Nationwide risk analysis of duodenoscope and linear echoendoscope contamination

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Background and Aims: Contaminated duodenoscopes and linear echoendoscopes (DLEs) pose a risk for infectious outbreaks. To identify DLEs and reprocessing risk factors, we combined the data from the previously published nationwide cross-sectional PROCESS 1 study (Prevalence of contamination of complex endoscopes in the Netherlands) with the follow-up PROCESS 2 study.

Methods: We invited all 74 Dutch DLE centers to sample ≥2 duodenoscopes during PROCESS 1, and all duodenoscopes as well as linear echoendoscopes during PROCESS 2. The studies took place 1 year after another. Local staff sampled each DLE at ≤6 sites according to uniform methods explained by online videos. We used 2 contamination definitions: (1) any microorganism with ≥20 colony-forming units (CFU)/20 mL (AM20) and (2) presence of microorganisms with GI or oral origin, independent of CFU count (MGOs). We assessed the factors of age and usage by performing an analysis of pooled data of both PROCESS studies; additional factors including reprocessing characteristics were only recorded in PROCESS 2.

Results: Ninety-seven percent of all Dutch centers (72 of 74; PROCESS 1, 66; PROCESS 2, 61) participated in one of the studies, sampling 309 duodenoscopes and 64 linear echoendoscopes. In total, 54 (17%) duodenoscopes and 8 (13%) linear echoendoscopes were contaminated according to the AM20 definition. MGOs were detected on 47 (15%) duodenoscopes and 9 (14%) linear echoendoscopes. Contamination was not age or usage dependent (all *P* values ≥.27) and was not shown to differ between the reprocessing characteristics (all *P* values ≥.01).

Conclusions: In these nationwide studies, we found that DLE contamination was independent of age and usage. These results suggest that old and heavily used DLEs, if maintained correctly, have a similar risk for contamination as new DLEs. The prevalence of MGO contamination of ~15% was similarly high for duodenoscopes as for linear echoendoscopes, rendering patients undergoing ERCP and EUS at risk for transmission of microorganisms. (Gastrointest Endosc 2020;92:681-91.)

Abbreviations: AER, automated endoscope reprocessor; AM20, any microorganism with ≥20 CFU/20 mL; CFU, colony-forming units; DLE, duodenoscope and linear echoendoscope; IFU, instructions for use; IQR, interquartile range; MGO, presence of microorganisms with GI or oral origin, independent of CFU count; PROCESS study, Prevalence of contamination of complex endoscopes in the Netherlands; SFERD, Dutch Steering Group for Flexible Endoscope Cleaning and Disinfection.

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INTRODUCTION

Worldwide, an increasing number of reports describe outbreaks of multidrug-resistant organisms caused by contaminated duodenoscopes.[1-6] Duodenoscopes are used for ERCP procedures, of which approximately 650,000 are performed in the United States annually.[7] Contaminated duodenoscopes and the subsequent outbreaks are commonly detected by transmission of multidrug-resistant organisms bearing distinct features that enable retrospective tracing. Often, these outbreaks are not properly reported, registered, and/or communicated by manufacturers, hospitals, and governmental bodies.[1,2,4] Although 400 patient infections and 20 deaths were officially reported between 2012 and 2017,[1,2,7] the actual number of patients affected by transmission of exogenous microorganisms and the corresponding burden of disease is likely to be much higher.[1]

Patients undergoing ERCP are exposed to exogenous microorganisms when duodenoscopes are not properly cleaned, and therefore remain contaminated. Recent studies show that the incidence of duodenoscope contamination ranges from 0.3% to 30%.[8-14] The first nationwide PROCESS (Prevalence of contamination of complex endoscopes in the Netherlands) study showed that 15% of patient-ready duodenoscopes were contaminated with GI or oral microorganisms, that is, bacteria originating from previous patients.[15] Contamination of reprocessed duodenoscopes is attributed to their complex design, which includes a side viewing tip, forceps elevator, and elevator wire channel.[16] Linear echoendoscopes, used for EUS procedures, have a similarly complex design with an additional balloon channel. Several studies have reported contamination of linear echoendoscopes,[9,17] raising the question of whether the prevalence of contamination in duodenoscopes and linear echoendoscopes (DLEs) is similar at a nationwide level.

The margin of safety of endoscope reprocessing is small and does not leave any room for error.[18-21] In clinical practice, however, reprocessing procedures are error prone, and adequate decontamination is not guaranteed.[15,22-28] Large multicenter studies show that contamination is independent of duodenoscope manufacturer,[9,15] type,[15] or endoscope age,[9] implying that all DLEs seem to have a similar risk for contamination. Risk factors for DLE contamination and potential subsequent interventions are still unknown and require additional investigation. Therefore, we conducted a second nationwide study, the PROCESS 2 study, to (re-)assess the level of contamination of DLEs. We combined the data from the PROCESS 1 and 2 studies to identify potential DLE and reprocessing risk factors for contamination of DLEs.

METHODS

Setting and design

We conducted 2 prospective nationwide cross-sectional studies among the 74 Dutch centers using DLEs: the PROCESS 1 and 2 studies. Although the prevalence data from PROCESS 1 have been published,[15] the data on endoscope age and usage have not been published before. During PROCESS 1, we invited centers to sample at least 2 reprocessed duodenoscopes and to include the newest Olympus TJF-Q180V (Olympus, Zoeterwoude, the Netherlands) as 1 of the 2 duodenoscopes if possible. During PROCESS 2, we invited centers to sample all reprocessed DLEs present in the endoscopy department.

