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Duodenoscope-associated infection prevention: A call for evidence-based decision making

Authors
Cori L. Ofstead[1], Brandy L. Buro[1], Krystina M. Hopkins[1], John E. Eiland[1], Harry P. Wetzler[1], David R. Lichtenstein[2]

Institutions
1 Ofstead & Associates, Inc., St. Paul, Minnesota, United States
2 Boston University Medical Center, Boston, Massachusetts, United States

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Corresponding author
Cori L. Ofstead, MSPH, President and CEO, Ofstead & Associates, Inc., 1360 Energy Park Drive, Suite 300, Saint Paul, MN 55108, United States
Fax: +1-651-647-6287
cori@ofsteadinsights.com

ABSTRACT

Background Recent outbreaks of duodenoscope-associated multidrug-resistant organisms (MDROs) have brought attention to the infection risk from procedures performed with duodenoscopes. Prior to these MDRO outbreaks, procedures with duodenoscopes were considered safe and low risk for exogenous infection transmission, provided they were performed in strict accordance with manufacturer instructions for use and multisociety reprocessing guidelines. The attention and efforts of the scientific community, regulatory agencies, and the device industry have deepened our understanding of factors responsible for suboptimal outcomes. These include instrument design, reprocessing practices, and surveillance strategies for detecting patient and instrument colonization. Various investigations have made it clear that current reprocessing methods fail to consistently deliver a pathogen-free instrument. The magnitude of infection transmission has been underreported due to several factors. These include the types of organisms responsible for infection, clinical signs presenting in sites distant from ERCP inoculation, and long latency from the time of acquisition to infection. Healthcare providers remain hampered by the ill-defined infectious risk innate to the current instrument design, contradictory information and guidance, and limited evidence-based interventions or reprocessing modifications that reduce risk. Therefore, the objectives of this narrative review included identifying outbreaks described in the peer-reviewed literature and comparing the findings with infections reported elsewhere. Search strategies included accessing peer-reviewed articles, governmental databases, abstracts for scientific conferences, and media reports describing outbreaks. This review summarizes current knowledge, highlights gaps in traditional sources of evidence, and explores opportunities to improve our understanding of actual risk and evidence-based approaches to mitigate risk.

Evolution of endoscopy-associated infection risk estimates

Original risk estimates

For many years, clinicians and policymakers believed endoscopy-associated infections were extremely rare. This belief was bolstered when a 1993 position paper by the American Society for Gastrointestinal Endoscopy estimated that infections associated with gastrointestinal endoscopy occurred in 1 in 1.8 million procedures [1] and other guidelines repeated this risk estimate [2 – 5].

Infection attack rates are calculated by identifying all exposed patients (denominator) and actively assessing them to determine the number infected or colonized (numerator) (▶ **Fig. 1**). However, the oft-repeated infection risk estimate was calculated using a numerator of 28 upper and lower gastrointestinal endoscopy cases, including endoscopic retrograde cholangiopancreatography (ERCP), derived from a 1993 literature review by Spach et al. [6]. and a denominator of 40 million,

$$\frac{\text{Number of exposed patients who became infected or colonized}}{\text{Total number of exposed patients}} = \text{Infection attack rate}$$

▶ **Fig. 1** Infection attack rate equation.

which was a "guesstimate" of the United States procedural volume in 1988 to 1992 [1]. Spach et al. cautioned against using their data to calculate infection risk and stated, "These recognized and reported cases, however, probably represent a minority of all infections transmitted by endoscopy, because they were primarily due to easily recognized bacterial infections characterized by short incubation periods and often occurring in large or unusual clusters." [6]. They concluded "Given the above limitations and lack of prospective studies, the true incidence of infections transmitted by endoscopy is impossible to determine" and recommended that prospective studies include monitoring patients for clinical disease and positive cultures following endoscopy [6].

Outbreaks following ERCP are often detected only because multidrug-resistant organisms (MDRO) attract the attention of clinicians and infection preventionists. Recognition of other infections may be limited by pitfalls that adversely impact detection, including the following issues that are described in this article:

- A failure to detect asymptomatic colonization due to a lack of routine post-ERCP screening cultures;
- Long lag times between procedures and the appearance of clinical infections;
- Remote infection sites in the body that are not recognized as ERCP-related; and
- The transmission of bacteria that are typically endogenous gut flora (assumed to have originated in the infected patient).

Although the inaccuracy of endoscopy-associated infection risk estimates was described in 2013 [7], the risk continues to be characterized as less than one in a million or "extremely rare" [8–10] without any substantiating evidence. The concept of negligible risk has been used to support clinical decision making (e.g., declining to notify or test exposed patients), even when serious reprocessing breaches were identified [11–13]. Additionally, incomplete risk estimates for endoscopic procedures adversely impact the informed consent process and can leave patients with a false sense of security. Thus, there remains a need to prospectively monitor large numbers of endoscopy patients to accurately determine attack rates.

