesizing results across the studies was a challenge.

3.1. Quality and safety

In a first study, 17 patients with cystic fibrosis were randomized to receive outpatient antibiotic therapy (OPAT) or inpatient antibiotic therapy (IPAT) following an initial 2–4 d inpatient stay (Table 1).[19] While the sample size was small, double-blinded randomization, a sample of patients representative of the larger cystic fibrosis community, and precise outcome measurement in all patients created a methodologically rigorous study, Newcastle-Ottawa score=8. There were no significant differences in intravenous complication rates (p=0.57) or in the number of intravenous line changes (p=0.5) between the OPAT and IPAT groups.[19] In a larger retrospective chart review study comparing to 410 IPAT patients with 539 OPAT patients, OPAT infusions were associated with > 50% reduction in adverse events, though the types of adverse events were not described (OPAT=9.3%, IPAT=19.8%), p < 0.0001.[18] However, the results are likely biased: the authors did not adjust for factors related to patients' health status that made them suitable candidates for OPAT, e.g., OPAT patients were younger, had fewer chronic comorbidities, and were judged clinically stable, Newcastle-Ottawa score=7.

In another study, side effects associated with chemotherapy infusion were compared in the clinic setting (first infusion) versus the home setting (all subsequent infusions). Among 48 patients with pre-terminal cancer and life expectancy < 6 months, the side effect rate was 0.66 (63/95) per clinic infusion and 0.75 (171/195) per home infusion, p=0.4014.[16] The two exposure groups were likely not comparable in factors predicting suitability for home infusion, Newcastle-Ottawa score=7. A second study of in-home versus in-hospital chemotherapy infusions in 152 patients receiving care at a Veterans Administration Medical Center reported only 27 complications total, and concluded that home infusion was not a significant risk factor for venous access device port complications, p=0.32.[17] There was no adjustment for factors related to patients' suitability for OPAT, Newcastle-Ottawa score=7.

3.2. Clinical outcomes

5 studies assessed OPAT outcomes (Table 1). Among 539 patients receiving OPAT, 94.6% were described as "cured" (infection cleared with a negative culture; no additional antibiotic therapy needed) or "improved" (partial resolution of clinical symptoms and/or additional antibiotic therapy needed) compared to 86.3% of IPAT patients, p < 0.001.[18] However, no adjustment for confounders was performed, and higher OPAT success rates were likely due to purposeful selection of younger, healthier patients for OPAT therapy. In contrast, a higher-quality cohort study evaluated outcomes for 72 OPAT patients matched to 93 IPAT patients on age (± 5 years), gender, and one of 15 DRGs.[24] The 93 IPAT patients were selected from a time period during which OPAT was not available for any patients, minimizing selection bias by the matching factors, Newcastle-Ottawa score=9. At 4-months, 59 (81.9%) of OPAT patients were considered cured compared to 75 (80.6%) IPAT patients, p=0.991.

Esmond et al. used a pre-post treatment comparison for cystic fibrosis patients with acute respiratory exacerbation, 15 of whom chose OPAT (all had used OPAT before) and 15 of whom chose IPAT.[20] Comparing pre- to post-infusion values, both OPAT and IPAT patients had statistically significant improvements in oxygen saturation and body mass index. IPAT patients also had significant improvement in forced expiratory volume in 1 s and forced volume capacity. Only forced volume capacity improvements were significantly greater for IPAT patients. However, factors such as the frequency and intensity of chest physiotherapy, indicated for use during acute respiratory exacerbations, and other patient characteristics that drove the choice of OPAT versus IPAT therapy were not measured or adjusted for in the analysis, lowering the Newcastle-Ottawa score to 7.

A more methodologically valid retrospective chart review study compared pre-post antibiotic treatment improvements in white blood cell count, expiratory flow rate, forced vital capacity, forced expiratory volume in 1 second, weight, and other outcomes.[21] Twenty-five patients with cystic fibrosis' OPAT experience was compared with their prior, most recent IPAT experience. Only changes in white blood cell count were found to be significantly different between the IPAT and OPAT experiences, but this difference was small and not clinically relevant: IPAT improvement $= -4.72 \pm 0.36$; OPAT improvement $= -3.64 \pm 0.38$. Using patients as their own comparators minimized bias, as characteristics that might influence the association between OPAT and clinical outcomes did not change between experiences, Newcastle-Ottawa score=9. In a randomized trial comparing OPAT to IPAT after a 2–4 d stay for 17 patients with CF, there were no significant differences between groups in overall improvement in lung function, Newcastle-Ottawa score=8.[19].

A retrospective chart review of 2650 male patients' experience with home versus medical setting infusion for hemophilia found that 28.6% of home infusion patients and 32.2% of medical setting infusion patients had a hemorrhagic bleeding complication.[22] Controlling for patient and other characteristics (e.g., age, race), home-infused patients had a 40% reduced likelihood of a bleeding complication requiring hospitalization (95% CI, 0.50–0.70). The Newcastle-Ottawa score=9. A patient self-reported survey was used to compare the severity and duration of hereditary angioedema attacks between 21 patients receiving home infusions immediately after an attack's onset, and 18 receiving infusions at a medical facility shortly after an attack's onset, as time elapsed to reach the facility.[23] Both groups had similar demographic and clinical characteristics. On a 1–10 scale, with 10 being the highest, home infusion patients reported lower attack severity (mean 4.75 ± 2.46) than medical facility infusion patients (5.67 ± 2.69), p < 0.005. Attacks lasted 8.0 ± 13.5 h in home and 34.2 ± 27.5 h in medical facility infusion patients, p < 0.0001; a 77% reduction. The average number of pain medications taken per week was substantially lower in home infusion patients, 0.38 ± 0.98 versus 1.75 ± 3.13 respectively, p < 0.0001, 76% reduction. Home infusion patients reported a significantly higher number of injections with bleeding (7.81% of injections versus 0.58% in medical facility group) and pain (7.21% of injections versus 1.73% in medical facility group) but fewer drug-related side effects (mean rating of 0.01 on severity scale of 0–3, with 3 being the highest, versus 0.22 in the medical facility group). The study had comparable exposure groups, however, data were self-reported using an un-validated questionnaire, and the sample size was small, Newcastle-Ottawa score=6.