Reprocessing, the multistep process of postprocedure flushing, manual cleaning, automated cleaning, high-level disinfection, and drying, was performed according to each endoscope's instructions for use (IFUs) and according to the standard handbook of the Dutch Steering Group for Flexible Endoscope Cleaning and Disinfection (SFERD).[29] At the time of the PROCESS studies, microbiological surveillance was only recommended after repairs,[29] but centers could perform routine surveillance on their own initiative. No patient data or patient samples were collected and/or included in this study, therefore there was no need for approval by the Medical Ethical Research Committee.

Sample collection and culture methods

The sampling, culturing, and methods of interpretation were the same for both studies and described extensively for PROCESS 1 (see Supplementary Information, available online at www.giejournal.org).[15] In PROCESS 2, we provided additional sampling protocols for linear echoendoscopes, which included sampling of the balloon channel (Supplementary Tables 1-3, Appendices 1-6, available online at www.giejournal.org). Contamination was defined as (1) microbial growth with ≥20 CFU/20 mL of any type of microorganism (AM20) as used by the then current European Society of Gastrointestinal Endoscopy guidelines and Dutch SFERD handbook,[29,30] or (2) the presence of microbial growth (≥1 CFU/20 mL) of GI and/or oral microorganisms (MGOs).

Risk factors for contamination

Data on endoscope age and usage were recorded using questionnaires for both PROCESS studies. For PROCESS 2, an extended set of DLE and reprocessing factors was recorded. Age was defined as the time between the date of purchase of the endoscope and the sampling date. Usage was defined as the number of procedures for which the endoscope was used since the date of purchase until the date of sampling. Only endoscopes purchased first hand with usage registries at the time of purchase were included; second-hand endoscopes, loan endoscopes, and endoscopes whose usage was not recorded directly from the construction date were not included. Risk factors recorded for PROCESS 2 included biopsy channel replacement, reprocessing characteristics (manual cleaning detergent, automated cleaning detergent, disinfectant and type of automated endoscope reprocessor [AER]), moment of

sampling (drying cabinet or AER), and frequency of microbiological surveillance.

Statistical analysis

Categorical data are presented in percentages. Means (standard deviation) and medians (interquartile range [IQR]) are given for continuous and skewed data, respectively. Contamination rates were analyzed by multilevel logistic regression. This modeling technique allowed us to take into account the hierarchical structure of the data (and the correlation between measurements possibly caused by it): samples were taken at multiple locations per DLE, DLEs could be investigated in both PROCESS studies, and DLEs were grouped within their respective centers.

Using PROCESS 2 data, we assessed reprocessing characteristics. Variant types of each reprocessing characteristic could be included if there was at least 1 case of contamination and 1 case of noncontamination. The most frequently observed category was used as a reference. If possible, we categorized different factors to enable analysis of groups with larger power. Odds ratios with 95% confidence intervals were calculated for each characteristic. To correct for the increased possibility of a type I error as a result of testing in multiple subsets using 2 outcome definitions, we applied Bonferroni correction, giving $\alpha = 0.05/10 = 0.005$.

We pooled data from both PROCESS studies to analyze the endoscope age and usage. The model was adjusted for age and usage when analyzing duodenoscopes and linear echoendoscopes separately. In a second analysis using data from PROCESS 2 only, age and usage were reset if the biopsy channel was replaced. Odds ratios with 95% confidence intervals were calculated per year and per 100 procedures. We applied Bonferroni correction for the increased possibility of a type I error as a result of using both AM20 and MGO as outcome definitions, giving $\alpha = 0.05/2 = 0.025$. We performed the analyses using SPSS V21.0 (Chicago, Ill, USA) and R V3.4.1 (Vienna, Austria) using the lme4 package.[31]

Role of the funding source

A grant from the Dutch Ministry of Health funded the PROCESS studies. The funder was not involved in any part of this study, including study design, data collection, data analysis, data interpretation, or writing of the report.

RESULTS

PROCESS 2

The PROCESS 2 study was conducted between October 2016 and May 2017 in 61 of the 73 (84%) centers in the Netherlands performing ERCP and/or EUS procedures during this time period. Across these 61 centers, a total of 159 duodenoscopes and 64 linear echoendoscopes were included in the study. Contamination according to the AM20 definition was found on 21 (13%) duodenoscopes and 8 (13%) linear echoendoscopes (Table 1), originating from 20 (33%) centers (Supplementary Table 1). Prevalence rates per contamination category are shown in Supplementary Table 2. Contamination according to the MGO definition was found on 24 (15%) duodenoscopes and 9 (14%) linear echoendoscopes, originating from 24 (39%) centers. The median age was 5.5 years (IQR, 2.7-6.7 years) and the median usage was 266 procedures (IQR, 162-532 procedures) for duodenoscopes and 3.6 years (IQR, 1.3-5.8 years) and 270 procedures (128-443 procedures) for linear echoendoscopes, respectively (Table 2). In 30% of the DLEs, the biopsy channel was replaced (in 40 [30%] duodenoscopes and 16 [30%] linear echoendoscopes). Table 3 shows the adapted age and usage, which was reset to zero in the case of replacement of the biopsy channel.

