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Epidemic potential of *Escherichia coli* ST131 and *Klebsiella pneumoniae* ST258: A systematic review and meta-analysis

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ABSTRACT

Objectives - Observational studies have suggested that *Escherichia coli* sequence type (ST) 131 and *Klebsiella pneumoniae* ST258, both frequently resistant to multiple antibiotics, and first described in 2008 and 2009, respectively, have hyperendemic properties. This would be obvious from continuously high incidence and/or prevalence of carriage or infection with these bacteria in specific patient populations. Hyperendemicity could result from increased transmissibility, a longer duration of infectiousness, and/or a higher pathogenic potential as compared to other lineages of the same species.

Primary outcome measures - A systematic literature search was performed to assess the evidence of transmissibility, duration of infectiousness, and pathogenicity for *E. coli* ST131 and *K. pneumoniae* ST258. Meta-regression was performed to quantify these characteristics.

Results - The systematic literature search yielded 386 articles, of which 17 data sources provided information on transmissibility (*E. coli* ST131 n=10; *K. pneumoniae* ST258 n=7)), 2 on duration of infectiousness (*E. coli* ST131 n=2), and 305 on pathogenicity (*E. coli* ST131 n=278; *K. pneumoniae* ST256 n=27). Available data on duration of carriage and on transmissibility were insufficient for quantitative assessment. In multivariable meta-regression *E. coli* isolates causing infection were associated with ST131, compared to isolates only causing colonization, suggesting that *E. coli* ST131 can be considered more pathogenic than non-ST131 isolates. Date of isolation, location, and resistance mechanism also influenced the prevalence of ST131. *E. coli* ST131 was 3.4 (95% CI 2.0-5.8) times more pathogenic than non-ST131. For *K. pneumoniae* ST258 there were not enough data for meta-regression assessing the influence of colonization versus infection on ST258 prevalence.

Conclusions - With the currently available data, it cannot be confirmed nor rejected, that *E. coli* ST131 or *K. pneumoniae* ST258 are hyperendemic clones.

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STRENGTHS AND LIMITATIONS

- A comprehensive literature search combined with meta-regression analyses was performed to quantify evidence of hyperendemicity of *E. coli* ST131 and *K. pneumoniae* ST258 focussing on transmissibility, durations of infectiousness, and pathogenicity.
- There is a large heterogeneity in reported prevalences and a limited amount of data available on transmissibility and duration of infectiousness.
- With the currently available data, it cannot be confirmed nor rejected, that *E. coli* ST131 or *K. pneumoniae* ST258 are hyperendemic clones.

INTRODUCTION

Infections caused by *Escherichia coli* and *Klebsiella pneumoniae* producing extended-spectrum beta-lactamases (ESBL) or carbapenamases are increasing worldwide. There is growing evidence that certain clonal lineages of these species, such as *E. coli* sequence type (ST) 131 and *K. pneumoniae* ST258, have more epidemic potential than other lineages within their species group. *E. coli* ST131 was first described in 2008[1] and *K. pneumoniae* ST258 in 2009[2]. *E. coli* ST131 is reported from around the globe, both in healthcare settings and in the community[3,4], and is mostly associated with ESBL production and fluoroquinolone resistance.[3,5] *K. pneumoniae* ST258 is mainly associated with *Klebsiella pneumoniae* carbapenemase (KPC) production, and other resistance mechanisms[6], and is widespread in the USA, and expanding in Europe.[6–8] In the scientific literature *E. coli* ST131 and *K. pneumoniae* ST258 are widely considered hyperendemic clones.[3,5,6,8,9] But the evidence underlying these assumptions is not that obvious.[3,5] If *E. coli* ST131 or *K. pneumoniae* ST258 are truly hyperendemic clones, interventions may be targeted to these specific clones.

The characteristics of hyperendemicity follow from a simple model in which patients can be susceptible, colonized, or infected (Figure 1). Susceptible hosts can acquire colonization through transmission, either directly (from another colonized or infected person) or indirectly (from the environment or via the hands of health care workers). Both colonized and infected patients contribute to transmission, as long as they are infectious, which can be expressed with the duration of colonization. Duration of colonization can be influenced by fitness cost associated with resistance or by antibiotic use. Colonization can proceed to infection, which typically occurs in a fraction of colonized patients[10] and the

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rate of this progression can be expressed as the pathogenicity level. Decolonization can occur in both colonized and infected persons.

To be hyperendemic, a clone has to have advantages over other clones in at least one of the traits transmissibility, duration of colonization, or pathogenicity. Therefore, we define a hyperendemic clone as 'a clone that is more transmissible, has a longer duration of colonization, and/or is more pathogenic than other clones of the same species'. The presence of any or more of these traits will then lead to a continuously high incidence and/or prevalence of carriage or disease in a specific patient population. We performed a systematic review to quantitatively estimate these critical parameters for *E. coli* ST131 and *K. pneumoniae* ST258.

METHODS

Search strategy

A PubMed search was performed to retrieve relevant articles published until February 11, 2014. The complete search string can be found in Supplementary Text 1. A cross-reference check was performed to include relevant articles not found during the search. Only English, full-text articles were included. Articles unavailable online were requested from the authors. The MOOSE statement[11] was followed for reporting in this paper.

Study selection

Titles and abstracts were independently reviewed by two reviewers (MRH and MJDD) and selected for further review if they met the inclusion criteria. Selections were compared between the two reviewers and if consensus was not reached, a third reviewer (MCJB or MJMB) was consulted.

The inclusion criteria for articles on transmissibility were that possible transmissions should be described, and the number of cases should be reported. Outbreak reports were included. Articles focusing on duration of colonization should include at least two cultures per patient taken at two different time points. Pathogenicity was defined as the difference in the prevalence of ST131 or ST258 in infections (clinical isolates) compared to colonization. We considered a clone to be more pathogenic when the relative abundance of this clone in isolates causing infections is higher compared to isolates associated with colonization. Therefore, articles on pathogenicity of *E. coli* ST131 or *K. pneumoniae*

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ST258 should report the prevalence or incidence of infections among patients colonized with *E. coli* ST131 or *K. pneumoniae* ST258, the prevalence of *E. coli* ST131 or *K. pneumoniae* ST258 among patients colonized with *E. coli* or *K. pneumoniae*, respectively, or the prevalence of *E. coli* ST131 or *K. pneumoniae* ST258 among at least 10 clinical isolates of *E. coli* or *K. pneumoniae*, respectively.

Articles were excluded if they did not contain original data (such as reviews, commentaries, or articles reusing existing datasets), if they considered *E. coli* or *K. pneumoniae* only in non-human sources, or if there was no clear information on the isolate collection or selection.

Data extraction

Data were extracted by the same two reviewers independently and crosschecked using a standard form developed by the researchers. Data were collected on population and setting, recording if participants were inpatients, outpatients/community residents, travelers, or from another/unknown group. The area/region where the study took place was recorded and categorized into (mainly) from Africa, Asia, Australia, Europe, North America, and South America. It was recorded whether data collection took place during an outbreak period, and if a selection on antibiotic susceptibility or resistance was made, divided into selection on ESBL/AmpC-producing isolates (including third generation cephalosporin-resistant isolates), carbapenem-resistant or carbapenemase-producing Enterobacteriaceae (CRE/CPE, e.g., KPC, OXA-48), other resistance profiles (e.g., ciprofloxacin-resistant, fluoroquinolone-susceptible, or multi-drug resistant), or no selection on resistance. Furthermore, the method to detect sequence types was documented, split up into multi-locus sequence typing (MLST, when all isolates were typed by MLST), extrapolation based on pulsed-field gel electrophoresis (PFGE, when only selected isolates were typed with MLST and the sequence types were inferred based on PFGE type), polymerase chain reaction (PCR, when all isolated underwent PCR-screening for ST-specific alleles), extrapolation based on PCR (mainly MLST for *E. coli* isolates that were positive for O25b-ST131 by PCR), or other/unknown (such as fumC/fimH typing). Also, the sample site of the included isolates (percentage of isolates isolated from blood, urine, gastrointestinal, respiratory, wound/abscess, or other sites) and time period of the study were recorded. For the time period, the middle date was used in the model if the study covered a longer time period.

For transmissibility, if available, information was gathered on admission prevalence, number of cases, number of uncolonized patients, and transmission measure given. For duration of colonization, the number of cases and duration of colonization was recorded. For pathogenicity, information was

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collected on the prevalence or incidence of infections in patients colonized with *E. coli* ST131 or *K. pneumoniae* ST258, the prevalence of *E. coli* ST131 or *K. pneumoniae* ST258 in patients colonized with *E. coli* or *K. pneumoniae*, respectively, and/or the prevalence of *E. coli* ST131 or *K. pneumoniae* ST258 in patients infected with *E. coli* or *K. pneumoniae*, respectively.

Quality of the included articles was assured by only including papers with a proper selection of isolates. Furthermore, quality was implicitly incorporated in the data that were collected on the detection method used, the sample sites, whether data were collected during an outbreak, and the setting and time period in which data were collected.

Several studies allowed splitting the data into multiple 'data sources'. For example, if data was available per year or per country, these were recorded separately. Figure 2 shows a flow diagram with the included and excluded articles. Since only 17 data sources were available on transmissibility (10 on *E. coli* ST131 and 7 on *K. pneumoniae* ST258) and 2 on duration of colonization (both on *E. coli* ST131), we could only describe these without quantifying summary measures. For pathogenicity, enough data was available on *E. coli* to do a meta-regression analysis and calculate summary measures.

Meta-regression pathogenicity

In order to evaluate the pathogenicity of *E. coli* ST131 and *K. pneumoniae* ST258 and to assess which factors influence this, meta-regression was performed using all reported data on the prevalence of *E. coli* ST131 in clinical (infection) or screening (colonization) isolates of *E. coli* and for all reported data on the prevalence of *K. pneumoniae* ST258 in clinical (infection) isolates of *K. pneumoniae*. The prevalence estimates (calculated as the number of ST131- or ST258-positive isolates divided by the total number of *E. coli* or *K. pneumoniae* isolates, respectively) and standard errors (SEs) were logit transformed in the analysis. Heterogeneity between studies was evaluated with Cochrans's Q and the I^2 statistic.[12] Because of high heterogeneity ($I^2 > 75\%$), a meta-analysis using a generalized linear mixed effect model with random effects per data source was used to assess sources of variability in the overall prevalence estimates. Univariate analyses were performed to identify covariates associated with the overall prevalence estimates. All covariates with a p-value < 0.20 were included in the multivariate model, and backward selection was performed using the likelihood ratio test. There, as we are performing an exploratory analysis, a cut-off of $p < 0.10$ was used to determine statistical significance. The variable describing sample site was not included in the models, because of great dependency on the type of isolate (clinical or screening isolate, e.g. blood isolates representing infection), and the effect of culture

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site might not be comparable for isolates representing colonization or infection. The estimated between-study variance (τ^2) was evaluated for the model with and without explanatory parameters. The exponent of the coefficient for colonization/ infection found in the metaregression model is an odds ratio, which can be interpreted as a risk ratio. This was taken as a measure of how much more pathogenic *E. coli* ST131 was compared to non-ST131. I.e., a value of 2 would indicate that per colonized day colonization with ST131 leads two times more often to an infection as compared to colonization with non-ST131. All analyses were performed in R v. 3.0.3 (http://CRAN.R-project.org) using the 'metafor' package.

RESULTS

In all, 285 useful data sources were identified (see Figure 2 for the consecutive steps followed for identification). For transmissibility 14 data sources were identified, for duration of carriage 2, and for pathogenicity 269. Most studies (n=206, 72%) were performed in Europe and North America, and 266 (93%) were performed in a non-outbreak setting (Table 1). *E. coli* isolates were most selected on ESBL production or resistance against third-generation cephalosporins, and *K. pneumoniae* isolates on being CRE/CPE. Colonization isolates were most often from gastro-intestinal origin (85.2%), and infection isolates from urine (54.8%) or blood (24.5%).

Table 1: Characteristics of included studies

	EC trans-missibility (n=7)	KP trans-missibility (n=7)	EC duration (n=2)	EC pathogenicity colonization (n=25)	EC pathogenicity infection (n=214)	KP pathogenicity colonization (n=2)	KP pathogenicity infection (n=27)	KP pathogenicity colonization & infection (n=1)
Number of isolates (mean, sd)				66 (77)	112 (325)	20 (23)	43 (70)	
Number of isolates (median, iqr)				39 (21 - 64)	45 (18 - 100)	20 (12 - 28)	20 (14 - 43·5)	
Population - inpatients	2 (28.6%)	5 (71.4%)	1 (50.0%)	6 (24.0%)	104 (48.6%)	2 (100.0%)	18 (66.7%)	0 (0.0%)
Population - outpatients/community	4 (57.1%)	2 (28.6%)	0 (0.0%)	15 (60.0%)	23 (10.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Population - mixed	1 (14.3%)	0 (0.0%)	0 (0.0%)	2 (8.0%)	56 (26.2%)	0 (0.0%)	2 (7.4%)	1 (100.0%)
Population - travellers	0 (0.0%)	0 (0.0%)	1 (50.0%)	2 (8.0%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Population - other/unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	29 (13.6%)	0 (0.0%)	7 (25.9%)	0 (0.0%)
Continent - Africa	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	13 (6.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

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Continent - Asia	1 (14.3%)	0 (0.0%)	0 (0.0%)	6 (24.0%)	35 (16.4%)	0 (0.0%)	4 (14.8%)	0 (0.0%)
Continent - Australia	0 (0.0%)	0 (0.0%)	1 (50.0%)	3 (12.0%)	9 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Continent - Europe	3 (42.9%)	6 (85.7%)	1 (50.0%)	11 (44.0%)	81 (37.9%)	2 (100.0%)	12 (44.4%)	0 (0.0%)
Continent - North America	3 (42.9%)	1 (14.3%)	0 (0.0%)	5 (20.0%)	74 (34.6%)	0 (0.0%)	6 (22.2%)	1 (100.0%)
Continent - South America	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.9%)	0 (0.0%)	5 (18.5%)	0 (0.0%)
Outbreak setting	1 (14.3%)	7 (100.0%)	0 (0.0%)	1 (4.0%)	4 (1.9%)	1 (50.0%)	8 (29.6%)	0 (0.0%)
Selection - ESBL/3GC-R	6 (85.7%)	0 (0.0%)	1 (50.0%)	17 (68.0%)	156 (72.9%)	2 (100.0%)	0 (0.0%)	0 (0.0%)
Selection - CRE/CPE	0 (0.0%)	6 (85.7%)	0 (0.0%)	0 (0.0%)	6 (2.8%)	0 (0.0%)	25 (92.6%)	1 (100.0%)
Selection - other	1 (14.3%)	0 (0.0%)	1 (50.0%)	2 (8.0%)	32 (15.0%)	0 (0.0%)	2 (7.4%)	0 (0.0%)
Selection - none	0 (0.0%)	1 (14.3%)	0 (0.0%)	6 (24.0%)	20 (9.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Detection - MLST	5 (71.4%)	3 (42.9%)	0 (0.0%)	7 (28.0%)	116 (54.2%)	1 (50.0%)	18 (66.7%)	0 (0.0%)
Detection - extrapolation based on PFGE	1 (14.3%)	2 (28.6%)	0 (0.0%)	3 (12.0%)	15 (7.0%)	1 (50.0%)	9 (33.3%)	1 (100.0%)
Detection - extrapolation based on PCR	1 (14.3%)	0 (0.0%)	2 (100.0%)	14 (56.0%)	70 (32.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Detection - CH	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	12 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Detection - other/unknown	0 (0.0%)	2 (28.6%)	0 (0.0%)	1 (4.0%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Site - blood	1 (14.3%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	54 (25.2%)	0 (0.0%)	5 (18.5%)	0 (0.0%)
Site - urine	2 (28.6%)	2 (28.6%)	1 (50.0%)	2 (8.0%)	122 (57.0%)	0 (0.0%)	10 (37.0%)	1 (100.0%)
Site - gastro-intestinal tract	4 (57.1%)	3 (42.9%)	1 (50.0%)	22 (88.0%)	4 (1.9%)	1 (50.0%)	6 (22.2%)	0 (0.0%)
Site - respiratory tract	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	3 (1.4%)	1 (50.0%)	2 (7.4%)	0 (0.0%)
Site - wound	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Site - other/unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	30 (14.0%)	0 (0.0%)	4 (14.8%)	0 (0.0%)

EC: *E. coli*, KP: *K. pneumoniae*. Site: site from which most isolates were identified

Transmissibility

There were 14 studies reporting transmissibility of *E. coli* ST131 (n=7) and *K. pneumoniae* ST258 (n=7), some being case-reports or describing single possible transmission events (Table 2). Transmission events for *E. coli* ST131 have been described or suggested in household (n=3), day care (n=1), and hospital settings (n=4). For *K. pneumoniae* ST258 all sources reported on transmission events in hospital settings, and all included CRE/CPE.

Transmissibility can be quantified by the number of transmissions per patient or patient-days at risk, which requires information on the number of index cases, number of transmissions and number of days or patients at risk. Yet, one or more of these aspects, especially time at risk, is missing in all studies but one. Most studies are cross-sectional studies, in which transmission cannot be proven.

Differences in transmission capacity between *E. coli* ST131 and non-ST131, or between *K. pneumoniae* ST258 and non-ST258, have not been quantified, precluding any conclusion on the relative transmissibility of *E. coli* ST131 and *K. pneumoniae* ST258 compared to other clonal lineages.

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Table 2: Summary of articles describing transmissibility of *E. coli* ST131 and *K. pneumoniae* ST258

Author	Country	Year	Setting	Organism	Index cases (n)	Secondary cases (n)	Un-colonized	Exposure time
Blanc 2014[13]	France	2012	Day care centers	*E. coli* ST131	7			
Giuffrè 2013[14]	Italy	2012	Neonatal intensive care unit	*E. coli* ST131	15		88	
Adler 2012 [15]	Israel	2008-2009	Geriatric rehabilitation wards	*E. coli* ST131	21	23	367	
				E. coli non-ST131	31	36	367	
Hilty 2012[16]	Switzerland	2008-2010	University hospital	*E. coli* ST131	13	2	36	48 index inpatients for a total of 400 000 patient-days
				E. coli non-ST131	27	2	48	
			Household	*E. coli* ST131	15	7	19	
				E. coli non-ST131	42	13	49	
Owens 2011[17]	USA	Before 2011	Household	*E. coli* ST131	2			
Johnson 2010[18]	USA	Before 2010	Household	*E. coli* ST131	1	1	1	
Ender 2009[19]	USA	Before 2009	Hospital	*E. coli* ST131	1	1		
Giuffrè 2013[20]	Italy	2012	Neonatal intensive care unit	*K. pneumoniae* ST258	10		44	
Tofteland 2013[21]	Norway	2010	Intensive care unit	*K. pneumoniae* ST258	6			
Morris 2012[22]	Ireland	2011	2 Hospitals	*K. pneumoniae* ST258	11			
Agodi 2011[23]	Italy	2009	Hospital	*K. pneumoniae* ST258	16			
Won 2011[24]	USA	2008	Acute care hospitals and long-term acute care hospitals	*K. pneumoniae* ST258	33 (+ 7 presumed cases)			
Marchese 2010[25]	Italy	2009	Neuro-rehabilitation unit	*K. pneumoniae* ST258	4 (+3 at time of publication)			
Mammina 2010[26]	Italy	2009	Intensive care unit	*K. pneumoniae* ST258	13			

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Duration of carriage

The duration of carriage of *E. coli* ST131 was investigated in two studies. In one study colonization with *E. coli* was still apparent after 12 months in 64% (n=9) and 40% (n=14) of those carrying *E. coli* ST131 or other STs, respectively (p=0.12).[27] In another study, of two patients acquiring colonization with *E. coli* ST131 during travel, one was a prolonged carrier with this strain. The definition of prolonged carriage was not given however.[28] The duration of carriage of *K. pneumoniae* ST258 has not been determined.

Pathogenicity

E. coli

From 239 data sources, we retrieved data from 25,722 *E. coli* isolates (1,657 associated with colonization and 24,065 with infection). Prevalence of *E. coli* ST131 in these studies ranged from 0% to 100% (Supplementary Figure 1), with high statistical heterogeneity between studies (I^2=98.1%, 95% CI 97.7%-98.4%).

In univariable meta-regression the *E. coli* ST131 prevalence in individual studies increased in time, and appeared to be influenced by whether isolates were associated with infection or colonization, resistance patterns used for isolate selection, and location where the study was performed (*p*-value < 0.20; Table 3). These variables were included in the multivariable meta-regression model, and time, location, and selection remained significantly associated with *E. coli* ST131 prevalence (Table 4). No significant effects were present for study population, microbiological methods used to detect ST131, or whether the study was performed in an outbreak situation or not.

The prevalence of ST131 was highest if *E. coli* isolates were selected upon the presence of ESBL production or third generation cephalosporin resistance, and lowest if derived from non-selective media. Prevalence of *E. coli* ST131 was highest in North America, and lowest in South America. The estimated prevalence of ST131 in *E. coli*, given particular values of the covariates, can be derived from the regression equation (Table 4). For example, the estimated logit (prevalence ST131) for isolates causing infection, selected on presence of ESBL, in North America in January 2010 is given by -3.0020 + 12*0.0180 + 1.2353 + 1.4858 + 0.3395 = 0.2746, which corresponds to a prevalence of ST131 of exp(0.2746)/(1+exp(0.2746)) = 56.8%. The estimated prevalence in the reference category (January 2009, colonization, no selection on resistant profile, Europe) is exp(-2.940)/(1+exp(-2.940)) = 5.0%.

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In the multivariable meta-regression model *E. coli* ST131 was significantly associated with infection compared to colonization, suggesting that ST131 isolates are more pathogenic than non-ST131 isolates. From the infection/colonization coefficient we can calculate the relative pathogenicity of *E. coli* ST131 compared to non-ST131. We found that *E. coli* ST131 is 3.4 (95% CI 2.0-5.8) times more pathogenic than non-ST131. Supplementary Figure 2 shows the proportion of ST131 found in infection isolates compared to colonization isolates as estimated by the meta-regression model.

The estimated between-study variance (τ^2) reduced from 1.28 in the model without parameters to 0·90 in the final model, implying that a high level of heterogeneity remained.

Table 3: Effect of covariates on prevalence of ST131 in *E. coli* (univariable random effects meta-regression models)

	P-value
Study period (per month[a])	< 0.0001
Infection or colonization	0.0011
Colonization	
Infection	
Outbreak setting	0.9893
Selection of isolates based on resistance pattern	< 0.0001
no selection on resistance profile	
ESBL/3GC-R	
CRE/CPE	
other	
Study population	0.9383
Inpatients	
Outpatients / community	
Mixed	
Travelers	
Other / unknown	
Location	0.0071
Europe	
North America	
South America	
Australia	
Asia	
Africa	
Method used to detect ST131	0.5312
MLST	
Extrapolation based on PFGE	
PCR	

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Extrapolation based on PCR	
Other/unknown	

CRE/CPE: carbapenem-resistant Enterobacteriaceae/carbapenemase-producing Enterobacteriaceae

ESBL/3GC-R: extended-spectrum beta-lactamases/third-generation cephalosporin resistance

MLST: multi-locus sequence typing

PCR: polymerase chain reaction

PFGE: pulsed-field gel electrophoresis

[a]Reference date: 1 January 2009

Table 4: Effect of covariates on prevalence of ST131 in *E. coli* (multivariable random effects meta-regression model)

	Estimate (SE[a])	**P-value**
Intercept	-3.0020 (0.3351)	
Study period (per month[b])	0.0180 (0.0025)	<0.0001
Infection or colonization		<0.0001
Colonization	Reference	
Infection	1.2353 (0.2649)	
Selection of isolates based on resistance pattern		<0.0001
no selection on resistance profile	Reference	
ESBL/3GC-R	1.4858 (0.2578)	
CRE/CPE	0.5575 (0.5632)	
other	0.9444 (0.2951)	
Location		<0.0001
Europe	Reference	
North America	0.3395 (0.1770)	
South America	-2.1666 (1.2034)	
Australia	-0.4926 (0.3658)	
Asia	-0.2399 (0.2133)	
Africa	-0.0390 (0.3770)	

CRE/CPE: carbapenem-resistant Enterobacteriaceae/carbapenemase-producing Enterobacteriaceae

ESBL/3GC-R: extended-spectrum beta-lactamases/third-generation cephalosporin resistance

SE: standard error

[a]Parameter estimates (SEs) are presented on a logit scale.

[b]Reference date: 1 January 2009.

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K. pneumoniae

There were 27 and two data sources providing information on the prevalence of ST258 *K. pneumoniae* in clinical and colonizing isolates, respectively (Supplementary Figure 3). Because of limited data on colonization, quantitative analyses were performed for clinical isolates only.

In the univariable meta-regression model, study period, outbreak setting yes/no, selection of isolates based on resistance pattern, study population, geographic location, and method used to detect ST258 were all associated with a higher prevalence of ST258 with a *p*-value < 0.20 and were, thus, included in the multivariable model (Table 5). This model yielded a significant increasing effect in time of the prevalence of ST258 in *K. pneumoniae* isolates, as well as an effect of resistance patterns on the prevalence of ST258 in *K. pneumoniae* (Table 6). ST258 prevalence was associated with selection of isolates on CRE-positivity, but the number of data sources describing isolates that are not CRE/CPE is low (not selected on resistance pattern, n=1 or selected on ESBL, n=1). Furthermore, study population characteristics also appeared to influence ST258 prevalence in *K. pneumoniae*, with higher prevalence of ST258 in inpatients, compared to "other" populations. Yet, the "other" group is not defined accurately, precluding firm conclusions. No data sources were available for outpatients or persons residing in the community. Finally, reported ST258 prevalence was higher in Asia and Australia than in other continents.

The method of sequence type detection (9 data sources with extrapolation based on MLST of selected isolates; 18 data sources using MLST for all isolates) or whether data was collected during an outbreak (8 data sources) or not (n=19) were not associated with a higher prevalence of ST258.

The estimated prevalence of ST258 in *K. pneumoniae*, given particular values of the covariates, can be derived from the regression equation. For example, the estimated logit (prevalence of ST258) for isolates selected on presence of CRE in hospital inpatients in North America in January 2010 is given by -0.8794 + 12*0.0588 + 2.4991 + 0.7178 = 3.0431, which corresponds to a prevalence of ST258 of exp(3.0431)/(1+exp(3.0431)) = 95.4%. The estimated prevalence in the reference category (January 2009, non CRE/CPE, hospital inpatients, Europe) is exp(-0.8794)/(1+exp(-0.8794)) = 29.3%.

The estimated between-study variance (τ^2) reduced from 7.87 in the model without parameters to 1.43 in the final model, indicating a considerable improvement, but still a high level of heterogeneity.

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ST258 was not detected in the two studies reporting on colonization with *K. pneumonia*, that included in 36 and 4 isolates.[146,173] This precludes any quantification of the pathogenicity of *K. pneumoniae* ST258.

The only study in which both colonization and infection with *K. pneumoniae* ST258 were investigated included a set of seven KPC-producing *K. pneumoniae* ST258 isolates collected from a long-term acute care facility in South Florida.[194] Three patients were colonized, and four had both colonization and infection. Again, the sample size is too small for drawing conclusions.

Table 5: Effect of covariates on prevalence of ST258 in clinical isolates of *K. pneumoniae* (univariable random effects meta-regression models)

	P-value
Study period (per month[a])	0.0875
Outbreak setting	0.0147
No	
Yes	
Selection of isolates based on resistance pattern	0.1333
Non-CRE/CPE	
CRE/CPE	
Study population	0.0071
Inpatients	
Mixed	
Other/unknown	
Location	0.0415
Europe	
North America	
South America	
Asia (including Australia)	
Method used to detect ST258	0.1569
MLST	
Extrapolation based on PFGE	

CRE/CPE: carbapenem-resistant Enterobacteriaceae/carbapenemase-producing Enterobacteriaceae

MLST: multi-locus sequence typing

PFGE: pulsed-field gel electrophoresis

[a]Reference date: 1 January 2009

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Table 6: Effect of covariates on prevalence of ST258 in clinical isolates of *K. pneumoniae* (multivariable random effects meta-regression model)

	Estimate (SE[a])	P-value
Intercept	-0.8794 (1.1010)	0.4244
Study period (per month[b])	0.0588 (0.0257)	0.0221
Selection of isolates based on resistance pattern		
Non-CRE/CPE	Reference	0.0264
CRE/CPE	2.4991 (1.1257)	
Study population		< 0.0001
Inpatients	Reference	
Mixed	-5.7152 (1.4969)	
Other/unknown	-2.9060 (0.7049)	
Location		0.0553
Europe	Reference	
North America	0.7178 (0.9240)	
South America	0.6296 (0.9180)	
Asia (including Australia)	-2.4943 (0.9626)	

CRE/CPE: carbapenem-resistant Enterobacteriaceae/carbapenemase-producing Enterobacteriaceae

SE: standard error

[a]Parameter estimates (SEs) are presented on a logit scale.

[b]Reference date: 1 January 2009.

DISCUSSION

Based on published information we conclude that there is evidence that *E. coli* ST131 is more pathogenic than *E. coli* non-ST131, but not for increased transmissibility or prolonged duration of carriage. Because of the heterogeneity in the data it cannot be concluded (nor rejected) that *E. coli* ST131 is a hyperendemic clone. For *K. pneumoniae* ST258 the published data precluded any conclusion on increased transmissibility, longer duration of carriage or increased pathogenicity.

Several limitations in our study should be acknowledged. Because of our search strategy, the prevalence of *E. coli* ST131 and *K. pneumoniae* ST258 that were retrieved are likely overestimations of the real prevalence. We required the articles to report ST131/ST258 in their title and/or abstract and therefore articles that did not report this or that did not detect ST131/ST258 in their study may have been missed. Since the prevalence is dependent on factors including time, location, resistance pattern, population studied and possibly variables not included in this review (e.g., patient-specific details like age, gender),

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we deemed it not meaningful to estimate an overall prevalence of ST131 in *E. coli* or ST258 in *K. pneumoniae*.

We also did not create a funnel plot to assess publication bias, as such an analysis also assumes that there is one overall effect or prevalence. Thus, publication bias cannot be excluded. It is possible that identification of *E. coli* ST131 or *K. pneumoniae* ST258 stimulates publication, because of the current interest in these clones. However, this will most likely equally influence studies reporting infection and colonization isolates, which would not influence our conclusions. In our analysis, we used grouped variables (e.g., continent instead of country), as there are limitations to the number of variables that can be studied.

There could also be differences in detecting infection and colonization associated isolates. Infection isolates are mainly collected retrospectively, when a pattern or outbreak is recognized, whereas colonization isolates are more often collected prospectively. Yet, since determination of sequence types is unambiguous it is unlikely that such differences have affected our conclusions.

Our analysis clearly demonstrates that more – and better designed – studies are needed to determine whether *E. coli* ST131 and *K. pneumoniae* ST258 are truly hyperendemic clones. This would be possible with a prospective cohort study of a population (e.g., the general population or hospitalized patients) with a certain contact structure, in which carriage with *E. coli* or *K. pneumoniae* is regularly (e.g. weekly or monthly) determined. For determination of transmissibility genotyping should be performed, preferably with highly discriminatory methods, and preferably with inclusion of multiple isolates per patient.[195] The duration of exposure to persons colonized or infected with *E. coli* ST131/*K. pneumoniae* ST258 should be determined to calculate the number of acquisitions per unit of time. Carriers could be studied in more detail to determine the duration of carriage and the infection rate (and duration until infection), preferably with inclusion of the effects of antibiotic use on these parameters. There should be a sufficient duration of follow-up, and isolates should be characterized to determine whether multiple isolates represent persistent carriage or recolonization with different strains.

In conclusion, current evidence does not allow the conclusion that *E. coli* ST131 and *K. pneumoniae* ST258 are hyperendemic clones.

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DECLARATION OF INTERESTS

All authors have no competing interests to declare.

