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Defining Relatedness in Studies of Transmission of Antimicrobial-Resistant Organisms: Variability in Definitions across Studies and Impact of Different Approaches on Study Conclusions

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Abstract

OBJECTIVE—Comparison of studies evaluating patient-to-patient transmission of organisms is difficult, given the lack of standardized criteria. We used fluoroquinolone-resistant *Escherichia coli* (FQREC) as a model to characterize variability in definitions of relatedness across studies and to evaluate the resultant impact on study conclusions.

DESIGN—Narrative review and cohort study.

METHODS—The narrative review compared relatedness criteria across studies of FQREC. Additionally, an existing database was used to compare relatedness of isolates on the basis of molecular criteria alone versus molecular plus clinical criteria with different temporal cutoffs (hospitalization overlap of ≥ 1 day or allowance for nonoverlap of hospitalization dates of ≤7 days or ≤30 days).

RESULTS—Forty-six articles met narrative review inclusion criteria. Sixteen studies exclusively utilized molecular criteria to define relatedness. Thirty studies included molecular and clinical criteria. Of these, 6 included temporal data (ie, time period of isolate identification), 10 included patient location, and 14 included proximity and temporal criteria. For the database analysis, 353 patients were colonized with FQREC. There were 2 main clusters containing 48 and 17 related isolates within 49 pulsed-field gel electrophoresis types. Among the clusters, 18.4% of isolates

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were related by molecular criteria. Incorporating clinical criteria, fewer isolates were considered related: 5.7% of isolates using 30-day criteria, 3.1% using 7-day criteria, and 1.4% using 1-day overlap.

CONCLUSIONS—There is considerable variability in definitions of relatedness of FQREC. Utilizing molecular criteria alone to define relatedness overestimates transmission compared with definitions including clinical criteria. Standard definitions of relatedness in studies of antimicrobial-resistant organisms are needed.

Increasing antimicrobial resistance is a pressing public health crisis.[1] In order to develop effective infection control strategies, improved understanding of the relative contribution of patient-to-patient transmission versus selection pressure (ie, antimicrobial use) to the emergence of antimicrobial-resistant organisms is needed. Several studies have assessed organism relatedness in order to determine the relative importance of patient-to-patient transmission.[2–4] However, there is no standard definition for patient-to-patient transmission across studies. Some studies have used exclusively molecular criteria to determine genetic relatedness and used genetic relatedness alone as a suggestion of patient-to-patient transmission.[5,6] Other studies employing more rigorous definitions have required genetic relatedness along with clinical relatedness characteristics, such as overlap in hospital stay of varying durations or location proximity among subjects.[7,8] The degree of variability in definitions of patient-to-patient transmission across studies has not been assessed, and the impact of this variability on study conclusions is unknown, making comparisons across studies difficult.

In this study, we used fluoroquinolone-resistant *Escherichia coli* (FQREC) as a model to address these broader questions. Our goal in this study was to conduct a narrative review of the literature to characterize differences in definitions of relatedness across studies of FQREC. In addition, we sought to use an existing research database[9] to evaluate the impact of different definitions of relatedness on study conclusions regarding relatedness of FQREC.

METHODS

Narrative Review

A search of PubMed, the Cochrane database, Medline, and Google scholar was conducted for articles of all study designs focusing on patient-to-patient transmission of FQREC. The search terms used included “fluoroquinolone-resistant *E. coli* + pulsed-field gel electrophoresis,” “fluoroquinolone-resistant *E. coli* + relatedness,” “fluoroquinolone-resistant *E. coli* + patient transmission,” “fluoroquinolone-resistant *E. coli* + ribotyping,” “fluoroquinolone-resistant *E. coli* + multilocus enzyme electrophoresis,” and “fluoroquinolone-resistant *E. coli* + PCR.” Each of the previous searches was repeated, substituting “quinolone-resistant *E. coli*” for “fluoroquino-lone-resistant *E. coli*.” The search was limited to articles published in the English language involving human subjects. The search was further enhanced by reviewing the bibliography of included articles to find studies not previously identified.