Reprocessing characteristics. Reprocessing characteristics, assessed only during PROCESS 2, are shown in Table 4. In the Dutch centers included in the study (n = 61), more than 50% of the 217 DLEs were cleaned and disinfected with Neodisher products (Dr Weigert, Assen, the Netherlands), and 48% were disinfected in Wassenburg AERs (Wassenburg Medical, Dodewaard, the Netherlands). Contamination rates of AM20 and MGO for DLEs did not depend on the different reprocessing characteristics (Table 4, all P values $\geq$.01). This outcome did not change when the detergents and disinfectants were categorized into 2 groups (ie, detergents in alkaline and nonalkaline variants and disinfectants in peracetic acid or glutaraldehyde; all P values $\geq$.22). In total, 138 (63%) DLEs in 30 (51%) centers were subjected to surveillance cultures, of which 106 (48%) of the DLEs were sampled monthly or quarterly. Contamination, however, was not shown to be dependent on surveillance (all P values $\geq$.41).

PROCESS 1

PROCESS 1 was conducted between June 2015 and March 2016.[15] In total, 66 of the 74 (89%) eligible centers in the Netherlands during this time period participated. The centers included 150 duodenoscopes. We have presented the contamination prevalence results (AM20, 22% [n = 33]; MGO, 15% [n = 23]) of these duodenoscopes in a previous publication.[15] The endoscope age and usage data for PROCESS 1 as shown in Table 2 have not been presented before. The duodenoscopes had a median age of 4.4 years (IQR, 2.2-6.6 years) and had been used for a median of 180 procedures (IQR, 88-385 procedures).

Age and usage

PROCESS 1 and 2: pooled data. Overall, 97% (72 of 74) of all eligible Dutch centers participated in at least 1 of the 2 studies. In the PROCESS 1 and 2 studies pooled together, 373 DLEs were included and tested, consisting

TABLE 1. PROCESS 1 and 2: prevalence of AM20 and MGO contamination

	PROCESS 2			PROCESS 1*			PROCESS 1 and 2 pooled		
	N	AM20, n (%)	MGO, n (%)	N	AM20, n (%)	MGO, n (%)	N	AM20, n (%)	MGO, n (%)
All DLEs							373	62 (17)	56 (15)
Duodenoscopes	159	21 (13)	24 (15)	150	33 (22)	23 (15)	309	54 (17)	47 (15)
Olympus									
TJF-Q180V	68	9 (13)	8 (12)	69	15 (22)	15 (22)	137	24 (18)	23 (17)
TJF-160VR	45	6 (13)	6 (13)	43	13 (30)	6 (14)	88	19 (22)	12 (14)
TJF-160R	6	1 (17)	1 (17)	8	1 (13)	0	14	2 (14)	1 (7)
TJF-140R	1	0	1	2	0	0	3	0	1 (33)
TJF-145	–	–	–	2	0	0	0	0	0
Pentax									
ED34-i10T	14	0	2 (14)	11	3 (27)	0	25	3 (12)	2 (8)
ED-3490TK	11	3 (27)	3 (27)	8	0	0	19	3 (16)	3 (16)
ED-3680TK	–	–	–	1	0	1	1	0	1
Fujifilm									
ED-530XT8	7	1 (14)	2 (29)	5	0	0	12	1 (8)	2 (17)
ED-530XT	7	1 (14)	1 (14)	1	1	1	8	2 (25)	2 (25)
Linear echoendoscopes	64	8 (13)	9 (14)						
Olympus									
GF-UCT180	28	4 (14)	5 (18)						
GF-UCT140-AL5	3	0	0						
GF-UCT140P-AL5	1	0	0						
Pentax									
EG-3870UTK	17	3 (18)	3 (18)						
EG-3270UK	10	1 (10)	1 (10)						
FG-36UX	1	0	0						
Fujifilm									
EG-580UT	4	0	0						

AM20, Microbial growth with ≥20CFU/20 mL of any type of microorganism; *MGO*, presence of any microbial growth of GI or oral microorganisms; *DLE*, duodenoscopes and linear echoendoscopes.
*PROCESS 1 contamination results have been published before.[15]

of 309 (83%) duodenoscopes and 64 (17%) linear echoendoscopes. Eighty-one duodenoscopes were tested only once in PROCESS 1, 90 duodenoscopes were tested only once in PROCESS 2, and 69 duodenoscopes originating from 36 centers were tested in both PROCESS studies (Fig. 1). Ten different types of duodenoscopes and 7 types of linear echoendoscope were included from 3 manufacturers (ie, Olympus, Pentax, and Fujifilm). In total, 1866 sites were sampled (Supplementary Table 3). Table 1 shows the prevalence of contamination in the pooled duodenoscopes (AM20, 17% [n = 54]; MGO, 15% [n = 47]) and all DLEs collectively (AM20, 17% [n = 62]; MGO, 15% [n = 56]). The contaminated DLEs originated from 48 (67%) centers (Supplementary Table 1). The analysis of the pooled data from both PROCESS studies showed that contamination by AM20 and MGO in both duodenoscopes and linear echoendoscopes were not dependent on age or usage (all *P* values ≥.27; Fig. 2).

