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Anti-infectious decontamination strategies in Dutch intensive care units: A survey study on contemporary practice and heterogeneity

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ABSTRACT

Purpose: Despite increasing evidence and updated national guidelines, practice of anti-infectious strategies appears to vary in the Netherlands. This study aimed to determine the variation of current practices of anti-infectious strategies in Dutch ICUs.
Materials and methods: In 2018 and 2019 an online survey of all Dutch ICUs was conducted with detailed questions on their anti-infectious strategies.
Results: 89% (63 of 71) of the Dutch ICUs responded to the online survey. The remaining ICUs were contacted by telephone. 47 (66%) of the Dutch ICUs used SDD, 14 (20%) used SOD and 10 (14%) used neither SDD nor SOD. Within these strategies considerable heterogeneity was observed in the start criteria of SDD/SOD, the regimen adjustments based on microbiological surveillance and the monitoring of the interventions.
Conclusions: The proportion of Dutch ICUs applying SDD or SOD increased over time. Considerable heterogeneity in the regimens was reported. The impact of the observed differences within SDD and SOD practices on clinical outcome remains to be explored.

1. Introduction

Severe infections are the main reasons for intensive care unit (ICU) admission, but more importantly also frequently complicate ICU treatment [1,2]. Tailored anti-infectious strategies are thus an essential part of ICU treatment. Selective decontamination of the digestive tract (SDD) and selective oropharyngeal decontamination (SOD) are anti-infectious strategies originally described as preventive regimens, which aim to control and prevent infections in critically ill patients [3,4]. The baseline hypothesis of SDD (and SOD) regimens in critically ill patients is related to endogenous or acquired colonization and overgrowth of potential pathogenic microorganisms (PPM) [3-6]. The goal of SDD is to eradicate PPM from the oropharyngeal and digestive tract, and thereby reducing the risk of infections, such as ventilator-associated pneumonia (VAP) and bloodstream infections. Classical SDD in the ICU setting consists of 4 interconnected pillars of management: (1) nonabsorbable antibiotics (AB) applied to oropharynx and digestive tract to prevent secondary endogenous infections, (2) systemic AB with minimal effect on colonization resistance (CR) to treat primary endogenous infections, (3) monitoring and adjusting the interventions based on microbial (surveillance) cultures, and (4) a high level of hygiene to prevent exogenous infections [3,4]. In contrast, in SOD only local oropharyngeal antibiotics are applied and its main goal is to prevent VAP.

SDD, and to a lesser extent SOD are clinically effective, although most studies have been performed in countries with low levels of antibiotic resistance such as the Netherlands [7-11]. Moreover, SDD and SOD have not been associated with an increase in antimicrobial resistance [8,10,12-18]. The application of SDD and SOD as infection prevention regimens for intensive care patients has been strongly recommended in Dutch national guidelines [18-20]. However, specific elaboration on the essentiality of the different components is largely lacking. These different components may be divided into basic, optional and additional ones. Basic components were mandatory in the

Abbreviations: AB, Antibiotics; CR, Colonization resistance; ESBL, extended spectrum beta-lactamase; FTE, Full-time-equivalent; HRMO, Highly resistant microorganisms; ICU, Intensive care unit; IQR, Interquartile range; NICE, Netherlands intensive care evaluation; NVIC, "Nederlandse Vereniging voor Intensive Care" (Dutch intensive care society); PPM, Potential pathogenic microorganisms; SC, Standard care; SDD, Selective decontamination of the digestive tract; SOD, Selective oropharyngeal decontamination; VAP, Ventilator associated pneumonia.

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intervention arms of large SDD/SOD trials, and included the indication to initiate the SOD/SDD regimen, the use of nonabsorbable topical antibiotics, the use of systemic antibiotics (only in SDD), the application of antibiotic containing paste around tracheostomies, the use of suppositories in case of colostomy/ileostomy and microbial surveillance. Optional components were possibilities in these studies and included the intensification of topical antimicrobial therapy, nebulization of antimicrobials and the discouragement/prohibition of specific antibiotics. Several additional components, such as SDD component drug monitoring and promotion of intestinal decontamination were not originally part of the SDD/SOD regimens, but have been explored in recent studies [21-23]. Our survey study aimed to determine which anti-infectious regimen is used nowadays in Dutch ICUs, their change in use over time, and whether organizational ICU characteristics were associated with the use of a specific regimen. Secondly, we describe in detail the practical application of the anti-infectious strategies in a large sample of Dutch ICUs, with an emphasis on variability in basic, optional and additional components.