The abstract of every identified article was reviewed. Only those articles describing FQREC isolates that also commented on transmission or relatedness in human subjects were further analyzed. Since *E. coli* with different resistance mechanisms may have different transmissibility, articles that specifically evaluated extended-spectrum *β*-lactamase (ESBL)–producing *E. coli* were excluded. Because this review focused on patient-to-patient transmission in the hospital setting, articles concerning transmission of FQREC within agricultural settings and studies of exclusively outpatient populations were excluded.

Specific data elements extracted included the year and site of study, study design, patient population, number of human subjects, number of FQREC isolates included for genotypic analysis, source of FQREC isolate (ie, blood, stool), presence of FQREC colonization versus infection, type of molecular data employed to determine relatedness, criteria for molecular relatedness, whether clinical epidemiologic data were considered in assessing relatedness, number of related isolates determined by molecular criteria, and number of identified related isolates determined by combining clinical and molecular criteria (if applicable).

Cohort Study

The second part of this study was a methodologic study of the impact of different definitions of relatedness on determination of relatedness of FQREC. This analysis was based on a previously described data set for a study conducted by the authors.[9] As described previously, this study was performed at 2 hospitals within the University of Pennsylvania Health System: (1) the Hospital of the University of Pennsylvania, a 725-bed academic tertiary care medical center; and (2) Penn Presbyterian Medical Center, a 344-bed urban community hospital. All patients hospitalized at the 2 study sites were eligible for inclusion, provided they had been hospitalized for at least 3 days. Perirectal swabs were obtained from eligible subjects to detect FQREC colonization.[10] Levofloxacin was used as a marker for susceptibility to fluoroquinolones (FQs). The genetic relatedness of FQREC isolates was determined by pulsed-field gel electrophoresis (PFGE). All subjects colonized with *E. coli* demonstrating reduced FQ susceptibility (as determined by a levofloxacin minimum inhibitory concentration ≥0.125 μg/mL) were included in this study and were considered FQREC. Clinical data related to location of subjects in the hospital, date of culture, and hospitalization dates were documented. The number (and proportion) of FQREC isolates determined to be secondary to patient-to-patient transmission on the basis of different criteria was compared, as follows: (1) genetic criteria: genetic relatedness was determined by isolates that had 80% or greater similarity by PFGE; and (2) clinical criteria: temporal overlap of hospitalization of at least 1 day, allowance for nonoverlap of hospitalization dates of 7 days or fewer, and allowance for nonoverlap of hospitalization dates of 30 days or fewer.

This study was reviewed and approved by the Institutional Review Board of the University of Pennsylvania.

RESULTS

Narrative Review

We identified 706 articles on the basis of the above search criteria. All abstracts were reviewed for content. Duplicates and ineligible articles based on the criteria detailed in “Methods” were excluded, leaving 75 articles. These articles were reviewed in full, and ineligible articles were excluded, so that 46 articles remained. The bibliographies of these articles were reviewed, with 7 additional relevant articles identified. However, none of these articles met inclusion criteria.

Figure 1 and Table 1 show a flow diagram and summary of the included articles, respectively. Sample sizes for molecular analysis ranged from 4 to 353 FQREC isolates. Thirty-nine of the studies employed PFGE, with definitions of criteria for molecular relatedness ranging from 67% to 100% similarity. Seven studies employed random amplification of polymorphic DNA typing, with criteria for molecular relatedness including no band difference, 2 or fewer band difference, and similarity coefficient (S_{AB}) values of 90% or greater. The molecular methods utilized in the remaining studies were as follows (molecular criteria for relatedness in parentheses): 2 studies used enterobacterial repetitive

intergenic consensus–polymerase chain reaction (PCR; <2 band difference or identical), 2 studies used automated ribotyping (identical or unlisted criteria), 2 studies used repetitive sequence–based PCR (≥95% similarity or unlisted criteria), 1 study used infrequent restriction site PCR (unlisted criteria), and 1 study used single-enzyme amplified fragment length polymorphism (≥95% similarity).

