

Title:

Linking individual-level data on diagnoses and dispensing for research on antibiotic use:
evaluation of a novel data source from English secondary care

Running title:

Evaluation of linkage in Hospital Treatment Insights (HTI)

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Key messages:

- The Hospital Treatment Insights (HTI) database links admissions, diagnoses and procedures in the widely-used Hospital Episode Statistics (HES) database with dispensing information stored in hospital pharmacy systems for a subset of 43/153 acute hospital trusts in England.
- Available from January 2010, HTI for the first time allows to analyse associations between diagnoses and hospital dispensing for individual patients in a relatively large number of NHS hospitals.
- Successful linkage of diagnoses and dispensing depends on HES and the local pharmacy systems having a minimum number of patient identifiers in common such as the NHS number, date of birth, gender and postcode. While HES contains identifiers for every patient, hospital pharmacies only retain identifiers when drugs are ordered specifically for a named patient. Where medication is administered from drugs stored on the ward without informing the pharmacy about the receiving patient, the dispensation cannot be linked to HES and is therefore not captured in HTI.
- Linkage of antibiotic dispenses was found to vary with individual antibiotic and ward settings. Capture of dispensing was good for specific antibiotics, but low linkage of highly-used treatments prevents HTI from being used for widespread antibiotic surveillance.
- Principles and findings may be generalised to other drug classes. For each drug of interest, the proportion of dispenses captured should be taken into account when designing future studies using HTI.

Prior presentations:

An abstract for this study was displayed as a poster at the International Conference on Pharmacoepidemiology & Therapeutic Risk Management 2017 in Montreal. The study was entirely funded by QuintilesIMS UK, the custodian of the HTI database.

Abstract

1

2 **Purpose:** There has been a focus on stewardship programmes to curb inappropriate antibiotic
3 prescribing and reduce antimicrobial resistance. In-hospital, patient-level prescribing linked to
4 indication is needed to support surveillance, evaluation of stewardship initiatives, as well as
5 other antibiotic research. We evaluated whether a novel dataset linking hospital pharmacy
6 records to Hospital Episode Statistics (HES) data can be used for antibiotic research.

7

8 **Methods:** Using the Hospital Treatment Insights (HTI) database, which links HES to pharmacy
9 records from 43 out of 153 hospital trusts in England, we estimated the proportion of missed
10 linkage and identified characteristics associated with missing data.

11

12 **Results:** Linkage of antibiotics to patients was inconsistent and dependent on drug type and
13 clinical setting, so that linkage for some specific antibiotics was high (80-100%), but overall, only
14 27.6% (CI: 27.4% - 27.8%) for all antibiotics dispensed. Linkage was best for quinolones
15 (62.6%; CI: 61.8% - 63.8%), but only 21.1% (CI: 21.1% - 21.2%) for penicillins. Linkage was
16 lower for common antibiotics and in emergency departments, however 80% linkage was
17 achieved for individual drugs like clindamycin, especially on wards with reduced ward stock use.

18

19 **Conclusions:** For those antibiotics with high linkage, HTI might be used to study associations
20 between indication, dispensing and outcomes. However, the majority of common antibiotics had
21 insufficient linkage, likely due to extensive use of ward stocks. Therefore, HTI in its current form
22 is not suitable for general antibiotic surveillance or evaluation of stewardship initiatives. For
23 drugs in HTI other than antibiotics, linkage should be similarly evaluated before a study is
24 conducted.

25

26

27 Introduction

28

29 Owing to a continued rise in resistance¹ and a slowing in the development of new antibiotics,²
30 antimicrobial resistance (AMR) is currently poised to threaten the way we think about
31 healthcare. A recognised risk factor for the emergence of resistance is excessive use of
32 antibiotic treatment.³ To tackle this issue, antimicrobial stewardship (AMS) programmes are
33 being implemented across the world to promote the effective use of antibiotics.⁴⁻⁷ In hospitals,
34 appropriate and prudent treatment is particularly important, because the combination of
35 vulnerable patients with high rates of co-morbidity, frequent antibiotic use² and heavy
36 dependence on broad-spectrum agents can create potent hotspots of AMR.³

37

38 To facilitate effective and efficient AMR policies, further research on the uptake and impact of
39 current hospital interventions is urgently needed. These efforts are hampered by the
40 unavailability of longitudinal patient-level data due to a continued lack of wide-spread electronic
41 prescribing in English secondary care.⁸ As a result, only aggregated data on hospital prescribing
42 exists on a national level.⁹ While this aggregated information allows us to monitor overall trends
43 in antibiotic usage, it prevents detailed enquiry into the association between indication and
44 prescribing. Any impact specifically attributable to initiatives is difficult to discern from general
45 trends in the population.³

46

47 Linking information between the Hospital Episode Statistics (HES) database and the dispensing
48 records stored in hospital pharmacy databases might offer a solution. However, success
49 depends on these databases having a minimum number of patient identifiers in common such
50 as the NHS number, date of birth, gender and postcode. While HES contains identifiers for
51 every patient, hospital pharmacies only retain identifiers when drugs are ordered specifically for
52 a named patient. Where a medication is instead stored on the ward, clinical personnel can

53 administer it without informing the pharmacy about the receiving patient. In this case, no patient
54 identifier is entered into the pharmacy system and the dispensation cannot be linked to HES.

