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Risk Factors Associated with Community-Acquired Urinary Tract Infections Caused by Extended-Spectrum β-Lactamase-Producing *Escherichia coli*: a Systematic Review

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Abstract

Purpose of Review This review aims to characterize the current body of knowledge regarding risk factors for community-acquired urinary tract infection (CA-UTI) caused by extended-spectrum β-lactamase-producing (ESBL) uropathogenic *Escherichia coli* (UPEC). Our purpose is to identify major knowledge gaps, suggest potential areas for improved public health intervention, and propose future research directions.

Recent Findings This review contains two parts. Part one reviews 15 studies that included 2,930 ESBL-producing UPEC infections in 10 countries. Of the 103 risk factors for these infections examined, only two of eight commonly-assessed factors demonstrated concordant significant results across studies. Part two focuses on 19 studies that examined 2,042 ESBL-producing extraintestinal pathogenic *E. coli (*ExPEC) strains isolated from environmental, food, or animal sources and discovered evidence for occurrence of all six pandemic ExPEC lineages associated with CA-UTI in these sources.

Summary This review has demonstrated inconsistent evidence regarding patient level risk factors associated with CA-UTI caused by ESBL-producing UPEC. However, reviewed studies reveal exposures to food, animal, or environmental sources to be potential risk factors for infection with common ESBL-producing *E. coli*.

Keywords Antimicrobial resistance · Extended-spectrum β-lactamase · Risk factors · Urinary tract infection · Community-acquired urinary tract infection · Multilocus sequence typing

Introduction

Community-acquired urinary tract infections (CA-UTI) are the most prevalent bacterial infection in women and are, overall, a common reason for the prescription of oral antibiotics [1]. It is estimated that approximately 150 million people worldwide develop urinary tract infections every year. Of the many pathogens known to cause these infections, the most common is uropathogenic *Escherichia coli* (UPEC) [2].

Antimicrobial resistance is a growing public health concern in the clinical management of CA-UTI caused by UPEC. Multidrug-resistant *E. coli* are of increasing concern due to their associated high rates of treatment failure and large economic burden [1]. CA-UTI is treated empirically, and in the USA, the Infectious Disease Society of America (IDSA) recommends the use of nitrofurantoin, trimethoprim/sulfamethoxazole (TMP-SXZ), or fosfomycin for the treatment of acute uncomplicated cystitis/UTI [3]. While most UPEC strains in the USA remain susceptible to nitrofurantoin, this drug is recommended only for acute uncomplicated cystitis and cannot be used for more severe infections such as pyelonephritis. The increasing frequency of resistance of UPEC to TMP-SXZ and fluoroquinolones, as well as earlier-generation beta-lactam drugs (ampicillin, cephalexin) have led to greater use of broader spectrum beta-lactam antimicrobial agents in many regions of the world [4].

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Extended-spectrum β-lactamase (ESBL)-producing organisms are characterized by their ability to produce enzymes that hydrolyze third-generation cephalosporins and aztreonam [5]. ESBL-producing Enterobacteriaceae organisms, including *E. coli,* are considered "serious threat" hazard level pathogens by the US Centers for Disease Control and Prevention [6]. ESBL-producing *E. coli* are frequently resistant to multiple classes of antimicrobial agents in addition to beta-lactams.

In the NCBI PubMed database, the term "extended-spectrum beta-lactamase-producing *E. coli*" first appeared in a publication in 1990 [6]. UTIs caused by ESBL-producing *E. coli* are becoming increasingly common among community-acquired infections [7]. These cases began to be reported in community onset infections in 1998, first in Ireland, Israel, Spain, and France [8]. However, factors that contribute to this increasing prevalence of ESBL-producing UPECs in communities are not clearly understood. A better understanding of risk factors associated with such infections is needed to improve clinical management of ESBL UPEC infections.