AUTHOR CONTRIBUTIONS

MJDD and MRH performed the systematic literature search, reviewed and summarized data from each selected article, performed the analyses, and wrote the first draft of the manuscript. MJDD, MRH, MJMB, and MCJB all revised the manuscript.

DATA SHARING STATEMENT

Extracted data are available from the authors.

REFERENCES

1. Nicolas-Chanoine M-HH, Blanco J, Leflon-Guibout V, et al. Intercontinental emergence of *Escherichia coli* clone O25:H4-ST131 producing CTX-M-15. *J Antimicrob Chemother* 2008;61:273–81.

2. Samuelsen Ø, Naseer U, Tofteland S, et al. Emergence of clonally related *Klebsiella pneumoniae* isolates of sequence type 258 producing plasmid-mediated KPC carbapenemase in Norway and Sweden. *J Antimicrob Chemother* 2009;63:654–8.

3. Nicolas-Chanoine M-H, Bertrand X, Madec J-Y. *Escherichia coli* ST131, an Intriguing Clonal Group. *Clin Microbiol Rev* 2014;27:543–74.

4. Rogers BA, Sidjabat HE, Paterson DL. *Escherichia coli* O25b-ST131: a pandemic, multiresistant, community-associated strain. *J Antimicrob Chemother* 2011;66:1–14.

5. Banerjee R, Johnson JR. A new clone sweeps clean: the enigmatic emergence of *Escherichia coli* sequence type 131. *Antimicrob Agents Chemother* 2014;58:4997–5004.

6. Woodford N, Turton JF, Livermore DM. Multiresistant Gram-negative bacteria: the role of high-risk clones in the dissemination of antibiotic resistance. *FEMS Microbiol Rev* 2011;35:736–55.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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7. Kitchel B, Rasheed JK, Patel JB, et al. Molecular epidemiology of KPC-producing *Klebsiella pneumoniae* isolates in the United States: clonal expansion of multilocus sequence type 258. *Antimicrob Agents Chemother* 2009;53:3365–70.

8. Grundmann H, Livermore DM, Giske CG, et al. Carbapenem-non-susceptible Enterobacteriaceae in Europe: Conclusions from a meeting of national experts. *Eurosurveillance* 2010;15.

9. Rogers BA, Doi Y. Who is leading this dance? Understanding the spread of *Escherichia coli* sequence type 131. *Infect Control Hosp Epidemiol* 2013;34:370–2.

10. Bonten MJ, Weinstein RA. The role of colonization in the pathogenesis of nosocomial infections. *Infect Control Hosp Epidemiol* 1996;17:193–200.

11. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;283:2008–12.

12. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ Br Med J* 2003;327:557–60.

13. Blanc V, Leflon-Guibout V, Blanco J, et al. Prevalence of day-care centre children (France) with faecal CTX-M-producing *Escherichia coli* comprising O25b:H4 and O16:H5 ST131 strains. *J Antimicrob Chemother* 2014;69:1231–7.

14. Giuffrè M, Cipolla D, Bonura C, et al. Outbreak of colonizations by extended-spectrum beta-lactamase-producing *Escherichia coli* sequence type 131 in a neonatal intensive care unit, Italy. *Antimicrob Resist Infect Control* 2013;2:8.

15. Adler A, Gniadkowski M, Baraniak A, et al. Transmission dynamics of ESBL-producing *Escherichia coli* clones in rehabilitation wards at a tertiary care centre. *Clin Microbiol Infect* 2012;18:E497–505.

16. Hilty M, Betsch BY, Bögli-Stuber K, et al. Transmission dynamics of extended-spectrum beta-lactamase-producing Enterobacteriaceae in the tertiary care hospital and the household setting. *Clin Infect Dis* 2012;55:967–75.

17. Owens RC, Johnson JR, Stogsdill P, et al. Community transmission in the United States of a CTX-M-15-producing sequence type ST131 *Escherichia coli* strain resulting in death. *J Clin Microbiol* 2011;49:3406–8.

18. Johnson JR, Anderson JT, Clabots C, et al. Within-household sharing of a fluoroquinolone-resistant *Escherichia coli* sequence type ST131 strain causing pediatric osteoarticular infection. *Pediatr Infect Dis J* 2010;29:473–5.

19. Ender PT, Gajanana D, Johnston B, et al. Transmission of an extended-spectrum-beta-lactamase-producing *Escherichia coli* (sequence type ST131) strain between a father and daughter resulting in septic shock and Emphysematous pyelonephritis. *J Clin Microbiol* 2009;47:3780–2.

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20. Giuffrè M, Bonura C, Geraci DM, et al. Successful control of an outbreak of colonization by *Klebsiella pneumoniae* carbapenemase-producing *K. pneumoniae* sequence type 258 in a neonatal intensive care unit, Italy. *J Hosp Infect* 2013;85:233–6.

21. Tofteland S, Naseer U, Lislevand JH, et al. A long-term low-frequency hospital outbreak of KPC-producing *Klebsiella pneumoniae* involving Intergenus plasmid diffusion and a persisting environmental reservoir. *PLoS One* 2013;8:e59015.

22. Morris D, Boyle F, Morris C, et al. Inter-hospital outbreak of *Klebsiella pneumoniae* producing KPC-2 carbapenemase in Ireland. *J Antimicrob Chemother* 2012;67:2367–72.

23. Agodi A, Voulgari E, Barchitta M, et al. Containment of an outbreak of KPC-3-producing *Klebsiella pneumoniae* in Italy. *J Clin Microbiol* 2011;49:3986–9.

24. Won SY, Munoz-Price LS, Lolans K, et al. Emergence and rapid regional spread of *Klebsiella pneumoniae* carbapenemase-producing enterobacteriaceae. *Clin Infect Dis* 2011;53:532–40.

25. Marchese A, Coppo E, Barbieri R, et al. Emergence of KPC-2 carbapenemase-producing *Klebsiella pneumoniae* strains and spread of an isolate of sequence type 258 in the neuro-rehabilitation unit of an Italian hospital. *J Chemother* 2010;22:212–4.

26. Mammina C, Palma DM, Bonura C, et al. Outbreak of infection with *Klebsiella pneumoniae* sequence type 258 producing *Klebsiella pneumoniae* Carbapenemase 3 in an intensive care unit in Italy. *J Clin Microbiol* 2010;48:1506–7.

27. Titelman E, Hasan CM, Iversen A, et al. Faecal carriage of extended-spectrum beta-lactamase-producing Enterobacteriaceae is common 12 months after infection and is related to strain factors. *Clin Microbiol Infect* 2014;20:O508–15.

28. Rogers BA, Kennedy KJ, Sidjabat HE, et al. Prolonged carriage of resistant *E. coli* by returned travellers: clonality, risk factors and bacterial characteristics. *Eur J Clin Microbiol Infect Dis* 2012;31:2413–20.

29. Habeeb MA, Haque A, Iversen A, et al. Occurrence of virulence genes, 16S rRNA methylases, and plasmid-mediated quinolone resistance genes in CTX-M-producing *Escherichia coli* from Pakistan. *Eur J Clin Microbiol Infect Dis* 2014;33:399–409.

30. López-Cerero L, Navarro MD, Bellido M, et al. *Escherichia coli* belonging to the worldwide emerging epidemic clonal group O25b/ST131: risk factors and clinical implications. *J Antimicrob Chemother* 2014;69:809–14.

31. Giufre M, Accogli M, Farina C, et al. Predominance of the fimH30 subclone among multidrug-resistant *Escherichia coli* strains belonging to sequence type 131 in Italy. *J Infect Dis* 2014;209:629–30.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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32. Al-Agamy MH, Shibl AM, Hafez MM, et al. Molecular characteristics of extended-spectrum beta-lactamase-producing *Escherichia coli* in Riyadh: emergence of CTX-M-15-producing *E. coli* ST131. *Ann Clin Microbiol Antimicrob* 2014;13:4.

33. Rogers BA, Ingram PR, Runnegar N, et al. Community-onset *Escherichia coli* infection resistant to expanded-spectrum cephalosporins in low-prevalence countries. *Antimicrob Agents Chemother* 2014;58:2126–34.

34. Dimude JU, Amyes SGB. Molecular diversity associated with the dissemination of CTX-M-15 beta-lactamase gene in blood culture isolates of *Escherichia coli* from Edinburgh. *Scand J Infect Dis* 2013;45:32–7.

35. Karfunkel D, Carmeli Y, Chmelnitsky I, et al. The emergence and dissemination of CTX-M-producing *Escherichia coli* sequence type 131 causing community-onset bacteremia in Israel. *Eur J Clin Microbiol Infect Dis* 2013;32:513–21.

36. Nielsen JB, Albayati A, Jørgensen RL, et al. An abbreviated MLVA identifies *Escherichia coli* ST131 as the major extended-spectrum beta-lactamase-producing lineage in the Copenhagen area. *Eur J Clin Microbiol Infect Dis* 2013;32:431–6.

37. Van der Donk CFM, Schols JMGA, Driessen CJ, et al. Prevalence and spread of multidrug resistant *Escherichia coli* isolates among nursing home residents in the southern part of The Netherlands. *J Am Med Dir Assoc* 2013;14:199–203.

38. Doi Y, Park YS, Rivera JI, et al. Community-associated extended-spectrum beta-lactamase-producing *Escherichia coli* infection in the United States. *Clin Infect Dis* 2013;56:641–8.

39. Helldal L, Karami N, Florén K, et al. Shift of CTX-M genotypes has determined the increased prevalence of extended-spectrum beta-lactamase-producing *Escherichia coli* in south-western Sweden. *Clin Microbiol Infect* 2013;19:E87–90.

40. Hammami S, Saidani M, Ferjeni S, et al. Characterization of extended spectrum beta-lactamase-producing *Escherichia coli* in community-acquired urinary tract infections in Tunisia. *Microb Drug Resist* 2013;19:231–6.

41. Kudinha T, Johnson JR, Andrew SD, et al. Distribution of phylogenetic groups, sequence type ST131, and virulence-associated traits among *Escherichia coli* isolates from men with pyelonephritis or cystitis and healthy controls. *Clin Microbiol Infect* 2013;19:E173–80.

42. Kudinha T, Johnson JR, Andrew SD et al. Genotypic and phenotypic characterization of *Escherichia coli* isolates from children with urinary tract infection and from healthy carriers. *Pediatr Infect Dis J* 2013;32:543–8.

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43. Weissman SJ, Adler A, Qin X, Zerr DM. Emergence of extended-spectrum beta-lactam resistance among *Escherichia coli* at a US academic children's hospital is clonal at the sequence type level for CTX-M-15, but not for CMY-2. *Int J Antimicrob Agents* 2013;41:414–20.

44. Banerjee R, Johnston B, Lohse C, et al. *Escherichia coli* sequence type 131 is a dominant, antimicrobial-resistant clonal group associated with healthcare and elderly hosts. *Infect Control Hosp Epidemiol* 2013;34:361–9.

45. Kim B, Kim J, Seo M-R, et al. Clinical characteristics of community-acquired acute pyelonephritis caused by ESBL-producing pathogens in South Korea. *Infection* 2013;41:603–12.

46. Aoike N, Saga T, Sakata R, et al. Molecular characterization of extraintestinal *Escherichia coli* isolates in Japan: relationship between sequence types and mutation patterns of quinolone resistance-determining regions analyzed by pyrosequencing. *J Clin Microbiol* 2013;51:1692–8.

47. Olesen B, Hansen DS, Nilsson F, et al. Prevalence and characteristics of the epidemic multiresistant *Escherichia coli* ST131 clonal group among extended-spectrum beta-lactamase-producing *E. coli* isolates in Copenhagen, Denmark. *J Clin Microbiol* 2013;51:1779–85.

48. Qin X, Hu F, Wu S, et al. Comparison of adhesin genes and antimicrobial susceptibilities between uropathogenic and intestinal commensal *Escherichia coli* strains. *PLoS One* 2013;8:e61169.

49. Denisuik AJ, Lagacé-Wiens PRS, Pitout JD, et al. Molecular epidemiology of extended-spectrum beta-lactamase-, AmpC beta-lactamase- and carbapenemase-producing *Escherichia coli* and *Klebsiella pneumoniae* isolated from Canadian hospitals over a 5 year period: CANWARD 2007-11. *J Antimicrob Chemother* 2013;68 Suppl 1:i57–65.

50. Yano H, Uemura M, Endo S, et al. Molecular characteristics of extended-spectrum beta-lactamases in clinical isolates from *Escherichia coli* at a Japanese tertiary hospital. *PLoS One* 2013;8:e64359.

51. Chmielarczyk A, Pobiega M, Wójkowska-Mach J, et al. Molecular epidemiology, plasmid analysis, virulence, and resistance of *Escherichia coli* isolated from neonatal intensive care units in Poland. *Diagn Microbiol Infect Dis* 2013;76:542–5.

52. Seiffert SN, Hilty M, Kronenberg A, et al. Extended-spectrum cephalosporin-resistant *Escherichia coli* in community, specialized outpatient clinic and hospital settings in Switzerland. *J Antimicrob Chemother* 2013;68:2249–54.

53. Reyna-Flores F, Barrios H, Garza-Ramos U, et al. Molecular epidemiology of *Escherichia coli* O25b-ST131 isolates causing community-acquired UTIs in Mexico. *Diagn Microbiol Infect Dis* 2013;76:396–8.

54. Mnif B, Harhour H, Jdidi J, et al. Molecular epidemiology of extended-spectrum beta-lactamase-producing *Escherichia coli* in Tunisia and characterization of their virulence factors and plasmid addiction systems. *BMC Microbiol* 2013;13:147.

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55. Williamson DA, Freeman JT, Porter S, et al. Clinical and molecular correlates of virulence in *Escherichia coli* causing bloodstream infection following transrectal ultrasound-guided (TRUS) prostate biopsy. *J Antimicrob Chemother* 2013;68:2898–906.

56. Kang C-I, Cha MK, Kim SH, et al. Clinical and molecular epidemiology of community-onset bacteremia caused by extended-spectrum beta-lactamase-producing *Escherichia coli* over a 6-year period. *J Korean Med Sci* 2013;28:998–1004.

57. Kudinha T, Johnson JR, Andrew SD, et al. *Escherichia coli* sequence type 131 as a prominent cause of antibiotic resistance among urinary *Escherichia coli* isolates from reproductive-age women. *J Clin Microbiol* 2013;51:3270–6.

58. Hu Y-Y, Cai J-C, Zhou H-W, et al. Molecular typing of CTX-M-producing E*scherichia Coli* isolates from environmental water, swine feces, specimens from healthy humans, and human patients. *Appl Environ Microbiol* 2013;79:5988–96.

59. Van der Donk C, van de Bovenkamp J, Bamelis H, et al. Prevalence and spread of multidrug-resistant *Escherichia coli* including ST131 in different patient populations in the Euroregion Meuse-Rhine. *Future Microbiol* 2013;8:1027–37.

60. Banerjee R, Strahilevitz J, Johnson JR, et al. Predictors and molecular epidemiology of community-onset extended-spectrum beta-lactamase-producing *Escherichia coli* infection in a Midwestern community. *Infect Control Hosp Epidemiol* 2013;34:947–53.

61. Blanco J, Mora A, Mamani R, et al. Four main virotypes among extended-spectrum beta-lactamase-producing isolates of *Escherichia coli* O25b:H4-B2-ST131: bacterial, epidemiological, and clinical characteristics. *J Clin Microbiol* 2013;51:3358–67.

62. Colpan A, Johnston B, Porter S, et al. *Escherichia coli* sequence type 131 (ST131) subclone H30 as an emergent multidrug-resistant pathogen among US veterans. *Clin Infect Dis* 2013;57:1256–65.

63. Dahbi G, Mora A, López C, et al. Emergence of new variants of ST131 clonal group among extraintestinal pathogenic *Escherichia coli* producing extended-spectrum beta-lactamases. *Int J Antimicrob Agents* 2013;42:347–51.

64. Horner C, Fawley W, Morris K, et al. *Escherichia coli* bacteraemia: 2 years of prospective regional surveillance (2010-12). *J Antimicrob Chemother* 2014;69:91–100.

65. Banerjee R, Johnston B, Lohse C, et al. The clonal distribution and diversity of extraintestinal *Escherichia coli* isolates vary according to patient characteristics. *Antimicrob Agents Chemother* 2013;57:5912–7.

66. Ha YE, Kang C-I, Cha MK, et al. Epidemiology and clinical outcomes of bloodstream infections caused by extended-spectrum beta-lactamase-producing *Escherichia coli* in patients with cancer. *Int J Antimicrob Agents* 2013;42:403–9.

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67. Brolund A, Edquist PJ, Mäkitalo B, et al. Epidemiology of extended-spectrum beta-lactamase-producing *Escherichia coli* in Sweden 2007-2011. *Clin Microbiol Infect* 2014;20:O344–52.

68. Aschbacher R, Giani T, Corda D, et al. Carbapenemase-producing Enterobacteriaceae during 2011-12 in the Bolzano area (Northern Italy): increasing diversity in a low-endemicity setting. *Diagn Microbiol Infect Dis* 2013;77:354–6.

69. Calhau V, Ribeiro G, Mendonça N, et al. Prevalent combination of virulence and plasmidic-encoded resistance in ST 131 *Escherichia coli* strains. *Virulence* 2013;4:726–9.

70. Ferjani S, Saidani M, Ennigrou S, et al. Multidrug resistance and high virulence genotype in uropathogenic *Escherichia coli* due to diffusion of ST131 clonal group producing CTX-M-15: an emerging problem in a Tunisian hospital. *Folia Microbiol (Praha)* 2014;59:257–62.

71. Markovska R, Schneider I, Ivanova D, et al. Predominance of IncL/M and IncF plasmid types among CTX-M-ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* in Bulgarian hospitals. *APMIS* 2013;122:608–15.

72. Ma L, Siu LK, Lin J-C, et al. Updated molecular epidemiology of carbapenem-non-susceptible *Escherichia coli* in Taiwan: first identification of KPC-2 or NDM-1-producing *E. coli* in Taiwan. *BMC Infect Dis* 2013;13:599.

73. Brisse S, Diancourt L, Laouénan C, et al. Phylogenetic distribution of CTX-M- and non-extended-spectrum-beta-lactamase-producing *Escherichia coli* isolates: group B2 isolates, except clone ST131, rarely produce CTX-M enzymes. *J Clin Microbiol* 2012;50:2974–81.

74. Chandramohan L, Revell PA. Prevalence and molecular characterization of extended-spectrum-beta-lactamase-producing Enterobacteriaceae in a pediatric patient population. *Antimicrob Agents Chemother* 2012;56:4765–70.

75. Musumeci R, Rausa M, Giovannoni R, et al. Prevalence of plasmid-mediated quinolone resistance genes in uropathogenic *Escherichia coli* isolated in a teaching hospital of northern Italy. *Microb Drug Resist* 2012;18:33–41.

76. Oteo J, Cercenado E, Fernández-Romero S, et al. Extended-spectrum-beta-lactamase-producing *Escherichia coli* as a cause of pediatric infections: report of a neonatal intensive care unit outbreak due to a CTX-M-14-producing strain. *Antimicrob Agents Chemother* 2012;56:54–8.

77. Gibreel TM, Dodgson AR, Cheesbrough J, et al. Population structure, virulence potential and antibiotic susceptibility of uropathogenic *Escherichia coli* from Northwest England. *J Antimicrob Chemother* 2012;67:346–56.

78. Chung H-C, Lai C-H, Lin J-N, et al. Bacteremia caused by extended-spectrum-beta-lactamase-producing *Escherichia coli* sequence type ST131 and non-ST131 clones: comparison of demographic data, clinical features, and mortality. *Antimicrob Agents Chemother* 2012;56:618–22.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2015-009971 on 17 March 2016. Downloaded from http://bmjopen.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

79. Tiruvury H, Johnson JR, Mariano N, et al. Identification of CTX-M beta-lactamases among *Escherichia coli* from the community in New York City. *Diagn Microbiol Infect Dis* 2012;72:248–52.

80. Giufrè M, Graziani C, Accogli M, et al. *Escherichia coli* of human and avian origin: detection of clonal groups associated with fluoroquinolone and multidrug resistance in Italy. *J Antimicrob Chemother* 2012;67:860–7.

81. Novais A, Rodrigues C, Branquinho R, et al. Spread of an OmpK36-modified ST15 *Klebsiella pneumoniae* variant during an outbreak involving multiple carbapenem-resistant Enterobacteriaceae species and clones. *Eur J Clin Microbiol Infect Dis* 2012;31:3057–63.

82. Matsumura Y, Nagao M, Iguchi M, et al. Molecular and clinical characterization of plasmid-mediated AmpC beta-lactamase-producing *Escherichia coli* bacteraemia: a comparison with extended-spectrum beta-lactamase-producing and non-resistant *E. coli* bacteraemia. *Clin Microbiol Infect* 2013;19:161–8.

83. Yokota S, Sato T, Okubo T, et al. Prevalence of fluoroquinolone-resistant *Escherichia coli* O25:H4-ST131 (CTX-M-15-nonproducing) strains isolated in Japan. *Chemotherapy* 2012;58:52–9.

84. Johnson JR, Urban C, Weissman SJ, et al. Molecular epidemiological analysis of *Escherichia coli* sequence type ST131 (O25:H4) and $bla_{\text{CTX-M-15}}$ among extended-spectrum-beta-lactamase-producing *E. coli* from the United States, 2000 to 2009. *Antimicrob Agents Chemother* 2012;56:2364–70.

85. Williamson DA, Roberts SA, Paterson DL, et al. *Escherichia coli* bloodstream infection after transrectal ultrasound-guided prostate biopsy: implications of fluoroquinolone-resistant sequence type 131 as a major causative pathogen. *Clin Infect Dis* 2012;54:1406–12.

86. Kim YA, Qureshi ZA, Adams-Haduch JM, et al. Features of infections due to *Klebsiella pneumoniae* carbapenemase-producing *Escherichia coli*: emergence of sequence type 131. *Clin Infect Dis* 2012;55:224–31.

87. Ho PL, Yeung MK, Lo WU, et al. Predominance of pHK01-like incompatibility group FII plasmids encoding CTX-M-14 among extended-spectrum beta-lactamase-producing *Escherichia coli* in Hong Kong, 1996-2008. *Diagn Microbiol Infect Dis* 2012;73:182–6.

88. Dimou V, Dhanji H, Pike R, et al. Characterization of Enterobacteriaceae producing OXA-48-like carbapenemases in the UK. *J Antimicrob Chemother* 2012;67:1660–5.

89. Burke L, Humphreys H, Fitzgerald-Hughes D. The revolving door between hospital and community: extended-spectrum beta-lactamase-producing *Escherichia coli* in Dublin. *J Hosp Infect* 2012;81:192–8.

90. Park SH, Byun J-H, Choi S-M, et al. Molecular epidemiology of extended-spectrum beta-lactamase-producing *Escherichia coli* in the community and hospital in Korea: emergence of ST131 producing CTX-M-15. *BMC Infect Dis* 2012;12:149.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2015-009971 on 17 March 2016. Downloaded from http://bmjopen.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

91. Reuland EA, Overdevest ITMA, Al Naiemi N, et al. High prevalence of ESBL-producing Enterobacteriaceae carriage in Dutch community patients with gastrointestinal complaints. *Clin Microbiol Infect* 2013;19:542–9.

92. Kuroda H, Yano H, Hirakata Y, et al. Molecular characteristics of extended-spectrum beta-lactamase-producing *Escherichia coli* in Japan: emergence of CTX-M-15-producing *E. coli* ST131. *Diagn Microbiol Infect Dis* 2012;74:201–3.

93. Gibreel TM, Dodgson AR, Cheesbrough J, et al. High metabolic potential may contribute to the success of ST131 uropathogenic *Escherichia coli*. *J Clin Microbiol* 2012;50:3202–7.

94. Matsumura Y, Yamamoto M, Nagao M, et al. Emergence and spread of B2-ST131-O25b, B2-ST131-O16 and D-ST405 clonal groups among extended-spectrum-beta-lactamase-producing *Escherichia coli* in Japan. *J Antimicrob Chemother* 2012;67:2612–20.

95. Österblad M, Kirveskari J, Hakanen AJ, et al. Carbapenemase-producing Enterobacteriaceae in Finland: the first years (2008-11). *J Antimicrob Chemother* 2012;67:2860–4.

96. Naseer U, Olsson-Liljequist BE, Woodford N, et al. Multi-locus variable number of tandem repeat analysis for rapid and accurate typing of virulent multidrug resistant *Escherichia coli* clones. *PLoS One* 2012;7:e41232.

97. Golding GR, Persaud N, Levett PN, et al. Characterization of *Escherichia coli* urinary tract infection isolates in remote northern Saskatchewan communities: the Northern Antibiotic Resistance Partnership. *Diagn Microbiol Infect Dis* 2012;74:242–7.

98. Hussain A, Ewers C, Nandanwar N, et al. Multiresistant uropathogenic *Escherichia coli* from a region in India where urinary tract infections are endemic: genotypic and phenotypic characteristics of sequence type 131 isolates of the CTX-M-15 extended-spectrum beta-lactamase-producing lineage. *Antimicrob Agents Chemother* 2012;56:6358–65.

99. Van der Donk CFM, van de Bovenkamp JHB, De Brauwer EIGB, et al. Antimicrobial resistance and spread of multi drug resistant *Escherichia coli* isolates collected from nine urology services in the Euregion Meuse-Rhine. *PLoS One* 2012;7:e47707.

100. Adams-Sapper S, Diep BA, Perdreau-Remington F, et al. Clonal composition and community clustering of drug-susceptible and -resistant *Escherichia coli* isolates from bloodstream infections. *Antimicrob Agents Chemother* 2013;57:490–7.

101. López-Cerero L, Bellido M del M, Serrano L, et al. *Escherichia coli* O25b:H4/ST131 are prevalent in Spain and are often not associated with ESBL or quinolone resistance. *Enferm Infecc Microbiol Clin* 2013;31:385–8.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2015-009971 on 17 March 2016. Downloaded from http://bmjopen.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

102. Mavroidi A, Miriagou V, Liakopoulos A, et al. Ciprofloxacin-resistant *Escherichia coli* in Central Greece: mechanisms of resistance and molecular identification. *BMC Infect Dis* 2012;12:371.

103. Overdevest I, Willemsen I, Rijnsburger M, et al. Extended-spectrum beta-lactamase genes of *Escherichia coli* in chicken meat and humans, The Netherlands. *Emerg Infect Dis* 2011;17:1216–22.

104. Leverstein-van Hall MA, Dierikx CM, Cohen Stuart J, et al. Dutch patients, retail chicken meat and poultry share the same ESBL genes, plasmids and strains. *Clin Microbiol Infect* 2011;17:873–80.

105. Courpon-Claudinon A, Lefort A, Panhard X, et al. Bacteraemia caused by third-generation cephalosporin-resistant *Escherichia coli* in France: prevalence, molecular epidemiology and clinical features. *Clin Microbiol Infect* 2011;17:557–65.

106. Vidal-Navarro L, Pfeiffer C, Bouziges N, et al. Faecal carriage of multidrug-resistant Gram-negative bacilli during a non-outbreak situation in a French university hospital. *J Antimicrob Chemother* 2010;65:2455–8.

107. Rodriguez-Villalobos H, Bogaerts P, Berhin C, et al. Trends in production of extended-spectrum beta-lactamases among Enterobacteriaceae of clinical interest: results of a nationwide survey in Belgian hospitals. *J Antimicrob Chemother* 2011;66:37–47.

108. Mora A, Blanco M, López C, et al. Emergence of clonal groups O1:HNM-D-ST59, O15:H1-D-ST393, O20:H34/HNM-D-ST354, O25b:H4-B2-ST131 and ONT:H21,42-B1-ST101 among CTX-M-14-producing *Escherichia coli* clinical isolates in Galicia, northwest Spain. *Int J Antimicrob Agents* 2011;37:16–21.

109. Coelho A, Mora A, Mamani R, et al. Spread of *Escherichia coli* O25b:H4-B2-ST131 producing CTX-M-15 and SHV-12 with high virulence gene content in Barcelona (Spain). *J Antimicrob Chemother* 2011;66:517–26.

110. Xu L, Shabir S, Bodah T, et al. Regional survey of CTX-M-type extended-spectrum beta-lactamases among Enterobacteriaceae reveals marked heterogeneity in the distribution of the ST131 clone. *J Antimicrob Chemother* 2011;66:505–11.

111. Ruiz SJ, Montealegre MC, Ruiz-Garbajosa P, et al. First characterization of CTX-M-15-producing *Escherichia coli* ST131 and ST405 clones causing community-onset infections in South America. *J Clin Microbiol* 2011;49:1993–6.

112. Simner PJ, Zhanel GG, Pitout J, et al. Prevalence and characterization of extended-spectrum beta-lactamase- and AmpC beta-lactamase-producing *Escherichia coli*: results of the CANWARD 2007-2009 study. *Diagn Microbiol Infect Dis* 2011;69:326–34.

113. Dhanji H, Patel R, Wall R, et al. Variation in the genetic environments of $bla_{CTX-M-15}$ in *Escherichia coli* from the faeces of travellers returning to the United Kingdom. *J Antimicrob Chemother* 2011;66:1005–12.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2015-009971 on 17 March 2016. Downloaded from http://bmjopen.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

114. Kim J, Bae IK, Jeong SH, et al. Characterization of IncF plasmids carrying the *bla*$_{CTX-M-14}$ gene in clinical isolates of *Escherichia coli* from Korea. *J Antimicrob Chemother* 2011;66:1263–8.

115. Van der Bij AK, Peirano G, Goessens WHF, et al. Clinical and molecular characteristics of extended-spectrum-beta-lactamase-producing *Escherichia coli* causing bacteremia in the Rotterdam Area, Netherlands. *Antimicrob Agents Chemother* 2011;55:3576–8.

116. Titelman E, Karlsson IM, Ge Y, Giske CG. In vitro activity of CXA-101 plus tazobactam (CXA-201) against CTX-M-14- and CTX-M-15-producing *Escherichia coli* and *Klebsiella pneumoniae*. *Diagn Microbiol Infect Dis* 2011;70:137–41.

117. Cao X, Cavaco LM, Lv Y, et al. Molecular characterization and antimicrobial susceptibility testing of *Escherichia coli* isolates from patients with urinary tract infections in 20 Chinese hospitals. *J Clin Microbiol* 2011;49:2496–501.

118. Mshana SE, Imirzalioglu C, Hain T, et al. Multiple ST clonal complexes, with a predominance of ST131, of *Escherichia coli* harbouring *bla*$_{CTX-M-15}$ in a tertiary hospital in Tanzania. *Clin Microbiol Infect* 2011;17:1279–82.

119. Blanco J, Mora A, Mamani R, et al. National survey of *Escherichia coli* causing extraintestinal infections reveals the spread of drug-resistant clonal groups O25b:H4-B2-ST131, O15:H1-D-ST393 and CGA-D-ST69 with high virulence gene content in Spain. *J Antimicrob Chemother* 2011;66:2011–21.

120. Shin J, Kim DH, Ko KS. Comparison of CTX-M-14- and CTX-M-15-producing *Escherichia coli* and *Klebsiella pneumoniae* isolates from patients with bacteremia. *J Infect* 2011;63:39–47.

121. Croxall G, Hale J, Weston V, et al. Molecular epidemiology of extraintestinal pathogenic *Escherichia coli* isolates from a regional cohort of elderly patients highlights the prevalence of ST131 strains with increased antimicrobial resistance in both community and hospital care settings. *J Antimicrob Chemother* 2011;66:2501–8.

122. Simner PJ, Hoban DJ, Lagacé-Wiens PRS, et al. Fluoroquinolone resistance in *Escherichia coli* isolated from patients attending Canadian hospitals is associated with the ST131 clone. *Diagn Microbiol Infect Dis* 2011;71:323–4.