PROCESS 2: reset age and usage. Analysis of the reset age and usage using data from PROCESS 2 only did not demonstrate that contamination was age or usage dependent (all *P* values ≥.66; Fig. 3).

DISCUSSION

In the PROCESS 1 and 2 studies, we found that contamination of DLEs according to the MGO and AM20 definitions was independent of endoscope age and usage. These results suggest that older and more heavily used DLEs, if maintained correctly, have a similar risk for contamination as new DLEs. Furthermore, the prevalence of high MGO contamination of ~15% was comparable for duodenoscopes and linear echoendoscopes, rendering patients undergoing ERCP as well as EUS at risk for transmission of microorganisms. These results are in line with

TABLE 2. PROCESS 1 and 2: age and usage

	N	All endoscopes	AM20		MGO	
			Contaminated	Not contaminated	Contaminated	Not contaminated
Duodenoscopes						
PROCESS 2						
Age	148	5.5 (2.7-6.7)	5.7 (5.0-7.1)	5.3 (2.5-6.7)	6.3 (4.8-7.2)	5.3 (2.5-6.7)
Usage	118	266 (162-532)	257 (196-614)	269 (138-530)	344 (212-590)	260 (149-520)
PROCESS 1						
Age	142	4.4 (2.2-6.6)	4.9 (3.6-7.0)	4.2 (2.1-6.6)	4.4 (2.7-7.1)	4.4 (2.1-6.6)
Usage	111	180 (88-385)	400 (88-701)	175 (88-349)	279 (94-530)	175 (88-373)
PROCESS 1 and 2 pooled						
Age*	290	4.9 (2.5-6.7)	5.4 (3.7-7.1)	4.7 (2.2-6.7)	5.6 (3.4-7.1)	4.9 (2.2-6.6)
Usage*	229	231 (105-450)	287 (130-670)	228 (101-441)	282 (282-567)	230 (101-445)
Linear echoendoscopes						
PROCESS 2						
Age†	58	3.6 (1.3-5.8)	5.6 (0.8-6.5)	3.5 (1.3-5.7)	2.9 (1.8-4.9)	3.7 (1.3-6.0)
Usage†	50	270 (128-443)	405 (34-841)	243 (134-424)	305 (147-411)	250 (112-450)

Age is presented in years (median, IQR); usage is presented in number of procedures (median, IQR).
AM20, Microbial growth with ≥20 CFU/20 mL of any type of microorganism; *MGO*, presence of any microbial growth of GI or oral microorganisms.
*Information on age was missing for 19 (6%) duodenoscopes; on usage for 80 (26%) duodenoscopes.
†Information on age was missing for 6 (9%) linear echoendoscopes; on usage for 14 (22%) linear echoendoscopes.

TABLE 3. PROCESS 2: age and usage reset in cases of biopsy channel replacement

	N	All endoscopes	AM20		MGO	
			Contaminated	Not contaminated	Contaminated	Not contaminated
Duodenoscopes*						
Replaced biopsy channel	40		8 (20)	32 (80)	9 (23)	31 (77)
Original biopsy channel	95		9 (10)	86 (90)	12 (13)	83 (87)
Age†	132	3.4 (1.4-6.0)	4.7 (1.6-6.0)	3.4 (1.4-6.0)	4.7 (1.4-6.3)	3.4 (1.4-5.8)
Usage†	109	203 (61-440)	213 (38-362)	200 (64-447)	219 (31-510)	197 (63-437)
Linear echoendoscopes*						
Replaced biopsy channel	16		3 (19)	13 (81)	2 (13)	14 (87)
Original biopsy channel	38		4 (11)	34 (89)	6 (16)	32 (84)
Age†	51	2.4 (1.1-4.2)	1.5 (0.4-5.1)	2.5 (1.1-4.1)	2.4 (1.7-3.9)	2.5 (0.9-4.9)
Usage†	42	188 (61-386)	55 (34-515)	198 (75-378)	305 (147-411)	163 (43-378)

Age is presented in years (median, IQR); usage is presented in number of procedures (median, IQR).
AM20, Microbial growth with ≥20 CFU/20 mL of any type of microorganism; *MGO*, presence of any microbial growth of GI or oral microorganisms.
*Information on biopsy channel replacement was only recorded during PROCESS 2 and was missing in 24 (15%) duodenoscopes and 10 (16%) linear echoendoscopes.
†Age and usage were reset to zero on the date of the biopsy channel replacement if the channel was replaced.

previous reports showing that duodenoscopes of all manufacturers and types can be a source for outbreaks.[1,2] Our results also support the notion that outbreaks are inevitable when the current design of DLEs are processed using error-prone reprocessing procedures with an insufficient margin of safety. Effective control measures, such as feasible sterilization instead of disinfection, and eventually radical redesign of DLEs are required.

