



DDS, finalement on va où?

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MÉDECINE INTENSIVE-RÉANIMATION, CHU DE LILLE

INSERM U1285, UNIVERSITÉ DE LILLE

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Liens d'intérêt

- ▶ Lecture : Pfizer, MSD, Biomérieux, Medtronic, Ficher and Paykel, Shionogi
- ▶ Comité d'experts : Mundi Pharma

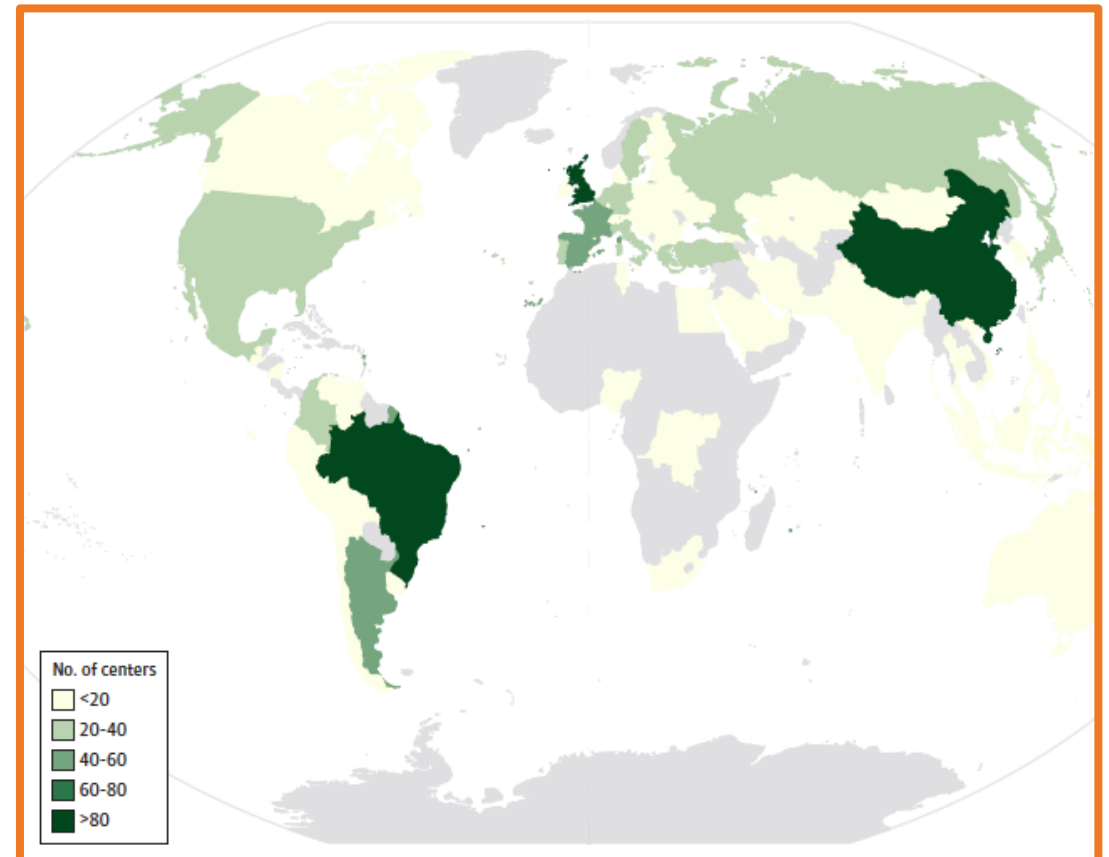
Plan

- ▶ Introduction
- ▶ Définitions et rationnel
- ▶ Efficacité de la décontamination digestive sélective (DDS)
- ▶ Antibiorésistance et microbiome
- ▶ Conclusions

Prevalence and Outcomes of Infection Among Patients in Intensive Care Units in 2017

Jean-Louis Vincent, MD, PhD; Yasser Sakr, MD, PhD; Mervyn Singer, MB, BS; Ignacio Martin-Loeches, MD; Flavia R. Machado, MD, PhD;

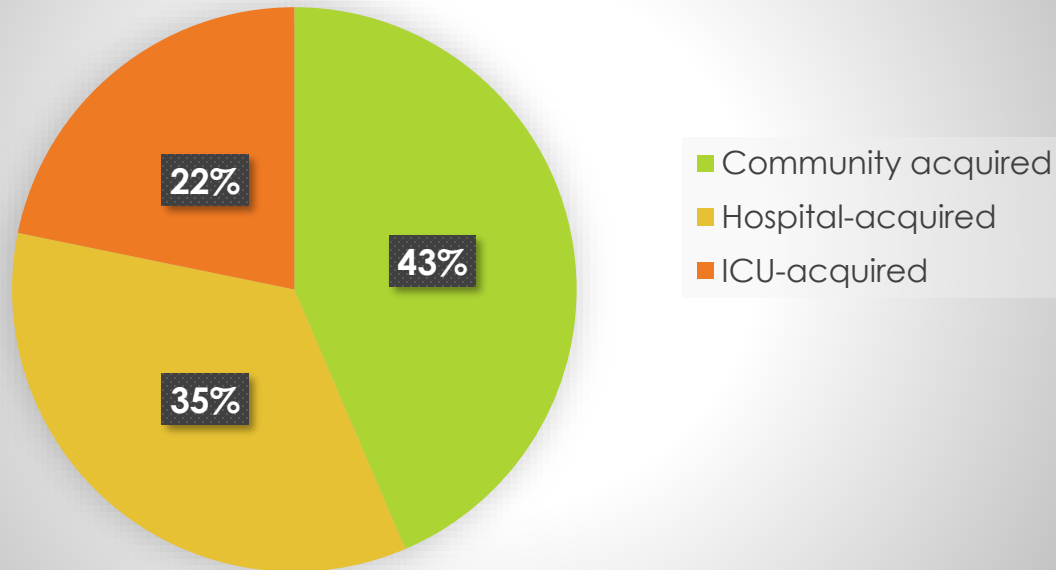
- ▶ Observational 24-hour point prevalence study
- ▶ Longitudinal follow-up, 1 150 centers, 88 countries
- ▶ 15 165 patients hospitalized in the ICU >24h
- ▶ 8135 (54%) patients with suspected or confirmed infection