3.3. Quality of life (QOL)

In a survey of 30 patients using the Cystic Fibrosis Quality of Life Questionnaire, those with CF receiving OPAT reported significant improvements from baseline to post-therapy follow-up in 5 domains: physical functioning, chest symptoms, emotional response to their disease, interpersonal relationships, and career concerns (Table 2).[20] Patients receiving IPAT reported statistically significant improvement in 2 domains: chest symptoms and a reduction in their concerns about the future. When the OPAT and IPAT groups were compared, there were no significant differences in pre-post improvements; however, none of the comparisons were adjusted for potential confounding factors such as the presence of other comorbidities, whether or not they were clinical stable, and/or other factors that made some patients suitable candidates for OPAT, and the sample size was small, Newcastle-Ottawa score=6. Wolter et al. randomized IPAT versus OPAT study (Newcastle-Ottawa score=8) used the Chronic Respiratory Disease Questionnaire (CRDQ) to measure QOL on Day 0 and on the day after therapy completion among patients with CF.[19] Patients randomized to OPAT reported significantly less family, personal, and sleep disruption associated with receiving care at home, while IPAT patients reported significantly greater feelings of disease control and less fatigue.

In the first non-OPAT study, among 34 patients with Fabry disease and 49 patients with Gaucher disease who had experience with home and hospital infusion of enzyme replacement therapy, 95% and 85% respectively preferred home infusion and 94% and 87% agreed that home infusions were less disruptive to their family lives, citing greater convenience, easier childcare, and no traveling.[25] This study was methodologically poor; there was no adjustment for factors that might influence the suitability of home versus hospital infusion for a particular episode of care, the sample size was small, likely not generalizable to the larger community of patients with these diseases, and outcomes were self-reported using an un-validated questionnaire, Newcastle-Ottawa score=5. In a randomized crossover trial, 37 patients with multiple myeloma received 3 months of home infusions and 3 months of in-hospital infusions reported small but not statistically significant improvements in role, emotional, cognitive and social QOL with in-home versus in-hospital infusions.[26] The study's only limitation was its sample size, Newcastle-Ottawa score=8. Finally, compared to patients with hereditary angioedema who received in-clinic infusions, clinically and demographically similar patients who

Please cite this article as: Polinski JM, et al. Home infusion: Safe, clinically effective, patient preferred, and cost saving. *Healthcare* (2016), http://dx.doi.org/10.1016/j.hjdsi.2016.04.004

Table 1
Articles regarding the safety, quality of and clinical outcomes associated with home infusion.

Author	Year	Title	Type of infusion/ disease	Type of study	Number of study patients	Intervention and comparison groups	Inclusion criteria	Results: quality of infusion care and clinical outcomes	Newcastle-Ottawa score
Safety and quality									
Beijer	2007	Intravenous ATP infusions can be safely administered in the home setting: a study in pre-terminal cancer patients.	ATP infusion/pre-terminal cancer patients	Cross sectional	51 patients; 266 infusions	Baseline first infusion in clinic versus subsequent in-home infusions	• adult patients • confirmed cancer with treatment options restricted to supportive care • life expectancy <6 months • WHO performance status 1 or 2 • at least one complaint: fatigue, anorexia, or $>5\%$ weight loss in previous 6 months	• Majority (63% of infusions, 176/266) were without side effects. • Baseline infusion side effects were on average 0.66 (63/95)per infusion, and 0.75 (129/175) side effects per home infusion	7
Brown	1997	Mode of chemotherapy does not affect complications with an implantable venous access device.	Chemotherapy/ cancer	Retrospective chart review	152 patients; 158 ports	Patients receiving home infusion compared with patients receiving in-hospital infusions	• adult oncology patients aged 18 or older who received continuous follow up at the Little Rock VAMC • had a single implantable venous access device in subclavian vein • received care between May 1, 1992 and May 31, 1994	• In patients receiving home infusions exclusively, 8/35 (23%) of ports had complications; there was no statistically significant difference in port complications when compared with patients receiving in-hospital infusions, $p=0.32$. • In patients who received both home and in-hospital infusions, there were complications in 10/42 (25%) ports; there was no statistically significant difference in complications with compared with patients only receiving infusions in the hospital, $p=0.13$.	7
Martone	2008	Outpatient parenteral antibiotic therapy with daptomycin: insights from a patient registry.	Antibiotics/gram-positive infections (various)	Cross sectional, via chart review	949	Patients who received OPAT ($N=539$) versus patients receiving IPAT only ($N=410$) in 2005	• enrolled in the Cubicin Outcomes Registry and Experience (CORE 2005) study • received at least one dose of daptomycin • not part of a controlled clinical trial • age unspecified	• Fifty (9.3%) of 539 OPAT patients and 81 (19.8%) of 410 IPAT patients experienced at least one adverse event, $p<0.0001$. • 31 (5.8%) of 539 OPAT patients and 34 (8.3%) of 410 IPAT patients experienced at least one adverse event associated with daptomycin therapy, $p=0.12$.	7
Wolter	1997	Home intravenous therapy in cystic fibrosis: a prospective randomized trial examining clinical, quality of life and cost aspects.	Antibiotics/cystic fibrosis	Randomized controlled trial	17 patients; 31 admissions	Home vs hospital treatment. All patients spent 2–4 days in the hospital. Patients were then randomized to receive home infusions or to remain in hospital to receive infusions.	• diagnosis of cystic fibrosis • acute respiratoroy exacerbation presenting to two Brisbane hospitals • Age ≥ 16 years	• There were no significant differences in intravenous complication rates ($p=0.57$) or in the number of intravenous line changes ($p=0.5$) between the OPAT and IPAT groups.	8
Clinical outcomes									
Esmond	2006	Comparison of hospital and home intravenous antibiotic therapy in adults with cystic fibrosis.	Antibiotics/cystic fibrosis	Quasi-experimental pre-post design	30	Home vs hospital treatment	• Diagnosis of CF confirmed by sweat test or genotyping • Aged ≥ 18 • Acute respiratory	From day 0 to post treatment, there were signficant imporvements in all physiological clinical outcomes for the hospitalized group: • FEV1, day 0= mean 32.3 ± 16.9,	7