2. Materials and methods

A survey on anti-infectious strategies was developed by the authors (survey details in supplement) aiming to collect detailed information on the application of SDD, SOD and standard care. The survey was converted to an electronic document using SurveyMonkey (www.surveymonkey.com), which uses a direct check of adequate answering of the questions. The questions had pre-defined categories and if applicable space for free text. Each survey started with general questions on hospital and ICU characteristics, such as details on type of hospital, level and size of ICU, size of staff, and categories of patients admitted. After indicating which strategy was used (SDD/SOD/standard care (SC)) the survey followed three routes of relevant questions. The year of initiation of this strategy was asked.

The methods of application of basic, optional and additional components of the 4 pillars of SDD/SOD regimens were questioned in detail. Basic components included the indication to initiate SOD/SDD regimen, the use of nonabsorbable topical antibiotics, the use of systemic antibiotics (only in SDD), the application of paste around tracheostomies, the use of suppositories in case of colostomy/ileostomy and microbial surveillance (frequency, which body sites, determination of microorganisms and their susceptibility to AB). Optional components included the intensification of topical antibiotics, the nebulization of antimicrobials and the discouragement/prohibition of specific antibiotics (in order to preserve colonization resistance). Additional components included drug monitoring and promotion of intestinal decontamination. An invitation e-mail with a link to the survey was sent out to the medical directors of all 71 ICUs in the Netherlands via the Dutch Intensive Care Society (NVIC) in October and November 2018. A repeated request was sent in September 2019. One representative per unit was invited to respond and the response of only one representative per unit was included. Non-responding ICUs or those who did not complete the survey were contacted by telephone and/or email from September 2019 to January 2020. Next the attending intensivists of non-responding ICUs were contacted by telephone in June 2020 to ask the current anti-infectious regimen (SDD, SOD or SC). Missing organizational data was obtained via the website of NICE (Netherlands Intensive Care Evaluation; www.stichting-nice.nl).

2.1. Statistical analysis

Descriptive statistics, n (%) for categorical and median (+ interquartile range) for continuous data were examined for all organizational aspects, SDD/SOD/SC characteristics and microbiological data. Differences between groups were analysed with Fisher Exact test (Type of hospital), Kruskall-Wallis test (Number of ICU beds, number of intensivists per unit and number of nurses per unit) and Pearson chi-square test (University-affiliated region). Statistical significance was established at $p < 0.05$. Practice heterogeneity of certain components was defined as <70% of centres applying the component of interest. Data on composition of SDD/SOD mouth paste and suspension were categorised into reported combinations. All statistical analyses were conducted in SPSS.

3. Results

Between October 2018 and November 2019, 63 of 71 ICUs (89%) in the Netherlands responded to the survey. 51 surveys were complete and 12 had incomplete data (mostly data on microbiological aspects were missing). ICUs who did not respond to the survey were contacted by telephone in June 2020 and only information was obtained on ICU characteristics and the type of anti-infectious regimen used (Table S1).

Overall 47 (66%) of the ICUs use SDD, 14 (20%) SOD, and 10 (14%) use neither SDD nor SOD. The proportion of ICUs using SDD and SOD increased over time (Fig. 1).

3.1. Organizational characteristics

Characteristics of responding ICUs are presented in Table 1 (a more detailed description is provided in Table S1). SDD was used in ICUs of all 8 Dutch university hospitals, in 20 out of 26 (77%) teaching hospitals and in 19 out of 37 (51%) non-teaching hospitals. SOD was used by 0%, 15% and 27% of these hospitals, respectively. The median number of full-time-equivalent (FTE) intensivists in ICUs applying SOD or standard care was 5.1 (IQR 5.0–9.0) FTE and 4.2 (IQR 3.0–4.5) FTE, respectively. In ICUs applying SDD the median number of FTE intensivists was 6.4 (IQR 4.8–10.0). SDD use was associated with larger numbers of beds per ICU (14 [IQR 10–24] vs 12 [IQR 8–16] for SOD and 6 [IQR 6–9] for SC; $p = 0.003$), larger numbers of full-time-equivalent intensivists (median 6.4 vs. 5.1 (SOD) vs. 4.2 (SC); $p = 0.012$) and nurses (median 55 vs 40.8 (SOD)vs. 27 (SC); $p = 0.027$). Application of SDD, SOD or SC also differed between university-affiliated regions. All ICUs in the Amsterdam region used SDD, in contrast to only 45% of ICUs in the Utrecht and Maastricht region.

3.2. Anti-infectious ICU practice

The next section addresses the following components of SDD or SOD practice: Indication to start and stop SDD/SOD; practice of systemic AB use; practice of nonabsorbable AB use; the adjustments of topical therapy, microbiological surveillance and monitoring of potentially toxic topical antibiotic levels. Practice on hygiene control was not a subject of the current survey.

3.3. SDD practice

Results on the methodology of SDD practice are summarized in Tables 2–4 (More detailed description is provided in Tables S2, S3 and S4).