123. Titelman E, Iversen A, Kahlmeter G, et al. Antimicrobial susceptibility to parenteral and oral agents in a largely polyclonal collection of CTX-M-14 and CTX-M-15-producing *Escherichia coli* and *Klebsiella pneumoniae*. *APMIS* 2011;119:853–63.

124. Peirano G, van der Bij AK, Gregson DB, et al. Molecular epidemiology over an 11-year period (2000 to 2010) of extended-spectrum beta-lactamase-producing *Escherichia coli* causing bacteremia in a centralized Canadian region. *J Clin Microbiol* 2012;50:294–9.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2015-009971 on 17 March 2016. Downloaded from http://bmjopen.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

125. Molina-López J, Aparicio-Ozores G, Ribas-Aparicio RM, et al. Drug resistance, serotypes, and phylogenetic groups among uropathogenic *Escherichia coli* including O25-ST131 in Mexico City. *J Infect Dev Ctries* 2011;5:840–9.

126. Sidjabat HE, Derrington P, Nimmo GR, et al. *Escherichia coli* ST131 producing CTX-M-15 in Australia. *J Antimicrob Chemother* 2010;65:1301–3.

127. Tian G-B, Garcia J, Adams-Haduch JM, et al. CTX-M as the predominant extended-spectrum beta-lactamases among Enterobacteriaceae in Manila, Philippines. *J Antimicrob Chemother* 2010;65:584–6.

128. Platell JL, Cobbold RN, Johnson JR, et al. Clonal group distribution of fluoroquinolone-resistant *Escherichia coli* among humans and companion animals in Australia. *J Antimicrob Chemother* 2010;65:1936–8.

129. Naseer U, Haldorsen B, Simonsen GS, et al. Sporadic occurrence of CMY-2-producing multidrug-resistant *Escherichia coli* of ST-complexes 38 and 448, and ST131 in Norway. *Clin Microbiol Infect* 2010;16:171–8.

130. Johnson JR, Johnston B, Clabots C, et al. *Escherichia coli* sequence type ST131 as an emerging fluoroquinolone-resistant uropathogen among renal transplant recipients. *Antimicrob Agents Chemother* 2010;54:546–50.

131. Lee MY, Choi HJ, Choi JY, et al. Dissemination of ST131 and ST393 community-onset, ciprofloxacin-resistant *Escherichia coli* clones causing urinary tract infections in Korea. *J Infect* 2010;60:146–53.

132. Peirano G, Richardson D, Nigrin J, et al. High prevalence of ST131 isolates producing CTX-M-15 and CTX-M-14 among extended-spectrum-beta-lactamase-producing *Escherichia coli* isolates from Canada. *Antimicrob Agents Chemother* 2010;54:1327–30.

133. Severin JA, Mertaniasih NM, Kuntaman K, et al. Molecular characterization of extended-spectrum beta-lactamases in clinical *Escherichia coli* and *Klebsiella pneumoniae* isolates from Surabaya, Indonesia. *J Antimicrob Chemother* 2010;65:465–9.

134. Cerquetti M, Giufrè M, García-Fernández A, et al. Ciprofloxacin-resistant, CTX-M-15-producing *Escherichia coli* ST131 clone in extraintestinal infections in Italy. *Clin Microbiol Infect* 2010;16:1555–8.

135. Peirano G, Costello M, Pitout JDD. Molecular characteristics of extended-spectrum beta-lactamase-producing *Escherichia coli* from the Chicago area: high prevalence of ST131 producing CTX-M-15 in community hospitals. *Int J Antimicrob Agents* 2010;36:19–23.

136. Smet A, Martel A, Persoons D, et al. Characterization of extended-spectrum beta-lactamases produced by *Escherichia coli* isolated from hospitalized and nonhospitalized patients: emergence of CTX-M-15-producing strains causing urinary tract infections. *Microb Drug Resist* 2010;16:129–34.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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137. Dahmen S, Bettaieb D, Mansour W, et al. Characterization and molecular epidemiology of extended-spectrum beta-lactamases in clinical isolates of Enterobacteriaceae in a Tunisian University Hospital. *Microb Drug Resist* 2010;16:163–70.

138. Oteo J, Cercenado E, Cuevas O, et al. AmpC beta-lactamases in *Escherichia coli*: emergence of CMY-2-producing virulent phylogroup D isolates belonging mainly to STs 57, 115, 354, 393, and 420, and phylogroup B2 isolates belonging to the international clone O25b-ST131. *Diagn Microbiol Infect Dis* 2010;67:270–6.

139. Díaz MA, Hernández-Bello JR, Rodríguez-Baño J, et al. Diversity of *Escherichia coli* strains producing extended-spectrum beta-lactamases in Spain: Second nationwide study. *J Clin Microbiol* 2010;48:2840–5.

140. Bert F, Johnson JR, Ouattara B, et al. Genetic diversity and virulence profiles of *Escherichia coli* isolates causing spontaneous bacterial peritonitis and bacteremia in patients with cirrhosis. *J Clin Microbiol* 2010;48:2709–14.

141. Johnson JR, Johnston B, Clabots C, et al. *Escherichia coli* sequence type ST131 as the major cause of serious multidrug-resistant *E. coli* infections in the United States. *Clin Infect Dis* 2010;51:286–94.

142. Brolund A, Hæggman S, Edquist PJ, et al. The DiversiLab system versus pulsed-field gel electrophoresis: characterisation of extended spectrum beta-lactamase producing *Escherichia coli* and *Klebsiella pneumoniae*. *J Microbiol Methods* 2010;83:224–30.

143. Jouini A, Ben Slama K, Vinué L, et al. Detection of unrelated *Escherichia coli* strains harboring genes of CTX-M-15, OXA-1, and AAC(6')-Ib-cr enzymes in a Tunisian hospital and characterization of their integrons and virulence factors. *J Chemother* 2010;22:318–23.

144. Pitout JDD, Campbell L, Church DL, et al. Molecular characteristics of travel-related extended-spectrum-beta-lactamase-producing *Escherichia coli* isolates from the Calgary Health Region. *Antimicrob Agents Chemother* 2009;53:2539–43.

145. Morris D, Boyle F, Buckley V, et al. CTX-M enzymes are the predominant extended-spectrum beta-lactamases produced by Enterobacteriaceae in Ireland. *J Antimicrob Chemother* 2009;64:864–6.

146. Hrabák J, Empel J, Bergerová T, et al. International clones of *Klebsiella pneumoniae* and *Escherichia coli* with extended-spectrum beta-lactamases in a Czech Hospital. *J Clin Microbiol* 2009;47:3353–7.

147. Suzuki S, Shibata N, Yamane K, et al. Change in the prevalence of extended-spectrum-beta-lactamase-producing *Escherichia coli* in Japan by clonal spread. *J Antimicrob Chemother* 2009;63:72–9.

148. Literacka E, Bedenic B, Baraniak A, et al. bla_{CTX-M} genes in *Escherichia coli* strains from Croatian Hospitals are located in new ($bla_{CTX-M-3a}$) and widely spread ($bla_{CTX-M-3a}$ and $bla_{CTX-M-15}$) genetic structures. *Antimicrob Agents Chemother* 2009;53:1630–5.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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149. Pitout JDD, Campbell L, Church DL, et al. Using a commercial DiversiLab semiautomated repetitive sequence-based PCR typing technique for identification of *Escherichia coli* clone ST131 producing CTX-M-15. *J Clin Microbiol* 2009;47:1212–5.

150. Arpin C, Quentin C, Grobost F, et al. Nationwide survey of extended-spectrum beta-lactamase-producing Enterobacteriaceae in the French community setting. *J Antimicrob Chemother* 2009;63:1205–14.

151. Blanco M, Alonso MP, Nicolas-Chanoine M-H, et al. Molecular epidemiology of *Escherichia coli* producing extended-spectrum beta -lactamases in Lugo (Spain): dissemination of clone O25b:H4-ST131 producing CTX-M-15. *J Antimicrob Chemother* 2009;63:1135–41.

152. Pitout JDD, Gregson DB, Campbell L, et al. Molecular characteristics of extended-spectrum-beta-lactamase-producing *Escherichia coli* isolates causing bacteremia in the Calgary Health Region from 2000 to 2007: emergence of clone ST131 as a cause of community-acquired infections. *Antimicrob Agents Chemother* 2009;53:2846–51.

153. Johnson JR, Menard M, Johnston B, et al. Epidemic clonal groups of *Escherichia coli* as a cause of antimicrobial-resistant urinary tract infections in Canada, 2002 to 2004. *Antimicrob Agents Chemother* 2009;53:2733–9.

154. Oteo J, Diestra K, Juan C, et al. Extended-spectrum beta-lactamase-producing *Escherichia coli* in Spain belong to a large variety of multilocus sequence typing types, including ST10 complex/A, ST23 complex/A and ST131/B2. *Int J Antimicrob Agents* 2009;34:173–6.

155. Clermont O, Dhanji H, Upton M, et al. Rapid detection of the O25b-ST131 clone of *Escherichia coli* encompassing the CTX-M-15-producing strains. *J Antimicrob Chemother* 2009;64:274–7.

156. Naseer U, Haldorsen B, Tofteland S, et al. Molecular characterization of CTX-M-15-producing clinical isolates of *Escherichia coli* reveals the spread of multidrug-resistant ST131 (O25:H4) and ST964 (O102:H6) strains in Norway. *APMIS* 2009;117:526–36.

157. Oteo J, Orden B, Bautista V, et al. CTX-M-15-producing urinary *Escherichia coli* O25b-ST131-phylogroup B2 has acquired resistance to fosfomycin. *J Antimicrob Chemother* 2009;64:712–7.

158. Sidjabat HE, Paterson DL, Adams-Haduch JM, et al. Molecular epidemiology of CTX-M-producing *Escherichia coli* isolates at a tertiary medical center in western Pennsylvania. *Antimicrob Agents Chemother* 2009;53:4733–9.

159. Lau SH, Reddy S, Cheesbrough J, et al. Major uropathogenic *Escherichia coli* strain isolated in the northwest of England identified by multilocus sequence typing. *J Clin Microbiol* 2008;46:1076–80.

160. Yumuk Z, Afacan G, Nicolas-Chanoine M-H, et al. Turkey: a further country concerned by community-acquired *Escherichia coli* clone O25-ST131 producing CTX-M-15. *J Antimicrob Chemother* 2008;62:284–8.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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161. Cagnacci S, Gualco L, Debbia E, et al. European emergence of ciprofloxacin-resistant *Escherichia coli* clonal groups O25:H4-ST 131 and O15:K52:H1 causing community-acquired uncomplicated cystitis. *J Clin Microbiol* 2008;46:2605–12.

162. Jones GL, Warren RE, Skidmore SJ, et al. Prevalence and distribution of plasmid-mediated quinolone resistance genes in clinical isolates of *Escherichia coli* lacking extended-spectrum beta-lactamases. *J Antimicrob Chemother* 2008;62:1245–51.

163. Vasoo S, Madigan T, Cunningham SA, et al. Prevalence of rectal colonization with multidrug-resistant Enterobacteriaceae among international patients hospitalized at Mayo Clinic, Rochester, Minnesota. *Infect Control Hosp Epidemiol* 2014;35:182–6.

164. March A, Aschbacher R, Pagani E, et al. Changes in colonization of residents and staff of a long-term care facility and an adjacent acute-care hospital geriatric unit by multidrug-resistant bacteria over a four-year period. *Scand J Infect Dis* 2014;46:114–22.

165. Nicolas-Chanoine M-H, Robert J, Vigan M, et al. Different factors associated with CTX-M-producing ST131 and non-ST131 *Escherichia coli* clinical isolates. *PLoS One* 2013;8:e72191.

166. Izdebski R, Baraniak A, Fiett J, et al. Clonal structure, extended-spectrum beta-lactamases, and acquired AmpC-type cephalosporinases of *Escherichia coli* populations colonizing patients in rehabilitation centers in four countries. *Antimicrob Agents Chemother* 2013;57:309–16.

167. Liss MA, Peterson EM, Johnston B, et al. Prevalence of ST131 among fluoroquinolone-resistant *Escherichia coli* obtained from rectal swabs before transrectal prostate biopsy. *Urology* 2013;81:548–55.

168. Birgy A, Mariani-Kurkdjian P, Bidet P, et al. Characterization of extended-spectrum-beta-lactamase-producing *Escherichia coli* strains involved in maternal-fetal colonization: prevalence of *E. coli* ST131. *J Clin Microbiol* 2013;51:1727–32.

169. Nüesch-Inderbinen MT, Abgottspon H, Zurfluh K, et al. Cross-sectional study on fecal carriage of Enterobacteriaceae with resistance to extended-spectrum cephalosporins in primary care patients. *Microb Drug Resist* 2013;19:362–9.

170. Arvand M, Moser V, Pfeifer Y. Prevalence of extended-spectrum-beta-lactamase-producing *Escherichia coli* and spread of the epidemic clonal lineage ST131 in nursing homes in Hesse, Germany. *J Antimicrob Chemother* 2013;68:2686–8.

171. Roy S, Krishnan R, Mukherjee S, et al. Prevalence of ST131 virulence-associated strains among CTX-M-producing *Escherichia coli* in the gut of hospitalized neonates in India. *Diagn Microbiol Infect Dis* 2013;77:158–9.

172. Severin JA, Lestari ES, Kloezen W, et al. Faecal carriage of extended-spectrum beta-lactamase-producing Enterobacteriaceae among humans in Java, Indonesia, in 2001-2002. *Trop Med Int Health* 2012;17:455–61.

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173. Dolejska M, Brhelova E, Dobiasova H, et al. Dissemination of IncFII(K)-type plasmids in multiresistant CTX-M-15-producing Enterobacteriaceae isolates from children in hospital paediatric oncology wards. *Int J Antimicrob Agents* 2012;40:510–5.

174. Li B, Sun J-Y, Liu Q-Z, et al. High prevalence of CTX-M beta-lactamases in faecal *Escherichia coli* strains from healthy humans in Fuzhou, China. *Scand J Infect Dis* 2011;43:170–4.

175. Peirano G, Laupland KB, Gregson DB, et al. Colonization of returning travelers with CTX-M-producing *Escherichia coli*. *J Travel Med* 2011;18:299–303.

176. Leflon-Guibout V, Blanco J, Amaqdouf K, et al. Absence of CTX-M enzymes but high prevalence of clones, including clone ST131, among fecal *Escherichia coli* isolates from healthy subjects living in the area of Paris, France. *J Clin Microbiol* 2008;46:3900–5.

177. Lascols C, Peirano G, Hackel M, et al. Surveillance and molecular epidemiology of *Klebsiella pneumoniae* isolates that produce carbapenemases: first report of OXA-48-like enzymes in North America. *Antimicrob Agents Chemother* 2013;57:130–6.

178. Castanheira M, Farrell SE, Wanger A, et al. Rapid expansion of KPC-2-producing *Klebsiella pneumoniae* isolates in two Texas hospitals due to clonal spread of ST258 and ST307 lineages. *Microb Drug Resist* 2013;19:295–7.

179. Rodríguez-Zulueta P, Silva-Sánchez J, Barrios H, et al. First outbreak of KPC-3-producing *Klebsiella pneumoniae* (ST258) clinical isolates in a Mexican Medical Center. *Antimicrob Agents Chemother* 2013;57:4086–8.

180. Di Carlo P, Gulotta G, Casuccio A, et al. KPC - 3 *Klebsiella pneumoniae* ST258 clone infection in postoperative abdominal surgery patients in an intensive care setting: analysis of a case series of 30 patients. *BMC Anesthesiol* 2013;13:13.

181. Hrabák J, Papagiannitsis CC, Študentová V, et al. Carbapenemase-producing *Klebsiella pneumoniae* in the Czech Republic in 2011. *Euro Surveill* 2013;18:20626.

182. Jain R, Walk ST, Aronoff DM, et al. Emergence of Carbapenemaseproducing *Klebsiella pneumoniae* of Sequence type 258 in Michigan, USA. *Infect Dis Rep* 2013;5:e5.

183. Cejas D, Fernandez Canigia L, Nastro M, et al. Hyperendemic clone of KPC producing *Klebsiella pneumoniae* ST 258 in Buenos Aires hospitals. *Infect Genet Evol* 2012;12:499–501.

184. Warburg G, Hidalgo-Grass C, Partridge SR, et al. A carbapenem-resistant *Klebsiella pneumoniae* epidemic clone in Jerusalem: sequence type 512 carrying a plasmid encoding aac(6')-Ib. *J Antimicrob Chemother* 2012;67:898–901.

185. Richter SN, Frasson I, Franchin E, et al. KPC-mediated resistance in *Klebsiella pneumoniae* in two hospitals in Padua, Italy, June 2009-December 2011: massive spreading of a KPC-3-encoding plasmid and involvement of non-intensive care units. *Gut Pathog* 2012;4:7.

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186. Adler A, Paikin S, Sterlin Y, et al. A swordless knight: epidemiology and molecular characteristics of the *bla*$_{KPC}$-negative sequence type 258 *Klebsiella pneumoniae* clone. *J Clin Microbiol* 2012;50:3180–5.

187. Mammina C, Bonura C, Di Bernardo F, et al. Ongoing spread of colistin-resistant *Klebsiella pneumoniae* in different wards of an acute general hospital, Italy, June to December 2011. *Euro Surveill* 2012;17.

188. Mataseje LF, Boyd DA, Willey BM, et al. Plasmid comparison and molecular analysis of *Klebsiella pneumoniae* harbouring *bla*$_{KPC}$ from New York City and Toronto. *J Antimicrob Chemother* 2011;66:1273–7.

189. Giakkoupi P, Papagiannitsis CC, Miriagou V, et al. An update of the evolving epidemic of *bla*$_{KPC-2}$-carrying *Klebsiella pneumoniae* in Greece (2009-10). *J Antimicrob Chemother* 2011;66:1510–3.

190. Andrade LN, Curiao T, Ferreira JC, et al. Dissemination of *bla*$_{KPC-2}$ by the spread of *Klebsiella pneumoniae* clonal complex 258 clones (ST258, ST11, ST437) and plasmids (IncFII, IncN, IncL/M) among Enterobacteriaceae species in Brazil. *Antimicrob Agents Chemother* 2011;55:3579–83.

191. Gomez SA, Pasteran FG, Faccone D, et al. Clonal dissemination of *Klebsiella pneumoniae* ST258 harbouring KPC-2 in Argentina. *Clin Microbiol Infect* 2011;17:1520–4.

192. Baraniak A, Grabowska A, Izdebski R, et al. Molecular characteristics of KPC-producing Enterobacteriaceae at the early stage of their dissemination in Poland, 2008-2009. *Antimicrob Agents Chemother* 2011;55:5493–9.

193. Cuzon G, Naas T, Truong H, et al. Worldwide diversity of *Klebsiella pneumoniae* that produce beta-lactamase *bla*$_{KPC-2}$ gene. *Emerg Infect Dis* 2010;16:1349–56.

194. Endimiani A, Depasquale JM, Forero S, et al. Emergence of *bla*$_{KPC}$-containing *Klebsiella pneumoniae* in a long-term acute care hospital: a new challenge to our healthcare system. *J Antimicrob Chemother* 2009;64:1102–10.

195. Paterson GK, Harrison EM, Murray GGR, et al. Capturing the cloud of diversity reveals complexity and heterogeneity of MRSA carriage, infection and transmission. *Nat Commun* 2015;6:6560.

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Figure legends

Figure 1: Simple model

Figure 2: Flowchart of article selection

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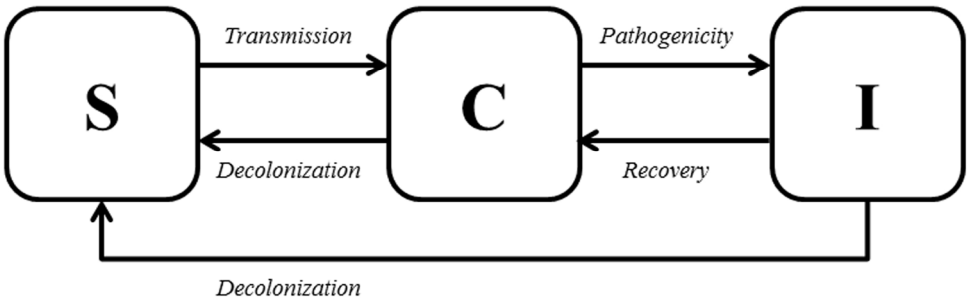

Figure 1: Simple model
209x67mm (300 x 300 DPI)

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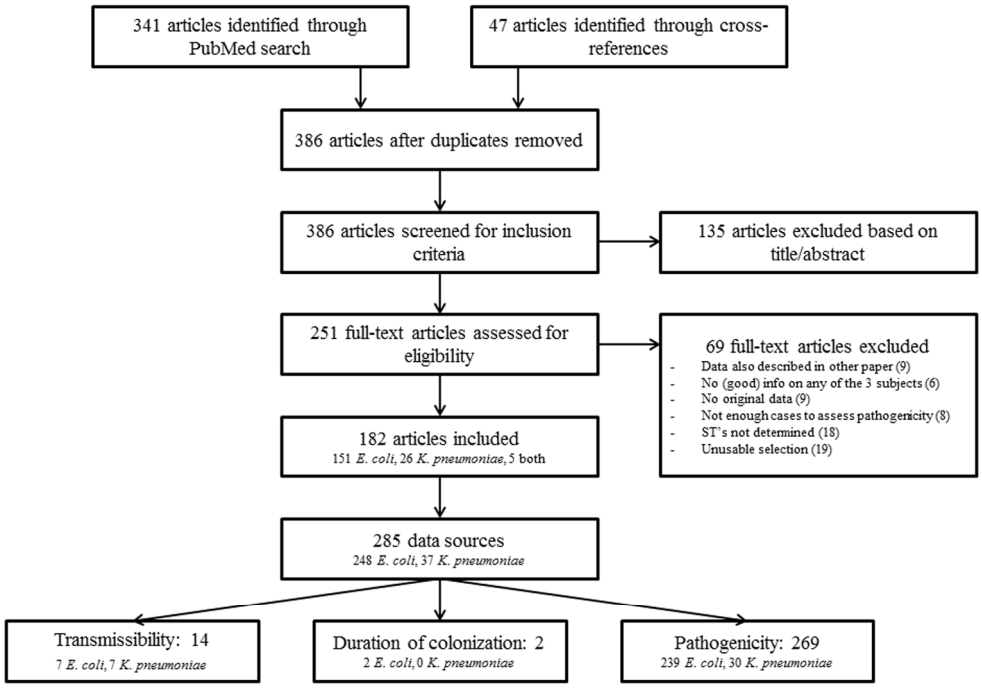

Figure 2: Flowchart of article selection
254x190mm (300 x 300 DPI)

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Supplementary Material

Supplementary Text 1. Search string.

((k. pneumoniae[All Fields] AND (st258[All Fields] OR st 258[All Fields] OR (((“sequence”[All Fields] AND type[All Fields]) OR sequence type[All Fields]) AND 258[All Fields]))) OR (e. coli[All Fields] AND (st131[All Fields] OR st 131[All Fields] OR (((“sequence”[All Fields] AND type[All Fields]) OR sequence type[All Fields]) AND 131[All Fields]))))

AND

(

(“transmission”[Subheading] OR transmissi*[All Fields] OR transmit*[All Fields] OR spread*[All Fields] OR disease outbreaks[All Fields] OR (disease[All Fields] AND outbreaks[All Fields]) OR outbreak*[All Fields] OR “gene transfer, horizontal“[MeSH Terms] OR (gene[All Fields] AND (“transfer”[All Fields] OR “transfers”[All Fields]) AND horizontal[All Fields]) OR horizontal gene transfer*[All Fields] OR conjugation*[All Fields] OR ((“plasmids”[MeSH Terms] OR plasmid*[All Fields]) AND (“transfer”[All Fields] OR “transfers”[All Fields])))

OR

(((colonis*[All Fields] OR coloniz*[All Fields]) AND (duration*[All Fields] OR (“period”[All Fields] OR “periods”[All Fields]) OR times[All Fields])) OR (infectious[All Fields] AND (“period”[All Fields] OR “periods”[All Fields] OR times[All Fields] OR interval[All Fields] OR intervals[All Fields])) OR (“generation”[All Fields] AND (times[All Fields] OR interval[All Fields] OR intervals[All Fields])))

OR

(“pathogenicity”[Subheading] OR pathogenic*[All Fields] OR virulen*[All Fields] OR “virulence”[MeSH Terms] OR infectiv*[All Fields] OR infectious[All Fields] OR infectious*[All Fields])

)

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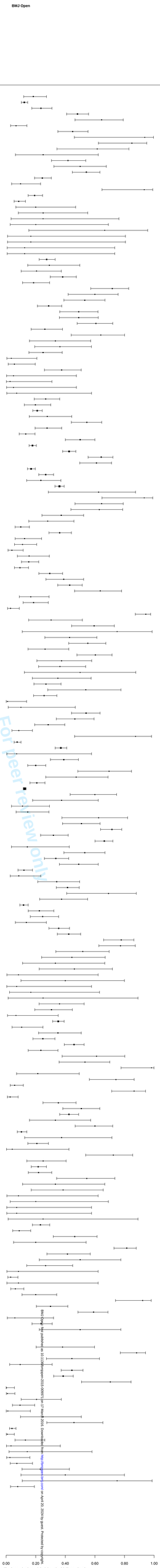
Supplementary Figure 1: Forest plot showing proportion ST131 in *E. coli*