55

56 We set out to evaluate the extent of this issue and to explore whether a linkage approach can
57 be utilised for research on antibiotic usage and surveillance in English hospitals. We described
58 the proportion of observed antibiotic dispensing after linkage using the Hospital Treatment
59 Insights (HTI) dataset, which links HES records with patient records from hospital pharmacies
60 for 43 English trusts. We compared total dispensing within all HTI hospitals against aggregated
61 pharmacy data on the hospital-level used by Public Health England.⁹ We estimated the
62 proportion of dispensed antibiotics that were captured in the database and investigated factors
63 influencing the recording of data.

64

65 **Methods**

66

67 *Data sources*

68

69 Hospital Treatment Insights¹ is a database of electronic health records from English secondary
70 care. It is maintained by QuintilesIMS (<https://www.quintilesims.com>), a leading provider of
71 information, services and technology for the healthcare industry. HTI links hospital patient
72 records in the HES² database with dispensing information stored in hospital pharmacy systems
73 for a subset of 43 consenting trusts out of a total of 153 acute hospital trusts in England. In
74 these participating trusts, HES already routinely captures hospital activity information such as
75 demographics, admission and administrative data, diagnoses and procedures. Where
76 dispensing data could be linked to patients, HTI retrospectively enriches the available HES data
77 from 2010 onwards with patient-level data on brand, type, date and quantity of dispensed drugs.

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78 Linkage was performed by NHS Digital as a trusted third party using a 15-step deterministic
79 linkage algorithm (Supplement Table 1). Due to the data sharing agreement with NHS Digital,
80 no information on the nature of the trusts (e.g. geography or specialty of the hospital) included
81 in HTI was made available to the researchers. Therefore, data had to be treated as if it
82 originated from a single hospital.

83

84 Between 2010 and 2015, HTI included 7.7 million admitted hospital patients (Figure 1). For 3.6
85 million (47.2%) of these patients, additional information on dispensed drugs was available. 3.9
86 million (52.8%) patients had no medication information in HTI. Although some of these patients
87 might genuinely not have been prescribed a drug, it is more likely that most of them received a
88 drug but, for reasons exemplified below, dispensing could not be linked to the patient within HTI.
89 Diagnoses and issued medications in HTI are not jointly recorded in the same IT system at the
90 point of care. Instead, they are mapped at a later point in time by NHS Digital based on
91 personal identifiers recorded in hospital pharmacy systems during dispensation. This can be
92 done if medication is explicitly requested for a named patient. If instead the drug is bulk-
93 dispensed to the hospital ward for interim storage and used on demand, hospital pharmacy
94 systems do not obtain feedback as to which patient eventually received the medication. Without
95 this information, medication from ward stock cannot be linked and has to be excluded from HTI.
96 This might happen for example in day case patients, who account for 35.1% of all inpatient
97 episodes¹⁰. These day case patients bring in their own medication and may only require
98 additional ward stock anaesthesia for procedures such as cataract surgery or endoscopy. They
99 may therefore account for many of the patients without any medication information. A further
100 clinical inpatient setting with possibly high ward stock usage and no additional drugs would be
101 maternity care of women without comorbid disease. Whether HTI can indeed be used for
102 antibiotic research on drug usage depends largely on the extent to which similar issues prevent
103 HTI from accurately capturing antibiotic dispensing.¹¹

104

105 Aggregated reference levels of antibiotic dispensing in HTI hospitals were taken from the
106 Hospital Pharmacy Audit (HPA) database, which has been used for antibiotic surveillance by
107 Public Health England.⁹ Analogous to HTI, HPA is curated by QuintilesIMS and collected from
108 hospital pharmacy systems, covering 99% of hospital beds in England.¹² However, unlike HTI it
109 does not contain patient specific information and is not, therefore, subject to data linkage. As a
110 result, HPA includes bulk dispensing to wards excluded in HTI, allowing for it to be used as a
111 measure of total hospital dispensing.

