Table S1. Case-control studies assessing risk factors of resistance in community-onset or community-acquired bloodstream infections and urinary tract infections

First author, year	Studied group	Studied bacteria-resistance pair
Rodríguez-Baño, 2010 [1]	CO-BSI	ESBL-p *E. coli*
Hsieh, 2010 [2]	CO-BSI	ESBL-p *E. coli*
Park, 2011 [3]	CO-BSI	ESBL-p *E. coli*
Park, 2014 [4]	CO-BSI	ESBL-p *E. coli*
Kim, 2019 [5]	CO-BSI	ESBL-p *E. coli* or *Klebsiella* spp.
Lee, 2017 [6]	CO-BSI	ESBL-p Enterobacteriacea
Zahar, 2017 [7]	CO-BSI	ESBL-p Enterobacteriaceae
Lin, 2019 [8]	CO-BSI	3GC-R *E. coli*
Lee, 2014 [9]	CO-BSI	3GC-R *E. coli*, *K.pneumoniae*
Sung, 2012 [10]	CA-BSI (CO-like)	3GC-R *E. coli*, *Klebsiella*, *Enterobacter*, *Citrobacter*
Gottesman, 2018 [11]	CA-BSI	ESBL-p *E. coli*
Pedersen, 1999 [12]	CA-BSI	*E. Coli* R to ampicillin, sulphonamides, trimethoprim
Ortega, 2016 [13]	CA-BSI	3GC-R *E. coli* or *Klebsiella* spp.
Wi, 2018 [14]	CO-BSI	MRSA
Lim, 2014 [15]	CO-BSI	MRSA
Fan, 2014 [16]	CO-UTI	ESBL-p *E. coli*
Pérez Heras, 2017 [17]	CO-UTI	ESBL-p *E. coli*
Søgaard, 2017 [18]	CO-UTI	ESBL-p *E. coli*
Tüzün, 2019 [19]	CO-UTI	ESBL-p *E. coli*
Boix-Palop, 2017 [20]	CO-UTI	ESBL-p *K. pneumoniae*
Kung, 2015 [21]	CO-UTI	ESBL-p Enterobacteriacea
Calbo, 2006 [22]	CO-UTI (CA like)	ESBL-p *E. coli*
Zhu, 2019 [23]	CA-UTI (CO like)	ESBL-p *E. coli*
Topaloglu, 2010 [24]	CA-UTI (CO like)	ESBL-p *E. coli* or *Klebsiella* spp.
Yilmaz, 2008 [25]	CA/CO-UTI	ESBL-p *E. coli* or *K. pneumoniae*
Colodner, 2004 [26]	NH-UTI	ESBL-p *E. coli* or *Klebsiella* spp.
Albaramki, 2019 [27]	CA-UTI	ESBL-p *E. coli* or *Klebsiella* spp.
Guzmán, 2019 [28]	CA-UTI	ESBL-p *E. coli*
Koksal, 2019 [29]	CA-UTI	ESBL-p *E. coli* or *Klebsiella* spp.
Azap, 2010 [30]	CA-UTI	ESBL-p *E. coli*
Rodríguez-Baño, 2008 [31]	CA-UTI	ESBL-p *E. coli*
Castillo-Tokumori, 2017 [32]	CA-UTI	ESBL-p *E. coli*
Megged, 2014 [33]	CA-UTI	ESBL-p Enterobacteriacea
Chervet, 2018 [34]	CA-UTI (CO like)	ESBL-p Enterobacteriacea
Jacmel, 2017 [35]	CA-UTI (CO like)	ESBL-p Enterobacteriacea
Brosh-Nissimov, 2019 [36]	CA-UTI (CO like)	ESBL-p Enterobacteriacea
Colodner, 2008 [37]	CA-UTI (CO like)	*E. Coli* R to quinolones
Seija, 2014 [38]	CA-UTI (CO like)	*E. Coli* R to fluoroquinolones
Killgore, 2004 [39]	CA-UTI (CO like)	*E. Coli* R to ciprofloxacin
Chaniotaki, 2004 [40]	CA-UTI (CO like)	*E. Coli* R to quinolones
Dromigny, 2005 [41]	CA-UTI (CO like)	*E. Coli* R to ampicillin, amoxicillin, nalidixic acid, fluoroquinolones, TMP/SMX
Hillier, 2007 [42]	CA-UTI (CO like)	All bacteria, R to ampicillin, TMP
Anesi, 2016 [43]	CO-UTI	3GC-R Enterobacteriacea
Lee, 2015 [44]	CO-UTI	AmpC β-lactamase-producing Enterobacteriacea