							exacerbation	post-tx $=37.4 \pm 19.7$, p=0.005 • FVC, day 0=41.6 ± 20.8, post-tx =53.9 ± 26.8, p=0.001 • SaO2, day 0=92.7 ± 5.0, post-tx =94.7 ± 3.4, p=0.02 • BMI, day 0=19.0 ± 2.3, post-tx =19.4 ± 2.5, p=0.05 For the home infusion group, significant improvements from day 0 to day post-treatment were for: • SaO_2, day 0=93.5 ± 3.4, post-tx =95.4 ± 2.7, p=0.01 • BMI, day 0=19.3 ± 3.0, post-tx 19.5 ± 2.9, p=0.05 • FEV1 and FVC were improved but were not statistically significant When pre-post changes were compared between the home and hospital groups, only FVC had a statistically significant greater improvement in the hospital compared to home, p=0.01	
Martone	2008	Outpatient parenteral antibiotic therapy with daptomycin: insights from a patient registry.	Antibiotics/gram-positive infections (various)	Cross sectional, via chart review	949	Patients who received OPAT (N=539) versus patients receiving IPAT only (N=410) in 2005	• enrolled in the Cubicin Outcomes Registry and Experience (CORE 2005) study • received at least one dose of daptomycin • not part of a controlled clinical trial • age unspecified	• "Cure" or "improved" success rates were higher in OPAT patients (510∕539, 94.6%) than in IPAT patients (354∕410, 86.3%) ($p < 0.001$, chi-square test) for all infections. • Patients with endocarditis had better clinical success rates with OPAT (13/14, 92.9%) than with IPAT (6/15, 40.0%) (p=0.005). • Patients with bacteremia also had better clinical success rates with OPAT (71/73, 97.3%) than with IPAT 116/143, 81.2%) ($p < 0.0001$). • There were no significant differences in success rates for patients with osteomyelitis, cSSSI, ucSSSI, and other infections.	7
Pond	1994	Home versus hospital intravenous antibiotic therapy in the treatment of young adults with cystic fibrosis.	Antibiotics/Cystic fibrosis	Quasi-experimental pre-post design	25	Patients' home infusion experience was compared to their most recent, previous in-hospital infusion experience	• attending Leeds adult cystic fibrosis clinic • had received home infusion treatment • age ≥ 18 years	• Among home patients, white blood cell counts decreased significantly less (3.64 point decrease) than among hospital infusion patients (4.72 points). This difference was statistically significant but did not appear to be clinically meaningful. • All other variables improved to a similar degree in both home infusion and in-hospital infusion patients: peak expiratory flow rate, forced vital capacity, forced expiratory volume, neutrophil count, plasma viscosity, total IgG, CRP, northern CXR score, weight, clinical score, and Shwachman-Kulczyki score.	9

Please cite this article as: Polinski JM, et al. Home infusion: Safe, clinically effective, patient preferred, and cost saving. *Healthcare* (2016), http://dx.doi.org/10.1016/j.hjdsi.2016.04.004

Table 1 (*continued*)

