Techniques in Gastrointestinal Endoscopy 000 (2019) 1–6

Contents lists available at ScienceDirect

Techniques in Gastrointestinal Endoscopy

journal homepage: www.techgiendoscopy.com/locate/tgie

Endoscope-associated infections: A brief summary of the current state and views toward the future

Arjan W. Rauwers, MD, MSc[a], Judith A. Kwakman, MD, MSc[a], Margreet C. Vos, MD, PhD[b,1], Marco. J. Bruno, MD, PhD[a,b,*]

[a] Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center, PO box 2040, 3000 CA Rotterdam, The Netherlands
[b] Department of Medical Microbiology and Infectious Diseases, Erasmus MC University Medical Center, Rotterdam, The Netherlands

ARTICLE INFO

Keywords:
Endoscopic retrograde cholangiopancreatography
Duodenoscope
Contamination
Reprocessing
Disinfection
Infection

ABSTRACT

World-wide reports of duodenoscope-associated outbreaks of multidrug resistant micro-organisms are an indication that transmission of infection via contaminated endoscopes occurs more frequently than previously thought. To reduce the incidence of endoscope contamination, open communication between manufacturers, institutions, and government agencies is urgently needed. Endoscope risk factor studies and thorough investigation of outbreaks by experts are instrumental in lowering and ultimately eliminating infections. These studies should yield improvements in endoscope design, endoscope reprocessing, as well as hospital surveillance and infection control measures. Current reprocessing methods have a very small margin of safety, allowing no room for error. Strictly following the manufacturer's instructions regarding reprocessing does not adequately guarantee complete removal of micro-organisms. New reprocessing measures to reduce contamination show promising results, but they are costly to implement and do not assure zero contamination risk. Redesign of endoscopes to facilitate better cleaning and ultimately sterilization instead of disinfection might provide a solution. Going forward, the focus should extend beyond the forceps elevator to include the entire instrument since every aspect of the duodenoscope can be contaminated by infectious organisms. Single-use duodenoscopes would completely eliminate the risk of transmission of exogenous micro-organisms, but they not the Food and Drug Administration-approved, and are likely to be costly and of unproven efficacy. Indeed, balancing cost-effectiveness of any redesign or use of disposable endoscopes with the actual risk of transmitting exogenous micro-organisms will ultimately determine which solutions are adopted and utilized.

Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; ATP, adenosine triphosphate; ERCP, endoscopic retrograde cholangiopancreatography; ESGE, European Society of Gastrointestinal Endoscopy; FDA, Food and Drug Administration; HLD, high-level disinfection; IFU, Instructions for Use; MDRO, multidrug-resistant organisms

Conflict of interest

Rauwers and Kwakman reported no relevant financial activities.

Prof. Dr Bruno has had the following relevant financial activities outside the submitted work:
- Consultant for 3M.
- Grant from 3M for an investigator-initiated study for the benefit of the Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands.
- Consultant and lecturer for Boston Scientific.
- Grants from Boston Scientific for investigator-initiated studies and industry-initiated studies for the benefit of the Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands.
- Consultant and lecturer for Cook Medical.
- Grants from Cook Medical for investigator-initiated studies and industry initiated studies for the benefit of the Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands.
- Grants from Pentax Medical for the benefit of the Dept. of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands.

Prof. Dr Vos has had the following relevant financial activities outside the submitted work:
- Grant from 3M for an investigator-initiated study.
- Grant from Pentax Medical for an investigator-initiated study.
- Grant from IMS innovations for an investigator-initiated study.

* Corresponding author.
E-mail address: m.bruno@erasmusmc.nl (M.J. Bruno).

[1] Both authors contributed equally to this manuscript.

https://doi.org/10.1016/j.tgie.2019.04.006
1096-2883/

1. Introduction

This issue of Techniques in Gastrointestinal Endoscopy is dedicated to raising awareness for the existence and extent of endoscope-related infections. In this article, we will discuss future directions and opportunities that may limit and eventually eliminate endoscope-related infections. Short-term measures to reduce the chance of endoscope contamination with current-design reusable endoscopes are essential. Further development of endoscope design, reprocessing techniques, and control measures to prevent contamination are needed to eventually eliminate endoscope-related infections.

2. The current state

Endoscope-associated infections due to contaminated endoscopes continue to be reported worldwide [1-3]. Although endoscope-associated infections are in particular duodenoscope-related, recent reports also discuss outbreaks related to gastroscopes [4,5], colonoscopes [6], and bronchoscopes [7-9]. Patients infected via endoscopes are mostly detected during outbreak investigations or carriage by epidemiologically linked patients. Infections with multidrug-resistant micro-organisms are easily recognizable and thus most frequently reported. It is needless to state that these infections are only the tiny tip of the iceberg as persistent contamination of antibiotic sensitive (nonresistant) micro-organisms and contamination lasting only 1 or 2 procedures, remain unnoticed. A better estimate of the problem is the number of contaminated endoscopes despite “adequate” reprocessing. Recent studies have mainly assessed duodenoscope contamination incidence rates ranging from 0.3% to 30% [10-16], although linear echoendoscopes with a similar complex design [11,12,17], gastroscopes [12,18,19], and colonoscopes can also be contaminated [12,18,19]. *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* are frequently involved in endoscopy-related outbreaks, probably due to their persistence in biofilms. Subject to heavy wear and tear, damaged parts such as biopsy channels are vulnerable to biofilm formation.