3.3.1. Indications for start and discontinuation of SDD

Most centres started SDD for patients expected to be on mechanical ventilation for more than 48 h (79%) or with an expected ICU stay of more than 72 h (48%). Reasons to discontinue SDD were ICU discharge (83%), while 12 out of 42 (29%) centres discontinued when oral intake was started.

3.3.2. Systemic antibiotics in SDD

ICUs used cefotaxime ($n = 27$; (64%)), ceftriaxone ($n = 14$; (33%)) or cefuroxime (n = 1; (2%)) as systemic prophylactic AB component, most frequently for a total duration of 4 days. Most centres (>78%) discouraged, but more than 88% did not forbid the use of certain systemic AB (most frequently discouraged AB: amoxicillin ± clavulanic acid, piperacillin/tazobactam, and penicillin; Table S3).

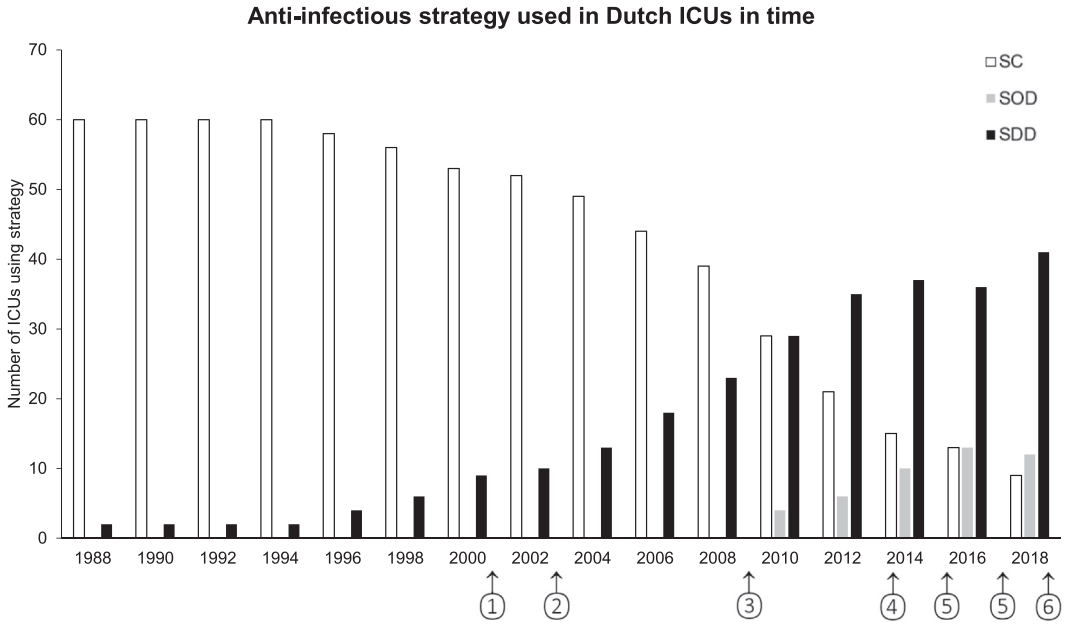

Fig. 1. Anti-infectious strategy used in Dutch ICUs in time. Use of anti-infectious strategy between 1988 and 2018 in 62 Dutch ICUs. SC-standard care; SOD-selective oropharyngeal decontamination; SDD- Selective decontamination of the Digestive tract. Studies and guidelines (year of publication): ① SWAB national guideline (2001) ② de Jonge et al. – Lancet (2003) [8]; ③ de Smet et al. – N Engl J Med (2009) [9]; ④ SWAB national guideline revision (2014) [29]; ⑤ Oostdijk et al. – JAMA (2014, revision 2017) [10]; ⑥ SWAB national guideline revision (2018) [19] + Wittekamp et al. – JAMA (2018) [11].

3.3.3. Practice on nonabsorbable antibiotics in SDD

In 39 out of 42 (92%) centres tobramycin, colistin and amphotericin B were the components of nonabsorbable antibiotics in suspension and mouth paste for topical application. Nystatin was used instead of amphotericin B in only 3 of the 42 (7%) ICUs. The frequency of suspension and paste application was four times daily in 93% of ICUs.

Measures to improve local decontamination were surveyed and included the following: (1) the adjustment of topical SDD regimens; (2) the use of SDD suppositories or enemas; (3) application of paste around tracheostomies; (4) additional measures to stimulate intestinal decontamination, and (5) the use of antimicrobial nebulization.

