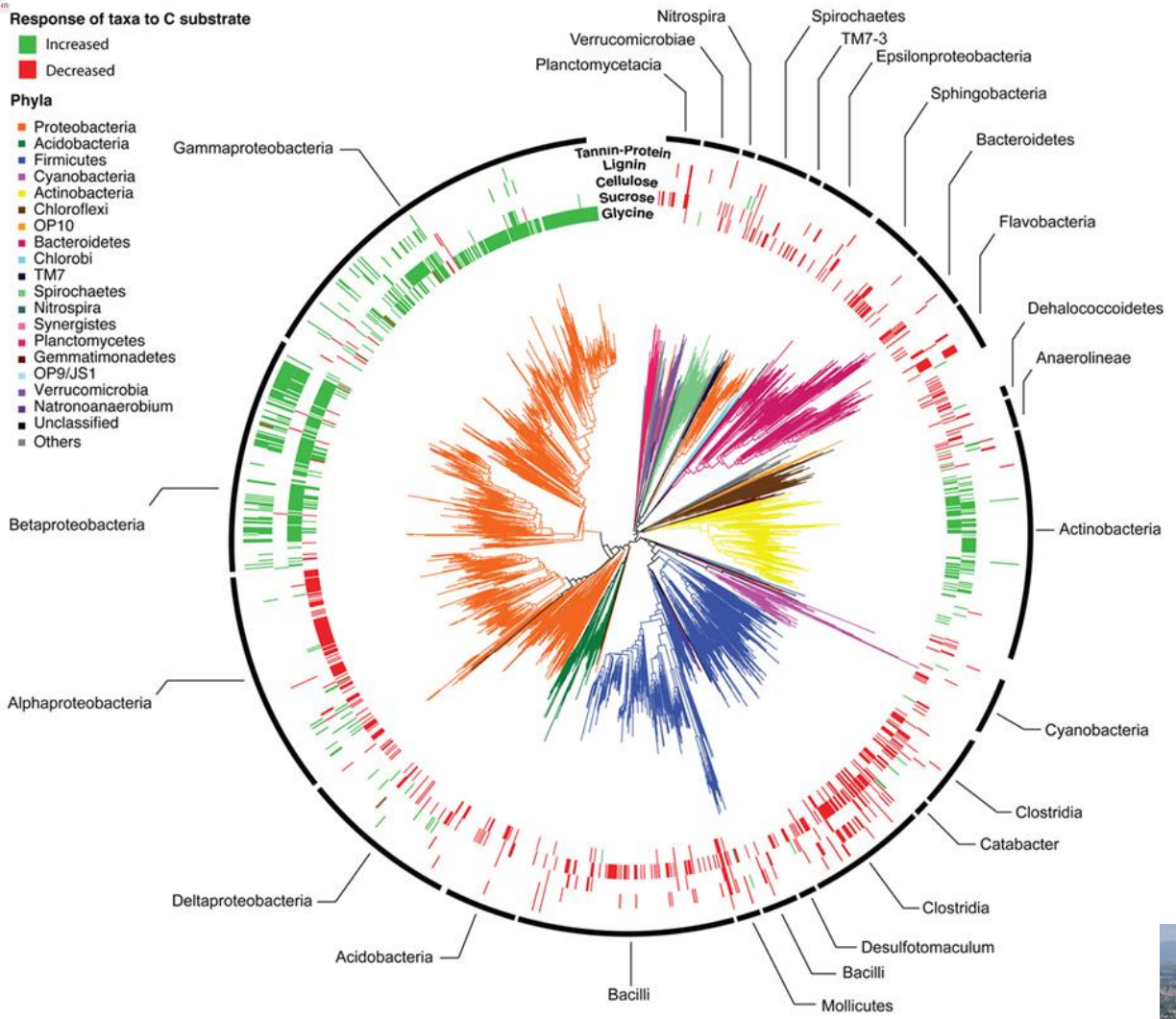
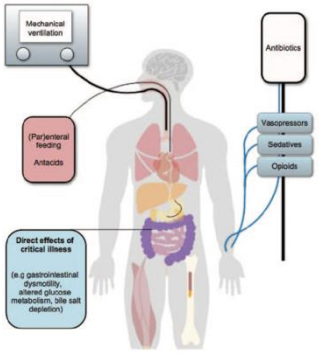
Le Microbiote, comment l'inclure dans nos pratiques