The widespread clinical use of antimicrobial agents has resulted in the selection of antimicrobial drug-resistant (AMR) bacterial strains, and yet, it remains unclear if this factor alone contributes to the widespread dissemination of AMR UPECs in community settings. Population-based studies of CA-UTI have shown that a large proportion (> 50%) of AMR infections are caused by just five to six lineages of *E. coli*, referred to as pandemic extraintestinal pathogenic *E. coli* (ExPEC) lineages, defined by multilocus sequence typing (MLST) [9, 10•]. Therefore, the community prevalence of AMR CA-UTI may be largely influenced by ExPEC genotypes circulating in a community, instead of initial selection of resistant strains by antimicrobial agents. Thus, UPEC resistance selection alone appears to be insufficient to determine community prevalence of AMR CA-UTI.

Most studies that assess risk factors for AMR infections focus on factors related to the selection of AMR strains and inevitably identify host-related factors, such as previous use of antibiotics, underlying medical conditions (e.g., diabetes and urinary tract anatomical defects) or medical procedures (e.g., catheterization). These studies do not take into consideration risk factors related to transmission and sources of AMR UPEC organisms. The observation that a large proportion of AMR CA-UTIs in a community may be caused by only a few ExPEC lineages suggests that there are point sources of these strains to which people are exposed. There is growing evidence that a substantial proportion of CA-UTI may be caused by UPEC strains that contaminate food products [11, 12•, 13–15, 16••]. Food animals may serve as this point source. In major food exporting countries, antimicrobial agents are used in large quantities in animal husbandry to prevent infectious disease and promote growth [17–19]. Hence, it is conceivable that AMR UPECs are initially selected in such animal reservoirs, contaminate human food and the environment, and ultimately enter the human intestine and then enter the bladder to cause UTI. One question posed in this review, therefore, is whether ESBL-producing UPECs originate from sources outside of the human host.

This review is divided into two parts. The first part considers the current body of knowledge regarding risk factors for CA-UTI caused by ESBL-producing UPEC. We then undertake a more detailed examination of potential risk factors for transmission of ESBL-producing UPEC by reviewing the current body of knowledge that addresses the role of food and environmental sources for ESBL-producing ExPECs that cause CA-UTI. We identify new risk factors for transmission of ESBL-producing UPECs with the hope to inform research agendas, public policy, and public health intervention strategies.

Methods

Data Sources and Search Strategy

Two independent authors conducted two literature searches using the databases PubMed, Embase, and Web of Science. In both queries, we limited the search to articles published between 2014 and 2019, the five most recent years. To include highly influential works published before this time period, we included articles published before 2014 that were cited greater than 50 times. Only articles published in English were included.

The first search focused on risk factors for CA-UTI caused by ESBL-producing UPEC and was conducted on January 8th, 2019. It included the search terms: ("Community-Acquired Infections"[Mesh] or "Community-Acquired") and ("Urinary Tract Infection*" or "Urinary Tract Infections"[Mesh]) and ("Drug Resistance, Microbial"[Mesh] or "antimicrobial resistance" or "antibiotic resistant") ("urinary tract infection" or "urinary tract infection"/exp) and ("community acquired" OR "community acquired infection"/exp) and ("antibiotic resistance"/exp. OR "antibiotic resistance" OR "antimicrobial resistance"). Our second search, which focused on ESBL-producing ExPECs found in food and environmental sources, was conducted on April 8th, 2019 and included the search terms; ("extraintestinal pathogenic *Escherichia coli*"/exp or "extraintestinal pathogenic *Escherichia coli*") and ("antibiotic resistance"/exp or "antibiotic resistance" or "antimicrobial resistance"/exp or "antimicrobial resistance" or "antibiotic resistant") and ("food"/exp or "food" or "animal"/exp or "animal" or "environment"/exp or "environment").