3.3.4. Adjustments of topical SDD regimen

Intensifying topical antimicrobials in case of persistent presence of PPM (defined as 1 or 2 positive surveillance cultures by 88% of centres) was most frequently applied by doubling the frequency of topical application (28 of 42; 85%). Of note, 2 centres never changed their SDD regimen. Over 90% of centres used SDD suppositories or enemas, mostly in case of a blind bowel loop after bowel surgery. Four of 42 (11%) centres prescribed suppositories or enemas to all patients on SDD. In contrast, SDD enemas are used to improve decontamination in 21 out of 34 (62%) centres. In addition, promotion of intestinal motility as measure to improve decontamination is used at initiation of SDD by 20 out of 34 centres (59%), and on indication by 82% of centres. 95% of SDD centres applied paste around the tracheostomies, usually two to four times daily. Nebulization as part of SDD was reported by 57% of centres (Table S4). Indications to start antimicrobial nebulization varied between hospitals, but the majority initiated nebulization after one (40%) or two (35%) positive surveillance respiratory tract cultures of PPM. Gram-negative bacteria were treated with colistin (35%), colistin or tobramycin (35%), or tobramycin (25%). Respiratory tract cultures growing Gram-positive bacteria are mostly left untreated (65%), while yeasts were treated by 65% of nebulizing centers (amphotericin B). Most centers stopped antimicrobial nebulization after two consecutive negative cultures.

Table 1
Antimicrobial strategy based on hospital- and ICU-characteristics.

	SC	SOD	SDD	*p*-value
Number of centres (%)	10 (14)	14 (20)	47 (66)	n.a.
Type of hospital				0.07
University hospital	0	0	8 (100)	
Teaching hospital	2 (8)	4 (15)	20 (77)	
Non-teaching hospital	8 (22)	10 (27)	19 (51)	
Number of ICU beds	6 [6–9]	12 [8–16]	14 [10–24]	0.003
# intensivists per unit	4.2 [3.0–4.5]	5.1 [5.0–9.0]	6.4 [4.8–10.0]	0.012
# nurses per unit	27 [20–38]	40.8 [28–75]	55 [37–99]	0.027
University-affiliated region				0.06
Amsterdam	0	0	13 (100)	
Groningen	1 (7)	3 (22)	10 (71)	
Leiden	0	2 (40)	3 (60)	
Maastricht	4 (45)	1 (11)	4 (45)	
Nijmegen	2 (25)	1 (13)	5 (63)	
Rotterdam	2 (15)	3 (23)	8 (62)	
Utrecht	1 (11)	4 (45)	4 (45)	

Data are presented in absolute numbers (percentages) or median [interquartile range]. ICU: Intensive care unit, SDD - Selective Decontamination of the Digestive tract, SOD – Selective Oropharyngeal Decontamination, SC - Standard Care, n.a. – not applicable.

3.3.5. Monitoring of SDD regimen

All centres performed microbial surveillance cultures to monitor resistance and/or efficacy of the SDD regimen. Results of 36 responding centres are shown in Tables 3, 4, S3 and S4. On admission all centres took rectal or perineal cultures, 92% throat cultures, and 89% sputum cultures. 27 out of 36 (78%) centres performed complete microbial surveillance cultures including throat, sputum and rectum/perineal, while sputum cultures were omitted by 22% of centres. Surveillance cultures were taken twice weekly by the large majority of centres. Results on the type of microbiological culture are presented in Table 4. Most ICUs use targeted testing on the presence of highly resistant microorganisms (HRMO) or extended spectrum beta-lactamase (ESBL) Enterobacteriaceae both on admission and during surveillance. Most centres performed routine microbiological cultures to screen for the presence of Gram-negative bacteria and *Candida* species. However, heterogeneity

Table 2
SDD and SOD methodology – treatment characteristics.