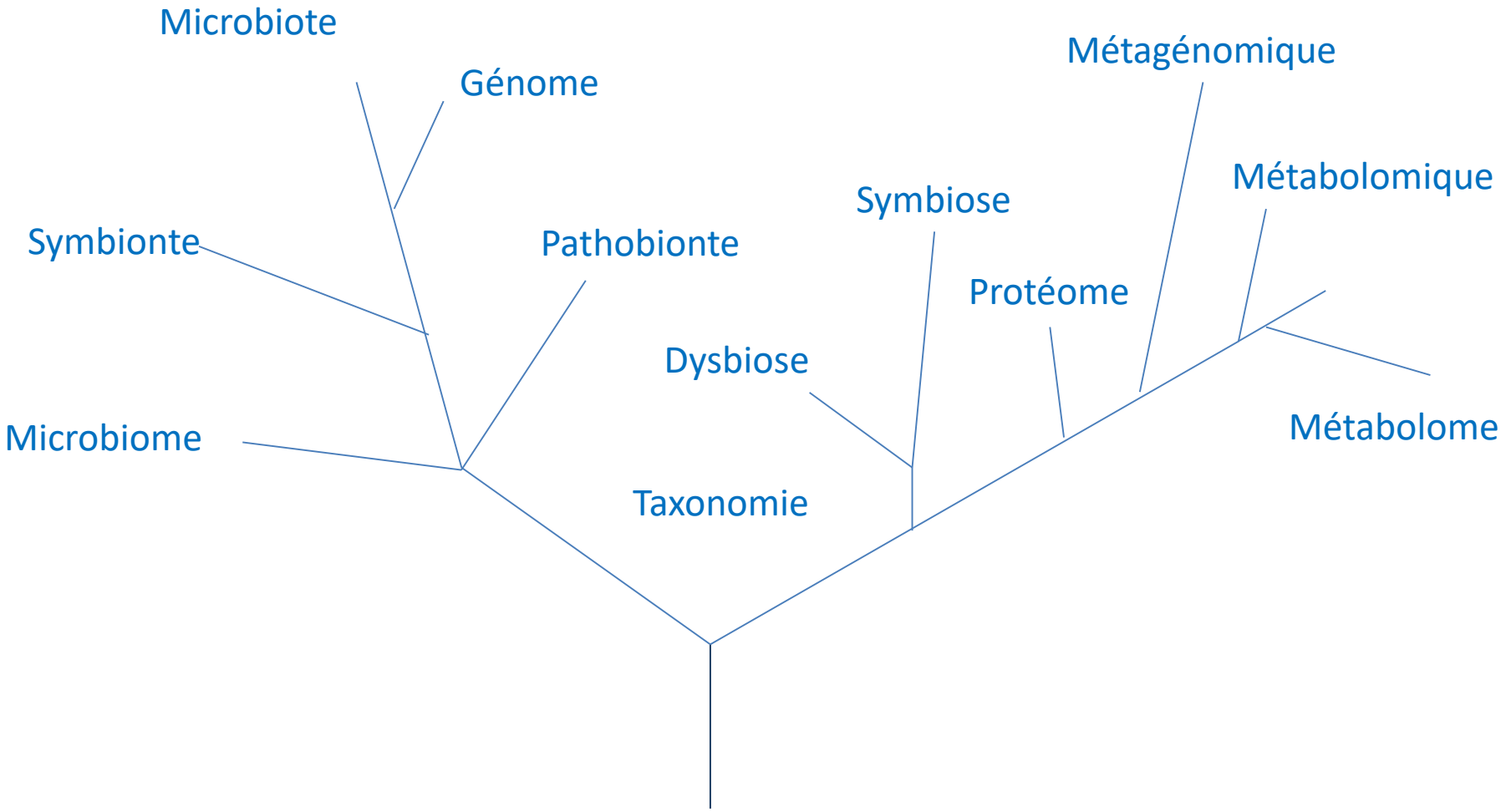
Dr J Mootien

Heinrich Anton de Bary
1831 (Francfort)-1888 (Strasbourg)
Médecin, biologiste, botaniste