Of the included studies, 16 exclusively utilized molecular criteria in their definition of relatedness. Thirty studies included a combination of molecular and clinical criteria. Of these, 6 studies included information on the date or time period of identification of the isolates. Temporal criteria ranged from isolates collected during the same year to those identified as isolated on the same day of hospitalization. Ten of 30 studies included information on the location of the subjects. The proximity factors used ranged from noting that isolates were collected from the same country to identifying the individual room and nursing staff caring for the subject. Finally, 14 studies used both proximity and temporal criteria. However, while these studies enumerated the clinical criteria used, the majority did not define which isolates the authors qualified as responsible for patient-to-patient transmission.

Cohort Study

As described previously,[9] a total of 353 patients were identified as colonized with FQREC in the prior study and were included in this study. Table 2 shows a summary of the results. Among the 353 FQREC, there were 49 PFGE types. There were 2 main clusters: 1 cluster contained 48 isolates (12a–12f cluster), and the other contained 17 isolates (16a–16c cluster). Among the 2 large clusters, by PFGE (ie, molecular criteria), 48 + 17 isolates (*n* = 65) out of 353 (18.4%) isolates would be considered related. However, using a combination of molecular criteria and clinical criteria, the *n* (%) that would be classified as related is substantially lower (Table 2).

DISCUSSION

In this study, we provide a narrative review of the literature on patient-to-patient transmission of FQREC and evaluate the impact of different definitions of relatedness on study conclusions. In the narrative review, we found considerable variation in the definitions used to report relatedness in the medical literature. In our analysis of a preexisting data set, we found that employing different criteria for relatedness resulted in substantively different study conclusions.

Our study provides a comprehensive comparison of different definitions of antimicrobial-resistant organism relatedness across studies. Of the reviewed studies, more than half exclusively used molecular criteria to define relatedness. Among those studies that also incorporated clinical criteria, the specific criteria employed were oftentimes not clearly delineated, and there was substantial variability in clinical criteria used. The high degree of variability found in this narrative review emphasizes the lack of a standard epidemiologic definition of relatedness. The concern with this degree of variability is that it makes comparison across studies difficult. Studies utilizing purely molecular approaches are likely to report falsely high patient-to-patient transmission rates, since patients hospitalized months or even years apart with genetically similar isolates are unlikely to represent true person-to-person transmission. For example, patients with nonoverlapping hospitalization might have molecularly indistinguishable isolates secondary to acquisition of dominant strains that exist in the community. On the other hand, more rigorous definitions requiring genetic relatedness along with clinical criteria (eg, overlap in hospital stay) might miss transmission events should an intermediate (ie, hospital employee or environmental source) be involved. While additional studies are necessary to identify the most accurate definition of relatedness of

antimicrobial-resistant organisms, this review highlights the importance of standardizing reporting of relatedness in order to allow for comparison of studies and more accurately determine the relative importance of patient-to-patient transmission.

In the second part of the study, we found that the relatedness rates of FQREC differ significantly if molecular criteria alone are utilized versus a combination of molecular and various clinical criteria. A combination of molecular criteria and moderately stringent clinical variables will likely provide a more accurate estimate of true cases of patient-to-patient transmission of FQREC. We propose that, in addition to molecular criteria, the definition of patient-to-patient transmission for future studies should include 30-day criteria, as defined in our study. We believe that this temporal criteria will appropriately exclude genetically similar isolates from patients who have been hospitalized months to years apart (and therefore are unlikely to be representative of true patient-to-patient transmission) but will allow for enough time to account for potential transfer of isolates between intermediates (eg, healthcare workers). Of note, these findings are not limited to FQREC; a study in imipenem-resistant *Pseudomonas aeruginosa* showed variability in estimated rates of relatedness when utilizing strictly molecular criteria versus a combination of molecular and clinical criteria.[11] However, other studies by the same authors in ESBL-producing *E. coli* and *Klebsiella pneumoniae* did not show a similar discrepancy between relatedness as defined by hospital overlap and PFGE results.[2,3] This implies that criteria for the definition of relatedness must be independently investigated for each organism and that optimal infection control interventions may differ among gram-negative organisms.

There are several potential limitations of our study. The study was carried out in a university health system and might not be generalizable to other settings. In addition, future studies that include evaluation of environmental samples would help to elucidate the role of the environment in the transmission of FQREC and define optimal overlap periods.

