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Powell, N, Honeyford, K and Sandoe, J orcid.org/0000-0003-0193-8677 (2020) Impact of penicillin allergy records on antibiotic costs and patient length of hospital stay: a single centre observational retrospective cohort. Journal of Hospital Infection, 106 (1). pp. 35-42. ISSN 0195-6701

https://doi.org/10.1016/j.jhin.2020.05.042

Impact of penicillin allergy records on antibiotic costs and patient length of hospital stay: a single centre observational retrospective cohort.

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Abstract

Introduction

Patients with penicillin allergy records are usually prescribed non-penicillin antibiotics and have worse health outcomes. This study explored the impact of penicillin allergy records on antibiotic treatment costs and on patient length of stay.

Methods

Patients prescribed a systemic antibacterial agent between April 2016 and March 2018 in a 750 bed English hospital were included. The following data were extracted for each patient hospital spell; age, sex, co-morbidity, infection treated, antibiotic usage (DDD), hospital length of stay, and penicillin allergy status.

Multivariable log-linear modelling was used to determine the association between patients labelled as penicillin allergic and total antibiotic costs and length of stay.

Using the above models, we estimated the potential reduction in total costs and hospital bed days of 'de-labelling' patients with penicillin allergy records.

Results

Penicillin allergy records were present in 14.3% of hospital admissions and were associated with an increase in non-penicillin antibiotic prescribing, a 28.4% increase in antibiotic costs and 5.5% longer length of hospital stay, relative to patients without a penicillin allergy record. Patients with penicillin allergy records accounted for an excess antibiotic spend of £10,637 (2.61% of annual antibiotic drug spend) and 3,522 excess bed days (3.87% of annual bed days). De-labelling 50% of patients with a self-reported allergy record would save an estimated £5,501 in antibiotic costs and £503,932 through reduced excess bed days

Conclusion

De-labelling patients with a self-reported allergy record has potential to reduce antibiotic costs but its biggest cost impact is via reduction in excess bed days.

Introduction

Six percent of the general population [1] and between 15-20% of hospital inpatients [2, 3] have a penicillin allergy record. Penicillin antibiotics are first-line treatment for many common hospital infections, but patients with penicillin allergy records are usually prescribed second line antibiotics; a practice associated with negative patient and healthcare system outcomes including treatment failure [1, 4, 5], and increased risks of side effects, [5] infections with resistant bacteria and *Clostridioides (Clostridium) difficile*-associated diarrhoea. [1, 6] Patients with penicillin allergy records also experience increased length of hospital stay, [7]

and increased antibiotic treatment costs. [8, 9, 10] These associated risks are avoidable in 95% of patients with a reported penicillin allergy as studies show that, despite the record, they are able to tolerate penicillin after allergy assessment. [11] Removing a penicillin allergy record from a patient's medical record following allergy assessment and confirmation that they are able to tolerate penicillin, is called de-labelling. Current allergy services in the UK and worldwide are insufficient to undertake the necessary testing to identify all the patients with penicillin allergy records who are not allergic and able to safely take penicillin.[11] Some researchers have conducted inpatient de-labelling studies, delivered without direct allergy specialist input and instead a pharmacist or a hospital doctor carried out the de-labelling, and shown that it is possible to safely de-label between 24 and 80% of patients with penicillin allergy records through taking a thorough allergy history and offering an oral challenge dose if required. [12, 13, 14, 15] These studies used direct oral penicillin challenge tests without prior skin testing in low risk patients, forgoing the need for skin allergy testing.

Despite the negative consequences of penicillin allergy records and the well described impact of de-labelling on improving antibiotic stewardship there is little evidence of routine de-labelling as part of patient pathways in the UK.[16] We are not aware of any national UK guidance that supports penicillin allergy de-labelling as part of antibiotic stewardship programmes. Perhaps this is because the majority of the studies looking at health-system impact of penicillin allergy records have been done outside the UK.

This study sets out to determine the impact of penicillin allergy records on antibiotic treatment costs and on patient length of stay, and to quantify the potential to reduce cost and patient length of stay through de-labelling a proportion of patients with incorrect penicillin allergy records.

