

Review

Wastewater drains: epidemiology and interventions in 23 carbapenem-resistant organism outbreaks

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Abstract

For many years, patient-area wastewater drains (ie, sink and shower drains) have been considered a potential source of bacterial pathogens that can be transmitted to patients. Recently, evolving genomic epidemiology tools combined with new insights into the ecology of wastewater drain (WWD) biofilm have provided new perspectives on the clinical relevance and hospital-associated infection (HAI) transmission risks related to these fixtures. To further clarify the clinical relevance of WWD-associated pathogen transmission, reports of outbreaks attributed to WWDs were selected for review that (1) investigated the outbreak epidemiology of WWD-associated transmission of bacterial pathogens, (2) utilized advanced microbiologic methods to establish clonality of outbreak pathogens and/or resistance genes, or (3) described interventions implemented to mitigate transmission of the outbreak pathogens from WWDs. These reports were collated, compared, and analyzed, and the results are presented here.

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Background

While the basic elements of healthcare-associated pathogen epidemiology and acquisition are well recognized, new insights into the complexity of transmission events, particularly with respect to carbapenem-resistant organisms (CROs), have begun to evolve dramatically. The first recognition of and validation of transmission clusters of gram-negative pathogens occurred as a result of the recognition of new resistance patterns in *Klebsiella pneumoniae* and *Acinetobacter baumannii*.¹ Improved species-specific typing technologies and, recently, the rapidly escalating use of sequencing have greatly facilitated what is now recognized as genomic epidemiology. Although water tap and/or aerator *Pseudomonas* outbreaks were recognized and remediated in the 1990s,¹ only when Berrouane et al² identified and corrected a whirlpool drain-associated *Pseudomonas* outbreak in 2000 did wastewater drain (WWD) systems begin to be evaluated as a potential source of environmental CRO transmission to patients. In 2003, Yomoda et al³ described the first reported outbreak associated with the transferrable *bla*(IMP) carbapenamase genes among *Pseudomonas* spp cultured from WWDs.³ Subsequently, 20 additional reports describing both the epidemiology and the mitigation initiatives were published; they serve as the basis for this review. All of these outbreaks were caused by CROs: *Pseudomonas* spp (n = 9), *K. pneumoniae* (n = 3), *K. oxytoca* (n = 3), *Escherichia coli* (n = 3), multiple CROs (n = 3), *Acinetobacter* (n = 1), and *Serratia* (n = 1).

Methods

The PubMed database (1990–2018) was searched using multiple text terms: “healthcare drains” and “wastewater drains” as well as “sink drains” and “shower drains” individually and combined with the terms “biofilm” and “outbreaks.” All studies that met the following inclusion criteria were analyzed and compared: (1) investigated the clinical outbreak epidemiology of WWD-associated transmission of CROs, (2) utilized advanced microbiologic methods to establish clonality of outbreak pathogens and/or resistance genes, or (3) described interventions implemented to mitigate transmission of the outbreak pathogens from WWDs.

Results

Demographic features

All 23 WWD-associated outbreaks included in this review occurred in acute-care hospitals and involved CROs. Among them, 16 outbreaks (69%) occurred in Europe, 3 outbreaks (13%) occurred in the United States, 3 outbreaks (13%) occurred in Australia, and 1 (4%) occurred in Canada. Also, 22 outbreaks (95%) were associated with high-risk patient settings. Furthermore, 19 outbreaks (87%) were related to a single CRO: *P. aeruginosa* (n = 9),^{3–5,11,15,17,19,21} *K. pneumoniae* (n = 3),^{6,7,12} *E. coli* (n = 3),^{18,20,22} *K. oxytoca* (n = 3),^{8,10,16} and a *Serratia* species (n = 1)¹³ (Table 1). In addition, 4 outbreaks (17%) involved between 2 and 6 species of CROs that shared the same resistance gene or genes.^{9,14,23,24} Of the 17 outbreaks reported since 2013, 6 (35%) were associated with metallo- β -lactamase-producing CROs: 5 occurred in Europe and 1 occurred in Australia.^{9,10,15,18,21,22} In the past 17 years, 8 reports have described WWD-associated outbreaks without evaluating mitigation intervention.^{25–32} In these studies, 1 or more CROs were identified as the outbreak strain (Obs). These outbreaks occurred in 8 intensive care

