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VALUE IN HEALTH

The Influence of Case Mix, Site Selection, and Methods Biases on Costs of Hospitalization For Acute Exacerbations of Chronic Obstructive Airways Disease and Lower Respiratory Tract Infections

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ABSTRACT

Objective: To compare costs of hospitalization for lower respiratory tract infection (LRTI) in patients who received antibiotics before admission to those who did not, and in patients with and without underlying chronic obstructive airways disease (COAD) or diabetes mellitus.

Methods: All hospitalizations in a population of 366,849 residents in Tayside Scotland from 1993 to 1994 were analyzed. Three groups of patients were identified by primary discharge diagnosis in 1993/94 and previous admissions from 1980 to 1992: 1) acute exacerbation of COAD; 2) LRTI plus a secondary diagnosis of COAD or previous admission with COAD; 3) LRTI but no secondary COAD or previous admission with COAD. Setting specific costs were applied (e.g., general medicine, intensive care, geriatrics). Dispensed antibiotic prescribing in the 28 days before admission was identified from all community pharmacies. Nonparametric statistical tests were used.

Results: Patients with COAD were more likely to have received antibiotics before admission: COAD (n = 893) 49%; COAD + LRTI (n = 316) 43%; LRTI only (n = 822) 33%. Patients who received antibiotics before admission had lower hospital costs than patients who did not. Mean total costs per admission: COAD £1604 versus £1625 (p = .5); COAD + LRTI £2281 versus £2297 (p = .5); LRTI only £2365 versus £3233; (p = .009). Increasing age and diabetes mellitus were associated with higher hospital costs in all three groups.

Conclusion: Economic models of the value of preventing hospital admissions for COAD or LRTI will be subject to case mix bias unless they adjust for age, community antibiotic use, and comorbidity.

Introduction

Lower respiratory tract infection (LRTI) is the most common community-acquired infection causing admission to hospital in the UK [1]. These infections are usually treated with parenteral antibiotics but parenteral administration is both more costly and more dangerous than oral administration [2]. Oral treatment is as effective as parenteral treatment, provided that the drugs selected are effective against the pathogens that cause LRTI and are well absorbed after oral administration [3].

If LRTI can be treated with oral therapy in hospitals, it follows that hospitalization might be avoided by improving the selection of antibiotic therapy in the community [4], or by improving compliance with the drugs prescribed [5]. Other interventions such as vaccination may also prevent hospitalization for LRTI [6–9].

The aim of the present study was to provide information about the costs of hospitalization for community-acquired LRTI to be used in economic modeling of the cost-effectiveness of interventions that might prevent hospitalization, which is the major cost driver in most healthcare systems. There are three common sources of bias in healthcare costs: site selection, method of cost allocation, and case mix [10]. This study was designed to answer two specific questions about case mix:

1. Do patients who receive antibiotic treatment before hospital admission have different hospital costs from those who do not receive treatment?

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2. What is the effect of comorbidity with chronic obstructive airways disease (COAD) or diabetes on hospital costs for patients admitted with lower respiratory tract infection?

Methods

Study Population

All residents in Scotland who register with a primary care doctor are assigned a unique community health number that is then used to index all of their primary and secondary healthcare records. The subjects for the analysis were drawn from the population (n = 366,849) who were known to be resident in Tayside from January 1989 to December 1994. The analysis was restricted to adults aged 40–99 who had emergency admissions to any of the hospitals providing acute secondary care in Tayside (Fig. 1).

Organization of Hospital Care in Tayside. There are three providers of acute secondary care in Tayside, located in Dundee, Perth, and Brechin. Only in Dundee are there specialist communicable diseases and respiratory wards.