Methods

Ethics

This study was categorised as a service evaluation, not requiring NHS Research Ethics Committee approval. The patient data were used in accordance with local NHS Trust Policy and in line with general data protection regulations.

Design

All patients who were prescribed antibiotics during the study period were included. Patients with a penicillin allergy or sensitivity record in their electronic health records were considered "allergic". All inpatient spells were included.

Setting

Study was conducted in a district general hospital with 750 inpatient beds. The trust serves a local population of 430,000 people, a figure that can increase significantly during holiday seasons.

Participants

Inclusion criteria: any inpatient (adult or child) prescribed a systemic antibacterial agent(s) (BNF chapter 5.1) between April 2016 and March 2018 inclusive was eligible. Exclusion criteria, children less than 1 year of age and adults over 100 years of age were excluded to reduce the risk of unintentional identification.

Data sources and variables

Data were extracted from the electronic prescribing and medication administration system (EPMA; JAC Computer Services). Variables included: age, sex, co-morbidity (International Statistical Classification of

Diseases and Related Health Problems 10th Revision (ICD-10) [17] administrative code, see supplementary material for codes used), infection treated during the inpatient stay (ICD-10) inpatient spell administrative diagnostic code, see supplementary material for codes used), name of antibiotic (s), inpatient and discharge antibiotic usage in defined daily doses DDD, [18] hospital length of stay, whether the patients had a penicillin allergy record, whether the patient had a penicillin sensitivity recorded (combined to give one penicillin allergy record). Patient allergy and sensitivity status is manually entered to the patient's EPMA record, this information is retained within the EPMA system between inpatient spells.

Antibiotic DDD were calculated per patient spell were used to calculate treatment costs using local antibiotic prices.

Statistical methods

The unit for analysis was a spell (period of continuous hospital stay) during which antibiotics were prescribed at some point during the stay. For each spell, the total antibiotic costs were determined using local antibiotic costs. Length of spell was calculated in days and fractions of days, based on time and date of admission and discharge from the hospital. Any identified comorbidities and infections coded during the spell were included in the analysis. Initial descriptive analyses of patient characteristics for spells, compared patients with and without recorded penicillin allergy. Differences were assessed using Chi-squared and Mann-Whitney tests for continuous data. Antibiotics were grouped by antibiotic class. Differences in prescribing between patients with and without penicillin "allergy" records were compared using Chi-squared tests.

Both costs and length of stay were highly skewed, we therefore used a pre-specified log-linear regression model to investigate the relationship between penicillin allergy records and antibiotic class prescribed, total antibiotic costs and total length of stay, taking account of potential confounders: age, gender, co-morbidities and the infection being treated. Sensitivity analysis showed that taking into account of clustering at patient level had no impact on results; we therefore used models treating each hospital stay as independent observations.

As there was evidence that costs were different for the two years of the data, we included a binary variable for year of study in the models.

The results of the multivariable log-linear model are log(outcome) scale coefficients which are the actual results of the linear regression on log(COSTS). This was then be interpreted as an 'impact' which reflected the multiplicative association of an increase in one unit of that predictor variable on the central tendency of the outcome. When reporting results we focused on the outcome scale, which was easier to interpret. We also reported the coefficients on the log(outcome) scale for clarity.

In order to estimate the potential reduction in total costs and hospital bed days of 'de-labelling' patients with penicillin allergy records we estimated the total costs and bed days based on the coefficients derived from the models. Twenty-five percent of spells occurring in penicillin allergic patients were randomly selected and recoded in the dataset as no longer penicillin allergic, total costs and hospital bed days were then calculated based on the coefficients derived from the models and the modified dataset. This process was repeated for de-labelling 50%, 75% and 100%.

Results

Between April 2016 and March 2018, 38,816 inpatients were treated with antibiotics, 5,549 (14.3%) of which had a penicillin allergy record. These patients had antibiotics prescribed during 53,408 spells, 8,423 (15.8%) involving patients with a penicillin allergy record. i.e. there were on average 1.4 spells per patient during which an antibiotic was prescribed.