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Table 1. Epidemiologic Features of 26 Wastewater Drain-Associated Outbreaks

Reference	Outbreak Organism	Drain Type (% Positive)	Longest Interval Between Cases	Duration of Outbreak before first direct WWD Intervention	Initial Interventions (months)	Subsequent Interventions
2	MDR Pa	Whirlpool Drain 1/1 (100)	N/A	N/A	EIPI (1 mo)	1. Unit closed 2. Whirlpool system replaced
4	MDR Pa	Sinks 21/124 (17)	2 mo	12 mo	1. EIPI 2. Bleach sink decontamination protocol, "no lasting impact" (12 mo)	ICU closed, sinks removed, splash-minimizing sinks installed
5	MDR Ab	Sink	1 mo	9 mo	1. EIPI 2. Single sink replacement (9 mo)	Weekly bleach system flushing protocol using plugged sink flooding of waste pipes. Sinks negative for ObS at 6 mo. Subsequently, new sinks positive and 19 patients colonized
6	KPC	"Multiple patient sinks"	N/A	N/A	1. EIPI 2. Hydrogen peroxide vapor protocol (N/A)	Multiple environmental interventions
7	ESBL Kp	"Sink and surround"	6 mo	7 mo	BIPI (4 mo)	Sink systems replaced
8	ESBL Ko	Sinks 149/910 (16.4)	7 mo	6 mo	1. EIPI 2. Escalating bleach drain disinfection protocols (2) failed (20 mo)	1. Third protocol, thrice daily bleach decontamination decreased positive rate to 4.9%. Rate returned to baseline (16.4%) when compliance decreased. 2. Sink system replacement 3. Continued daily bleach protocol
9	3 MβL + species	Primarily shower drains also room sinks	10 mo	36 mo	1. EIPI 2. "Enhanced cleaning of all sinks and shower drains" 3. Mechanical "biofilm removal" 4. Double-strength phenolic disinfectant 5. Use of a "chlorine-based product" was ineffective (33 mo).	No intervention was effective.
10	MβL Ko	Sinks	4 mo	24 mo	1. EIPI 2. Sink removal 3. Hyperchlorination protocol (27 mo)	Sinks and portions of horizontal drain system replaced
11	MDR Pa	Sink and Showers	3 mo	80 mo	EIPI (80 mo)	EIPI decreased but did not eliminate the ObS
11	MDR Pa	Sink and Shower	4 mo	1 mo	BIPI (1 mo)	EIPI
12	MDR Kp with <i>bla</i> KPC-2 plasmid	Sink 4/19 (21)	13 mo	N/A	Sinks and traps replaced but relapsed colonization confirmed recurrent	None. Continued contamination of drains with ObS but no new cases over several months
13	<i>Serratia</i> , <i>Ec</i> with <i>bla</i> IMP-4 resistance gene	Sinks 11/11 (100)	12 mo	N/A	1. "Enhanced" sink cleaning with bleach. "Heavy growth was found a week later in the drains." 8/11 sinks were positive for ObS after 6 treatments.	1. Steam plunger tool "ineffective" over 24 mo 2. Sink replacement planned
14	Multiple sp. sharing resistance genes	Sinks 13/13 (100)	N/A	?	EIPI had no impact on incidence density.	Removal of all sink systems and installation of electronic "drain siphon" heating system

Table 1. (Continued)

