

**Increasing outpatient treatment of mild community-acquired pneumonia: systematic review and meta-analysis**

James D Chalmers<sup>1</sup>, Ahsan R Akram<sup>1</sup>, Adam T Hill<sup>1</sup>

**1. Royal Infirmary of Edinburgh, Edinburgh, United Kingdom**

**Corresponding author**

**Dr James Chalmers**

**Department of Respiratory Medicine**

**Royal Infirmary of Edinburgh**

**51 Little France Crescent**

**Old Dalkeith Road**

**Edinburgh**

**EH16 4SA**

**E-mail: jamesdchalmers@googlemail.com**

Telephone : +44 1312426662

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## ABSTRACT

### **Objective**

To identify, synthesise and interpret the evidence relating to strategies to increase the proportion of low risk patients with community-acquired pneumonia treated in the community.

### **Data sources**

A systematic review of intervention studies conducted between 1981-2010.

### **Review**

Articles were included if they compared strategies to increase outpatient care with usual care. Outcomes were: the proportion of patients treated as outpatients, mortality, hospital readmissions, health related quality of life, return to usual activities and patient satisfaction with care.

### **Results**

The main analysis included 6 studies. The interventions in these studies were generally complex, but all involved the use of a severity score to identify low risk patients. Overall, a significantly larger numbers of patients were treated in the community with these interventions: odds ratio(OR) 2.31(95% CI 2.03-2.63). The interventions appear safe, with no significant differences in mortality OR 0.83(0.59-1.17), hospital readmissions OR 1.08(0.82-1.42) or patient satisfaction with care OR 1.21(0.97-1.49) between the intervention and control groups. There was insufficient data regarding quality of life or return to usual activities. All studies had significant limitations.

### **Conclusions**

The available evidence suggests that interventions to increase the proportion of patients treated in the community are safe, effective and acceptable to patients.

## **Introduction**

Community-acquired pneumonia (CAP) is the most common infectious disease presenting to emergency departments in western countries.<sup>1</sup> Population based studies of CAP in Europe suggest an incidence of CAP requiring hospitalisation of 1.98-2.6/1000 population per year.<sup>2,3</sup>

Approximately 75% of cases are managed in the community where mortality is very low. The mortality rate in hospitalised patients is reported to be between 5%-15%.<sup>4,5</sup>

Treatment of community-acquired pneumonia costs over 8 billion dollars annually in the United States.<sup>6</sup> More than 90% of that expenditure relates to the cost of inpatient care.<sup>6</sup> The initial decision, made by the attending physician, to admit the patient to hospital or discharge the patient from hospital is therefore crucial.

In recent years, severity assessment tools such as the Pneumonia severity index (PSI) and the CURB65 score have been developed.<sup>4,5</sup> These tools allow patients to be categorised into groups at low, intermediate and high risk for 30-day mortality. Patients at low risk for mortality are more likely to be suitable for outpatient care. These tools are now promoted by almost all national and international guidelines to aid clinicians in making the site of care decision.<sup>1</sup>

Strategies to increase the proportion of patients treated in the community have the potential to significantly decrease hospital costs, but must be safe and acceptable to patients.<sup>7</sup>

In this study, we systematically reviewed the published literature to identify, synthesise and interpret the evidence relating to strategies to increase the proportion of low risk patients with community-acquired pneumonia treated in the community.

The aim of the study was to establish if these interventions could increase the proportion of patients treated in the community without compromising patient satisfaction with care,

healthy related quality of life and return to usual activities or increasing hospital readmissions or mortality.

## Methods

This was a systematic review and meta-analysis conducted and reported according to PRISMA recommendations.<sup>8</sup>

### **Search strategy**

The present review was based on a search of PUBMED and EMBASE for articles using keywords ‘Outpatient’, ‘discharge’, ‘home’, ‘hospitalisation/hospitalization’ or ‘guideline’ in combination with ‘community-acquired pneumonia’ was performed between January 1981 and April 2010.. Non relevant studies were excluded based on title and abstract review only. Full articles of all potentially appropriate abstracts were retrieved and reviewed by investigators. No language restriction was applied. Only peer-reviewed data was included, therefore conference abstracts were excluded. The search strategy was supplemented by reviewing of reference lists, bibliographies and the investigators files.