Author	Year	Title	Type of infusion/ disease	Type of study	Number of study patients	Intervention and comparison groups	Inclusion criteria	Results: quality of infusion care and clinical outcomes	Newcastle-Ottawa score
Soucie	2001	Home-based factor infusion therapy and hospitalization for bleeding complications among males with hemophilia.	Factor VIII or Factor IX concentrate/Hemophilia A or B	Cross sectional, via chart review	2650	Patients receiving home infusion versus patients receiving infusions in a medical setting	• Physician diagnosis of hemophilia A or B • Male • All ages	• 360/1257 (28.6%) of home infusion patients had a bleeding complication for which they were hospitalized compared to 448/1393 (32.2%) of patients receiving infusions in a medical setting patients, RR $=0.80$ $(0.70-0.90)$. • Compared to patients receiving infusions in a medical setting, patients receiving home infusions were 40% less likely to have a hospitalized bleeding complication, RR$=0.60$ $(0.50-0.70)$.	9
Tourangeau	2012	Safety and efficacy of physician-supervised self-managed C1 inhibitor replacement therapy.	C1INH/Hereditary angioedema	Cross sectional	39	Patients who self-infused C1INH at home versus patients who received C1INH infusion in a medical setting during December 2007 - March 2008	• Physician diagnosis of hereditary angioedema • were receiving on-demand C1INH at home or at a medical facility • Age ≥ 18	• On a 1–10 scale, attack severity was lower among home infusion patients (4.75 ± 2.46) than clinic setting infusion patients (5.67 ± 2.69), $p < 0.005$. • Attack duration (in hours) was lower for home infusion patients (8.0 ± 13.5) than for the medical setting patients (34.2 ± 27.5), $p < 0.0001$. • The number of pain medications taken per week was also lower in home infusion patients (0.38 ± 0.98) compares with medical setting infusion patients (1.75 ± 3.13), $p < 0.0001$. • The percent of injections with bleeding was higher in home infusion patients ($7.81\% \pm 26.9$) than in medical setting infusion patients ($0.58\% \pm 7.6$), $p < 0.0001$. • The home infusion patients reported a higher percentage of injections with pain/inflammation at the injection site ($7.21\% \pm 25.9$ versus $1.73\% \pm 13.1$). • On a 0–3 scale, there was more difficulty with home injection (0.31 ± 0.60) than with medical setting injection (0.03 ± 0.17), $p < 0.0001$. • On a 0–3 scale, the home infusion patients reported less severe drug side effects (0.01 ± 0.16) than the medical setting infusion group (0.22 ± 0.71).	6
Wolter	1997	Home intravenous therapy in cystic fibrosis: a prospective randomized trial	Antibiotics/cystic fibrosis	Randomized controlled trial	17 patients; 31 admissions	Home vs hospital treatment. All patients spent 2–4 days in the hospital. Patients were then	• diagnosis of cystic fibrosis • acute respiratoroy	• There was no statistical difference between home infusion patients and in-hospital infusion	8

		examining clinical, quality of life and cost aspects.				randomized to receive home infusions or to remain in hospital to receive infusions.	exacerbation presenting to two Brisbane hospitals • Age ≥ 16 years	patients in their overall improvement in lung function (FEV1 p=0.27; FVC p=0.30)	
Yong	2009	A cost analysis of Outpatient Parenteral Antibiotic Therapy (OPAT): an Asian perspective.	Antibiotics/Infection (various)	Case control	165	Home infusion treatment vs hospital treatment. Cases were matched retrospectively with control matched on age, gender, and DRG.	• OPAT pts from Jan 1, 2005 to Aug 31, 2006 • To receive 4 days minimum care • Age ≥ 16	• At the end of the 4-month follow-up period, 59 (81.9%) OPAT patients were considered cured. Of the 13 (18.1%) OPAT patients who were re-admitted to the hospital due to relapse of their primary conditions, 12 were eventually cured and discharged from hospital; 1 died during hospitalization owing to the underlying medical condition. • For the inpatient-only group, 75 (80.6%) were considered cured at the end of the 4-month follow-up period. Eighteen (19.4%) were re-admitted with problems related to their primary condition. Seventeen of these patients were ultimately cured and discharged from hospital; one died during hospitalization. • There was no significant difference in the number cured between the two groups, p =0.991.	9

Table 2
Articles regarding the quality of life, costs, and length of stay associated with home infusion.

Author	Year	Title	Type of infusion/ disease	Type of study	Number of study patients	Intervention and comparison groups	Inclusion criteria	QOL measure used/assessment dates	Results: Patient-centered QOL or Costs
Patient satisfaction and quality of life									
Esmond	2006	Comparison of hospital and home intravenous antibiotic therapy in adults with cystic fibrosis.	Antibiotics/cystic fibrosis	Quasi-experimental pre-post design	30	Home vs hospital treatment	• Diagnosis of CF confirmed by sweat test or genotyping • Aged ≥ 18 • Acute respiratory exacerbation	• Cystic fibrosis Quality of Life (QOL) questionnaire • Administered on Day 0 (pre- home or in-hospital infusion) and day immediately post-treatment completion	• In the home group, there were improvements in all 9 quality of life domains between Day 0 and Day post-Rx, with statistically significant changes in 5: 1. physical functioning, Day 0 = 62.0 ± 14.0, Post-Rx = 72.0 ± 15.6, p = 0.02 2. chest symptoms, Day 0 = 49.7 ± 21.9, Post-Rx = 68.8 ± 23.2, p = 0.03 3. emotional responses, Day 0 = 66.0 ± 23.5, Post-Rx = 78.5 ± 17.6, p = 0.01 4. interpersonal relationships, Day 0 45.9 ± 25.7, Post-Rx 52.8 ± 22.0, p = 0.049) 5. career concerns, Day 0 40.3 ± 29.4, Post-Rx = 50.3 ± 20.0, p = 0.02 • In the hosptial group, 2 quality of life domains showed statistically significant changes: 1. chest symptoms (Day 0 47.0 [22.6], Post-Rx 70.3 [15.2], p = 0.006) 2. future concerns (Day 0 42.3 [24.5], Post-Rx 51.6 [21.3], p = 0.04) • When the home infusion and hospital infusion groups were compared, there were no significant differences in pre-post changes between groups.
Milligan	2006	Intravenous enzyme replacement therapy: better in home or hospital?	Enzyme replacement therapy/Gaucher and Fabry disease	Cross sectional	45	Patients receiving home infusion therapy or in-hospital infusion therapy	• Confirmed diagnosis of Fabry or Gaucher disease by enzyme assay and DNA analysis • receiving enzyme replacement therapy with agalsidase alfa or glucocerebrosidase • age not specified	Survey designed for this study, with questions about stress, and how treatment affected family life	Patients receiving in-hospital infusions: • 9/20 (45%) with Fabry disease and 9/25 (36%) with Gaucher disease found in-hospital infusion treatment stressful • 12/20 (60%) with Fabry and 7/25 (28%) with Gaucher disease said hospital infusion treatment affected their family life Patients receiving home infusions: • 2/20 (10%) with Fabry disease and 2/25 (8%) with Gaucher disease found