	SDD ($n = 42$)	SOD ($n = 12$)
Reasons to start SDD/SOD (basic)[a]		
>24 h of expected ICU stay	8 (19)	2 (17)
>48 h of expected ICU stay	1 (2)	–
>72 h of expected ICU stay	20 (48)	1 (8)
>48 h of mechanical ventilation	33 (79)	7 (58)
Specific category of patients	5[b] (12)	3[c] (24)
All patients	1 (2)	–
Reasons to discontinue SDD/SOD regimen (basic)[a]		
ICU discharge	35 (83)	7 (58)
Extubation	10 (24)	7 (58)
Oral intake	12 (29)	3 (25)
Microbiological resistance to products used	13 (31)	4 (33)
(Suspected) allergic reaction to products used	19 (45)	8 (67)
Persistent presence of resistant micro-organisms	1 (2)	3 (25)
Refusal by patient	2 (5)	–
After burn surgery is completed	1 (2)	–
Reasons not to start anti-infectious regimen[a]		
None	19 (45)	7 (58)
Known allergy	4 (9,5)	1 (8)
No enteral tube (no suspension)	3 (7)	n.a.
Nausea	1 (2)	–
Known colonization with MO resistant to SDD components	10 (24)	2 (17)
Refusal or intolerance of patients	4 (9,5)	–
Specific patient category	3[d] (7)	2[e] (17)
Components of SDD/SOD suspension and mouthpaste (basic)		
Tobramycin/Polymyxin E (colistin)/Amphotericin B	30 (71)	9 (75)
Tobramycin/Polymyxin B/Amphotericin B	9 (21)	2 (17)
Tobramycin/Polymyxin B/Nystatin	2 (5)	–
Tobramycin/Polymyxin E (colistin)/Nystatin	1 (2)	1 (8)
When do you intensify SDD ($n = 35$)/SOD ($n = 8$) paste/suspension? (optional)		
Never	2 (6)	5 (62.5)
After 1 positive surveillance culture	4 (11)	1 (12.5)
After 2 positive surveillance cultures	23 (66)	2 (25)
After 2 positive surveillance cultures only paste, suspension never	4 (11)	n.a.
After 3 positive surveillance cultures	2 (6)	–
Additional measures to stimulate decontamination (additional)[a] (SDD; $n = 34$)		
Start measures to promote intestinal motility when started on SDD (e.g. laxatives)	20 (59)	n.a.
Start measures to promote intestinal motility on indication	28 (82)	n.a.
Use of SDD suppository or enema	21 (62)	n.a.
Routinely exchange invasive materials (e.g. IV lines)	3 (9)	n.a.
Amphotericin B bladder rinsing in case of candiduria	5 (15)	n.a.
Use of SDD suppository or enema		
Yes	38 (90.5)	n.a.
No	4 (9.5)	n.a.
Indications for use of SDD suppository or enema[a] ($n = 38$)		
Every patient receiving SDD (additional)	4 (10.5)	n.a.
Blind bowel loop after bowel surgery (basic)	34 (90)	n.a.
No enteral passage for several days (additional)	3 (8)	n.a.
Use of SDD/SOD paste applied on skin around tracheostomy (basic)		
Yes	40 (95)	12 (100)
No	2 (5)	–
Nebulization as part of anti-infectious regime (optional; SDD n = 35; SOD n = 8)		
Yes[f]	20 (57)	1 (12.5)
Systemic antibiotic used as prophylaxis (basic)		
Cefotaxime 3000 mg/day	2 (5)	n.a.
Cefotaxime 4000 mg/day	25 (59.5)	n.a.
Ceftriaxone 1000 mg/day	1 (2)	n.a.
Ceftriaxone 2000 mg/day	13 (31)	n.a.
Cefuroxime 3 × 1500 mg/day	1 (2)	n.a.

(continued on next page)

Table 2 (*continued*)

	SDD ($n = 42$)	SOD ($n = 12$)
Duration of systemic antibiotic as prophylaxis (basic)		
"I don't know"	1 (2)	n.a.
2 days	1 (2)	n.a.
3 days	3 (7)	n.a.
4 days	33 (79)	n.a.
5 days	1 (2)	n.a.
Until no more PPM in sputum culture	3 (7)	n.a.

Data are presented in absolute numbers (percentages). Basic, optional or additional component of regimen (see method section).
Abbreviations: SDD - Selective Decontamination of the Digestive tract, SOD – Selective Oropharyngeal Decontamination, ICU – Intensive care unit, n.a. – Not applicable, MO – Microorganisms, IV – Intravenous, mg – Milligrams, PPM – Potential pathogenic microorganisms.
[a] Multiple answers allowed.
[b] Pancreatitis (2); immunocompromised (1); admission for elective gastro-intestinal surgery (1); admission for oesophagectomy until passage of stool on general ward (1).
[c] All ICU patients expected admission >48 h and no oral intake (1); only patients expected to be on mechanical ventilation for more than 24 h (1); all mechanically ventilated patients (1).
[d] Different regime in haematological patients (1); "limited burden of disease" (1); "specific type of surgery" (1).
[e] Patients with chronic respiratory failure with ventilation at home (1); palliative care (1).
[f] Details see supplemental table S4.

exists for other microorganisms, such as *Haemophilus* and *Staphylococcus aureus*, and for antimicrobial susceptibility.

The definition of SDD failure also varied considerably. Persistent presence of PPM was considered as SDD failure by 28 of 35 (80%), selection of antibiotic-resistant bacteria by 21 of 35 (60%), renewed detection of PPM by 18 of 35 (51%), and the occurrence of an infectious episode on SDD by 11 of 35 (31%) centres. All centres responded with an intervention when SDD failure was detected. The most frequently applied interventions were intensifying the topical SDD regimen (91%). When micro-organisms in surveillance cultures were resistant to one of the SDD components, 86% of ICUs continued SDD. In contrast, only 60% continued SDD in an adjusted manner, when PPM were resistant to 2 SDD components.