The actual risk for a patient of becoming infected (ie, transmission) by a contaminated endoscope is not yet known. Duodenoscope-associated outbreaks have shown attack rates (the number of infected or colonized cases/number of exposed persons) from 12% to 41% [20-24]. However, in a nonoutbreak setting, it is unclear what the actual risk of transmission of exogenous micro-organisms is when using a contaminated endoscope. Outbreaks have been reported to be associated with multiple factors, including reprocessing protocol breaches [4,24,25], inadequate endoscope maintenance [10,26], duodenoscope design issues [22], and ineffective or even absence of microbiological surveillance [20,21,27,28]. Moreover, the true extent of the problem is unknown as detected outbreaks are not adequately reported, registered and/or communicated by manufacturers, hospitals, and governmental bodies [1,2]. A worldwide survey reported that nearly one fifth of the responding institutions experienced at least 1 endoscope-associated outbreak [29].

Providing minimal invasive diagnosis and therapeutic options, endoscopy has established itself as an essential part of contemporary medicine with both low procedural risks and costs. The total volume, complexity, and invasiveness of endoscopic procedures are expected to continue rising in the coming decades. Safe endoscopic procedures without avoidable microbiological transmission risk in this day and age of increasing reports of antibiotic resistant bacteria and attributable deaths [30] are only possible if all parties involved (gastroenterologists, medical microbiologists, government agencies, regulatory bodies, and manufacturers) acknowledge the issue and act concertedly.

3. Future view 1: short-term measures

3.1. Transparent communication

More transparent communication and thorough assessment of adverse events (ie, outbreaks, device failures, and reprocessing risks) by hospitals and manufacturers, whether involving endoscopes or reprocessing equipment, is essential. The US Food and Drug Administration (FDA) has emphasized that if adverse events are not reported in a proper and timely manner, patient safety may be put at risk [31]. Investigation of the outbreaks by experts, including dismantling the persistently contaminated endoscope, is instrumental to assess and improve endoscope design, scope reprocessing and surveillance measures. Although up to 40 duodenoscope-associated outbreaks have been reported [2,32], few reports describe investigation of the endoscope concerned [22,23,26,33-35]. One independent investigation ultimately contributed to a design modification and worldwide recall of the Olympus TJF-Q180V duodenoscope [22,34,35], including 4400 duodenoscopes in the United States [36].

In 2015, the FDA demanded postmarket surveillance studies on the Instructions for Use related to duodenoscope reprocessing by all three major manufacturers of these instruments: Fujifilm, Olympus, and Pentax [37]. After all 3 manufacturers initially failed to conduct these studies [31], the first interim results demonstrated higher-than-expected contamination rates of up to 3% for high concern organisms [37]. In response to this, the FDA stated that reprocessing alone may not be sufficient to avoid duodenoscope-associated infections [31]. Awareness that endoscope contamination is a clinical reality and cannot be neglected should enforce a proactive attitude of all relevant professionals working with endoscopes. Close and regular communications are required between reprocessing staff, medical device experts, infection control professionals, medical microbiologists, and gastroenterologists in order to control endoscope-related infections.

3.2. Endoscope risk factors

To develop tailored measures to control endoscope contamination, more information about endoscope-specific risk factors such as vulnerable design issues, endoscope durability, and optimal inspection frequency are needed. Currently, attention focuses on complex design endoscopes, as persistent contamination of the forceps elevator [10,24,26,38], and the protection cap [22,33], have been a source for multiple outbreaks. Although several type specific design issues have been raised [22,33], contamination of duodenoscopes and linear echoendoscopes does not seem to depend on manufacturer or type [11,39]. Moreover, not only the forceps elevator but the whole endoscope should be critically assessed. All endoscope locations including channels can be contaminated [39], and all endoscope types are at risk of contamination [12]. Borescope studies show that the inside of all types of gastrointestinal endoscopes are often damaged [40,41], which can affect the risk of contamination [42], as damage to internal parts may facilitate biofilm formation.

The American Society for Gastrointestinal Endoscopy warns that endoscope longevity and durability are understood incompletely [43]. Several outbreak investigations have shown that normally-functioning duodenoscopes were ultimately found to harbor critical abnormalities [10,26,33] which may have contributed to contamination. Timely, routine inspections and preventive maintenance could prevent use of damaged endoscopes. Affected centers and professional societies have advocated that guidelines should become available pertaining endoscope evaluation and maintenance schedules [7,10,17,26,44]. Nowadays, manufactures advise yearly inspections of duodenoscopes [36,45-47]. Contamination of

duodenoscopes and linear echoendoscopes, however, is independent of physical age and therefore usage-based inspections could be considered [11]. We advocate the implementation of an endoscope-specific log file in which users and manufacturers keep track of previous endoscope repairs and culture results (where performed).

3.3. Process control

Although improvements in endoscope designs and reprocessing techniques are to be expected, the majority of hospitals will continue to use current-design endoscopes and high-level disinfection (HLD), at least in the decade to come. Therefore strict process control, regular intensive training of cleaning personnel and regular audits remain essential [48], as the current reprocessing technique has a very small margin of safety [49-52] and is error-prone [53-55]. Surveys show a large variation of compliance with reprocessing practices [14,29,56,57]. A worldwide survey among 163 institutions showed that manual cleaning of endoscopes is not routinely performed in 20% of institutions [29]. This is alarming because without manual cleaning, adequate disinfection of the endoscope is not possible. Repeated surveys can help to identify persistent reprocessing flaws and create a critical awareness as well as promote knowledge-sharing among institutions [56,58]. Endoscope manufactures may develop tools to assess (and thereby enhance) compliance with Instructions for Use after they have completed the FDA-ordered human factors studies [31]. Even when novel reprocessing techniques including sterilization become available, protocol adherence including meticulous manual cleaning will remain imperative to reduce the risk of endoscope-related infections.