Author (pub. year)	ST131 (n)	Total (n)	ST131 (%)
Infection			
Habeeb, 2014 [29]	18	98	18.4
Clermont, 2009 (other) [30]	114	928	12.3
Lopez−Cerero, 2014 (ESBL) [30]	35	149	23.5
Giufre, 2014 [31]	83	172	61.3
Al−Agamy, 2014 [32]	20	31	64.5
Rogers, 2014 (other) [33]	6	90	6.7
Rogers, 2014 (ESBL) [33]	40	89	44.9
Dimude, 2013 [34]	7	7	100
Karfunkel, 2013 (2009) [35]	17	20	85
Karfunkel, 2013 (2007) [35]	8	13	61.5
Karfunkel, 2013 (2003) [35]	2	8	25
Nielsen, 2013 [36]	28	67	41.8
van der Donk, 2013 [37]	14	28	50
Doi, 2013 [38]	58	107	54.2
Helldal, 2013 (2008) [39]	54	221	24.4
Helldal, 2013 (2004) [39]	4	41	9.8
Hammami, 2013 [40]	14	15	93.3
Kudinha, 2013a [41]	49	254	8.5
Kudinha, 2013b (Inpatients) [42]	18	212	6.4
Weissman, 2013 (2007) [43]	3	15	20
Weissman, 2013 (2006) [43]	3	12	25
Weissman, 2013 (2005) [43]	1	4	25
Weissman, 2013 (2004) [43]	1	5	20
Weissman, 2013 (2003) [43]	2	3	66.7
Weissman, 2013 (2002) [43]	0	2	0
Weissman, 2013 (2001) [43]	0	2	0
Weissman, 2013 (2000) [43]	0	3	0
Weissman, 2013 (1999) [43]	0	3	0
Banerjee, 2013 [44]	71	259	27.4
Kim, 2013a [45]	7	24	29.2
Aoike, 2013 [46]	7	34	20.6
Olesen, 2013 [57]	44	115	38.3
Qin, 2013 (Inpatients) [48]	13	70	18.6
Denisuk, 2013 (ESBL 2011) [49]	33	46	71.7
Denisuk, 2013 (ESBL 2010) [49]	18	30	60
Denisuk, 2013 (ESBL 2009) [49]	25	47	53.2
Denisuk, 2013 (Other 2007−2011) [49]	33	115	28.7
Denisuk, 2013 (ESBL 2008) [49]	27	55	49.1
Denisuk, 2013 (ESBL 2007) [49]	26	53	49.1
Yano, 2013 [50]	37	61	60.7
Chmielarczyk, 2013 (other) [51]	17	65	26.2
Chmielarczyk, 2013 (ESBL) [51]	16	25	64
Seiffert, 2013 (Outpatients/community) [52]	6	18	28.6
Seiffert, 2013 (Inpatients) [52]	8	22	36.4
Reyne−Flores, 2013 [53]	14	56	25
Minf, 2013 (2009) [54]	1	29	3.4
Minf, 2013 (2006) [54]	2	36	5.6
Minf, 2013 (2003−2004) [54]	21	56	37.5
Minf, 2013 (2002) [54]	0	9	0
Minf, 2013 (2001) [54]	0	18	0
Minf, 2013 (2000) [54]	0	9	0
Minf, 2013 (1989−1990) [54]	0	6	0
Williamson, 2013 [55]	27	101	38.3
Kang, 2013 [56]	15	76	19.7
Kudinha, 2013c (Mixed) [57]	131	623	13
Hu, 2013 (Inpatients) [58]	10	36	27.8
van der Donk, 2013 (Outpatients/community) [59]	48	88	32
van der Donk, 2013 (Inpatients) [59]	26	94	15.4
Banerjee, 2013b (other) [60]	21	158	13.3
Banerjee, 2013b (ESBL) [60]	47	94	50
Blanco, 2013 [61]	166	931	17.4
Colpan, 2013 (other) [62]	201	472	7.2
Colpan, 2013 (ESBL) [62]	79	123	64.2
Dahbi, 2013 [63]	47	77	61
Horner, 2013 [64]	130	770	16.9
Banerjee, 2013c [65]	80	299	25.4
Ha, 2013 [66]	12	51	23.5
Brolund, 2013 [67]	329	913	36
Aschbacher, 2013 [68]	5	8	62.5
Calhau, 2013 [69]	14	15	93.3
Ferjani, 2014 [70]	20	31	64.5
Markovska, 2013 [71]	17	27	63
Ma, 2013 (2012) [72]	16	43	37.2
Ma, 2013 (2010) [72]	9	32	28.1
Brisse, 2012 (Other) [73]	15	152	9.9
Brisse, 2012 (ESBL) [73]	55	152	36.2
Chandramohan, 2012 [74]	7	56	12.5
Musumeci, 2012 (2006) [75]	8	72	11.1
Musumeci, 2012 (2004) [75]	3	76	3.9
Oteo, 2012 [76]	7	45	15.6
Gibrael, 2012 (2009) [77]	23	150	15.3
Gibrael, 2012 (2007) [77]	14	150	9.3
Chung, 2012 [78]	36	122	29.5
Tiruvury, 2012 [79]	21	54	38.9
Giufre, 2012 [80]	58	135	39.1
Novais, 2012 [81]	21	33	63.6
Matsumura, 2012a (other) [82]	9	54	16.7
Matsumura, 2012a (ESBL) [82]	15	81	25.9
Yokota, 2012 (MLST) [83]	3	100	3
Yokota, 2012 (Extrapolation PFGE) [83]	85	90	94.4
Johnson, 2012 (2009) [84]	7	23	30.4
Johnson, 2012 (2008−2009) [84]	25	42	54.8
Johnson, 2012 (2008) [84]	1	1	100
Johnson, 2012 (2007−2008) [84]	12	28	62.5
Johnson, 2012 (2007) [84]	32	58	63
Johnson, 2012 (2004−2009) [84]	10	38	26.3
Johnson, 2012 (2004−2008) [84]	38	63	60.3
Johnson, 2012 (2004−2007 children) [84]	9	24	37.5
Johnson, 2012 (2002−2009 children) [84]	12	33	36.4
Johnson, 2012 (2005) [84]	2	4	50
Johnson, 2012 (2000−2006) [84]	7	20	35
Williamson, 2012 [85]	24	89	13.3
Kim, 2012 [86]	7	13	53.8
Ho, 2012 (2007−2008) [87]	30	117	25.6
Ho, 2012 (1996−1998) [87]	0	50	0
Dmou, 2012 [88]	1	10	10
Burke, 2012 [89]	54	100	54
Park, 2012 (Outpatients/community) [90]	26	56	46.4
Park, 2012 (Inpatients) [90]	21	74	28.4
Reuland, 2012 [91]	6	70	8.6
Kuroda, 2012 [92]	7	8	87.5
Gibrael, 2012 [93]	37	500	7.4
Matsumura, 2012b [94]	215	581	37
Osterlund, 2012 [95]	0	6	0
Naseer, 2012 [96]	39	100	58.3
Golding, 2012 [97]	33	165	20
Hussain, 2012 [98]	16	23	69.6
van der Donk, 2012 [99]	9	19	47.4
Adams−Sapper, 2013 [100]	51	246	20.7
Lopez−Cerero, 2013 [101]	540	4308	12.5
Mavrodi, 2012 [102]	21	35	60
Overdevest, 2011 [103]	6	16	37.5
Leverstein−van Hall, 2011 [104]	3	27	11.1
Courpon−Claudinon, 2011 [105]	6	41	14.6
Vidal−Navarro, 2010 [106]	10	16	62.5
Rodriguez−Villalobos, 2011 [107]	29	57	50.9
Mora, 2011 [108]	108	151	86.6
Coelho, 2011 [109]	30	94	31.9
Xu, 2011 [110]	154	232	66.4
Ruiz, 2011 [111]	2	14	14.3
Simner, 2011a (2009) [112]	25	47	53.2
Simner, 2011a (2008) [112]	42	125	49.1
Simner, 2011a (2007) [112]	26	53	49.1
Dhanji, 2011 [113]	21	174	12.1
Kim, 2011 [114]	3	35	8.6
van der Bij, 2011 [115]	14	41	32
Titelman, 2011a [116]	63	152	41.4
Cao, 2011 [117]	9	13	100
Mshana, 2011 [118]	12	32	37.5
Blanco, 2011 [119]	59	500	11.8
Shin, 2011 [120]	20	89	22.5
Croxall, 2011 (Outpatients/community) [121]	19	77	24.7
Croxall, 2011 (Inpatients) [121]	6	44	13.6
Simner, 2011b [122]	64	180	3
Titelman, 2011b [123]	63	149	42.3
Peirano, 2012 (2010) [124]	49	63	77.8
Peirano, 2012 (2009) [124]	34	44	77.3
Peirano, 2012 (2008) [124]	14	27	51.9
Peirano, 2012 (2007) [124]	8	18	44.4
Peirano, 2012 (2006) [124]	3	9	33.3
Peirano, 2012 (2005) [124]	6	13	46.2
Peirano, 2012 (2004) [124]	0	5	0
Peirano, 2012 (2003) [124]	2	5	40
Peirano, 2012 (2002) [124]	0	6	0
Peirano, 2012 (2001) [124]	1	6	16.7
Peirano, 2012 (2000) [124]	0	1	0
Molina−Lopez, 2011 [125]	13	36	36.1
Sidjabat, 2010 [126]	15	49	30.6
Tian, 2010 [127]	1	15	6.7
Platell, 2010 [128]	205	582	35.2
Naseer, 2010 [129]	4	38	10.5
Johnson, 2010a [130]	14	40	35
Lee, 2010 [131]	32	129	24.8
Peirano, 2010a [132]	96	209	45.9
Severin, 2010 [133]	16	68	23.5
Cerquetti, 2010 [134]	11	18	61.1
Peirano, 2010b [135]	16	30	53.3
Smet, 2010 (Outpatients/community) [136]	28	28	100
Smet, 2010 (Inpatients) [136]	3	14	21.4
Dahmen, 2010 [137]	23	31	74.2
Oteo, 2010 [138]	7	121	5.8
Diaz, 2010 [139]	32	37	86.5
Bert, 2010 [140]	3	110	2.7
Johnson, 2010b (Other) [141]	24	68	70.6
Johnson, 2010b (ESBL) [141]	30	59	64.7
Brolund, 2010 [142]	96	226	42.5
Jouini, 2010 [143]	6	18	33.3
Pitout, 2009a [144]	33	55	60
Morris, 2009 [145]	36	348	10.3
Hrabak, 2009 [146]	3	8	37.5
Suzuki, 2009 [147]	27	130	20.8
Literacka, 2009 [148]	0	11	0
Pitout, 2009b [149]	21	29	72.4
Arpin, 2009 [150]	10	40	25
Blanco, 2009 (2007) [151]	54	249	21.7
Blanco, 2009 (2006) [151]	23	105	21.9
Pitout, 2009c (2007) [152]	12	22	54.5
Pitout, 2009c (2006) [152]	3	9	33.3
Pitout, 2009c (2005) [152]	5	13	38.5
Pitout, 2009c (2004) [152]	0	5	0
Pitout, 2009c (2003) [152]	1	5	20
Pitout, 2009c (2002) [152]	0	6	0
Pitout, 2009c (2001) [152]	0	6	0
Pitout, 2009c (2000) [152]	0	1	0
Johnson, 2009 [153]	46	199	0
Oteo, 2009a [154]	8	91	8.8
Clermont, 2009 (Europe 2006−2007) [155]	19	41	46.3
Clermont, 2009 (Europe 2006) [155]	2	20	10
Clermont, 2009 (Europe 2004−2007) [155]	84	103	81.6
Clermont, 2009 (N−America 2004−2006) [155]	17	41	41.5
Clermont, 2009 (Africa 2004−2006) [155]	5	10	50
Clermont, 2009 (Asia 2004−2005) [155]	8	30	26.7
Clermont, 2009 (S−America 2001−2005) [155]	0	5	0
Clermont, 2009 (Europe 2002 − 2003) [155]	4	129	3.1
Clermont, 2009 (Asia 1999) [155]	0	5	0
Clermont, 2009 (Europe 1994−2003) [155]	8	128	6.3
Naseer, 2009 [156]	9	45	20
Oteo, 2009b [157]	24	26	92.3
Sidjabat, 2009 [158]	21	70	30
Lau, 2008 [159]	52	88	59.1
Yumuk, 2008 [160]	1	17	5.9
Cagnacci, 2008 [161]	35	148	23.6
Jones, 2008 [162]	5	10	50
Colonization			
Vasoo, 2014 [163]	8	21	38.1
March, 2014 [164]	52	59	89.7
Blanc, 2014 [13]	12	27	44.4
Nicolas−Chanoine, 2013 [165]	2	21	9.5
Izdebski, 2013 (Europe) [166]	76	171	41.9
Izdebski, 2013 (Asia) [166]	79	205	38.5
Lisa, 2013 [167]	19	27	70.4
Kudinha, 2013a [41]	0	135	0
Kudinha, 2013b (Outpatients/community) [42]	1	115	0.87
Banerjee, 2013a [44]	7	34	20.6
Birgy, 2013 [168]	6	64	11.1
Qin, 2013 (Outpatients/community) [48]	0	41	0
Nuesch−Inderbinen, 2013 [169]	4	16	25
Arvand, 2013 [170]	11	24	45.8
Kudinha, 2013c (Outpatients/community) [57]	13	330	3.94
Roy, 2013 [171]	1	123	0.81
Hu, 2013 (Outpatients/community) [58]	6	46	13
Severin, 2012 [172]	0	14	0
Dolejska, 2012 [173]	1	7	14.3
Overdevest, 2011 [103]	1	39	2.6
Li, 2011 [174]	4	55	7.3
Peirano, 2011 (Travelers) [175]	6	26	23.1
Peirano, 2011 (Outpatients/community) [175]	2	5	40
Hrabak, 2009 [146]	1	1	100
Leflon−Guibout, 2008 [176]	4	51	7.8



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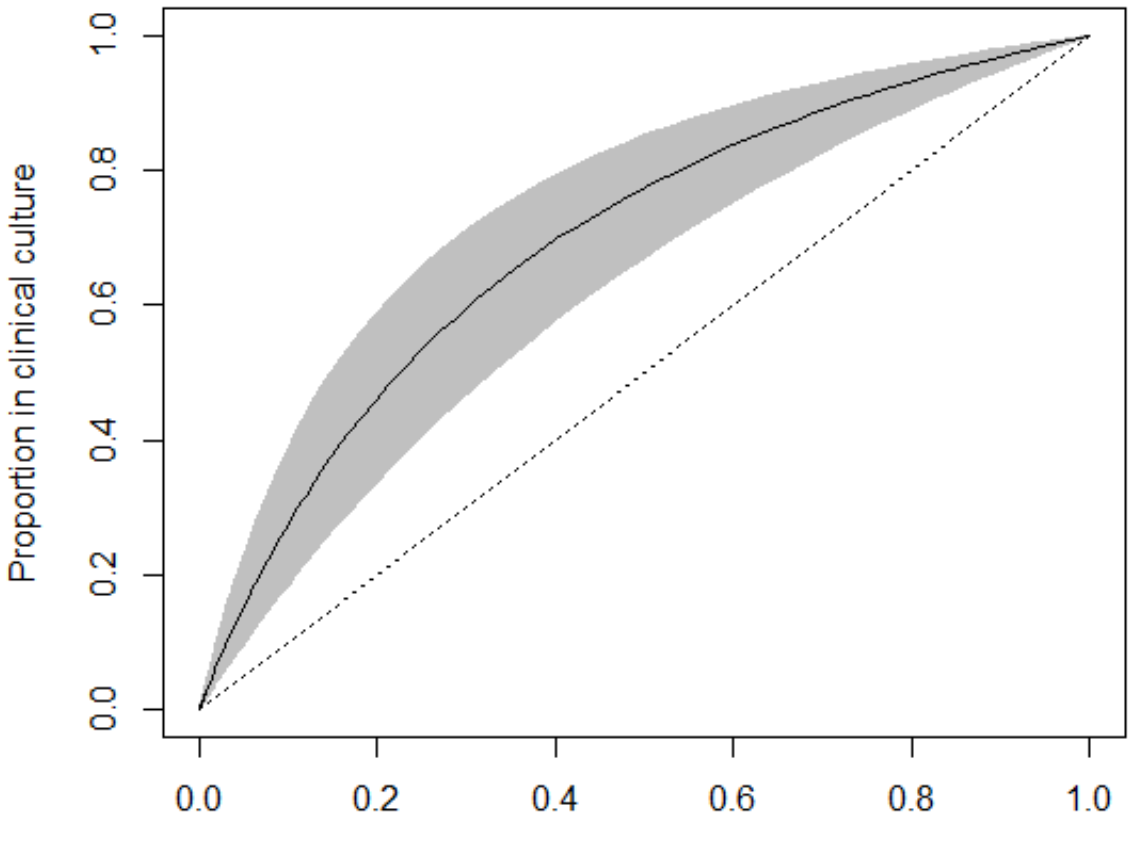
Supplementary Figure 2: Differences in proportion ST131 in colonization versus infection as given by the metaregression model.



The confidence interval should be interpreted as the confidence interval for the mean effect and not the individual effect. If one would average the proportions *E. coli* ST131 found in 100 studies, the mean should fall within the limits of the confidence interval of this graph 95% of the times.

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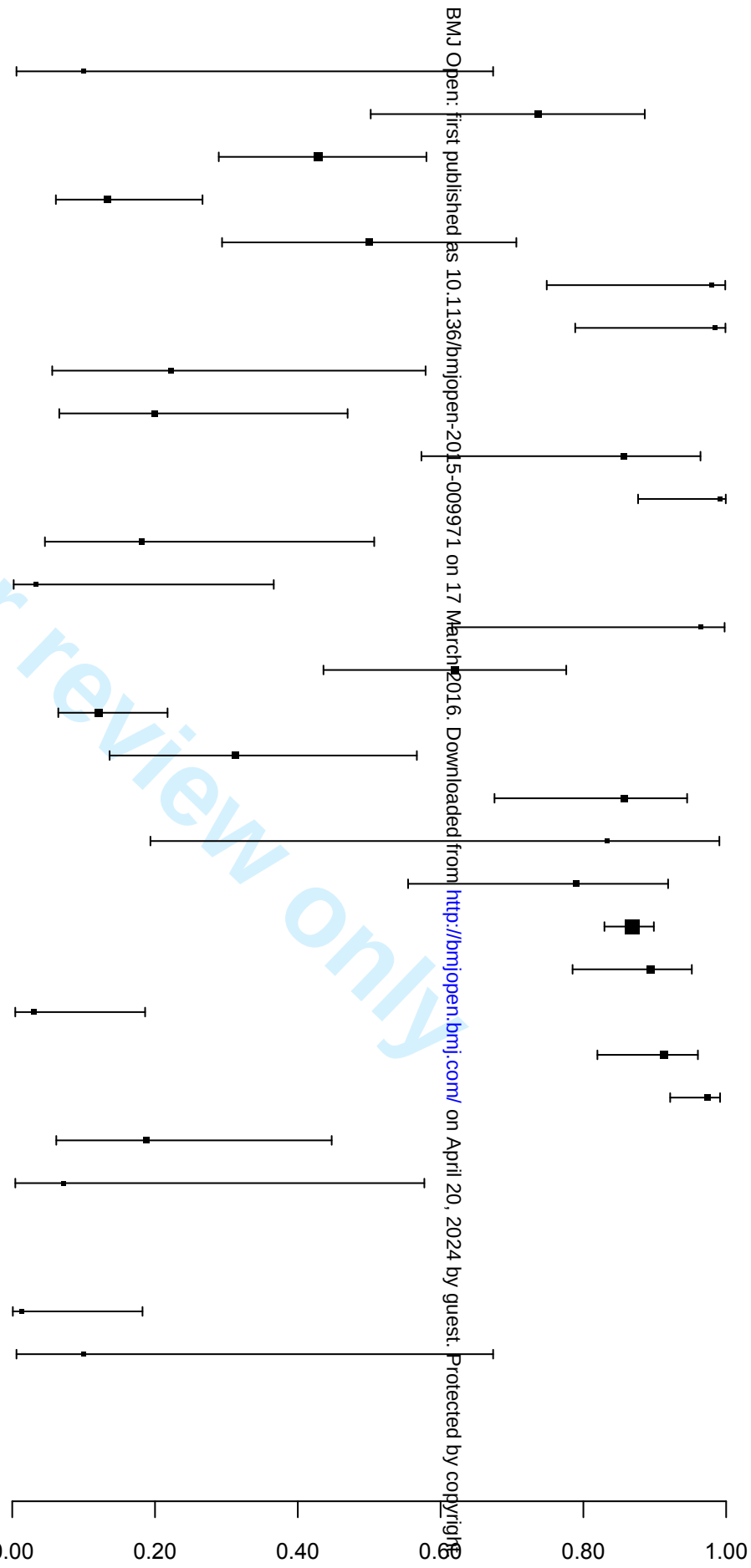
Supplementary Figure 3: Forest plot showing proportion ST258 in *K. pneumoniae*

Author (pub. year)	*ST258 (n)*	*Total (n)*	*ST258 (%)*
Infection			
Lascols, 2013 (S−America) [177]	0	4	0
Lascols, 2013 (N−America) [177]	14	19	72.2
Lascols, 2013 (Europe) [177]	18	42	0
Lascols, 2013 (Asia/Australia) [177]	6	45	0
Castanheira, 2013 [178]	10	20	50
Rodriguez−Zulueta, 2013 [179]	24	24	100
Di Carlo, 2013 [180]	30	30	100
Aschbacher, 2013 [68]	2	9	22.2
Hrabak, 2014 [181]	3	15	20
Jain, 2013 [182]	12	14	85.7
Cejas, 2012 [183]	57	57	100
Warburg, 2012 [184]	2	11	18.2
Dimou, 2012 [88]	0	14	0
Morris, 2012 [185]	13	13	100
Richter, 2012 [186]	18	29	62.1
Adler, 2012 [187]	9	74	12.2
Osterblad, 2012 [95]	5	16	31.3
Mammina, 2012 [188]	24	28	85.7
Mataseje, 2011 (MLST) [188]	2	2	100
Mataseje, 2011 (Extrapolation PFGE)	15	19	78.9
Giakkoupi, 2011 [189]	322	371	86.8
Andrade, 2011 [190]	51	57	89.5
Shin, 2011 [120]	1	33	3
Gomez, 2011 [191]	63	69	91.3
Baraniak, 2011 [192]	111	114	97.4
Cuzon, 2010 [193]	3	16	18.8
Hrabak, 2009 [146]	0	6	0
Colonization			
Dolejska, 2012 [173]	0	36	0
Hrabak, 2009 [146]	0	4	0



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MOOSE Checklist for Meta-analyses of Observational Studies

Item No	Recommendation	Reported on Page No
Reporting of background should include		
1	Problem definition	3-4
2	Hypothesis statement	4
3	Description of study outcome(s)	4
4	Type of exposure or intervention used	-
5	Type of study designs used	-
6	Study population	N/A
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	4
8	Search strategy, including time period included in the synthesis and key words	4 + Supplementary Text 1
9	Effort to include all available studies, including contact with authors	4
10	Databases and registries searched	4
11	Search software used, name and version, including special features used (eg, explosion)	N/A
12	Use of hand searching (eg, reference lists of obtained articles)	4
13	List of citations located and those excluded, including justification	-
14	Method of addressing articles published in languages other than English	4
15	Method of handling abstracts and unpublished studies	4
16	Description of any contact with authors	4
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	5
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	-
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	5
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	N/A
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	5
22	Assessment of heterogeneity	6
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	6-7
24	Provision of appropriate tables and graphics	7
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	10 + Supplementary Figure 1 and 2
26	Table giving descriptive information for each study included	7-8 (Table 1)
27	Results of sensitivity testing (eg, subgroup analysis)	-
28	Indication of statistical uncertainty of findings	10-14

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Item No	Recommendation	Reported on Page No
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	16
30	Justification for exclusion (eg, exclusion of non-English language citations)	-
31	Assessment of quality of included studies	16
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	16
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	N/A
34	Guidelines for future research	16
35	Disclosure of funding source	17

From: Stroup DF, Berlin JA, Morton SC, et al, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. *JAMA*. 2000;283(15):2008-2012. doi: 10.1001/jama.283.15.2008.

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BMJ Open

Epidemic potential of Escherichia coli ST131 and Klebsiella pneumoniae ST258: A systematic review and meta-analysis.

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Primary Subject Heading:	Infectious diseases
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Keywords:	MICROBIOLOGY, Systematic review, Meta-regression, Escherichia coli, Klebsiella pneumoniae, hyperendemicity

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Epidemic potential of *Escherichia coli* ST131 and *Klebsiella pneumoniae* ST258: A systematic review and meta-analysis

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Key words: Systematic review, meta-regression, *Escherichia coli*, *Klebsiella pneumoniae*, hyperendemicity

Word count: 3593

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ABSTRACT

Objectives - Observational studies have suggested that *Escherichia coli* sequence type (ST) 131 and *Klebsiella pneumoniae* ST258 have hyperendemic properties. This would be obvious from continuously high incidence and/or prevalence of carriage or infection with these bacteria in specific patient populations. Hyperendemicity could result from increased transmissibility, longer duration of infectiousness, and/or higher pathogenic potential as compared to other lineages of the same species. The aim of our research is to quantitatively estimate these critical parameters for *E. coli* ST131 and *K. pneumoniae* ST258, in order to investigate whether *E. coli* ST131 and *K. pneumoniae* ST258 are truly hyperendemic clones.

Primary outcome measures - A systematic literature search was performed to assess the evidence of transmissibility, duration of infectiousness, and pathogenicity for *E. coli* ST131 and *K. pneumoniae* ST258. Meta-regression was performed to quantify these characteristics.

Results - The systematic literature search yielded 639 articles, of which 19 data sources provided information on transmissibility (*E. coli* ST131 n=9; *K. pneumoniae* ST258 n=10)), 2 on duration of infectiousness (*E. coli* ST131 n=2), and 324 on pathogenicity (*E. coli* ST131 n=285; *K. pneumoniae* ST258 n=39). Available data on duration of carriage and on transmissibility were insufficient for quantitative assessment. In multivariable meta-regression *E. coli* isolates causing infection were associated with ST131, compared to isolates only causing colonization, suggesting that *E. coli* ST131 can be considered more pathogenic than non-ST131 isolates. Date of isolation, location, and resistance mechanism also influenced the prevalence of ST131. *E. coli* ST131 was 3.2 (95% CI 2.0-5.0) times more pathogenic than non-ST131. For *K. pneumoniae* ST258 there were not enough data for meta-regression assessing the influence of colonization versus infection on ST258 prevalence.

Conclusions - With the currently available data, it cannot be confirmed nor rejected, that *E. coli* ST131 or *K. pneumoniae* ST258 are hyperendemic clones.

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STRENGTHS AND LIMITATIONS

- A comprehensive literature search combined with meta-regression analyses was performed to quantify evidence of hyperendemicity of *E. coli* ST131 and *K. pneumoniae* ST258 focussing on transmissibility, durations of infectiousness, and pathogenicity.
- There is a large heterogeneity in reported prevalences and a limited amount of data available on transmissibility and duration of infectiousness.
- With the currently available data, it cannot be confirmed nor rejected, that *E. coli* ST131 or *K. pneumoniae* ST258 are hyperendemic clones.

INTRODUCTION

Infections caused by *Escherichia coli* and *Klebsiella pneumoniae* producing extended-spectrum beta-lactamases (ESBL) or carbapenamases are increasing worldwide. There is growing evidence that certain clonal lineages of these species, such as *E. coli* sequence type (ST) 131 and *K. pneumoniae* ST258, have more epidemic potential than other lineages within their species group. *E. coli* ST131 was first described in 2008[1] and *K. pneumoniae* ST258 in 2009[2]. *E. coli* ST131 is reported from around the globe, both in healthcare settings and in the community[3,4], and is mostly associated with ESBL production and fluoroquinolone resistance.[3,5] *K. pneumoniae* ST258 is mainly associated with *Klebsiella pneumoniae* carbapenemase (KPC) production, and other resistance mechanisms[6], and is widespread in the USA, and expanding in Europe.[6–8] In the scientific literature *E. coli* ST131 and *K. pneumoniae* ST258 are widely considered hyperendemic clones.[3,5,6,8,9] But the evidence underlying these assumptions is not that obvious.[3,5] If *E. coli* ST131 or *K. pneumoniae* ST258 are truly hyperendemic clones, interventions may be targeted to these specific clones.

From a simple model in which patients can be susceptible, colonized, or infected (Figure 1), the he characteristics of hyperendemicity follow as explained below. Susceptible hosts can acquire colonization through transmission, either directly (from another colonized or infected person) or indirectly (from the environment or via the hands of health care workers). Both colonized and infected patients contribute to transmission, as long as they are infectious, which can be expressed with the duration of colonization. Duration of colonization can be influenced by fitness cost associated with resistance or by antibiotic use. Colonization can proceed to infection, which typically occurs in a fraction of colonized patients[10] and

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the rate of this progression can be expressed as the pathogenicity level. Decolonization can occur in both colonized and infected persons.

To be hyperendemic, a clone has to have advantages over other clones in at least one of the traits transmissibility, duration of colonization, or pathogenicity. Therefore, we define a hyperendemic clone as 'a clone that is more transmissible, has a longer duration of colonization, and/or is more pathogenic than other clones of the same species'. The presence of any or more of these traits will then lead to a continuously high incidence and/or prevalence of carriage or disease in a specific patient population. We performed a systematic review to quantitatively estimate these critical parameters for *E. coli* ST131 and *K. pneumoniae* ST258, in order to investigate whether *E. coli* ST131 and *K. pneumoniae* ST258 are truly hyperendemic clones.

METHODS

Search strategy

A PubMed and EMBASE search was performed to retrieve relevant articles published until January 1, 2015. The complete search string can be found in Supplementary Text 1. A cross-reference check was performed to include relevant articles not found during the search. Only English, full-text articles were included. Articles unavailable online were requested from the authors. The MOOSE statement[11] was followed for reporting in this paper.

Study selection

Titles and abstracts were independently reviewed by two reviewers (MRH and MJDD) and selected for further review if they met the inclusion criteria. Selections were compared between the two reviewers and if consensus was not reached, a third reviewer (MCJB or MJMB) was consulted.

The inclusion criteria for articles on transmissibility were that possible transmissions should be described, and the number of cases should be reported. Outbreak reports were included. Articles focusing on duration of colonization should include at least two cultures per patient taken at two different time points. Pathogenicity was defined as the difference in the prevalence of ST131 or ST258 in infections (clinical isolates) compared to colonization. We considered a clone to be more pathogenic when the relative abundance of this clone in isolates causing infections is higher compared to isolates

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associated with colonization. Therefore, articles on pathogenicity of *E. coli* ST131 or *K. pneumoniae* ST258 should report the prevalence or incidence of infections among patients colonized with *E. coli* ST131 or *K. pneumoniae* ST258, the prevalence of *E. coli* ST131 or *K. pneumoniae* ST258 among patients colonized with *E. coli* or *K. pneumoniae*, respectively, or the prevalence of *E. coli* ST131 or *K. pneumoniae* ST258 among at least 10 clinical isolates of *E. coli* or *K. pneumoniae*, respectively.

Articles were excluded if they did not contain original data (such as reviews, commentaries, or articles reusing existing datasets), if they considered *E. coli* or *K. pneumoniae* only in non-human sources, or if there was no clear information on the isolate collection or selection.

Data extraction

Data were extracted by the same two reviewers independently and crosschecked using a standard form developed by the researchers. Data were collected on population and setting, recording if participants were inpatients, outpatients/community residents, travelers, or from another/unknown group. The area/region where the study took place was recorded and categorized into (mainly) from Africa, Asia, Australia, Europe, North America, and South America. It was recorded whether data collection took place during an outbreak period, and if a selection on antibiotic susceptibility or resistance was made, divided into selection on ESBL/AmpC-producing isolates (including third generation cephalosporin-resistant isolates), carbapenem-resistant or carbapenemase-producing Enterobacteriaceae (CRE/CPE, e.g., KPC, OXA-48), other resistance profiles (e.g., ciprofloxacin-resistant, fluoroquinolone-susceptible, or multi-drug resistant), or no selection on resistance. Furthermore, the method to detect sequence types was documented, split up into multi-locus sequence typing (MLST, when all isolates were typed by MLST), extrapolation based on pulsed-field gel electrophoresis (PFGE, when only selected isolates were typed with MLST and the sequence types were inferred based on PFGE type), polymerase chain reaction (PCR, when all isolated underwent PCR-screening for ST-specific alleles), extrapolation based on PCR (mainly MLST for *E. coli* isolates that were positive for O25b-ST131 by PCR), or other/unknown (such as fumC/fimH typing). Also, the sample site of the included isolates (percentage of isolates isolated from blood, urine, gastrointestinal, respiratory, wound/abscess, or other sites) and time period of the study were recorded. For the time period, the middle date was used in the model if the study covered a longer time period.

For transmissibility, if available, information was gathered on admission prevalence, number of cases, number of uncolonized patients, and transmission measure given. For duration of colonization, the

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number of cases and duration of colonization was recorded. For pathogenicity, information was collected on the prevalence or incidence of infections in patients colonized with *E. coli* ST131 or *K. pneumoniae* ST258, the prevalence of *E. coli* ST131 or *K. pneumoniae* ST258 in patients colonized with *E. coli* or *K. pneumoniae*, respectively, and/or the prevalence of *E. coli* ST131 or *K. pneumoniae* ST258 in patients infected with *E. coli* or *K. pneumoniae*, respectively.

Quality of the included articles was assured by only including papers with a proper selection of isolates. Furthermore, quality was implicitly incorporated in the data that were collected on the detection method used, the sample sites, whether data were collected during an outbreak, and the setting and time period in which data were collected.

Several studies allowed splitting the data into multiple 'data sources'. For example, if data was available per year or per country, these were recorded separately. Figure 2 shows a flow diagram with the included and excluded articles. Since only 19 data sources were available on transmissibility (9 on *E. coli* ST131 and10 on *K. pneumoniae* ST258) and 2 on duration of colonization (both on *E. coli* ST131), we could only describe these without quantifying summary measures. For pathogenicity, enough data was available on *E. coli* to do a meta-regression analysis and calculate summary measures.

Meta-regression pathogenicity

In order to evaluate the pathogenicity of *E. coli* ST131 and *K. pneumoniae* ST258 and to assess which factors influence this, meta-regression was performed using all reported data on the prevalence of *E. coli* ST131 in clinical (infection) or screening (colonization) isolates of *E. coli* and for all reported data on the prevalence of *K. pneumoniae* ST258 in clinical (infection) isolates of *K. pneumoniae*. The prevalence estimates (calculated as the number of ST131- or ST258-positive isolates divided by the total number of *E. coli* or *K. pneumoniae* isolates, respectively) and standard errors (SEs) were logit transformed in the analysis. Heterogeneity between studies was evaluated with Cochrans's Q and the I^2 statistic.[12] Because of high heterogeneity ($I^2 > 75\%$), a meta-analysis using a generalized linear mixed effect model with random effects per data source was used to assess sources of variability in the overall prevalence estimates. Univariate analyses were performed to identify covariates associated with the overall prevalence estimates. All covariates with a p-value < 0.20 were included in the multivariate model, and backward selection was performed using the likelihood ratio test. There, as we are performing an exploratory analysis, a cut-off of $p < 0.10$ was used to determine statistical significance. The variable describing sample site was not included in the models, because of great dependency on the type of

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isolate (clinical or screening isolate, e.g. blood isolates representing infection), and the effect of culture site might not be comparable for isolates representing colonization or infection. The estimated between-study variance (τ^2) was evaluated for the model with and without explanatory parameters. The exponent of the coefficient for colonization/ infection found in the metaregression model is an odds ratio, which can be interpreted as a risk ratio. This was taken as a measure of how much more pathogenic *E. coli* ST131 was compared to non-ST131. I.e., a value of 2 would indicate that per colonized day colonization with ST131 leads two times more often to an infection as compared to colonization with non-ST131. All analyses were performed in R v. 3.0.3 (http://CRAN.R-project.org) using the 'metafor' package.

RESULTS

In all, 345 useful data sources were identified (see Figure 2 for the consecutive steps followed for identification). For transmissibility 19 data sources were identified, for duration of carriage 2, and for pathogenicity 324. Most studies (n=206, 72%) were performed in Europe and North America, and 266 (93%) were performed in a non-outbreak setting (Table 1). *E. coli* isolates were most selected on ESBL production or resistance against third-generation cephalosporins, and *K. pneumoniae* isolates on being CRE/CPE. Colonization isolates were most often from gastro-intestinal origin (85.2%), and infection isolates from urine (54.8%) or blood (24.5%).