### **Study inclusion criteria and quality assessment**

Data was independently extracted from each relevant study by 2 abstractors and these abstractors carried out quality assessment using standardised criteria.<sup>9</sup> Quality assessments were performed separately and disagreements resolved by a third independent abstractor. Studies were included if they met the following criteria: 1) original publication; 2) describe an intervention aimed to increase the proportion of patients treated in the community; 3) include a control group in which the intervention was withheld; 4) include data reporting the safety of the intervention.

Studies reporting outpatient care but without control data were not included.

### **End-points**

The primary outcome was the proportion of patients treated in the community in the intervention groups compared to the control groups. Measures of safety were also assessed as

follows: mortality; readmission to hospital in community treated patients; patient satisfaction with care; health related quality of life and return to work or usual activities.

### **Statistical analysis**

Statistical analysis was performed using Review Manager, version 5. For pooled data, odds ratios (OR) with 95% confidence intervals (CI) are reported. A fixed-effects model was used to pool the results of individual studies. Heterogeneity of study results were assessed by calculating an  $\chi^2$  test of heterogeneity and the  $I^2$  test for inconsistency. Significant heterogeneity was predefined as a  $\chi^2$  test  $p < 0.1$  or an  $I^2$  test  $> 50\%$ . Publication bias was assessed using the Funnel plot method.

### **Results**

The literature review identified 6 studies for inclusion in the meta-analysis.<sup>10-15</sup> Details of the literature review are shown in figure 1.

Details of each study are shown in Table 1.

The interventions used in each study were generally complex, but all included a scoring system to identify low risk patients. In 5 studies, the PSI was used to help determine where patients should be treated in the intervention arm. In 1 study the authors derived their own criteria for inpatient care and then implemented this. No clinical trials using any of the other available severity scores were identified.

### **Description of included studies**

In the study by Atlas et al<sup>10</sup>, a single centre intervention, the authors implemented a practice guideline for patients with low PSI scores. The study included patients with PSI scores I-III and excluded patients with significant hypoxaemia, patients with immunosuppression, injecting drug users and other co-morbidities that were considered a contraindication to outpatient care. The intervention involved promoting the use of the PSI in the emergency

department and supporting discharge by providing nursing visits at home, standardised antibiotic treatment (clarithromycin monotherapy) and access to a primary care physician. Care after the intervention was compared to a retrospective control cohort identified from case-note review. Significantly more patients were treated as outpatient in the intervention compared to the control cohort.<sup>10</sup>

In the study by Marrie et al<sup>11</sup>, the intervention was the implementation of the critical pathway composed of 3 parts: 1- promoting the use of the PSI; 2- treatment with levofloxacin; 3- implementation of a practice guideline that included standard microbiological tests, Intravenous (IV) to oral switch criteria and hospital discharge criteria. 9 hospitals implemented this critical pathway while 10 hospitals managed patients according to their usual practice. This did not include pneumonia severity scoring or the other components of the critical pathway.<sup>11</sup>

In the study by Dean et al<sup>12</sup>, a clinical practice guideline based on the American Thoracic Society guidelines were introduced. The guideline included a decision support system to determine site of care that included a scoring system. This study is unique in not using the PSI to determine initial site of care, instead the authors determined their own criteria for outpatient care and incorporated these into the guideline. The study is also unique as it took place in community based walk in medical centres rather than emergency departments as was the case in the other studies. Data for 12 months after the introduction of the guideline was compared to a retrospective control group of patients treated before implementation of the guideline.<sup>12</sup>

In the study by Carratala et al<sup>13</sup>, patients were randomised to outpatient versus inpatient management. Outpatients were treated with oral levofloxacin and in-patients treated with sequential IV then oral levofloxacin. Patients were excluded if they were intolerant of quinolones, if they were pregnant or breast feeding and if they had respiratory failure,

unstable comorbidities, pneumonia complications (pleural effusion or lung abscess) or were unable to take oral medications.<sup>13</sup> Outcomes were determined at 30-days after randomisation and included mortality, the number of readmissions as well as adverse drug reactions and patient satisfaction with care.