Data Sources

Hospital discharge data were obtained from the Scottish Morbidity Record database 1 (SMR1) [11]. This database records information about each hospital discharge from acute hospitals, including: date and source of the admission (from the community or another hospital), the hospital, the specialty, up to six diagnostic codes, and the date and destination at discharge (i.e., died or discharged to the community or another hospital). From 1989 to 1996 the diagnostic codes in SMR1 are from the International Classification of Disease, version 9 (ICD9) and are further classified into a primary code (a single code giving the primary reason for hospitalization) and secondary codes (all remaining codes) [11]. Community drug utilization data were obtained from the Tayside Scripts Facility, which contains data about drugs dispensed from community pharmacies in Tayside from 1989 [11]. The TSF database currently holds records for all antibiotic prescriptions dispensed from 1993 to 1995 inclusive. Dates of death were obtained from the Tayside Community Health Index database, which contains information about all subjects registered with primary care practices in Tayside [11].

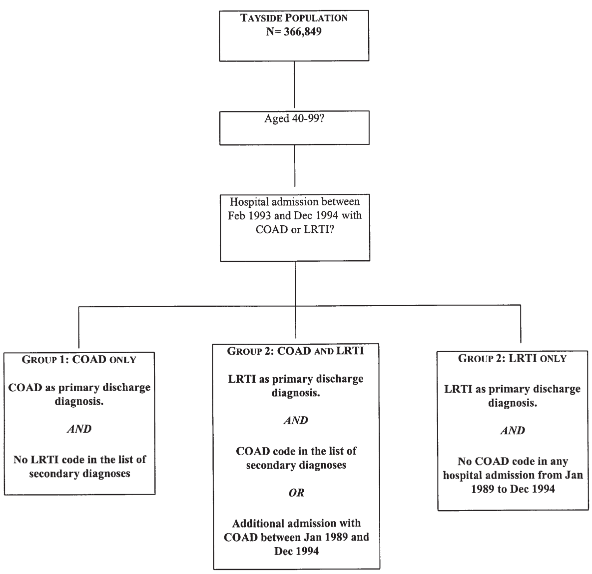

Figure 1 Flow chart to show the derivation of the study population.

Identification of Patients and Comorbidities

Lower Respiratory Tract Infection. LRTI was identified from the SMR1 database by ICD9 codes 466 (acute bronchitis); 480–486 and 487 A (community acquired pneumonia); 511 (bacterial pleurisy); 513 (abscess of the lung); and 514 (hypostatic pneumonia).

Chronic Obstructive Airways Disease. COAD was identified from the SMR1 database by ICD9 codes 491 (chronic bronchitis) and 496 (other specified chronic obstructive airways disease).

Diabetes Mellitus. Diabetes mellitus was ascertained from the Diabetes Audit and Research in Tayside Scotland (DARTS) database [12]. DARTS integrates data from multiple sources (inpatient episodes, outpatient clinic records, laboratory investigations, dispensed prescribing, and community eye screening) to compile a register of all diabetics in Tayside. The DARTS register has been validated by comparison with primary and secondary care source records [12].

Classification of Patients

All hospitalizations in the study population were identified from February 1993 to December 1994 (January 1993 was used as a screening period for antibiotic treatment before admission). In addition, hospitalization from 1989 to 1993 was used to identify admissions for COAD before the start of the study period.

Hospitalizations eligible for analysis between February 1993 and December 1994 were classified into three groups:

Group 1: Acute exacerbations of COAD. These patients had one of the COAD codes as the primary diagnosis and did not have any LRTI code in the list of secondary diagnoses.

Group 2: Lower respiratory tract infection and COAD. These patients had one of the LRTI codes as the primary diagnosis but either had COAD as a secondary diagnosis for the same hospitalization, or had a previous hospitalization with COAD as a primary or secondary diagnosis. Patients with COAD as a primary diagnosis and LRTI as a secondary diagnosis were also included in this group.

Group 3: Lower respiratory tract infection only. These patients had one of the LRTI codes as the primary diagnosis and had no hospitalization from 1989 to 1994 with COAD as a primary or secondary code.

Prescribing Before Hospital Admission

Antibacterial drugs were identified from Chapter 5.1 of the British National Formulary, September 1995. All oral antibacterials were included with the exception of 5.1.11 (metronidazole or tinidazole, drugs used only for treatment of infections caused by protozoa or anaerobic bacteria) and 5.1.13 (fosfomycin, nitrofurantoin, or hexamine hippurate, drugs used only for urinary tract infections). Exposure to oral antibiotics within 28 days before admission to hospital was determined from the TSF database.