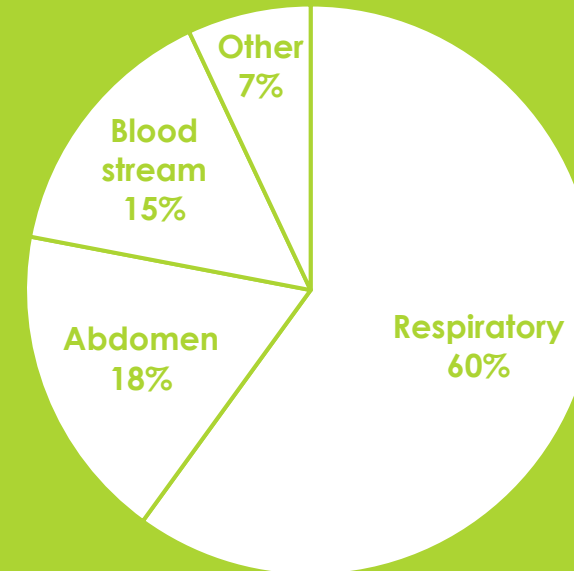
Prevalence and Outcomes of Infection Among Patients in Intensive Care Units in 2017

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Type of infection



SITE OF INFECTION



ICU-acquired infection independently associated with **higher risk of mortality** compared with community-acquired infection

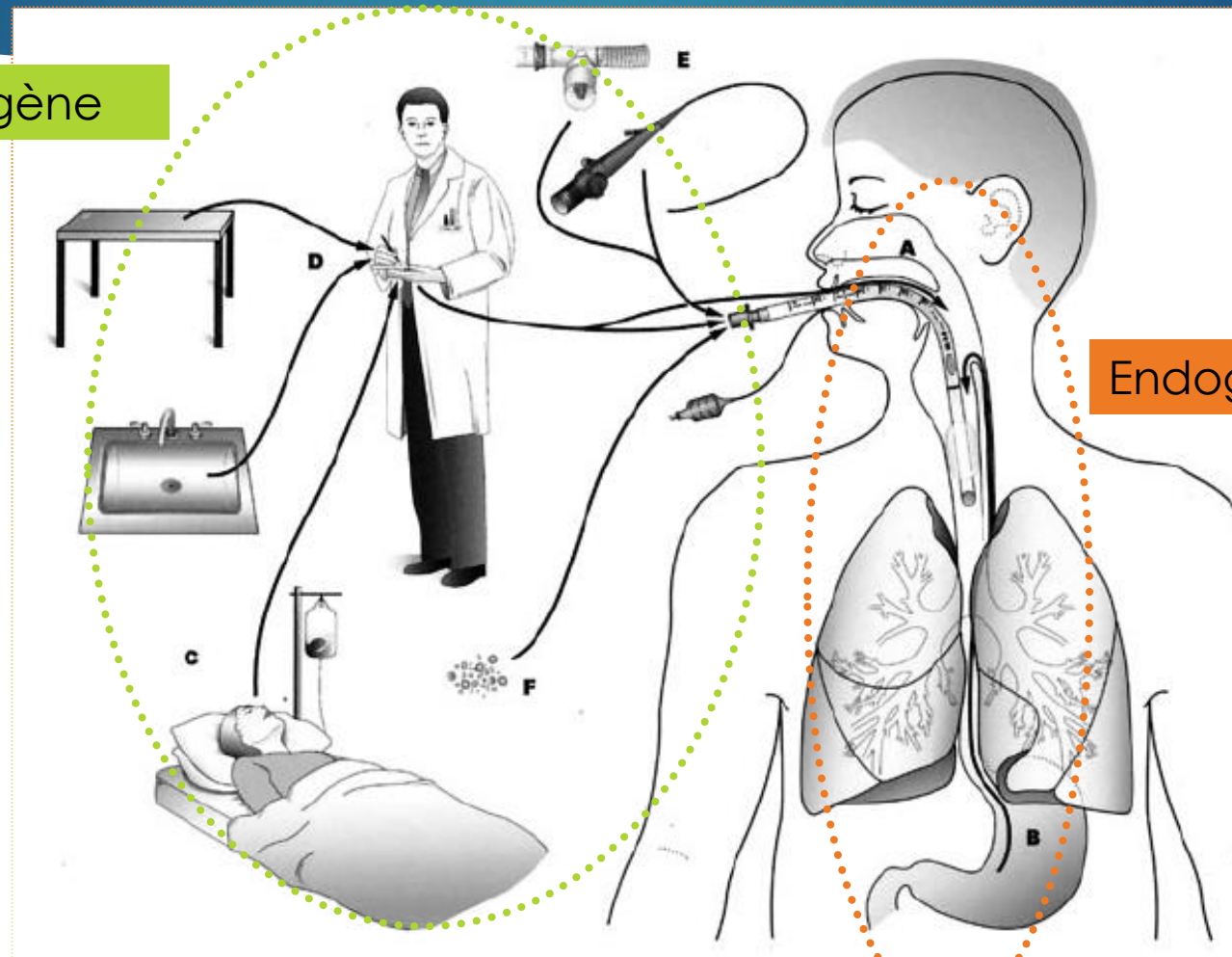
OR **1.32** [95%CI, 1.10-1.60]; P = 0.003