Reference	Outbreak Organism	Drain Type (% Positive)	Longest Interval Between Cases	Duration of Outbreak before first direct WWD Intervention	Initial Interventions (months)	Subsequent Interventions
15	MβL Pa	44 sinks positive for ObS	20 mo	50 mo	BIPI (49 mo)	1. EIPI 2. Sink drain replacement decreased but did not eliminate outbreak strain.
16	ESBL Ko	Sinks 11/56 (20) Showers 1/19 (5.2)	11 mo	12 mo	EIPI (11 mo)	Sinks replaced
17	MDR Pa	Sink 4/4 (100%)	5 mo	7 mo	BIPI (10 mo)	1. EIPI 2. Sink drain systems replaced; 1 patient became colonized with ObS in 6 mo follow-up.
18	ESBL Ec	17 Sinks and “many” showers	4 mo	21 mo	EIPI revealed that all isolates were resistant to QAC (14 mo).	1. “Biofilm removal” 2. Daily bleach protocol decreased incidence of OS infection
19	MβL Pa	Sinks 12/12 (100)	7 mo	61 mo	Sink replacement but 3/11 recolonized “on average” 13 weeks later. Drains positive after 10 weeks of acetic acid treatment protocol	Weekly acetic acid treatment protocol continued but did not eliminate OSB contamination.
20	ESBL Ec	Sinks	N/A	1 mo	EIPI (3 mo)	1. ICU closed 2. Sinks replaced. “Increased incidence rate has decreased.”
21	MβL Pa	Sinks 11/24 (46)	40 mo	84 mo	1. EIPI (80 mo)	1. Sink drain replacement 2. Unit Closed and rebuilt
22	MβL Ec	Sink 1/1 (100)	N/A	< 1 mo	1. EIPI 2. Bleach treatment protocol (9 mo)	Single sink system replaced
23	Multiple species sharing resistance genes including MβL	Sinks 32/32 (100)	N/A	N/A	1. EIPI 2. After daily treatment with glucoprotamin for 4 mo. 9/32 (28%) remained positive.	Sink system replaced
24	2 strains of MDR in P-traps	Sink P-traps 149/437 (34)	24 mo	30 mo	All sinks replaced but recolonization with ObSs was confirmed.	1. Twice weekly bleach treatment 2. P-trap replacement for patient stay >7 days 3. Outcome: ongoing recontamination but no new patient acquisition for 36 mo.

NOTE. CRE, carbapenem-resistant Enterobacteriaceae; Ec, *Escherichia coli*; ESBL, extended-spectrum β-lactamase; Ko, *Klebsiella oxytoca*; Kp, *Klebsiella pneumoniae*; KPC, *Klebsiella pneumoniae* carbapenemase; MβL, metallo-β-lactamase; MDR, multidrug resistant; Ab, *Acinetobacter*; N/A, not available; ObS, outbreak strain; Pa, *Pseudomonas aeruginosa*; WWD, wastewater drains; BIPI, basic infection prevention interventions; CHG, chlorhexidine gluconate; EIPI, enhanced infection prevention interventions; N/A, not available; ObS, outbreak strain; QAC, quaternary ammonium compound.

units (ICUs) and 1 burn treatment unit and were reported in Europe (n = 5), Australia (n = 1), Thailand (n = 1), and Japan (n = 1).

Aside from the 5 studies in which only 1 sink drain was cultured, 12 studies reported culturing samples from between 1 and 910 WWDs as part of a preintervention outbreak analysis (Table 1).^{3,5,11,22} The proportion of positive WWDs ranged between 16% and 100% (mean, 60%). As part of evaluations prior to performing WWD cultures, 15 sites performed several hundred environmental cultures of dry patient-zone surfaces, including sink bowls and sink surrounds. The results of these cultures revealed that these sites were rarely positive for ObS organisms (<1%). In each of the 9 studies identifying *Pseudomonas* as the outbreak CRO, sink water taps were excluded as a source of the

outbreak. Various systems for genotypic testing were employed to define clonality in 13 studies (56%), and in 10 studies, pulse-field gel electrophoresis was used (primarily before 2013).