Table 1: Characteristics of included studies

	EC trans-missibility (n=9)	KP trans-missibility (n=10)	EC duration (n=2)	EC pathogenicity colonization (n=35)	EC pathogenicity infection (n=249)	KP pathogenicity colonization (n=3)	KP pathogenicity infection (n=35)	KP pathogenicity colonization & infection (n=1)
Number of isolates (mean, sd)				58 (67)	129 (357)	59 (69)	40 (64)	
Number of isolates (median, iqr)				36 (21 - 62)	53 (20 - 115)	36 (20 - 87)	20 (14 - 41)	
Population - inpatients	2 (22.2%)	8 (80.0%)	1 (50.0%)	11 (31.4%)	128 (51.4%)	3 (100.0%)	24 (68.6%)	0 (0.0%)
Population - outpatients/community	6 (66.7%)	2 (20.0%)	0 (0.0%)	18 (51.4%)	25 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Population - mixed	1 (11.1%)	0 (0.0%)	0 (0.0%)	2 (5.7%)	63 (25.3%)	0 (0.0%)	2 (5.7%)	1 (100.0%)
Population - travellers	0 (0.0%)	0 (0.0%)	1 (50.0%)	3 (8.6%)	3 (1.2%)	0 (0.0%)	1 (2.9%)	0 (0.0%)
Population - other/unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	30 (12.0%)	0 (0.0%)	9 (25.7%)	0 (0.0%)

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Continent - Africa	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.7%)	16 (6.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Continent - Asia	2 (22.2%)	0 (0.0%)	0 (0.0%)	9 (25.7%)	42 (16.9%)	0 (0.0%)	4 (11.4%)	0 (0.0%)
Continent - Australia	0 (0.0%)	0 (0.0%)	1 (50.0%)	3 (8.6%)	10 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Continent - Europe	4 (44.4%)	7 (70.0%)	1 (50.0%)	14 (40.0%)	96 (38.6%)	2 (66.7%)	14 (40.0%)	0 (0.0%)
Continent - North America	3 (33.3%)	1 (10.0%)	0 (0.0%)	7 (20.0%)	79 (31.7%)	1 (33.3%)	11 (31.4%)	1 (100.0%)
Continent - South America	0 (0.0%)	2 (20.0%)	0 (0.0%)	0 (0.0%)	6 (2.4%)	0 (0.0%)	6 (17.1%)	0 (0.0%)
Outbreak setting	3 (33.3%)	10 (100.0%)	0 (0.0%)	1 (2.9%)	4 (1.6%)	1 (33.3%)	8 (22.9%)	0 (0.0%)
Selection - ESBL/3GC-R	8 (88.9%)	0 (0.0%)	1 (50.0%)	23 (65.7%)	182 (73.1%)	2 (66.7%)	0 (0.0%)	0 (0.0%)
Selection - CRE/CPE	0 (0.0%)	9 (90.0%)	0 (0.0%)	0 (0.0%)	8 (3.2%)	1 (33.3%)	29 (82.9%)	1 (100.0%)
Selection - other	1 (11.1%)	0 (0.0%)	1 (50.0%)	5 (14.3%)	31 (12.4%)	0 (0.0%)	5 (14.3%)	0 (0.0%)
Selection - none	0 (0.0%)	1 (10.0%)	0 (0.0%)	7 (20.0%)	28 (11.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Detection - MLST	6 (66.7%)	4 (40.0%)	0 (0.0%)	10 (28.6%)	134 (53.8%)	1 (33.3%)	25 (71.4%)	0 (0.0%)
Detection - extrapolation based on PFGE	1 (11.1%)	3 (30.0%)	0 (0.0%)	3 (8.6%)	15 (6.0%)	1 (33.3%)	9 (25.7%)	1 (100.0%)
Detection - extrapolation based on PCR	2 (22.2%)	0 (0.0%)	2 (100.0%)	21 (60.0%)	83 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Detection - CH	0 (0.0%)	1 (10.0%)	0 (0.0%)	0 (0.0%)	13 (5.2%)	1 (33.3%)	0 (0.0%)	0 (0.0%)
Detection - other/unknown	0 (0.0%)	2 (20.0%)	0 (0.0%)	1 (2.9%)	4 (1.6%)	0 (0.0%)	1 (2.9%)	0 (0.0%)
Site - blood	1 (11.1%)	3 (30.0%)	0 (0.0%)	0 (0.0%)	64 (25.7%)	0 (0.0%)	7 (20.0%)	0 (0.0%)
Site - urine	2 (22.2%)	3 (30.0%)	1 (50.0%)	2 (5.7%)	143 (57.4%)	1 (33.3%)	12 (34.3%)	1 (100.0%)
Site - gastro-intestinal tract	6 (66.7%)	3 (30.0%)	1 (50.0%)	32 (91.4%)	5 (2.0%)	1 (33.3%)	7 (20.0%)	0 (0.0%)
Site - respiratory tract	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	3 (1.2%)	1 (33.3%)	3 (8.6%)	0 (0.0%)
Site - wound	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Site - other/unknown	0 (0.0%)	1 (10.0%)	0 (0.0%)	0 (0.0%)	33 (13.3%)	0 (0.0%)	6 (17.1%)	0 (0.0%)

EC: *E. coli*, KP: *K. pneumoniae*. Site: site from which most isolates were identified

Transmissibility

There were 19 studies reporting transmissibility of *E. coli* ST131 (n=9) and *K. pneumoniae* ST258 (n=10), some being case-reports or describing single possible transmission events (Table 2). Transmission events for *E. coli* ST131 have been described or suggested in household (n=4), day care (n=1), nursing home (n=1), and hospital settings (n=4). For *K. pneumoniae* ST258 all sources reported on transmission events in hospital settings, and all included CRE/CPE.

Transmissibility can be quantified by the number of transmissions per patient or patient-days at risk, which requires information on the number of index cases, number of transmissions and number of days or patients at risk. Yet, one or more of these aspects, especially time at risk, is missing in all studies but one. Most studies are cross-sectional studies, in which transmission cannot be proven.

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Differences in transmission capacity between *E. coli* ST131 and non-ST131, or between *K. pneumoniae* ST258 and non-ST258, have not been quantified, precluding any conclusion on the relative transmissibility of *E. coli* ST131 and *K. pneumoniae* ST258 compared to other clonal lineages.

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Table 2: Summary of articles describing transmissibility of *E. coli* ST131 and *K. pneumoniae* ST258

Author	Country	Year	Setting	Organism	Resistance mechanism	Index cases (n)	Secon-dary cases (n)	Un-colonized	Exposure time
Veenemans 2014[13]	The Netherlands	2013	Nursing homes	*E. coli* ST131	ESBL	5 and 3			
Kojima 2014[14]	Japan	2009-2010	Household	*E. coli* ST131	ESBL	1	2		
Blanc 2014[15]	France	2012	Day care centers	*E. coli* ST131	ESBL	7			
Giuffrè 2013[16]	Italy	2012	Neonatal intensive care unit	*E. coli* ST131	ESBL	15		88	
Adler 2012[17]	Israel	2008-2009	Geriatric rehabilitation wards	*E. coli* ST131	ESBL	21	23	367	
				E. coli non-ST131	ESBL	31	36	367	
Hilty 2012[18]	Switzerland	2008-2010	University hospital	*E. coli* ST131	ESBL	13	2	36	48 index inpatients for a total of 400,000 patient-days
				E. coli non-ST131	ESBL	27	2	48	
			Household	*E. coli* ST131	ESBL	15	7	19	
				E. coli non-ST131	ESBL	42	13	49	
Owens 2011 [19]	USA	Before 2011	Household	*E. coli* ST131	ESBL	2			
Johnson 2010[20]	USA	Before 2010	Household	*E. coli* ST131	Fluoro-quinolone resistance	1	1	1	
Ender 2009[21]	USA	Before 2009	Hospital	*E. coli* ST131	ESBL	1	1		
Marquez 2014[22]	Uruguay	2011	Intensive care unit	*K. pneumoniae* ST258	KPC	1	1	3	
Garza-Ramos 2014[23]	Mexico	2012-2013	2 Hospitals	*K. pneumoniae* ST258	KPC	15 and 3			
Gaibani 2014[24]	Italy	2010	Hospital	*K. pneumoniae* ST258	KPC	11			
Giuffrè 2013[25]	Italy	2012	Neonatal intensive care unit	*K. pneumoniae* ST258	KPC	10		44	
Tofteland 2013[26]	Norway	2010	Intensive care unit	*K. pneumoniae* ST258	KPC	6			
Morris 2012[27]	Ireland	2011	2 Hospitals	*K. pneumoniae* ST258	KPC	11			
Agodi 2011[28]	Italy	2009	Hospital	*K. pneumoniae* ST258	KPC	16			
Won 2011[29]	USA	2008	Acute care hospitals and long-term acute care hospitals	*K. pneumoniae* ST258	KPC	33 (+ 7 presumed cases)			

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Marchese 2010[30]	Italy	2009	Neuro-rehabilitation unit	*K. pneumoniae* ST258	KPC	4 (+3 at time of publication)
Mammina 2010[31]	Italy	2009	Intensive care unit	*K. pneumoniae* ST258	KPC	13

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Duration of carriage

The duration of carriage of *E. coli* ST131 was investigated in two studies. In one study colonization with *E. coli* was still apparent after 12 months in 64% (n=9) and 40% (n=14) of those carrying *E. coli* ST131 or other STs, respectively (p=0.12).[32] In another study, of two patients acquiring colonization with *E. coli* ST131 during travel, one was a prolonged carrier with this strain. The definition of prolonged carriage was not given however.[33] The duration of carriage of *K. pneumoniae* ST258 has not been determined.

Pathogenicity

E. coli

From 285 data sources, we retrieved data from 34,253 *E. coli* isolates (2,041 associated with colonization and 32,212 with infection). Prevalence of *E. coli* ST131 in these studies ranged from 0% to 100% (Supplementary Figure 1), with high statistical heterogeneity between studies (I^2=96.9%).

In univariable meta-regression the *E. coli* ST131 prevalence in individual studies increased in time, and appeared to be influenced by whether isolates were associated with infection or colonization, resistance patterns used for isolate selection, and location where the study was performed (*p*-value < 0.20; Table 3). These variables were included in the multivariable meta-regression model, and time, location, and selection remained significantly associated with *E. coli* ST131 prevalence (Table 4). No significant effects were present for study population, microbiological methods used to detect ST131, or whether the study was performed in an outbreak situation or not.

The prevalence of ST131 was highest if *E. coli* isolates were selected upon the presence of ESBL production or third generation cephalosporin resistance, and lowest if derived from non-selective media. Prevalence of *E. coli* ST131 was highest in North America, and lowest in South America. The estimated prevalence of ST131 in *E. coli*, given particular values of the covariates, can be derived from the regression equation (Table 4). For example, the estimated logit (prevalence ST131) for isolates causing infection, selected on presence of ESBL, in North America in January 2010 is given by 2.9668 + 12*0.0140 + 1.1545 + 1.3826 + 0.4436 = 0.1819, which corresponds to a prevalence of ST131 of exp(0.1819)/(1+exp(0.1819)) = 54.5%. The estimated prevalence in the reference category (January 2009, colonization, no selection on resistant profile, Europe) is exp(-2.9668)/(1+exp(-2.9668)) = 4.9%.

In the multivariable meta-regression model *E. coli* ST131 was significantly associated with infection compared to colonization, suggesting that ST131 isolates are more pathogenic than non-ST131 isolates.

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From the infection/colonization coefficient we can calculate the relative pathogenicity of *E. coli* ST131 compared to non-ST131. We found that *E. coli* ST131 is 3.2 (95% CI 2.0-5.0) times more pathogenic than non-ST131. Supplementary Figure 2 shows the proportion of ST131 found in infection isolates compared to colonization isolates as estimated by the meta-regression model.

The estimated between-study variance (τ^2) reduced from 1.68 in the model without parameters to 1.1 in the final model, implying that a high level of heterogeneity remained.

Table 3: Effect of covariates on prevalence of ST131 in *E. coli* (univariable random effects meta-regression models)

	P-value
Study period (per month[a])	0.0011
Infection or colonization	0.0002
Colonization	
Infection	
Outbreak setting	0.9112
Selection of isolates based on resistance pattern	< 0.0001
no selection on resistance profile	
ESBL/3GC-R	
CRE/CPE	
other	
Study population	0.6219
Inpatients	
Outpatients / community	
Mixed	
Travelers	
Other / unknown	
Location	< 0.0001
Europe	
North America	
South America	
Australia	
Asia	
Africa	
Method used to detect ST131	0.3598
MLST	
Extrapolation based on PFGE	
PCR	
Extrapolation based on PCR	
Other/unknown	

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CRE/CPE: carbapenem-resistant Enterobacteriaceae/carbapenemase-producing Enterobacteriaceae

ESBL/3GC-R: extended-spectrum beta-lactamases/third-generation cephalosporin resistance

MLST: multi-locus sequence typing

PCR: polymerase chain reaction

PFGE: pulsed-field gel electrophoresis

[a]Reference date: 1 January 2009

Table 4: Effect of covariates on prevalence of ST131 in *E. coli* (multivariable random effects meta-regression model)

	Estimate (SE[a])	**P-value**
Intercept	-2.9668 (0.2959)	
Study period (per month[b])	0.0140 (0.0023)	<0.0001
Infection or colonization		<0.0001
Colonization	Reference	
Infection	1.1545 (0.2281)	
Selection of isolates based on resistance pattern		<0.0001
no selection on resistance profile	Reference	
ESBL/3GC-R	1.3826 (0.2207)	
CRE/CPE	0.5994 (0.4879)	
other	0.9058 (0.2709)	
Location		<0.0001
Europe	Reference	
North America	0.4436 (0.1675)	
South America	-2.2868 (0.6101)	
Australia	-0.4209 (0.3407)	
Asia	-0.3657 (0.1927)	
Africa	-0.2246 (0.3154)	

CRE/CPE: carbapenem-resistant Enterobacteriaceae/carbapenemase-producing Enterobacteriaceae

ESBL/3GC-R: extended-spectrum beta-lactamases/third-generation cephalosporin resistance

SE: standard error

[a]Parameter estimates (SEs) are presented on a logit scale.

[b]Reference date: 1 January 2009.

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K. pneumoniae

There were 35 and three data sources providing information on the prevalence of ST258 *K. pneumoniae* in clinical and colonizing isolates, respectively (Supplementary Figure 3). Because of limited data on colonization, quantitative analyses were performed for clinical isolates only.

In the univariable meta-regression model, outbreak setting yes/no, selection of isolates based on resistance pattern, study population, and geographic locationwere all associated with a higher prevalence of ST258 with a *p*-value < 0.20 and were, thus, included in the multivariable model (Table 5). If data were collected during an outbreak of *K. pneumoniae*, this was associated with a higher prevalence of ST258 (Table 6). Furthermore, the model yielded a significant effect of resistance patterns on the prevalence of ST258 in *K. pneumoniae* . ST258 prevalence was associated with selection of isolates on CRE-positivity, but the number of data sources describing isolates that are not CRE/CPE is low and varied (n=5). Furthermore, study population characteristics also appeared to influence ST258 prevalence in *K. pneumoniae*, with higher prevalence of ST258 in inpatients, compared to "other" populations. Yet, the "other" group is not defined accurately, precluding firm conclusions. Only one data source was available for outpatients or persons residing in the community. Finally, reported ST258 prevalence was lower in Asia and Australia than in other continents.

The estimated prevalence of ST258 in *K. pneumoniae*, given particular values of the covariates, can be derived from the regression equation. For example, the estimated logit (prevalence of ST258) for isolates selected on presence of CRE in hospital inpatients in North America during an outbreak is given by -0.0.0320 + 2.8038 + 0.3332 = 3.1050, which corresponds to a prevalence of ST258 of exp(3.1050)/(1+exp(3.1050) = 95.7%. The estimated prevalence in the reference category (during an outbreak, non CRE/CPE, hospital inpatients, Europe) is exp(-0.0320)/(1+exp(-0.0320)) = 50.8%.

The estimated between-study variance (τ^2) reduced from 6.43 in the model without parameters to 2.25 in the final model, indicating a considerable improvement, but still a high level of heterogeneity.

ST258 was not detected in two studies reporting on colonization with *K. pneumonia*, that included in 36 and 4 isolates.[184,219] Only from the study of van Duin et al.[224] we can deduce a prevalence of ST258 in *K. pneumoniae* of 31% in colonizing isolates. This precludes any quantification of the pathogenicity of *K. pneumoniae* ST258.

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The only study in which both colonization and infection with *K. pneumoniae* ST258 were investigated included a set of seven KPC-producing *K. pneumoniae* ST258 isolates collected from a long-term acute care facility in South Florida.[245] Three patients were colonized, and four had both colonization and infection. Again, the sample size is too small for drawing conclusions.

Table 5: Effect of covariates on prevalence of ST258 in clinical isolates of *K. pneumoniae* (univariable random effects meta-regression models)

	P-value
Study period (per month[a])	0.6109
Outbreak setting	0.0052
Selection of isolates based on resistance pattern	0.0543
Non-CRE/CPE	
CRE/CPE	
Study population	0.0265
Inpatients	
Mixed	
Other/unknown	
Location	0.1013
Europe	
North America	
South America	
Asia (including Australia)	
Method used to detect ST258	0.2253
MLST	
Extrapolation based on PFGE	

CRE/CPE: carbapenem-resistant Enterobacteriaceae/carbapenemase-producing Enterobacteriaceae

MLST: multi-locus sequence typing

PFGE: pulsed-field gel electrophoresis

[a]Reference date: 1 January 2009

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Table 6: Effect of covariates on prevalence of ST258 in clinical isolates of *K. pneumoniae* (multivariable random effects meta-regression model)

	Estimate (SE[a])	P-value
Intercept	-0.0320 (1.0008)	0.9745
Outbreak setting		< 0.05
Yes	Reference	
No	-1.7725 (0.7833)	
Selection of isolates based on resistance pattern		< 0.01
Non-CRE/CPE	Reference	
CRE/CPE	2.8038 (0.9445)	
Study population		< 0.01
Inpatients	Reference	
Mixed	-3.8232 (1.5480)	
Other/unknown	-2.2908 (0.7255)	
Location		< 0.05
Europe	Reference	
North America	0.3332 (0.7607)	
South America	0.4213 (0.9038)	
Asia (including Australia)	-2.0716 (0.7833)	

CRE/CPE: carbapenem-resistant Enterobacteriaceae/carbapenemase-producing Enterobacteriaceae

SE: standard error

[a]Parameter estimates (SEs) are presented on a logit scale.

[b]Reference date: 1 January 2009.

DISCUSSION

Based on published information we conclude that there is evidence that *E. coli* ST131 is more pathogenic than *E. coli* non-ST131, but not for increased transmissibility or prolonged duration of carriage. Because of the heterogeneity in the data it cannot be concluded (nor rejected) that *E. coli* ST131 is a hyperendemic clone. For *K. pneumoniae* ST258 the published data precluded any conclusion on increased transmissibility, longer duration of carriage or increased pathogenicity.

Several limitations in our study should be acknowledged. Because of our search strategy, the prevalence of *E. coli* ST131 and *K. pneumoniae* ST258 that were retrieved are likely overestimations of the real prevalence. We required the articles to report ST131/ST258 in their title and/or abstract and therefore articles that did not report this or that did not detect ST131/ST258 in their study may have been missed. Since the prevalence is dependent on factors including time, location, resistance pattern, population

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studied and possibly variables not included in this review (e.g., patient-specific details like age, gender), we deemed it not meaningful to estimate an overall prevalence of ST131 in *E. coli* or ST258 in *K. pneumoniae*.

We also did not create a funnel plot to assess publication bias, as such an analysis also assumes that there is one overall effect or prevalence. Thus, publication bias cannot be excluded. It is possible that identification of *E. coli* ST131 or *K. pneumoniae* ST258 stimulates publication, because of the current interest in these clones. However, this will most likely equally influence studies reporting infection and colonization isolates, which would not influence our conclusions. Also, the finding of ESBL or KPC might instigate investigation of sequence types. As 70% of the included studies on *E. coli* selected isolates based on the presence of ESBL or 3GC-R our findings might be more applicable to ESBL-producing *E. coli* ST131 than all *E. coli* ST131 in general. The same holds for *K. pneumoniae*, for which around 90% of included studies selected isolates based on the presence of carbapenemase production of carbapenem resistance, mainly corresponding to KPC-production. In our analysis, we used grouped variables (e.g., continent instead of country), as there are limitations to the number of variables that can be studied.

There could also be differences in detecting infection and colonization associated isolates. Infection isolates are mainly collected retrospectively, when a pattern or outbreak is recognized, whereas colonization isolates are more often collected prospectively. Yet, since determination of sequence types is unambiguous it is unlikely that such differences have affected our conclusions.

Our analysis clearly demonstrates that more – and better designed – studies are needed to determine whether *E. coli* ST131 and *K. pneumoniae* ST258 are truly hyperendemic clones. This would be possible with a prospective cohort study of a population (e.g., the general population or hospitalized patients) with a certain contact structure, in which carriage with *E. coli* or *K. pneumoniae* is regularly (e.g. weekly or monthly) determined. As *K. pneumoniae* ST258 is mainly a healthcare-associated pathogen, choice of study population might be different than for *E. coli* ST131, that is also a community-associated pathogen. For determination of transmissibility genotyping should be performed, preferably with highly discriminatory methods, and preferably with inclusion of multiple isolates per patient.[246] The duration of exposure to persons colonized or infected with *E. coli* ST131/*K. pneumoniae* ST258 should be determined to calculate the number of acquisitions per unit of time. Carriers could be studied in more detail to determine the duration of carriage and the infection rate (and duration until infection), preferably with inclusion of the effects of antibiotic use on these parameters. There should be a

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sufficient duration of follow-up, and isolates should be characterized to determine whether multiple isolates represent persistent carriage or recolonization with different strains.

In conclusion, current evidence does not allow the conclusion that *E. coli* ST131 and *K. pneumoniae* ST258 are hyperendemic clones.

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DECLARATION OF INTERESTS

All authors have no competing interests to declare.

AUTHOR CONTRIBUTIONS

MJDD and MRH performed the systematic literature search, reviewed and summarized data from each selected article, performed the analyses, and wrote the first draft of the manuscript. MJDD, MRH, MJMB, and MCJB all revised the manuscript.

DATA SHARING STATEMENT

No additional data available

REFERENCES

1 Nicolas-Chanoine M-HH, Blanco J, Leflon-Guibout V, *et al.* Intercontinental emergence of Escherichia coli clone O25:H4-ST131 producing CTX-M-15. *J Antimicrob Chemother* 2008;61:273–81. doi:10.1093/jac/dkm464

2 Samuelsen Ø, Naseer U, Tofteland S, *et al.* Emergence of clonally related Klebsiella pneumoniae isolates of sequence type 258 producing plasmid-mediated KPC carbapenemase in Norway and Sweden. *J Antimicrob Chemother* 2009;63:654–8. doi:10.1093/jac/dkp018

3 Nicolas-Chanoine M-H, Bertrand X, Madec J-Y. Escherichia coli ST131, an Intriguing Clonal Group. *Clin Microbiol Rev* 2014;27:543–74. doi:10.1128/CMR.00125-13

4 Rogers BA, Sidjabat HE, Paterson DL. Escherichia coli O25b-ST131: a pandemic, multiresistant, community-associated strain. *J Antimicrob Chemother* 2011;66:1–14. doi:10.1093/jac/dkq415

5 Banerjee R, Johnson JR. A new clone sweeps clean: the enigmatic emergence of Escherichia coli sequence type 131. *Antimicrob Agents Chemother* 2014;58:4997–5004. doi:10.1128/AAC.02824-14

6 Woodford N, Turton JF, Livermore DM. Multiresistant Gram-negative bacteria: the role of high-risk clones in the dissemination of antibiotic resistance. *FEMS Microbiol Rev* 2011;35:736–55. doi:10.1111/j.1574-6976.2011.00268.x

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7 Kitchel B, Rasheed JK, Patel JB, *et al.* Molecular epidemiology of KPC-producing Klebsiella pneumoniae isolates in the United States: clonal expansion of multilocus sequence type 258. *Antimicrob Agents Chemother* 2009;53:3365–70. doi:10.1128/AAC.00126-09

8 Grundmann H, Livermore DM, Giske CG, *et al.* Carbapenem-non-susceptible Enterobacteriaceae in Europe: Conclusions from a meeting of national experts. *Eurosurveillance* 2010;15.http://www.ncbi.nlm.nih.gov/pubmed/21144429 (accessed 20 May2015).

9 Rogers BA, Doi Y. Who is leading this dance? Understanding the spread of Escherichia coli sequence type 131. *Infect Control Hosp Epidemiol* 2013;34:370–2. doi:10.1086/669874

10 Bonten MJ, Weinstein RA. The role of colonization in the pathogenesis of nosocomial infections. *Infect Control Hosp Epidemiol* 1996;17:193–200. doi:10.1086/647274

11 Stroup DF, Berlin JA, Morton SC, *et al.* Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;283:2008–12.http://www.ncbi.nlm.nih.gov/pubmed/10789670 (accessed 28 Mar2015).

12 Higgins JPT, Thompson SG, Deeks JJ, *et al.* Measuring inconsistency in meta-analyses. *BMJ Br Med J* 2003;327:557–60. doi:10.1136/bmj.327.7414.557

13 Veenemans J, Overdevest IT, Snelders E, *et al.* Next-generation sequencing for typing and detection of resistance genes: performance of a new commercial method during an outbreak of extended-spectrum-beta-lactamase-producing Escherichia coli. *J Clin Microbiol* 2014;52:2454–60. doi:10.1128/JCM.00313-14

14 Kojima Y, Harada S, Aoki K, *et al.* Spread of CTX-M-15 extended-spectrum β-lactamase-producing Escherichia coli isolates through household contact and plasmid transfer. *J Clin Microbiol* 2014;52:1783–5. doi:10.1128/JCM.03342-13

15 Blanc V, Leflon-Guibout V, Blanco J, *et al.* Prevalence of day-care centre children (France) with faecal CTX-M-producing Escherichia coli comprising O25b:H4 and O16:H5 ST131 strains. *J Antimicrob Chemother* 2014;69:1231–7. doi:10.1093/jac/dkt519

16 Giuffrè M, Cipolla D, Bonura C, *et al.* Outbreak of colonizations by extended-spectrum β-lactamase-producing Escherichia coli sequence type 131 in a neonatal intensive care unit, Italy. *Antimicrob Resist Infect Control* 2013;2:8. doi:10.1186/2047-2994-2-8

17 Adler A, Gniadkowski M, Baraniak A, *et al.* Transmission dynamics of ESBL-producing Escherichia coli clones in rehabilitation wards at a tertiary care centre. *Clin Microbiol Infect* 2012;18:E497–505. doi:10.1111/j.1469-0691.2012.03999.x

18 Hilty M, Betsch BY, Bögli-Stuber K, *et al.* Transmission dynamics of extended-spectrum β-lactamase-producing Enterobacteriaceae in the tertiary care hospital and the household setting. *Clin Infect Dis* 2012;55:967–75. doi:10.1093/cid/cis581

19 Owens RC, Johnson JR, Stogsdill P, *et al.* Community transmission in the United States of a CTX-M-15-producing sequence type ST131 Escherichia coli strain resulting in death. *J Clin Microbiol* 2011;49:3406–8. doi:10.1128/JCM.00993-11

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20 Johnson JR, Anderson JT, Clabots C, *et al.* Within-household sharing of a fluoroquinolone-resistant Escherichia coli sequence type ST131 strain causing pediatric osteoarticular infection. *Pediatr Infect Dis J* 2010;29:473–5. doi:10.1097/INF.0b013e3181c89bd7

21 Ender PT, Gajanana D, Johnston B, *et al.* Transmission of an extended-spectrum-beta-lactamase-producing Escherichia coli (sequence type ST131) strain between a father and daughter resulting in septic shock and Emphysematous pyelonephritis. *J Clin Microbiol* 2009;47:3780–2. doi:10.1128/JCM.01361-09

22 Marquez C, Ingold A, Echeverría N, *et al.* Emergence of KPC-producing Klebsiella pneumoniae in Uruguay: infection control and molecular characterization. *New microbes new Infect* 2014;2:58–63. doi:10.1002/nmi2.40

23 Garza-Ramos U, Barrios H, Reyna-Flores F, *et al.* Characteristics of KPC-2-producing Klebsiella pneumoniae (ST258) clinical isolates from outbreaks in 2 Mexican medical centers. *Diagn Microbiol Infect Dis* 2014;79:483–5. doi:10.1016/j.diagmicrobio.2014.05.010

24 Gaibani P, Colombo R, Arghittu M, *et al.* Successful containment and infection control of a Carbapenem-resistant Klebsiella pneumoniae outbreak in an Italian hospital. *New Microbiol* 2014;37:87–90.http://www.ncbi.nlm.nih.gov/pubmed/24531175 (accessed 20 May2015).

25 Giuffrè M, Bonura C, Geraci DM, *et al.* Successful control of an outbreak of colonization by Klebsiella pneumoniae carbapenemase-producing K. pneumoniae sequence type 258 in a neonatal intensive care unit, Italy. *J Hosp Infect* 2013;85:233–6. doi:10.1016/j.jhin.2013.08.004

26 Tofteland S, Naseer U, Lislevand JH, *et al.* A long-term low-frequency hospital outbreak of KPC-producing Klebsiella pneumoniae involving Intergenus plasmid diffusion and a persisting environmental reservoir. *PLoS One* 2013;8:e59015. doi:10.1371/journal.pone.0059015

27 Morris D, Boyle F, Morris C, *et al.* Inter-hospital outbreak of Klebsiella pneumoniae producing KPC-2 carbapenemase in Ireland. *J Antimicrob Chemother* 2012;67:2367–72. doi:10.1093/jac/dks239

28 Agodi A, Voulgari E, Barchitta M, *et al.* Containment of an outbreak of KPC-3-producing Klebsiella pneumoniae in Italy. *J Clin Microbiol* 2011;49:3986–9. doi:10.1128/JCM.01242-11

29 Won SY, Munoz-Price LS, Lolans K, *et al.* Emergence and rapid regional spread of Klebsiella pneumoniae carbapenemase-producing Enterobacteriaceae. *Clin Infect Dis* 2011;53:532–40. doi:10.1093/cid/cir482

30 Marchese A, Coppo E, Barbieri R, *et al.* Emergence of KPC-2 carbapenemase-producing Klebsiella pneumoniae strains and spread of an isolate of sequence type 258 in the neuro-rehabilitation unit of an Italian hospital. *J Chemother* 2010;22:212–4. doi:10.1179/joc.2010.22.3.212

31 Mammina C, Palma DM, Bonura C, *et al.* Outbreak of infection with Klebsiella pneumoniae sequence type 258 producing Klebsiella pneumoniae Carbapenemase 3 in an intensive care unit in Italy. *J Clin Microbiol* 2010;48:1506–7. doi:10.1128/JCM.00315-10

32 Titelman E, Hasan CM, Iversen A, *et al.* Faecal carriage of extended-spectrum β-lactamase-producing Enterobacteriaceae is common 12 months after infection and is related to strain factors. *Clin Microbiol Infect* 2014;20:O508–15. doi:10.1111/1469-0691.12559

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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33 Rogers BA, Kennedy KJ, Sidjabat HE, *et al.* Prolonged carriage of resistant E. coli by returned travellers: clonality, risk factors and bacterial characteristics. *Eur J Clin Microbiol Infect Dis* 2012;31:2413–20. doi:10.1007/s10096-012-1584-z

34 Papagiannitsis CC, Študentová V, Jakubů V, *et al.* High prevalence of ST131 among CTX-M-producing Escherichia coli from community-acquired infections, in the Czech Republic. *Microb Drug Resist* 2015;21:74–84. doi:10.1089/mdr.2014.0070

35 Osawa K, Shigemura K, Shimizu R, *et al.* Molecular characteristics of extended-spectrum β-lactamase-producing Escherichia coli in a university teaching hospital. *Microb Drug Resist* 2015;21:130–9. doi:10.1089/mdr.2014.0083

36 Hristea A, Olaru ID, Adams-Sapper S, *et al.* Characterization of ESBL-producing Escherichia coli and Klebsiella pneumoniae from bloodstream infections in three hospitals in Bucharest, Romania: a preliminary study. *Infect Dis (London, England)* 2015;47:46–51. doi:10.3109/00365548.2014.959043

37 Salipante SJ, Roach DJ, Kitzman JO, *et al.* Large-scale genomic sequencing of extraintestinal pathogenic Escherichia coli strains. *Genome Res* 2015;25:119–28. doi:10.1101/gr.180190.114

38 Can F, Azap OK, Seref C, *et al.* Emerging Escherichia coli O25b/ST131 clone predicts treatment failure in urinary tract infections. *Clin Infect Dis* 2015;60:523–7. doi:10.1093/cid/ciu864

39 Zhao L, Zhang J, Zheng B, *et al.* Molecular epidemiology and genetic diversity of fluoroquinolone-resistant Escherichia coli isolates from patients with community-onset infections in 30 Chinese county hospitals. *J Clin Microbiol* 2015;53:766–70. doi:10.1128/JCM.02594-14

40 Hansen F, Olsen SS, Heltberg O, *et al.* Characterization of third-generation cephalosporin-resistant Escherichia coli from bloodstream infections in Denmark. *Microb Drug Resist* 2014;20:316–24. doi:10.1089/mdr.2013.0157

41 Berman H, Barberino MG, Moreira ED, *et al.* Distribution of strain type and antimicrobial susceptibility of Escherichia coli isolates causing meningitis in a large urban setting in Brazil. *J Clin Microbiol* 2014;52:1418–22. doi:10.1128/JCM.03104-13

42 Peirano G, Pitout JDD. Fluoroquinolone-resistant Escherichia coli sequence type 131 isolates causing bloodstream infections in a canadian region with a centralized laboratory system: rapid emergence of the H30-Rx sublineage. *Antimicrob Agents Chemother* 2014;58:2699–703. doi:10.1128/AAC.00119-14

43 Shakir SM, Goldbeck JM, Robison D, *et al.* Genotypic and phenotypic characterization of invasive neonatal Escherichia coli clinical isolates. *Am J Perinatol* 2014;31:975–82. doi:10.1055/s-0034-1370341

44 Peirano G, Ahmed-Bentley J, Fuller J, *et al.* Travel-related carbapenemase-producing Gram-negative bacteria in Alberta, Canada: the first 3 years. *J Clin Microbiol* 2014;52:1575–81. doi:10.1128/JCM.00162-14

45 Sana F, Mabrouka S, Claudine Q, *et al.* Prevalence and characterization of uropathogenic Escherichia coli harboring plasmid-mediated quinolone resistance in a Tunisian university hospital. *Diagn Microbiol Infect Dis* 2014;79:247–51. doi:10.1016/j.diagmicrobio.2014.03.011

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46 Önnberg A, Söderquist B, Persson K, *et al.* Characterization of CTX-M-producing Escherichia coli by repetitive sequence-based PCR and real-time PCR-based replicon typing of CTX-M-15 plasmids. *APMIS* 2014;122:1136–43. doi:10.1111/apm.12270

47 Oteo J, González-López JJ, Ortega A, *et al.* Inhibitor-resistant TEM- and OXA-1-producing Escherichia coli isolates resistant to amoxicillin-clavulanate are more clonal and possess lower virulence gene content than susceptible clinical isolates. *Antimicrob Agents Chemother* 2014;58:3874–81. doi:10.1128/AAC.02738-13

48 Rodríguez I, Thomas K, Van Essen A, *et al.* Chromosomal location of blaCTX-M genes in clinical isolates of Escherichia coli from Germany, The Netherlands and the UK. *Int J Antimicrob Agents* 2014;43:553–7. doi:10.1016/j.ijantimicag.2014.02.019

49 O'Hara JA, Hu F, Ahn C, *et al.* Molecular epidemiology of KPC-producing Escherichia coli: occurrence of ST131-fimH30 subclone harboring pKpQIL-like IncFIIk plasmid. *Antimicrob Agents Chemother* 2014;58:4234–7. doi:10.1128/AAC.02182-13

50 Inwezerua C, Mendonça N, Calhau V, *et al.* Occurrence of extended-spectrum beta-lactamases in human and bovine isolates of Escherichia coli from Oyo state, Nigeria. *J Infect Dev Ctries* 2014;8:774–9.http://www.ncbi.nlm.nih.gov/pubmed/24916877 (accessed 2 Nov2015).