Hospital Costs

Estimation of costs of hospitalization was based on analysis of length of stay in specific specialties and hospitals. Information about hospital costs in the financial year 1993–94 was obtained from the Information and Statistics Division [13]. This publication includes detailed costs by specialty for every hospital in Scotland. Costs are divided into direct patient care (staff costs for medical, nursing or professions allied to medicine, drugs, investigations, operations and other therapeutic procedures) and allocated (management, hotel or other overheads). The perspective of providers or purchasers of secondary care is considered for the economic analysis.

Mortality. Deaths of any citizen of Tayside from any cause are registered on the Tayside Community Health database [11]. Data were available up to the end of July 1997, providing a minimum of two years mortality for all patients from date of entry to the study.

Episodes and Periods of Care. Each admission to a single specialty was termed an episode of care. Multiple consecutive episodes of care were termed a period of care. The criteria for linking episodes of care were the interval between the episodes (<24 hours) and the coding for source of admission and destination at discharge. The first episode always began with admission from the community and the last episode always ended with discharge to the community. However, within a period of care patients may have been transferred between two or more clinical specialties.

All statistical analyses were based on the cost per period of care. This was the sum of costs of consecutive episodes of care in different hospital settings (e.g., general medical, geriatric long stay). The total cost per period of care was calculated from the number of inpatient days and the average cost per day for each specific hospital setting. To investigate the potential confounding effect of mortality in hospital on length of hospital stay, we compared the median duration of periods of care which ended in the death of the patient to those periods from which the patient was discharged alive.

Base Case and Sensitivity Analysis for Site Selection and Methods Bias. The base case calculated the cost per period of care from the total cost per hospital day (direct patient care plus allocated costs) for each specific hospital setting in Tayside. Site selection bias was investigated by substituting the average total cost per hospital day for all equivalent hospital settings in Scotland for the Tayside hospital cost. Methods bias was investigated by substituting direct patient care costs for total cost per hospital day.

Statistical Analysis

The same patient could appear in Groups 1 and 2 if they had separate admissions with COAD alone and COAD plus LRTI during the study period. In contrast, patients in Group 3 could not appear in either Group 1 or 2 because patients were excluded from Group 3 if they had a COAD code in any admission from 1989 to 1994. Comparisons between groups were therefore only made for Group 1 versus Group 3 and Group 2 versus Group 3.

Non-parametric tests were used throughout. Within-group comparisons for the effect of single variables (antibiotics and diabetes) on cost were made with the Wilcoxon test. Within-group tests of the effect of age on cost were made with the Kruskal–Wallis test. Between-group comparisons of costs controlling for the effects of other variables were made with the adjusted Wilcoxon test. Between-cohort comparisons of mortality were made with a proportional hazards model and Kaplan Meier plots.

Results

In comparison to patients with COAD (Groups 1 and 2), patients with LRTI only (Group 3) were less likely to receive antibiotics before admission, more likely to have diabetes mellitus, and had a different distribution of age and episodes of care (Table 1). The median age was highest in Group 3 (76 vs. 74 for Group 2 and 70 for Group 1), but Group 3 also had the highest proportion of patients less than 60 years old (Table 1). Patients in Group 3 were less likely to have episodes of care in respiratory medicine, but more likely to have episodes in the intensive care unit, geriatric assessment, and other specialties (Table 1).

Death in hospital occurred much less frequently in Group 1 compared with Groups 2 or 3. In Group 1, only 6% of the periods of care ended with death in hospital, compared to 40% for Group 2 and 47% for Group 3 (Table 1). In Group 3 patients who died in hospital had significantly longer length of stay than patients who were discharged alive (median 14 days vs. 9 days, 95% CI of difference between medians 2–6 days; $p < .0001$ Mann Whitney test). However there was no significant difference in the other two groups (12 days vs. 10 days in Group 2 and 8 days vs. 9 days in Group 1; $p > .2$ both groups). The rate ratio for mortality in the LRTI only cohort (Group 3) versus the COAD only cohort (Group 1) was 2.0 (95% CI 1.74–2.33) unadjusted for age or sex and 1.99 (95% CI 1.72–2.31) adjusted for age and sex.