Ill-defined infection risk estimates may jeopardize patient safety. Therefore, the objectives of this narrative review include identifying outbreaks and reprocessing failures described in peer-reviewed literature and comparing the findings with evidence reported elsewhere. Traditional search strategies were used to identify articles indexed in PubMed that described infections, reprocessing breaches, and residual contamination on duodenoscopes. In addition, researchers reviewed evidence of infections and reprocessing failures described in governmental databases and reports, abstracts for scientific conferences, and media reports describing outbreaks.

Risks based on retrospective analyses

Recent retrospective studies have documented higher rates of post-endoscopy infection, which provide a starkly different view of infection risk. Additionally, advances in genetic testing and molecular technology now allow investigators to detect outbreak organisms and link them directly to contaminated endoscopes [14].

Responding to concerns about historic infection risk estimate accuracy [15] and a safety communication from the US Food and Drug Administration (FDA) regarding pathogen transmission associated with ERCP [16], Wang et al. used claims data to determine the risk of endoscopy-associated infections requiring emergency care or hospitalization within seven days of procedures [17]. The researchers hypothesized that facility-related factors may contribute to post-endoscopy infections. They reviewed records for 2,347,894 colonoscopy, gastroscopy, bronchoscopy, and cystoscopy procedures in ambulatory surgery centers (ASCs) in six states [17]. The overall infection risk varied by procedure type and was far higher than previously asserted (1.1, 3.0, and 15.6 per 1,000 for screening colonoscopy, esophagogastroduodenoscopy, and bronchoscopy, respectively) [17]. The risk differed by setting, with serious infections transmitted to more than 10% of patients in certain ASCs [17]. This demonstrated that endoscopy-associated infections were not "very rare" (defined by the World Health Organization [WHO] as <1/10,000 patients) or even "rare" (<1/1,000 patients) [18], even for gastrointestinal endoscopes lacking elevator mechanisms.

There is a paucity of data from large multisite studies on infection risk for patients who have undergone ERCP. Loor et al. analyzed surveillance data to determine the impact of pre-operative ERCP on cholecystectomy surgical site infection (SSI) risk [19]. Patients undergoing pre-operative ERCP had more than double the SSI rate (4.1% vs 1.8%), with more resistant pathogens (1.1% vs 0.2%) compared to those without pre-operative ERCP [19]. This suggests pathogen transmission during ERCP may remain undetected until later invasive procedures. The study was conducted in an institution that had previously found 60% of patient-ready endoscopes harbored bacteria (including gram-negative organisms linked to contaminated AER rinse water) despite adherence to reprocessing guidelines [20]. Researchers from that hospital subsequently described the transmission of an MDRO from a patient with a pre-existing infection to a gastroscope that harbored the pathogen through 12 reprocessing cycles and procedures involving nine other patients [21]. These studies established that repeated cycles of reprocessing in that facility did not remove potential pathogens from endoscopes, and thus it is possible that the post-ERCP SSIs reported by Loor et al. could have been transmitted by contaminated duodenoscopes.

Risk based on outbreaks reported in peer-reviewed journals

When attack rates were calculated using data from 15 duodenoscope-associated outbreaks, the lowest rate was 6 %, and attack rates were ≥ 20 % in nine outbreaks (▶ **Table 1**). Only three manuscripts explicitly reported attack rates, which ranged from 14 % to 41 % [22 – 24]. In five manuscripts, investigators documented secondary transmission to close contacts of ERCP patients and included these in the total number of infections. Sometimes the number of exposed patients was not reported, or exposed patients were not notified or tested (▶ **Table 1**). Rectal culture sensitivity is uncertain and may underestimate transmission from a contaminated endoscope. Together, these factors limit the ability to calculate accurate attack rates.

Peer-reviewed literature is often considered to be the definitive source of scientific evidence. However, the information about duodenoscope-associated outbreaks in journals was often incomplete or contradicted by evidence found elsewhere, such as FDA adverse event (AE) (MAUDE) reports, Centers for Disease Control and Prevention (CDC) investigations, and health department inspections. ▶ **Table 2** provides additional details about four outbreaks described in peer-reviewed articles included in ▶ **Table 1**. Different sources of information often reported contradictory numbers of affected patients and infection rates for the same outbreak (e. g., Illinois: 26.5 % [25] to 46.0 % [26]). There was poor alignment regarding other aspects of the outbreaks, including the number of duodenoscopes involved, pathogens found, and the presence of reprocessing breaches (▶ **Table 2**).

Infections reported to federal and state agencies

In 2017 – 2019, numerous reports of breaches and infections attributed to contaminated duodenoscopes were submitted to the FDA (▶ **Table 3**). MAUDE reports often provide information about microbial culture results, device damage or malfunctions, affected patients, reprocessing breaches, and endoscope maintenance issues. For example, in 2019, a series of reports described 32 ERCP patients infected with vancomycin- and carbapenem-resistant organisms in one institution since 2013, including 12 cases and one death in 2018. Serious reprocessing breaches were identified by the manufacturer, including problems with point-of-care precleaning, delayed reprocessing, manual cleaning, irrigation systems, handling, and transport [27, 28]. Despite these reported breaches, the reports indicated the state health department investigated and observed "no abnormalities" [27]. This outbreak has not been published in peer-reviewed literature or news media, nor has it been factored into infection risk estimates and trends. This example and our review of infections reported to federal and state agencies strongly suggest that infections are underreported.