Study Selection and Data Extraction

Risk Factors for ESBL-Producing CA-UTI

All study abstracts were reviewed by each of the two independent authors and were considered to be eligible for inclusion

for full-text review if they reported risk factors associated with CA-UTI caused by ESBL-producing *E. coli*. Studies deemed relevant by both authors were reviewed in full. All disagreements were resolved by consensus prior to proceeding to data extraction. Study populations comprised of both adult and pediatric patients (Table 1).

Data extraction was conducted by two independent authors and exported to a single Excel spreadsheet for evaluation. Relevant recorded information included author names, year of publication, sample size, location of study, study design, risk factors investigated, outcome measurement methods, statistical analysis methods, and limitations. We evaluated evidence in

Table 1 Characteristics of studies included in review

Lead author, year of publication	Country	Setting or sample origin	Species	Study type CC, R P	Number of samples assessed (*n*)	Total number ESBL positive (*n*)	% ESBL (%)
Risk factors for ESBL-producing CA-UTI							
Søgaard 2017	Denmark	Laboratory Information System/database	Human	CC	3390	339	10%
Sittichanbuncha 2016	Thailand	University Hospital	Human	R	399	159	40%
Pérez Heras 2017	Spain	Tertiary Care Hospital	Human	R	229	21	9%
Martin 2016	France	Private Practice laboratories	Human	R	51,643	1694	3%
Lee 2018	Korea	University Hospital	Human	CC	150	50	33%
Kim 2017	Korea	University Hospital	Human	R	186	31	17%
Jacmel 2017	France	Pediatric Emergency Department, Hospital	Human	P	403	22	5%
Hertz 2016	Denmark	University Hospital	Human	CC	442	98	22%
Hernández Marco 2017	Spain	Pediatric Hospital	Human	CC	537	19	4%
Fan 2014	Taiwan	Children's Hospital	Human	CC	312	104	33%
Chervet 2018	France	Parisian suburb laboratory platform	Human	P	849	36	4%
Castillo-Tokumori 2017	Peru	Main Hospital	Human	CC	1158	67	6%
Azap 2010	Turkey	Four Tertiary-care Hospitals	Human	P	269	17	6%
Almomani 2018	Jordan	University Hospital	Human	CC	591	251	42%
Alcántar-Curiel 2015	Mexico	Mexico's Naval Referral Hospital	Human	CC	70	22	31%
Sources of ESBL-producing ExPEC							
DeRauw 2019	Belgium	STEC infection	Calves	CC	9	1	11%
Ewers 2014	Europe	Naturally occurring infections	Mammals	P	1152	1152	100%
Ghodousi 2016	Italy	Retail chicken meat	Chicken	CC	237	237	100%
Ghodousi 2015	Italy	Retail chicken meat	Chicken	P	163	132	81%
Gomi 2015	Japan	Waste water + hospital water	N/A	P	32	32	100%
Guo 2015	Australia	Feces and clinical isolates	Dog	P	47	18	38%
Hussain 2017	India	Broiler and free-range chicken meat	Chicken	P	168	63	38%
LeCuyer 2018	USA	Urinary tract infection	Dog	P	295	14	5%
Liu 2015	USA	Urinary tract infection	Cat	P	2686	76	3%
Liu 2016	China	Naturally occurring infection	Dog	P	165	40	24%
Liu 2017	China	Urine, blood and feces	Cat, Dog	P	174	16	9%
Liu 2018	China	River and lake water	N/A	P	74	8	11%
Maeyama 2018	Japan	Urinary tract infection	Cat, Dog	P	381	78	20%
Nebbia 2014	Italy	Urinary tract infection	Cat	P	138	7	5%
Solà-Ginés 2015	Spain	Colibacillosis cases	Chicken	P	32	11	34%
Solà-Ginés 2015	Spain	Broiler farm fly carcass	House Flies	P	682	42	6%
Vounba 2018	Senegal	Colibacillosis cases	Chicken	P	58	54	93%
Zogg 2018	Switzerland	Urinary tract infection	Cat, Dog	P	64	35	55%
Zurfluh 2015	Switzerland	Unwashed vegetables	Vegetables	P	169	26	15%

support of possible risk factors by examining total number of significant study findings, sample size and author-listed limitations. Risk factors were deemed to be commonly assessed if they were included in more than three studies (Table 2).