The cost of hospitalization was lower in patients who had antibiotics before admission in all three groups, but the difference was only statistically significant within Group 3 (Table 2). Costs of hospitalization were higher for patients with diabetes mellitus within all three groups but the difference was only statistically significant within Group 3 (Table 2). Costs of hospitalization increased significantly with age in all three groups (Table 2).

Costs of hospitalization were highest in Group 3 (Table 3). The statistical significance of the difference between Groups 1 and 3 was not changed by adjustment for antibiotics, diabetes, and age, whereas adjustment reduced the statistical significance of the difference between Groups 2 and 3 (Table 3). The results were sensitive to site selection bias. Use of national costs instead of local costs increased the costs in all three groups and reduced the differences in costs between groups. Differences between Groups 3 and 1 were no longer statistically significant with national costs (Table 4). The comparisons between groups were not sensitive to methods bias. Use of direct patient

Table 1 Information about case mix

	Group 1: Acute exacerbation of COAD only (n = 893)		Group 2: Lower respiratory tract infection and COAD (n = 316)		Group 3: Lower respiratory tract infection only (n = 822)	
	Number	%	Number	%	Number	%
Received antibiotics before admission	436	49%	136	43%	275	34%
Diabetes mellitus	74	8%	30	9%	84	10%
Age						
<60	129	14%	38	12%	136	17%
61–70	319	36%	77	24%	127	15%
71–80	315	35%	126	40%	293	36%
>80	130	15%	75	24%	266	32%
Died in hospital	57	6%	126	40%	384	47%
Total episodes of care	1049	100%	396	100%	1074	100%
Distribution of episodes of care:						
General medicine	379	36%	142	36%	448	42%
Respiratory medicine	544	52%	165	42%	213	20%
Communicable diseases	27	3%	11	3%	32	3%
Intensive care unit	24	2%	12	3%	56	5%
Geriatric assessment	42	4%	45	11%	190	18%
Geriatric long stay	4	0%	6	2%	37	3%
Other	29	3%	15	4%	98	9%

Table 2 Influence of case mix variables on mean hospital cost of periods of care (£) within each group. The hospital cost is the total cost (direct patient care cost plus allocated cost).

	Group 1: COAD only	Group 2: COAD and LRTI	Group 3: LRTI only
Antibiotic	£1604	£2281	£2365
No antibiotic	£1625	£2297	£3233
P (Wilcoxon)	0.49	0.51	0.009
Diabetic	£1660	£2808	£3564
Non-diabetic	£1611	£2236	£2872
P (Wilcoxon)	0.18	0.46	0.0365
Age:			
<60	£1281	£1059	£2276
61–70	£1597	£2265	£2334
71–80	£1679	£2509	£3298
>80	£1834	£2573	£3181
P (Kruskal-Wallis)	0.0001	0.0008	0.0001

care costs instead of total costs reduced the mean cost in all three groups but had little effect on the statistical significance of the differences between groups (Table 4).

Discussion

Case Mix Bias

There were differences in case mix between the groups (Table 1) and each of the case mix variables had a significant effect on costs of hospitalization in at least one of the groups (Table 2). Age was the most important case mix variable, in that increasing age was associated with a statistically significant increase in costs of hospitalization in all groups (Table 2). There is ample evidence to show the importance of adjusting for age when estimating the costs of hospital-acquired infection [14–16]. Age is also an important determinant of both mortality and length of stay for patients with community-acquired pneumonia [17]. It is therefore not surprising that our results show that age is an important determinant of the costs of hospitalization in all three cohorts.