3.4. Control measures

According the FDA, following current reprocessing practices is not sufficient to avoid all duodenoscope-associated infections [31]. Therefore, the efficacy of scope decontamination should be verifiable with easily applied and effective control measures. Microbiological surveillance is the gold standard and considered as the bare minimum by the majority of the international guidelines to prevent the use of persistently contaminated endoscopes [44,59-61]. Negative culture results, however, do not guarantee a total absence of micro-organisms. Several outbreak investigations were not able to retrieve the concerning micro-organism from the contaminated endoscope [23,33,62,63]. Furthermore, there is no (international) consensus on the sampling and culturing method of endoscopes. This complicates the comparison of culture outcomes from studies around the globe. The optimal culture frequency is also subject of debate, varying between weekly to yearly cultures. Culture-and-quarantine strategies may be challenging for some centers from the viewpoint of economics: obtaining culture results takes at least 48-72 hours and quarantining endoscopes while awaiting these culture results thus requires the purchase of extra endoscopes to overcome scope downtime. Other tests for which the result is readily available, such as adenosine triphosphate tests and bioburden assays measuring protein, hemoglobin, or carbohydrates, have several limitations. Testing is performed mainly after manual cleaning to allow the endoscope to proceed to HLD, as post-HLD testing is not sensitive enough to negate the presence of micro-organisms. Although the correlation between adenosine triphosphate test results and culture outcomes seems poor [64], these tests could also prove useful to enhance manual cleaning protocol adherence and thereby reduce the incidence of post-HLD endoscope contamination.

4. Future view 2: new reprocessing methods for current-design heat labile endoscopes

4.1. Spaulding criteria: still applicable?

The Spaulding classification has been used for decades and categorizes reusable medical devices in 3 classes based on the risk of transmission of micro-organisms. Duodenoscopes are classified as “semi-critical” devices, meaning that they come in contact with nonintact skin or mucous membranes, requiring HLD [65]. However, the Spaulding classification may be outdated for flexible endoscopes since the procedures for which these devices are being used have become more invasive. Endoscopes are contaminated with a microbiological load up to 7-10 $\log_{10}$ [49-52], while reprocessing reduces this load at a maximum of 6-12 $\log_{10}$ [49-52]. This means that reprocessing leaves no room for error [53-55]. This is of particular relevance to duodenoscopes which are even more difficult to reprocess than straight-channel endoscopes due to their more complex design [22,49].

Sterilization reduces a much higher load of micro-organisms, but is only required for critical instruments that come in contact with sterile tissue [65]. Endoscopic retrograde cholangiopancreatography (ERCP) and therapeutic endoscopic ultrasound have become more invasive while breaching more often natural mucosal barriers, for example, through papillotomy, ampullectomy, and endoscopic necrosectomy. In addition, patients presenting for endoscopic procedures have become increasingly complex with additional comorbidity and immune compromise. The possibility of an infection due to translocation of endogenous micro-organisms, that is, those originating from the patient him/herself, has always been a potential risk that is inherent to ERCP [66]. Importantly, outbreaks now show that duodenoscopes are vectors for transmission of exogenous micro-organism, that is, those originating from a previously treated patient with that same endoscope.

In an outbreak setting it was shown that biliary obstruction (ie, cholangiocarcinoma and biliary stent placement) was associated with an increased risk of transmission of exogenous micro-organisms [67]. This leads to the question as to whether or not duodenoscopes are in fact critical devices which should be sterilized to exclude avoidable transmission risks for the patient. Current-design heat liable endoscopes cannot endure regular high temperature sterilization methods. Therefore, reprocessing methods with a larger margin of safety should be developed which are both suitable for use with current design duodenoscopes and safer for cleaning staff personnel.

4.2. Double HLD or low temperature sterilization

In 2015, the FDA suggested 4 supplemental measures in addition to regular reprocessing to reduce endoscope contamination rates. These measures, repeat HLD, ethylene oxide (EtO) sterilization [15,16,68-70], the use of a liquid chemical sterilant and surveillance culturing [10,11,15,17] have been explored in several studies. Although some of these studies show that a reduction of contamination is feasible, no studies convincingly show a zero contamination rate. Most of the suggested measures require extensive logistical and financial investments including the purchase of extra endoscopes to overcome scope downtime. Double HLD could be easily implemented in daily practice and does not require extensive additional costs. Studies assessing the effect of this method were unable to show a zero contamination rate [13,16,69], even if a second manual cleaning step was added [69].

Performing 2 cycles of HLD or EtO sterilization after single HLD has not led to lower contamination rates compared to the standard procedure using single HLD [13]. EtO sterilization uses low temperatures and has been used effectively to clean contaminated duodenoscopes after outbreaks [71] or when contamination persisted despite

repeated processing cycles. However, this form of sterilization comes with several limitations. EtO has an increased turn-around time requiring the purchase of additional duodenoscopes, it can damage duodenoscopes, and it is toxic and carcinogenic to personnel [72,73]. Furthermore, complete sterilization has not yet been proven in randomized trials [13,71] and the addition of EtO does not appear to be cost-effective [74]. Hydrogen peroxide ozone sterilization [75] and disinfection using plasma-activated water [76] have both so far only been tested in small studies. Both methods showed promising results, but have yet to be proven in clinical trials. For now, none of these additional measures to the current reprocessing cycle seem to be able to a guarantee a zero contamination rate of reusable endoscopes.