Monitoring of systemic levels of SDD components was performed by 46% of ICU. The most frequent reasons for monitoring were acute kidney injury and illnesses prone to disrupted intestinal barrier integrity.

3.4. SOD practice

Selected results on the methodology of SOD practice are presented in Tables 2 and 3 (more details are provided in Tables S4-S6).

3.4.1. Indications for start and discontinuation of SOD

An expected duration of mechanical ventilation of more than 48 h was the most frequently used indication to start SOD. Extubation or ICU discharge were the main reasons to discontinue SOD.

3.4.2. Practice on nonabsorbable antibiotics in SOD

Most hospitals used a combination of tobramycin, colistin and amphotericin B for the mouth paste, applied four times daily in most cases (83%). All centres applied SOD paste around tracheostomies. Only 1 out of 12 centers used antimicrobial nebulization as part of their anti-infectious regimen.

3.4.3. Monitoring SOD regimen

Surveillance cultures were taken twice weekly in 7 out of 8 centres. These surveillance cultures usually included throat, sputum and rectal samples. Most hospitals (63%) never changed their local SOD regimen in case of persisted presence of PPM. Results on the type of microbiological cultures in SOD are depicted in Table S6.

2 of 8 centres perform drug level monitoring of SOD components in case of acute kidney injury.

4. Discussion

In this nationwide cross-sectional survey, we collected detailed information on practice of anti-infectious strategies in all Dutch ICUs. The implemented type of anti-infectious strategies evolved in time, with an increasing number of centres applying SDD, or SOD to a lesser extent. In general, change of policy and implementation of new evidence and guidelines require time with clinical practice usually significantly lagging behind. Barriers that limit implementation can be classified into a lack of awareness, lack of familiarity, lack of agreement, self-efficacy, outcome expectancy, the inability to overcome the inertia of previous practice, and presence of external barriers to perform recommendations [24]. For SDD/SOD implementation, a lack of agreement especially on the risk of emergence of antibiotic resistance during SDD has long been a major limiting factor [25-28]. The observed increase of SDD implementation over time in Dutch ICU parallels the accumulating evidence on outcome benefits of SDD and no clear evidence of increasing antibiotic resistance, reinforced by recent Dutch guidelines [8,10,12-19,29,30]. The fear of emerging antibiotic resistance, costs, difficulty in obtaining the preparation and limited efficacy studies in settings with high levels of baseline AB resistance, may explain the paucity of SDD adoption in other countries [31,32].

In our survey the use of SDD (66%), SOD (20%) or standard care (14%) strategies was associated with the size of ICUs and regional affiliations. The observation that small-sized ICUs less frequently implemented SDD or SOD is most likely related to the limited number of admitted patients potentially eligible for such strategies, constraining the feasibility of implementation. The regional differences on the other hand, are most likely explained by regional lack of agreement propagated by local champions.

SDD practice for ICU, as originally described by Stoutenbeek, van Saene and co-workers is based on four interconnected pillars: (1) the use of nonabsorbable antibiotics to eradicate PPM in the digestive and oropharyngeal tract, that cause secondary endogenous infections (2) systemic antibiotics to eradicate PPM causing primary endogenous infections, while minimally affecting colonization resistance (CR) (3) monitoring and adjusting interventional components accordingly; and (4) a high level of hygiene to prevent exogenous infections [3,4,7]. In the current survey we observed that most Dutch ICUs using SDD adhere to the basic components of the interventional arms as used in the large recent clinical trials [8-10], in which the efficacy of SDD and to a lesser extent of SOD as bundles of care was demonstrated. In contrast to minor differences observed in the first two pillars, considerable variation was apparent in the third pillar, more specifically in the optional

Table 3
SDD and SOD methodology – monitoring characteristics and treatment failure.