Smithson, 2012 [45]	CA-UTI	*E. Coli* R to quinolones
Bosch-Nicolau, 2017 [46]	CA-UTI (CO like)	All bacteria, R to amoxicillin-clavulanate, cefuroxime, cefotaxime, ciprofloxacin
Filiatrault et al., 2012 [47]	CA-UTI	All bacteria, R to ciprofloxacin, TMP/SMX

*Table footnotes. Abbreviations: 3GC = third generation cephalosporins; CA = community acquired; CO = community onset; CO-like = CA infection which definition actually corresponds to a CO infection; *E. coli* = *Escherichia coli*; ESBL-p = Extended-Spectrum β-Lactamase producing; *K. pneumoniae* = *Klebsiella pneumoniae*; MRSA = methicillin-resistant *Staphylococcus aureus*; NH = non-hospitalized; R = resistant; S = susceptible; SMX = sulfamethoxazole; TMP = trimethoprim.

Table S2. Classifications, windows of exposure and collections of antibiotic use in case-control studies assessing risk factors of resistance in community-onset or community-acquired bloodstream infections and urinary tract infections

	Bacteremia, no. (total=15)	UTI, no. (total = 32)
Studied antibiotic(s) and sub classifications		
Global use	13	23
Beta lactam antibiotics	3	2
Penicillins	4	12
Penicillins and beta-lactamase inhibitors	3	6
Cefuroxime / 2nd generation cephalosporins	3	5
Cephalosporins / 3rd generation cephalosporins	4	17
Narrow/broad-spectrum penicillins	0	1
Any of ampicillin, ampicillin/sulbactam, cefalotin	0	1
Carbapenems	1	3
Mecillinam	0	1
(Fluoro)quinolones	7	20
Cotrimoxazole	0	10
Nitrofurantoin	1	7
Aminosides	1	6
Macrolides	1	5
Clindamycin	0	1
Doxycyclin	0	1
Fosfomycin	0	3
Vancomycin	1	2
Anti-anaerobic	1	0
Metronidazole	0	2
Narrow/broad-spectrum antibiotics	0	1
Window of exposure		
15 days	1	0
1 month	4	5
2 months	1	0
3 months	7	17
6 months	1	4
12 months	1	3
"recent"	0	1
within 31-365 days before the index date	0	1
Not specified*	0	1
Collection		
Analysis of medical records	8	19
Patient interviews	0	6
Prospective evaluation without further details	3	1
Delivered antibiotics in pharmacy databases	2	2
Not specified*	2	4

*Table footnotes.

* Some papers did not specify the window of exposure [40] or the way antibiotic exposure was collected [4,15,21,22,25,40].

Table S3. Definitions of community-onset and community-acquired infections in case-control studies assessing risk factors of resistance in bloodstream infections and urinary tract infections

Studies focusing on "Community Onset" bacteremia (total = 11)

<48h (no. = 4)

≤48h + not transferred from other hospitals (no. =3)

<48h + not hospitalized within 2 (no. =1) or 4 (no. =1) weeks before admission + not transferred from other hospitals

Residing in a long-term healthcare facility, or community-acquired (no. = 1)

Presenting at the ED (no. = 1)

Studies focusing on "Community Acquired" bacteremia (total = 4)

≤48h (no. = 1)

≤48h + not HCA (no. =2)

Present or incubating at admission to hospital + exclusion of patients hospitalized within the past 30 days (no. = 1)

Studies focusing on "Community Onset" UTI (no. = 9)

≤48h (no. = 3)

Presenting at the ED (no. = 1)

<48h or outpatients (no. = 1)

Presenting at the ED, or outpatient practices, or within 72 hours of hospital admission from the ED/outpatient clinic (no. = 1)

Presenting at the ED, and no hospitalization or long-term care facility stay within the preceding month (no. = 2)

Identified in a laboratory + referred by general practitioners (no. = 1)

Study focusing on "Non hospitalized" UTI (no. = 1)

Study focusing on "Community onset/community acquired" UTI without further definition (no. = 1)