112

113 *Study design*

114

115 We conducted a retrospective cross-sectional study evaluating the proportion of antibiotic
116 treatment that could be linked to a patient in English hospitals contributing to HTI between 1st
117 April 2011 and 31st March 2015. Systemic antibiotics were defined using the classes *J01* and
118 *J03A* of the European Pharmaceutical Market Research Association's anatomical classification
119 used in both HTI and HPA.¹³ This definition is roughly equivalent to the class *J01* in the World
120 Health Organisation's substance-based Anatomical Therapeutic Chemical (ATC) classification
121 system, with a few notable exceptions like nitrofurantoin.¹⁴ Quantities were calculated as
122 number of dispensed packs per month, without making an attempt to estimate the amount of
123 defined daily doses contained in a pack. While this might lead to an over- or underestimation of
124 the true proportion of linkage if linkage depends on dosage, packs provided a fast option to
125 compare average linkage which can be easily extended to other classes of drugs.

126

127 All antibiotic dispenses in HTI falling within the study period were extracted using the above
128 definition. A quality control of the extract was performed, assessing it for clinically unlikely
129 outliers due to data entry errors. Three antibiotic agents, ceftadizime, colistin, and
130 sulfamethoxypyridazine, were excluded from the analysis, as some hospitals were found to
131 report number of tablets dispensed instead of number of packs in a considerable number of

132 cases. For other included antibiotics, the number of matching identifiers used for linkage was
133 examined.

134
135 Dispensing was then aggregated and compared to quantities reported in HPA for the same set
136 of hospitals. The overall proportion of antibiotics that could be linked to a patient was estimated
137 as the percentage of HPA dispensing found in HTI and appropriate 95%-confidence intervals
138 (CI) were calculated using bootstrapping with 2,000 samples. Linkage was stratified by form,
139 therapeutic agent and ward. Drugs were classified as oral, intravenous or another form (topical,
140 lung administration, rectal, etc.) using EphMRA's New Form Code. Antibiotic agents were
141 grouped by antibiotic class and changes in linkage of these classes were compared over time.
142 Dispensing was stratified by the five ward specialties with the highest observed usage in HPA:
143 Accidents & Emergencies (A&E), general medicine, geriatrics, intensive care and respiratory
144 medicine (thoracic medicine and respiratory clinics). Finally, linkage of individual antibiotic
145 agents was contrasted across wards, using drugs indicated for methicillin-resistant
146 *Staphylococcus aureus* (MRSA) infections by the British National Formulary as an example.

147
148 Approval for this study was obtained by the Clinical Practice Research Datalink's Independent
149 Scientific Advisory Committee for MHRA database research (ISAC) as part of the protocol
150 16/102.

151
152 All analyses were carried out using R software version 3.3.1 for Windows.¹⁵

154 **Results**

155
156 On average, 27.6% (CI: 27.4% - 27.8%) of all antibiotics dispensed in hospitals contributing to
157 HTI could be linked to an individual patient (Table 1). The general strength of linkage was high,

158 with more than 85% of the linkage based on NHS number and one or more additional identifiers
159 (see Supplement Table 1).

160

161 The proportion of packs linked to a patient depended on the form of the drug, the antibiotic
162 agent and the type of ward. Respiratory medicine and geriatrics had an above average linkage
163 of 48.3% (CI: 47.2% - 49.8%) and 39.6% (CI: 38.9% - 40.6%) respectively (Table 1).
164 Emergency departments had much lower linkage of antibiotics, with 4.4% (CI: 4.3% - 4.4%) of
165 dispensed antibiotics recorded in intensive care and 8.7% (CI: 8.7%- 8.7%) recorded in A&E.
166 Linkage for general medicine was 13.2% (CI: 12.9% - 13.7%). Together, these five ward
167 specialties were responsible for almost half of all antibiotic dispensing in the study period.
168 Among other wards, exceptionally high linkage across all antibiotics was found in radiotherapy
169 (89.0%, CI: 88.1% - 89.9%), whereas only 0.4% (CI: 0.4% - 0.4%) of antibiotics used in
170 operating theatres were recorded.

171

172 Oral antibiotics had a linkage of 37.2% (CI: 37.1% - 37.3%) while intravenous dispensing,
173 accounting for almost two thirds of all antibiotic dispensing in hospitals, was less well captured
174 with 21.9% (CI: 21.6% - 22.2%) linked to a patient. The highest linkage was achieved in other
175 forms of antibiotics, but those only accounted for a small fraction of all dispenses.