Yealy et al<sup>14</sup> conducted a cluster-randomised trial at 32 emergency departments in Pennsylvania and Connecticut, USA. Centres were randomised to 1 of 3 intensities of pneumonia guideline implementation. The intervention included instructions to use the PSI, and to manage patients in class I-III without oxygen desaturation as outpatients. The guideline also suggested administration of antibiotics for inpatients within 4 hours, and recommended appropriate empiric antibiotic therapy. The low intensity strategy simply involved writing to medical directors of hospitals suggesting that they develop pneumonia quality improvement strategies and mailing the emergency department with the guideline. The moderate and high intensity strategies included the measures for the low-intensity group but also an on-site teaching session on how to use the PSI and to encourage outpatient treatment. The high intensity group also included a number of additional reminders and feedback systems.<sup>14</sup>

In the study by Renaud et al<sup>15</sup>, an observational study, 8 emergency departments in which the PSI was used to determine site of care were compared with 8 emergency departments in which the PSI was not used. PSI user hospitals were provided with posters and pocket cards reminding them to use the PSI, while control hospitals were not. No other interventions were used. Each hospital completed data collection for 3-5 months and the primary outcome was the proportion of patients discharged from the emergency department.<sup>15</sup>

The results of these studies are summarised in Table 1.

**Table 1.** Characteristics of included studies.

**Outpatient management using clinical guidelines**

We included 5 studies in the meta-analysis for outpatient care. The study by Carratala et al<sup>13</sup> was unique in randomising all patients to outpatient or inpatient treatment rather than implementing a clinical guideline to increase the proportion of patients treated in the community, therefore this was not included in this part of the analysis. The definition of outpatient treatment was only specifically given in the study by Yealy et al<sup>14</sup>, defined as discharge from the emergency department to the community within 24 hours. In the other studies, outpatient treatment was assumed to meet the same definition.

The analysis included a total of 2,817 patients in the intervention groups and 2,052 patients in the control groups. In raw analysis, 64.6% of patients in the intervention group were treated in the community compared to 48.7% of patients in the control groups.

In the meta-analysis, the interventions were associated with a significant increase in outpatient managed, with an odds ratio of 2.31 (95% confidence interval 2.03-2.63). The Forest plot is shown (Figure 2). There was no significant heterogeneity.

### **Safety of the intervention**

For the 2 measures of safety, mortality was not increased OR 0.83 (0.59-1.17)- Figure 3.

For hospital readmissions, the studies by Atlas et al<sup>10</sup>, Dean et al<sup>12</sup>, Yealy et al<sup>14</sup> and Renaud et al<sup>15</sup> reported readmissions only for patients initially treated in the community in both intervention and control groups. The definition of readmissions was unclear in the study by Marrie et al.<sup>11</sup> Carratala et al<sup>13</sup> compared readmissions in patients discharged from the emergency department to those patients initially hospitalised and then subsequently discharged.

Separately, none of these studies showed an increase in hospital readmissions. Similarly, the pooled analysis showed no increase in hospital readmissions, OR 1.08 (0.82-1.42)- figure 4.

There was no significant heterogeneity in these analyses.

### **Patient satisfaction with care**

Only 3 studies reported data for patient satisfaction with care between intervention and control groups. In the studies by Carratala<sup>13</sup> and Atlas et al<sup>10</sup>, patients were asked to rate their satisfaction with care at 4 weeks on a scale 1-5 (very unsatisfactory to very satisfactory) with 4 or 5 considered satisfied. In the study by Yealy et al<sup>14</sup>, telephone interviews were conducted at day 30 and patients were asked if they were satisfied with their initial site of care, their emergency department care and their overall medical care.

Pooling the results of the 3 studies, there was no difference between the intervention and control groups OR 1.21 (0.97-1.49),  $p=0.09$ , in the proportion of patients reporting satisfaction with overall care. There was no significant heterogeneity in the analysis (Figure 5). This conclusion was based predominantly on the results of the study by Yealy et al<sup>14</sup>, which was significantly larger than the other 2 studies.