5. Future view 3: redesign of endoscopes

5.1. Peer-review is essential

The expectation is that redesigned endoscopes will facilitate improved reprocessing or sterilization, thereby preventing the risk of transmission of micro-organisms. However, lessons can be learned from the introduction of recently adapted duodenoscope models. The current risk classification of endoscopes in both Europe and the US state that new endoscope models are given market authorization without the need for additional scrutiny by regulatory bodies if the modified design is sufficiently similar to previously approved designs [77,78]. In 2010, Olympus introduced the TJF-Q180V duodenoscope with a sealed elevator channel, based on a previously approved design with an open elevator wire channel [1]. In 2014, only after the occurrence of multiple outbreaks related to the use of the TJF-Q180V, the FDA indicated that the design modifications had a potential impact on safety. Subsequently, after a 2016 modification to the elevator wire channel sealing, did the FDA consider the modified design to be equivalent [36,79] to previous models. Ultimately, this leads Olympus to recall the TGF-Q180V worldwide [36,80]. The lesson to be learned is that successive design adjustments of endoscope models can ultimately result in a substantial functional change as compared to the original “legacy” model with a resulting potential safety risk. This questions whether this system of semiautomatic “renewal” of market authorization is not outdated and poses safety risks that can be avoided.

5.2. Reusable endoscopes with single-use parts

Newly introduced duodenoscope models have disposable protection caps [81,82], including models with a disposable forceps elevator or with a sterilizable removable elevator mechanism [83,84]. These adjustments should facilitate adequate cleaning of crevices surrounding the forceps elevator, but these changes have not yet been proven in peer-reviewed studies. Current design adjustments have focused on the tip and the forceps elevator but multiple sites within the duodenoscope have shown to be predilections for contamination [39]. More innovative designs should also address other parts, in particular the damage-sensitive biopsy channel as this site has shown to be often contaminated.

5.3. Single-use endoscopes

A very important and relevant issue is the fact that it is still unknown which percentage of postprocedure infections is to be attributed to contaminated endoscopes. The use of single-use endoscopes would eliminate any risk of transmission from exogenous micro-organisms. The use of disposable bronchoscopes and ureteroscopes has already been tested in clinical practice, and a disposable duodenoscope is in the latter stages of development [85-87]. Apart from whether single-use endoscopes perform as well as reusable endoscopes, implementation will ultimately depend on their cost-effectiveness. A recent report estimated the total per-procedure costs of reusable duodenoscopes at $297-$818, depending on the ERCP volume [88]. Although extrapolation to other practices is limited as the analysis was performed in a US tertiary center, the report stated that the use of single-use instead of reusable duodenoscopes would add significant costs. Furthermore, the costs of the HLD reprocessing infrastructure would remain largely the same because these facilities would still be required for the cleaning and disinfection of gastroscopes and colonoscopes until these are disposable as well. Another cost exploration report conservatively estimated reprocessing costs of one reusable endoscope at $114-$280, excluding purchase and maintenance costs [89]. The bigger picture, however, also includes costs for managing colonized individuals and infected patients, infection prevention, risk management and litigation, and implementation of previously described supplemental reprocessing measures [74]. Surveillance costs can vary, as currently there is no consensus on which microbiological surveillance method to use and its frequency. In a US tertiary center performing monthly cultures, annual costs per endoscope were $1500 to which the purchase of extra duodenoscopes to overcome downtime was not added [70]. In addition to the burden patients have to endure because of repeated culturing or isolation measures, outbreak management also poses a large financial strain to the health care system. The costs of other nonendoscope-related nosocomial outbreaks ranged from €10,778-€356,754 or even up to $804,263 [90,91] of which about 50% lost revenues were caused by missed income due to closed beds. Future studies incorporating all hidden expenses should determine if the costs of single-use duodenoscopes are justified.

6. Conclusion

Endoscope-related infectious outbreaks of micro-organisms including multidrug-resistant micro-organisms call for stringent control measures and critical assessment of current-design endoscopes in the short term, and for the development of innovative reprocessing techniques and radically different endoscopes designs in the long term. To date, the ideal reprocessing method that guarantees absence of exogenous micro-organisms of reprocessed endoscopes with an acceptable turnover time while being safe for staff and endoscopes remains elusive. Newly introduced duodenoscope models with disposable parts are the first step toward the development of durable endoscopes that potentially have a lower risk of contamination. Single-use endoscopes may provide yet another solution; however, cost may be a barrier to wide-scale implementation. Ultimately, the actual risk of transmission of exogenous micro-organisms through contaminated endoscopes and the burden of world-wide antibiotic resistance patterns, relative to the cost-effectiveness of any one measure designed to reduce or abolish the risk of infection, will dictate which solution holds the future.

Author contributions

Arjan W. Rauwers: drafting of the manuscript; critical revision of the manuscript for important intellectual content;

Judith A. Kwakman: critical revision of the manuscript for important intellectual content;

Marco J. Bruno: critical revision of the manuscript for important intellectual content;

Margreet C. Vos: critical revision of the manuscript for important intellectual content.

References

[1] United States Senate. Preventable tragedies: superbugs and how ineffective monitoring of medical device safety fails patients [U.S. Senate - Minority Staff Report]. Washington, United States 2016. Available from: https://www.help.senate.gov/imo/media/doc/Duodenoscope%20Investigation%20FINAL%20Report.pdf.