Root cause of duodenoscope-associated infections

Pathogen, procedural, and patient risk factors

ERCP-related infections develop as a result of a complex interplay between bacterial pathogens, procedural factors, and underlying pancreaticobiliary (PB) anatomy. Duodenoscopes are exposed to normal flora and potential pathogens during passage through the oral cavity, esophagus, and duodenum, and the risk of endogenous transmission has long been recognized [3, 14]. These bacteria, which are *endogenous,* can be introduced into the PB tree during ERCP, leading to a spectrum of infectious complications ranging from transient bacteremia to cholecystitis, cholangitis, and infected pancreatic fluid collections (e. g., pseudocyst, walled-off pancreatic necrosis or cystic neoplasm) [29]. Transient bacteremia occurs in up to 15 % of diagnostic and 28 % of therapeutic ERCP procedures, but infrequently progresses to sepsis among immunocompetent patients [30 – 33]. Although antibiotic prophylaxis has been shown to reduce the incidence of bacteremia associated with ERCP, pre-procedure antibiotic prophylaxis has not been shown to prevent cholangitis [31, 32].

PB infectious complications typically occur as a result of instrumentation or contrast injection into an incompletely drained PB tree [29]. Other risk factors may include underlying immunocompromised state. Bacterial contaminants already present on a "patient-ready" duodenoscope – termed *exogenous* pathogens – can produce a similar range of infectious PB complications as well as intestinal colonization that can persist or lead to remote sites of infection in the urinary tract, pulmonary tree or bloodstream up to months after the initial ERCP [25].

Exogenous flora and reprocessing effectiveness

Given the exposure of reusable duodenoscopes to blood, gastric secretions, enteric microbiota, and potential pathogens, effective reprocessing is essential to remove soil and bioburden and prevent the transmission of exogenous pathogens, including MDROs. Although manual cleaning and high-level disinfection (HLD) should theoretically eliminate all microbes except resilient bacterial spores, recent studies have demonstrated that duodenoscope reprocessing is not reliably effective (▶ **Table 4**) [34 – 38].

Reprocessing failures may occur in part due to the complex distal end of duodenoscopes, which have elevator mechanisms. The elevator, open wires, and channels are exposed to bioburden during procedures, and the instrument design of conventional models does not allow disassembly or direct visualization during cleaning. Numerous infections have been attributed to pathogens detected on elevator mechanisms, wires, or channels [39 – 42]. However, outbreak strains have also been detected in other duodenoscope components including the suction-biopsy channel [22, 42 – 44].

In light of these reprocessing failures and outbreaks linked to contaminated duodenoscopes, the FDA recommended in 2015 that institutions adopt enhanced methods of reprocessing, such as double HLD or sterilization [45]. Since then, re-

▶ **Table 1** Duodenoscope-associated infections reported in peer-reviewed journal articles.

Source[1]	Location	Pathogens isolated from patients	Infected patients	Exposed to scopes	Post-exposure testing	Reported attack rate	Calculated attack rate	
							Rate[2]	Confidence[3]
Rauwers 2019 [43]	Utrecht, Netherlands	MDR *Klebsiella pneumoniae*	27[4]	102	81 (79.4 %)	35 % scope A 29 % scope B	32.5 % [26/80]	Medium
Bourigault 2018 [97]	Nantes, France	CR *K. pneumoniae* (OXA-48)	5	61	41 (67.2 %)	NR	12.2 % [5/41]	Medium
Shenoy 2018 [98]	Boston, MA, USA	*mcr*-1 *K. pneumoniae*	1[5]	5	5 (100 %)	NR	20 % [1/5]	High
Robertson 2017 [99]	Glasgow, Scotland	*Salmonella enteritidis*	4[6]	9	9 (100 %)	NR	37.5 % [3/8]	High
Kim 2016 [23]	Los Angeles, CA, USA	CR *K. pneumoniae* ($bla_{OXA-232}$)	15	115	104 (90.4 %)	14.4 %	14.4 % [15/104]	Medium
Kola 2015 [100]	Berlin, Germany	CR *K. pneumoniae* (OXA-48)	12 [6 ERCP]	26	23 (88.5 %)	NR	26.1 % [6/23]	Medium
Marsh 2015 [101]	Pittsburgh, PA, USA	CR *K. pneumoniae* ESBL *K. pneumoniae*	34 [12 ERCP]	UNK	UNK	NR	–	–
Wendorf 2015 [96]	Seattle, WA, USA	AmpC *E. coli* CR *E. coli*	35	UNK	49	NR	–	–
Verfaillie 2015 [39]	Rotterdam, Netherlands	VIM-2 *P. aeruginosa*	30 [22 ERCP]	251	UNK	NR	–	–
Qiu 2015 [102]	Hangzhou, China	*P. aeruginosa*	3	3	3 (100 %)	NR	100 % [3/3]	High
Smith 2015 [72]	Milwaukee, WI, USA	NDM-1 *E. coli*	4[7]	27	18 (66.7 %)	NR	23.5 % [4/17]	Medium
Epstein 2014 [25]	Chicago, IL, USA	NDM, CR *E. coli*	39 [35 ERCP]	226	102 (45.1 %)	NR	26.5 % [27/102]	Low
Alrabaa 2013 [40]	Tampa, FL, USA	CR *K. pneumoniae*	10	51	46 (90.2 %)	NR	21.7 % [10/46]	Medium
Carbonne 2010 [22]	Paris, France	CR *K. pneumoniae* (KPC-2)	12 [7 ERCP][5]	17	16 (94.1 %)	41 %	43.8 % [7/16]	Medium
Aumeran 2010 [44]	Clermont-Ferrand, France	ESBL *K. pneumoniae*	16	253	253 (100 %)	NR	6.3 % [16/253]	High