Sources of ESBL-Producing ExPEC

Study abstracts were reviewed by two independent authors and were considered to be eligible for inclusion for full-text review if they reported analyzing ESBL-producing ExPEC isolates from food, animal, or environmental sources and included multilocus sequence typing (MLST) data based on the Achtman scheme [20]. Studies deemed relevant by both authors were reviewed in full, and all disagreements were resolved by consensus prior to proceeding to data extraction .

Data extraction was conducted by two independent authors and exported to a single Excel spreadsheet for evaluation. Relevant recorded information included author names, year of publication, sample size, location of study, study design, and ExPEC sequence types.

Results

Risk Factors for ESBL-Producing CA-UTI

The initial multidatabase search query returned 414 studies matching search criteria; 88 were removed as duplicates and 326 abstracts were reviewed. Two hundred and fifty-eight studies were deemed to be irrelevant by two independent researchers and 68 studies were reviewed in full. Fifty-three studies were excluded: 51 for wrong outcomes measured or non-CA-UTI comparator, 1 for being a review, and 1 for being a non-English publication. This review focuses on 15 studies that examined 60,924 patient urine samples that included 2,930 ESBL-producing *E. coli* infections [21•, 22•, 23•, 24, 25•, 26, 27•, 28•, 29•, 30•, 31••, 32•, 33, 34•, 35•]. Of these 15 studies, eight used case control, three used prospective cohort, and four used retrospective cohort study designs. The number of cases caused by ESBL-producing UPEC examined in each study ranged from 21 to 1694. Study settings included hospital inpatient, community clinic, and hospital outpatient services. The majority of studies took place in Europe (7), while other study locations included South Korea (2), Thailand (1), China (1), Peru (1), Mexico (1), Turkey (1), and Jordan (1). Table 1 lists all studies identified with relevant characteristics. Studies compared cases (CA-UTI caused by ESBL-producing *E. coli*) with controls defined as CA-UTI caused by non-ESBL-producing *E. coli* (14) or CA-UTI caused by non-ESBL-producing *E. coli* resistant to at least one antibiotic (1). There were 103 unique risk factors assessed by all identified studies. Of the 103 risk factors, 8 were deemed commonly assessed by this review. The most frequent risk factors assessed were: previous hospitalization (11), antibiotic use within the past 3 months (9), male sex (9), pre-existing condition of type II diabetes (5), previous UTI (6), recurrent UTI (5), previous catheterization (5), and urinary tract abnormality (4). Evidence in support of potential risk factors was commonly reported using odds ratios (OR), with significance reported as 95% confidence intervals (CI) and associated *p* values. Common statistical methods included univariate logistic regression, multivariate logistic regression, chi-squared test, and Fisher's exact *t* test.

Statistically significant associations between commonly assessed potential risk factors and CA-UTI caused by ESBL-producing *E. coli* were found to vary between studies. For example, seven (78%) of nine studies found a statistically significant association between antibiotic use in the past 3 months. Male sex was found to be a significant risk factor for ESBL-producing *E. coli* infection in five (56%) of nine studies. Previous hospitalization was the most common risk factor examined across studies and was found to be a significant potential risk factor in 8 (73%) of 11 studies. Previous UTI caused by any organism was also found to be significantly associated with CA-UTI caused by ESBL-producing *E.*