Rationnel

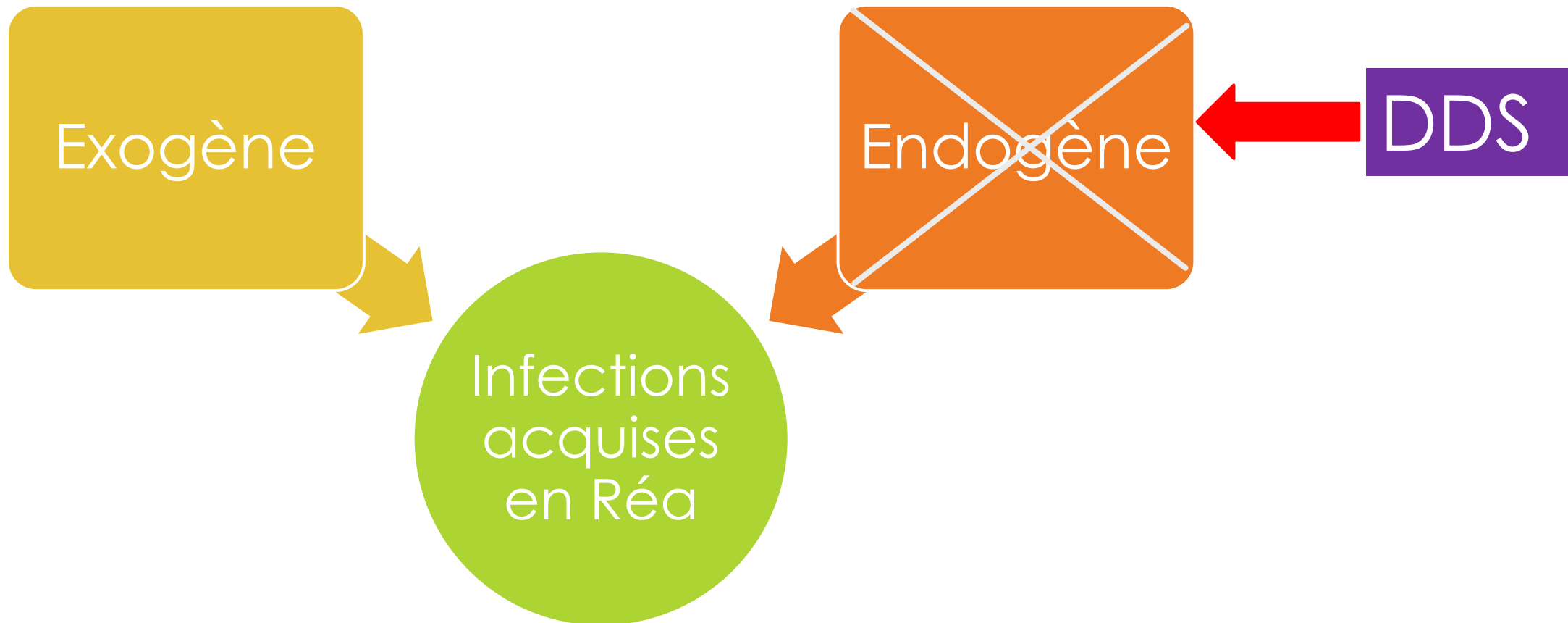
Safdar N, Respir Care 2005

Exogène

Endogène



Rationnel



Définition

Wittekamp B, ICM 2020

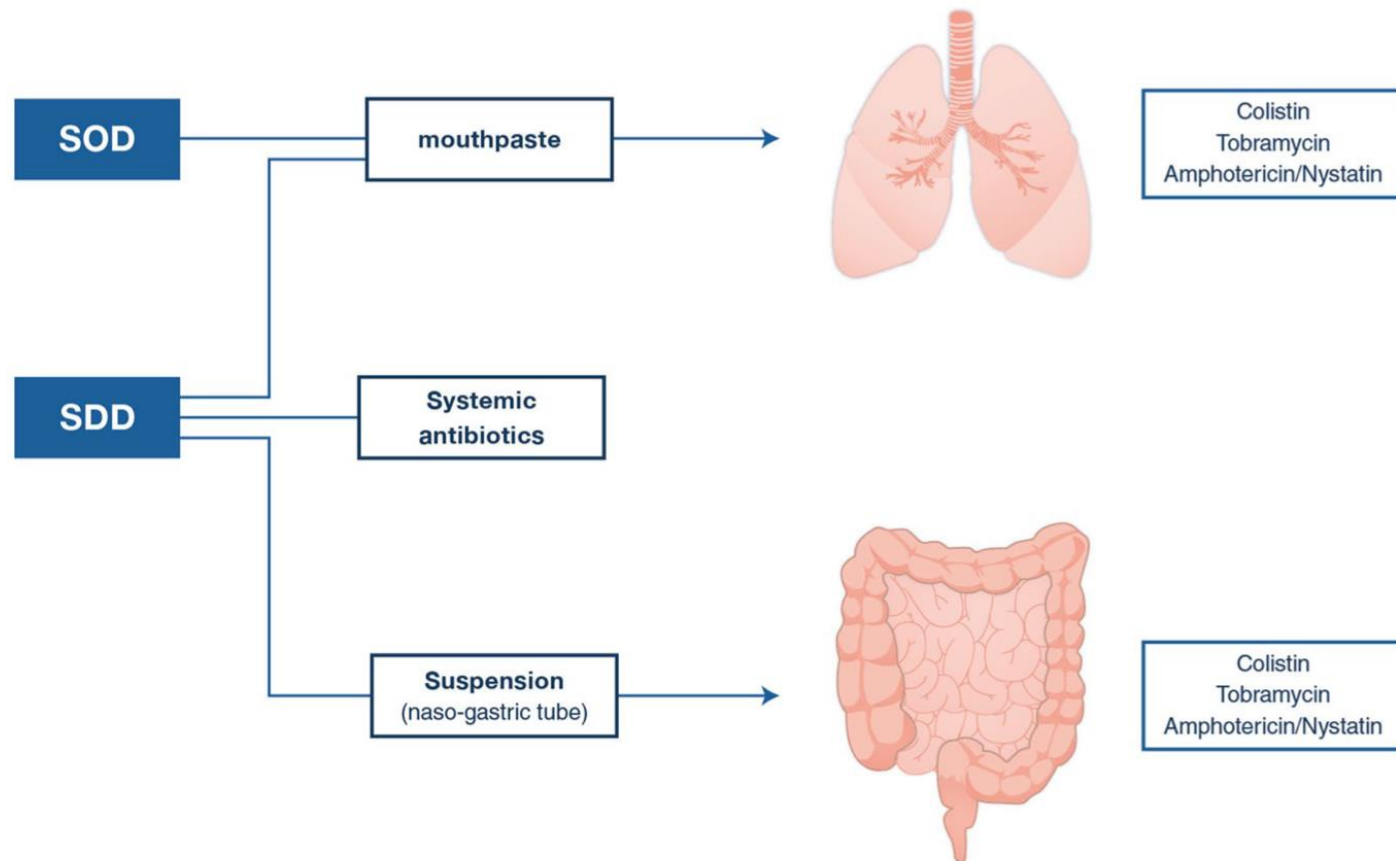


Fig. 1 Components of SDD and SOD. *SDD* selective digestive tract decontamination, *SOD* selective oropharyngeal decontamination

SOD, selective oral decontamination
SDD, selective digestive decontamination

[Intervention Review]

Topical antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving mechanical ventilation

Minozzi S, 2021

- ▶ **41 études, 11,004 patients**
- ▶ durée ventilation mécanique 2-6 j
- ▶ durée de séjour en Réa 11-33 j
- ▶ immunodépression 0-22%
- ▶ >40% possible risque de biais de sélection
- ▶ 5 études à risque élevé de biais de détection des infections respiratoires basses (IRB)

[Intervention Review]

Topical antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving mechanical ventilation

Minozzi S, 2021

ATB systémique et locale

- ▶ Réduit la **mortalité** vs placebo ou pas de traitement **RR (risque relatif) 0.84, 95% IC (intervalle de confiance) 0.73 - 0.96** (18 études, 5290 patients, certitude de l'évidence: **HAUTE**)
- ▶ Réduit probablement les **infections respiratoires basses (IRB)** **RR 0.43, 95% IC 0.35 to 0.53** (17 études, 2951 patients, certitude de l'évidence: **MODEREE**)

[Intervention Review]

Topical antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving mechanical ventilation

Minozzi S, 2021

Majorité des études aux Pays-Bas ou des réanimations à faible incidence de BMR

- ▶ Réduit probablement la **mortalité** vs placebo ou pas de traitement (**RR 0,96, 95% IC 0,87-1.05**, 22 études, 4213 patients; certitude de l'évidence: **MODEREE**)
- ▶ Pourrait réduire les IRB (**RR 0.57, 95% IC 0.44-0.74**; 19 études; 2698 patients; certitude de l'évidence: **FAIBLE**)

Decontamination Strategies and Bloodstream Infections With Antibiotic-Resistant Microorganisms in Ventilated Patients

L'utilisation de soins de bouche CHX, SOD, ou SDD associée à une réduction des bactériémies à BGN MR?