51 Micenková L, Šišková P, Bosák J, *et al.* Characterization of Human Uropathogenic ESBL-Producing Escherichia coli in the Czech Republic: Spread of CTX-M-27-Producing Strains in a University Hospital. *Microb Drug Resist* 2014;20:610–7. doi:10.1089/mdr.2014.0013

52 Xia S, Fan X, Huang Z, *et al.* Dominance of CTX-M-type extended-spectrum β-lactamase (ESBL)-producing Escherichia coli isolated from patients with community-onset and hospital-onset infection in China. *PLoS One* 2014;9:e100707. doi:10.1371/journal.pone.0100707

53 Morgand M, Vimont S, Bleibtreu A, *et al.* Extended-spectrum beta-lactamase-producing Escherichia coli infections in children: Are community-acquired strains different from nosocomial strains? *Int J Med Microbiol* 2014;304:970–6. doi:10.1016/j.ijmm.2014.06.003

54 Suwantarat N, Rudin SD, Marshall SH, *et al.* Infections caused by fluoroquinolone-resistant Escherichia coli following transrectal ultrasound-guided biopsy of the prostate. *J Glob Antimicrob Resist* 2014;2:71–6. doi:10.1016/j.jgar.2013.07.003

55 Maluta RP, Logue CM, Casas MRT, *et al.* Overlapped sequence types (STs) and serogroups of avian pathogenic (APEC) and human extra-intestinal pathogenic (ExPEC) Escherichia coli isolated in Brazil. *PLoS One* 2014;9:e105016. doi:10.1371/journal.pone.0105016

56 Dashti AA, Vali L, El-Shazly S, *et al.* The characterization and antibiotic resistance profiles of clinical Escherichia coli O25b-B2-ST131 isolates in Kuwait. *BMC Microbiol* 2014;14:214. doi:10.1186/s12866-014-0214-6

57 Freeman JT, Rubin J, McAuliffe GN, *et al.* Differences in risk-factor profiles between patients with ESBL-producing Escherichia coli and Klebsiella pneumoniae: a multicentre case-case comparison study. *Antimicrob Resist Infect Control* 2014;3:27. doi:10.1186/2047-2994-3-27

58 Hussain A, Ranjan A, Nandanwar N, *et al.* Genotypic and phenotypic profiles of Escherichia coli isolates belonging to clinical sequence type 131 (ST131), clinical non-ST131, and fecal non-ST131

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BMJ Open: first published as 10.1136/bmjopen-2015-009971 on 17 March 2016. Downloaded from http://bmjopen.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

lineages from India. *Antimicrob Agents Chemother* 2014;58:7240–9. doi:10.1128/AAC.03320-14

59 Dahbi G, Mora A, Mamani R, *et al.* Molecular epidemiology and virulence of Escherichia coli O16:H5-ST131: comparison with H30 and H30-Rx subclones of O25b:H4-ST131. *Int J Med Microbiol* 2014;304:1247–57. doi:10.1016/j.ijmm.2014.10.002

60 Zhang J, Zheng B, Zhao L, *et al.* Nationwide high prevalence of CTX-M and an increase of CTX-M-55 in Escherichia coli isolated from patients with community-onset infections in Chinese county hospitals. *BMC Infect Dis* 2014;14:659. doi:10.1186/s12879-014-0659-0

61 Usein C-R, Condei M, Cristea D, *et al.* Escherichia coli ST131 causing invasive infections in Romanian patients--a threat we can no longer ignore. *Roum Arch Microbiol Immunol*;73:5–8.http://www.ncbi.nlm.nih.gov/pubmed/25518564 (accessed 23 Nov2015).

62 Wu Y-H, Cheng M-F, Lai C-H, *et al.* The role of Sequence Type (ST) 131 in adult community-onset non-ESBL-producing Escherichia coli bacteraemia. *BMC Infect Dis* 2014;14:579. doi:10.1186/s12879-014-0579-z

63 Guillard T, Bertrand X, de Champs C, *et al*. Aac(6')Ib-cr is the major plasmid-mediated quinolone resistance determinant in extended-spectrum beta-lacatamase-producing *Escherichia coli* in Eastern France. *Journal of Global Antimicrobial Resistance,* 2014;2:111-113.

64 Habeeb MA, Haque A, Iversen A, *et al.* Occurrence of virulence genes, 16S rRNA methylases, and plasmid-mediated quinolone resistance genes in CTX-M-producing Escherichia coli from Pakistan. *Eur J Clin Microbiol Infect Dis* 2014;33:399–409. doi:10.1007/s10096-013-1970-1

65 López-Cerero L, Navarro MD, Bellido M, *et al.* Escherichia coli belonging to the worldwide emerging epidemic clonal group O25b/ST131: risk factors and clinical implications. *J Antimicrob Chemother* 2014;69:809–14. doi:10.1093/jac/dkt405

66 Giufre M, Accogli M, Farina C, *et al.* Predominance of the fimH30 subclone among multidrug-resistant Escherichia coli strains belonging to sequence type 131 in Italy. *J Infect Dis* 2014;209:629–30. doi:10.1093/infdis/jit583

67 Ferjani S, Saidani M, Ennigrou S, *et al.* Multidrug resistance and high virulence genotype in uropathogenic Escherichia coli due to diffusion of ST131 clonal group producing CTX-M-15: an emerging problem in a Tunisian hospital. *Folia Microbiol (Praha)* 2014;59:257–62. doi:10.1007/s12223-013-0292-0

68 Al-Agamy MH, Shibl AM, Hafez MM, *et al.* Molecular characteristics of extended-spectrum β-lactamase-producing Escherichia coli in Riyadh: emergence of CTX-M-15-producing E. coli ST131. *Ann Clin Microbiol Antimicrob* 2014;13:4. doi:10.1186/1476-0711-13-4

69 Rogers BA, Ingram PR, Runnegar N, *et al.* Community-onset Escherichia coli infection resistant to expanded-spectrum cephalosporins in low-prevalence countries. *Antimicrob Agents Chemother* 2014;58:2126–34. doi:10.1128/AAC.02052-13

70 Nicolas-Chanoine M-H, Robert J, Vigan M, *et al.* Different factors associated with CTX-M-producing ST131 and non-ST131 Escherichia coli clinical isolates. *PLoS One* 2013;8:e72191. doi:10.1371/journal.pone.0072191

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2015-009971 on 17 March 2016. Downloaded from http://bmjopen.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

71 Nordberg V, Quizhpe Peralta A, Galindo T, *et al.* High proportion of intestinal colonization with successful epidemic clones of ESBL-producing Enterobacteriaceae in a neonatal intensive care unit in Ecuador. *PLoS One* 2013;8:e76597. doi:10.1371/journal.pone.0076597

72 Dimude JU, Amyes SGB. Molecular diversity associated with the dissemination of CTX-M-15 beta-lactamase gene in blood culture isolates of Escherichia coli from Edinburgh. *Scand J Infect Dis* 2013;45:32–7. doi:10.3109/00365548.2012.708781

73 Karfunkel D, Carmeli Y, Chmelnitsky I, *et al.* The emergence and dissemination of CTX-M-producing Escherichia coli sequence type 131 causing community-onset bacteremia in Israel. *Eur J Clin Microbiol Infect Dis* 2013;32:513–21. doi:10.1007/s10096-012-1765-9

74 Nielsen JB, Albayati A, Jørgensen RL, *et al.* An abbreviated MLVA identifies Escherichia coli ST131 as the major extended-spectrum β-lactamase-producing lineage in the Copenhagen area. *Eur J Clin Microbiol Infect Dis* 2013;32:431–6. doi:10.1007/s10096-012-1764-x

75 van der Donk CFM, Schols JMGA, Driessen CJ, *et al.* Prevalence and spread of multidrug resistant Escherichia coli isolates among nursing home residents in the southern part of The Netherlands. *J Am Med Dir Assoc* 2013;14:199–203. doi:10.1016/j.jamda.2012.09.026

76 Adams-Sapper S, Diep BA, Perdreau-Remington F, *et al.* Clonal composition and community clustering of drug-susceptible and -resistant Escherichia coli isolates from bloodstream infections. *Antimicrob Agents Chemother* 2013;57:490–7. doi:10.1128/AAC.01025-12

77 Doi Y, Park YS, Rivera JI, *et al.* Community-associated extended-spectrum β-lactamase-producing Escherichia coli infection in the United States. *Clin Infect Dis* 2013;56:641–8. doi:10.1093/cid/cis942

78 López-Cerero L, Bellido M del M, Serrano L, *et al.* Escherichia coli O25b:H4/ST131 are prevalent in Spain and are often not associated with ESBL or quinolone resistance. *Enferm Infecc Microbiol Clin* 2013;31:385–8. doi:10.1016/j.eimc.2012.09.005

79 Helldal L, Karami N, Florén K, *et al.* Shift of CTX-M genotypes has determined the increased prevalence of extended-spectrum β-lactamase-producing Escherichia coli in south-western Sweden. *Clin Microbiol Infect* 2013;19:E87–90. doi:10.1111/1469-0691.12086

80 Hammami S, Saidani M, Ferjeni S, *et al.* Characterization of extended spectrum β-lactamase-producing Escherichia coli in community-acquired urinary tract infections in Tunisia. *Microb Drug Resist* 2013;19:231–6. doi:10.1089/mdr.2012.0172

81 Kudinha T, Johnson JR, Andrew SD, *et al.* Distribution of phylogenetic groups, sequence type ST131, and virulence-associated traits among Escherichia coli isolates from men with pyelonephritis or cystitis and healthy controls. *Clin Microbiol Infect* 2013;19:E173–80. doi:10.1111/1469-0691.12123

82 Kudinha T, Johnson JR, Andrew SD, *et al.* Genotypic and phenotypic characterization of Escherichia coli isolates from children with urinary tract infection and from healthy carriers. *Pediatr Infect Dis J* 2013;32:543–8. doi:10.1097/INF.0b013e31828ba3f1

83 Weissman SJ, Adler A, Qin X, *et al.* Emergence of extended-spectrum β-lactam resistance among Escherichia coli at a US academic children's hospital is clonal at the sequence type level for CTX-

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M-15, but not for CMY-2. *Int J Antimicrob Agents* 2013;41:414–20. doi:10.1016/j.ijantimicag.2013.01.006

84 Banerjee R, Johnston B, Lohse C, *et al.* Escherichia coli sequence type 131 is a dominant, antimicrobial-resistant clonal group associated with healthcare and elderly hosts. *Infect Control Hosp Epidemiol* 2013;34:361–9. doi:10.1086/669865

85 Kim B, Kim J, Seo M-R, *et al.* Clinical characteristics of community-acquired acute pyelonephritis caused by ESBL-producing pathogens in South Korea. *Infection* 2013;41:603–12. doi:10.1007/s15010-013-0441-z

86 Aoike N, Saga T, Sakata R, *et al.* Molecular characterization of extraintestinal Escherichia coli isolates in Japan: relationship between sequence types and mutation patterns of quinolone resistance-determining regions analyzed by pyrosequencing. *J Clin Microbiol* 2013;51:1692–8. doi:10.1128/JCM.03049-12

87 Olesen B, Hansen DS, Nilsson F, *et al.* Prevalence and characteristics of the epidemic multiresistant Escherichia coli ST131 clonal group among extended-spectrum beta-lactamase-producing E. coli isolates in Copenhagen, Denmark. *J Clin Microbiol* 2013;51:1779–85. doi:10.1128/JCM.00346-13

88 Qin X, Hu F, Wu S, *et al.* Comparison of adhesin genes and antimicrobial susceptibilities between uropathogenic and intestinal commensal Escherichia coli strains. *PLoS One* 2013;8:e61169. doi:10.1371/journal.pone.0061169

89 Denisuik AJ, Lagacé-Wiens PRS, Pitout JD, *et al.* Molecular epidemiology of extended-spectrum β-lactamase-, AmpC β-lactamase- and carbapenemase-producing Escherichia coli and Klebsiella pneumoniae isolated from Canadian hospitals over a 5 year period: CANWARD 2007-11. *J Antimicrob Chemother* 2013;68 Suppl 1:i57–65. doi:10.1093/jac/dkt027

90 Yano H, Uemura M, Endo S, *et al.* Molecular characteristics of extended-spectrum β-lactamases in clinical isolates from Escherichia coli at a Japanese tertiary hospital. *PLoS One* 2013;8:e64359. doi:10.1371/journal.pone.0064359

91 Chmielarczyk A, Pobiega M, Wójkowska-Mach J, *et al.* Molecular epidemiology, plasmid analysis, virulence, and resistance of Escherichia coli isolated from neonatal intensive care units in Poland. *Diagn Microbiol Infect Dis* 2013;76:542–5. doi:10.1016/j.diagmicrobio.2013.04.016

92 Seiffert SN, Hilty M, Kronenberg A, *et al.* Extended-spectrum cephalosporin-resistant Escherichia coli in community, specialized outpatient clinic and hospital settings in Switzerland. *J Antimicrob Chemother* 2013;68:2249–54. doi:10.1093/jac/dkt208

93 Reyna-Flores F, Barrios H, Garza-Ramos U, *et al.* Molecular epidemiology of Escherichia coli O25b-ST131 isolates causing community-acquired UTIs in Mexico. *Diagn Microbiol Infect Dis* 2013;76:396–8. doi:10.1016/j.diagmicrobio.2013.03.026

94 Mnif B, Harhour H, Jdidi J, *et al.* Molecular epidemiology of extended-spectrum beta-lactamase-producing Escherichia coli in Tunisia and characterization of their virulence factors and plasmid addiction systems. *BMC Microbiol* 2013;13:147. doi:10.1186/1471-2180-13-147

95 Williamson DA, Freeman JT, Porter S, *et al.* Clinical and molecular correlates of virulence in

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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Escherichia coli causing bloodstream infection following transrectal ultrasound-guided (TRUS) prostate biopsy. *J Antimicrob Chemother* 2013;68:2898–906. doi:10.1093/jac/dkt276

96 Kang C-I, Cha MK, Kim SH, *et al.* Clinical and molecular epidemiology of community-onset bacteremia caused by extended-spectrum β-lactamase-producing Escherichia coli over a 6-year period. *J Korean Med Sci* 2013;28:998–1004. doi:10.3346/jkms.2013.28.7.998

97 Kudinha T, Johnson JR, Andrew SD, *et al.* Escherichia coli sequence type 131 as a prominent cause of antibiotic resistance among urinary Escherichia coli isolates from reproductive-age women. *J Clin Microbiol* 2013;51:3270–6. doi:10.1128/JCM.01315-13

98 Hu Y-Y, Cai J-C, Zhou H-W, *et al.* Molecular typing of CTX-M-producing escherichia coli isolates from environmental water, swine feces, specimens from healthy humans, and human patients. *Appl Environ Microbiol* 2013;79:5988–96. doi:10.1128/AEM.01740-13

99 van der Donk C, van de Bovenkamp J, Bamelis H, *et al.* Prevalence and spread of multidrug-resistant Escherichia coli including ST131 in different patient populations in the Euroregion Meuse-Rhine. *Future Microbiol* 2013;8:1027–37. doi:10.2217/fmb.13.61

100 Banerjee R, Strahilevitz J, Johnson JR, *et al.* Predictors and molecular epidemiology of community-onset extended-spectrum β-lactamase-producing Escherichia coli infection in a Midwestern community. *Infect Control Hosp Epidemiol* 2013;34:947–53. doi:10.1086/671725

101 Blanco J, Mora A, Mamani R, *et al.* Four main virotypes among extended-spectrum-β-lactamase-producing isolates of Escherichia coli O25b:H4-B2-ST131: bacterial, epidemiological, and clinical characteristics. *J Clin Microbiol* 2013;51:3358–67. doi:10.1128/JCM.01555-13

102 Colpan A, Johnston B, Porter S, *et al.* Escherichia coli sequence type 131 (ST131) subclone H30 as an emergent multidrug-resistant pathogen among US veterans. *Clin Infect Dis* 2013;57:1256–65. doi:10.1093/cid/cit503

103 Dahbi G, Mora A, López C, *et al.* Emergence of new variants of ST131 clonal group among extraintestinal pathogenic Escherichia coli producing extended-spectrum β-lactamases. *Int J Antimicrob Agents* 2013;42:347–51. doi:10.1016/j.ijantimicag.2013.06.017

104 Horner C, Fawley W, Morris K, *et al.* Escherichia coli bacteraemia: 2 years of prospective regional surveillance (2010-12). *J Antimicrob Chemother* 2014;69:91–100. doi:10.1093/jac/dkt333

105 Banerjee R, Johnston B, Lohse C, *et al.* The clonal distribution and diversity of extraintestinal Escherichia coli isolates vary according to patient characteristics. *Antimicrob Agents Chemother* 2013;57:5912–7. doi:10.1128/AAC.01065-13

106 Ha YE, Kang C-I, Cha MK, *et al.* Epidemiology and clinical outcomes of bloodstream infections caused by extended-spectrum β-lactamase-producing Escherichia coli in patients with cancer. *Int J Antimicrob Agents* 2013;42:403–9. doi:10.1016/j.ijantimicag.2013.07.018

107 Brolund A, Edquist PJ, Mäkitalo B, *et al.* Epidemiology of extended-spectrum β-lactamase-producing Escherichia coli in Sweden 2007-2011. *Clin Microbiol Infect* 2014;20:O344–52. doi:10.1111/1469-0691.12413

108 Aschbacher R, Giani T, Corda D, *et al.* Carbapenemase-producing Enterobacteriaceae during

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2011-12 in the Bolzano area (Northern Italy): increasing diversity in a low-endemicity setting. *Diagn Microbiol Infect Dis* 2013;77:354–6. doi:10.1016/j.diagmicrobio.2013.08.029

109 Calhau V, Ribeiro G, Mendonça N, *et al.* Prevalent combination of virulence and plasmidic-encoded resistance in ST 131 Escherichia coli strains. *Virulence* 2013;4:726–9. doi:10.4161/viru.26552

110 Markovska R, Schneider I, Ivanova D, *et al.* Predominance of IncL/M and IncF plasmid types among CTX-M-ESBL-producing Escherichia coli and Klebsiella pneumoniae in Bulgarian hospitals. *APMIS* 2014;122:608–15. doi:10.1111/apm.12204

111 Ma L, Siu LK, Lin J-C, *et al.* Updated molecular epidemiology of carbapenem-non-susceptible Escherichia coli in Taiwan: first identification of KPC-2 or NDM-1-producing E. coli in Taiwan. *BMC Infect Dis* 2013;13:599. doi:10.1186/1471-2334-13-599

112 Brisse S, Diancourt L, Laouénan C, *et al.* Phylogenetic distribution of CTX-M- and non-extended-spectrum-β-lactamase-producing Escherichia coli isolates: group B2 isolates, except clone ST131, rarely produce CTX-M enzymes. *J Clin Microbiol* 2012;50:2974–81. doi:10.1128/JCM.00919-12

113 Weissman SJ, Johnson JR, Tchesnokova V, *et al.* High-resolution two-locus clonal typing of extraintestinal pathogenic Escherichia coli. *Appl Environ Microbiol* 2012;78:1353–60. doi:10.1128/AEM.06663-11

114 Musumeci R, Rausa M, Giovannoni R, *et al.* Prevalence of plasmid-mediated quinolone resistance genes in uropathogenic Escherichia coli isolated in a teaching hospital of northern Italy. *Microb Drug Resist* 2012;18:33–41. doi:10.1089/mdr.2010.0146

115 Oteo J, Cercenado E, Fernández-Romero S, *et al.* Extended-spectrum-β-lactamase-producing Escherichia coli as a cause of pediatric infections: report of a neonatal intensive care unit outbreak due to a CTX-M-14-producing strain. *Antimicrob Agents Chemother* 2012;56:54–8. doi:10.1128/AAC.05103-11

116 Gibreel TM, Dodgson AR, Cheesbrough J, *et al.* Population structure, virulence potential and antibiotic susceptibility of uropathogenic Escherichia coli from Northwest England. *J Antimicrob Chemother* 2012;67:346–56. doi:10.1093/jac/dkr451

117 Chung H-C, Lai C-H, Lin J-N, *et al.* Bacteremia caused by extended-spectrum-β-lactamase-producing Escherichia coli sequence type ST131 and non-ST131 clones: comparison of demographic data, clinical features, and mortality. *Antimicrob Agents Chemother* 2012;56:618–22. doi:10.1128/AAC.05753-11

118 Peirano G, van der Bij AK, Gregson DB, *et al.* Molecular epidemiology over an 11-year period (2000 to 2010) of extended-spectrum β-lactamase-producing Escherichia coli causing bacteremia in a centralized Canadian region. *J Clin Microbiol* 2012;50:294–9. doi:10.1128/JCM.06025-11

119 Tiruvury H, Johnson JR, Mariano N, *et al.* Identification of CTX-M β-lactamases among Escherichia coli from the community in New York City. *Diagn Microbiol Infect Dis* 2012;72:248–52. doi:10.1016/j.diagmicrobio.2011.11.008

120 Giufrè M, Graziani C, Accogli M, *et al.* Escherichia coli of human and avian origin: detection of clonal groups associated with fluoroquinolone and multidrug resistance in Italy. *J Antimicrob*

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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Chemother 2012;67:860–7. doi:10.1093/jac/dkr565

121 Novais A, Rodrigues C, Branquinho R, *et al.* Spread of an OmpK36-modified ST15 Klebsiella pneumoniae variant during an outbreak involving multiple carbapenem-resistant Enterobacteriaceae species and clones. *Eur J Clin Microbiol Infect Dis* 2012;31:3057–63. doi:10.1007/s10096-012-1665-z

122 Matsumura Y, Nagao M, Iguchi M, *et al.* Molecular and clinical characterization of plasmid-mediated AmpC β-lactamase-producing Escherichia coli bacteraemia: a comparison with extended-spectrum β-lactamase-producing and non-resistant E. coli bacteraemia. *Clin Microbiol Infect* 2013;19:161–8. doi:10.1111/j.1469-0691.2012.03762.x

123 Yokota S, Sato T, Okubo T, *et al.* Prevalence of fluoroquinolone-resistant Escherichia coli O25:H4-ST131 (CTX-M-15-nonproducing) strains isolated in Japan. *Chemotherapy* 2012;58:52–9. doi:10.1159/000336129

124 Johnson JR, Urban C, Weissman SJ, *et al.* Molecular epidemiological analysis of Escherichia coli sequence type ST131 (O25:H4) and blaCTX-M-15 among extended-spectrum-β-lactamase-producing E. coli from the United States, 2000 to 2009. *Antimicrob Agents Chemother* 2012;56:2364–70. doi:10.1128/AAC.05824-11

125 Williamson DA, Roberts SA, Paterson DL, *et al.* Escherichia coli bloodstream infection after transrectal ultrasound-guided prostate biopsy: implications of fluoroquinolone-resistant sequence type 131 as a major causative pathogen. *Clin Infect Dis* 2012;54:1406–12. doi:10.1093/cid/cis194

126 Ho PL, Yeung MK, Lo WU, *et al.* Predominance of pHK01-like incompatibility group FII plasmids encoding CTX-M-14 among extended-spectrum beta-lactamase-producing Escherichia coli in Hong Kong, 1996-2008. *Diagn Microbiol Infect Dis* 2012;73:182–6. doi:10.1016/j.diagmicrobio.2012.03.009

127 Dimou V, Dhanji H, Pike R, *et al.* Characterization of Enterobacteriaceae producing OXA-48-like carbapenemases in the UK. *J Antimicrob Chemother* 2012;67:1660–5. doi:10.1093/jac/dks124

128 Burke L, Humphreys H, Fitzgerald-Hughes D. The revolving door between hospital and community: extended-spectrum beta-lactamase-producing Escherichia coli in Dublin. *J Hosp Infect* 2012;81:192–8. doi:10.1016/j.jhin.2012.04.021

129 Park SH, Byun J-H, Choi S-M, *et al.* Molecular epidemiology of extended-spectrum β-lactamase-producing Escherichia coli in the community and hospital in Korea: emergence of ST131 producing CTX-M-15. *BMC Infect Dis* 2012;12:149. doi:10.1186/1471-2334-12-149

130 Reuland EA, Overdevest ITMA, Al Naiemi N, *et al.* High prevalence of ESBL-producing Enterobacteriaceae carriage in Dutch community patients with gastrointestinal complaints. *Clin Microbiol Infect* 2013;19:542–9. doi:10.1111/j.1469-0691.2012.03947.x

131 Kuroda H, Yano H, Hirakata Y, *et al.* Molecular characteristics of extended-spectrum β-lactamase-producing Escherichia coli in Japan: emergence of CTX-M-15-producing E. coli ST131. *Diagn Microbiol Infect Dis* 2012;74:201–3. doi:10.1016/j.diagmicrobio.2012.06.011

132 Gibreel TM, Dodgson AR, Cheesbrough J, *et al.* High metabolic potential may contribute to the

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success of ST131 uropathogenic Escherichia coli. *J Clin Microbiol* 2012;50:3202–7. doi:10.1128/JCM.01423-12

133 Matsumura Y, Yamamoto M, Nagao M, *et al.* Emergence and spread of B2-ST131-O25b, B2-ST131-O16 and D-ST405 clonal groups among extended-spectrum-β-lactamase-producing Escherichia coli in Japan. *J Antimicrob Chemother* 2012;67:2612–20. doi:10.1093/jac/dks278

134 Österblad M, Kirveskari J, Hakanen AJ, *et al.* Carbapenemase-producing Enterobacteriaceae in Finland: the first years (2008-11). *J Antimicrob Chemother* 2012;67:2860–4. doi:10.1093/jac/dks299

135 Naseer U, Olsson-Liljequist BE, Woodford N, *et al.* Multi-locus variable number of tandem repeat analysis for rapid and accurate typing of virulent multidrug resistant Escherichia coli clones. *PLoS One* 2012;7:e41232. doi:10.1371/journal.pone.0041232

136 Golding GR, Persaud N, Levett PN, *et al.* Characterization of Escherichia coli urinary tract infection isolates in remote northern Saskatchewan communities: the Northern Antibiotic Resistance Partnership. *Diagn Microbiol Infect Dis* 2012;74:242–7. doi:10.1016/j.diagmicrobio.2012.07.003

137 Hussain A, Ewers C, Nandanwar N, *et al.* Multiresistant uropathogenic Escherichia coli from a region in India where urinary tract infections are endemic: genotypic and phenotypic characteristics of sequence type 131 isolates of the CTX-M-15 extended-spectrum-β-lactamase-producing lineage. *Antimicrob Agents Chemother* 2012;56:6358–65. doi:10.1128/AAC.01099-12

138 van der Donk CFM, van de Bovenkamp JHB, De Brauwer EIGB, *et al.* Antimicrobial resistance and spread of multi drug resistant Escherichia coli isolates collected from nine urology services in the Euregion Meuse-Rhine. *PLoS One* 2012;7:e47707. doi:10.1371/journal.pone.0047707

139 Mavroidi A, Miriagou V, Liakopoulos A, *et al.* Ciprofloxacin-resistant Escherichia coli in Central Greece: mechanisms of resistance and molecular identification. *BMC Infect Dis* 2012;12:371. doi:10.1186/1471-2334-12-371

140 Peirano G, Asensi MD, Pitondo-Silva A, Pitout JD. Molecular characteristics of extended-spectrum β-lactamase-producing Escherichia coli from Rio de Janeiro, Brazil. *Clin Microbiol Infect* 2011;17:1039-43. doi: 10.1111/j.1469-0691.2010.03440.x

141 Peirano G, van Greune CH, Pitout JD. Characteristics of infections caused by extended-spectrum β-lactamase-producing Escherichia coli from community hospitals in South Africa. *Diagn Microbiol Infect Dis* 2011;69:449-53. doi: 10.1016/j.diagmicrobio.2010.11.011

142 Overdevest I, Willemsen I, Rijnsburger M, *et al.* Extended-spectrum β-lactamase genes of Escherichia coli in chicken meat and humans, The Netherlands. *Emerg Infect Dis* 2011;17:1216–22. doi:10.3201/eid1707.110209

143 Leverstein-van Hall MA, Dierikx CM, Cohen Stuart J, *et al.* Dutch patients, retail chicken meat and poultry share the same ESBL genes, plasmids and strains. *Clin Microbiol Infect* 2011;17:873–80. doi:10.1111/j.1469-0691.2011.03497.x

144 Courpon-Claudinon A, Lefort A, Panhard X, *et al.* Bacteraemia caused by third-generation cephalosporin-resistant Escherichia coli in France: prevalence, molecular epidemiology and clinical features. *Clin Microbiol Infect* 2011;17:557–65. doi:10.1111/j.1469-0691.2010.03298.x

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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145 Rodriguez-Villalobos H, Bogaerts P, Berhin C, *et al.* Trends in production of extended-spectrum beta-lactamases among Enterobacteriaceae of clinical interest: results of a nationwide survey in Belgian hospitals. *J Antimicrob Chemother* 2011;66:37–47. doi:10.1093/jac/dkq388

146 Mora A, Blanco M, López C, *et al.* Emergence of clonal groups O1:HNM-D-ST59, O15:H1-D-ST393, O20:H34/HNM-D-ST354, O25b:H4-B2-ST131 and ONT:H21,42-B1-ST101 among CTX-M-14-producing Escherichia coli clinical isolates in Galicia, northwest Spain. *Int J Antimicrob Agents* 2011;37:16–21. doi:10.1016/j.ijantimicag.2010.09.012