[2] Rubin ZA, Kim S, Thaker AM, Muthusamy VR. Safely reprocessing duodenoscopes: current evidence and future directions. Lancet Gastroenterol Hepatol 2018;3(7):499–508.
[3] Petersen BT, Koch J, Ginsberg GG. Infection using ERCP endoscopes. Gastroenterology 2016;151(1):46–50.
[4] Bajolet O, Ciocan D, Vallet C, de Champs C, Vernet-Garnier V, Guillard T, et al. Gastroscopy-associated transmission of extended-spectrum beta-lactamase-producing pseudomonas aeruginosa. J Hosp Infect 2013;83(4):341–3.
[5] Parr A, Querry A, Pasculle A, Morgan D, Muto C. Carbapenem-resistant klebsiella pneumoniae cluster associated with gastroscope exposure among surgical intensive care unit patients at University of Pittsburgh Medical Center. Open Forum Infect Dis 2016;3(suppl 1):248.
[6] Reddick E. Investigation of salmonellosis outbreak following a hospital endoscopy: a public health case study. Can J Infect Control 2017;32(3):156–9.
[7] Dickson A, Kondal P, Hilken L, Helgesen M, Sjolin W, Jensen D. Possible pseudotransmission of Enterobacter cloacae associated with an endobronchial ultrasound scope. Am J Infect Control 2018;46(11):1296–8.
[8] Cetre JC, Nicolle MC, Salord H, Perol M, Tigaud S, David G, et al. Outbreaks of contaminated broncho-alveolar lavage related to intrinsically defective bronchoscopes. J Hosp Infect 2005;61(1):39–45.
[9] Alipour N, Karagoz A, Taner A, Gaeini N, Alipour N, Zeytin H, et al. Outbreak of Hospital Infection from biofilm-embedded pan drug-resistant pseudomonas aeroginosa, due to a contaminated bronchoscope. J Prev Med (Wilmington) 2017;2(2).
[10] Ross AS, Baliga C, Verma P, Duchin J, Gluck M. A quarantine process for the resolution of duodenoscope-associated transmission of multidrug-resistant *Escherichia coli*. Gastrointest Endosc 2015;82(3):477–83.
[11] Brandabur JJ, Leggett JE, Wang L, Bartles RL, Baxter L, Diaz GA, et al. Surveillance of guideline practices for duodenoscope and linear echoendoscope reprocessing in a large healthcare system. Gastrointest Endosc 2016;84(3):392–9. e3.
[12] Saliou P, Le Bars H, Payan C, Narbonne V, Cholet F, Jezequel J, et al. Measures to improve microbial quality surveillance of gastrointestinal endoscopes. Endoscopy 2016;48(8):704–10.
[13] Snyder GM, Wright SB, Smithey A, Mizrahi M, Sheppard M, Hirsch EB, et al. Randomized comparison of 3 high-level disinfection and sterilization procedures for duodenoscopes. Gastroenterology 2017;153(4):1018–25.
[14] Alfa MJ, Olson N, DeGagne P, Jackson M. A survey of reprocessing methods, residual viable bioburden, and soil levels in patient-ready endoscopic retrograde cholangiopancreatography duodenoscopes used in Canadian centers. Infect Control Hosp Epidemiol 2002;23(4):198–206.
[15] Decristoforo P, Kaltseis J, Fritz A, Edlinger M, Posch W, Wilflingseder D, et al. High-quality endoscope reprocessing decreases endoscope contamination. Clin Microbiol Infect 2018;24(10):1101.e1-e6.
[16] Bartles RL, Leggett JE, Hove S, Kashork CD, Wang L, Oethinger M, et al. A randomized trial of single versus double high-level disinfection of duodenoscopes and linear echoendoscopes using standard automated reprocessing. Gastrointest Endosc 2018;88(2):306–13 e2.
[17] Chapman CG, Siddiqui UD, Manzano M, Konda VJ, Murillo C, Landon EM, et al. Risk of infection transmission in curvilinear array echoendoscopes: results of a prospective reprocessing and culture registry. Gastrointest Endosc 2017;85(2):390–7.e1.
[18] Bisset L, Cossart YE, Selby W, West R, Catterson D, O'Hara K, et al. A prospective study of the efficacy of routine decontamination for gastrointestinal endoscopes and the risk factors for failure. Am J Infect Control 2006;34(5):274–80.
[19] Ribeiro MM, de Oliveira AC. Analysis of the air/water channels of gastrointestinal endoscopies as a risk factor for the transmission of microorganisms among patients. Am J Infect Control 2012;40(10):913–6.
[20] Carbonne A, Thiolet JM, Fournier S, Fortineau N, Kassis-Chikhani N, Boytchev I, et al. Control of a multi-hospital outbreak of KPC-producing Klebsiella pneumoniae type 2 in France, September to October 2009. Euro Surveill 2010;15(48):19734.
[21] Valderrama S, Miranda CJL, ÁPG Rubio, Gualtero S, Fraile GCC, Escobar Y, et al. Successful control of an endoscopic retrograde cholangiopancreatography−associated nosocomial outbreak caused by *Klebsiella pneumoniae* carbapenemase producing *Klebsiella pneumoniae* in a University Hospital in Bogota, Colombia. Open Forum Infect Dis 2016;3(suppl_1):1398.
[22] Verfaillie CJ, Bruno MJ, Voor in 't Holt AF, Buijs JG, Poley JW, Loeve AJ, et al. Withdrawal of a novel-design duodenoscope ends outbreak of a VIM-2-producing *Pseudomonas aeruginosa*. Endoscopy 2015;47(6):493–502.
[23] Kola A, Piening B, Pape UF, Veltzke-Schlieker W, Kaase M, Geffers C, et al. An outbreak of carbapenem-resistant OXA-48—producing *Klebsiella pneumonia* associated to duodenoscopy. Antimicrob Resist Infect Control 2015;4(1):8.
[24] Alrabaa SF, Nguyen P, Sanderson R, Baluch A, Sandin RL, Kelker D, et al. Early identification and control of carbapenemase-producing *Klebsiella pneumoniae*, originating from contaminated endoscopic equipment. Am J Infect Control 2013;41(6):562–4.
[25] Aumeran C, Poincloux L, Souweine B, Robin F, Laurichesse H, Baud O, et al. Multidrug-resistant *Klebsiella pneumoniae* outbreak after endoscopic retrograde cholangiopancreatography. Endoscopy 2010;42(11):895–9.
[26] Wendorf KA, Kay M, Baliga C, Weissman SJ, Gluck M, Verma P, et al. Endoscopic retrograde cholangiopancreatography-associated AmpC *Escherichia coli* outbreak. Infect Control Hosp Epidemiol 2015;36(6):634–42.
[27] Kovaleva J, Meessen NE, Peters FT, Been MH, Arends JP, Borgers RP, et al. Is bacteriologic surveillance in endoscope reprocessing stringent enough? Endoscopy 2009;41(10):913–6.