Wittekamp B, JAMA 2018

POPULATION



5561 Men 3104 Women

Adult patients who were not pregnant, with expected duration of invasive mechanical ventilation of ≥ 24 hours

Median age: **64.1** years
(range, 18-98)

LOCATIONS

13
ICUs in Europe



INTERVENTION

8665 Patients randomized

2251

Standard of care

Daily CHX
body washing
and hand hygiene

2108

CHX 2% mouthwash

4 times daily

2224

SOD

Mouthpaste
with colistin,
tobramycin,
and nystatin
4 times daily

2082

SDD

Mouthpaste and
gastrointestinal
suspension
with colistin,
tobramycin,
and nystatin
4 times daily

Decontamination Strategies and Bloodstream Infections With Antibiotic-Resistant Microorganisms in Ventilated Patients

Wittekamp B, JAMA 2018

FINDINGS

Standard of care

2.1% bloodstream infection

31.9% 28-day mortality

CHX mouthwash

1.8% bloodstream infection

32.9% 28-day mortality

Limites

Pas d'ATB systémique

SOD, SDD arrêtées après extubation

Adjusted hazard ratios (95% CIs) vs **standard of care**
for bloodstream infection
with multidrug-resistant gram-negative bacteria

1.13 (0.68-1.88) for **CHX**

0.89 (0.55-1.45) for **SOD**

0.70 (0.43-1.14) for **SDD**

JAMA | **Original Investigation** | **CARING FOR THE CRITICALLY ILL PATIENT**

Effect of Selective Decontamination of the Digestive Tract on Hospital Mortality in Critically Ill Patients Receiving Mechanical Ventilation A Randomized Clinical Trial

The SuDDICU Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group

Effect of Selective Decontamination of the Digestive Tract on Hospital Mortality in Critically Ill Patients Receiving Mechanical Ventilation

A Randomized Clinical Trial

The SuDDICU Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group

QUESTION Among critically ill patients receiving mechanical ventilation, what is the effect of selective decontamination of the digestive tract (SDD) on hospital mortality?

POPULATION



3780 Men 2202 Women

Adults receiving mechanical ventilation in an intensive care unit

Mean age: 58 years

LOCATIONS

19 Intensive care units in Australia



INTERVENTION



5982 Patients randomized

2791

SDD

6-Hourly oral paste and gastric suspension of colistin, tobramycin, and nystatin, plus 4-day IV antibiotic course

3191

Standard care

Standard care without SDD

PRIMARY OUTCOME

90-Day in-hospital mortality

Effect of Selective Decontamination of the Digestive Tract on Hospital Mortality in Critically Ill Patients Receiving Mechanical Ventilation A Randomized Clinical Trial

The SuDDICU Investigators for the Australian and New Zealand Intensive Care

FINDINGS

In-hospital deaths

SDD

753 of 2791 patients



Standard care

928 of 3191 patients



SDD did not significantly reduce in-hospital mortality:

Mean difference, **-1.7%** (95% CI, -4.8% to 1.3%)

Odds ratio, **0.91** (95% CI, 0.82-1.02); $P = .12$

Effect of Selective Decontamination of the Digestive Tract on Hospital Mortality in Critically Ill Patients Receiving Mechanical Ventilation
A Randomized Clinical Trial

The SuDDICU Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group

Outcomes and adverse events	Selective decontamination of the digestive tract (n = 2791)	Standard care (n = 3191)	Difference, % (95% CI)
Microbiological secondary outcomes^b			
Any antibiotic-resistant organism found, No. (%)	583 (20.9)	1036 (32.5)	AD, -11.0 (-14.7 to -7.3)
Any blood organism found, No. (%)	156 (5.6)	259 (8.1)	AD, -1.95 (-3.47 to -0.43)
Positive for <i>Clostridioides difficile</i> , No. (%)	14 (0.5)	29 (0.9)	AD, -0.24 (-0.59 to 0.10)
Defined daily dose of antibiotics over 28 d, mean (95% CI) ^a	0.81 (0.75-0.88)	0.85 (0.78-0.91)	MD, -0.035 (-0.13 to 0.06)

- ▶ ICU mortality, MV-free days, ICU-free days, adverse events: NS

Association Between Selective Decontamination of the Digestive Tract and In-Hospital Mortality in Intensive Care Unit Patients Receiving Mechanical Ventilation

A Systematic Review and Meta-analysis


- ▶ 32 RCT, 24 389 patients
- ▶ Risk ratio (RR) for mortality (SDD vs standard care)
0.91 (95% credible interval [CrI], 0.82-0.99; $I^2 = 33.9\%$)
- ▶ Beneficial association of SDD evident in trials with an iv agent
RR 0.84 (0.74-0.94), but not in trials without an iv agent RR, 1.01 (0.91-1.11), (P value interaction = 0.02)

Association Between Selective Decontamination of the Digestive Tract and In-Hospital Mortality in Intensive Care Unit Patients Receiving Mechanical Ventilation

A Systematic Review and Meta-analysis

- ▶ SDD associated with reduced risk of VAP
RR 0.44 (0.36-0.54)
- ▶ and ICU-acquired bacteremia
RR 0.68 (0.57-0.81)
- ▶ Available data regarding the incidence of positive cultures of antimicrobial-resistant organisms were not amenable to pooling and were of **very low certainty**