Mortality was markedly different between the groups, both in hospital and following hospital discharge. Monthly mortality in both the LRTI only and LRTI + COAD groups was significantly higher than in the COAD only group in each of the first four months after admission to hospital (Fig. 2). Mortality from community-acquired pneumonia is usually estimated to be about 20% [18,19]. Our study was confined to patients over the age of 40, which would increase mortality because 97% of deaths from pneumonia occur in patients over the age of 65 [17]. Furthermore, even when reporting outcome of pneumonia in the elderly, previous studies have excluded patients with rapidly fatal underlying disease, excluded deaths that were not thought to be directly due to pneumonia, and

Table 3 Mean hospital costs (£) per period of care and per patient for episodes of care by specialty. The mean cost per patient for episodes of care is the total cost of all episodes of care divided by the number of people in the group. Statistical analysis is provided both unadjusted and adjusted for case mix variables. The hospital cost is the total cost (direct patient care cost plus allocated cost).

	Mean cost (£)			P (unadjusted)		P (controlling for antibiotics, diabetes and age)	
	Group 1: COAD only	Group 2: COAD and LRTI	Group 3: LRTI only	Gp 1 vs 3	Gp 2 vs 3	Gp 1 vs 3	Gp 2 vs 3
Mean cost per period of care	1615	2290	2943	0.001	0.086	0.001	0.271
Mean cost per patient of episodes of care by specialty							
General medicine	542	641	773	0.001	0.002	0.001	0.071
Respiratory medicine	649	638	283	0.001	0.001	0.001	0.001
Infectious diseases	138	191	145	0.333	0.752	0.712	0.210
Intensive Care Unit	73	212	295	0.001	0.058	0.018	0.461
Geriatric Assessment	126	456	753	0.001	0.001	0.001	0.009
Geriatric Long Stay	6	35	268	0.001	0.036	0.001	0.154
All Other Units	81	118	425	0.001	0.001	0.001	0.009

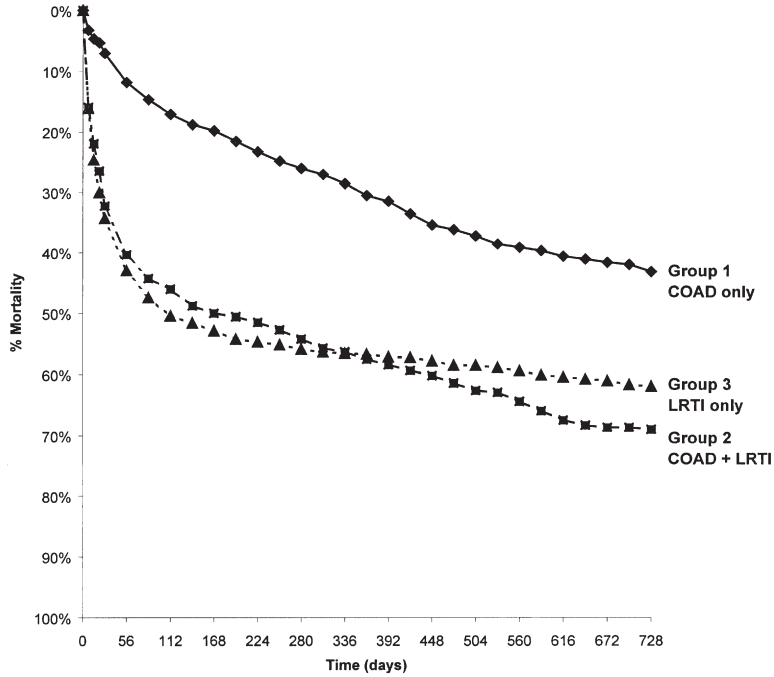

Figure 2 Mortality from all causes in the two years following admission of patients to hospital with COAD or LRTI.

restricted follow up to the acute hospital setting [17,20]. Our results show that pneumonia has an impact on total mortality for at least four months after diagnosis (Fig. 2).