### **Return to usual activities and quality of life**

There was insufficient data to pool studies of return to usual activities or quality of life. Atlas et al<sup>10</sup> reported return to daily activities, with 92% of patients in the intervention and 85% in the retrospective control group reporting return to usual activities ( $p>0.05$ ). They also reported no difference in patients reporting general health excellent or very good at 4 weeks. The study by Marrie et al<sup>11</sup> reported quality of life using the short-form 36 physical component summary scale (SF36) and reported no significant difference between intervention and control hospitals. Carratala et al<sup>13</sup> also assessed health related quality of life using the SF36 tool and found no significant difference at day 7 or day 30 in health related quality of life between patients managed as in-patients or outpatients. Yealy et al<sup>14</sup> assessed return to work and usual activities at day 30 and found no significant differences in these

parameters between the low, moderate and high intensity guideline implementation groups. Finally, Renaud et al<sup>15</sup> and Dean et al<sup>12</sup> did not assess return to usual activities or quality of life.

### **Publication Bias**

In each of the analyses, inspection of funnel plots did not suggest any evidence of publication bias.

### **Quality assessment**

Each of the included studies had significant limitations. The studies by Atlas et al<sup>10</sup> and Dean et al<sup>12</sup> utilised a retrospective control cohort design, a method associated with a significant risk of bias. Similarly, the centres included in the study by Renaud et al<sup>15</sup> were not randomised. Instead the study included hospitals that had decided independently to implement the PSI and control hospitals that had not. There is no way of knowing to what extent other aspects of CAP management were different in these centres, or that the PSI was not used in the control hospitals. The cluster randomisation design utilised in the studies by Marrie et al<sup>11</sup> and Yealy et al<sup>14</sup> are more robust, however, as the pneumonia severity index is a well known and widely used instrument, randomisation at hospital level cannot ensure the intended practice at the individual physician level. The study by Carratala et al<sup>13</sup> was more robust, as a randomised controlled trial in 2 centres but was underpowered to detect mortality, which is rare in low risk patients. The study also had to exclude a large proportion of patients as many otherwise low risk patients are not suitable for outpatient care. All of the guideline interventions were composed of multiple components and therefore evaluating which of these components were responsible for the effects seen is not straightforward.

## **Discussion**

This systematic review and meta-analysis demonstrates that, based on the available evidence, strategies to increase the proportion of patients treated in the community are safe, effective and acceptable to patients. Increased use of outpatient care for low risk patients, primarily defined using the pneumonia severity index, was associated with no significant increase in hospital readmissions, patient mortality or patient dissatisfaction with care.<sup>10-15</sup> There was limited data on other safety outcomes such as health related quality of life and return to usual activities.

Each of the 6 included studies had significant limitations and each used a variety of different methods to encourage outpatient management. All of these studies, however, were based on the principle that patients at low risk of death, and without important contraindications to outpatient treatment, such as inability to take oral medication or unstable co-morbidities, can be treated safely at home. The studies were conducted in the United States, Canada, France and Spain, suggesting that these results can be generalised to different healthcare systems.<sup>10-15</sup>

The Pneumonia severity index was developed in 1997 with the aim of identifying a population of patients at low risk for mortality who may be suitable for outpatient therapy.<sup>4</sup>

This score has been shown to be reliable in a large number of validation studies.<sup>16-20</sup> Evidence suggests that since the introduction of the pneumonia severity index the length of stay for patients with community-acquired pneumonia may have decreased and more patients may be initially treated in the community.<sup>21</sup> There is, however, evidence from a number of studies including those included in this meta-analysis that a larger proportion of patients could be safely treated in the community.<sup>10-15</sup>

Outpatient management has several potential advantages. More than 90% of hospital costs are associated with in-patient care and even small increases in the proportion of patients

treated at home can result in large economic savings.<sup>6,22</sup> Hospital acquired infections such as methicillin resistant *Staphylococcus aureus* and *Clostridium difficile* are an increasing problem in the UK and internationally.<sup>23,24</sup> Reducing the proportion of patients treated in hospital will reduce the risk of patients developing these hospital complications.

### **Barriers to outpatient treatment**

All of the quality improvement studies found a proportion of low risk patients still requiring inpatient treatment. Physician judgement is critical in the implementation of severity scores.<sup>25</sup> A number of studies have investigated reasons why low risk patients require hospitalisation and show that co-morbid illnesses, inability to take oral medications, severity not adequately captured by the PSI and hypoxaemia are frequent in low risk patients.<sup>25,26</sup> These factors must be taken into consideration when implementing outpatient management strategies.