In conclusion, our study reveals the considerable variation in definitions used to report relatedness of FQREC. In addition, it demonstrates that use of different criteria results in substantial differences in estimated relatedness rates. Future studies are needed to determine the most accurate criteria for defining relatedness for specific antimicrobial-resistant organisms. Standardized definitions of relatedness will allow for future comparisons to be made among studies, subsequent determination of the relative importance of patient-to-patient transmission in acquisition of specific antimicrobial-resistant organisms, and, ultimately, more efficient allocation of resources toward infection control interventions.

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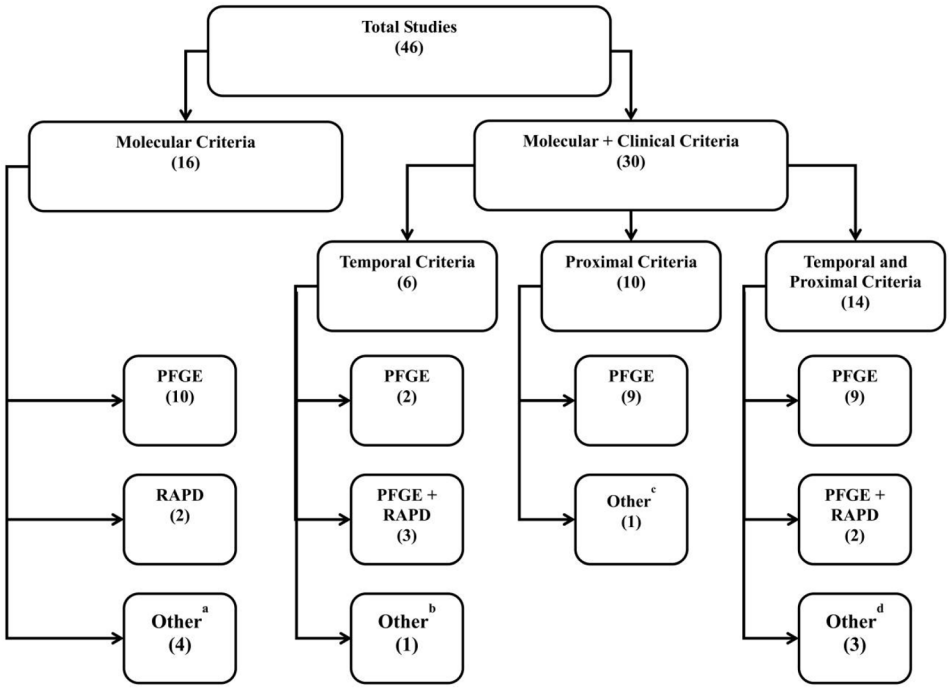

FIGURE 1.

Summary of the articles included in the narrative review. The number of articles of each type is shown in parentheses. PFGE, pulsed-field gel electrophoresis; RAPD, random amplification of polymorphic DNA. a = studies that utilized enterobacterial repetitive intergenic consensus–polymerase chain reaction (PCR), repetitive sequence–based PCR, infrequent restriction site PCR, and single enzyme amplified fragment length polymorphism. b = study that utilized a combination of repetitive element–based PCR profiling, multilocus sequence typing, and PFGE. c = study that utilized a combination of ribotyping followed by PFGE. d =studies that utilized a combination of PFGE and plasmid typing, PFGE and automated ribotyping, and enterobacterial repetitive intergenic consensus–PCR.