Prescription of antibiotics before hospitalization was associated with lower costs of hospitalization in all three groups, and particularly those with LRTI only. Treatment with antibiotics before admission could have either a positive or negative confounding effect on length of hospital stay. Patients who are hospitalized with lower respiratory tract infections caused by beta-lactamase–producing organisms are more likely to have received antibiotics before admission [21]. Our local hospital antibiotic policy follows national guidelines and recommends amoxycillin alone for acute exacerbations of COAD and amoxycillin plus erythromycin for pneumonia, with or without COAD [22]. We have previously shown that patients with acute exacerbations of COAD have a lower rate of response to amoxycillin if they have received antibiotics before admission [22]. Thus, antibiotic treatment before hospitalization could be associated with a longer duration of hospitalization if it is associated with a higher probability of infection with antibiotic resistant organisms, and hence of failure to respond to first line antibiotic treatment. Conversely, antibiotic treatment before hospital admission was associated with reduced hospital mortality from community-acquired pneumonia in a recent study from Italy [23]. This result could be due to a beneficial effect of antibiotic treatment before hospital admission. However, it is more likely that community antibiotic treatment acts as a marker for patients with less severe illness, because those with severe illness are admitted straight

Table 4 Sensitivity of between group comparisons to methods bias (total costs vs. direct patient care costs) and site selection bias (local costs vs. national costs). The costs are the mean cost per period of care (£).

				P (controlling for antibiotics, diabetes and age)	
	Group 1: COAD only	Group 2: COAD and LRTI	Group 3: LRTI only	Gp 1 vs 3	Gp 2 vs 3
Default: Total costs (direct patient care+allocated), local	1615	2290	2943	0.001	0.271
Total costs, national	2071	2690	3054	0.105	0.980
Direct patient care costs only, local	927	1315	1661	0.001	0.339
Direct patient care costs, national	1355	1752	1934	0.151	0.995

to hospital. In the present study community antibiotic treatment was associated with shorter duration of hospital stay, particularly in patients with LRTI alone.

Comorbidity can also have either a positive or negative confounding effect on hospital length of stay [24]. This study investigated the possible confounding effect of five selected secondary discharge diagnoses on additional length of hospital stay due to hospital acquired infection. The five secondary diagnoses were pulmonary embolism, renal failure, obesity, diabetes mellitus, and chronic lung disease. All of these diagnoses had a negative confounding effect in patients at low risk of infection but a positive confounding effect in patients at high risk of infection. Previous studies had assumed that underlying chronic problems would always have a positive confounding effect on length of hospital stay. The authors postulated that patients who also had diabetes mellitus or chronic lung disease might be admitted to hospital with mild acute problems, whereas patients without underlying disease would only be admitted with severe acute problems [24]. In the present study diabetes mellitus had a positive confounding effect on length of stay in all three groups, whereas chronic lung disease had a negative confounding effect in that length of stay and costs were lower in Group 2 than Group 3.

Site Selection Bias

Comparison of costs of hospitalization between countries reveals striking differences. For example the costs of hospitalization for invasive infections caused by Haemophilus influenzae Type B have been shown to vary almost tenfold across seven countries. In ascending order, the costs per case were $1,121 in Chile, $2,608 in Israel, $4,298 in the UK, $4,767 in Finland, $5,048 in Switzerland, $5,495 in Australia, and $10,000 in the USA [6]. Our results are influenced by site selection in that differences between Group 1 (COAD only) and Group 3 (LRTI only) were no longer statistically significant when national costs were substituted for local costs (Table 4). The most likely explanation is the relatively low local costs of Respiratory Medicine (£97 per day compared with a national average of £158 per day, Table 5). Respiratory Medicine accounted for a much higher proportion of periods of care in Group 1 compared with Group 3 (52% vs. 20%; Table 1).

Methods Bias

Much of the literature on costs of hospitalization is concerned with the economic impact of earlier discharge from hospital. In this context, use of average costs is misleading, particularly for surgical patients [25]. This is because the distribution of hospital costs is uneven over time and is usually higher in the first few days of an admission [26]. However, the aim of our study was to provide estimates of the value of preventing a hospital admission, rather than shortening length of hospital stay. In this context the use of average costs may be a reasonable estimate of the marginal cost per case.