1822-1895

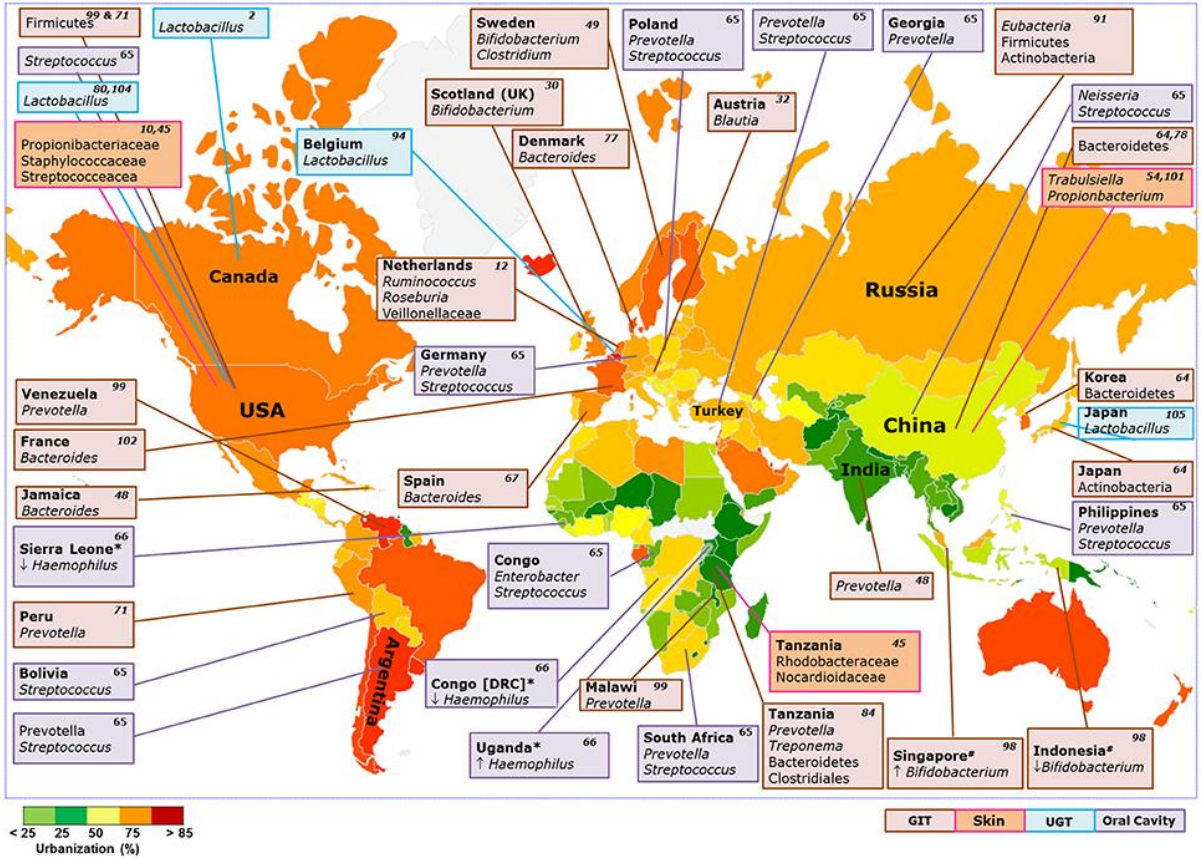
Theodor Escherich
1857(Ansbach) - 1911(Vienne)
Pédiatre, bactériologiste

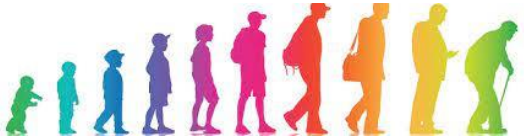
Titre de l'ouvrage :Die Erscheinung der Symbiose
"association vivante d'espèces différentes"
Publication : Strasbourg - K. J. Trübner - 1879


Microbiote
Génome
Métagénomique
Métabolomique
Symbiose
Symbiont
Pathobionte
Protéome
Dysbiose
Microbiome
Métabolome
Taxonomie