									home infusion stressful • 5/20 (20%) with Fabry and 2/25 (8%) with Gaucher disease said home infusion treatment affected family life Preference for home versus in-hospital infusion: • 95% with Fabry disease and 85% with Gaucher disease preferrcd home infusion. • Home therapy was reported to be more effective than hospital-based therapy by 9l% with Fabry disease and 86% with Gaucher disease • 30% with Fabry disease and 36% with Gaucher disease felt safer receiving therapy at home • 35% of patients with Fabry disease and 24% of padente with Gaucher disease felt safer receiving therapy in the hospital • 17% in both disease groups said that there was no difference in safety between home and hospital
Smith	2004	Home care versus hospital care in patients with multiple myeloma treated with pamidronate.	Pamidronate/multiple myeloma	Randomized controlled crossover trial	37	Cross over: Patients randomized to group 1 received 3 months of home infusions followed by 3 months of in-hospital infusions; patients randomized to gorup 2 received 3 months of in-hospital infusions followed by 3 months of home infusions	• < 80 years old • life expectancy > 6 months • symptomatic stage II or III multiple myeloma • either in plateau phase following initial chemotherapy or receiving chemotherapy for active disease	• EORTC QLQ-C39 questionnaire • survey assessed at baseline (pre-randomization), at 3 months (post-first treatment round, and at 6 months (post-second treatment round)	• Comparing patients who had just received home care with patients who had just received hospital care: • there were no significant differences in EORTC QLQ-C39 scores for 5 functional domains: physical, role, e• • motional, cognitive, social. • there was a slight trend toward preference for home treatment. • global health status/QOL was higher for patients who received home infusions, but this result was not statistically significant. • On a 0–100 analog scale that measured acceptability of care location, the average score for home treatment was 91.8; for hospital care, 69.7. This difference was statistically significant.
Tourangeau	2012	Safety and efficacy of physician-supervised self-managed C1 inhibitor replacement therapy.	C1INH/Hereditary angioedema	Cross sectional	39	Patients who self-infused C1INH at home versus patients who received C1INH infusion in a medical setting during December 2007 - March 2008	• Physician diagnosis of hereditary angioedema • were receiving on-demand C1INH at home or at a medical facility • Age ≥ 18	SF36, hereditary angioedema disease-specific questions	• Compared to the medical setting group, the home group reported statistically significant less interference with family life ($p < 0.0001$), social life ($p < 0.0001$), nights of disrupted sleep ($p < 0.0001$),

Please cite this article as: Polinski JM, et al. Home infusion: Safe, clinically effective, patient preferred, and cost saving. *Healthcare* (2016), http://dx.doi.org/10.1016/j.hjdsi.2016.04.004

Table 2 (*continued*)

Author	Year	Title	Type of infusion/ disease	Type of study	Number of study patients	Intervention and comparison groups	Inclusion criteria	QOL measure used/assessment dates	Results: Patient-centered QOL or Costs
									and days that family or friends had to miss school or work due to the subject's hereditary angioedema ($p = 0.045$) • Using the SF-36, the home group showed significantly greater improvement in their aggregated physical scores during the course of the study (positive change in the clinic group, median 0.49, IQR –1.14 to 2.50; positive change in the home group, median 2.23, IQR 0.78–5.56; $p = 0.043$).
Wolter	1997	Home intravenous therapy in cystic fibrosis: a prospective randomized trial examining clinical, quality of life and cost aspects.	Antibiotics/cystic fibrosis	Randomized controlled trial	17 patients; 31 admissions	Home vs hospital treatment. All patients spent 2–4 days in the hospital. Patients were then randomized to receive home infusions or to remain in hospital to receive infusions.	• diagnosis of cystic fibrosis • acute respiratoroy exacerbation presenting to two Brisbane hospitals • Age $\geq$ 16 years	Chronic Respiratory Disease Questionnaire (CRDQ) administered on Day 0 and Post-Rx; lower scores are BETTER	• Compared to home patients, hospital patients reported less fatigue, better mastery and better total QOL scores ($p < 0.05$). • In contrast, home patients had better family, personal, sleep and total disruption ratings ($p \leq 0.005$).
Home infusion costs and length of stay									
Grayson	1995	Home intravenous antibiotic therapy. A safe and effective alternative to inpatient care.	Antibiotics/Infection (various)	Cross sectional	20	Home treatment cost for present treatment episode versus vs hospital costs for the most recent, prior treatment episode that occurred in hospital.	• Stable clinical and psychological condition • established long-term venous access • need for ongoing parenteral abx therapy with dosing no more than twice daily • adequate social support structure • Age $\geq$ 18		• The daily mean cost of home treatment was \$147 (SD $\pm$ \$57) vs estimated hospital costs of \$259 (SD $\pm$ \$76) • Overall cost savings for each course of treatment at home versus in-hospital was an average \$2,974 (SD $\pm$ \$2,806)
Remonnay	2002	Economic evaluation of *anti*neoplasic chemotherapy administered at home or in hospitals.	Chemotherapy/ cancer	Randomized controlled crossover trial	42	Patients randomized to group 1 received two home infusions followed by two hospital-based infusions. Patients randomized to group 2 received two hospital-based infusions followed by two home infusions.	• had not received chem during the previous 2 months • lived in geographical sector covered by home health agency • lived with family member • patient's personal physician consented to participation • had permanent access to a vein or implantable venous access system		• Healthcare personnel costs were significantly greater for at-home care (\$69.1) versus in-hospital day-care (\$51.7), $p < 0.0001$, for one administration of chemotherapy. • Median cost of one medication administration is \$136.7 in home and \$74.0 in hospital day-care unit ($p < 0.0001$). This reflects medication purchasing methods in home care vs. hospital. • Overall, marginall costs