Evidence suggests that physicians over-estimate the severity of low risk patients.<sup>26</sup> It is notable that each of the successful quality improvement studies in this meta-analysis included some degree of physician education and feedback. This is well-demonstrated in the study by Yealy et al, in which low intensity implementation of guidelines, in which physicians were simply provided with the guidelines were significantly less effective than the moderate/high intensity group in which guidelines were supplemented with physician education and feedback. There is evidence that the PSI and other severity assessment tools are under-utilised in some centres.<sup>27</sup>

This study did not identify any clinical studies or trials of severity scores other than the PSI, and a site specific score developed by Dean and colleagues, to increase the proportion of patients treated in the community. It is uncertain if the results of this meta-analysis can be generalised to other methods or scoring systems.<sup>5,28,29</sup>

### **Limitations of the included studies**

As discussed above, potential bias must be considered in interpreting these results. Although the meta-analysis found no indication of publication bias, the methodology of each study varied substantially. The studies by Atlas *et al* and Dean *et al* used retrospective control cohorts. When different methodology are used to collect data for the intervention and control groups, the risk of bias is increased. The analysis of patient satisfaction with care was largely based on a single study (Yealy *et al*)<sup>14</sup> and therefore further studies on this end-point would be desirable. This meta-analysis was an aggregate meta-analysis rather than an individual patient data level analysis. The latter offers several advantages<sup>30</sup> and the use of aggregate methods in this study is a limitation. The pooled results should be treated with caution as, although there was no statistical heterogeneity, there were differences between studies in the interventions used and the characteristics of the health-care systems in which they were implemented.

### **Implementation and future studies**

The results of this meta-analysis suggest that emergency departments should be encouraged to develop strategies to manage more patients in the community, using validated criteria to ensure these interventions are safe. Further interventional studies are required, particularly in respect of severity criteria other than the PSI that have not yet been tested for guiding outpatient management. Limited data are available for important end-points such as health related quality of life, symptom resolution and return to work and usual activities and further studies in this area are needed.

### **Conclusion**

Current evidence suggests that strategies to increase the proportion of patients treated in the community are safe, effective and acceptable to patients.

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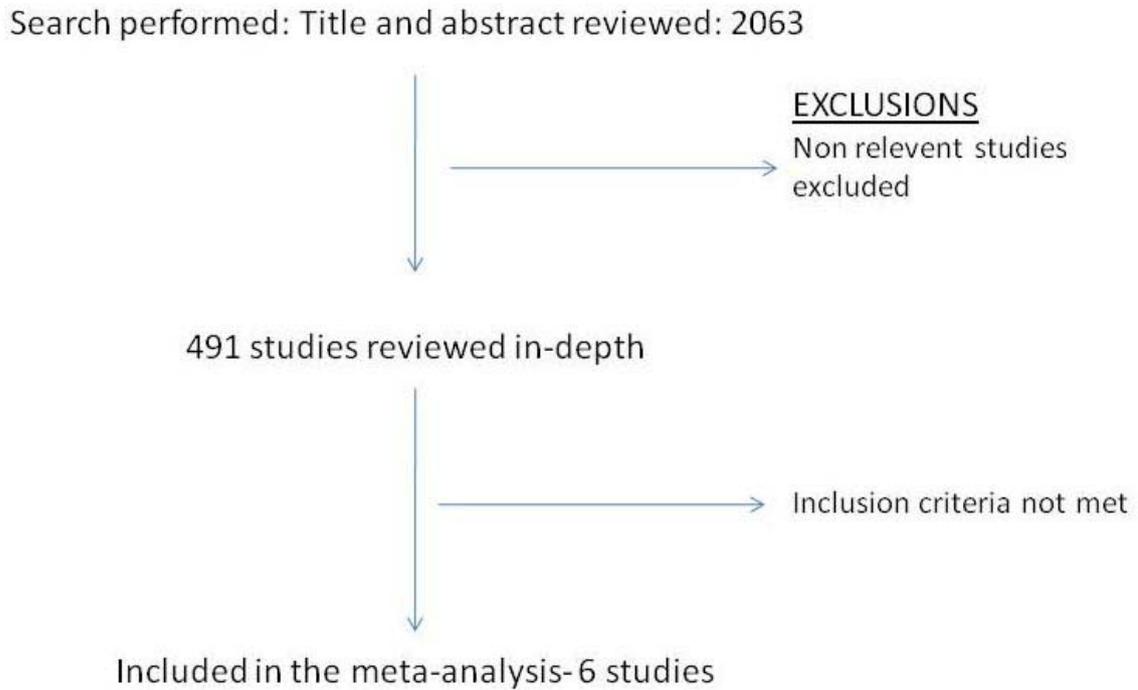
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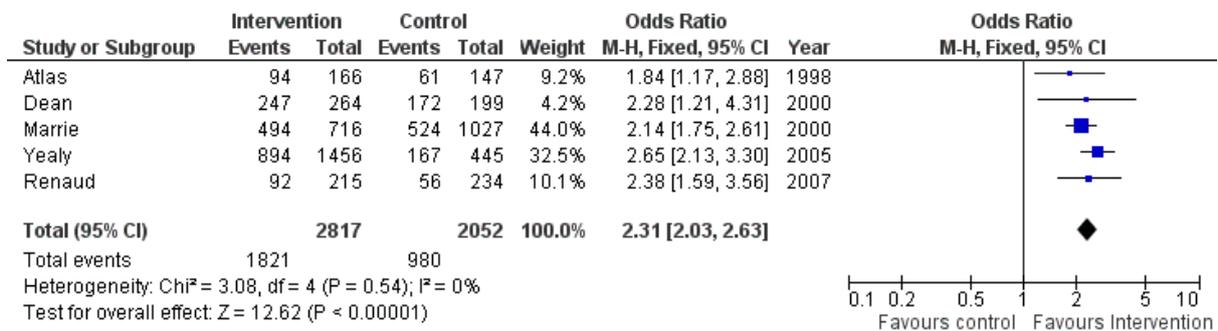
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Figure legends