TABLE 1

Narrative Review Findings

Study	Year published	Patient population/site	No. of FQREC isolates for genotypic analysis	Type of molecular data	Criteria for molecular relatedness	Clinical data included
Bauernfeind[4]	1994	ICU patients with ciprofloxacin-resistant *Escherichia coli* infections at hospital in Munich	9	PFGE	Not given, but identified related as identical and unrelated as "totally different"	Ward location, date of isolation
Baum[12]	2000	Fecal colonization of patients undergoing or who recently underwent a peripheral bone marrow transplant at a transplantation unit in Germany	11	PFGE	Not listed; state "genotypic identity was demonstrated"	None
Blanco[13]	2011	Ambulatory (71%) and hospitalized (29%) patients with *E. coli* infections from 5 hospitals in different Spanish regions	125	PFGE	≥85% similarity	Hospital site
Carratala[14]	1996	Fecal colonization of 25 patients with hematologic malignancies who received cytostatic chemotherapy and subsequently developed neutropenia, treated with norfloxacin prophylaxis in a hospital in Spain	10	PFGE	Not listed; state "marked difference in banding patterns suggest the isolates belonged to different strains"	None
Chang[15]	2007	Patients hospitalized at a university hospital in Taiwan with FQREC infections	74	RAPD	Not listed	None
Chen[16]	2001	Patients with clinical *E. coli* infections resistant to ciprofloxacin hospitalized at an acute care center in Taiwan	65	PFGE	<3 band difference to each other with a similarity of at least 67% correlation	None
Cheong[17]	2001	Patients with FQREC bacteremia in a Korean hospital	40	PFGE	Not listed	None
Christiansen[7]	2011	Isolates obtained from hospitals and general practitioners submitted to the department of clinical microbiology at a hospital in Denmark from patients with FQREC infections	104	PFGE	≤6 band differences with a similarity level of >85%	Same hospital within an interval of 1–3 days between sampling
Eom[18]	2002	Patients with *E. coli*–positive urine culture at a hospital in Korea	32	PFGE	Tenover criteria[19]	Ward location, 3-month time period of isolation, community- or hospital-acquired infection
Garau[20]	1999	Patients with FQREC bacteremia in a hospital in Spain (isolates for molecular analysis from patients with bacteremia of community origin)	16	PFGE	Not listed	None

Study	Year published	Patient population/site	No. of FQREC isolates for genotypic analysis	Type of molecular data	Criteria for molecular relatedness	Clinical data included
Grude[21]	2008	Patients with UTIs in Norway; 86% outpatients, 14% inpatients	35	PFGE	≤3 band difference	"Domicile information"
Johnson[22]	2010	Renal transplant recipients with *E. coli* bacteriuria identified in clinic visits or hospital admissions at a US hospital care system	39 (50% FQREC)	PFGE	>94% relatedness	None
Johnson[23]	2010	Hospitalized patients with *E. coli* infections from across the United States	127	PFGE	>94% relatedness	Location
Kariuki[8]	2007	Patients with community-acquired UTIs (inpatient and outpatient) in Kenya	17	PFGE	Indistinguishable = single outbreak strain; <4 band difference = closely related; 2–6 band difference = potentially part of outbreak; Tenover criteria[19]	Location, year, inpatient vs outpatient
Kern[24]	1994	Patients admitted to a medical service with at least 1 clinical specimen positive for ofloxacin-resistant *E. coli* (19/32 with leukemia) at a German hospital; isolates for molecular analysis from bacteremic leukemia patients	9	PFGE	Not listed	Days/months between isolation of genotypically related strains, ward location
Kern[25]	2005	Fecal colonization of patients admitted to a hematology-oncology service at a hospital in Germany	For serotyping followed by PFGE/ RAPD: 36 patients; RAPD: isolates from 82 patients (1–7 per patient)	PFGE and RAPD	≤2 band difference for RAPD; PFGE: not listed	Year of study
Kuntaman[26]	2005	Fecal colonization of hospitalized patients at admission, patients on discharge after ≥5 days of hospitalization, patients visiting a primary healthcare center, and healthy relatives or household members from admitted patients selected from 2 cities in Indonesia	196	ERIC-PCR	Identical	Hospital department, city, time period
Lautenbach[27]	2006	Hospitalized patients at 2 hospitals in the United States with fecal surveillance cultures	133	PFGE	Tenover criteria[19]	Identified by same annual survey
Lautenbach[9]	2010	Hospitalized patients at 2 hospitals in the United States with fecal surveillance cultures	353	PFGE	≥80% similarity	Overlap in the dates of hospitalization
Lehn[28]	1996	Hospitalized patients from various departments at a medical center in Germany with FQREC infections	19	PFGE	Not listed; state "clonally distinct"	Location in hospital, year and period (3-month blocks)