[28] Fraser TG, Reiner S, Malczynski M, Yarnold PR, Warren J, Noskin GA. Multidrug-resistant *Pseudomonas aeruginosa* cholangitis after endoscopic retrograde cholangiopancreatography: failure of routine endoscope cultures to prevent an outbreak. Infect Control Hosp Epidemiol 2004;25(10):856–9.
[29] Kenters N, Tartari E, Hopman J, El-Sokkary RH, Nagao M, Marimuthu K, et al. Worldwide practices on flexible endoscope reprocessing. Antimicrob Resist Infect Control 2018;7(1):153.
[30] Cassini A, Hogberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. Lancet Infect Dis 2019;19(1):56–66.
[31] FDA. Statement from Jeff Shuren, M.D., J.D., Director of the Center for Devices and Radiological Health, on updated safety communication about rates of duodenoscope contamination from preliminary postmarket data 2018. Available from: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm628096.htm.
[32] García-Cano J, Perez-Miranda M, Enric B, González-Huix F, López-Rosés L, Vila JJ. Sa1206 duodenoscope-transmited infection: results from a national spanish survey. Gastrointest Endosc 2016;83(5):AB255.
[33] Shenoy ES, Pierce VM, Walters MS, Moulton-Meissner H, Lawsin A, Lonsway D, et al. Transmission of mobile colistin resistance (mcr-1) by duodenoscope. Clin Infect Dis 2018;68(8):1327–34.
[34] Loeve AJ. Investigational report on a TJF-Q180V duodenoscope following contamination after cleaning and disinfection Available on request from the Dutch Healthcare Inspectorate/National Institute for Public Health and the Environment, Bilthoven, The Netherlands. Available on request from the Dutch Healthcare Inspectorate/National Institute for Public Health and the Environment.
[35] Bruijn ACPd, Drongelen AWv. Desinfection of the Olympus TJF-Q180V ERCP endoscope. RIVM Adviespunt Medische en Consumentenproducten. Projectnummer: V/080118/01/AH. Bilthoven, the Nederlands: National Institute for Public Health and the Environment / Rijksinstituut voor Volksgezondheid en Milieu RIVM; 2012.
[36] FDA. FDA clears Olympus TJF-Q180V duodenoscope with design modifications intended to reduce infection risk 2016. Available from: www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm481956.htm.
[37] FDA. The FDA Provides interim results of duodenoscope reprocessing studies conducted in real-world settings: FDA safety communication 2018 [updated 10-12-2018. Available from: https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm628020.htm.
[38] Epstein L, Hunter JC, Arwady MA, Tsai V, Stein L, Gribogiannis M, et al. New Delhi metallo-beta-lactamase-producing carbapenem-resistant *Escherichia coli* associated with exposure to duodenoscopes. JAMA 2014;312(14):1447–55.
[39] Rauwers AW, Voor In 't Holt AF, Buijs JG, de Groot W, Hansen BE, Bruno MJ, et al. High prevalence rate of digestive tract bacteria in duodenoscopes: a nationwide study. Gut 2018;67(9):1637–45.
[40] Thaker AM, Kim S, Sedarat A, Watson RR, Muthusamy VR. Inspection of endoscope instrument channels after reprocessing using a prototype borescope. Gastrointest Endosc 2018;88(4):612–9.
[41] Ofstead CL, Wetzler HP, Heymann OL, Johnson EA, Eiland JE, Shaw MJ. Longitudinal assessment of reprocessing effectiveness for colonoscopes and gastroscopes: results of visual inspections, biochemical markers, and microbial cultures. Am J Infect Control 2017;45(2):e26–33.
[42] Lee DH, Kim DB, Kim HY, Baek HS, Kwon SY, Lee MH, et al. Increasing potential risks of contamination from repetitive use of endoscope. Am J Infect Control 2015;43(5):e13–7.
[43] Committee AQAIE, Petersen BT, Chennat J, Cohen J, Cotton PB, Greenwald DA, et al. Multisociety guideline on reprocessing flexible gastrointestinal endoscopes: 2011. Gastrointest Endosc 2011;73(6):1075–84.
[44] Beilenhoff U, Biering H, Blum R, Brljak J, Cimbro M, Dumonceau JM, et al. Prevention of multidrug-resistant infections from contaminated duodenoscopes: position statement of the European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastroenterology Nurses and Associates (ESGENA). Endoscopy 2017;49(11):1098–106.
[45] Fujifilm Medical System U.S.A.Urgent medical device corecctioncorrection and removal 2017 [updated 21-07-2017. Available from: https://www.fujifilmusa.com/products/medical/endoscopy/pdf/UrgentFieldCorrectionAndRemoval_ED530XT_072117.pdf.
[46] Pentax of America Inc.ED34−i10T traditional 510(k) submission 2017. Available from: https://www.accessdata.fda.gov/cdrh_docs/pdf16/K163614.pdf.
[47] Olympus Medical System Corp.Customer letter: urgent medical device removal and corrective action. Elevator mechanism replacement, updated operation manual, and new reprocessing instructions for the Olympus TJF-Q180V Duodenoscope 2016 [updated 15-01-2016. Available from: http://medical.olympusamerica.com/sites/us/files/pdf/160115-Olympus-TJF-Q180V-Customer-Letter.pdf.
[48] AQAiE Committee, AH Calderwood, Day LW, Muthusamy VR, Collins J, Hambrick 3rd RD, et al. ASGE guideline for infection control during GI endoscopy. Gastrointest Endosc 2018;87(5):1167–79.
[49] Rutala WA, Weber DJ. Outbreaks of carbapenem-resistant enterobacteriaceae infections associated with duodenoscopes: what can we do to prevent infections? Am J Infect Control. 2016;44(5 Suppl):e47–51.
[50] Roberts CG. Studies on the bioburden on medical devices and the importance of cleaning. Disinfection, sterilization and antisepsis: principles and practices in healthcare facilities. Washington, DC: Association for Professional in Infection Control and Epidemiology; 2001. p. 63–9.
[51] Alfa MJ, Degagne P, Olson N. Worst-case soiling levels for patient-used flexible endoscopes before and after cleaning. Am J Infect Control 1999;27(5):392–401.
[52] Rutala WA, Weber DJ. FDA labeling requirements for disinfection of endoscopes: a counterpoint. Infect Control Hosp Epidemiol 1995;16(4):231–5.