Please cite this article as: Polinski JM, et al. Home infusion: Safe, clinically effective, patient preferred, and cost saving. *Healthcare* (2016), http://dx.doi.org/10.1016/j.hjdsi.2016.04.004

									were significantly greater at home, \$232.5 than in hospital day care, \$157.9 ($p < 0.0001$). • Total average costs (including overhead)were less in home (\$252.6) than in-hospital (\$277.3). Overhead accounted for 43% of in-hospital average cost and 8% of in-home average cost. • Aligning medication costs in a theorectical comparison, the overall average home cost would be \$190.0 vs \$277.3 in-hospital ($p < 0.0001$), a significant savings.
Wolter	1997	Home intravenous therapy in cystic fibrosis: a prospective randomized trial examining clinical, quality of life and cost aspects.	Antibiotics/Cystic fibrosis	Randomized controlled trial	17 patients; 31 admissions	Home vs hospital treatment. All patients spent 2–4 days in the hospital. Patients were then randomized to receive home infusions or to remain in hospital to receive infusions.	• diagnosis of cystic fibrosis • acute respiratoroy exacerbation presenting to two Brisbane hospitals • Age ≥ 16 years		• Home therapy was considerably cheaper for families than was hospitalization (mean \$23.77 $\pm$ \$17.77) per day of hospitalization and \$15.08 $\pm$ \$13.48) per day of home therapy).
Yong	2009	A cost analysis of Outpatient Parenteral Antibiotic Therapy (OPAT): an Asian perspective.	Antibiotics/Infection (various)	Case control	165	Home infusion treatment vs hospital treatment. Cases were matched retrospectively with control matched on age, gender, and DRG.	• OPAT pts from Jan 1, 2005 to Aug 31, 2006 • To receive 4 days minimum care • Age ≥ 16		• The mean total costs of treatment in the OPAT setting and inpatient setting were \$12,736 (median \$8863; range \$196–97,578) and \$12 403 (median \$3910; range \$736–388,758), respectively. • The difference in the mean total cost of treatment was not statistically significant ($P = 0.706$). • In contrast to total treatment costs, the difference in mean cost of treatment per day was found to be statistically significant ($P < 0.001$). • The mean cost per day for OPAT patients was \$278 (median \$230; range \$49–1027), whilst the mean cost per day for inpatient-only care was \$457 (median \$344; range \$163–2103).

self-infused at home reported greater improvement in their SF36 physical score ($p < 0.0001$) and less adverse impact on their family and social lives ($p < 0.0001$).[23] Family and friends missed fewer days of school/work due to the patient's condition ($p = 0.045$), Newcastle-Ottawa score = 6.

3.4. Costs and length of stay (LOS)

Grayson et al. used a self-controlled design to compare 20 patients' OPAT costs to the IPAT costs associated with their admission diagnoses immediately prior to their discharge to the OPAT program (Table 2).[27] OPAT costs included the pharmacy and laboratory fees associated with the infused antibiotic, consumables (needles, syringes, etc.), and home health nurse visits. IPAT costs included nursing care, routine ward expenses, catering, and pharmacy expenses. On average, OPAT expenditures totaled $\$147 \pm \$57$ per day versus $\$259 \pm \$76$ per day for IPAT. The mean cost savings associated with a full course of OPAT versus of IPAT treatment was $\$2974 \pm \$2806$. Cost variations were primarily dependent on the chosen antibiotic and the dosing frequency. The self-controlled design was a strength, but the sample size was small, and it was unclear whether these patients were representative of the larger community receiving OPAT, Newcastle-Ottawa score = 7. In a second US-based study of patients with cystic fibrosis, those randomized to OPAT had mean costs of $\$15 \pm \$14$ per day compared to $\$24 \pm \$18$ per day among patients randomized to IPAT.[19] The hospital's average total treatment costs to achieve a cure were: OPAT (3 IPAT days + 10 OPAT days) = $2476, compared with IPAT = $5028 (11.4 days of IPAT), a savings of $2552 per patient. As described above, the Newcastle-Ottawa score = 8.