Patients from spells involving penicillin allergic patients were more likely to be older, female and with comorbidities; asthma, coronary heart disease, chronic kidney disease, chronic obstructive pulmonary disease and diabetes. The most common infections in these spells were lower respiratory tract infection and "systemic infections not grouped elsewhere" (21.5% and 12.5% respectively). Lower respiratory tract infection, "systematic infections not grouped elsewhere", bone and joint infections, skin and skin structure infections, intra-abdominal infections, and urinary tract infections were all more prevalent in patients with a penicillin allergy record, as summarised in Table 1.

Table 1 goes here

Table 2 summarises the outcome by patient group and year.

Total hospital antibiotic costs, using local prices for antibiotics, for the 53,408 spells over two years was £930,290. A mean cost per spell of £17.42. Costs for spells in patients with a penicillin allergy record were significantly higher than those with no record. Total costs and costs per spell were also significantly higher in 2016/17 than 2017/18, univariate analysis using Mann-Whitney test, $p<0.01$ in both cases. Costs were highly skewed by small numbers of patients whose antibiotic costs were very high. In addition, the analysis was confounded by infection type. For example, there were proportionally more bone and joint infections in patients with a penicillin allergy record, these infections often require more prolonged therapy, with broader spectrum agents like glycopeptides.

Table 2 goes here

Table 3 goes here

Table 3 shows the different antibiotics administered to patients over the two year period of study. The penicillin antibiotic group were the most commonly administered antibiotics to patients with no recorded allergy, with penicillin administered in over 70% of patient spells. Aminoglycosides were the most commonly administered antibiotics to penicillin allergic patients, but were administered in approximately 40% of patient spells in both groups. There were significant differences for all other antibiotic classes. Non-penicillin allergic patients were more likely to receive metronidazole and cephalosporins. In contrast, penicillin allergic patients had higher odds of receiving clindamycin carbapenems, glycopeptides, macrolides, quinolones and tetracyclines.

Association between penicillin allergy and hospital encounter antibiotic costs.

An un-adjusted log-linear model suggested that a penicillin allergy record was associated with a 30.5% (95% CI: 17.4-45.4%) increase in costs of antibiotic therapy per patient per hospital spell when compared to patients with no penicillin allergy record. After adjusting for age, comorbidities and infection type, an adjusted log-linear model suggested that there was still a significant impact of penicillin allergy records on antibiotic cost of 28.4% (95% CI: 19.7-37.8%). Table 4.

Table 4 goes here

Association between penicillin allergy and hospital length of stay.

An un-adjusted log-linear model suggested that the impact of penicillin allergy was an increase in length of stay per patient per hospital spell of 17.0% (95% CI: 13.0-21.1%) compared to patients with no known penicillin allergy. After adjusting for patient factors, age, comorbidities and infection type, an adjusted log-linear model suggested that there was still a significant impact of penicillin allergy on hospital length of stay, but it had reduced to 5.5% (95% CI: 2.5-8.6%). The detailed results of the adjusted multivariable log-linear model are presented in Table 5.

Table 5 goes here

Potential benefits of de-labelling penicillin allergic or sensitive patients

Table 6 goes here

We used our model to estimate the cost of de-labelling penicillin allergic patients. For an individual patient the saving was estimated to be £2.61. Based on the model and the two years of data we estimate a potential saving of £5501 in one year, by de-labelling 50% of patients who were labelled as penicillin allergic and admitted to hospital in that year. De-labelling 50% of all penicillin allergic patients could save an estimated 1761.2 bed days, 1.9% of total inpatient bed days

Discussion

Key findings

Penicillin allergy records were present in 14.3% of hospital admissions and were associated with an increase in non-penicillin antibiotic prescribing, a 28.4% increase in antibiotic costs and 5.5% longer length of hospital stay, relative to patients without a penicillin allergy record. Patients with penicillin allergy records accounted for an estimated annual excess antibiotic spend of £10,637 (2.61% of annual antibiotic drug spend) and 3,522 excess bed days (3.87% of annual bed days). De-labelling 50% of patients with a penicillin allergy record in the study hospital (a medium sized General District Hospital) could save £5,501 in antibiotic costs and 1,762 bed days per year or £503,932 (£286 per excess bed day). [19]

The prevalence of penicillin allergy in this study is comparable to other studies. [7, 12, 13] We showed penicillin allergy was associated with an increased rate of prescribing of glycopeptides, quinolones and carbapenems again reported by others. [7, 20] The importance of consideration of the type of infection as a confounder is illustrated by the higher number of patients with orthopaedic infections in the penicillin allergy group, which is likely to be a chance occurrence. These patients for example, will likely include orthopaedic implant infections which are more likely to be treated with glycopeptides regardless of penicillin allergy status. In such patients, it is not the penicillin allergy that is driving glycopeptide use but the type of infection, so delabelling would not affect antibiotic prescribing in this situation. Analyses that do not include the type of infection therefore risk over-estimate the impact of a delabelling service.