MDR, multidrug resistant; NR, not reported in source article; CR, carbapenem-resistant; NDM: New Delhi beta-lactamase producing; *mcr-1*, Mobile colistin resistance gene 1; AmpC, cefoxitin/third-generation cephalosporin resistant, carbapenem sensitive; ESBL, extended-spectrum beta-lactamase producing; VIM-2, Verona integron-borne metallo-beta-lactamase producing

[1] When an outbreak has multiple published sources, only the first publication was included in this table.

[2] Attack rates were calculated by dividing the number of outbreak patients with duodenoscope exposure by the number of patients with duodenoscope exposure who were subsequently tested. Patients identified by investigators as index or source patients were removed from the numerator and denominator for accuracy.

[3] Confidence ranked as follows: High: 100 % of exposed patients were tested; Medium: ≥ 66 % of exposed patients were tested; Low: < 66 % of exposed patients were tested.

[4] Number of infected patients includes an index patient identified by investigators.

[5] Investigators clearly identified the source patient as the individual who introduced the pathogen into the scope; we excluded the source patient from the number of patients infected during the outbreak.

[6] Investigators hypothesized—but did not confirm—that the index patient was also the source patient.

[7] Investigators identified a source patient but included this patient in the number of patients exposed and tested; we excluded the source patient from the number of patients infected and from the denominator in the attack rate calculation.

searchers have determined that double HLD is no more effective than single HLD [34 – 38], with double-HLD failure rates ranging from 2 % [38] to 44 % [37] (▶ **Table 4**). Although sterilization should theoretically be failproof, several researchers have reported microbial growth in samples from duodenoscopes following sterilization with ethylene oxide (23 % [36], 18 % [46]) and peracetic acid (2 %) [38] and from ureteroscopes following hydrogen peroxide gas sterilization (13 %) [47].

Similar reprocessing failures have been found with curvilinear array echoendoscopes (EUS), which also have an elevator mechanism. Chapman et al. performed 540 microbial cultures on 18 patient-ready EUS endoscopes and found 4.2 % were po-

▶ **Table 2** Comparison of evidence from multiple sources describing four duodenoscope-associated outbreaks.

Location [Pathogen]	Source	Source type	Case patients[1]	Exposed	Tested	Positive test	Attack rate (Positive/Tested)	Comments
Tampa General Hospital, Tampa, FL [CR *K. pneumoniae*]	Alrabaa 2013 [40]	Journal article	10	51	46	10	21.7 %[2] [10/46]	▪ Reprocessing breaches reported ▪ Bio-debris visible under elevator
	Sanderson 2010 [103]	APIC abstract	16 [9 ERCP]	51	46	9	19.6 %[2] [9/46]	▪ Endoscope contamination (*Escherichia coli*, *Pseudomonas*, *Serratia* spp.)
	Sanderson 2010 [104]	APIC presentation	14 total Site A: 7 Site B: 7	Site A: 51 Site B: 140	Site A: 22 Site B: 140	Site A: 7 Site B: 7	Site A: 31.8 %[2] [7/22] Site B: 5 % [7/140]	▪ Endoscope contamination (*Pseudomonas aeruginosa*, *Proteus mirabilis*, and *E. coli*) ▪ Secondary transmission to other hospitals was found
Advocate Lutheran General Hospital, Chicago, IL [NDM-producing CR *E. coli*]	Epstein 2014 [25]	Journal article	39 [35 ERCP]	226	102	27	26.5 %[2] [27/102]	▪ No reprocessing breaches reported, but IFU deviations are described
	Ray 2018 [90]	Journal article	31	UNK	UNK	UNK	–	▪ Secondary transmission to 10 patients at 6 other hospitals
	Frias 2014 [26]	CDC MMWR	44	91	50	23	46.0 % [23/50]	▪ No reprocessing breaches reported
	Epstein 2013 [41]	CDC Epi-Aid Trip Report	26 [23 ERCP]	96	45	17	37.8 % [17/45]	▪ Endoscope damage reported ▪ Inadequate hand hygiene and PPE
	CMS 2014 [105]	Statement of Deficiencies	38	243	114	38	33.3 %[2] [38/114]	▪ Reprocessing breaches reported
UCLA Medical Center, Los Angeles, CA [CR *K. pneumoniae*]	Kim 2016 [23]	Journal article	15	115	104	15	14.4 % [15/104]	▪ No reprocessing breaches reported
	Humphries 2017 [73]	Journal article	16[3]	179	150	8	5.3 %[2] [8/150]	▪ No reprocessing breaches reported
	Yang 2018 [106]	Journal article	16[3]	UNK	UNK	UNK	–	▪ Endoscopes and reprocessing practices were not evaluated
	UCLA 2015 [107]	Public statement	7	>100	UNK	UNK	–	▪ No reprocessing breaches reported
	Rubin 2015 [108]	FDA Panel presentation	14	179	149	6	4.0 %[2] [6/149]	▪ 3 deaths reported ▪ No reprocessing breaches reported
	CMS 2015 [109]	Statement of Deficiencies	UNK	UNK	UNK	UNK	–	▪ Reprocessing issues are described; Immediate Jeopardy declared ▪ No environmental cultures after outbreak