Table 2 Commonly assessed risk factors

	Number of studies investigated (*n*)	Number of patients assessed (*n*)	Number of ESBL infections positive for risk factor (*n*)	Number of studies finding significant association (*n*)	% of studies finding significant association (%)	% of pooled patients assessed who are ESBL+ (%)
Previous antibiotic use (previous 3 months)	9	612	159	7	78%	26%
Previous hospitalization	11	1149	236	8	73%	21%
Gender (male)	9	1539	232	5	56%	15%
Type II diabetes	5	526	100	1	20%	19%
Previous UTI	6	131	103	6	100%	79%
Recurrent UTI	5	342	84	5	100%	25%
Catherization	5	80	32	3	60%	40%
Urinary tract abnormality	4	178	45	3	75%	25%

coli, reported in six of six studies. Recurrent UTI, defined as 3 episodes of UTI in the previous 12 months, was found to be a significant potential risk factor in 5 of 5 studies. The potential risk factors with the highest percentage of patients who were infected with ESBL-producing UPEC were previous UTI (79%) and previous catheterization (60%) (Table 2).

Sources of ESBL-Producing ExPEC

The initial multidatabase search query returned 514 studies matching our criteria; 99 were removed as duplicates and 415 abstracts were reviewed. Three hundred seventy-one studies were deemed irrelevant by two independent researchers and 44 studies were reviewed in full by each author. Twenty-five studies were excluded: 23 for wrong outcomes reported, 1 for being a review, and 1 because it was not published in full. This review focuses on 19 studies that examined 2042 ESBL-producing ExPEC specimens isolated from environmental, food, or animal sources [36•, 37, 38•, 39, 40•, 41, 42•, 43•, 44•, 45•, 46•, 47•, 48, 49•, 50•, 51•, 52–54]. Sources of ExPEC sampled included vegetables (1), houseflies (1), dogs (7) cats (6), horses (1), cattle (2), chicken (5), and water samples (2). Two thousand forty-two ESBL-producing ExPEC isolates were recovered. Sixteen (84%) of 19 studies reported ESBL producers of ExPEC pandemic lineages (ST10, ST69, ST73, ST95, ST127, ST131) [9].

In the course of this review, all six pandemic UPEC lineages with evidence of ESBL production were discovered. The most commonly recovered pandemic sequence type was ST131, which appeared in 12 (63%) of 19 studies, followed by ST10 which appeared in 7 (37%) of 19 studies (Fig. 1).

Discussion

We found conflicting reports of factors associated with CA-UTI caused by ESBL-producing *E. coli*. The reviewed studies were not concordant for significant association in six of the eight commonly assessed risk factors. This may have resulted from differences in types of variables sought, definitions used, sample size, and other factors associated with study design. Conversely, this review found agreement in all studies for previous UTI episodes and recurrent UTI as potential risk factors for UTI caused by ESBL-producing *E. coli* (Table 2). These risk factors are not new as they can serve as risks for any AMR infections. The above studies identified only risk factors associated with host-related characteristics. Previous UTI episodes and recurrent UTI may represent the same type of disease occurrence and likely select for AMR UPECs because of repeated exposures to antimicrobial agents. However, factors associated with selection of AMR UPECs are outside of the scope of this review.

In this review, we wished to identify factors associated with the increasing global prevalence of CA-UTI caused by ESBL-producing UPECs. Selection of AMR UPEC strains does not necessarily lead to increased community prevalence of AMR CA-UTI. Additionally, only 1 of the 15 studies used a comparison group that included only AMR CA-UTI caused by non-ESBL-producing *E. coli* [31••]. The remaining studies used controls which were defined as infection caused by non-ESBL-producing *E. coli* and did not explicitly exclude susceptible cases. This may impact the ability of such studies to distinguish risk factors for ESBL-producing infection from the more general risk factors for AMR.