In the current study, we found that contamination was not dependent on age or usage. Other studies, including a large multicenter study, also found that contamination was not age dependent,[9,32] although in 2 single-center studies, contamination of GI endoscopes was associated with either age or usage.[10,33] DLEs are subject to heavy wear and tear, including (1) repeated bending of the vulnerable distal end, (2) damage caused by endoscope accessories (eg, forceps or baskets), and (3) mechanical as well as chemical strain with each reprocessing cycle. Undetected damage in duodenoscopes is known to cause outbreaks.[8,34,35] Recent borescope studies show that biopsy channels are frequently damaged,[36-38] which adds to the risk of contamination.[39] In this study,

TABLE 4. PROCESS 2: reprocessing characteristics

		AM20			MGO		
	N	Contaminated, n (%)	Not contaminated, n (%)	*P* value	Contaminated, n (%)	Not contaminated, n (%)	*P* value
Manual cleaning detergent	217*						
Neodisher MediClean Forte†‡	145	23 (16)	122 (84)	Reference	27 (19)	118 (81)	Reference
Neodisher endo Clean†‡	33	2 (6)	31 (94)	.47	2 (6)	31 (94)	.38
Neodisher endo DIS active†‡	4	0	4		1 (25)	3 (75)	.89
Neodisher MediClean†‡	4	0	4		0	4	
Neodisher Steelco†‡	4	2 (50)	2 (50)	.37	0	4	
Medivators Intercept Detergent	11	1 (9)	10 (91)	.68	1 (9)	10 (91)	.60
Dr Peppe Instru Zym‡	7	0	7		0	7	
Wassenburg EndoHigh Detergent†‡	5	1 (20)	4 (80)	1.0	1 (20)	4 (80)	.93
Olympus EndoDet	4	0	4		0	4	
Automated cleaning detergent	216*						
Neodisher MediClean Forte	81	10 (12)	71 (88)	Reference	12 (15)	69 (85)	Reference
Neodisher endo Clean	42	3 (7)	39 (93)	.66	1 (2)	41 (98)	.33
Neodisher SC	9	2 (22)	7 (78)	.65	1 (11)	8 (89)	.87
Getinge Poka-Yoke DLC	30	7 (23)	23 (77)	.30	10 (33)	20 (67)	.14
Olympus EndoDet	35	5 (14)	30 (86)	.81	5 (14)	30 (86)	.81
Medivators Intercept Detergent	11	1 (9)	10 (91)	.82	1 (9)	10 (91)	.73
Wassenburg EndoHigh Detergent	8	1 (13)	7 (88)	.96	1 (13)	7 (88)	.89
Disinfectant	220*						
Neodisher endo SEPT PAC	65	9 (14)	56 (86)	Reference	9 (14)	56 (86)	Reference
Neodisher endo SEPT GA	45	4 (9)	41 (91)	.60	2 (4)	43 (96)	.38
Neodisher Septo DN (GA)	16	2 (13)	14 (88)	.95	1 (6)	15 (94)	.61
Getinge Aperlan Poka-Yoke (PAA)	30	7 (23)	23 (77)	.40	10 (33)	20 (67)	.14
Olympus PAA	35	5 (14)	30 (86)	.95	5 (14)	30 (86)	.79
Olympus GA	4	0	4		1 (25)	3 (75)	.85
Medivators Rapicide PAA	15	1 (7)	14 (93)	.63	3 (20)	12 (80)	.84
Wassenburg EndoHigh PAA	5	0	5		0	5	
Wassenburg EndoHigh GTA	5	1 (20)	4 (80)	.81	1 (20)	4 (80)	.81
AER	220*						
Wassenburg WD440 PT	68	8 (12)	60 (88)	Reference	8 (12)	60 (88)	Reference
Wassenburg WD440	38	4 (11)	34 (89)	.93	2 (5)	36 (95)	.40
Getinge ED-FLOW	24	7 (29)	17 (71)	.11	9 (38)	15 (62)	.01
Getinge Poka-Yoke AER	6	0	6		1 (17)	5 (83)	.86
Olympus ETD3	21	5 (24)	16 (76)	.35	5 (24)	16 (76)	.16
Olympus ETD Double	11	0	11		1 (9)	10 (91)	.82
Olympus ETD4+	7	0	7		0	7	
Steelco EW2	19	2 (11)	17 (90)	.96	2 (11)	17 (90)	.90
Steelco EW1	3	1 (33)	2 (67)	.40	1 (33)	2 (67)	.27
Belimed WD 430	8	1 (13)	7 (87)	.95	0	8	
Medivators Advantage Plus	11	1 (9)	10 (91)	.83	1 (9)	10 (91)	.77
Medivators	4	0	4		2 (50)	2 (50)	.21

(*continued on the next page*)

TABLE 4. Continued

	N	AM20 Contaminated, n (%)	AM20 Not contaminated, n (%)	AM20 *P* value	MGO Contaminated, n (%)	MGO Not contaminated, n (%)	MGO *P* value
Moment of sampling	216*						
Storage cabinet	196	28 (14)	168 (86)	Reference	31 (16)	165 (84)	Reference
AER	20	1 (5)	19 (95)	.58	2 (10)	18 (90)	.72
Frequency surveillance cultures	219*						
Only in case of an incident	81	15 (19)	66 (81)	Reference	15 (19)	66 (81)	Reference
At least 1× per month	51	4 (8)	47 (92)	.48	7 (14)	44 (86)	.80
Every 2 or 3 months	55	10 (18)	45 (82)	.87	9 (16)	46 (84)	.91
Every 6 or 12 months	32	0	32	-	2 (6)	30 (94)	.41

AM20, Microbial growth with ≥20 CFU/20 mL of any type of microorganism; *MGO*, presence of any microbial growth of GI or oral microorganisms; *GA*, glutaraldehyde; *PAC* or *PAA*, peracetic acid; *AER*, automated endoscope reprocessor.
*Information on reprocessing characteristics was only recorded during PROCESS 2.
†Detergent with alkaline boosters.
‡Detergent with enzymatic boosters.