▶ **Table 2** (Continuation)

Location [Pathogen]	Source	Source type	Case patients[1]	Exposed	Tested	Positive test	Attack rate (Positive/Tested)	Comments
Virginia Mason Medical Center, Seattle, WA [CRE *E. coli* and AmpC *E. coli*]	Wendorf 2015 [96]	Journal article	35	UNK	49	UNK	–	▪ No reprocessing breaches reported ▪ Endoscope defects (7 of 8 scopes) ▪ Endoscope contamination (AmpC *E. coli* on 2 scopes)
	Ross 2015 [42]	Journal article	32	1149	UNK	UNK	–	▪ Endoscope defects (4 of 8 scopes) ▪ Endoscope contamination (AmpC *E. coli* on 4 scopes)
	Hunter 2014 [110]	CDC Epi-Aid Trip Report	9	UNK	UNK	UNK	–	▪ No reprocessing breaches reported, but IFU deviations described ▪ Endoscope defects (8 of 8 scopes)
	FDA 2014 [111, 112]	MAUDE reports	37	UNK	UNK	UNK	–	▪ 4 deaths reported
	CMS 2015 [113]	Statement of Deficiencies	39	1239	UNK	UNK	–	▪ Reprocessing breaches reported ▪ Outbreak detected during health department study ▪ Cited for failure to report outbreak to health department

CR: carbapenem-resistant; UNK: unknown; –: not reported or not calculated
[1] Number of case patients included individuals infected or colonized by the outbreak strain and may include patients that were not identified via a formal screening process. If outbreak investigators reported secondary transmission, the number of patients infected via ERCP is noted in brackets.
[2] Calculated by Ofstead.
[3] Outbreak investigators clearly identified the source patient as the individual who introduced the pathogen into the scope; we excluded the source patient from the number of patients infected during the outbreak.

sitive for gram-negative organisms [48]. Bartles et al. sampled 45 EUS and ERCP endoscopes 2,925 times and found microbial growth in 7.7 % overall, with growth detected in both the elevator mechanism and the channel [34]. Reprocessing effectiveness studies for other endoscope types reported that microbial growth was found on 35 % [49], 41 % [50], 47 % [51], 58 % [52], 60 % [20, 53], 64 % [54], and 71 % [55] of endoscopes. High-concern organisms (HCOs) were found in most of these studies, which establishes that current reprocessing practices are not reliably effective.

Researchers have identified several factors that impact reprocessing effectiveness, including human factors [52, 56 – 59], endoscope durability and maintenance issues [43, 47, 51, 53, 60 – 63], reprocessing equipment malfunctions [52, 55, 64, 65], and difficulty drying endoscopes before storage [55, 61, 66]. When HLD or sterilization failed, investigators frequently identified endoscopes with damage or residual soil. In 2010, researchers reported that reprocessing personnel disliked reprocessing tasks, felt pressure to work quickly when reprocessing endoscopes, and experienced physical discomfort from working with endoscopes. These human factors led to reprocessing steps being performed incorrectly or skipped 99 % of the time [56]. Recent studies have documented widespread nonadherence, with personnel skipping steps or cutting corners due to time pressure and inadequate training and supervision [35, 47, 52, 55, 59]. On the other hand, persistent contamination has been reported even when technicians followed manufacturers' instructions for use (IFU) and guidelines [52 – 54].