Epidemiologic features

Of the 23 outbreaks reviewed here, 3 (13%) were relatively short (ie, 1, 4, and 6 months in duration), which precluded the evaluation of their timelines. The study durations of the other 20 outbreaks ranged from 7 to 96 months (mean 37 months), with 14 (70%) lasting 2 or more years. A total of 344 patients (range, 1–84; median, 15 per study) were either colonized or infected with outbreak strains. (Patients identified by screening

cultures were not included.) In the studies reviewed, the actual number of clinical cases identified per month was typically quite low ($n = 1-10$; median <1). Indeed, no clinical cases were identified during 578 of the 850 months evaluated (68%). The longest interval between cases ranged from 1 to 40 months (mean, 10.2 months) in the 17 studies from which such information could be obtained (Table 1). The attributable mortality rate reported in 9 studies ranged from 0 to 50% (mean, 33%).

Interventions to mitigate outbreaks

The duration of the outbreaks before implementation of initial mitigation activities directed at WWDs was often substantial in the 21 studies that allowed for such a determination (Table 1). While the interval was only 1 month in 3 studies,^{11,20,22} it was between 6 and 12 months in 7 studies^{4-8,16,17} (mean, 8.8 months) and between 24 and 84 months in an additional 7 studies (mean, 53 months).^{9-11,15,19,21,24} Once an outbreak was recognized, 19 sites implemented multiple enhanced infection prevention interventions such as increased hand hygiene education, hand hygiene monitoring, reinforced contact precautions, cohorting infected and colonized patients, cohorting staff caring for such patients, and increased emphasis on daily as well as terminal cleaning practices. Also, 10 sites initiated screening protocols and isolation of asymptomatic Obs gastrointestinal carriers. Although some reports may have included cases identified retrospectively, 2 studies were primarily retrospective, implementing interventions only after an Obs was cultured from 1 or more WWDs.^{11,21}

All sites utilized a wide range of focused WWD mitigation interventions with or without the enhanced infection prevention interventions following recognition of WWD colonization by Obs organisms (Table 1). Such initial interventions included liquid disinfectant-based protocols using bleach,^{9,13,22} acetic acid protocols,^{9,19} "double-strength phenolic disinfection,"⁹ a glucoprotamin disinfection protocol,²³ the use of a "steam plunger tool,"¹³ and a hydrogen peroxide vapor protocol.²³ Furthermore, 5 studies described environmental structural interventions as part of the initial outbreak control activities, including single sink replacement^{5,10,12} and multiple sink system replacements.^{19,24}

All 21 sites with outbreaks that were studied for >1 month documented ongoing patient infection or colonization with the Obs organism(s) and/or persistent WWD colonization with the Obs pathogen(s) despite initial remediation activities. In 7 sites, the failure of these interventions led to subsequent interventions including a bleach-based WWD system flooding protocol,^{5,9,18,24} multiple environmental interventions,⁶ a thrice daily bleach treatment protocol,¹⁸ "biofilm removal," and a daily bleach treatment protocol (Table 1).¹⁹ While not quantified, 7 studies noted that the design of sinks and sink areas might have had a role in outbreak perpetuation.^{9,11,13,15,16,24} Also, 14 sites described WWD system replacement, usually of multiple sinks,^{3,4,6-8,13-16,20-24} as part of subsequent interventions. Overall, 16 of 21 reports (76%) did not describe culture-based WWD evaluation of the effectiveness of these apparently final interventions.^{3,4,6-8,10,11,13,14,16,17,20-23} Although 3 reports described a partial response to interventions,^{15,18,24} 6 studies described objectively confirmed failure of final mitigation activities.^{5,9,11,15,19,24} Of the studies evaluating a response to mitigation activities, only 4 sites used culture-based assessment of the effectiveness of sink system replacement, and all 4