Two UK studies have demonstrated an association between penicillin allergy and increased antibiotic costs. Li *et al.* reported the acquisition costs of antibiotics prescribed for patients with penicillin allergy to be 1.82–2.58-fold higher than for first-line antibiotics, representing an excess antibiotic drug spend in their hospital of £225,056 - £556,640 using 2012 BNF prices.[9] In the same hospital group, Bermingham *et al*. compared the antibiotic costs in penicillin allergic and non-allergic patients who met sepsis criteria and were subsequently managed as per the sepsis pathway. [10] They found antibiotic costs to be 2.17 times higher for first dose and 2.61 times higher for overall antimicrobial costs in the penicillin allergy group. Bermingham estimated this to be an excess antibiotic spend in patients managed as sepsis of £90,157 per annum (using 2019 BNF prices) in the three acute study hospitals. [10] A Danish study [8] found a similar increase in acquisition costs in the penicillin allergy group. The acquisition costs associated with penicillin allergy records in our study are a more modest £10,637 per year. This can be explained, in part, by our use of local prices which are on average a third of BNF prices; the smaller size of our hospital; comparatively low use of antibiotics when compared to other English hospitals; and, the fact that we accounted for confounding by indication for antibiotics.[10] Bermingham used a sample size of 100 patients (50% with a reported penicillin allergy record) and Li used a sample size of 102 patients with penicillin allergy records to estimate the impact of penicillin allergy labels on antibiotic costs, both potentially introduced bias.

In our study there was a 5.5% longer length of hospital stay associated with penicillin allergy records. This is a similar magnitude, but lower, than the 9.9% longer stay found in a Californian study. [7] We are unaware of other European studies looking at length of hospital stay to compare our findings.

Our study hospital has approximately 230,000 bed days per year which is 0.68% of the annual English hospital bed base (approximately 34 million bed days in England). [21] If we use these data to extrapolate our findings to national data then penicillin allergy records would be associated with 517,941 excess bed

days per year or £148,131,126 using an average excess bed day figure of £286 [19] with an additional excess antibiotic drug spend of £1,564,265; both could potentially be halved by implementing a hospital-wide penicillin allergy de-labelling intervention that de-labelled 50% of those patients with penicillin allergy records and prescribed penicillin first line where indicated.

Strengths and limitations

The large cohort is a strength of this study but as a single centre study the findings may not be generalizable to other NHS hospitals. This study confirms the findings of two UK studies that demonstrated increased antibiotic costs but found a much smaller effect, perhaps because we reduced the risk of bias by including all patients prescribed antibiotics. The impact on length of stay is similar into the finding of a large Californian study.

We included patient gender, age, co-morbidities and infections treated during the inpatient stay to account for potential confounders, which is a strength over other studies, but there are other confounders and unknown factors which may also affect the analysis, that have not been accounted for. [1] A randomised controlled study is required to confirm whether de-labelling would realise these reductions in hospital length of stay. With some confidence we would expect de-labelling to increase penicillin antibiotic use and decrease second line antibiotic (e.g. quinolones, vancomycin) use and therefore likely reduce drug spend. The improvements in antibiotic stewardship and modest reductions in drug spend as a consequence of penicillin allergy de-labelling may not be sufficient to persuade hospital managers and NHS health policy makers that de-labelling is cost effective without demonstrating additional benefits, such as reduced length of hospital stay. There were repeat attendances for some patients, and therefore de-labelling one patient may actually correspond to more than one patient encounter. This is a limitation of our approach, which we believe is more likely to under-estimate savings than over-estimate.