None of the 15 studies selected in the first review examined risk factors associated with transmission of ESBL-producing UPEC, which would affect community AMR prevalence. An increasing number of studies have suggested that non-human reservoirs, such as food products, could serve as a potential source of human ExPEC exposure [11, 13, 16••]. Historically, diseases such as CA-UTI are seldom described as occurring as outbreaks. However, recent molecular epidemiological investigations have revealed that many CA-UTI cases, which appear sporadic, are caused by distinct sets of *E. coli* genotypes, suggesting point or common source exposures [55, 56]. Thus, UPEC may be acquired from contaminated food products or

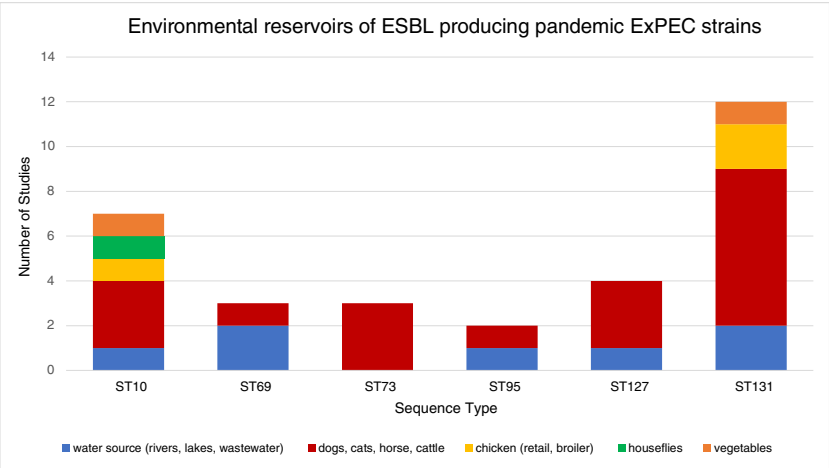

Fig. 1 Aggregated data of environmental exposures of pandemic ExPEC lineages from ESBL producers

other external sources (e.g., water, environment) [10•, 13, 57, 58]. In fact, the ST69 UPEC lineage—as genotyped by MLST—was first suggested to disseminate by contaminated food in the US in 1999 [15]. More recently, one study found UPEC sequence type 131 recovered from poultry meat to be closely related to CA-UTI clinical isolates of ST131 by phylogenetic analysis and ColV plasmid interrogation [12•]. By pulsed field gel electrophoresis (PFGE), raw poultry has been implicated as a possible source of human ExPEC strains in Canada [13], although these *E. coli* strains did not express ESBL. A study in the Netherlands discovered a high frequency of ESBL genes in *E. coli* strains isolated from raw chicken samples, many of which were shown to be identical to those found in human rectal swabs and blood cultures [59]. Despite these data, the effect and magnitude of food or food animals as a source of ESBL-producing UPEC is yet to be well established.

Furthermore, among the publications included in this review, we found extensive evidence of the presence of ESBL-producing pandemic UPEC lineages in food animals, companion animals, and other environmental sources (Fig. 1). These lineages are implicated in the vast majority of human cases of CA-UTI, which may suggest that there are common sources of these strains to which people are exposed. The relationship between food or food animals and AMR infections has been well established for enteric bacterial pathogens such as *Salmonella*, *Campylobacter*, and Shiga toxin–producing *E. coli* (STEC) [18, 57, 60–67]. Antibiotic use in animal husbandry is recognized as a key contributor to AMR selection in these enteric pathogens causing human gastrointestinal infections [17, 68]. The prevalence of AMR enteric infections in communities, however, is largely influenced by outbreaks and dissemination of these enteric pathogens by contaminated food products. It is therefore not inconceivable that food animals and food products, which have been shown to be contaminated with ESBL-producing *E. coli*, could cause CA-UTI and affect community prevalence of AMR CA-UTI [68–70]. Thus, exposures to certain types of food products or environmental sources may serve as important risk factors for CA-UTI caused by ESBL-producing UPEC. The intensification of food animal production, expanding use of antimicrobial agents in animal husbandry, and globalization of food trade may be contributing to the increasing global prevalence of CA-UTI caused by ESBL-producing *E. coli*.