confirmed ongoing or recurrent WWD colonization with Obs organisms.^{5,13,15,24}

Discussion

Wastewater drain-associated CRO outbreaks

All 23 WWD-associated outbreaks were attributed to 1 or more CROs and occurred in acute-care hospitals. While a recent study has documented pathogenic yeast sink drain colonization and contamination of surrounding surfaces,³³ no WWD-associated outbreaks have been attributed to yeasts, fungi, or gram-positive organisms. Essentially, all outbreaks that fit the inclusion criteria for this report occurred in hospital areas where substantial populations of immunologically compromised patients were cared for, and these outbreaks were attributed to many different species of CRO. Only 1 rapidly contained outbreak, related to a single colonized sink, occurred on a general medical ward.²² As would be expected from the known global distribution of CROs, outbreaks associated with pathogens exhibiting metallo- β -lactamase genes were reported in Europe ($n = 6$) and Australia ($n = 1$) but not North America. While the level of sink colonization with Obs organisms ranged widely (16%–100%), the majority of implicated WWDs (61%) were Obs positive, and 5 of the sites that cultured >1 sink found all WWDs colonized with Obs pathogens.^{13,14,17,19,23} The review analysis revealed a very wide range in the duration of outbreaks (1–91 months), with 61% outbreaks lasting 2 or more years. Generally, the shorter outbreaks reflected a combination of rapid recognition of WWD Obs colonization and a limited period of follow-up after implementing initial mitigation interventions. While it is possible that they were incompletely characterized, some of the longer-duration outbreaks appeared to reflect relatively late identification of a WWD source of the outbreak⁸ and/or partial use of retrospective data collation.^{11,21} Although not specifically described, it is likely that the very low incidence density of clinical cases, the typically long interval between cases, and the 68% of months without documented Obs infection or colonization both adversely impacted the recognition of an ongoing outbreak and confounded the assessment of possible responses to initial as well as subsequent mitigation interventions. Attributable mortality ranged widely from 0 to 50%, but it clustered near the mean of 33% in 6 of the 9 studies reporting this outcome.

Initial interventions reflected a wide range of traditional infection prevention activities that were specifically enhanced once an outbreak was suspected and prior to identification of WWDs having an ongoing role in the outbreak. Once WWD Obs colonization was identified, all sites implemented a wide range of liquid disinfection protocols while continuing enhanced infection prevention activities. Daily bleach protocols as part of initial mitigation activities were specifically identified as being ineffective in 9 reports.^{4,5,8,9,13,22} While Lowe et al noted that increasing a daily bleach protocol to thrice daily decreased Obs-positive drain cultures from 16.4% of sinks to 4.9%, an interruption in protocol compliance resulted in the sink colonization rate returning to 16.4%.⁸ Other WWD disinfection protocols found to be ineffective included a "phenolic disinfectant,"⁹ an acetic acid protocol,¹⁹ a glucoprotamin protocol,²³ and the addition of a vaporized hydrogen peroxide system protocol to other interventions.⁵²

Concomitantly or more usually in the setting of the limited effectiveness of enhanced infection prevention interventions and

disinfectant-based protocols, many sites initiated WWD replacement activities. Although the removal of a single implicated sink was done in 2 studies, ongoing WWD colonization led to a more complex bleach protocol being implemented at 1 site, which was incompletely effective,⁵ and additional sink system replacements at the other site, which was incompletely evaluated.¹⁰ Replacement of multiple sinks was planned but not evaluated in 1 report.²⁶ Although all sinks were replaced as an initial intervention in the recent report by Gbaguidi-Haore et al,²⁴ colonization of the P-trap systems persisted. As a result, twice weekly bleach treatments of all sinks and P-trap replacement for sinks were associated with patient stays of >7 days. While no new clinical cases were identified during 36 months of follow-up, Obs WWD colonization continued to be documented.²⁴ Unfortunately, none of the 9 sites that initiated multiple sink system replacements described the direct objective evaluation of the impact of the intervention on WWD colonization over time.^{7,8,10,12,16,21–23} An additional report noted that “no new cases were documented following sink system replacement,” but the duration of follow-up was not described.¹² Five reports specifically noted the ineffectiveness or incomplete effectiveness of WWD system replacement.^{5,13,15,19,24}

The primary limitation of this analysis of WWD-associated outbreaks relates to variations in the degree to which the epidemiology and mitigation interventions were evaluated and/or described. Despite this limitation, the similarities between the reports, particularly related to the finding of high frequencies of WWD Obs colonization (mean, 60%), the very low incidence density of cases (<1 per month), the typically long interval between cases with 68% of months having no identified cases, as well as the documentation of multilevel mitigation failures are notable and highly consistent in these reports.