Study	Year published	Patient population/site	No. of FQREC isolates for genotypic analysis	Type of molecular data	Criteria for molecular relatedness	Clinical data included
Maslow[29]	2005	Fecal colonization of patients residing in a long-term care facility in the United States	25	PFGE	≤3 band difference = clonal; 4–6 band difference considered related; Tenover criteria[19]	Facility, date of admission, duration of residence in facility recorded, specifics not listed
McDonald[30]	2001	Adult inpatients, adult outpatients, adults with documented hospital-acquired infections, and pediatric patients with FQREC infections from 44 hospitals in Taiwan	36	PFGE	>80% similarity	Hospital site, day of isolation
Mihu[31]	2010	ICU patients with *E. coli* bloodstream infections from a US cancer institution + clinical isolates of *E. coli* from 14 other geographically dispersed institutions	22	PFGE and/or automated ribotyping	Not listed, but state identical ribotype and PFGE pattern "suggesting an endemic clone"	Further evaluated for clonality only if same center; evaluated only from 2004 to 2005
Oethinger[32]	1996	Pediatric and adult febrile, neutropenic cancer patients with FQREC bacteremia admitted to cancer centers in Europe, North America, and the Middle East and other hospitalized surgical patients with FQREC clinical infections in Germany	60	PFGE and RAPD	PFGE: dice coefficient of similarity ≥90%; RAPD genotypes: ≤2 band difference	Center, year and month of isolation, and department for German hospital
Oethinger[33]	1998	Colonization and clinical infections in cancer patients with neutropenia secondary to cancer or cytotoxic therapy who received oral ofloxacin as prophylaxis in a hospital in Germany	46 (multiple isolates per patient)	PFGE and RAPD	PFGE: Dice coefficient of similarity ≥0.90; RAPD: ≤2 band difference	Time period
Park[34]	1998	Patients with leukemia and FQREC bacteremia who received ciprofloxacin as a regimen for selective gut decontamination in a stem cell transplantation center in Korea	28 (1 FQ susceptible)	Infrequent restriction site PCR	Not listed	None included in transmission claim
Pereira[35]	2007	Patients with ciprofloxacin-resistant *E. coli* UTIs from 17 Brazilian hospitals; 43% of patients with UTIs were outpatients	95	PFGE	Pfaller criteria[36]	Hospital site
Perrin[37]	1999	Patients with UTIs in 3 centers (1 hospital and 2 chronic care facilities) in France	4	PFGE	Note identical or similar (differ by 1–3 bands to determine whether isolates from same patient should be included; for comparison, state "no close relationships")	"Geographical area"
Pitout[5]	2008	Patients with ciprofloxacin-resistant Enterobacteriaceae infections from community clinics and hospitals within the Calgary health region	Not stated	PFGE	≥80%; possibly related 4–6 band difference; Tenover criteria[19]	None

Study	Year published	Patient population/site	No. of FQREC isolates for genotypic analysis	Type of molecular data	Criteria for molecular relatedness	Clinical data included
Reuter[38]	2005	FQREC bacteremia in patients with neutropenia and hematologic malignancies from a hospital in Germany	9	PFGE	Tenover criteria[19]	None included in transmission claim
Rhomberg[39]	2006	Patients with clinical infections from 10–16 US medical centers	38	Ribotyping followed by PFGE if needed to further discriminate	Tenover criteria[19]	Hospital site
Sheng[40]	2002	Inpatients and outpatients with clinical infections from various departments and wards throughout a hospital in Taiwan	23	PFGE	Not specified; “generally different PFGE patterns were noted, only a few revealed the same or similar patterns”	Time and place of occurrence
Shin[41]	2008	Patients with UTIs at a tertiary care hospital in Korea	8 qnrB positive *E. coli* analyzed	PFGE	≥80% similarity	Hospital floor and wards; specifics not noted
Tascini[42]	1999	Neutropenic patients on a hematologic ward with bacteremia in a hospital in Italy	19	PFGE and RAPD	PFGE and RAPD: S_{AB} values ≥90%	Time period (month vs year)
Uchida[43]	2009	Inpatients and outpatients with FQREC in Japan and 9 other Asian countries	219	PFGE	80% similarity	Location site
Uchida[44]	2010	FQREC isolates from patients at university hospitals, research centers, or their networking hospitals in 8 Asian countries	36 isolates of the common type (based on QRDR mutation patterns; common type was isolated from 3 or more countries)	PFGE	>70% similarity	Country
Usein[45]	2008	64 inpatients (5 children and 59 adults) and 23 outpatients with FQREC and symptoms of infection collected at a lab in Romania	51	PFGE	≥80%; possibly related 4–6 band difference; Tenover criteria[19]	Inpatient vs outpatient, adult vs child, “no epidemiological relationship found,” but specifics not given
van Belkum[46]	2001	Fecal colonization of patients admitted to a hematology unit in the Netherlands	17	RAPD and PFGE	RAPD: identical; PFGE: identical	Date of isolation, department
van Hees[6]	2011	Fecal colonization and infection site cultures of hematology patients receiving ciprofloxacin prophylaxis at a hospital in the Netherlands	37	Single-enzyme amplified fragment length polymorphism	≥95% similar	None
van kraaij[47]	1998	Fecal colonization and clinical infections of hematologic cancer patients at a hospital in the Netherlands	11	RAPD	Not listed	None
Vigil[48]	2009	Patients treated for MDR *E. coli* bacteremia (fluoroquinolone + at least 1 of the following: piperacillin, ceftazidime, or cefepime) at a cancer center in the United States	37	Repetitive sequence-based PCR	>95% similarity	None