Selective digestive decontamination-Con

James C. Hurley^{1,2*} 



ICM 2023

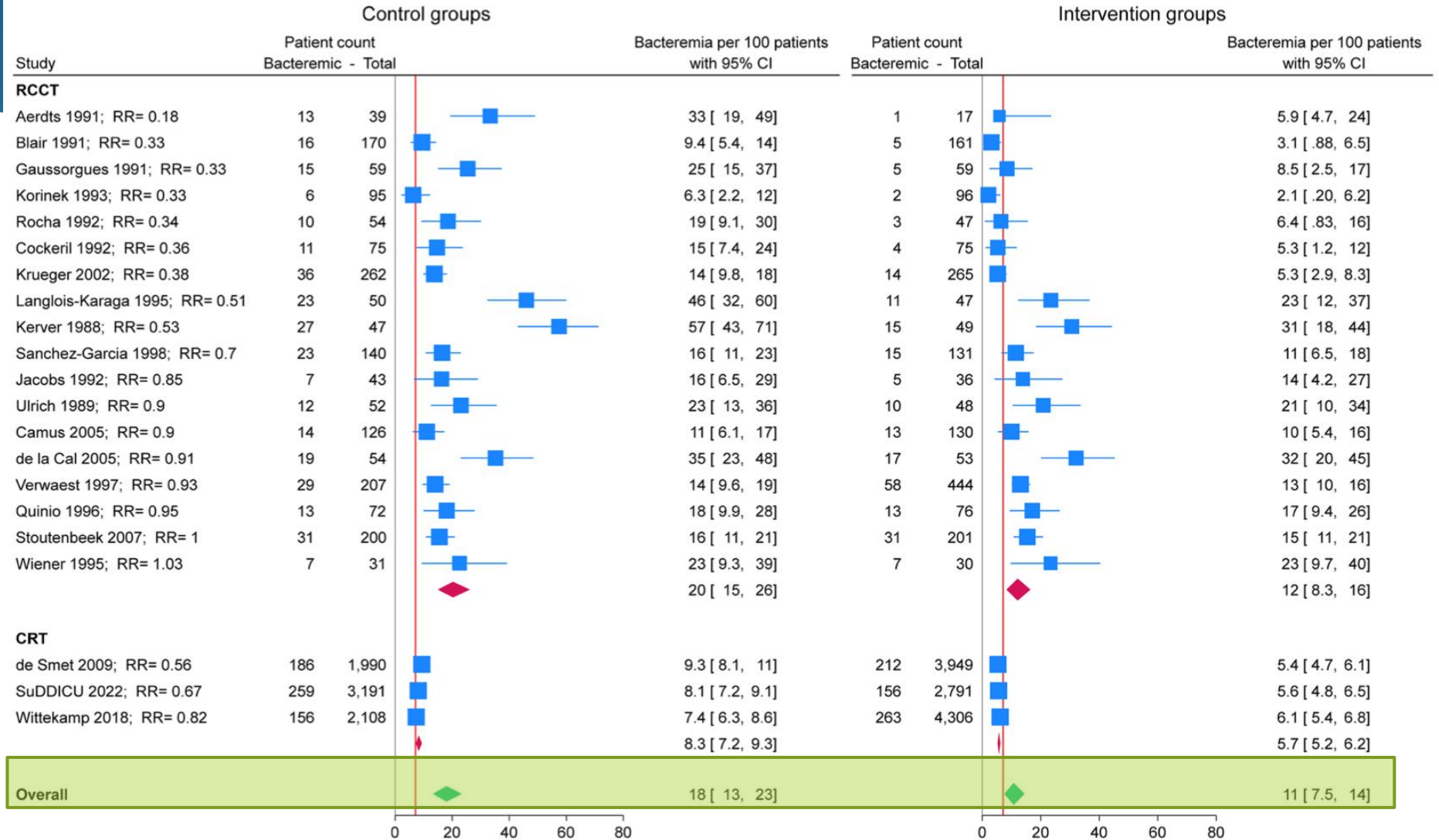
- ▶ Significantly less mortality among 27 studies (5699 patients) with patients individually randomized in concurrent trials (RCT) but not among 3 studies (18,335 patients) with groups randomized in cluster randomized trials (CRT): difference 15% vs 0%
- ▶ Is SDD safe?
- ▶ Incidence of BSI overestimated in RCTs?



ICM 2023

Selective digestive decontamination-Con

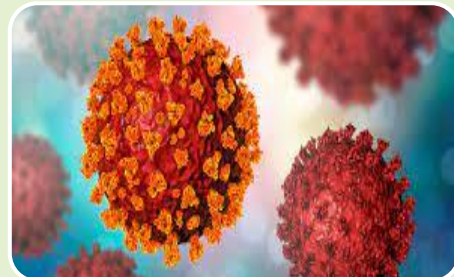
James C. Hurley^{1,2*}



Populations spécifiques



Brain injury



COVID-19



Immunocompromised



ECMO

Selective digestive tract decontamination in critically ill adults with acute brain injuries: a post hoc analysis of a randomized clinical trial



Young PJ, ICM 2023

- ▶ Post hoc analysis from a crossover, cluster randomized clinical trial
- ▶ ICUs randomly assigned to SDD or SC for two alternating 12-month periods
- ▶ Patients with an acute brain injury included
- ▶ SDD group ($n = 968$) : **oral** paste and **gastric** suspension containing colistin, tobramycin, and nystatin for the duration of mechanical ventilation, plus a 4-day course of an **intravenous antibiotic**
- ▶ Patients in the control group ($n = 1093$): standard care

Selective digestive tract decontamination in critically ill adults with acute brain injuries: a post hoc analysis of a randomized clinical trial



Young PJ, ICM 2023

Characteristic	SDD (N=968)	Standard care (N=1093)	Difference % (95% CI)	Odds ratio (95% CI)	p value
Primary outcome: in-hospital death within 90 d, no. (%)					
Primary analysis	313 (32.3)	415 (38)	- 6.2% (- 8.9% to - 3.5%)	0.76 (0.63 to 0.92)	0.004
Adjusted analysis ^a				0.74 (0.57 to 0.97)	0.03
Adjusted analysis ^b				0.78 (0.59 to 1.04)	0.082

a Adjusted for baseline Age, Sex, APACHE II/III score and diagnosis (operative vs non-operative)

b Adjusted for time from ICU admission to enrolment, systemic steroids, oral chlorhexidine, and on intravenous antibiotics at time of enrolment, in addition to the other variables from the previous model

Selective digestive tract decontamination in critically ill adults with acute brain injuries: a post hoc analysis of a randomized clinical trial



Young PJ, ICM 2023

Clinical secondary outcomes

Death in the ICU, no. (%)	247 (25.5)	323 (29.6)	- 5.0% (- 8.4% to - 1.5%)	0.79 (0.65 to 0.97)	0.02
Days alive and free of mechanical ventilation					
Mean \pm SD	57.2 \pm 38.3	52.1 \pm 39.5	5.60 (2.17 to 9.03)		0.001
Median (IQR)	81 (3 to 87)	78 (1 to 87)			
Days alive and free of ICU admission					
Mean \pm SD	54 \pm 37.3	49.2 \pm 38.4	5.18 (1.85 to 8.50)		0.002
Median (IQR)	76 (0 to 84)	72 (0 to 83)			
Days alive and free of hospital admission					
Mean \pm SD	39.8 \pm 34.2	36.3 \pm 34.5	3.72 (0.70 to 6.75)		0.02
Median (IQR)	50 (0 to 72)	38 (0 to 72)			

Selective digestive tract decontamination in critically ill adults with acute brain injuries: a post hoc analysis of a randomized clinical trial