The epidemiology, but not the mitigation interventions, was described in 9 additional reports since 2000.^{25–32} All of these 9 studies were associated with CROs in ICUs, and 66% of the hospitals were located in Europe. Taken together, these 9 reports support the epidemiologic aspects of the 23 studies reviewed overall.

An additional limitation of this analysis is the fact that only 26% of studies utilized cultures to evaluate subsequent interventions on Obs contamination of the implicated WWDs. Despite this limitation, the well-documented failure of multiple interventions, including drain system replacement, is consistent with our evolving understanding of the epidemiology of the WWD-biofilm-associated microbiome.^{34,35} Notably, the wastewater system laboratory work described by Kotay et al³⁵ defined the resilience of horizontal drain system biofilm colonization and its ability to continuously support CRO-infected sink drain systems as a result of rapid regrowth of drain biofilm following mechanical biofilm removal. In this context, in the 9 reports discussed above, sink replacement failed to successfully mitigate ongoing WWD Obs colonization and/or transmission.^{5,9,10,12–15,18,19}

These reports were also limited by an inability to quantify rates of actual patient acquisition because none of the study sites utilized or reported CRO screening to define a direct relationship between individual WWD cultures and clinical cultures. While it is likely that many of the colonized WWDs did not continually transmit Obs organisms to patients directly, or more likely, indirectly,³⁶ the consistent and substantial maximal interval between Obs clinical cases (mean, 10.2 months) provides strong support for there being an ongoing causal relationship between contaminated WWDs and ongoing patient acquisition of CROs. In addition, the nature of these reports and their potential for

selection bias limits the direct use of these studies to estimate how frequently WWD-associated outbreaks are occurring in acute-care hospitals. While it is possible that publication bias could overestimate the true incidence of outbreaks, Roux et al³⁷ documented widespread endemic CRO WWD colonization in 2013. In the only multisite evaluation of ICU WWD CRO colonization published to date, they confirmed CRO contamination in 89 sinks in the ICUs of 9 hospitals in France despite the fact that all sites were using various liquid-disinfectant protocols to suppress pathogen colonization.³⁷ Despite ongoing mitigation activities, colonization with CROs, primarily *K. pneumoniae* and *Enterobacter cloacae*, was found in 0 to 81% of sink drains tested (mean, 31%).³⁷ While additional studies of this type are needed, the findings of Roux et al support the possibility that WWD CRO-related outbreaks are more frequent than is currently recognized, particularly in high-risk patient settings. An additional factor that may be leading to the underrecognition of WWD CRO transmission is the high level of clonality of carbapenem-resistant *K. pneumoniae* in North America, where 70% have similar antibiograms belonging to sequence type 258.³⁸ Indeed, in the United States, the only recognized outbreak of environmentally transmitted KPC was initially recognized because of the uncommon finding of clostrix resistance, which led to the recognition of additional cases over the ensuing weeks on the same hematology oncology unit.⁶

Drain-associated biofilm and the genetic transfer of resistance

Almost a decade ago, as genomic epidemiology became widely available, clusters of gram-negative healthcare-associated infections were found to have shared resistance plasmids not explained by patient-to-patient transmission,³⁹ which led to further studies of WWD biofilms.^{40–44} It is now recognized that both vertical sink and shower drains as well as horizontal drain system pipes contain complex biofilm-associated microbiomes often contain CROs as well as a wide range of environmental commensal organisms.^{40–44} Research has now confirmed the occurrence of plasmid-based intra- and interspecies carbapenamase exchange between WWD biofilm-associated pathogens. In 2008, Tokatli-dou et al²⁶ documented the clonal spread of a novel *bla*(VIM-12) metallo- β -lactamase gene among *K. pneumoniae*.²⁶ In 2013, Tofteland et al¹² confirmed the interspecies spread of a *bla*_{KPC-2} plasmid in WWD-outbreak-associated pathogens. More recently, Wendel et al⁴⁵ found that biofilm-associated Enterobacteriaceae and nonfermenters shared metallo- β -lactamase GIM-1 plasmids. Subsequently, Michalikova et al⁴⁶ quantified transferrable antibiotic resistance in 39.4% of 137 randomly selected environmental *Pseudomonas* spp, *Enterobacter* spp, and *Klebsiella* ssp, finding that the most frequent plasma-mediated antibiotic resistance was present in *E. coli* (89%) followed by *Pseudomonas* spp (41%). In studies by Khariman et al,³⁴ multiple variables were evaluated that impacted the horizontal transfer of carbapenamase plasmids; plasmid content, temperature, substrate as well as strain variables substantially impacted such transmission. Most recently, Stoesser et al⁴⁷ found that 14 of 15 ICU room WWDs (93%) contained multiple CRO species that showed *bla* KPCs. Although transmission of CROs from WWDs represents only 1 of several hospital water-system reservoirs from which pathogens are disseminated,^{40–45} studies over the past 8 years have begun to clarify the bioepidemiology of these critically important components of patient-care WWD environments.