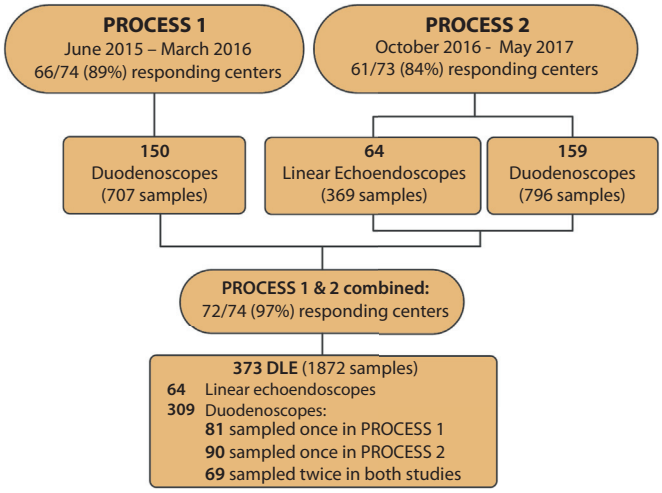

Figure 1. Flow diagram. *DLE*, Duodenoscopes and linear echoendoscopes; *PROCESS*, Prevalence of contamination of complex endoscopes in the Netherlands.

adequate and timely servicing is a plausible explanation as to why older and more heavily used DLEs had the same risk of contamination as new endoscopes. Fujifilm, Olympus, and Pentax recently recommended yearly technical inspections in their IFUs for specific duodenoscope types, [40-43] as is required by the Dutch guidelines.[44] However, time-based inspections still do not give clear guidance because yearly usage varies greatly between DLE procedures (PROCESS studies median yearly usage, 65; IQR, 41-109; similar to usage reported in other studies).[32] Therefore, manufacturers should assess the possibility of usage-based maintenance and inspections and their impact on the prevention of contamination.

Adequate preventive maintenance and servicing can potentially reset the endoscope, therefore the physical age and cumulative usage might not represent the actual state of the endoscope. Replacement of the biopsy channel potentially represents the most important part of endoscope maintenance. This channel is subject to heavy wear,[36-38] often replaced during repairs, and frequently contaminated (MGO contamination in the PROCESS studies: biopsy channel flushes, 5%; brush samples, 8%). However, using PROCESS 2 data with biopsy channel replacement as a surrogate marker for servicing, reset age and reset usage were also not associated with contamination. Biopsy channel replacement might not capture the whole story of complex repair histories because the PROCESS studies show that every DLE sampling site can harbor microorganisms. To assess usage as a contamination risk factor, future studies should potentially take the entire servicing history of an endoscope into account.

Guidelines and in vitro studies indicate potential differences in efficacy between detergents,[45-49] disinfectants,[48,50,51] and AERs.[52] In the current study, contamination was not shown to be dependent on reprocessing characteristics, which is in line with another multicenter study.[9] Instead of the assessed reprocessing factors, in our opinion, the variable manual cleaning step has the greatest impact on the reprocessing outcome. This is also complicated by other factors, including the complex DLE design, endoscope damage, and biofilm development. We also found that hospitals use different brands of detergents, disinfectants, and AERs together. Compatibility between these products and with different endoscopes is essential. In 2015, 2800 Custom Ultrasonics AERs (~20% of all USA AERs) had to be recalled when it became clear they were not compatible with closed-elevator channel endoscopes; this led to inconsistencies in duodenoscope disinfection and potentially contributed to outbreaks.[1] Transparent communication of adverse events by manufacturers of endoscopes and reprocessing equipment is essential. Furthermore, new

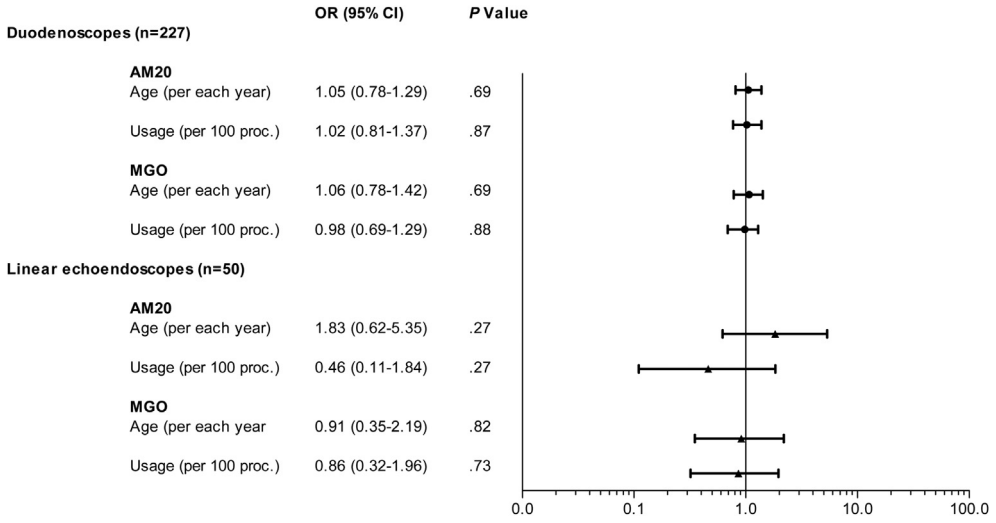

Figure 2. PROCESS 1 and 2: Odds ratios for age and usage on AM20 and MGO contamination in DLEs. Analysis of age and usage using pooled data from PROCESS 1 and 2. *AM20*, Microbial growth with ≥20 colony-forming units/20 mL of any type of microorganism; *DLE*, duodenoscopes and linear echoendoscopes; *MGO*, presence of any microbial growth of GI or oral microorganisms.