Young PJ, ICM 2023

Microbiological secondary outcomes	Absolute difference ^c , (95% CI)			
Positive for <i>Clostridioides difficile</i> whilst in ICU, no. (%)	1 (0.1)	9 (0.8)	- 0.56 (- 1.01 to - 0.11)	0.018
Any blood organism found, no (%)	52 (5.4)	79 (7.2)	- 1.53 (- 3.34 to 0.28)	0.09
Any blood organism found except coagulase negative <i>S. aureus</i> , no. (%)	27 (2.8)	60 (5.5)	- 1.91 (- 3.48, - 0.35)	0.02
Any antibiotic resistant organism found, no. (%)	198 (20.5)	374 (34.2)	- 13.9 (- 17.5, - 10.3)	<0.0001

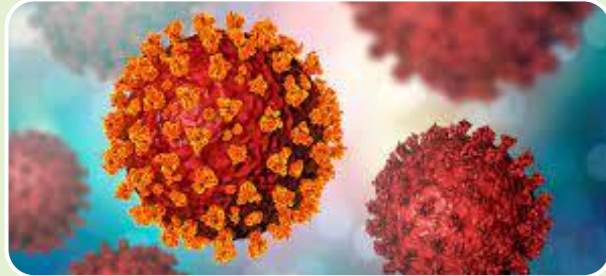
Populations spécifiques

Nicolas Massart

AIC 2022

Eur J Clin Microbiol Infect Dis 2023

AIC 2023



COVID-19

N=461

Multicentrique,
rétrospective

MSD



Immunocompromised

N = 295

Bicentrique
Avant/après

MSD



ECMO

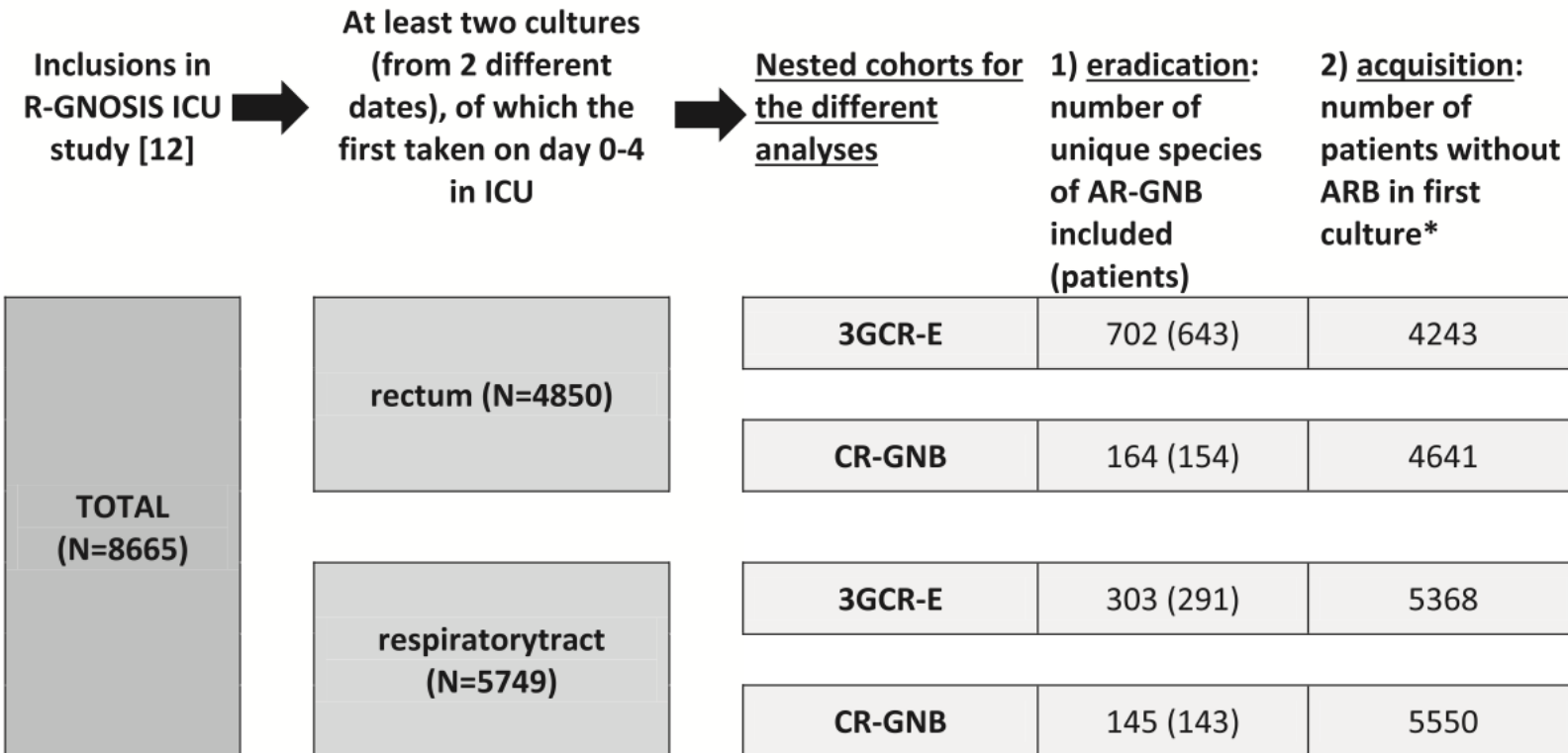
N = 241

Multicentrique,
rétrospective

MSD

The effects of topical antibiotics on eradication and acquisition of third-generation cephalosporin and carbapenem-resistant Gram-negative bacteria in ICU patients; a *post hoc* analysis from a multicentre cluster-randomized trial

Plantinga NL, CMI 2020



The effects of topical antibiotics on eradication and acquisition of third-generation cephalosporin and carbapenem-resistant Gram-negative bacteria in ICU patients; a *post hoc* analysis from a multicentre cluster-randomized trial

Plantinga NL, CMI 2020

- ▶ SDD associée avec plus d'éradication et moins d'acquisition de C3GR-E et CR- GNB dans le rectum que SC
 - csHR 1.76 (95% CI 1.31-2.36) éradication C3GR-E
 - csHR 3.17 (95% CI 1.60-6.29) éradication CR-GNB

 - csHR 0.51 (0.40-0.64) acquisition C3GR-E
 - csHR 0.56 (0.40-0.78) acquisition CR-GNB

The effects of topical antibiotics on eradication and acquisition of third-generation cephalosporin and carbapenem-resistant Gram-negative bacteria in ICU patients; a *post hoc* analysis from a multicentre cluster-randomized trial