Studies focusing on "Community Acquired" UTI (no. = 21)

No exclusion of HCA infections (no. = 11): <48h (no. = 1), presenting at the ED (no. = 3), GP practices (no. = 1), identified in an ambulatory laboratory (no. = 1), outpatients (no. = 5)

Exclusion of HCA infections (no. = 9): presenting at the ED or outpatients + not HCA (no. = 3), <48h + not HCA (no. = 1), <48h or ED + not HCA (no. =1), < = 72h + no hospitalization in the last two weeks prior to current UTI (no. = 1), not HCA (no. = 3)

Not specified (no. = 1) [30]

Table footnotes. Abbreviations: BSI = bloodstream infections; ED = emergency department; GP = general practitioner; HCA = healthcare associated; UTI = urinary tract infections.

Table S4. Main results of case-control studies assessing antibiotic use as a risk factor of resistance in CO-BSI or CA-BSI to ESBL-producing Enterobacteriacea, as a function of the control group

First author, year	Studied group	Number of cases	Number of controls	Exposure window	AB identified as a resistance RF	Odds ratio [95% CI]	Other antibiotics evaluated
Controls = non-ESBL-p Enterobacteriacea (no. = 10)							
Kim, 2019 [5]	CO-BSI	140	454	1 month	β-lactams or FQ	6·8 [2·3-20·2]	··
Lee, 2017 [6]	CO-BSI	65	1,076	1 month	Global use	15·3 [7·7–61·4]	··
Park, 2011* [3]	CO-BSI	50	100	3 months	Global use	4 [1·5-12·3]	··
Park, 2014† [4]	CO-BSI	60	180	3 months	3GC	16·4 [2·0-131·8]	1GC, 2GC, Penicillins, Quinolones
Rodríguez-Baño, 2010* [1]	CO-BSI	95	188	2 months	Global use / FQ / Cephalosporins	2·7 [1·5-4·9] / 4·7 [2·0-11·1] / 10·3 [2·1-50·3]	Aminopenicillins
Zahar, 2017 [7]	CA-BSI	22	335	1 year	··	··	β-Lactams, Cephalosporins, FQ, Carbapenems, Others, Macrolides, Nitrofurantoin, Aminoglycosides, Anti-anaerobic
Zahar, 2017 [7]	HCA-BSI	36	289	1 year	Anti-anaerobic	3·51 [1·6–7·5]	β-Lactams, Cephalosporins, FQ, Carbapenems, Others, Macrolides, Nitrofurantoin, Aminoglycosides,
Gottesman, 2018 [11]	CA-BSI	12	267	3 months	Quinolones	7 [1·7–29·4]	Global, Cefuroxime, Amoxicillin or penicillin, Amoxicillin/clavulanate
Controls = CO-sepsis (no. = 1)							
Rodríguez-Baño, 2010 [1]	CO-BSI	95	190	2 months	Global use / FQ	1·9 [1·03-3·5] / 2·8 [1·2-6·5]	Aminopenicillins, Cephalosporins
Controls = CO-BSI (no. = 1)							
Park, 2011* [3]	CO-BSI	50	100	3 months	Global use	3·9 [1·3-11·5]	··

Table footnotes. A study without multivariate analysis was excluded [2]. = case-case(control)-control study, † = no information on how antibiotic use was evaluated. Abbreviations: 1GC, 2GC, 3GC = first, second, third generation cephalosporins; BSI = blood stream infections; CA = community acquired; CI = confidence interval; CO = community onset; CO-like = CA infection which definition actually corresponds to a CO infection; ESBL-p = Extended-Spectrum β-Lactamase producing; FQ = fluoroquinolones; RF = risk factor.

Table S5. Main results of case-control studies assessing antibiotic use as a risk factor of resistance in CO-UTI or CA-UTI to ESBL-producing Enterobacteriacea, as a function of the control group