Glossaire

Diversité du microbiote

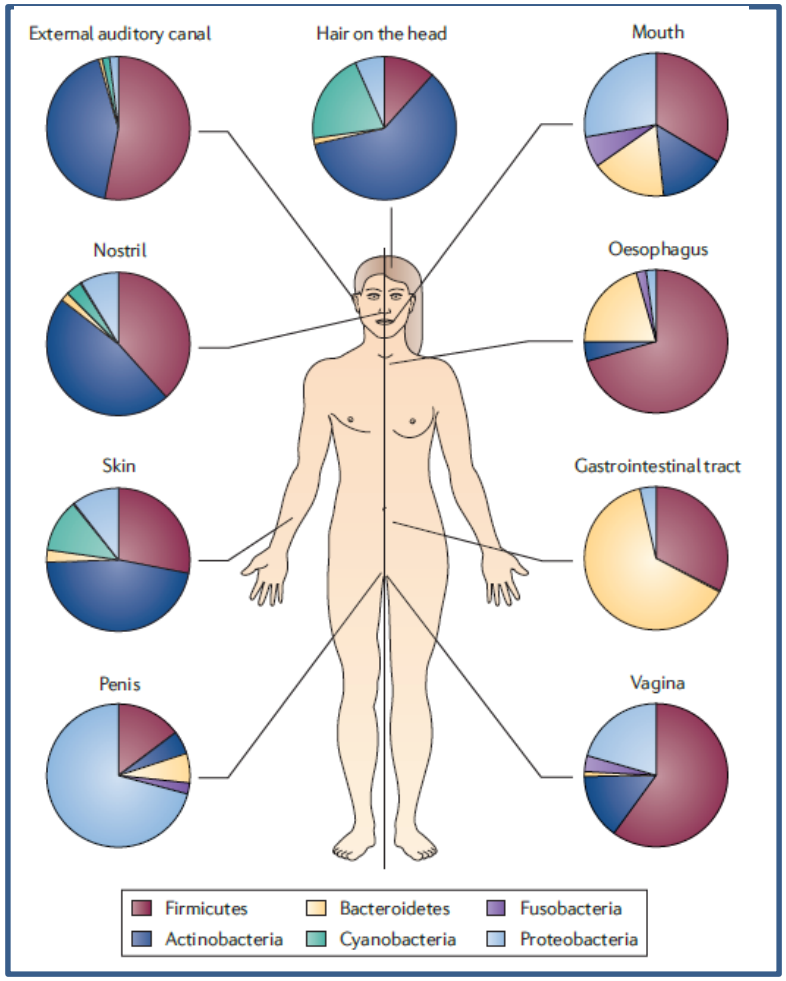




- Fœtus
  - Liquide amniotique (stérilité in utéro?)
- Colonisation à l'accouchement
  - voie basse (flore vaginale)
  - accouchement par césarienne (flore cutanée)

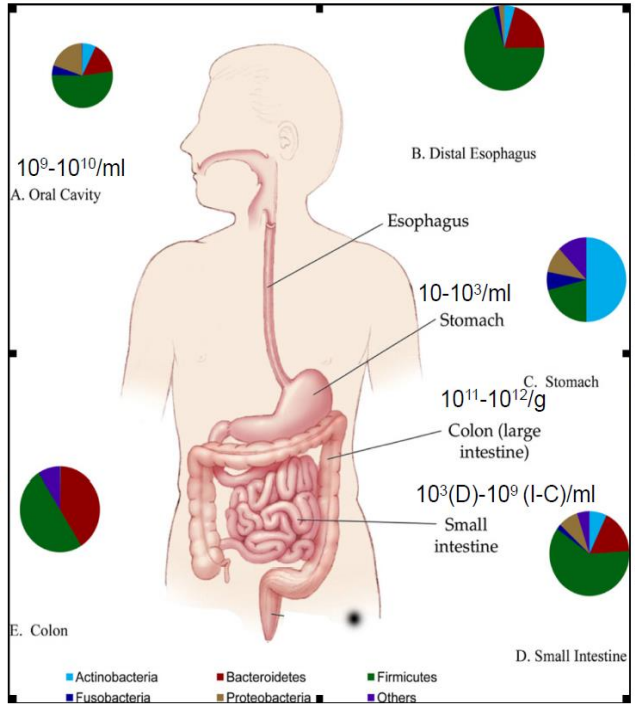
- Nourrisson
  - Mode d'alimentation, hygiène
- Flore adulte:
- Stabilité de cette flore
- Evolution dans le temps

Microbiote(s) …



Spor A Nature Review Microbiology , vol 9,2011

Firmicutes, Proteobactéries, Bacteroidetes, Actinobactéries, Fusobacteria
Rares: SR1, TM7, Cyanobactéries Spirochètes, Tenericutes, Synergistetes (Ahn J et al. 2011.PLoS One