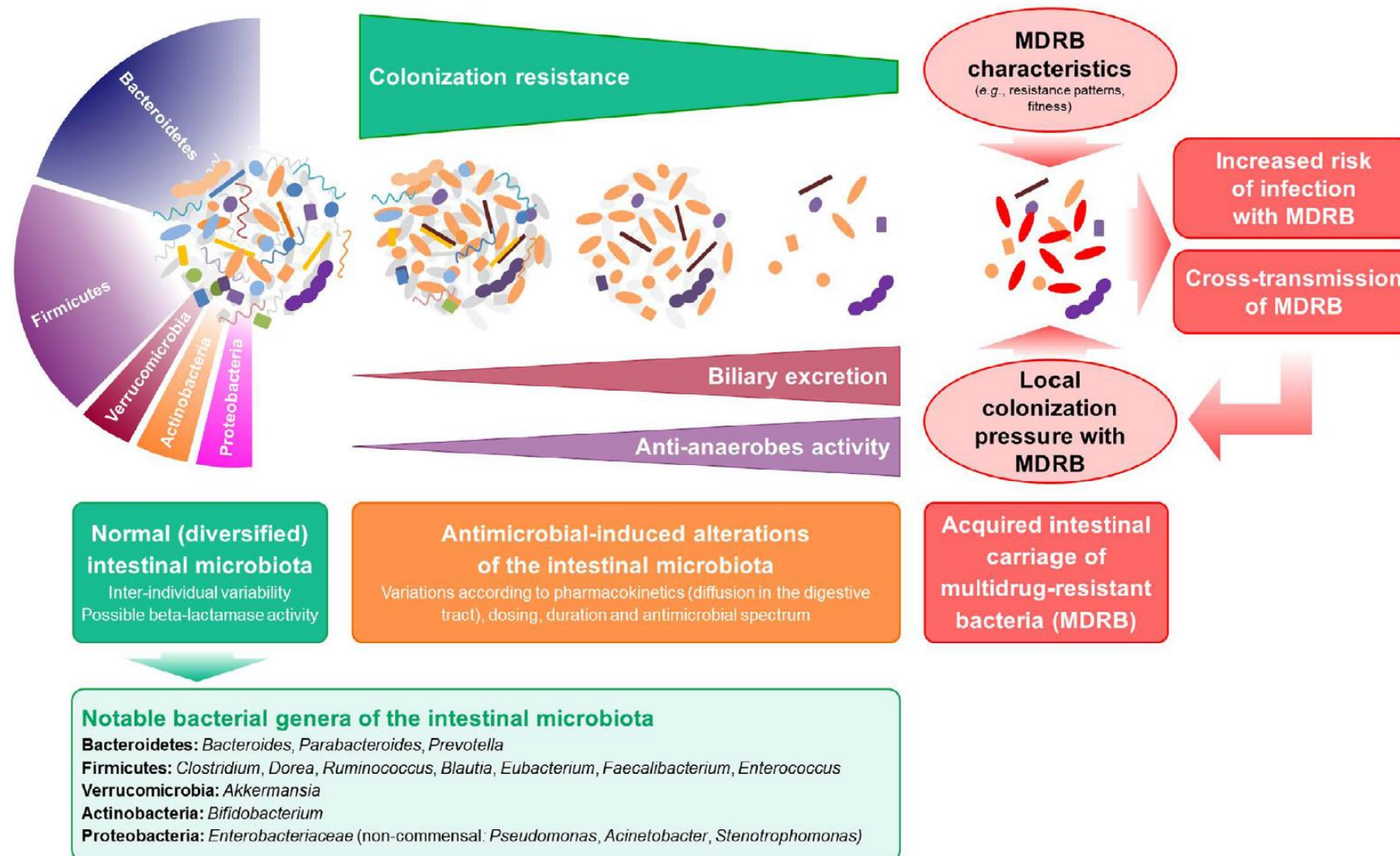
Plantinga NL, CMI 2020

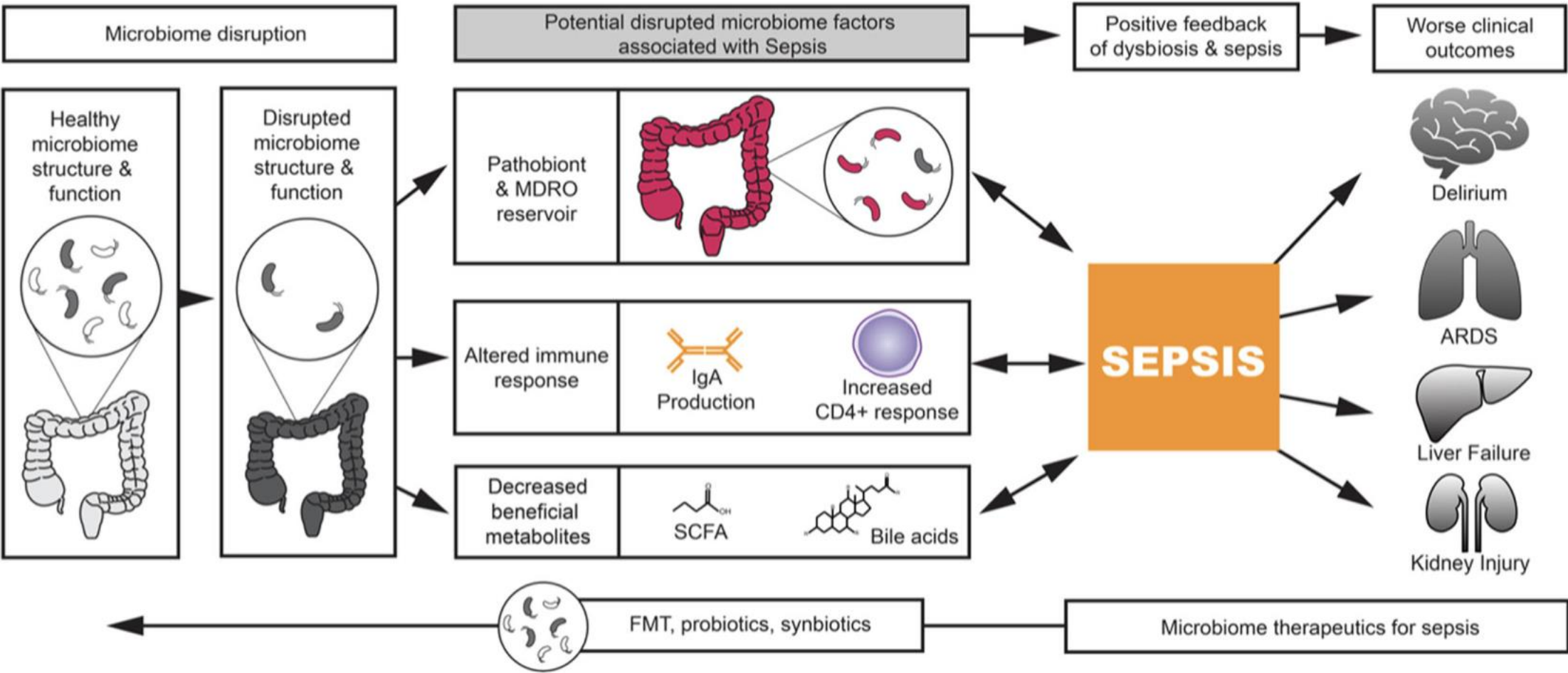
- ▶ SDD et SOD associée avec moins d'acquisition de C3GR-E et CR- GNB (respiratoire)
 - SDD: csHR 0.38 (0.28-0.50) acquisition C3GR-E
 - SOD: csHR 0.55 (0.42-0.71) acquisition C3GR-E