176

177 Regarding antibiotic groups, quinolones and carbapenems were recorded best, with 546,721
178 (62.6%; CI: 61.8 % - 63.8%) respectively 278,668 (46.9%; CI: 46.6% - 47.2%) dispensed packs
179 covered. Of all tetracyclines dispensed in hospital, 35.9% (CI: 35.8%-36.1%) could be linked to
180 an individual patient. Cephalosporins and macrolides corresponded to the average with 391,553
181 (28.5%; CI: 28.2% - 28.8%) and 639,042 (27.2%; CI: 27.1% - 27.3%) packs recorded in HTI.
182 Penicillins could only be related to a patient for 21.1% (CI: 21.1% - 21.2%) of dispensed packs.
183 This is especially noteworthy, as penicillins accounted for half of all packs dispensed.
184 Furthermore, the proportion of penicillins observed in HTI decreased slightly over the study

185 period (see Supplement Figure 1). In contrast, linkage of carbapenems increased at the
186 beginning of 2013 from 44% to 52%. All other classes of antibiotics fluctuated around their initial
187 levels.

188
189 Looking into individual antibiotic agents, linkage ranged from 100.0% (CI: 74.1% - 100.0%) in
190 telavancin, 97.4% (CI: 96.3% - 98.5%) in lymecycline and 92.1% in both linezolid (CI: 91.2% -
191 93.0%) and moxifloxacin (CI: 90.7% - 93.5%) to 3% in cefuroxime (CI: 3.4% - 3.6%), gentamicin
192 (CI: 3.3% - 3.4%) and penicillin G (CI: 3.0% - 3.1%) (Table 2). Limiting dispensing to specific
193 wards influenced the proportion of linkage observed, as exemplified by the linkage of MRSA
194 drugs in intensive care, general medicine, geriatrics and respiratory wards (Table 3). Higher
195 proportions of linkage could be achieved for many drugs when looking solely at respiratory or
196 geriatric wards. Drugs dispensed on general medicine wards, on the other hand, had almost
197 consistently lower linkage than average.

198 199 **Discussion**

200
201 Linkage of antibiotic dispenses varied with individual antibiotic and ward settings. Overall, in HTI
202 a quarter of antibiotic dispensing was linked to an individual patient. Linkage of frequently used
203 treatments was low, probably due to the fact that these drugs are less likely to be prescribed
204 directly from pharmacy and often held as ward stock. As a consequence, coverage of high
205 usage antibiotics like gentamicin, broad-spectrum penicillins and vancomycin was limited.
206 Alternative treatments (e.g. clindamycin, daptomycin and tigecycline) had a much higher linkage
207 across wards. The achieved proportion of linkage varied considerably depending on the ward
208 where they were dispensed. Looking specifically at patients in wards like geriatrics or
209 respiratory medicine improved the proportion of treatment observed and in multiple cases
210 yielded linkage of more than 80%. Patterns of linkage changed little across the study period,
211 with the exception of a sudden increase in linkage of carbapenems at the start of 2013. It is

212 possible that the reductions in dispenses from ward stock represent the impact of stewardship
213 initiatives promoting judicious use of carbapenems.

214
215 This is the first study evaluating the representativeness and completeness of data recorded in
216 HTI for research on antibiotic usage. We were able to identify and describe major factors
217 influencing linkage of antibiotic treatment. However, the results of this study were limited in
218 some ways. First, linkage was compared based on the number of dispensed packs to provide
219 an easy methodology for estimating linkage quality. This approach may over- or underestimate
220 the true proportion of linkage if linkage depends on the number of daily doses contained in a
221 pack, e.g. if larger packs are less likely to be linked. If a study is to be performed on HTI, those
222 results should therefore only act as a first indicator of feasibility and should be followed up by a
223 detailed analysis based on daily doses. Second, the identity of the participating hospitals was
224 not available to researcher and no hospital identifiers existed in the database at the time of
225 study. Consequently, no statement could be made about variations in demographics or
226 dispensing behaviour between individual hospitals. It is possible that findings in this study
227 mainly reflect the effect of low antibiotic recording in a subset of hospitals. The inclusion of an
228 anonymous trust identifier might reveal a subset of hospitals with high quality data linkage (e.g.
229 due to local resistance patterns), which would allow investigating associations between drug
230 usage and indications in more detail. Trust identifiers will be added to the database with the
231 next data update in spring 2017. Finally, no evaluation of successful linkage could be
232 performed. Linkage was conducted by NHS Digital as a trusted third party and we had no
233 access to identifiable patient data. Consequently, no individual patient files could be revisited
234 and records were treated as correctly linked where linkage was observed. False linkage could
235 not be investigated in this study. If the linkage algorithm falsely mapped dispenses and patients
236 in a large proportion of cases the findings in this study would overestimate true linkage.