	SDD	SOD
Drug monitoring of SDD (n = 35)/SOD (n = 8) components (additional)[a]		
No	19 (54)	6 (75)
Yes, standard	3 (9)	–
Yes, in case of AKI/CRRT	10 (29)	2 (25)
Yes, in case of typhlitis, abdominal sepsis, shock	4 (11)	–
Yes, other[b]	3 (9)	–
Frequency of performing surveillance cultures (basic) (SDD *n* = 36; SOD *n* = 8)		
Once a week	3 (9)	–
2 times per week	33 (92)	7 (87.5)
None, only when indicated	–	1 (12.5)
Body sites cultured as surveillance of SDD (n = 36)/SOD (n = 8) regimen (basic)[a]		
Rectal	29 (81)	4 (50)
Perineal	9 (25)	–
Throat	36 (100)	5 (62.5)
Nose	4 (11)	–
Sputum	28 (78)	5 (62.5)
Stoma	13 (36)	–
Wound	8 (22)	–
Urine	6 (17)	1 (12.5)
Considered to be "SDD-failure" (n = 35) / "SOD-failure" (n = 8) (additional)[a]		
Selection of antibiotic-resistant bacteria	21 (60)	6 (75)
Persistent presence of PPM	28 (80)	4 (50)
Renewed presence of PPM	18 (51)	2 (25)
Infection while applying SDD/SOD	11 (31)	5 (62.5)
Actions undertaken when "SDD-failure" (*n* = 35)/"SOD-failure" (n = 8) is observed (additional)[a]		
Stop SDD/SOD	5 (14)	2 (25)
Intensify SDD/SOD regimen	32 (91)	3 (37.5)
Continue SDD/SOD (reduction of colonization pressure)	6 (17)	4 (50)
Change SDD/SOD components	10 (29)	2 (25)
Check hygiene measures	3 (9)	–
Nothing	–	1 (12.5)
Actions undertaken when cultured micro-organisms are resistant to one of the SDD (n = 35) / SOD (n = 8) components (additional)[a]		
No actions	23 (66)	4 (50)
Stop applying SDD/SOD mouthpaste	4 (11)	3 (37.5)
Stop applying SDD suspension	6 (17)	n.a.
Intensify frequency of SDD/SOD application	2 (6)	–
Add/change antibiotic components	5 (14)	1 (12.5)
Actions undertaken when cultured micro-organisms are resistant to two of the SDD (n = 35) / SOD (n = 8) components (additional)[a]		
No actions	12 (34)	3 (37.5)
Stop applying SDD/SOD mouthpaste	14 (40)	4 (50)
Stop applying SDD suspension	14 (40)	n.a.
Intensify frequency of SDD/SOD application	1 (3)	–
Add/change antibiotic components	6 (17)	–
After >3 positive surveillance cultures with tobramycin and colistin resistant micro-organisms stop SDD and stop systemic antibiotics	1 (3)	–

Data are presented in absolute numbers (percentages). Basic, optional or additional component of regimen (see method section).
SDD - Selective Decontamination of the Digestive tract, SOD – Selective Oropharyngeal Decontamination, AKI – Acute kidney injury; CRRT - Continuous renal replacement therapy, PPM – Potential pathogenic microorganisms, n.a. – not applicable.
[a] Multiple answers allowed.
[b] In case of doubled dose of SDD (1); tobramycin in case of >4 weeks of application (1); tobramycin in case of >7 days of application (1).

component of nebulization, and in additional components such as monitoring of antibiotic serum levels of SDD components and promotion of intestinal decontamination. Although striving for uniformity in SDD practice is not an aim by itself, applying the SDD strategy in the most successful way may be of clinical importance [6]. Uncertainty remains as to whether and which of the individual components within the bundle of care are more pivotal than other. In parallel, in the surviving sepsis bundle adherence to all components of that bundle was associated with improved outcome but certain components appeared to be more essential than other [33-35]. A recent randomized controlled trial in non-Dutch European countries on SDD failed to show a mortality reduction. In contrast to previous SDD/SOD studies, the intervention arm in this study used some, but not all components of the classical SDD ICU regimen. Most importantly, the basic SDD component of systemic antibiotics and the optional component of strategy adjustment based on microbiological cultures monitoring were omitted [11]. Of note, in this study among mechanically ventilated ICU patients, SDD was associated with more eradication and less acquisition of third generation cephalosporin resistant and carbapenem-resistant Enterobacterales [16].

Heterogeneity of practice was most prominent in the decision criteria for adaptation of regimens following information derived from surveillance cultures, nebulization of antimicrobials, drug monitoring of antimicrobial SDD components and in measures that aim to improve decontamination. The composition of topical SDD/SOD components was largely similar, consisting of tobramycin, polymyxin and amphotericin in more than 88% of ICUs. A small number of ICUs used nystatin instead of amphotericin in the topical components, which has been shown to be equally effective as amphotericin B [36]. The most frequently used systemic antibiotic in SDD were 3rd generation cephalosporins (cefotaxime or ceftriaxone in >90%) and were mostly administered for 4 days.

Table 4
Microbiological culture procedures in centers using SDD.

	Micro-organism	On ICU admission		Surveillance during ICU stay	
		Determination	Antibiotic susceptibility	Determination	Antibiotic susceptibility
PPM	Enterobacteriaceae (not HRMO/ESBL)	28 (78)	26 (72)	32 (89)	32 (89)
	Enterobacteriaceae (HRMO/ESBL)	31 (86)	31 (86)	33 (92)	33 (92)
	Haemophilus influenzae	21 (58)	23 (64)	24 (67)	25 (69)
	Pseudomonas aeruginosa	28 (78)	29 (81)	33 (92)	34 (94)
	Other Gram-negative bacteria	29 (81)	28 (78)	33 (92)	33 (92)
	Staphylococcus aureus	24 (67)	24 (67)	29 (81)	28 (78)
	MRSA	23 (64)	23 (64)	23 (64)	22 (61)
	Candida species	31 (86)	19 (53)	35 (97)	23 (64)
	Streptococcal species	22 (61)	21 (58)	23 (64)	22 (61)
	Enterococcal species	22 (61)	22 (61)	23 (64)	22 (61)
	VRE	25 (69)	23 (64)	23 (64)	23 (64)
	Fungi, including Aspergillus species	22 (61)	12 (33)	24 (67)	13 (36)