147 Coelho A, Mora A, Mamani R, *et al.* Spread of Escherichia coli O25b:H4-B2-ST131 producing CTX-M-15 and SHV-12 with high virulence gene content in Barcelona (Spain). *J Antimicrob Chemother* 2011;66:517–26. doi:10.1093/jac/dkq491

148 Xu L, Shabir S, Bodah T, *et al.* Regional survey of CTX-M-type extended-spectrum β-lactamases among Enterobacteriaceae reveals marked heterogeneity in the distribution of the ST131 clone. *J Antimicrob Chemother* 2011;66:505–11. doi:10.1093/jac/dkq482

149 Ruiz SJ, Montealegre MC, Ruiz-Garbajosa P, *et al.* First characterization of CTX-M-15-producing Escherichia coli ST131 and ST405 clones causing community-onset infections in South America. *J Clin Microbiol* 2011;49:1993–6. doi:10.1128/JCM.00045-11

150 Simner PJ, Zhanel GG, Pitout J, *et al.* Prevalence and characterization of extended-spectrum β-lactamase- and AmpC β-lactamase-producing Escherichia coli: results of the CANWARD 2007-2009 study. *Diagn Microbiol Infect Dis* 2011;69:326–34. doi:10.1016/j.diagmicrobio.2010.10.029

151 Dhanji H, Patel R, Wall R, *et al.* Variation in the genetic environments of bla(CTX-M-15) in Escherichia coli from the faeces of travellers returning to the United Kingdom. *J Antimicrob Chemother* 2011;66:1005–12. doi:10.1093/jac/dkr041

152 Kim J, Bae IK, Jeong SH, *et al.* Characterization of IncF plasmids carrying the blaCTX-M-14 gene in clinical isolates of Escherichia coli from Korea. *J Antimicrob Chemother* 2011;66:1263–8. doi:10.1093/jac/dkr106

153 van der Bij AK, Peirano G, Goessens WHF, *et al.* Clinical and molecular characteristics of extended-spectrum-beta-lactamase-producing Escherichia coli causing bacteremia in the Rotterdam Area, Netherlands. *Antimicrob Agents Chemother* 2011;55:3576–8. doi:10.1128/AAC.00074-11

154 Titelman E, Karlsson IM, Ge Y, *et al.* In vitro activity of CXA-101 plus tazobactam (CXA-201) against CTX-M-14- and CTX-M-15-producing Escherichia coli and Klebsiella pneumoniae. *Diagn Microbiol Infect Dis* 2011;70:137–41. doi:10.1016/j.diagmicrobio.2011.02.004

155 Cao X, Cavaco LM, Lv Y, *et al.* Molecular characterization and antimicrobial susceptibility testing of Escherichia coli isolates from patients with urinary tract infections in 20 Chinese hospitals. *J Clin Microbiol* 2011;49:2496–501. doi:10.1128/JCM.02503-10

156 Mshana SE, Imirzalioglu C, Hain T, *et al.* Multiple ST clonal complexes, with a predominance of ST131, of Escherichia coli harbouring blaCTX-M-15 in a tertiary hospital in Tanzania. *Clin Microbiol Infect* 2011;17:1279–82. doi:10.1111/j.1469-0691.2011.03518.x

157 Blanco J, Mora A, Mamani R, *et al.* National survey of Escherichia coli causing extraintestinal

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infections reveals the spread of drug-resistant clonal groups O25b:H4-B2-ST131, O15:H1-D-ST393 and CGA-D-ST69 with high virulence gene content in Spain. *J Antimicrob Chemother* 2011;66:2011–21. doi:10.1093/jac/dkr235

158 Shin J, Kim DH, Ko KS. Comparison of CTX-M-14- and CTX-M-15-producing Escherichia coli and Klebsiella pneumoniae isolates from patients with bacteremia. *J Infect* 2011;63:39–47. doi:10.1016/j.jinf.2011.05.003

159 Croxall G, Hale J, Weston V, *et al.* Molecular epidemiology of extraintestinal pathogenic Escherichia coli isolates from a regional cohort of elderly patients highlights the prevalence of ST131 strains with increased antimicrobial resistance in both community and hospital care settings. *J Antimicrob Chemother* 2011;66:2501–8. doi:10.1093/jac/dkr349

160 Simner PJ, Hoban DJ, Lagacé-Wiens PRS, *et al.* Fluoroquinolone resistance in Escherichia coli isolated from patients attending Canadian hospitals is associated with the ST131 clone. *Diagn Microbiol Infect Dis* 2011;71:323–4. doi:10.1016/j.diagmicrobio.2011.07.016

161 Titelman E, Iversen A, Kahlmeter G, *et al.* Antimicrobial susceptibility to parenteral and oral agents in a largely polyclonal collection of CTX-M-14 and CTX-M-15-producing Escherichia coli and Klebsiella pneumoniae. *APMIS* 2011;119:853–63. doi:10.1111/j.1600-0463.2011.02766.x

162 Molina-López J, Aparicio-Ozores G, Ribas-Aparicio RM, *et al.* Drug resistance, serotypes, and phylogenetic groups among uropathogenic Escherichia coli including O25-ST131 in Mexico City. *J Infect Dev Ctries* 2011;5:840–9.http://www.ncbi.nlm.nih.gov/pubmed/22169782 (accessed 20 May2015).

163 Sidjabat HE, Derrington P, Nimmo GR, *et al.* Escherichia coli ST131 producing CTX-M-15 in Australia. *J Antimicrob Chemother* 2010;65:1301–3. doi:10.1093/jac/dkq098

164 Tian G-B, Garcia J, Adams-Haduch JM, *et al.* CTX-M as the predominant extended-spectrum beta-lactamases among Enterobacteriaceae in Manila, Philippines. *J Antimicrob Chemother* 2010;65:584–6. doi:10.1093/jac/dkp480

165 Platell JL, Cobbold RN, Johnson JR, *et al.* Clonal group distribution of fluoroquinolone-resistant Escherichia coli among humans and companion animals in Australia. *J Antimicrob Chemother* 2010;65:1936–8. doi:10.1093/jac/dkq236

166 Naseer U, Haldorsen B, Simonsen GS, *et al.* Sporadic occurrence of CMY-2-producing multidrug-resistant Escherichia coli of ST-complexes 38 and 448, and ST131 in Norway. *Clin Microbiol Infect* 2010;16:171–8. doi:10.1111/j.1469-0691.2009.02861.x

167 Johnson JR, Johnston B, Clabots C, *et al.* Escherichia coli sequence type ST131 as an emerging fluoroquinolone-resistant uropathogen among renal transplant recipients. *Antimicrob Agents Chemother* 2010;54:546–50. doi:10.1128/AAC.01089-09

168 Lee MY, Choi HJ, Choi JY, *et al.* Dissemination of ST131 and ST393 community-onset, ciprofloxacin-resistant Escherichia coli clones causing urinary tract infections in Korea. *J Infect* 2010;60:146–53. doi:10.1016/j.jinf.2009.11.004

169 Peirano G, Richardson D, Nigrin J, *et al.* High prevalence of ST131 isolates producing CTX-M-15 and CTX-M-14 among extended-spectrum-beta-lactamase-producing Escherichia coli isolates

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from Canada. *Antimicrob Agents Chemother* 2010;54:1327–30. doi:10.1128/AAC.01338-09

170 Severin JA, Mertaniasih NM, Kuntaman K, *et al.* Molecular characterization of extended-spectrum beta-lactamases in clinical Escherichia coli and Klebsiella pneumoniae isolates from Surabaya, Indonesia. *J Antimicrob Chemother* 2010;65:465–9. doi:10.1093/jac/dkp471

171 Cerquetti M, Giufrè M, García-Fernández A, *et al.* Ciprofloxacin-resistant, CTX-M-15-producing Escherichia coli ST131 clone in extraintestinal infections in Italy. *Clin Microbiol Infect* 2010;16:1555–8. doi:10.1111/j.1469-0691.2010.03162.x

172 Peirano G, Costello M, Pitout JDD. Molecular characteristics of extended-spectrum beta-lactamase-producing Escherichia coli from the Chicago area: high prevalence of ST131 producing CTX-M-15 in community hospitals. *Int J Antimicrob Agents* 2010;36:19–23. doi:10.1016/j.ijantimicag.2010.02.016

173 Smet A, Martel A, Persoons D, *et al.* Characterization of extended-spectrum beta-lactamases produced by Escherichia coli isolated from hospitalized and nonhospitalized patients: emergence of CTX-M-15-producing strains causing urinary tract infections. *Microb Drug Resist* 2010;16:129–34. doi:10.1089/mdr.2009.0132

174 Dahmen S, Bettaieb D, Mansour W, *et al.* Characterization and molecular epidemiology of extended-spectrum beta-lactamases in clinical isolates of Enterobacteriaceae in a Tunisian University Hospital. *Microb Drug Resist* 2010;16:163–70. doi:10.1089/mdr.2009.0108

175 Oteo J, Cercenado E, Cuevas O, *et al.* AmpC beta-lactamases in Escherichia coli: emergence of CMY-2-producing virulent phylogroup D isolates belonging mainly to STs 57, 115, 354, 393, and 420, and phylogroup B2 isolates belonging to the international clone O25b-ST131. *Diagn Microbiol Infect Dis* 2010;67:270–6. doi:10.1016/j.diagmicrobio.2010.02.008

176 Díaz MA, Hernández-Bello JR, Rodríguez-Baño J, *et al.* Diversity of Escherichia coli strains producing extended-spectrum β-lactamases in Spain: Second nationwide study. *J Clin Microbiol* 2010;48:2840–5. doi:10.1128/JCM.02147-09

177 Bert F, Johnson JR, Ouattara B, *et al.* Genetic diversity and virulence profiles of Escherichia coli isolates causing spontaneous bacterial peritonitis and bacteremia in patients with cirrhosis. *J Clin Microbiol* 2010;48:2709–14. doi:10.1128/JCM.00516-10

178 Johnson JR, Johnston B, Clabots C, *et al.* Escherichia coli sequence type ST131 as the major cause of serious multidrug-resistant E. coli infections in the United States. *Clin Infect Dis* 2010;51:286–94. doi:10.1086/653932

179 Vidal-Navarro L, Pfeiffer C, Bouziges N, *et al.* Faecal carriage of multidrug-resistant Gram-negative bacilli during a non-outbreak situation in a French university hospital. *J Antimicrob Chemother* 2010;65:2455–8. doi:10.1093/jac/dkq333

180 Brolund A, Hæggman S, Edquist PJ, *et al.* The DiversiLab system versus pulsed-field gel electrophoresis: characterisation of extended spectrum β-lactamase producing Escherichia coli and Klebsiella pneumoniae. *J Microbiol Methods* 2010;83:224–30. doi:10.1016/j.mimet.2010.09.004

181 Jouini A, Ben Slama K, Vinué L, *et al.* Detection of unrelated Escherichia coli strains harboring

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genes of CTX-M-15, OXA-1, and AAC(6')-Ib-cr enzymes in a Tunisian hospital and characterization of their integrons and virulence factors. *J Chemother* 2010;22:318–23. doi:10.1179/joc.2010.22.5.318

182 Pitout JDD, Campbell L, Church DL, *et al.* Molecular characteristics of travel-related extended-spectrum-beta-lactamase-producing Escherichia coli isolates from the Calgary Health Region. *Antimicrob Agents Chemother* 2009;53:2539–43. doi:10.1128/AAC.00061-09

183 Morris D, Boyle F, Buckley V, *et al.* CTX-M enzymes are the predominant extended-spectrum beta-lactamases produced by Enterobacteriaceae in Ireland. *J Antimicrob Chemother* 2009;64:864–6. doi:10.1093/jac/dkp297

184 Hrabák J, Empel J, Bergerová T, *et al.* International clones of Klebsiella pneumoniae and Escherichia coli with extended-spectrum β-lactamases in a Czech Hospital. *J Clin Microbiol* 2009;47:3353–7. doi:10.1128/JCM.00901-09

185 Suzuki S, Shibata N, Yamane K, *et al.* Change in the prevalence of extended-spectrum-beta-lactamase-producing Escherichia coli in Japan by clonal spread. *J Antimicrob Chemother* 2009;63:72–9. doi:10.1093/jac/dkn463

186 Literacka E, Bedenic B, Baraniak A, *et al.* blaCTX-M genes in escherichia coli strains from Croatian Hospitals are located in new (blaCTX-M-3a) and widely spread (blaCTX-M-3a and blaCTX-M-15) genetic structures. *Antimicrob Agents Chemother* 2009;53:1630–5. doi:10.1128/AAC.01431-08

187 Pitout JDD, Campbell L, Church DL, *et al.* Using a commercial DiversiLab semiautomated repetitive sequence-based PCR typing technique for identification of Escherichia coli clone ST131 producing CTX-M-15. *J Clin Microbiol* 2009;47:1212–5. doi:10.1128/JCM.02265-08

188 Arpin C, Quentin C, Grobost F, *et al.* Nationwide survey of extended-spectrum {beta}-lactamase-producing Enterobacteriaceae in the French community setting. *J Antimicrob Chemother* 2009;63:1205–14. doi:10.1093/jac/dkp108

189 Blanco M, Alonso MP, Nicolas-Chanoine M-H, *et al.* Molecular epidemiology of Escherichia coli producing extended-spectrum {beta}-lactamases in Lugo (Spain): dissemination of clone O25b:H4-ST131 producing CTX-M-15. *J Antimicrob Chemother* 2009;63:1135–41. doi:10.1093/jac/dkp122

190 Pitout JDD, Gregson DB, Campbell L, *et al.* Molecular characteristics of extended-spectrum-beta-lactamase-producing Escherichia coli isolates causing bacteremia in the Calgary Health Region from 2000 to 2007: emergence of clone ST131 as a cause of community-acquired infections. *Antimicrob Agents Chemother* 2009;53:2846–51. doi:10.1128/AAC.00247-09

191 Johnson JR, Menard M, Johnston B, *et al.* Epidemic clonal groups of Escherichia coli as a cause of antimicrobial-resistant urinary tract infections in Canada, 2002 to 2004. *Antimicrob Agents Chemother* 2009;53:2733–9. doi:10.1128/AAC.00297-09

192 Oteo J, Diestra K, Juan C, *et al.* Extended-spectrum beta-lactamase-producing Escherichia coli in Spain belong to a large variety of multilocus sequence typing types, including ST10 complex/A, ST23 complex/A and ST131/B2. *Int J Antimicrob Agents* 2009;34:173–6. doi:10.1016/j.ijantimicag.2009.03.006

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193 Clermont O, Dhanji H, Upton M, *et al.* Rapid detection of the O25b-ST131 clone of Escherichia coli encompassing the CTX-M-15-producing strains. *J Antimicrob Chemother* 2009;64:274–7. doi:10.1093/jac/dkp194

194 Naseer U, Haldorsen B, Tofteland S, *et al.* Molecular characterization of CTX-M-15-producing clinical isolates of Escherichia coli reveals the spread of multidrug-resistant ST131 (O25:H4) and ST964 (O102:H6) strains in Norway. *APMIS* 2009;117:526–36. doi:10.1111/j.1600-0463.2009.02465.x

195 Oteo J, Orden B, Bautista V, *et al.* CTX-M-15-producing urinary Escherichia coli O25b-ST131-phylogroup B2 has acquired resistance to fosfomycin. *J Antimicrob Chemother* 2009;64:712–7. doi:10.1093/jac/dkp288

196 Sidjabat HE, Paterson DL, Adams-Haduch JM, *et al.* Molecular epidemiology of CTX-M-producing Escherichia coli isolates at a tertiary medical center in western Pennsylvania. *Antimicrob Agents Chemother* 2009;53:4733–9. doi:10.1128/AAC.00533-09

197 Lau SH, Reddy S, Cheesbrough J, *et al.* Major uropathogenic Escherichia coli strain isolated in the northwest of England identified by multilocus sequence typing. *J Clin Microbiol* 2008;46:1076–80. doi:10.1128/JCM.02065-07

198 Yumuk Z, Afacan G, Nicolas-Chanoine M-H, *et al.* Turkey: a further country concerned by community-acquired Escherichia coli clone O25-ST131 producing CTX-M-15. *J Antimicrob Chemother* 2008;62:284–8. doi:10.1093/jac/dkn181

199 Cagnacci S, Gualco L, Debbia E, *et al.* European emergence of ciprofloxacin-resistant Escherichia coli clonal groups O25:H4-ST 131 and O15:K52:H1 causing community-acquired uncomplicated cystitis. *J Clin Microbiol* 2008;46:2605–12. doi:10.1128/JCM.00640-08

200 Jones GL, Warren RE, Skidmore SJ, *et al.* Prevalence and distribution of plasmid-mediated quinolone resistance genes in clinical isolates of Escherichia coli lacking extended-spectrum beta-lactamases. *J Antimicrob Chemother* 2008;62:1245–51. doi:10.1093/jac/dkn406

201 Fam NS, Defasque S, Bert F, *et al.* Faecal carriage of extended-spectrum β-lactamase (ESBL)-producing enterobacteria in liver disease patients from two hospitals in Egypt and France: a comparative epidemiological study. *Epidemiol Infect* 2015;143:1247–55. doi:10.1017/S0950268814001812

202 Liss MA, Johnson JR, Porter SB, Clinical and microbiological determinants of infection after transrectal prostate biopsy. *Clin Infect Dis* 2015;60:979–87. doi:10.1093/cid/ciu1129

203 Valverde A, Turrientes MC, Norman F, *et al.* CTX-M-15-non-ST131 Escherichia coli isolates are mainly responsible of faecal carriage with ESBL-producing Enterobacteriaceae in travellers, immigrants and those visiting friends and relatives. *Clin Microbiol Infect* 2015;21:252.e1-4. doi: 10.1016/j.cmi.2014.09.021.

204 Stewardson AJ, Renzi G, Maury N, *et al.* Extended-spectrum β-lactamase-producing Enterobacteriaceae in hospital food: a risk assessment. *Infect Control Hosp Epidemiol* 2014;35:375–83. doi:10.1086/675609

205 Yaita K, Aoki K, Suzuki T, *et al.* Epidemiology of extended-spectrum β-lactamase producing

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Escherichia coli in the stools of returning Japanese travelers, and the risk factors for colonization. *PLoS One* 2014;9:e98000. doi:10.1371/journal.pone.0098000

206 Lupindu AM, Olsen JE, Ngowi HA, *et al.* Occurrence and characterization of Shiga toxin-producing Escherichia coli O157:H7 and other non-sorbitol-fermenting E. coli in cattle and humans in urban areas of Morogoro, Tanzania. *Vector Borne Zoonotic Dis* 2014;14:503–10. doi:10.1089/vbz.2013.1502

207 Vervoort J, Gazin M, Kazma M, *et al.* High rates of intestinal colonisation with fluoroquinolone-resistant ESBL-harbouring Enterobacteriaceae in hospitalised patients with antibiotic-associated diarrhoea. *Eur J Clin Microbiol Infect Dis* 2014;33:2215–21. doi:10.1007/s10096-014-2193-9

208 Han JH, Johnston B, Nachamkin I, *et al.* Clinical and molecular epidemiology of Escherichia coli sequence type 131 among hospitalized patients colonized intestinally with fluoroquinolone-resistant E. coli. *Antimicrob Agents Chemother* 2014;58:7003–6. doi:10.1128/AAC.03256-14

209 Vasoo S, Madigan T, Cunningham SA, *et al.* Prevalence of rectal colonization with multidrug-resistant Enterobacteriaceae among international patients hospitalized at Mayo Clinic, Rochester, Minnesota. *Infect Control Hosp Epidemiol* 2014;35:182–6. doi:10.1086/674853

210 March A, Aschbacher R, Pagani E, *et al.* Changes in colonization of residents and staff of a long-term care facility and an adjacent acute-care hospital geriatric unit by multidrug-resistant bacteria over a four-year period. *Scand J Infect Dis* 2014;46:114–22. doi:10.3109/00365548.2013.859392

211 Nicolas-Chanoine M-H, Gruson C, Bialek-Davenet S, *et al.* 10-Fold increase (2006-11) in the rate of healthy subjects with extended-spectrum β-lactamase-producing Escherichia coli faecal carriage in a Parisian check-up centre. *J Antimicrob Chemother* 2013;68:562–8. doi:10.1093/jac/dks429

212 Izdebski R, Baraniak A, Fiett J, *et al.* Clonal structure, extended-spectrum β-lactamases, and acquired AmpC-type cephalosporinases of Escherichia coli populations colonizing patients in rehabilitation centers in four countries. *Antimicrob Agents Chemother* 2013;57:309–16. doi:10.1128/AAC.01656-12

213 Liss MA, Peterson EM, Johnston B, *et al.* Prevalence of ST131 among fluoroquinolone-resistant Escherichia coli obtained from rectal swabs before transrectal prostate biopsy. *Urology* 2013;81:548–55. doi:10.1016/j.urology.2012.10.056

214 Birgy A, Mariani-Kurkdjian P, Bidet P, *et al.* Characterization of extended-spectrum-beta-lactamase-producing Escherichia coli strains involved in maternal-fetal colonization: prevalence of E. coli ST131. *J Clin Microbiol* 2013;51:1727–32. doi:10.1128/JCM.03255-12

215 Nüesch-Inderbinen MT, Abgottspon H, Zurfluh K, *et al.* Cross-sectional study on fecal carriage of Enterobacteriaceae with resistance to extended-spectrum cephalosporins in primary care patients. *Microb Drug Resist* 2013;19:362–9. doi:10.1089/mdr.2013.0013

216 Arvand M, Moser V, Pfeifer Y. Prevalence of extended-spectrum-β-lactamase-producing Escherichia coli and spread of the epidemic clonal lineage ST131 in nursing homes in Hesse, Germany. *J Antimicrob Chemother* 2013;68:2686–8. doi:10.1093/jac/dkt226

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217 Roy S, Krishnan R, Mukherjee S, *et al.* Prevalence of ST131 virulence-associated strains among CTX-M-producing Escherichia coli in the gut of hospitalized neonates in India. *Diagn Microbiol Infect Dis* 2013;77:158–9. doi:10.1016/j.diagmicrobio.2013.06.014

218 Severin JA, Lestari ES, Kloezen W, *et al.* Faecal carriage of extended-spectrum β-lactamase-producing Enterobacteriaceae among humans in Java, Indonesia, in 2001-2002. *Trop Med Int Health* 2012;17:455–61. doi:10.1111/j.1365-3156.2011.02949.x

219 Dolejska M, Brhelova E, Dobiasova H, *et al.* Dissemination of IncFII(K)-type plasmids in multiresistant CTX-M-15-producing Enterobacteriaceae isolates from children in hospital paediatric oncology wards. *Int J Antimicrob Agents* 2012;40:510–5. doi:10.1016/j.ijantimicag.2012.07.016

220 Li B, Sun J-Y, Liu Q-Z, *et al.* High prevalence of CTX-M β-lactamases in faecal Escherichia coli strains from healthy humans in Fuzhou, China. *Scand J Infect Dis* 2011;43:170–4. doi:10.3109/00365548.2010.538856

221 Peirano G, Laupland KB, Gregson DB, *et al.* Colonization of returning travelers with CTX-M-producing Escherichia coli. *J Travel Med* 2011;18:299–303. doi:10.1111/j.1708-8305.2011.00548.x

222 Leflon-Guibout V, Blanco J, Amaqdouf K, *et al.* Absence of CTX-M enzymes but high prevalence of clones, including clone ST131, among fecal Escherichia coli isolates from healthy subjects living in the area of Paris, France. *J Clin Microbiol* 2008;46:3900–5. doi:10.1128/JCM.00734-08

223 Diago-Navarro E, Chen L, Passet V, *et al.* Carbapenem-resistant Klebsiella pneumoniae exhibit variability in capsular polysaccharide and capsule associated virulence traits. *J Infect Dis* 2014;210:803–13. doi:10.1093/infdis/jiu157

224 van Duin D, Perez F, Rudin SD, *et al.* Surveillance of carbapenem-resistant Klebsiella pneumoniae: tracking molecular epidemiology and outcomes through a regional network. *Antimicrob Agents Chemother* 2014;58:4035–41. doi:10.1128/AAC.02636-14

225 Mezzatesta ML, Caio C, Gona F, *et al.* Carbapenem and multidrug resistance in Gram-negative bacteria in a single centre in Italy: considerations on in vitro assay of active drugs. *Int J Antimicrob Agents* 2014;44:112–6. doi:10.1016/j.ijantimicag.2014.04.014

226 Ageevets VA, Partina I V, Lisitsyna ES, *et al.* Emergence of carbapenemase-producing Gram-negative bacteria in Saint Petersburg, Russia. *Int J Antimicrob Agents* 2014;44:152–5. doi:10.1016/j.ijantimicag.2014.05.004

227 Tijet N, Sheth PM, Lastovetska O, *et al.* Molecular characterization of Klebsiella pneumoniae carbapenemase (KPC)-producing Enterobacteriaceae in Ontario, Canada, 2008-2011. *PLoS One* 2014;9:e116421. doi:10.1371/journal.pone.0116421

228 Hrabák J, Papagiannitsis CC, Študentová V, *et al.* Carbapenemase-producing Klebsiella pneumoniae in the Czech Republic in 2011. *Euro Surveill* 2013;18:20626.http://www.ncbi.nlm.nih.gov/pubmed/24229789 (accessed 20 May2015).

229 Lascols C, Peirano G, Hackel M, *et al.* Surveillance and molecular epidemiology of Klebsiella pneumoniae isolates that produce carbapenemases: first report of OXA-48-like enzymes in North

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America. *Antimicrob Agents Chemother* 2013;57:130–6. doi:10.1128/AAC.01686-12

230 Castanheira M, Farrell SE, Wanger A, *et al.* Rapid expansion of KPC-2-producing Klebsiella pneumoniae isolates in two Texas hospitals due to clonal spread of ST258 and ST307 lineages. *Microb Drug Resist* 2013;19:295–7. doi:10.1089/mdr.2012.0238

231 Rodríguez-Zulueta P, Silva-Sánchez J, Barrios H, *et al.* First outbreak of KPC-3-producing Klebsiella pneumoniae (ST258) clinical isolates in a Mexican Medical Center. *Antimicrob Agents Chemother* 2013;57:4086–8. doi:10.1128/AAC.02530-12

232 Di Carlo P, Gulotta G, Casuccio A, *et al.* KPC - 3 Klebsiella pneumoniae ST258 clone infection in postoperative abdominal surgery patients in an intensive care setting: analysis of a case series of 30 patients. *BMC Anesthesiol* 2013;13:13. doi:10.1186/1471-2253-13-13

233 Jain R, Walk ST, Aronoff DM, *et al.* Emergence of Carbapenemaseproducing Klebsiella Pneumoniae of Sequence type 258 in Michigan, USA. *Infect Dis Rep* 2013;5:e5. doi:10.4081/idr.2013.e5

234 Cejas D, Fernandez Canigia L, Nastro M, *et al.* Hyperendemic clone of KPC producing Klebsiellapneumoniae ST 258 in Buenos Aires hospitals. *Infect Genet Evol* 2012;12:499–501. doi:10.1016/j.meegid.2011.09.018

235 Warburg G, Hidalgo-Grass C, Partridge SR, *et al.* A carbapenem-resistant Klebsiella pneumoniae epidemic clone in Jerusalem: sequence type 512 carrying a plasmid encoding aac(6')-Ib. *J Antimicrob Chemother* 2012;67:898–901. doi:10.1093/jac/dkr552

236 Richter SN, Frasson I, Franchin E, *et al.* KPC-mediated resistance in Klebsiella pneumoniae in two hospitals in Padua, Italy, June 2009-December 2011: massive spreading of a KPC-3-encoding plasmid and involvement of non-intensive care units. *Gut Pathog* 2012;4:7. doi:10.1186/1757-4749-4-7

237 Adler A, Paikin S, Sterlin Y, *et al.* A swordless knight: epidemiology and molecular characteristics of the blaKPC-negative sequence type 258 Klebsiella pneumoniae clone. *J Clin Microbiol* 2012;50:3180–5. doi:10.1128/JCM.00987-12

238 Mammina C, Bonura C, Di Bernardo F, *et al.* Ongoing spread of colistin-resistant Klebsiella pneumoniae in different wards of an acute general hospital, Italy, June to December 2011. *Euro Surveill* 2012;17.http://www.ncbi.nlm.nih.gov/pubmed/22913977 (accessed 20 May2015).

239 Mataseje LF, Boyd DA, Willey BM, *et al.* Plasmid comparison and molecular analysis of Klebsiella pneumoniae harbouring bla(KPC) from New York City and Toronto. *J Antimicrob Chemother* 2011;66:1273–7. doi:10.1093/jac/dkr092

240 Giakkoupi P, Papagiannitsis CC, Miriagou V, *et al.* An update of the evolving epidemic of blaKPC-2-carrying Klebsiella pneumoniae in Greece (2009-10). *J Antimicrob Chemother* 2011;66:1510–3. doi:10.1093/jac/dkr166

241 Andrade LN, Curiao T, Ferreira JC, *et al.* Dissemination of blaKPC-2 by the spread of Klebsiella pneumoniae clonal complex 258 clones (ST258, ST11, ST437) and plasmids (IncFII, IncN, IncL/M) among Enterobacteriaceae species in Brazil. *Antimicrob Agents Chemother* 2011;55:3579–83. doi:10.1128/AAC.01783-10

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242 Gomez SA, Pasteran FG, Faccone D, *et al.* Clonal dissemination of Klebsiella pneumoniae ST258 harbouring KPC-2 in Argentina. *Clin Microbiol Infect* 2011;17:1520–4. doi:10.1111/j.1469-0691.2011.03600.x

243 Baraniak A, Grabowska A, Izdebski R, *et al.* Molecular characteristics of KPC-producing Enterobacteriaceae at the early stage of their dissemination in Poland, 2008-2009. *Antimicrob Agents Chemother* 2011;55:5493–9. doi:10.1128/AAC.05118-11

244 Cuzon G, Naas T, Truong H, *et al.* Worldwide diversity of Klebsiella pneumoniae that produce beta-lactamase blaKPC-2 gene. *Emerg Infect Dis* 2010;16:1349–56. doi:10.3201/eid1609.091389

245 Endimiani A, Depasquale JM, Forero S, *et al.* Emergence of blaKPC-containing Klebsiella pneumoniae in a long-term acute care hospital: a new challenge to our healthcare system. *J Antimicrob Chemother* 2009;64:1102–10. doi:10.1093/jac/dkp327

246 Paterson GK, Harrison EM, Murray GGR, *et al.* Capturing the cloud of diversity reveals complexity and heterogeneity of MRSA carriage, infection and transmission. *Nat Commun* 2015;6:6560. doi:10.1038/ncomms7560

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Figure legends

Figure 1: Simple model

Figure 2: Flowchart of article selection

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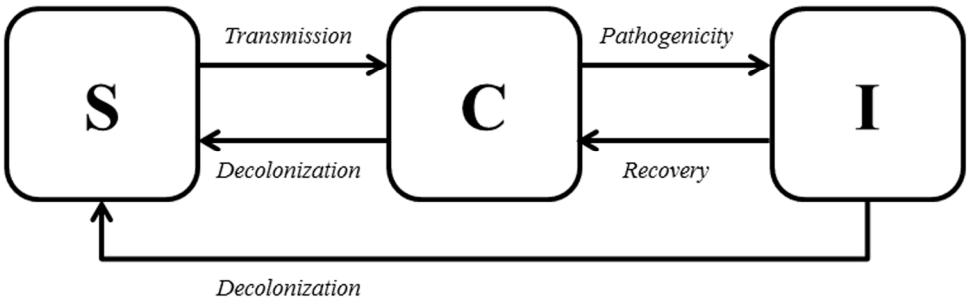

Figure 1: Simple model
209x67mm (300 x 300 DPI)

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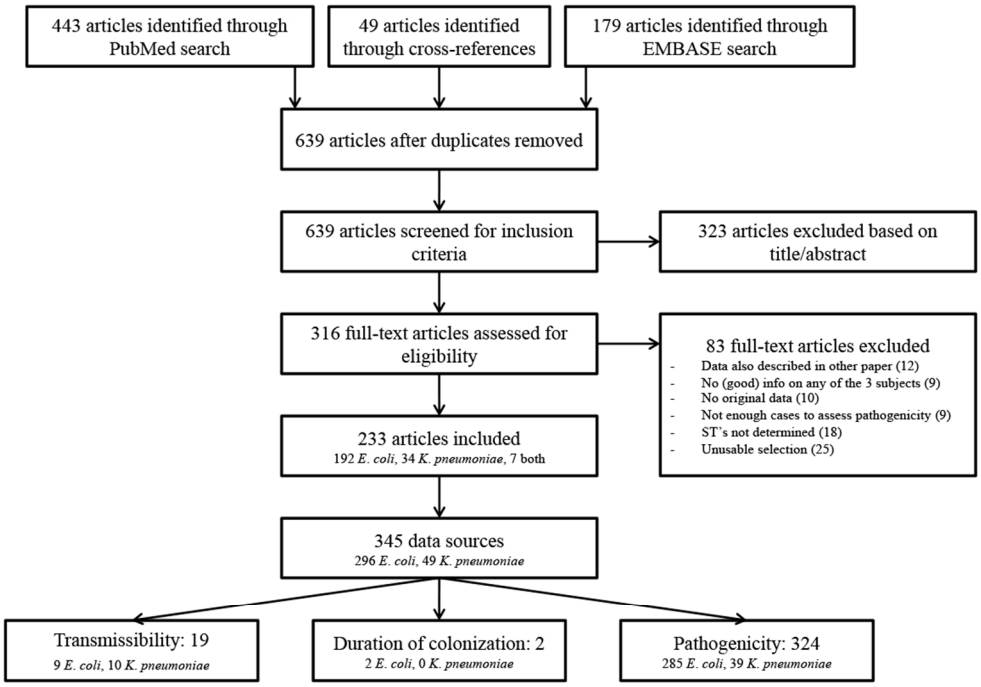

Figure 2: Flowchart of article selection
99x75mm (300 x 300 DPI)

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Supplementary Material

Supplementary Text 1. Search string.