Conclusion

This study shows that penicillin allergy records were associated with broad spectrum antibiotic use, increased antibiotic acquisitions costs and increased length of hospital stay. The excess antibiotic acquisition costs in this study were modest and lower than other studies. However, the impact of penicillin allergy records on hospital length of stay was sizable and may incentivise investment in a hospital wide penicillin allergy de-labelling programme.

Acknowledgements

We would like to thank Esther Dryden for co-ordinating the extraction of the data for this study

Contributors.

All authors contributed to the design of the study, interpretation of results and the manuscript write-up. KH carried out statistical analysis.

Disclaimer

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, the Department of Health and Social Care or Public Health England.

Conflict of interest statement

None to declare

Funding source

NP and JS carried out as part of routine work.

KH is funded by Imperial NIHR Biomedical Research Centre: NIHR-BRC-P68711.

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Condition	**Number of spells involving patients**	**Number of spells involving patients with a**	***p* value[1]**

	with no penicillin allergy record (%)	penicillin allergy record (%)	
Total	**44985**	**8423**	
Patient characteristics			
Gender			
Male	21447 (47.68)	2863 (33.99)	<0.01
Female	23538 (52.32)	5560 (66.01)	
Age[2]	64 (36, 78)	69 (50, 81)	<0.01
Year of admission			
2016/17	22315 (49.61)	4207 (49.95)	0.57
2017/18	22670 (50.39)	4216 (50.05)	
Comorbidities			
Asthma	3923 (8.72)	1044 (12.39)	<0.01
Cancer	6721 (14.94)	1300 (15.43)	0.25
Coronary heart disease	5700 (12.67)	1457 (17.3)	<0.01
Chronic kidney disease	10027 (22.29)	2335 (27.72)	<0.01
Chronic obstructive pulmonary disease	4858 (10.8)	1268 (15.05)	<0.01
Diabetes mellitus	6871 (15.27)	1687 (20.03)	<0.01
Smoker	5648 (12.56)	1047 (12.43)	0.76
Stroke	704 (1.56)	175 (2.08)	<0.01
Transient ischaemic attack	95 (0.21)	15 (0.18)	0.63
Infections			
Bone and joint infections	295 (0.66)	78 (0.93)	<0.01
Central nervous system infections	159 (0.35)	22 (0.26)	0.22
Congenital and neonatal infections	389 (0.86)	1 (0.01)	<0.01
Dental infections	147 (0.33)	37 (0.44)	0.13
Systemic infections not grouped else where	5512 (12.25)	1187 (14.09)	<0.01
Intra-abdominal infections	3599 (8)	758 (9)	<0.01
Intravascular infections	603 (1.34)	121 (1.44)	0.52
Lower Respiratory tract infections	9410 (20.92)	2083 (24.73)	<0.01
puerperal gynaecological infections	333 (0.74)	52 (0.62)	0.25
Sexually transmitted infections	79 (0.18)	15 (0.18)	1
Skin & skin structure infections	2413 (5.36)	575 (6.83)	<0.01
TB	34 (0.08)	3 (0.04)	0.29
Upper respiratory tract infections	600 (1.33)	87 (1.03)	0.03
Urinary tract infections	4795 (10.66)	1132 (13.44)	<0.01

[1]p value: result of Chi-squared test of association between penicillin allergy and condition.
[2]Age: median and interquartile range, p-value represents results of Wilcoxon Test.
Table 1 shows patient demographics, comorbidities and infection treated during inpatient stay and results using univariable comparative tests (Chi-squared).

Outcome	Median and IQR for patient spells with no recorded penicillin allergy		Median and IQR for patient spells with recorded penicillin allergy	
Patient length of stay (days)	2.94 (1.23, 6.96)		3.43 (1.34, 8.54)	
Costs (£)	£2.69 (1.37, 12.08)		£5.55 (1.49, 13.26)	
	No penicillin allergy record		Penicillin allergy record	
	Total costs	**Costs / spell**	**Total costs**	**Costs /spell**
Over the two year period of study	£747,480	£15.35	£182,810	£21.7
2016/17	£416,797.8	£18.7	£94,201	£22.4
2017/18	£330,681.8	£14.6	£88,608	£21.0

Table 2 Patient length of stay and antibiotic acquisition costs for patient spells with and without penicillin allergy