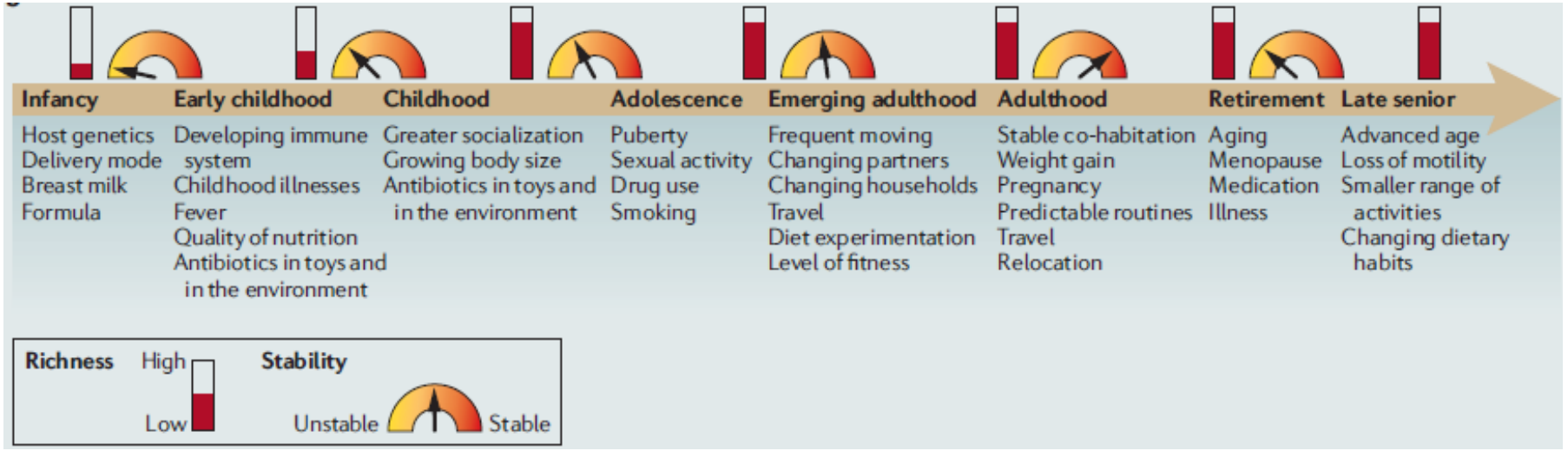


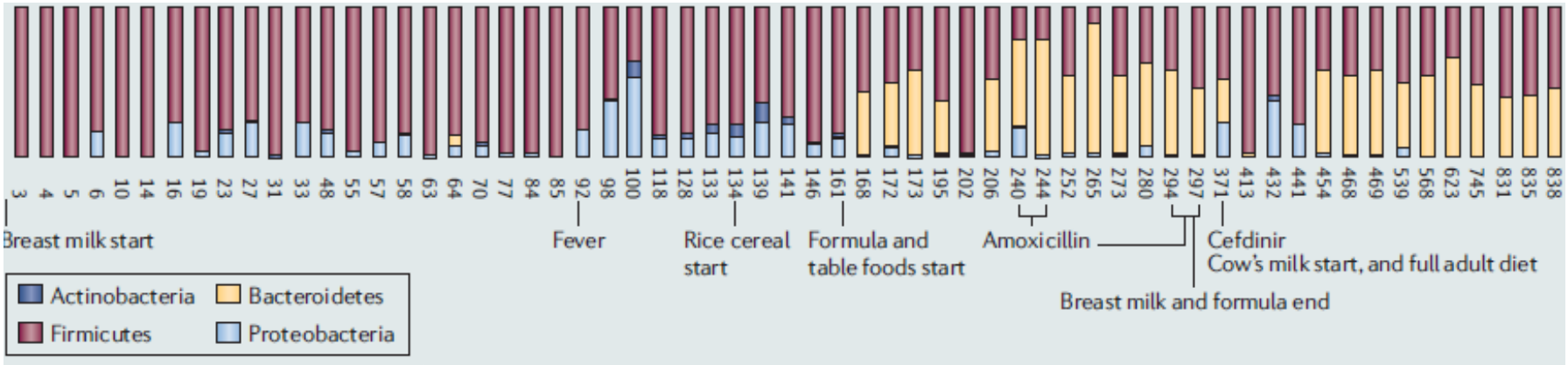
Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Fusobacteria, TM7
Streptococcus, Veillonella, Prevotella = les genres les plus fréquents
(Pei Z et al. 2004. PNAS)

Proteobacteria, Firmicutes, Actinobacteria, Bacteroidetes, Fusobacteria...
Helicobacter pylori
(Bick et al. 2006. PNAS)

Diversité restreinte/colon
Anaérobies facultatifs...