237

238 This study has highlighted some limitations, which must be taken into account for antibiotic
239 research using HTI as a data source. Further evaluation is needed on HTI for other therapeutic
240 agents with particular emphasis on the role of ward stock. Papers looking into the validity of
241 prescribing databases in primary care in England generally found a high conformity of the
242 quantity of drugs recorded when compared to external sources.^{16,17} High coverage of drugs was
243 also found for a secondary care database in the Taiwanese insurance-based healthcare
244 system.¹⁸ A study specifically investigating antibiotic prescribing in a Dutch secondary care
245 database was able to obtain treatment for all patients with community-acquired pneumonia,
246 although no validation of the obtained information was performed.¹⁹ The comparably low linkage
247 found for some antibiotics in this study likely reflects a high use of ward stock dispensing for
248 antibiotic treatment in English hospitals²⁰ and a current inability to capture this dispensing. This
249 conclusion is supported by findings on determining factors for linkage of dispensed drugs.
250 Linkage was lowest across settings in which antibiotic usage tended to be either common or
251 urgent, as is the case in A&E and intensive care. These situations potentially favour a higher
252 utilisation of ward stock because of time constraints and efficiency gains. Linkage was generally
253 higher for drugs like carbapenems and quinolones, which are used more cautiously and have
254 been subject to increased stewardship measures over the last 15 years.²¹ Yet, the high levels of
255 linkage in geriatrics and respiratory medicine, as compared to general medicine, cannot be fully
256 explained by these differences.

257

258 Although HTI in its current form does not seem to reflect a true picture of general antibiotic
259 dispensing in secondary care, therefore preventing it from being used for widespread antibiotic
260 surveillance, it has value for specific antibiotic research related to individual agents in specific
261 ward settings, and may be used for broader studies where the missing drug usage can be
262 estimated. There remains a pressing need for comprehensive and complete data to evaluate
263 the intended and unintended impacts of AMS programmes in hospitals. However, although
264 hospitals are clearly setting the course for e-prescribing,²² full adoption and availability for

265 secondary use might still take years. For now, linking HES to pharmacy data provides a
266 potential mechanism to investigate some patient-level drug usage across NHS hospitals. We
267 have shown that this is already possible for a number of antibiotics, in particular in medical
268 settings that rely less on ward stocks. Using hospital identifiers within HTI to identify sites with
269 above-average linkage could be used to further improve coverage and to enable the analysis of
270 more common antibiotics in HTI. Finally, reducing the reliance on ward stock in hospitals in the
271 panel might be a way to continue increasing this linkage. The unexpected large differences in
272 linkage rates between closely related wards, seen for example in general medicine and
273 geriatrics, suggest that it is feasible to do so. Further research will be needed to understand and
274 learn from the systematic differences in these ward level processes, the results of which may
275 aid in elevating the status of antibiotics from drugs used in everyday medicine to a limited
276 resource that requires prudent management.

277

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281

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284 Hospital Pharmacy Audit. IMS Health itself is funded by sales of information services to
285 industry, academia and governments around the world.

286

287 **Conflicts of interest**

288 All funding for this study was provided by QuintilesIMS UK, with no other external sources of
289 funding. P.R. was contracted by QuintilesIMS as a statistical programmer while the study was
290 performed. D.A. is Medical Director of the department of Real-World Evidence Solutions at
291 QuintilesIMS UK. L.S. has not received any funding for this study.

292

293 **Author contributions**

294 P.R. and L.S. developed the study protocol. P.R. performed the data extraction, analysis and
295 writing of the manuscript, supervised by L.S. D.A. and L.S. advised on the interpretation of the
296 study findings and revised the final manuscript.

297

Tables and Figures

Table 1 - Total number of antibiotics dispensed and proportion linked to an individual patient

	Total packs dispensed	Patient-linked packs		
		n	% of total	(95%-CI)
All	22,885,454	6,317,947	27.6	(27.4 – 27.8)
Dispensing ward				
Accident & Emergency	2,389,513	207,842	8.7	(8.7 – 8.7)
General Medicine	4,039,748	532,728	13.2	(12.9 – 13.7)
Geriatrics	1,364,470	540,037	39.6	(38.9 – 40.6)
Intensive Care	1,222,121	53,311	4.4	(4.3 – 4.4)
Respiratory Medicine	1,154,135	557,398	48.3	(47.2 – 49.8)
Other	12,715,467	4,426,631	34.8	(34.5 – 35.1)
Form				
Intravenous	14,358,600	3,144,292	21.9	(21.6 – 22.2)
Oral	8,518,627	3,169,344	37.2	(37.1 – 37.3)
Other	8,227	4,311	52.4	(51.3 – 53.7)
Antibiotic class				
Carbapenems	594,394	278,668	46.9	(46.6 – 47.2)
Cephalosporins	1,376,450	391,553	28.4	(28.2 – 28.8)
Macrolides	2,351,805	639,042	27.2	(27.1 – 27.3)
Penicillins	12,026,953	2,538,705	21.1	(21.1 – 21.2)
Quinolones	873,831	546,721	62.6	(61.8 – 63.8)
Tetracyclines	575,250	206,723	35.9	(35.8 – 36.1)
Others	5,086,771	1,716,535	33.7	(32.9 – 34.6)