[53] Ofstead CL, Wetzler HP, Snyder AK, Horton RA. Endoscope reprocessing methods: a prospective study on the impact of human factors and automation. Gastroenterol Nurs 2010;33(4):304–11.

[54] Dirlam Langlay AM, Ofstead CL, Mueller NJ, Tosh PK, Baron TH, Wetzler HP. Reported gastrointestinal endoscope reprocessing lapses: the tip of the iceberg. Am J Infect Control 2013;41(12):1188–94.

[55] Schaefer MK, Jhung M, Dahl M, Schillie S, Simpson C, Llata E, et al. Infection control assessment of ambulatory surgical centers. JAMA 2010;303(22):2273–9.

[56] Departement Welzijn VeG-Z.Beleidsrapport desinfectie van flexibele endoscopen met lumen. Depotnummer D/2017/3241/232 2017. Available from: https://www.departementwvg.be/sites/default/files/media/documenten/Beleidsrapport_desinfectie_flexibele_endoscopen_met_lumen_juli_2017.pdf.

[57] Thaker AM, Muthusamy VR, Sedarat A, Watson RR, Kochman ML, Ross AS, et al. Duodenoscope reprocessing practice patterns in U.S. endoscopy centers: a survey study. Gastrointest Endosc 2018;88(2):316–22.e2.

[58] Bruijn ACPd, Drongelen AWv. Control measures for the use of endoscope disinfectors: Progress progress of the implementation of the SFERD quality manual. 2018.

[59] Gastroenterological Society of Australia/Gastroenterological Nurses College of Australia. Infect. Control Endosc Mulgrave, Australia 2010. Available from: http://www.gesa.org.au/files/editor_upload/File/DocumentLibrary/Professional/Infection_Control_in_Endoscopy_Guidelines_2014.pdf.

[60] Dutch Association for Medical Microbiology (NVMM). Guideline: control of microbiological safety of thermolabile flexible high-risk gastrointestinal endoscopes/richtlijn controle op microbiologische veiligheid van thermolabiele flexibele hoog-risico gastro-intestinale endoscopen 2018. Available from: https://www.nvmm.nl/media/2222/180627-richtlijn-controle-op-microbiologische-veiligheid-van-thermolabiele-flexibele-gi-endoscopen-juiste-versie.pdf

[61] Ministere des Affaires sociales et de la sante. Guide technique: traitement des endoscopes souples thermosensibles a canaux 2016. Available from: http://nosobase.chu-lyon.fr/recommandations/Ministere_Sante/2016_EndoscopeSouple_Ministere.pdf.

[62] Bourigault C, Le Gallou F, Bodet N, Musquer N, Juvin ME, Corvec S, et al. Duodenoscopy: an amplifier of cross-transmission during a carbapenemase-producing *enterobacteriaceae* outbreak in a gastroenterology pathway. J Hosp Infect 2018;99(4):422–6.

[63] Humphries RM, Yang S, Kim S, Muthusamy VR, Russell D, Trout AM, et al. Duodenoscope-related outbreak of a carbapenem-resistant klebsiella pneumoniae identified using advanced molecular diagnostics. Clin Infect Dis 2017;65(7):1159–66.

[64] Olafsdottir LB, Whelan J, Snyder GM. A systematic review of adenosine triphosphate as a surrogate for bacterial contamination of duodenoscopes used for endoscopic retrograde cholangiopancreatography. Am J Infect Control 2018;46(6):697–705.

[65] Rutala WA, Weber DJ. Reprocessing semicritical items: current issues and new technologies. Am J Infect Control 2016;44(5 Suppl):e53–62.

[66] ASoP Committee, MA Khashab, Chithadi KV, Acosta RD, Bruining DH, Chandrasekhara V, et al. Antibiotic prophylaxis for GI endoscopy. Gastrointest Endosc 2015;81(1):81–9.

[67] Kim S, Russell D, Mohamadnejad M, Makker J, Sedarat A, Watson RR, et al. Risk factors associated with the transmission of carbapenem-resistant *Enterobacteriaceae* via contaminated duodenoscopes. Gastrointest Endosc 2016;83(6):1121–9.

[68] Higa JT, Choe J, Tombs D, Gluck M, Ross AS. Optimizing duodenoscope reprocessing: rigorous assessment of a culture and quarantine protocol. Gastrointest Endosc 2018;88(2):223–9.