Study Limitations The vast majority of risk factors investigated in the first review represent individual level risk factors that utilize simple demographic and health record information. No studies captured by this review investigated potential community level exposure risk factors, which may play a role in a patient's risk for CA-UTI caused by ESBL-producing *E. coli* and affect community prevalence of such infections. Of the eight commonly assessed risk factors addressed here, finding association with factors such as age, sex, and previous hospitalization provides limited opportunity for public health intervention. This demonstrates a clear need for studies that prioritize prevention of transmission as a motivation for risk factor investigation, as well as a need for new study designs that include strain genotype data that leverage community level data, such as places in the community for food product purchase and exposures.

Previous work on multidrug-resistant infections describes an existing need for standardization of risk factor definitions [71]. This review found that the coding of risk factor for analysis varied dramatically between studies. For example, many of the evaluated risk factors represented similar exposures. However, inconsistency in the time since exposure made comparison impossible between otherwise categorically similar exposures. A meta-analysis of the full breadth of findings was therefore difficult, and subsequent recommendations for clinical practice harder to suggest.

Currently, there are few studies that simultaneously and prospectively compared human isolates of ESBL-UPEC with *E. coli* strains isolated from food and environmental sources from the same geographic sites. Sampling of food or environmental products in most studies is frequently under-powered to sufficiently demonstrate links. Larger systematically well-designed studies are required to determine if contaminated food or environmental products act as a vehicle of ESBL-producing UPEC that cause human CA-UTI.

As is the case with many literature reviews, our results are limited by potential publication bias, as part one of this review only examined journal articles that reported positive associations. Our conclusions are also limited by the exclusion criteria that restricted our scope to articles written in English. UPEC strain types may cluster geographically and temporally, suggesting that risk factors for UTI may vary geographically and by time [10•, 72]. Although our review includes studies from several regions of the globe, geographic differences in UPEC genotype distribution may impact the generalizability of the results of this review.

Conclusion

The risk factors we found for CA-UTI caused by ESBL-producing UPEC reported in the reviewed articles include broad categories that may not be specifically related to UPEC organisms that produce ESBL. Factors such as previous UTI episodes and recurrent UTI may represent risk factors for any drug-resistant UTI and not necessarily UTI caused by ESBL-producing UPEC. Such observations may result from our current lack of precise understanding of mode of transmission of CA-UTI. Furthermore, this review found compelling evidence of the presence of ESBL-producing pandemic UPEC lineages that have been implicated in some human

cases of CA-UTI in food animals, companion animals, and other environmental sources. These results may suggest that there are in fact point sources of human exposure to these pathogens. Further studies investigating these source exposures may generate new information that can be used to devise focused and effective public health interventions.

Compliance With Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by the author.

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investigates risk factors for CA-UTI caused by ESBL-producing E. coli and finds recent hospitalization and antibiotic use are significant risk factors.

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30.• Jacmel L, Timsit S, Ferroni A, Auregan C, Angoulvant F, Chéron G. Extended-spectrum β -lactamase-producing bacteria caused less than 5% of urinary tract infections in a paediatric emergency centre. Acta Paediatr. 2017 Jan;106(1):142–7. **Included in part one of this review: This prospective observational study based in France examines risk factors for UTI caused by ESBL-producing E. coli in a pediatric population and finds urinary tract abnormalities, previous antibiotic use and prior hospitalization to be significant risk factors.**
31.•• Hertz FB, Schønning K, Rasmussen SC, Littauer P, Knudsen JD, Løbner-Olesen A, et al. Epidemiological factors associated with ESBL- and non ESBL-producing *E. coli* causing urinary tract infection in general practice. Infect Dis (Auckl). 2016;48(3):241–5 **This study evaluated risk factors for ESBL-producing *E. coli* causing UTI and utilizes a triple-case-control design. This was the only study captured within this review that used a control group that included only AMR CA-UTI caused by non-ESBL-producing *E. coli*.**
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such as ST131, ST127 and ST73, suggesting possible transmission between companion animals and humans.

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