Table 2 - Linkage of individual antibiotic agents in HTI (Apr 2011 – Mar 2015)

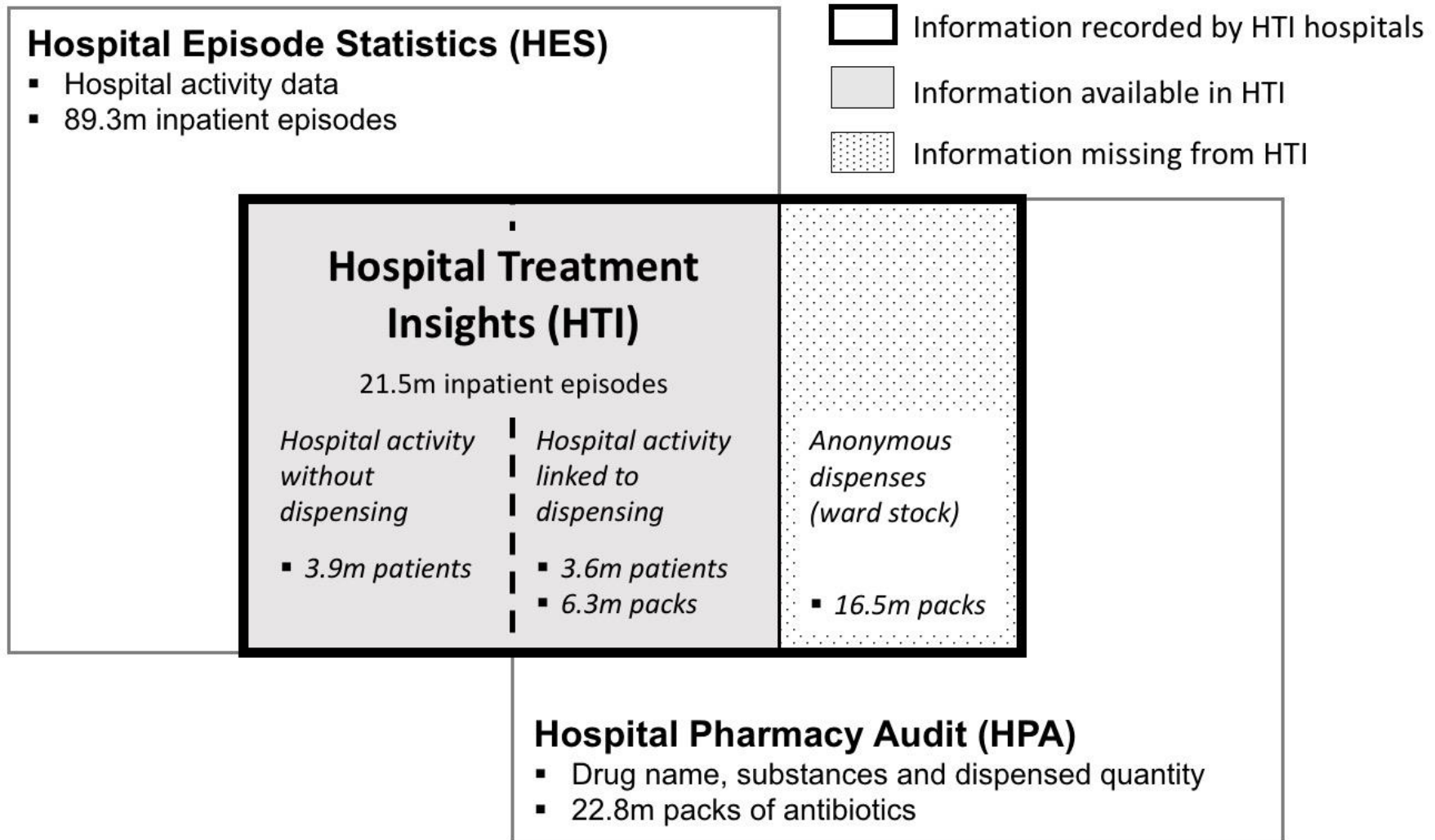
	Total packs (as recorded in HPA)	Patient – linked packs	
		n	% of total
Amikacin	44,119	19,569	44.35
Amoxicillin	1,552,520	323,235	20.82
Amoxicillin/Clavulanic Acid	2,318,864	595,729	25.69
Ampicillin	516	103	19.92
Ampicillin/Flucloxacillin	4,183	547	13.07
Azithromycin	514,125	177,580	34.54
Aztreonam	96,205	64,953	67.52
Cefaclor	19,125	10,723	56.07
Cefadroxil	1,751	676	38.60
Cefalexin	280,941	100,843	35.89
Cefixime	4,661	2,402	51.53
Cefotaxime	179,128	29,663	16.56
Cefpodoxime Proxetil	18	6	32.79
Cefradine	17,945	7,103	39.58
Ceftaroline Fosamil	70	41	59.40
Ceftriaxone	506,527	226,346	44.69
Cefuroxime	364,476	12,597	3.46
Cefuroxime Axetil	1,806	1,152	63.77
Chloramphenicol	154,784	91,252	58.95
Cilastatin/Imipenem	46,884	12,082	25.77
Ciprofloxacin	613,061	400,300	65.30
Clarithromycin	1,575,692	370,088	23.49
Clindamycin	378,721	233,180	61.57
Dalfopristin/Quinupristin	89	85	95.14
Daptomycin	55,118	47,221	85.67
Demeclocycline	11,098	7,077	63.76
Doripenem	0	0	–
Doxycycline	518,694	159,485	30.75
Ertapenem	246,339	137,143	55.67
Erythromycin	262,324	91,374	34.83
Flucloxacillin	1,546,681	382,220	24.71
Fosfomycin	416	147	35.20
Fusidic Acid	22,131	18,470	83.46
Gentamicin	916,173	30,513	3.33
Levofloxacin	165,184	82,624	50.02
Linezolid	28,520	26,267	92.10
Lymecycline	16,042	15,623	97.39
Meropenem	301,170	129,442	42.98
Minocycline	3,494	3,120	89.31
Moxifloxacin	54,147	49,883	92.12
Neomycin	9	8	92.38
Norfloxacin	1,015	887	87.47
Ofloxacin	40,424	13,026	32.22