	No penicillin allergy record		Penicillin allergy record		Odds ratio and 95% CIs for the administration of specific antibiotics in penicillin allergy patients compared to patients without.
Antibiotic class	No. of patient hospital spells encounters	% exposed to antibiotic group	No. of patient hospital encounters	% exposed to antibiotic group	
Total encounters	44985		8423		
Aminoglycosides	19078	42.41	3608	42.84	1.02 (0.97, 1.07)
Carbapenems	778	1.73	621	7.37	4.52 (4.06, 5.04)
Cephalosporins	5929	13.18	561	6.66	0.47 (0.43, 0.51)
Clindamycin	182	0.40	272	3.23	8.21 (6.80, 9.93)
Glycopeptide	1502	3.34	2685	31.88	13.55 (12.64, 14.51)
Macrolides	4845	10.77	1347	15.99	1.58 (1.48, 1.68)
Metronidizole	10328	22.96	1699	20.17	0.85 (0.80. 0.90)
Penicillins	34754	77.26	1101	13.07	0.04 (0.04, 0.05)
Quinolones	2118	4.71	2094	24.86	6.70 (6.27, 7.15)
Tetracyclines	4042	8.99	1102	13.08	1.52 (1.42, 1.64)
Other	4282	9.52	1384	16.43	1.87 (1.75, 2.00)

Table 3 Antibiotics administered to patients

	Log(costs) scale[1]	95% CI for log(costs) scale	Impact (%)[2]	95% CI of impact (%)	Standard Error	*p value*
Penicillin allergy	0.25	(0.180, 0.321)	28.4	(19.7, 37.8)	0.036	<0.0001
Age	-0.008	(-0.009,-0.006)	-0.8	(-0.9, -0.6)	0.001	<0.0001
Gender Male	0.145	(0.082, 0.208)	15.6	(8.6, 23.1)	0.032	<0.0001
Year	-0.525	(-0.590,-0.460)	-40.8	(-44.6, -36.9)	0.033	<0.0001
congenital and neonatal infections	-1.903	(-4.638, 0.833)	-85.1	(-99.0, 130.0)	1.396	0.173
central nervous system infections	0.631	(0.244, 1.018)	87.9	(27.6, 176.6)	0.197	0.001
systemic infections not grouped else where	1.447	(1.375, 1.519)	325	(295.4, 356.8)	0.037	<0.0001
Intra-abdominal infections	0.093	(-0.008, 0.193)	9.7	(-0.8, 21.3)	0.051	0.070
Lower Respiratory tract infections	1.039	(0.972, 1.105)	182.5	(164.3, 201.9)	0.034	<0.0001
puerperal gynaecological infections	-0.243	(-0.989, 0.503)	-21.6	(-62.8, 65.4)	0.381	0.524
Skin & skin structure infections	0.186	(0.088, 0.283)	20.4	(9.2, 32.7)	0.05	0.0002
Upper respiratory tract infections	0.594	(0.415, 0.774)	81.2	(51.5, 116.8)	0.092	<0.0001
Asthma	-0.054	(-0.166, 0.058)	-5.3	(-15.3, 6.0)	0.057	0.346
Cancer	0.784	(0.720, 0.847)	118.9	(105.5, 133.3)	0.032	<0.0001
Coronary heart disease	-0.057	(-0.158, 0.043)	-5.6	(-14.6, 4.4)	0.051	0.262
Chronic kidney disease	-0.338	(-0.420,-0.256)	-28.7	(-34.3, -22.6)	0.042	<0.0001
Chronic obstructive pulmonary disease	-0.47	(-0.595,-0.345)	-37.5	(-44.8, -29.2)	0.064	<0.0001
Diabetes mellitus	0.13	(0.054, 0.206)	13.9	(5.6, 22.9)	0.039	0.0008
Smoker	-0.017	(-0.116, 0.082)	-1.7	(-11.0, 8.6)	0.051	0.737
Transient ischaemic attack	0.135	(-0.051, 0.322)	14.5	(-5.0, 37.9)	0.095	0.155

Table 4 Results of log-linear multivariable model of JAC-costs (£).CHD Coronory heart disease, CKD chronic kidney disease, COPD chronic obstructive pulmonary disease, DM diabetes mellitus, TIA transient ischaemic attack