The costs of home versus inpatient infusion in France were compared in a randomized controlled crossover trial in which 42 patients were randomized to receive 2 home infusions followed by 2 inpatient infusions or vice versa.[28] Even though the costs of the infused chemotherapy drugs delivered at home ($137) were nearly twice those in the hospital ($74), the average costs per chemotherapy home infusion ($\$253 \pm \$82$) were significantly less than in hospital ($\$277 \pm \$62$), $p = 0.0002$, because the indirect costs associated with inpatient stays were so much higher than those associated with home infusion. The study's only limitation was its sample size, Newcastle-Ottawa score = 8. A final study in Singapore compared costs between OPAT patients and IPAT patients, matched by age, gender, and diagnosis. The IPAT patients were selected from the 12 months prior to OPAT's availability in Singapore.[24] The average treatment duration was 24.3 days for OPAT patients compared with 19 days for IPAT patients. Mean costs per day were $278 for OPAT and $457 for IPAT, $p < 0.001$. Even though the treatment duration was longer, each OPAT course of treatment saved approximately $1928 when compared with an IPAT treatment course. While the study did include matching factors to mitigate differences between exposure groups, other factors, such as disease severity, may have influenced the duration of OPAT therapy, Newcastle-Ottawa score = 7.

4. Discussion

In this systematic review, we found that home infusion care can provide safe, clinically effective care, improve quality of life, and reduce overall healthcare costs. Patients receiving home infusions were no more likely to experience adverse drug events or side effects (all $p > 0.05$), and had as good or better clinical outcomes. Patients overwhelmingly preferred receiving infusions at home. The costs associated with home infusion were consistently, significantly lower, with savings ranging between $1928 and $2974 per treatment course. Taken together, the available evidence suggests that the home infusion care delivery model represents a valuable approach to both improve quality and reduce costs for appropriate patients.

Six studies examined OPAT, one of the most common indications for home infusion therapy.[18–21,24,27] Intravenous antibiotic therapy is routinely prescribed following orthopedic surgeries, systemic infections, and acute respiratory exacerbations for vulnerable patients, and the evidence suggests that greater OPAT use is warranted. Home infusion is also well suited to medication delivery in many other clinical areas, including neurology, oncology, hematology, rheumatology, and gastroenterology, and the number of indications continues to expand as new medications enter the marketplace. The quality and costs associated with these clinical areas, as well as infused nutrition and palliative care infusion, merit additional study.

This review has strengths and limitations. While the methodological quality of the 13 studies varied, the majority did employ strategies that effectively mitigated confounding, including randomized designs, matching, self-controlled and case-crossover designs, and/or historical controls. Three of the 13 studies had a Newcastle-Ottawa score of 9, and most received a score of 7 or 8. The most common limitation was small sample size, reflecting the low prevalence of these diseases. Most importantly, however, each of the studies had a comparator group of patients receiving infusions in medical settings. The expenses included in cost calculations varied, as did the expenditure values for these components and the duration of infusion therapy. Costs associated with training pharmacists and nurses to perform home infusion were not included. Even with these limitations, all studies consistently reported cost savings, suggesting that the savings associated with home infusion are generalizable across therapy indications. Due to the substantial variability in the included studies, we did not attempt to pool data or conduct a meta-analysis, nor conduct a three-way comparisons of infusions delivered in inpatient and outpatient medical settings as compared to home.

5. Conclusions

In this systematic review, we found that compared with medical facility-based infusion, the available evidence consistently favored the quality, efficacy, patient satisfaction, and costs associated with home infusion. The Medicare Home Infusion Site of Care Act, presently under consideration by Congress, would expand Medicare reimbursement for home infusion services to all Medicare beneficiaries, not just those in medical facilities or homebound.[11] The Act's passage is a well-reasoned next step in realizing both improved care and lower costs for Medicare beneficiaries. As the overhaul of the healthcare payment system gains momentum, the home infusion care delivery model offers strong promise as one in a set of approaches that can achieve the triple aim.

References

1. Better, smarter, healthier: in historic announcement, HHS sets clear goals and timeline for shifting Medicare reimbursements from volume to value. ⟨http://www.hhs.gov/news/press/2015pres/01/2015126a.html⟩; 2015 Accessed 9.06.15.
2. Colla CH, Wennberg DE, Meara E, et al. Spending differences associated with the Medicare Physician Group Practice Demonstration. *J Am Med Assoc.* 2012;308(10):1015–1023.
3. McWilliams JM, Chernew ME, Landon BE, Schwartz AL. Performance differences in year 1 of pioneer accountable care organizations. *N Engl J Med.* 2015;372(20):1927–1936.
4. McWilliams JM, Chernew ME, Zaslavsky AM, Hamed P, Landon BE. Delivery system integration and health care spending and quality for Medicare beneficiaries. *JAMA Intern Med.* 2013;173(15):1447–1456.
5. Abrams L. Where surgery comes with a 90-day guarantee. The Atlantic 2012. September 26, 2012. ⟨www.theatlantic.com/health/archive/2012/09/where-surgery-comes-with-a-90-day-guarantee/262841⟩; 2012 September 26 Accessed 9.06.15.
6. The Medicare Participating Heart Bypass Center Demonstration ⟨Http://WWW.cms.Gov/Medicare/Demonstration-Projects/DemoProjectsEvalRpts/Downloads/Medicare_Heart_Bypass_Summary.pdf⟩; 2015 Accessed 9.06.15.
7. Nielsen M, Langner B, Zema C, Hacker T, Grundy P. Benefits of implementing the primary care patient-centered medical home. ⟨https://www.pcpcc.org/sites/default/files/media/benefits_of_implementing_the_primary_care_pcmh.pdf⟩; 2012 Accessed 9.06.15.
8. Medicare shared savings program performance year 1 results. ⟨http://www.cms.gov/Medicare/Medicare-Fee-for-service-payment/sharedsavingsprogram/Downloads/MSSP-PY1-final-performance-ACO.pdf⟩; 2014 accessed 9.06.15.
9. Unpacking the Medicare Shared Savings Proposed rule: geography and policy ⟨http://healthaffairs.org/blog/2015/01/22/unpacking-the-medicare-shared-savings-proposed-rule-[geography-and-policy/|⟩; 2015 Accessed 9.06.15.
10. Government Accountability Office. Home Infusion therapy: differences between medicare and private insurers coverage. ⟨www.gao.gov/new.items/d10426.pdf⟩; 2010 Accessed 9.06.15.
11. 114th Congress. Medicare Home infusion site of care act of 2015. In: Senate. S275. ⟨www.nhia.org/resource/legislative/documents/bills-114s275is.pdf⟩; 2015 Accessed 9.06.15.