Oxytetracycline	13,919	12,410	89.16
Penicillin G	186,962	5,663	3.03
Penicillin V	553,564	179,302	32.39
Piperacillin	0	0	–
Piperacillin/Tazobactam	5,782,414	1,000,979	17.31
Pivmecillinam	11,523	8,386	72.77
Polymethyl M	460	0	0.00
Rifabutin	1,777	1,395	78.54
Sulfadiazine	1,896	1,414	74.58
Sulfamethizole/Trimethoprim	633	217	34.27
Sulfamethoxazole/Trimethoprim	170,395	106,382	62.43
Teicoplanin	1,313,907	532,186	40.50
Telavancin	27	27	100.00
Temocillin	41,666	30,849	74.04
Tetracycline	2,110	1,824	86.44
Ticarcillin/Clavulanic Acid	28,060	11,694	41.67
Tigecycline	9,894	7,184	72.61
Tobramycin	136,028	86,051	63.26
Trimethoprim	637,583	164,564	25.81
Vancomycin	1,127,444	292,635	25.96

Table 3 - Differences in linkage of antibiotics used to treat methicillin resistant staphylococcus aureus infections

	<u>All wards</u>	<u>General medicine</u>	<u>Geriatrics</u>	<u>Respiratory</u>
	n % (95%-CI)	n % (95%-CI)	n % (95%-CI)	n % (95%-CI)
Teicoplanin	532,186 40.5 (40.2 – 40.8)	43,464 24.0 (23.5 – 24.5)	38,142 65.5 (64.2 – 66.7)	14,994 71.5 (69.1 – 74.0)
Vancomycin	292,635 26.0 (25.8 – 26.1)	31,388 18.9 (18.5 – 19.3)	37,653 50.4 (49.5 – 51.2)	14,746 36.1 (35.2 – 37.1)
Clindamycin	233,180 61.6 (61.2 – 61.9)	19,391 37.1 (36.5 – 37.7)	11,899 68.5 (67.0 – 69.9)	8,465 79.9 (77.9 – 82.0)
Daptomycin	47,221 85.7 (84.1 – 87.1)	2,602 40.2 (38.0 – 42.5)	1,977 80.4 (75.5 – 85.6)	2,367 99.3 (92.9 – 100.0)
Linezolid	26,267 92.1 (91.2 – 93.0)	1,587 60.4 (58.4 – 62.4)	1,297 72.4 (69.7 – 75.1)	1,884 80.0 (77.2 – 82.8)
Fusidic acid	18,470 83.5 (81.7 – 85.3)	1,147 55.7 (51.9 – 59.7)	1,011 61.2 (57.7 – 64.4)	792 78.4 (70.1 – 86.9)
Tigecycline	7,184 72.6 (71.8 – 73.5)	798 52.9 (51.4 – 54.4)	370 71.7 (68.9 – 74.5)	487 65.2 (62.5 – 68.1)
Ceftaroline	41 59.4 (51.4 – 68.0)	10 85.5 (85.5 – 85.5)	0 –	0 –
Telavancin	27 100.0 (74.1 – 100.0)	0 –	0 –	0 –