((k. pneumoniae[All Fields] AND (st258[All Fields] OR st 258[All Fields] OR ((("sequence"[All Fields] AND type[All Fields]) OR sequence type[All Fields]) AND 258[All Fields]))) OR (e. coli[All Fields] AND (st131[All Fields] OR st 131[All Fields] OR ((("sequence"[All Fields] AND type[All Fields]) OR sequence type[All Fields]) AND 131[All Fields]))))

AND

(

("transmission"[Subheading] OR transmissi*[All Fields] OR transmit*[All Fields] OR spread*[All Fields] OR disease outbreaks[All Fields] OR (disease[All Fields] AND outbreaks[All Fields]) OR outbreak*[All Fields] OR "gene transfer, horizontal"[MeSH Terms] OR (gene[All Fields] AND ("transfer"[All Fields] OR "transfers"[All Fields]) AND horizontal[All Fields]) OR horizontal gene transfer*[All Fields] OR conjugation*[All Fields] OR (("plasmids"[MeSH Terms] OR plasmid*[All Fields]) AND ("transfer"[All Fields] OR "transfers"[All Fields])))

OR

(((colonis*[All Fields] OR coloniz*[All Fields]) AND (duration*[All Fields] OR ("period"[All Fields] OR "periods"[All Fields]) OR times[All Fields])) OR (infectious[All Fields] AND ("period"[All Fields] OR "periods"[All Fields] OR times[All Fields] OR interval[All Fields] OR intervals[All Fields])) OR ("generation"[All Fields] AND (times[All Fields] OR interval[All Fields] OR intervals[All Fields])))

OR

("pathogenicity"[Subheading] OR pathogenic*[All Fields] OR virulen*[All Fields] OR "virulence"[MeSH Terms] OR infectiv*[All Fields] OR infectious[All Fields] OR infectious*[All Fields])

)

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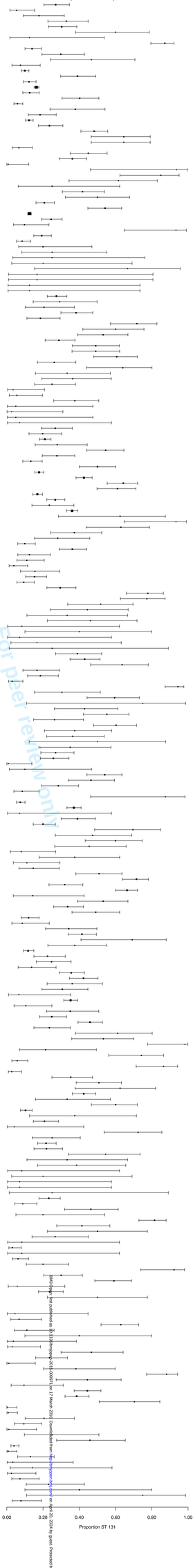
Supplementary Figure 1: Forest plot showing proportion ST131 in *E. coli*

Author (pub. year)	ST131 (n)	Total (n)	ST131 (%)
Infection			
Papagiannitsis, 2015 [34]	24	38	63.2
Osawa, 2015 [35]	28	72	38.9
Hristea, 2015 [36]	22	165	81.6
Sallpante, 2015 [37]	50	312	16
Can, 2015 [38]	35	294	11.9
Zhao, 2015 [39]	44	302	14.6
Hansen, 2014 [40]	34	68	50
Berman, 2014 [41]	1	36	2.8
Peirano, 2014 (2008–2010) [42]	161	319	50.5
Peirano, 2014 (2000–2007) [42]	151	358	42.2
Shakir, 2014 [43]	7	24	29.2
Peirano, 2014 [44]	0	4	0
Sana, 2014 [45]	32	68	47.1
Oennberg, 2014 [46]	41	152	27
Oteo, 2014 (Other) [47]	3	56	5.4
Oteo, 2014 (ESBL) [47]	8	45	17.8
Oteo, 2014 (CRE) [47]	22	67	32.8
Rodriguez, 2014 [48]	40	132	30.3
O'Hara, 2014 [49]	12	20	60
Inweszmus, 2014 [50]	1	8	12.5
Micenkova, 2014 [51]	95	109	87.2
Xia, 2014 [52]	32	229	14
Morgand, 2014 [53]	17	57	29.8
Suwantarat, 2014 [54]	7	15	46.7
Maluta, 2014 [55]	4	53	7.5
Dashti, 2014 [56]	83	832	10
Freeman, 2014 [57]	37	95	38.9
Hussain, 2014 (Inpatients) [58]	43	350	12.3
Dahlo, 2014 [59]	490	2995	16.4
Zhang, 2014 [60]	27	213	12.7
Usein, 2014 [61]	35	87	40.2
Wu, 2014 [62]	22	371	5.9
Guillard, 2014 [63]	14	37	37.8
Habeeb, 2014 [64]	18	98	18.4
Lopez–Cerero, 2014 (other) [65]	114	928	12.3
Lopez–Cerero, 2014 (ESBL) [65]	35	149	23.5
Giufre, 2014 [66]	83	172	48.3
Ferjani, 2014 [67]	20	31	64.5
Al–Agamy, 2014 [68]	20	31	64.5
Rogers, 2014 (other) [69]	6	90	6.7
Rogers, 2014 (ESBL) [69]	40	89	44.9
Nicolas–Chanoine, 2013 [70]	55	152	36.2
Nordberg, 2013 [71]	0	58	0
Dimude, 2013 [72]	7	7	100
Karfunkel, 2013 (2009) [73]	17	20	85
Karfunkel, 2013 (2007) [73]	8	13	61.5
Karfunkel, 2013 (2003) [73]	2	8	25
Nielsen, 2013 [74]	28	67	41.8
van der Donk, 2013 [75]	14	28	50
Adams–Sapper, 2013 [76]	51	246	20.7
Doi, 2013 [77]	58	107	54.2
Lopez–Cerero, 2013 [78]	540	4308	12.5
Helldal, 2013 (2008) [79]	54	221	24.4
Helldal, 2013 (2004) [79]	4	41	9.8
Hammami, 2013 [80]	14	15	93.3
Kudinha, 2013 [81]	49	254	19.3
Kudinha, 2013 (Inpatients) [82]	18	212	8.5
Weissman, 2013 (2007) [83]	3	15	20
Weissman, 2013 (2006) [83]	3	12	25
Weissman, 2013 (2005) [83]	1	4	25
Weissman, 2013 (2004) [83]	1	5	20
Weissman, 2013 (2003) [83]	2	3	66.7
Weissman, 2013 (2002) [83]	0	2	0
Weissman, 2013 (2001) [83]	0	2	0
Weissman, 2013 (2000) [83]	0	3	0
Weissman, 2013 (1999) [83]	0	3	0
Banerjee, 2013 [84]	71	259	27.4
Kim, 2013 [85]	7	24	29.2
Aolke, 2013 [86]	7	34	20.6
Olesen, 2013 [87]	44	115	38.3
Qin, 2013 (Inpatients) [88]	13	70	18.6
Denisuik, 2013 (ESBL 2011) [89]	33	46	71.7
Denisuik, 2013 (ESBL 2010) [89]	18	30	60
Denisuik, 2013 (ESBL 2009) [89]	25	47	53.2
Denisuik, 2013 (Other 2007–2011) [89]	33	115	28.7
Denisuik, 2013 (ESBL 2008) [89]	27	55	49.1
Denisuik, 2013 (ESBL 2007) [89]	26	53	49.1
Yano, 2013 [90]	37	61	60.7
Chmielarczyck, 2013 (other) [91]	17	65	26.2
Chmielarczyck, 2013 (ESBL) [91]	16	25	64
Seiffert, 2013 (Outpatients/community) [92]	6	18	33.3
Seiffert, 2013 (Inpatients) [92]	8	22	36.4
Reyna–Flores, 2013 [93]	14	56	25
Mnif, 2013 (2009) [94]	1	29	3.4
Mnif, 2013 (2006) [94]	2	36	5.6
Mnif, 2013 (2003–2004) [94]	21	56	37.5
Mnif, 2013 (2002) [94]	0	9	0
Mnif, 2013 (2001) [94]	0	18	0
Mnif, 2013 (period 2000) [94]	0	9	0
Mnif, 2013 (1989–1990) [94]	0	6	0
Williamson, 2013 [95]	27	101	26.7
Kang, 2013 [96]	15	76	19.7
Kudinha, 2013 (Mixed) [97]	131	623	21
Hu, 2013 (Inpatients) [98]	10	36	27.8
van der Donk, 2013 (Outpatients/community) [99]	48	88	54.5
van der Donk, 2013 (Inpatients) [99]	26	94	27.7
Banerjee, 2013 (other) [100]	21	158	13.3
Banerjee, 2013 (ESBL) [100]	47	94	50
Blanco, 2013 [101]	166	931	17.8
Colpan, 2013 (other) [102]	201	472	42.6
Colpan, 2013 (ESBL) [102]	79	123	64.2
Dahbi, 2013 [103]	47	77	61
Horner, 2013 [104]	130	770	16.9
Banerjee, 2013 [105]	80	299	26.8
Ha, 2013 [106]	12	51	23.5
Brolund, 2013 [107]	329	913	36
Aschbacher, 2013 [108]	5	8	62.5
Calhau, 2013 [109]	14	15	93.3
Markovska, 2013 [110]	17	27	63
Ma, 2013 (2012) [111]	16	43	37.2
Ma, 2013 (2010) [111]	9	32	28.1
Brisse, 2012 (Other) [112]	15	152	9.9
Brisse, 2012 (ESBL) [112]	55	152	36.2
Weissman, 2012 [113]	7	56	12.5
Musumeci, 2012 (2006) [114]	8	72	11.1
Musumeci, 2012 (2004) [114]	3	76	3.9
Oteo, 2012 [115]	7	45	15.6
Gibreel, 2012 (2009) [116]	23	150	15.3
Gibreel, 2012 (2007) [116]	14	150	9.3
Chung, 2012 [117]	36	122	29.5
Peirano, 2012 (2010) [118]	49	63	77.8
Peirano, 2012 (2009) [118]	34	44	77.3
Peirano, 2012 (2008) [118]	14	27	51.9
Peirano, 2012 (2007) [118]	8	18	44.4
Peirano, 2012 (2006) [118]	3	9	33.3
Peirano, 2012 (2005) [118]	6	13	46.2
Peirano, 2012 (2004) [118]	0	5	0
Peirano, 2012 (2003) [118]	2	5	40
Peirano, 2012 (2002) [118]	0	6	0
Peirano, 2012 (2001) [118]	1	6	16.7
Peirano, 2012 (2000) [118]	0	1	0
Tiruvury, 2012 [119]	21	54	38.9
Giufre, 2012 [120]	58	135	43
Novais, 2012 [121]	21	33	63.6
Matsumura, 2012 (other) [122]	9	54	16.7
Matsumura, 2012 (ESBL) [122]	15	81	18.5
Yokota, 2012 (MLST) [123]	3	100	3
Yokota, 2012 (Extrapolation PFGE) [123]	85	90	94.4
Johnson, 2012 (2009) [124]	7	23	30.4
Johnson, 2012 (2008–2009) [124]	25	42	59.5
Johnson, 2012 (2008) [124]	1	100	1
Johnson, 2012 (2007–2008) [124]	12	28	42.9
Johnson, 2012 (2007) [124]	32	58	55.2
Johnson, 2012 (2004–2009) [124]	10	38	26.3
Johnson, 2012 (2004–2008) [124]	38	63	60.3
Johnson, 2012 (2004–2007 children) [124]	9	24	37.5
Johnson, 2012 (2002–2009 children) [124]	12	33	36.4
Johnson, 2012 (2005) [124]	2	4	50
Johnson, 2012 (2000–2006) [124]	7	20	35
Williamson, 2012 [125]	24	89	27
Ho, 2012 (2007–2008) [126]	30	117	25.6
Ho, 2012 (1996–1998) [126]	0	50	0
Dmou, 2012 [127]	1	10	10
Burke, 2012 [128]	54	100	54
Park, 2012 (Outpatients/community) [129]	26	56	46.4
Park, 2012 (Inpatients) [129]	21	74	28.4
Reuland, 2012 [130]	6	70	8.6
Kuroda, 2012 [131]	7	8	87.5
Gibreel, 2012 [132]	37	500	7.4
Matsumura, 2012 [133]	215	581	37
Osterlund, 2012 [134]	0	6	0
Naseer, 2012 [135]	39	100	39
Golding, 2012 [136]	33	165	20
Hussain, 2012 [137]	16	23	69.6
van der Donk, 2012 [138]	9	19	47.4
Mavroidi, 2012 [139]	21	35	60
Peirano, 2011 [141]	10	22	45.5
Peirano, 2011 [140]	2	25	8
Overdevest, 2011 [142]	6	16	37.5
Leverstein–van Hall, 2011 [143]	3	27	11.1
Courpon–Claudinon, 2011 [144]	6	41	14.6
Rodriguez–Villalobos, 2011 [145]	29	57	50.9
Mora, 2011 [146]	108	151	71.5
Coelho, 2011 [147]	30	94	31.9
Xu, 2011 [148]	154	232	66.4
Ruiz, 2011 [149]	2	14	14.3
Simner, 2011 (2009) [150]	25	47	53.2
Simner, 2011 (2008) [150]	42	125	33.6
Simner, 2011 (2007) [150]	26	53	49.1
Dhanji, 2011 [151]	21	174	12.1
Kim, 2011 [152]	3	35	8.6
van de Bij, 2011 [153]	14	41	34.1
Titelman, 2011 [154]	63	152	41.4
Cao, 2011 [155]	9	13	69.2
Mshana, 2011 [156]	12	32	37.5
Blanco, 2011 [157]	59	500	11.8
Shin, 2011 [158]	20	89	22.5
Crowall, 2011 (Outpatients/community) [159]	19	77	24.7
Crowall, 2011 (Inpatients) [159]	6	44	13.6
Simner, 2011 [160]	64	180	35.6
Titelman, 2011 [161]	63	149	42.3
Molina–Lopez, 2011 [162]	13	36	36.1
Sidjabat, 2010 [163]	15	49	30.6
Tian, 2010 [164]	1	15	6.7
Platek, 2010 [165]	205	582	35.2
Naseer, 2010 [166]	4	38	10.5
Johnson, 2010 [167]	14	40	35
Lee, 2010 [168]	32	129	24.8
Peirano, 2010 [169]	96	209	45.9
Severin, 2010 [170]	16	68	23.5
Cerquetti, 2010 [171]	11	18	61.1
Peirano, 2010 [172]	16	30	53.3
Smet, 2010 (Outpatients/community) [173]	28	28	100
Smet, 2010 (Inpatients) [173]	3	14	21.4
Dahmen, 2010 [174]	23	31	74.2
Oteo, 2010 [175]	7	121	5.8
Diaz, 2010 [176]	32	37	86.5
Bert, 2010 [177]	3	110	2.7
Johnson, 2010 (Other) [178]	24	68	35.3
Johnson, 2010 (ESBL) [178]	30	59	50.8
Vidal–Navarro, 2010 [179]	10	16	62.5
Brolund, 2010 [180]	96	226	42.5
Jouini, 2010 [181]	6	18	33.3
Pitout, 2009 [182]	33	55	60
Morris, 2009 [183]	36	348	10.3
Hrabak, 2009 [184]	3	8	37.5
Suzuki, 2009 [185]	27	130	20.8
Literacka, 2009 [186]	0	11	0
Pitout, 2009 [187]	21	29	72.4
Arpin, 2009 [188]	10	40	25
Blanco, 2009 (2007) [189]	54	249	21.7
Blanco, 2009 (2006) [189]	23	105	21.9
Pitout, 2009 (2007) [190]	12	22	54.5
Pitout, 2009 (2006) [190]	3	9	33.3
Pitout, 2009 (2005) [190]	5	13	38.5
Pitout, 2009 (2004) [190]	0	5	0
Pitout, 2009 (2003) [190]	1	5	20
Pitout, 2009 (2002) [190]	0	6	0
Pitout, 2009 (2001) [190]	0	6	0
Pitout, 2009 (2000) [190]	0	1	0
Johnson, 2009 [191]	46	199	23.1
Oteo, 2009 [192]	8	91	8.8
Clermont, 2009 (Europe 2006–2007) [193]	19	41	46.3
Clermont, 2009 (Europe 2006) [193]	2	10	20
Clermont, 2009 (Europe 2004–2007) [193]	84	103	81.6
Clermont, 2009 (N–America 2004–2006) [193]	17	41	41.5
Clermont, 2009 (Africa 2004–2006) [193]	5	10	50
Clermont, 2009 (Asia 2004–2005) [193]	8	30	26.7
Clermont, 2009 (S–America 2001–2005) [193]	0	5	0
Clermont, 2009 (Europe 2002 – 2003) [193]	4	129	3.1
Clermont, 2009 (Asia 1999) [193]	0	5	0
Clermont, 2009 (Europe 1994–2003) [193]	8	128	6.3
Naseer, 2009 [194]	9	45	20
Oteo, 2009 [195]	24	26	92.3
Sidjabat, 2009 [196]	21	70	30
Lau, 2008 [197]	52	88	59.1
Yumuk, 2008 [198]	1	17	5.9
Cagnacci, 2008 [199]	35	148	23.6
Jones, 2008 [200]	5	10	50
Colonization			
Fam, 2015 (Europe) [201]	0	10	0
Fam, 2015 (Africa) [201]	3	44	6.8
Liss, 2015 [202]	51	81	63
Valverde, 2015 [203]	4	36	11.1
Stewardson, 2014 [204]	2	5	40
Yaita, 2014 [205]	0	13	0
Lazniu, 2014 [206]	1	33	3
Vervoort, 2014 [207]	14	30	46.7
Han, 2014 [208]	21	89	23.6
Hussain, 2014 (Outpatients/community) [58]	0	43	0
Vasoo, 2014 [209]	8	21	38.1
March, 2014 [210]	52	59	88.1
Blanc, 2014 [15]	12	27	44.4
Nicolas–Chanoine, 2013 [212]	2	21	9.5
Izdebski, 2013 (Europe) [213]	76	171	44.4
Izdebski, 2013 (Asia) [213]	79	205	38.5
Liss, 2013 [214]	19	27	70.4
Kudinha, 2013 [81]	0	135	0
Kudinha, 2013 (Outpatients/community) [82]	1	115	0.9
Banerjee, 2013 [84]	7	34	20.6
Birgy, 2013 [214]	6	64	9.4
Qin, 2013 (Outpatients/community) [88]	0	41	0
Nuesch–Inderbinen, 2013 [215]	4	16	25
Arvand, 2013 [216]	11	24	45.8
Kudinha, 2013 (Outpatients/community) [97]	13	330	3.9
Roy, 2013 [217]	1	123	0.8
Hu, 2013 (Outpatients/community) [98]	6	46	13
Severin, 2012 [218]	0	14	0
Dolejska, 2012 [219]	1	7	14.3
Overdevest, 2011 [142]	1	39	2.6
Li, 2011 [220]	4	55	7.3
Peirano, 2011 (Travelers) [221]	6	26	23.1
Peirano, 2011 (Outpatients/community) [221]	2	5	40
Hrabak, 2009 [184]	1	1	100
Lefon–Guibout, 2008 [222]	4	51	7.8



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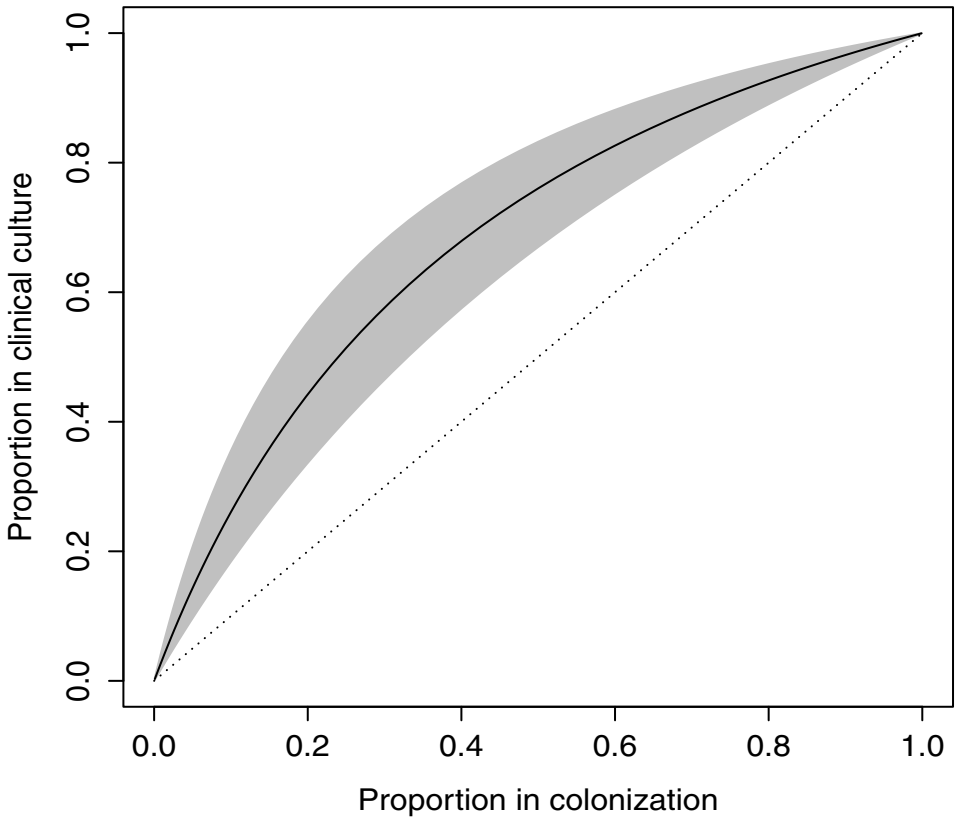
Supplementary Figure 2: Differences in proportion ST131 in colonization versus infection as given by the metaregression model.



The confidence interval should be interpreted as the confidence interval for the mean effect and not the individual effect. If one would average the proportions *E. coli* ST131 found in 100 studies, the mean should fall within the limits of the confidence interval of this graph 95% of the times.

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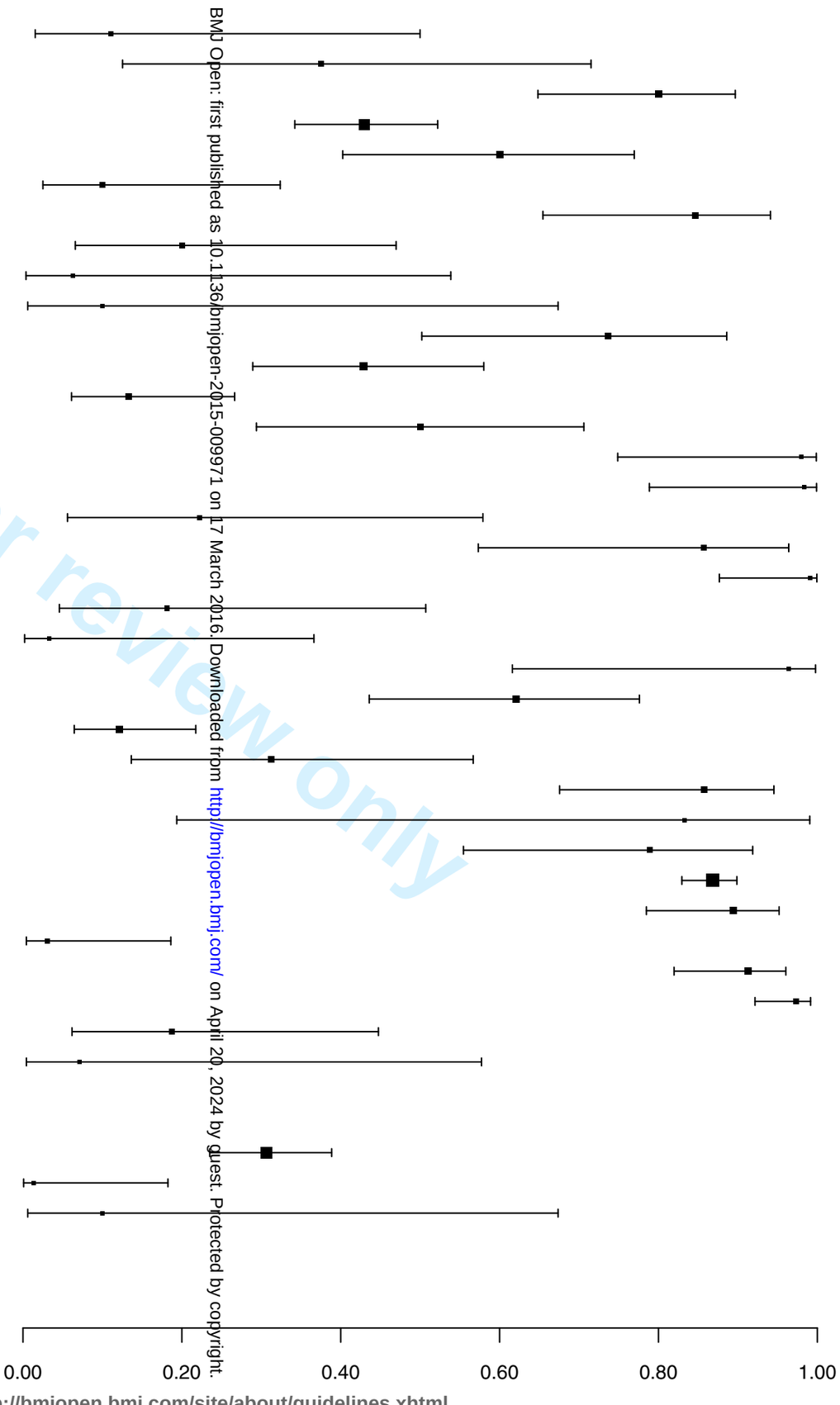
Supplementary Figure 3: Forest plot showing proportion ST258 in *K. pneumoniae*

Author (pub. year)	*ST258 (n)*	*Total (n)*	*ST258 (%)*
Infection			
Peirano, 2014 [44]	1	9	11.1
Diago–Navarro, 2014 (Other) [223]	3	8	37.5
Diago–Navarro, 2014 (CRE) [223]	32	40	80
van Duin, 2014 [224]	49	114	43
Mezzatesta, 2014 [225]	15	25	60
Ageevets, 2014 [226]	2	20	10
Tijet, 2014 [227]	22	26	84.6
Hrabak, 2014 [228]	3	15	20
Nordberg, 2013 [71]	0	7	0
Lascols, 2013 (S–America) [229]	0	4	0
Lascols, 2013 (N–America) [229]	14	19	73.7
Lascols, 2013 (Europe) [229]	18	42	42.9
Lascols, 2013 (Asia/Australia) [229]	6	45	13.3
Castanheira, 2013 [230]	10	20	50
Rodriguez–Zulueta, 2013 [231]	24	24	100
Di Carlo, 2013 [232]	30	30	100
Aschbacher, 2013 [108]	2	9	22.2
Jain, 2013 [230]	12	14	85.7
Cejas, 2012 [234]	57	57	100
Warburg, 2012 [235]	2	11	18.2
Dimou, 2012 [127]	0	14	0
Morris, 2012 [27]	13	13	100
Richter, 2012 [236]	18	29	62.1
Adler, 2012 [237]	9	74	12.2
Osterblad, 2012 [134]	5	16	31.3
Mammina, 2012 [238]	24	28	85.7
Mataseje, 2011 (MLST) [239]	2	2	100
Mataseje, 2011 (Extrapolation PFGE) [239]	15	19	78.9
Giakkoupi, 2011 [240]	322	371	86.8
Andrade, 2011 [241]	51	57	89.5
Shin, 2011 [158]	1	33	3
Gomez, 2011 [242]	63	69	91.3
Baraniak, 2011 [243]	111	114	97.4
Cuzon, 2010 [244]	3	16	18.8
Hrabak, 2009 [184]	0	6	0
Colonization			
van Duin, 2014 [224]	42	137	30.7
Dolejska, 2012 [219]	0	36	0
Hrabak, 2009 [184]	0	4	0



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MOOSE Checklist for Meta-analyses of Observational Studies

Item No	Recommendation	Reported on Page No
Reporting of background should include		
1	Problem definition	3-4
2	Hypothesis statement	4
3	Description of study outcome(s)	4
4	Type of exposure or intervention used	-
5	Type of study designs used	-
6	Study population	N/A
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	4
8	Search strategy, including time period included in the synthesis and key words	4 + Supplementary Text 1
9	Effort to include all available studies, including contact with authors	4
10	Databases and registries searched	4
11	Search software used, name and version, including special features used (eg, explosion)	N/A
12	Use of hand searching (eg, reference lists of obtained articles)	4
13	List of citations located and those excluded, including justification	-
14	Method of addressing articles published in languages other than English	4
15	Method of handling abstracts and unpublished studies	4
16	Description of any contact with authors	4
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	5
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	-
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	5
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	N/A
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	5
22	Assessment of heterogeneity	6
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	6-7
24	Provision of appropriate tables and graphics	7
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	10 + Supplementary Figure 1 and 2
26	Table giving descriptive information for each study included	7-8 (Table 1)
27	Results of sensitivity testing (eg, subgroup analysis)	-
28	Indication of statistical uncertainty of findings	10-14

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Item No	Recommendation	Reported on Page No
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	16
30	Justification for exclusion (eg, exclusion of non-English language citations)	-
31	Assessment of quality of included studies	16
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	16
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	N/A
34	Guidelines for future research	16
35	Disclosure of funding source	17

From: Stroup DF, Berlin JA, Morton SC, et al, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. *JAMA*. 2000;283(15):2008-2012. doi: 10.1001/jama.283.15.2008.

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