Reporting delays

Major outbreaks have been reported in peer-reviewed literature several years after investigations were initiated [40, 43, 67]. In 2014, our team learned of a 2013 ERCP-associated outbreak of New Delhi metallo-beta-lactamase-1 (NDM-1) that occurred in Milwaukee, Wisconsin. No further information was available until a 2015 media article reported that five endoscopy patients had superbug infections [68]. The MAUDE database includes three reports that appear pertinent but were submitted almost a year after the outbreak [69 – 71]. Clinicians from this institution published a report describing the investigation two years after the outbreak [72].

Reporting delays have also occurred because patients were asymptomatically colonized by pathogens from contaminated

▶ **Table 3** Infections described in reports submitted to FDA MAUDE database (2017 – 2019).

MAUDE	# of reports	Manufacturer	Infected	Pathogens	Contributing factors and other comments
8204386 [28] 8379810 [27]	33[1]	Olympus	32	VR *Enterococcus faecium*, CR *Enterobacteriaceae*, *Escherichia coli*	▪ 2 deaths in Texas ▪ Occurred in 2016 (20 patients) and 2018 – 2019 (12 patients) ▪ Reprocessing breach
8177954 [114]	6	Olympus	8 [6 ERCP]	MDR *P. aeruginosa*	▪ Cultures were negative for *P. aeruginosa*
8820754 [115]	6	Olympus	6	CR *Enterobacteriaceae*, NDM *K. pneumoniae*	▪ Endoscope damage
8538532 [116]	6	Olympus	5 or 6	*Enterococcus casseliflavus*	▪ Reprocessing breach
7027139 [117]	4	Olympus	4	OXA48-producing *K. pneumoniae*	▪ Endoscope damage
8201861 [118] 8201871 [119]	6	Olympus	4	*E. coli*, *E. faecium* (CR + and CR–)	▪ Reprocessing breach ▪ Endoscope contamination
7548459 [120]	1	Pentax	3[2]	MDR *P. aeruginosa*	
8730284 [121]	3	Olympus	3	*P. aeruginosa*	▪ Reprocessing breach
8825520 [122]	3	Olympus	3	MDR *K. pneumoniae*	▪ Cultures were negative for *K. pneumoniae*
8751568 [123]	1	Olympus	1[2]	ESBL *K. pneumoniae*	▪ Endoscope contamination
7791919 [124]	1	Olympus	1[2]	*E. casseliflavis*	
7424492 [125]	1	Olympus	1	MDR *Pseudomonas*	▪ Endoscope contamination ▪ Endoscope damage

MDR: Multi-drug resistant; VR: Vancomycin-resistant; NDM: New Delhi metallo-beta-lactamase-producing; ESBL: Extended-spectrum beta-lactamase producing; CR: Carbapenem-resistant/carbapenemase-producing

[1] Reports indicated there are a total of 33 MAUDE reports; we were able to obtain 31 of them.

[2] A source patient (the individual who introduced the pathogen into the endoscope) was clearly identified in the report; we excluded the source patient from the number of patients infected.

duodenoscopes [22, 44] and developed clinical signs of infection much later [23, 39, 43, 73]. Loor et al. established that SSIs are more common among cholecystectomy patients who had undergone ERCP in the 60 days before surgery [19]. The long-term sequelae of ERCP-associated colonization are not well described. However, a recent report related to superbug colonization following gastroscopy sheds light on the potential impact. Jousset et al. reported that 17 patients were exposed to carbapenemase-producing *K. pneumoniae* during procedures with a contaminated gastroscope [74]. One patient was persistently colonized with the pathogen despite aggressive treatment and experienced fatal sepsis due to this pathogen following prostate and bladder cancer surgery more than 4 years after exposure [74]. This AE was published in 2018, 9 years after the original outbreak. The possibility that patients colonized during ERCP may experience AEs much later should be studied.

FDA recommendations and post-market surveillance studies

In 2015, the FDA ordered three duodenoscope manufacturers to conduct studies to evaluate the real-world feasibility and effectiveness of reprocessing [75]. Manufacturers found reprocessing staff had difficulty understanding and following instructions and commonly missed steps [57]. Interim data indicated that HLD failure rates were much higher than the 0.4 % contamination rate anticipated by FDA [57, 76]. Final results showed HCOs were present in 4.1 % to 22.2 % of samples, depending on the duodenoscope model, and 0.3 % to 4.4 % had > 100 CFU of low- or moderate-concern organisms. The results released by the FDA represent only a fraction of the number of samples required by the FDA, and hundreds of samples were excluded from analysis for unknown reasons (▶ **Table 5**) [76 – 80]. The presence of low- and moderate-concern organisms is important because they can contribute to biofilm formation [81]. Although the post-market surveillance studies were designed to demonstrate effectiveness, several MAUDE reports describing microbial growth stated that technicians neglected to follow instructions and made reprocessing errors [82 – 84]. Despite these findings, FDA maintained that "…an individual's risk of acquiring infection from an inadequately reprocessed medical device remains relatively low given the large number of such devices in use" [76].