Please cite this article as: Polinski JM, et al. Home infusion: Safe, clinically effective, patient preferred, and cost saving. *Healthcare* (2016), http://dx.doi.org/10.1016/j.hjdsi.2016.04.004

12. MedPAC. Medicare coverage of payment for home infusion therapy. ⟨www.medpac.gov/documents/reports/chapter-6-medicare-coverage-of-and-payment-for-home-infusion-therapy-%28june-2012-report%29.pdf?sfvrsn=0⟩; 2012 Accessed 9.06.15.
13. Drozd EM, Hoban M. Impact on medicare expenditures from expanding coverage of infusion therapy of anti-infective drugs to the home setting. ⟨www.nhia.org/resource/legislative/documents/avalerefinalhomeinfusionreport.pdf⟩); 2014 Accessed 9.06.15.
14. National Home Infusion Association releases first-ever study of alternate-site infusion industry. ⟨www.nhia.org/press_release/pr101811.html⟩; 2010 Accessed 9.06.15.
15. Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa Hospital Research Institute. ⟨http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp⟩; Accessed 29.02.16.
16. Beijer S, Gielisse EAR, Hupperets PS, et al. Intravenous ATP infusions can be safely administered in the home setting: a study in pre-terminal cancer patients. *Invest New Drugs.* 2007;25:571–579.
17. Brown DF, Muirhead MJ, Travis PM, Vire SR, Weller JA, Hauer-Jensen M. Mode of chemotherapy does not affect complications with an implantable venous access device. *Cancer.* 1997;80(5):966–972.
18. Martone WJ, Lindfield KC, Katz DE. Outpatient parenteral antibiotic therapy with daptomycin: insights from a patient registry. *Intern J Clin Pr.* 2008;62(8):1183–1187.
19. Wolter JM, Bowler SD, Nolan PJ, McCormack JG. Home intravenous therapy in cystic fibrosis: a prospective randomized trial examining clinical, quality of life, and cost aspects. *Eur Respir J.* 1997;10(4):896–900.
20. Esmond G, Butler M, McCormack AM. Comparison of hospital and home intravenous antibiotic therapy in adults with cystic fibrosis. *J Clin Nurs.* 2006;15(1):52–60.
21. Pond MN, Newport M, Joanes D, Conway SP. Home versus hospital intravenous antibiotic therapy in the treatment of young adults with cystic fibrosis. *Eur Respir J.* 1994;7(9):1640–1644.
22. Soucie JM, Symons J, Evatt B, et al. Home-based factor infusion therapy and hospitalization for bleeding complications among males with haemophilia. *Haemophilia.* 2001;7(2):198–206.
23. Torangeau LM, Castaldo AJ, Davis DK, Koziol J, Christiansen SC, Zuraw BL. Safety and efficacy of physician-supervised self-managed c1 inhibitor replacement therapy. Internat Arch. *Allerg Immunol.* 2012;157(4):417–424.
24. Yong C, Fisher DA, Sklar GE, Li S-C. A cost analysis of outpatient parenteral antibiotic therapy (OPAT): an Asian perspective. *Intern J Antimicrob Agents.* 2009;33(1):46–51.
25. Milligan A, Hughes D, Goodwin S, Richfield L, Mehta A. Intravenous enzyme replacement therapy: better in home or hospital? *Br J Nurs.* 2006;15(6):330–333.
26. Smith AG, Soutar RL, Schey S, et al. Home care versus hospital care in patients with multiple myeloma treated with pamidronate. *Intern J Palliat Care Nurs.* 2004;10(3):144–149.
27. Grayson ML, Silvers J, Turnidge J. Home intravenous antibiotic therapy. *Med J Aust.* 1995;162(5):249–253.
28. Remonnay R, Devaux Y, Chauvin F, Dubost E, Carrere MO. Economic evaluation of antineoplasic chemotherapy administered at home or in hospitals. *Intern J Technol Assess Health Care.* 2002;18(3):508–519.

Conflict of interest

This statement accompanies the article Home infusion: Safe, clinically effective, patient preferred, and cost saving, authored by Jennifer M. Polinski and co-authored by Mary K. Kowal, Michael Gagnon, Troyen A. Brennan, William H. Shrank and submitted to *Healthcare* as an Article Type. Authors collectively affirm that this manuscript represents original work that has not been published and is not being considered for publication elsewhere.We also affirm that all authors listed contributed significantly to the project and manuscript. Furthermore we confirm that none of our authors have disclosures and we declare no conflict of interest.

Consultant arrangements: None
Stock/other equity ownership: None
Patent licensing arrangements: None
Grants/research support: None
Employment: None
Speakers' bureau: None
Expert witness: None.

Please cite this article as: Polinski JM, et al. Home infusion: Safe, clinically effective, patient preferred, and cost saving. *Healthcare* (2016), http://dx.doi.org/10.1016/j.hjdsi.2016.04.004