

## GUIDELINE

# Selective decontamination: SWAB guideline revised

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Selective decontamination is a prophylactic antibiotic regimen used in –mainly Dutch– intensive care units (ICUs) to prevent ICU-acquired infections. Selective decontamination of the digestive tract (SDD) consists of a mixture of topically applied antibiotics. Various combinations have been described, yet the most frequently used combination consists of tobramycin, colistin and amphotericin B, aiming to eradicate colonisation with aerobic Gram-negative bacteria and yeasts while leaving the anaerobic flora intact. The topical antibiotics are applied in the oropharynx using a mouth paste and in the intestinal tract using a suspension via a nasogastric tube. Both the mouth paste and suspension are applied four times daily from ICU admission until ICU discharge. In addition, a four-day course of intravenous antibiotics is administered during the first four days to treat incubating infections. Most studies used third-generation cephalosporins as systemic prophylaxis. A variant of SDD is selective oropharyngeal decontamination (SOD). SOD only consists of the mouth paste and the regimen does not contain the standard four-day course of intravenous antibiotics. Appropriate systemic antibiotics are only administered if there is a clinical suspicion of infection. Both strategies are used for ICU patients with an expected length of ICU stay of more than 48 hours and involve regular microbiological culturing and hygiene measures.

Recently, the Dutch guideline on the use of selective decontamination in ICU patients was updated.<sup>[1]</sup> The first guideline was published in 2001. It was recommended not to use SDD or SOD as robust evidence on improved outcome was lacking at that time. Since then multiple studies have been published including three large Dutch randomised trials. In 2014 an updated guideline was published. Mainly based on these three large Dutch studies,<sup>[2-4]</sup> the 2014 guideline advised to use selective decontamination (either SDD or SOD) in Dutch ICUs for patients with an ICU stay of more than 48 hours with no preference for SDD or SOD. The largest modification in

the 2018 guideline as compared with the 2014 guideline is the recommendation to use SDD instead of the recommendation to use either SOD or SDD.

The preference for SDD is merely based on two studies. One is a Dutch multicentre cross-over study in 16 ICUs by Oostdijk et al.<sup>[4]</sup> The primary endpoint was differences between SDD and SOD in ICU ecology determined by monthly point prevalence surveillance cultures. Mortality was a secondary endpoint in this study. Initially, the trial was published in 2014, reporting no difference in mortality. In 2017 the study was retracted and replaced by JAMA because of incorrectly reported mortality rates.<sup>[5]</sup> The trial was designed as a cluster randomised cross-over trial with 12 months of SDD compared with 12 months of SOD in which the order of interventions was randomised. Re-analysing the original trial data for an individual patient data meta-analysis<sup>[6]</sup> revealed that an error had occurred in coding the interventions in one of the 16 participating hospitals. As it was one of the largest participating ICUs, correcting the error led to significantly different mortality outcomes. The correct 28-day mortality was 25.7% during SOD and 23.8% during SDD with a corresponding adjusted odds ratio (aOR) of 0.850 (95% confidence interval (CI) 0.774-0.933). ICU and hospital mortality were also significantly different with aOR of 0.842 (95% CI 0.759-0.933) and 0.857 (95% CI, 0.783-0.938) respectively, both in favour of SDD. The other endpoints, including the primary endpoint, were not significantly affected by the error.

The other important study regarding the effects of SDD and SOD on mortality is an individual patient data meta-analysis by Plantinga et al.<sup>[6]</sup> In total, six studies were included containing data from 16,528 patients. All studies were performed in countries with a low prevalence of antibiotic-resistant bacteria. Hospital mortality was found to be 29.5% for SDD patients as compared with 31.5% and 32.4% for SOD and control group

patients, respectively, with corresponding aORs of 0.90 (95% CI 0.82-0.97) for SDD versus SOD and 0.82 (95% CI 0.72-0.93) for SDD versus control. Similar results were reported for ICU mortality. No differences in mortality were found in a subgroup analysis for surgical versus medical patients. The authors of the guideline take the view that based on these studies SDD is preferred over SOD with a high level of evidence.

Regarding the effects of SDD on antibiotic resistance, no major revisions were made in the 2018 guideline as compared with the 2014 guideline. A large meta-analysis published in 2013 including 64 studies found no increase in prevalence of colonisation or infection with resistant Gram-negative and Gram-positive bacteria during SDD.<sup>[7]</sup> Two Dutch trials studied the incidence of bacteraemia with resistant Gram-negative bacteria and found a significantly lower incidence during SDD as compared with control<sup>[8]</sup> and SOD respectively.<sup>[4]</sup> Ecological changes in a setting with low prevalence of antibiotic resistance have been studied by obtaining point prevalence cultures once monthly from all patients admitted to the ICU during 12 months of SDD and 12 months of SOD.<sup>[4]</sup> No differences were seen for respiratory tract colonisation with resistant pathogens during SDD versus SOD. Yet for intestinal tract colonisation lower prevalences were seen during SDD. During both interventions a gradual, significant increase was observed with aminoglycoside-resistant Gram-negative bacteria of 7% and 4% per month for SDD and SOD, respectively. Besides resistance against aminoglycosides, colistin resistance is of great concern. Colistin is used as a last resort antibiotic and colistin resistance is rising globally. Fortunately, resistance to colistin is rare in the Netherlands. Little is known about colistin resistance, yet the use of colistin is found to be a risk factor in acquiring colistin resistance.<sup>[9]</sup> During SDD and SOD all Dutch studies found low prevalences of colistin-resistant pathogens. Yet, acquisition of colistin resistance in Gram-negative bacteria during SDD was found to be fivefold higher during persistent intestinal colonisation with Gram-negative bacteria and even 15-fold higher if patients were colonised with aminoglycoside-resistant Gram negatives.<sup>[10]</sup> In the current guideline it is therefore recommended that besides regular culturing during SDD, the use of SDD is discouraged in patients colonised with Enterobacteriaceae and/or *Pseudomonas aeruginosa* resistant for aminoglycosides and carbapenems as additional acquisition of colistin resistance would result in a pan-resistant strain.

The current guideline preferring SDD over SOD will affect overall ICU budgets as the SDD regimen involves more culture taking and more topical antibiotics as compared with SOD. No differences were found in overall systemic antibiotic use.<sup>[2,3]</sup> A previous cost-analysis based on data from the study by De Smet et al.<sup>[3]</sup> included costs for microbiology, antibiotics and days admitted to the hospital.<sup>[11]</sup> 2009 was used as the reference

year for all costs. Both SOD and SDD were less expensive than control with total costs per patient of €41,941 for control group patients, €41,183 for SDD patients and €40,433 for SOD patients. Prices will differ between different hospitals due to pricing agreements with pharmacies. In the past the price of topical antibiotics fluctuated and therefore SDD costs will rise more when prices of the topical antibiotics increase as compared with total SOD costs. Especially the price of amphotericin B has increased considerably. Nystatin is used by a number of Dutch ICUs and can be considered to be a cheaper but safe antifungal component of SDD.

In conclusion, in 2018 the revised SWAB guideline on selective decontamination was published with as major modification SDD is preferred over SOD.

### Disclosures

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