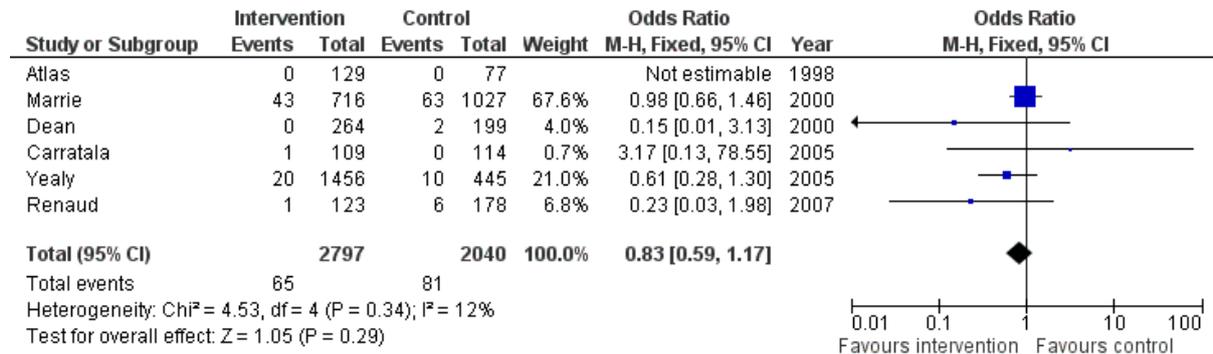
**Figure 1.** Process of literature review



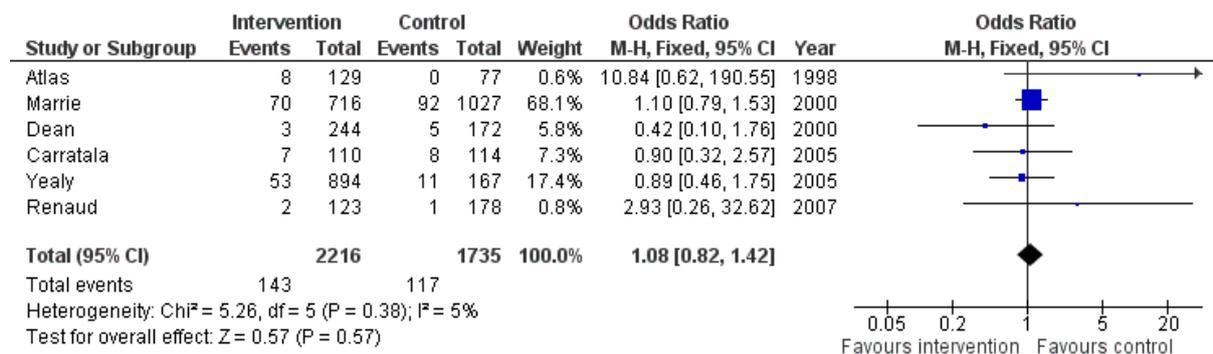
**Figure 2.** Forest plot- Proportion of patients treated in the community in the intervention and control cohorts. Events= patients treated in the community in each group.