Data are presented in absolute numbers (percentages).
Abbreviations: SDD - Selective Decontamination of the Digestive tract, ICU – Intensive care unit, HRMO - Highly resistant microorganisms, ESBL - Extended spectrum beta-lactamase, MRSA - Methicillin-resistant Staphylococcus aureus, VRE – Vancomycin-resistant Enterococci.

The choice for 3rd generation cephalosporins is based on the low level of cephalosporin resistance in the Dutch setting, its activity against causative microorganisms and the limited effect on colonization resistance. As preserving colonization resistance and preventing bacterial overgrowth [37] is considered an important part of SDD, the use of certain antibiotics like amoxicillin/clavulanic acid and clindamycin [38,39], are discouraged in classical SDD practice. In fact, up to 50% of Dutch ICUs discouraged the use of amoxicillin, amoxicillin/clavulanic acid and piperacillin/tazobactam. Drug monitoring of SDD components was performed by 16 of 35 (46%) ICUs that used SDD and 2 of 8 that used SOD. SDD components like tobramycin are theoretically none-absorbable but may be detectable in the systemic circulation, although rarely in the toxic range. Especially patients on renal replacement therapy or those prone for leaky intestines are at risk [21,40,41]. 57% of ICUs used antimicrobial nebulization when PPM were detected in the respiratory tract. However, it remains questionable whether the use of antibiotic nebulization to improve respiratory tract decolonization rate, has an effect on clinically relevant endpoints [42]. Although the use of antibiotic nebulization for Gram-negative bacteria in a prophylactic (SDD) setting has not been formally studied, therapeutic nebulization of aminoglycosides, in addition to systemic antibiotic therapy failed to show improved outcome in Gram-negative VAP [43,44]. In our study additional measures to improve gastro-intestinal tract decolonization were frequently applied as part of SDD regimens and included intensifying dosing frequency of topical SDD/SOD component (94% of ICUs), use of SDD suppositories or enema's in blind loops (>90%) and promotion of intestinal motility (standard 59%; on indication 82%). These measures have been introduced based on the hypothesis that improved decolonization of the digestive tract, as reservoir of nosocomial pathogens [45,46] decreases infection rates. Indeed Gram-negative rectal decolonization was associated with less ICU-acquired infections in SDD-treated patients [22,23], but it remains to be determined whether more rapid decolonization also results in improved outcome. Our survey also showed important differences in how the effect of SDD or SOD treatment was monitored, more specifically the practice of microbiological culturing. Almost all ICUs that used SDD performed basic throat and rectal/perineal cultures on admission and during regular surveillance (twice weekly in more than 90% of ICUs), but only one third of ICUs regularly performed optional wound and stoma cultures. A large proportion of ICUs performed these cultures on admission, but especially the practice of surveillance cultures was more variable.

The present survey provides a comprehensive overview of SDD and SOD practice in the Netherlands, a country with extensive experience with SDD and SOD in the ICU setting and an initiator of multiple large randomized controlled trials in this field. To our knowledge, this is the first study to examine SDD and SOD application on a detailed level in a nationwide setting. Moreover, the survey included almost all Dutch ICUs. Whether adding or omitting certain optional or additional components or practice variation may affect clinical outcome and rate of antimicrobial resistance is largely unclear, but the observed variation is a starting point for future studies. Observational studies addressing the association between specific measures and outcomes, such as decontamination and infection rates may pinpoint the most promising aspects that can be explored in future interventional studies.

Several limitations of our survey need to be considered. First, the quality of data was strongly dependent on the input and feedback provided by the individual ICUs without additional independent verification performed by the investigators. A period-prevalence study on SDD practice may provide further insight into the true implementation. Second, our survey was conducted in a country with relatively low antimicrobial resistance. How SDD or SOD practice is applied in countries with higher background levels of antimicrobial resistance is unexplored.

In conclusion, the level of adherence to national guidelines, uncertainty on the efficacy of the different individual SDD/SOD components, and uncertainty on optimal monitoring may have contributed to considerable heterogeneity in SDD/SOD practice among Dutch ICUs. Further studies should focus on the different components of SDD/SOD regimens to explore whether further optimisation and establishing of a best practice for SDD/SOD is possible.

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Declaration of Competing Interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2021.05.001.

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