First author, year	Studied group	Number of cases	Number of controls	Exposure window	AB identified as a resistance RF	Odds ratio [95% CI]	Other antibiotics evaluated
Controls = non-ESBL-p Enterobacteriacea (no. = 16)							
Søgaard, 2017* [18]	CO-UTI	339	3,390	Day -30 to -365	Macrolides Nitrofurantoin	1·5 [1·1-2·2] 1·5 [1·1-2·3]	Mecillinam, Sulfamethizole, TMP, Narrow/ broad-spectrum penicillins, narrow/ broad-spectrum AB
Tüzün, 2019 [19]	CO-UTI	154	151	6 months	Global use	2·3 [1·2–4·3]	FQ, Cephalosporins, β-lactams + β-lactamase inhibitor
Zhu, 2019 [23]	CA-UTI (CO like)	111	103	3 months	Global use	4·2 [1·9–9·1]	..
Boix-Palop, 2017* [20]	CO-UTI	83	155	3 months	Cephalosporins Quinolones	4·0 [1·8–9·2] 3·3 [1·4–7·9]	..
Kung, 2015† [21]	CO-UTI	62	376	3 months	..	..	Penicillins with/without β-lactamase inhibitor, Cephalosporins, FQ
Topaloglu, 2010 [24]	CA-UTI (CO like)	155	155	3 months	..	..	Global use, Penicillins, 2GC, 3GC+4GC, Others, Combinations, Suppression with TMP/SMX or nitrofurantoin
Yilmaz, 2008† [25]	CA/CO-UTI	62	62	3 months	Quinolones Cephalosporins	.. ..	Global use, Aminopenicillins, Aminoglycosides, Aminopenicillins + β-lactamase inhibitor, TMP/SMX
Colodner, 2004 [26]	NH-UTI	100	77	3 months	Global use 2GC 3GC Quinolones Penicillins	3·2 [1·8-5·9] 15·8 [1·7-143] 10·1 [4·2-24·0] 4·1 [1·8-9·0] 4·0 [1·6-9·0]	Macrolides, 1GC, TMP/SMX, Nitrofurantoin, Aminoglycosides
Calbo, 2006† [22]	CO-UTI (CA like)	19	55	1 year	Cefuroxime	21·4 [5·4–85·2]	3GC, Ciprofloxacin, Aminoglycosides

Albaramki, 2019 [27]	CA-UTI	77	77	3 months	..	..	Global use
Guzmán, 2019 [28]	CA-UTI	21	82	3 months	..	..	"First line β-lactams" (ampicillin, ampicillin/sulbactam, cefalotin)
Koksal, 2019 [29]	CA-UTI	66	112	3 months	..	..	Global use, Penicillins, Cephalosporins, FQ, Fosfomycin, Nitrofurantoin
Azap, 2010‡ [30]	CA-UTI	51	464	3 months	β-lactams	4·6 [2·0–10·7]	Global use, Quinolones
Rodríguez-Baño, 2008 [31]	CA-UTI	122 (93% had UTI)	244	3 months	Global use Aminopenicillins FQ 2GC + 3GC	2·9 [1·6-5·3] 2·8 [1·2-6·1] 1·9 [1·0-4·1] 3·2 [1·0-9·5]	Fosfomycin, Tromethamine
Castillo-Tokumori, 2017 [32]	CA-UTI	67	105	1 month	Global use	3·1 [1·4–6·7]	Penicillins, Cephalosporins, FQ
Megged, 2014 [33]	CA-UTI	80	80	1 month	Global use	4 [1·6–10·4]	..

Controls = uninfected patients from the general population (no. = 1)

| Søgaard, 2017* [18] | CO-UTI | 339 | 3390 | Day -30 to day -365 | Macrolides
Nitrofurantoin
Broad-spectrum AB
Mecillinam
Sulfamethizole Trimethoprim | 2·2 [1·3-3·8]
4·7 [1·9-11·2]
2·9 [1·1-7·7]
3·1 [1·3-7·8]
4·7 [2·4-9·2]
3·6 [1·6-8·0] | Narrow / broad-spectrum penicillins, narrow-spectrum AB |

*Table footnotes.** Studies without multivariate analysis were excluded [16,17,34–36].

* = case-case(control)-control study, † = no information on how antibiotic use was evaluated, ‡ = no definition of CA infections.

Abbreviations: 1GC, 2GC, 3GC, 4GC = first, second, third, fourth generation cephalosporins; AB = antibiotics; CA = community acquired; CA-like = CO infection which definition actually corresponds to a CA infection; CI = confidence interval; CO = community onset; CO-like = CA infection which definition actually corresponds to a CO infection; ESBL-p = Extended-Spectrum β-Lactamase producing, FQ = fluoroquinolones; RF = risk factor; SMX = sulfamethoxazole; TMP = trimethoprim.

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