[1]Numbers for log(costs) are coefficients from multivariable linear regression models on log(costs)

[2]Numbers for impact are exponentiation of the coefficients on the log(costs) and reflect the multiplicative effect on the central tendency for costs for each explanatory variable, based on coefficients from multivariable linear regression models on log(JAC costs)

Term	Log(los) scale[1]	95% CI for log(los) scale	Impact (%)[2]	95% CI of impact (%)	Standard Error	*p value*

Penicillin allergy	0.054	(0.025, 0.083)	5.5	(2.5, 8.6)	0.015	0.0003
Age	0.012	(0.011, 0.013)	1.2	(1.1, 1.3)	0	<0.0001
Gender male	-0.026	(-0.050,-0.002)	-2.6	(-4.9, -0.2)	0.012	0.032
Year	-0.078	(-0.101,-0.055)	-7.5	(-9.6, -5.4)	0.012	<0.0001
congenital and neonatal infections	1.297	(1.176, 1.418)	265.7	(224.0, 312.9)	0.062	<0.0001
central nervous system infections	0.54	(0.374, 0.706)	71.6	(45.3, 102.6)	0.085	<0.0001
systemic infections not grouped else where	0.616	(0.592, 0.640)	85.2	(80.8, 89.7)	0.012	<0.0001
Intra-abdominal infections	0.29	(0.257, 0.323)	33.6	(29.3, 38.1)	0.017	<0.0001
Lower Respiratory tract infections	0.463	(0.439, 0.488)	59	(55.1, 62.9)	0.013	<0.0001
puerperal gynaecological infections	0.019	(-0.240, 0.279)	2	(-21.3, 32.1)	0.132	0.884
Skin & skin structure infections	0.248	(0.211, 0.284)	28.1	(23.5, 32.9)	0.019	<0.0001
Upper respiratory tract infections	-0.201	(-0.413, 0.012)	-18.2	(-33.8, 1.2)	0.108	0.064
Asthma	-0.133	(-0.181,-0.084)	-12.4	(-16.6, -8.1)	0.025	<0.0001
Cancer	0.024	(-0.006, 0.054)	2.4	(-0.6, 5.6)	0.015	0.122
Coronary heart disease	0.134	(0.106, 0.162)	14.3	(11.1, 17.5)	0.014	<0.0001
Chronic kidney disease	0.041	(0.015, 0.066)	4.2	(1.5, 6.9)	0.013	0.002
Chronic obstructive pulmonary disease	-0.176	(-0.211,-0.142)	-16.1	(-19.0, -13.2)	0.018	<0.0001
Diabetes mellitus	0.034	(0.007, 0.062)	3.5	(0.7, 6.4)	0.014	0.014
Smoker	0.061	(0.020, 0.102)	6.3	(2.0, 10.7)	0.021	0.003
Transient ischaemic attack	0.215	(0.163, 0.268)	24	(17.7, 30.7)	0.027	<0.0001

Table 5 Results of log-linear multivariable model of Length of Stay (days).

[1]Numbers for log(LOS) are coefficients from multivariable linear regression models on log(LOS)

[2]Numbers for impact are exponentiation of the coefficients on the log(LOS) and reflect the multiplicative effect on the central tendency for length of stay for each explanatory variable, based on coefficients from multivariable linear regression models on log(LOS)

	Percentage de-labelled				
	0%	*25%*	*50%*	*75%*	*100%*
Number de-labelled	*0*	*1053*	*2106*	*3159*	*4212*
Total costs (£) (estimated from model)	*407525*	*404774*	*402024*	*399274*	*396888*
Savings (£)	*0*	*2751*	*5501*	*8251*	*10637*
Saving as % of total costs	*0*	*0.67*	*1.35*	*2.02*	*2.61*

Total length of stay (days) (estimated from model)	*90937.8*	*90057.2*	*89176.6*	*88296.4*	*87415.8*
Savings (number of days)	*0*	*880.6*	*1761.2*	*2641.4*	*3522*
Saving as % of total days	*0*	*0.97*	*1.9*	*2.9*	*3.87*

Table 6 Potential benefits of de-labelling penicillin sensitive patients, on total costs and bed days and costs in one year