The value of these studies is limited by the lack of information about types of institutions submitting data, duodenoscope models, reprocessing methods, personnel adherence, and microbial culture methods. In addition, manufacturers have not reported the proportion of samples with up to 99 CFU of low-

▶ **Table 4** Effectiveness of HLD, double HLD, and sterilization in real-world settings.

Study	HLD			Double HLD			Sterilization			High-concern organisms
	N	Any growth (%)[1]	High-concern organisms (%)	N	Any growth (%)[1]	High-concern organisms (%)	N	Any growth (%)	High-concern organisms (%)	
Gromski 2019 [38]	–	–	–	453	8 (1.8%)	2 (0.44%)	425[2]	9 (2.1%)	2 (0.47%)	▪ Double HLD: *Klebsiella pneumoniae; Enterobacter cloacae* ▪ Sterilization: *Streptococcus viridans; Enterococcus* spp.
Bartles 2018 [34]	1399	102 (7.3%)	5 (0.4%)	1526	122 (8.0%)	3 (0.2%)	–	–	–	▪ *Enterococcus* spp.; *Enterobacter cloacae*; *Aeromonas* spp.; ESBL +/- *Escherichia coli*
Rex 2017 [35]	–	–	–	A: 627 B: 783[3]	A: 59 (9.4%) B: 38 (4.9%)[3]	A: 5 (0.8%) B: 2 (0.3%)	–	–	–	▪ *Candida glabrata; Zygomycete; Enterococcus* spp.
Snyder 2017 [36]	174	28 (16.1%)	–	169	27 (16.0%)	–	173[4]	39 (22.5%)	–	▪ Species not reported
Visrodia 2017 [37]	20	12 (60%)	11 (55%)	18	8 (44.4%)[5]	–	–	–	–	▪ *Stenotrophomonas maltophilia; Klebsiella pneumoniae; Pseudomonas aeruginosa; Enterococcus faecalis; Cellulosimicrobium cellulans*

N: number of encounters during which samples were taken for microbial cultures; –: not evaluated
[1] Overall growth rate reported of any microorganisms, including high-concern organisms
[2] Liquid chemical sterilization using peracetic acid in a Steris 1E system
[3] A: Phase I of study when double HLD was implemented. B: Phase III of study where new personnel were trained on double HLD
[4] Ethylene oxide gas sterilization in a 3M Sterivac system after HLD in a System 83 Plus 9 Custom Ultrasonics AER
[5] Of 18 scopes that were re-reprocessed, they only cultured 17

▶ **Table 5** Results from post-market surveillance studies ordered by the FDA in 2015.

Manufacturer	Samples required by FDA	Interim analysis of all available samples (2018–2019)				Final analysis of properly collected samples (2020)				Samples discarded[1]
		Samples collected	Analyzed	HCO found	High colony counts[2]	Samples collected	Analyzed	HCO found	High colony counts[2]	
Olympus [77, 126]	1736	1583	1369	74 (5.4%)	6 (0.4%)	1932	1488	75 (5.0%)	9 (0.6%)	444 (23.0%)
Pentax [78, 127]	850	505	505	40 (7.9%)	18 (3.6%)	Data not reported	653	32 (4.9%)	29 (4.4%)	98 (13.0%)
Fujifilm [79, 80]	727	104	104	2 (1.9%)	1 (1.0%)	Data not reported	Data not reported[3]	Data not reported[3]	Data not reported[3]	0

HCO: high-concern organisms
[1] The number of discarded samples that contained 1–10 CFU or 11–99 CFU of low- or moderate-concern organisms was not specified
[2] Includes cases where there were >100 CFU of low- or moderate-concern organisms
[3] The final report stated "Fujifilm has not enrolled a sufficient number of sites or collected a sufficient number of samples to establish a real-world contamination rate." Data previously reported in the database appears to have been redacted.

or moderate-concern organisms. The presence of > 10 colonies is considered actionable by CDC and Australian guidelines [85, 86], and other international guidelines recommend a benchmark of 20 CFU [87, 88] (▶ **Table 5**). The exclusion of hundreds of samples raises questions about whether those samples had substantial bioburden and if microbes found were due to sampling errors. Despite these limitations, these data confirm that reprocessing does not reliably eliminate contamination.

Clinical implications of underestimating infection risks

Neglecting to notify or test exposed patients

In addition to delayed recognition and reporting of infections, a lack of transparency and poor inter-agency communication erode the ability of clinicians and infection preventionists to accurately assess infection risk and develop strategies to address breaches and patient exposure. In one case, hospital personnel observed blood on a patient-ready EUS endoscope, and investigators determined that four patients had been exposed to blood and bodily fluids because improper irrigation system connectors were used during cleaning and disinfection. Further investigation revealed that incorrect channel connectors had been used for 3 years, resulting in a lack of cleaning and HLD that placed numerous patients at risk [89]. The hospital notified 2,557 exposed patients, but did not recommend follow-up testing because the CDC and other experts advised that "the risk of transmission of any disease to patients is very remote" [13]. The lack of follow-up testing prevented characterization of actual infection risk.