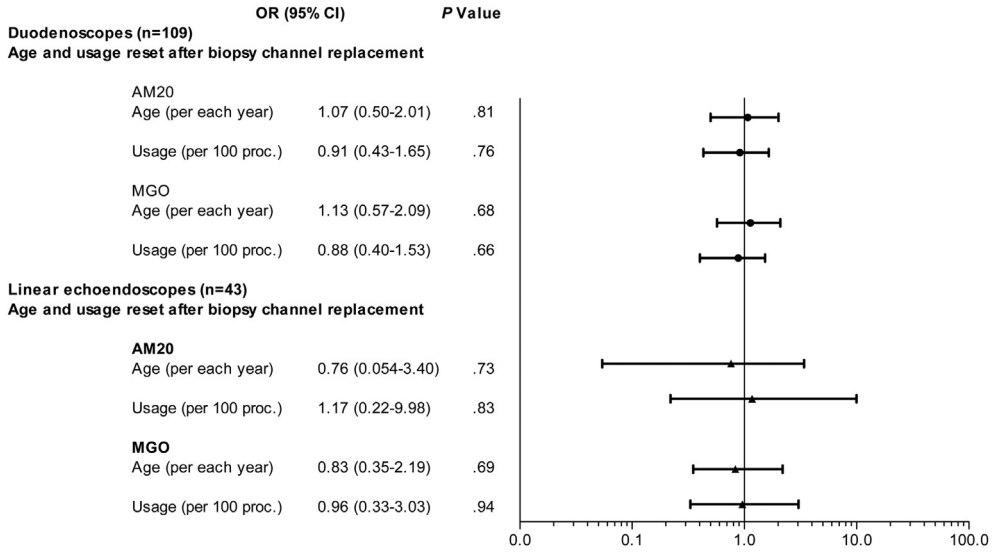

Figure 3. PROCESS 2: Odds ratios for reset age and usage on AM20 and MGO contamination in DLEs with information on biopsy channel replacement. Analysis of reset age and usage using data from PROCESS 2. *AM20*, Microbial growth with ≥20 CFU/20 mL of any type of microorganism; *CFU*, colony-forming units; *DLE*, duodenoscopes and linear echoendoscopes; *MGO*, presence of any microbial growth of GI or oral microorganisms.

reprocessing measures should be subject to peer-reviewed validation tests while ensuring compatibility with DLEs with adjusted designs.

When the contamination definition for high-concern organisms by the Centers for Disease Control and Prevention was used, the contamination prevalence for DLEs was 8% in this study, similar to the interim results of the postmarket surveillance studies ordered by the U.S. Food and Drug Administration.[53] Recent studies assessing surveillance,[9,13,17,53] culture and quarantine strategies,[8,9,54,55] double high-level disinfection,[14,56] and ethylene oxide sterilization[11] have reported promising lower contamination rates, showing that reduction of contamination is feasible. In addition to the assessed interventions, the lower rates may also be the result of continuous feedback and raised alertness by the culture results for these studies,[9,14,55,56] or less-sensitive sampling and culture methods. By not sampling all potential sites (eg, not including a channel brush[54,55] or channel flushes[14]), incubating cultures for only 48 hours,[14,54,56] or focusing only on carbapenem-resistant Enterobacteriaceae as the primary outcome,[11] contaminated endoscopes can be deemed false-negative, while still being a vector for transmission with subsequent infection. In our opinion, interventional measures should focus on the reduction of all MGOs. During PROCESS 2, 60% of the centers used a form of

microbiological surveillance, however contamination was not shown to be associated with surveillance. This is in line with reported outbreaks that occurred in settings where surveillance cultures were repeatedly negative.[3,57-60] Although microbiological surveillance will not entirely prevent contamination, it is essential for the identification of persistently contaminated DLEs. The other proposed measures require extensive financial investments; therefore, their value should be proven using sensitive culturing methods in a blinded and preferably multicenter setting before widespread implementation can be definitely recommended.

During both PROCESS studies, 15% of the endoscopes were contaminated with MGOs, indicating organic residue from previous patients. This suggests that reprocessing remained inadequate, especially because during PROCESS 2, a higher number of centers had at least 1 endoscope contaminated with MGOs (PROCESS 1, 29%; PROCESS 2, 39%). The prevalence of AM20 was lower during PROCESS 2, mainly consisting of less contamination with skin and water-borne flora. This may be the result of improved endoscope handling and protocol adherence by institutions after the first PROCESS study, (inter-)national alerts, and updates of IFUs and the Dutch Disinfection handbook.[29,42,44,61] The current study confirms that linear echoendoscopes can also be vectors for transmission,[9,10,14,17] but no echoendoscope-associated outbreaks have been reported to date. This might be because EUS is less invasive than ERCP, and risk factors for transmission during ERCP, such as an obstructed biliary system, do not play a role.[62,63] Also patients undergoing ERCP can be sicker and thus more prone to the development of infection if transmission occurs.