[69] Rex DK, Sieber M, Lehman GA, Webb D, Schmitt B, Kressel AB, et al. A double-reprocessing high-level disinfection protocol does not eliminate positive cultures from the elevators of duodenoscopes. Endoscopy 2018;50(6):588–96.

[70] Ma GK, Pegues DA, Kochman ML, Alby K, Fishman NO, Saunders M, et al. Implementation of a systematic culturing program to monitor the efficacy of endoscope reprocessing: outcomes and costs. Gastrointest Endosc 2018;87(1):104–9.e3.

[71] Naryzhny I, Silas D, Chi K. Impact of ethylene oxide gas sterilization of duodenoscopes after a carbapenem-resistant enterobacteriaceae outbreak. Gastrointest Endosc 2016;84(2):259–62.

[72] Kovaleva J. Infectious complications in gastrointestinal endoscopy and their prevention. Best Pract Res Clin Gastroenterol 2016;30(5):689–704.

[73] Rutala WA, Weber DJ. ERCP scopes: what can we do to prevent infections? Infect Control Hosp Epidemiol. 2015;36(6):643–8.

[74] Almario CV, May FP, Shaheen NJ, Murthy R, Gupta K, Jamil LH, et al. Cost utility of competing strategies to prevent endoscopic transmission of carbapenem-resistant enterobacteriaceae. Am J Gastroenterol 2015;110(12):1666–74.

[75] Molloy-Simard V, Lemyre JL, Martel K, Catalone BJ. Elevating the standard of endoscope processing: terminal sterilization of duodenoscopes using a hydrogen peroxide-ozone sterilizer. Am J Infect Control 2018;47(3):243–50.

[76] Balan GG, Rosca I, Ursu EL, Doroftei F, Bostanaru AC, Hnatiuc E, et al. Plasma-activated water: a new and effective alternative for duodenoscope reprocessing. Infect Drug Resist 2018;11:727–33.

[77] van Drongelen A, Hessels J, Geertsma R. RIVM letter report: comparison of market authorization systems of medical devices in USA and Europe. Bilthoven, the Nederlands. 2015.

[78] FDA. Is a new 510(k) required for a modification to the device? 2014. Available from: www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm134575.htm.

[79] FDA. Updated Information for healthcare providers regarding duodenoscopes silver spring, USA 2015. Available from: www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/ReprocessingofReusableMedicalDevices/UCM436588.pdf.

[80] Olympus Medical System Corp. Important update 2016. Available from: www.olympus-europa.com/medical/en/medical_systems/products_services/tjf_statement/tjf_statement_1.jsp.

[81] Olympus Medical System Corp. TJF-Q190V duodenoscope 2018. Available from: https://www.olympus-europa.com/medical/rmt/media/Content/Content-MSD/Documents/Brochures/E0428371_TJF-Q190V_A4_Flyer_EN_ABC02-2_FINAL_42669.pdf

[82] Fujifilm Europe. Duodenoscope ED-580XT 2018. Available from: https://www.fujifilm.eu/fileadmin/countries/EU/endoscopy/Brochures/Duodenoscope_Brochure_08_2018_72dpi.pdf.

[83] Endoskope KS. Highlights gastroenterology 2018. Available from: https://www.karlstorz.com/cps/rde/xbcr/karlstorz_assets/ASSETS/3544814.pdf

[84] Pentax Medical. DEC video duodenoscope ED34-i10T2 2017. Available from: https://www.pentaxmedical.com/pentax/download/fstore/uploadFiles/Pdfs/Brochures/EMEA_GI_BR_DEC%20Brochure_10_17.pdf.

[85] Butcher A. Endoscopy presentation for the investment community at DDW: Boston Scientific; 2018. Available from: http://investors.bostonscientific.com/~/media/Files/B/Boston-Scientific-IR/documents/events/endoscopy-investor-webcast-june-2018.pdf.

[86] Perbet S, Blanquet M, Mourgues C, Delmas J, Bertran S, Longere B, et al. Cost analysis of single-use (Ambu((R)) aScope) and reusable bronchoscopes in the ICU. Ann Intensive Care 2017;7(1):3.

[87] Usawachintachit M, Isaacson DS, Taguchi K, Tzou DT, Hsi RS, Sherer BA, et al. A prospective case-control study comparing lithovue, a single-use, flexible disposable ureteroscope, with flexible, reusable fiber-optic ureteroscopes. J Endourol 2017;31(5):468–75.

[88] Bang JY, Sutton B, Hawes R, Varadarajulu S. Concept of disposable duodenoscope: at what cost? Gut. 2019. doi: 10.1136/gutjnl-2019-318227.

[89] Ofstead CL, Quick MR, Eiland JE, Adams SJ. A glimpse at the true cost of reprocessing endoscopes. Int Assoc Healthc Cent Serv Mater Manag 2017. Available from: https://www.bostonscientific.com/content/dam/bostonscientific/uro-wh/portfolio-group/LithoVue/pdfs/Sterilization-Resource-Handout.pdf.

[90] Dik JW, Dinkelacker AG, Vemer P, Lo-Ten-Foe JR, Lokate M, Sinha B, et al. Cost-analysis of seven nosocomial outbreaks in an academic hospital. PLoS One 2016;11(2):e0149226.

[91] Mollers M, Lutgens SP, Schoffelen AF, Schneeberger PM, Suijkerbuijk AWM. Cost of nosocomial outbreak caused by NDM-1-containing klebsiella pneumoniae in the Netherlands, October 2015-January 2016. Emerg Infect Dis 2017;23(9):1574–6.