Our estimates of the cost per period of care are substantially higher than the estimates of the cost per case provided by Information and Statistics Division (ISD) [27]. For example, our cost per period of care ranged from £1611 for a nondiabetic patient with COAD to £3564 for a diabetic patient with LRTI (Table 2). The ISD's quoted average cost per case for General Medicine and Respiratory Medicine in Dundee are only £1219 and £1527, respectively [27]. This is because the ISD figures are based on the average cost of an episode of care, whereas our data show that periods of care are often composed of more than one episode of care in different settings (Table 1).

The contribution of direct patient care to total costs was not constant across specialties at the same site, or between specialties on different sites (Table 5). In general direct patient care accounted

Table 5 Costs per day (£) by specialty and site. Data from Information and Statistics Division [13]

	Local, Dundee			Local, Perth			Local, Angus			National		
	Total	Direct	Ratio*	Total	Direct	Ratio*	Total	Direct	Ratio*	Total	Direct	Ratio*
General medicine	175	120	69%	150	75	50%	143	85	59%	178	110	62%
Respiratory	97	54	56%	NA	NA	NA	NA	NA	NA	158	102	65%
Infectious diseases	447	304	68%	NA	NA	NA	NA	NA	NA	310	196	63%
Intensive care	901	624	69%	859	537	63%	244	168	69%	774	574	74%
Geriatric assessment	145	88	61%	122	52	43%	108	52	48%	120	69	58%
Geriatric long stay	79	39	49%	120	52	43%	130	78	60%	98	52	53%
Other	243	158	65%	304	203	67%	231	158	68%	219	141	64%

*Ratio = Direct costs/total costs

for a higher proportion of total costs in Intensive Care than in Geriatric Long Stay (74% vs. 53% for National figures). Nonetheless, substituting direct patient care costs for total costs did not influence the conclusions of this study (Table 4).

Limitations of the Study

Ascertainment of COAD was based on hospital discharge diagnoses from 1980 to 1994. The population of Tayside is relatively stable in that <5% of the population move in or out of the area in a year [11]. Nonetheless, the use of previous hospital discharge codes for ascertainment may have caused some misclassification bias if patients had never been admitted with COAD in the past, or had been admitted previously to a hospital outside the Tayside area. Either of these possibilities could result in patients with COAD being misclassified in the LRTI-only cohort. However, this would bias the results towards the null hypothesis (that there is no difference between Group 1 (COAD only) and Group 3 (LRTI only)).

The indication for antibiotic prescription in the 28 days before hospital admission is not known. The finding of lower costs in patients who received antibiotics before admission may be explained by patients with less severe illness being treated in the community before admission to hospital. If this is true then inclusion of data about antibiotic prescribing for indications other than respiratory tract infection would bias the results towards the null hypothesis (that there is no influence of community antibiotic treatment on costs of hospitalization).

An intervention that does prevent hospital admissions is unlikely to result in equivalent cash savings to the hospital and will not necessarily improve patient throughput [28]. Moreover, such an intervention is likely to increase costs to the primary care sector as well as to the patient's family or carergivers and may result in loss of welfare to the patient [28]. Consequently our results provide an estimate of the maximum value to the secondary care services of preventing a hospital admission with COAD or LRTI.

Implications of the Study

Case mix was the most important source of bias and our results suggest that a wide range of costs (£1281–£3564) should be used in sensitivity analysis of the value of preventing hospitalization with COAD or LRTI. Within the UK site selection is likely to be a much less important source of bias and any variation is likely to be encompassed within the range of costs used to allow for case mix bias. However, site selection bias is likely to be more important for international economic models [6]. Overall our data are likely to overestimate the marginal cost of hospitalization with COAD or LRTI. These data may be used in preliminary economic modeling of the impact of interventions that reduce hospitalization. However, randomized trials will be required to minimize bias and provide convincing evidence of cost-effectiveness.

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