Figure 1 – Schematic structure and source of inpatient data and antibiotic dispenses in Hospital Treatment Insights



References

1. Roca I, Akova M, Baquero F, et al. The global threat of antimicrobial resistance: science for intervention. *New Microbes New Infect.* 2016;6:22-29.
2. Shallcross LJ, Davies DSC. Antibiotic overuse: a key driver of antimicrobial resistance. *Br J Gen Pract.* 2014;64(629):604-605.
3. Llewelyn MJ, Hand K, Hopkins S, Walker AS. Antibiotic policies in acute English NHS trusts: implementation of “Start Smart—Then Focus” and relationship with *Clostridium difficile* infection rates. *J Antimicrob Chemother.* 2015;70(4):1230-1235.
4. Department of Health. *UK Five Year Antimicrobial Resistance Strategy 2013 to 2018.* London, UK; 2013.
5. Cantón R, Bryan J. Global antimicrobial resistance: from surveillance to stewardship. Part 2: stewardship initiatives. *Expert Rev Anti Infect Ther.* 2012;10(12).
6. Public Health England. *Start Smart - Then Focus: Antimicrobial Stewardship Toolkit for English Hospitals.*; 2015.
7. Public Health England. *Target Antibiotics Toolkit.*; 2014.
8. Cresswell KM, Bates DW, Williams R, et al. Evaluation of medium-term consequences of implementing commercial computerized physician order entry and clinical decision support prescribing systems in two “early adopter” hospitals. *J Am Med Informatics Assoc.* 2014;21(e2):e194-e202.
9. English Surveillance Programme for Antimicrobial Utilization and Resistance (ESPAUR). *Report 2016.* London; 2016.
10. Hospital Episode Statistics Analysis. *Hospital Episode Statistics: Admitted Patient Care, England - 2014-15.*; 2015.
11. Stephens P, Chikh K, Leufkens H. Prescribing of antipsychotics in people with dementia in acute general hospitals in England: 2010–2012. *Eur Geriatr Med.* 2014;5(6):394-398.
12. Cooke J, Stephens P, Ashiru-Oredope D, Johnson A, Livermore D, Sharland M. Antibacterial usage in English NHS hospitals as part of a national Antimicrobial Stewardship Programme. *Public Health.* 2014;128(8):693–697.
13. EphMRA. *Comparison of the WHO ATC Classification & EphMRA/PBIRG Anatomical Classification.*; 2016.
14. WHO Collaborating Centre for Drug Statistics Methodology. *Guidelines for ATC Classification and DDD Assignment 2015.* Oslo; 2015.
15. R Core Team. *R: A language and environment for statistical computing.* 2016.
16. Langley TE, Szatkowski L, Gibson J, et al. Validation of The Health Improvement Network (THIN) primary care database for monitoring prescriptions for smoking cessation medications. *Pharmacoepidemiol Drug Saf.* 2010;19:586-590.
17. Bourke A, Dattani H, Robinson M. Feasibility study and methodology to create a quality-evaluated database of primary care data. *Inform Prim Care.* 2004;12:171-177.
18. Cheng C-L, Kao Y-HY, Lin S-J, Lee C-H, Lai ML. Validation of the national health insurance research database with ischemic stroke cases in Taiwan. *Pharmacoepidemiol Drug Saf.* 2011;20(3):236-242.
19. van de Garde EMW, Natsch S, Prins JM, van der Linden PD. Antibiotic prescribing on admission to patients with pneumonia and prior outpatient antibiotic treatment: a cohort study on clinical outcome. *BMJ Open.* 2015;5(2).
20. MacKenzie FM, Gould IM, Bruce J, et al. The role of microbiology and pharmacy departments in the stewardship of antibiotic prescribing in European hospitals. *J Hosp Infect.* 2007;65(Suppl 2):73-81.
21. Gilchrist M, Wade P, Ashiru-Oredope D, et al. Antimicrobial Stewardship from Policy to Practice: Experiences from UK Antimicrobial Pharmacists. *Infect Dis Ther.* 2015;4(Suppl 1):51-64.
22. Hand K, Cumming D, Hopkins S, et al. Electronic prescribing system design priorities for antimicrobial stewardship: a cross-sectional survey of 142 UK infection specialists. *J*