Study	Year published	Patient population/site	No. of FQREC isolates for genotypic analysis	Type of molecular data	Criteria for molecular relatedness	Clinical data included
Vigil[49]	2010	Patients with a hematologic malignancy diagnosed with pyomyositis at a cancer center in the United States	6 (from 5 patients)	Broad clonal relationships determined by repetitive-element-based PCR profiling and MLST; PFGE used to resolve distinct chains	PFGE: >94% similarity	Date of diagnosis
Wagenlehner[50]	2000	Fecal colonization of patients receiving single-dose ciprofloxacin prophylaxis before urinary tract interventions at a urological department in Germany	39	PFGE	Note clonally identical pairs	None
Wang[51]	2008	FQREC infections in hospitalized pediatric patients in China	11 positive qnr *E. coli* strains	ERIC-PCR	<2 band difference	None
Xia[52]	2010	Hospitalized patients with diarrheal disease who had been treated with fluoroquinolones in China	36	PFGE	Not listed	None
Yoo[53]	1997	8 cases of *E. coli* bacteremia in patients with AML with neutropenia at a hospital in Korea	44 (8 “outbreak” + 36 other blood isolates)	PFGE and plasmid typing	≤6 band difference; Tenover criteria[19]	Hospital room location, time (3-month period)

NOTE. AML, acute myelocytic leukemia; ERIC-PCR, enterobacterial repetitive intergenic consensus polymerase chain reaction; FQ, fluoroquinolone; FQREC, fluoroquinolone-resistant *E. coli*; ICU, intensive care unit; MDR, multidrug resistant; MLST, multilocus sequence typing; PCR, polymerase chain reaction; PFGE, pulsed-field gel electrophoresis; QRDR, quinolone resistance determining regions; RAPD, random amplification of polymorphic DNA; S_{AB}, similarity coefficient; UTI, urinary tract infection.

TABLE 2

Cohort Study Results

		Isolates meeting criteria for patient-to-patient transmission	
Criteria	***n***	**No.**	**%**
12a–12f cluster	48		
PFGE		48	100
0 day[a]		2	4.2
7 day[b]		4	8.3
30 day[c]		10	20.8
16a–16c cluster	17		
PFGE		17	100
0 day[a]		3	17.6
7 day[b]		7	41.2
30 day[c]		10	58.8
Total samples	353		
PFGE		65	18.4
0 day[a]		5	1.4
7 day[b]		11	3.1
30 day[c]		20	5.7

NOTE. PFGE, pulsed-field gel electrophoresis.

[a] Genetically related isolates collected from subjects with temporal overlap of hospitalization of at least 1 day.

[b] Genetically related isolates collected from subjects with hospitalization dates separated by no more than 7 days.

[c] Genetically related isolates collected from subjects with hospitalization dates separated by no more than 30 days.