**Figure 3.** Forest plot- mortality among low risk patients in the intervention and control cohorts following implementation of measures to increase outpatient management. Events= deaths in each group.



**Figure 4.** Forest plot- readmissions following hospital discharge in the intervention and control cohorts. Events= readmissions following hospital discharge.



**Figure 5.** Forest plot- Satisfaction with care in the intervention and control cohorts following implementation of measures to increase outpatient management. Events= patients reporting satisfaction with care.

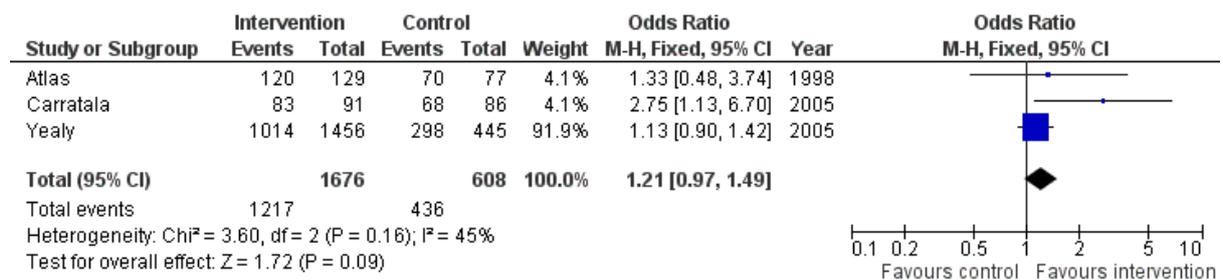






Table 1. Characteristics of included studies.

First author, initial	Year of publication	Setting	Design	Comparator 1 N	Comparator 2 N	Proportion of patients treated in the community	Readmission rate in each group	Mortality rates in each group
Atlas SJ <sup>10</sup>	1998	Single emergency department, Boston, MA USA	Prospective intervention with retrospective control group	Implementation of PSI based guideline N= 166	Retrospective control group prior to the intervention N= 147	56.6% vs. 41.5%	4.8% vs. 0%	No mortality in either group
Marrie TJ <sup>11</sup>	2000	19 Emergency departments, Canada	Implementation of a critical pathway with control hospitals	Critical pathway hospitals N= 716	Conventional management N= 1027	69% vs. 51%	0.7% increase in readmissions in the critical pathway group	0.1% higher in conventional management group
Dean NC <sup>12</sup>	2000	4 walk-in medical centres, Salt Lake City, Utah, USA	Implementation of a practice guideline with retrospective controls	Pneumonia practice guideline including site of care decision support N=264	Retrospective control cohort using conventional management N= 199	93.6% vs. 86.4%	1.1% vs. 2.5%	0% vs 1%
Carratala J <sup>13</sup>	2005	2 Emergency departments, Barcelona, Spain	Randomised controlled trial of outpatient versus inpatient management	Outpatient management N=109	Inpatient management N= 114	Not applicable*	6.3% vs. 7.0%	0.9% vs 0%
Yealy DM <sup>14</sup>	2005	32 Emergency departments, Pennsylvania and Connecticut, USA	Implementation of PSI based guidelines at low, moderate and high-intensity.	Moderate and high intensity implementation of guidelines N= 1456	Low intensity guideline implementation N= 445	61.4% vs. 37.5%	5.9% vs. 6.6%	1.4% vs. 2.3%
Renaud B <sup>15</sup>	2007	16 Emergency departments, France	Prospective observational study with control hospitals	Emergency departments using the PSI N= 215	Emergency departments not using the PSI N= 234	42.8% vs. 23.9%	1.6% vs. 0.6%	0.5% vs. 2.6%