- Extended waste water drains (WWD) associated carbapenem resistant organisms (CRO) outbreaks have been increasingly recognized during the past 10 years in 12 countries on 4 continents.
- Almost all outbreaks occurred in intensive care and hematology/oncology special treatment units.
- Low incidence density of clinical cases and the frequently long intervals between cases adversely impacted outbreak recognition as well as evaluation of mitigation interventions.
- In these outbreak settings most WWDs were colonized with outbreak strain organisms.
- Drain disinfection treatment protocols had limited, if any, lasting impact on CRO drain system colonization.
- Sink drain system replacement alone would appear to have a limited, if any, lasting impact on CRO colonization as a result of biofilm re-colonization from more distal components of the drain system.
- Sink drain biofilm colonizing gram-negative bacteria are readily capable of both intra-species as well as inter-species transfer of many forms of gene mediated antibiotic resistance.

Fig. 1. Summary of wastewater drain carbapenem-resistant organism outbreak characteristics.

As summarized in Figure 1, our rapidly evolving understanding of the role of patient-zone WWDs in CRO transmission clarifies the urgent need for further research to qualify and quantify the role of wet biofilm in healthcare environments with respect to both the epidemiology of CROs as well as other Enterobacteriaceae, yeasts, and possibly fungi in a range of healthcare settings. Given the finding that multiple, apparently initially successful, WWD mitigation interventions were later found to be substantially or completely unsuccessful (often after a delay of many months), an assessment of the effectiveness of interventions to mitigate drain biofilm-associated pathogen contamination and transmission might initially be best evaluated by mock-up sink laboratory investigations such as those described by Kotay et al.³⁵ Additionally, the likely role of healthcare worker hands in the transmission of WWD CROs³⁶ and the documentation that *bla*-KPC-carrying *K. pneumonia* was cultivable on plastic and steel for up to 5–6 days, and thereafter viable but noncultivable,⁴⁸ support the need for studies to clarify the role of intermediate fomites in CRO outbreaks. However, the potential role of WWD colonization in CRO outbreaks is not widely recognized. A review published in May 2017 providing detailed recommendations for interventions to optimize recognition and control of CRO stated, “Carbapenem-resistant *Enterobacteriaceae* have been found infrequently in the environment of infected or colonized patients,”^{49(p.586)} but these researchers failed to consider the possible role of WWDs in CRO acquisition. Although none of the 6 CRO outbreaks reported in 2017 investigated WWDs as a possible source for ongoing patient acquisition,^{50–56} greater awareness of the potential for WWDs to perpetuate CRO dissemination may lead to the routine evaluation of these sites in all CRO outbreak investigations in the future.

Clearly, further studies are needed to clarify and quantify the dynamics of WWD biofilm plasmid exchange because it is now clear that, as Wendel noted, “Drains may serve as a melting pot for horizontal gene transfer, for dissemination into new species, and as a reservoir to perpetuate future hospital outbreaks.”^{45(p.3605)}

While developing effective interventions to prevent transmission of WWD pathogens to patients is of immediate importance, it will be equally critical to concomitantly evaluate and mitigate WWD biofilm-colonizing plasmid-mediated antimicrobial resistance.

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