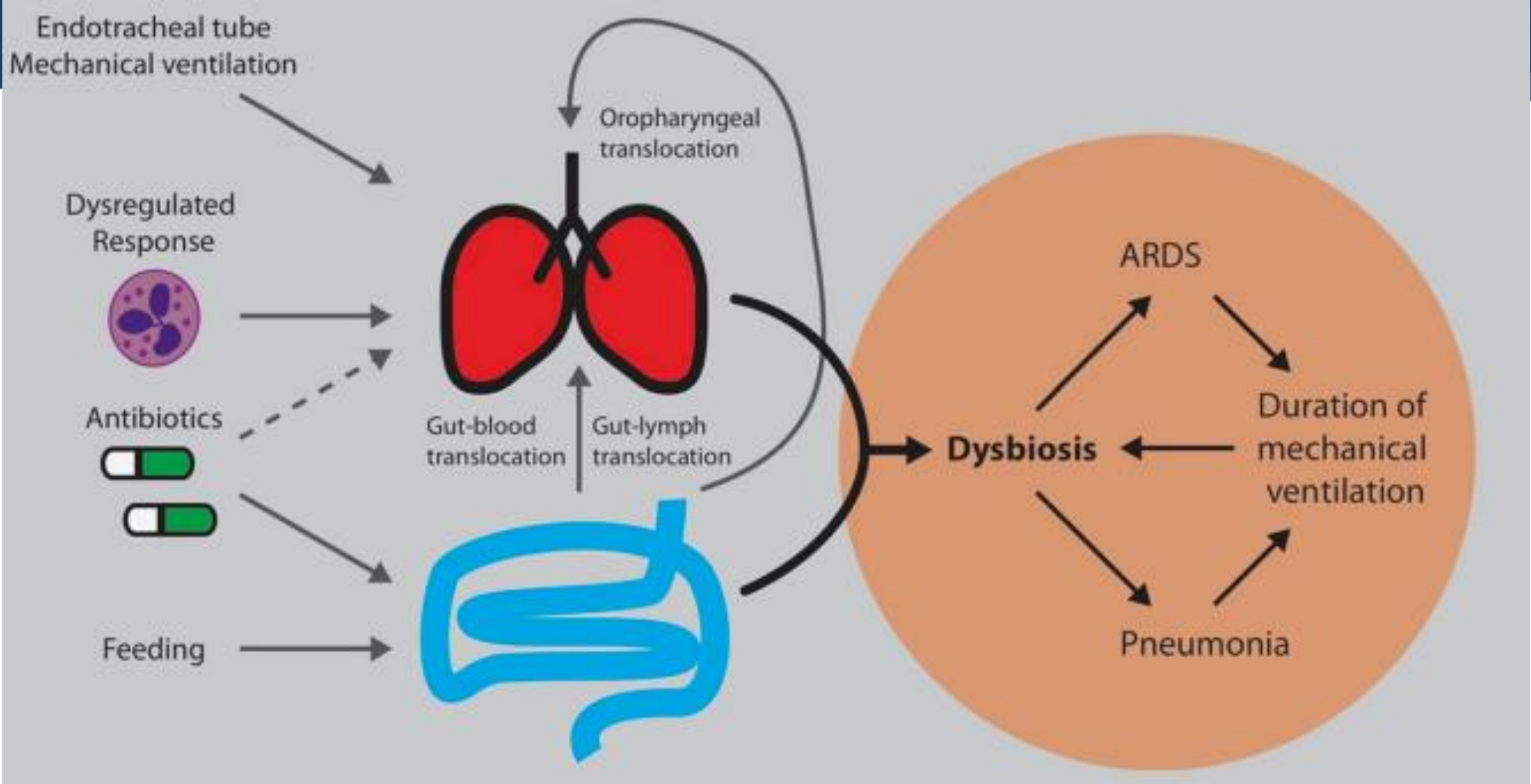
 - SDD: csHR 0.46 (0.33-0.64) acquisition CR-GNB
 - SOD: csHR 0.60 (0.44-0.81) acquisition CR-GNB

Antibiothérapie et microbiome

Woerther PL, IJAA 2018

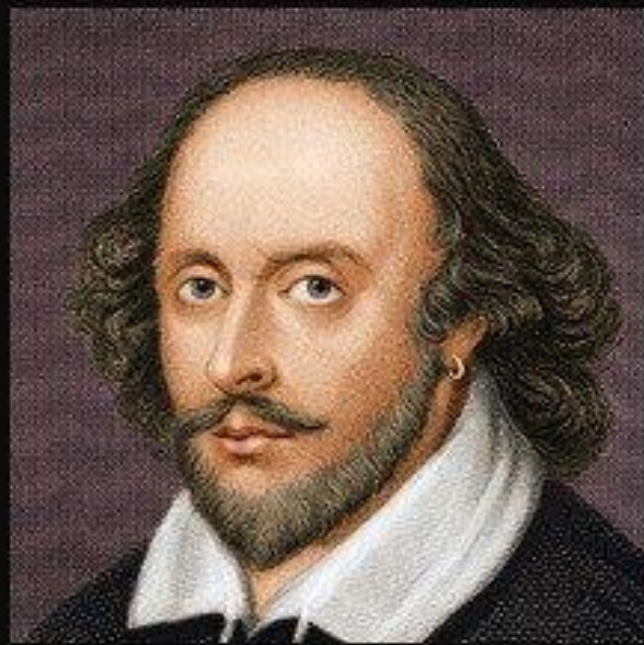






Conclusions

- ▶ SDD associée à une réduction de la mortalité et de l'incidence des IRB dans des réanimations avec une incidence faible d'antibio-résistance
- ▶ La réduction de la mortalité et des IAR plus importante avec la SDD vs SOD
- ▶ L'impact de la SDD sur la mortalité et de l'incidence des IRB dans des réanimation avec une incidence élevée d'antibio-résistance reste à déterminer
- ▶ L'impact de la SDD sur le microbiome digestif et pulmonaire est à évaluer



Sometimes, less is more.

~ William Shakespeare