Public health risks

Colonized or infected patients may serve as carriers, and secondary transmission has been documented in at least five outbreaks (▶ **Table 1**). Following an outbreak of NDM *Escherichia coli* in Chicago, 19 of 31 infected ERCP patients were eventually admitted to other hospitals for continuing care [90]. Ray et al. subsequently documented transmission of the superbug to 10 patients in six hospitals [90]. The risk of direct exposure and secondary transmission is heightened by a failure to adequately identify and report infections to stakeholders in local communities and beyond. Currently, there is no suitable reporting or notification system.

The impact of antimicrobial therapy on the risk of infection and superbug development is a major concern. The CDC and WHO have prioritized implementation of antimicrobial stewardship programs [91, 92]. Several institutions evaluated their use of prophylactic antimicrobials and found no significant effect on infectious complication rates [93, 94]. Du et al. noted that antibiotic prophylaxis guidelines do not consider patients' resistance profiles, and 62 % to 73 % were resistant to recommended antibiotics [95]. They attributed high rates of antimicrobial resistance to excessive antibiotic use [95]. Masadeh et al. observed that patients who received post-ERCP antibiotics were more likely to have resistant microbes [93]. Wendorf et al. hypothesized that antibiotics given to outbreak patients drove the development of additional resistance in the outbreak strain [96].

Evidence-based calculations of infection risk

Estimates of pathogen transmission with HCOs can be made using duodenoscope contamination rates that range from 0.3 % in academic centers with rigorous adherence to reprocessing guidelines and duodenoscope maintenance [34, 42] to 5 % in FDA post-market surveillance studies conducted in 26 US facilities [76 – 78, 80], 22 % in 67 Dutch hospitals [24], and 60 % in other high-volume settings [37]. With 750,000 estimated annual ERCP procedures, this means that 2,250 or 37,500, or even 412,500 procedures are performed with contaminated duodenoscopes annually in the United States. Using an average attack rate documented in settings where contaminated duodenoscopes were used (18.9 % [132/699]; ▶ **Table 1**), this translates into a per-procedure HCO transmission rate of 1 in 1,765 (0.3 % contaminated), 1 in 106 (5 % contaminated), 1 in 24 (22 % contaminated), or 1 in 10 ERCP procedures (60 % contaminated). These calculated transmission rates reflect the full spectrum of disease with most patients developing long-standing asymptomatic colonization and only a minority manifesting more severe forms of PB, urinary tract, pulmonary, or vascular infections.

Reducing the risk of ERCP-associated infections

Reducing the risk of ERCP-associated infection will require a multifaceted approach including:

1. Prioritizing the improvement of reprocessing effectiveness by:
   a) Establishing educational programs that support real-world competencies (e. g., hands-on and train-the-trainer programs; simulators)
   b) Providing rigorous training and oversight to ensure adherence to optimal practices
   c) Advocating for automation of manual cleaning and drying to reduce human error
   d) Implementing the full range of quality assurance steps to ensure reprocessing effectiveness (e. g., leak tests, visual inspection, cleaning verification tests, HLD and sterilization monitoring, and drying verification)
2. Implementing mandatory duodenoscope servicing by:
   a) Establishing an evidence-based schedule for routine inspections by biomedical department personnel or qualified repair technicians
   b) Addressing defects that could injure patients or predispose endoscopes to harbor soil and microbial contamination
3. Enhancing the evidence base for assessing risks associated with ERCP by:
   a) Conducting studies to evaluate real-world outcomes
   b) Publishing findings from research and investigations that identify risk factors
   c) Including sufficient information when reporting outbreaks, infections, or breaches (e. g., types of endo-

scopes; number of patients exposed, tested, and infected or colonized; reprocessing methods and breaches; and maintenance issues or damage)
   d) Evaluating antibiotic usage and its impact on transmission and resistance
   e) Sharing innovations that may improve reprocessing effectiveness and patient safety
4. Partnering with manufacturers and biomedical engineers to address risks by:
   a) Considering alternatives to conventional reusable devices (e.g., duodenoscopes that are sterilizable, single-use, or have disposable components that facilitate reprocessing)
   b) Evaluating the impact of these innovations on outcomes

Conclusions

Until recently, many clinicians and researchers believed the risk of post-ERCP infection was extremely low. There is now substantial evidence that duodenoscope reprocessing does not reliably eliminate soil or bioburden, allowing potential pathogens to remain on endoscopes. This clearly causes infections that harm patients and jeopardize public health, with evidence suggesting infections could be expected to occur in as few as 1 in 1,765 or as many as 10 % of ERCP procedures when contaminated duodenoscopes are used. Endoscopists can lead efforts in reducing risk by working with a multidisciplinary team that includes infection preventionists, reprocessing and endoscopy personnel, and biomedical engineers. This team should develop and implement evidence-based strategies to improve reprocessing practices and systemically evaluate and report patient outcomes.

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Competing interests

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