To the best of our knowledge, this is the first report to assess the association between DLE contamination and endoscope as well as reprocessing risk factors on a nationwide level. By pooling PROCESS 1 and 2 data, we could assess endoscope age and usage. Similar results for both PROCESS studies confirmed that the sampling and culturing method allows for a reliable and sensitive assessment of the DLE contamination rate.

The current study also has some limitations. Information on age and usage was not available for all DLEs, and the recorded repair history was limited to the biopsy channel. Furthermore, some factors that are exemplary of the complexity of reprocessing, for example, adherence to the multitude of steps, including meticulous manual cleaning, were not assessed in this study. Generalizability to other countries may be limited, depending on national differences in audit, surveillance, and maintenance strategies as well as availability and usage of endoscope types.

The persistent prevalence of high contamination for DLEs independent of type, age, usage, and reprocessing factors support the notion that current reprocessing techniques cannot guarantee adequate decontamination. To counter this, easy to apply and effective control measures should be devised and implemented to check for the efficacy of endoscope decontamination. Short-term reprocessing methods are required with a larger margin of safety counterbalanced with feasibility, welfare for staff, and suitability for use with existing model endoscopes. Ultimately, redesigned DLEs that can facilitate sterilization or single-use endoscopes must eliminate the risk of contamination. If not, contamination of DLEs will continue to occur with new outbreaks inevitable.

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SUPPLEMENTARY TABLE 1. Centers with ≥1 contaminated endoscope

	N	≥1 AM20 contaminated DLE, n (%)	≥1 MGO contaminated DLE, n (%)	≥1 MGO or AM20 contaminated DLE, n (%)
PROCESS 1	66	26 (39)	19 (29)	31 (47)
PROCESS 2	61	20 (33)	24 (39)	30 (49)
PROCESS 1 and 2 pooled	72	37 (51)	34 (47)	48 (67)

AM20, Microbial growth with ≥20 CFU/20 mL of any type of microorganism; *DLE*, duodenoscopes and linear echoendoscopes; *MGO*, presence of any microbial growth of GI or oral microorganisms.

SUPPLEMENTARY TABLE 2. DLEs contaminated with AM20

	N	AM20, n (%)	Gut flora ≥20 CFU, n (%)	Oral flora ≥20 CFU, n (%)	Skin flora ≥20 CFU, n (%)	Water-borne flora ≥20 CFU, n (%)
PROCESS 1						
Duodenoscopes	150	34 (23)	10 (7)	4 (3)	17 (11)	12 (8)
PROCESS 2	223	29 (13)	13 (6)	3 (1)	15 (7)	4 (2)
Duodenoscopes	159	21 (13)	9 (6)	3 (2)	12 (8)	2 (1)
Linear echoendoscopes	64	8 (13)	4 (6)	0	3 (5)	2 (3)

Microorganisms categorized by origin.
DLE, Duodenoscopes and linear echoendoscopes; *AM20*, microbial growth with ≥20 CFU/20 mL of any type of microorganism; *MGO*, presence of any microbial growth of GI or oral microorganisms.

SUPPLEMENTARY TABLE 3. Prevalence of AM20 and MGO contamination for sample sites

	PROCESS 2			PROCESS 1			PROCESS 1 and 2 pooled		
	N	AM20, n (%)	MGO, n (%)	N	AM20, n (%)	MGO, n (%)	N	AM20, n (%)	MGO, n (%)
Duodenoscopes									
All sample sites	796	34 (4)	42 (5)	707	51 (7)	36 (5)	1503	83 (6)	78 (5)
Biopsy channel	154	6 (4)	8 (5)	147	5 (3)	6 (4)	301	11 (4)	14 (5)
Suction channel	158	7 (4)	8 (5)	139	6 (4)	5 (4)	297	13 (4)	13 (4)
Forceps elevator	156	5 (3)	4 (3)	149	15 (10)	7 (5)	305	19 (6)	11 (4)
Brush	156	10 (6)	11 (7)	140	18 (13)	14 (10)	296	27 (9)	25 (8)
Protection cap	65	2 (3)	5 (8)	57	6 (11)	4 (7)	122	8 (7)	9 (7)
Elevator channel	61	3 (5)	3 (5)	53	0	0	114	3 (3)	3 (3)
Air/water channel	38	0	1 (3)	22	1 (5)	0	60	1 (2)	1 (2)
Brush air/water channel	8	1 (13)	2 (25)	–	–	–	8	1 (13)	2 (25)
Linear echoendoscopes									
All sample sites	369	17 (5)	19 (5)						
Biopsy channel	63	2 (3)	4 (6)						
Suction channel	62	4 (7)	6 (10)						
Forceps elevator	64	1 (2)	1 (2)						
Brush	64	3 (5)	3 (5)						
Elevator channel	58	5 (9)	2 (3)						
Air/water channel	27	2 (7)	2 (7)						
Brush balloon channel	31	0	1 (3)						

AM20, Microbial growth with ≥20 CFU/20 mL of any type of microorganism; *MGO*, presence of any microbial growth of GI or oral microorganisms.