Évolution du microbiote



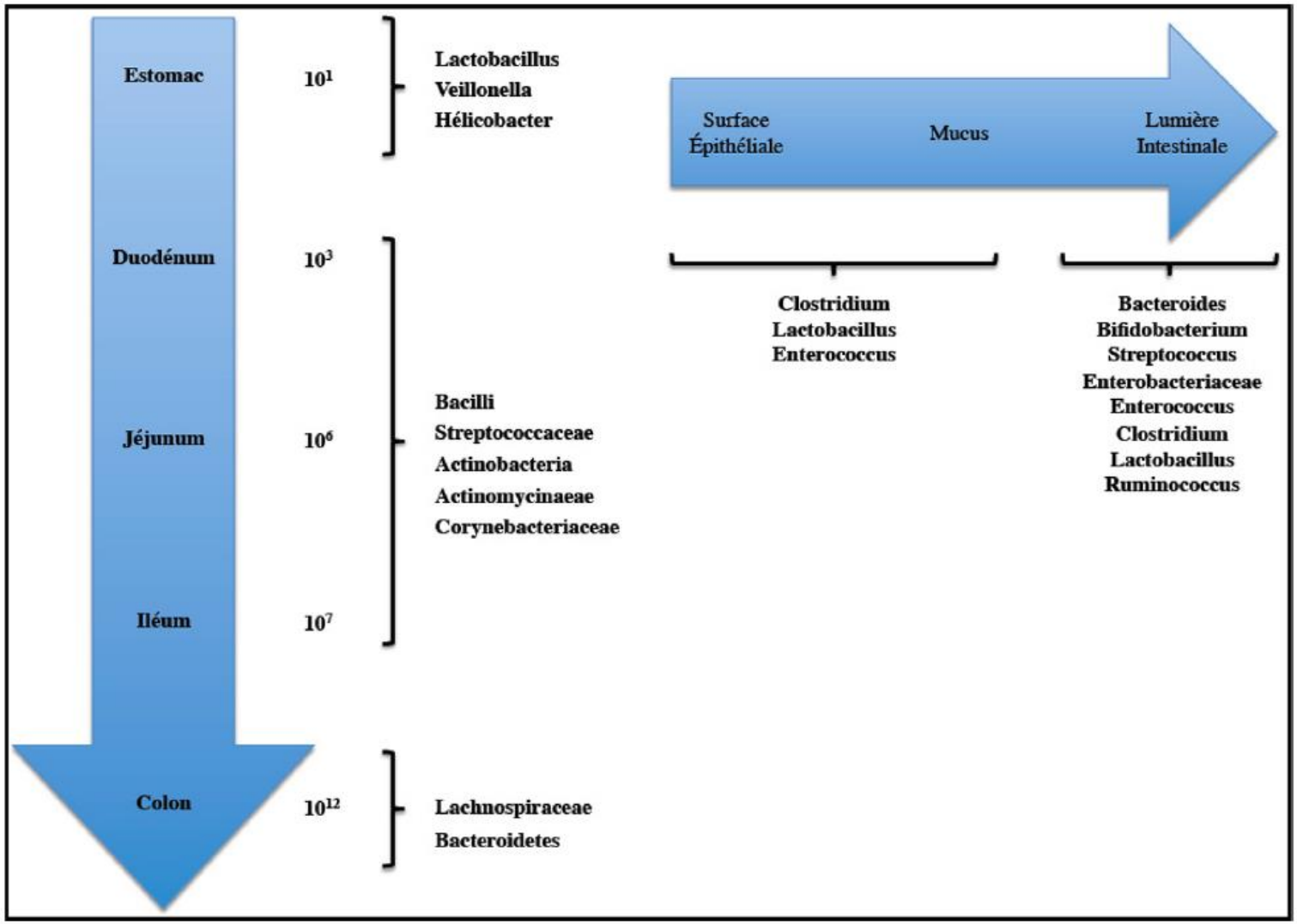


Spor A Nature Review Microbiology , vol 9,2011

Effets biologiques du microbiote intestinal sur son hôte humain

- Développement de l'immunité innée et adaptative
- Effet de barrière microbiologique
- Maintien de l'intégrité de l'épithélium
- Source d'énergie
- Biosynthèse de vitamines, transformation des sels biliaires, catabolisme des sucres végétaux complexes (cellulose, pectines) et des mucines
- Métabolisme des xénobiotiques

Composition et biogéographie du microbiote



Baraud D Réanimation 2016,25,328-339

The Pervasive Effects of an Antibiotic on the Human Gut Microbiota, as Revealed by Deep 16S rRNA Sequencing

Dethlefsen L, Huse S, Sogin ML, Relman DA (2008)
PLoS Biol 6(11): e280. doi:10.1371/journal.pbio.0060280

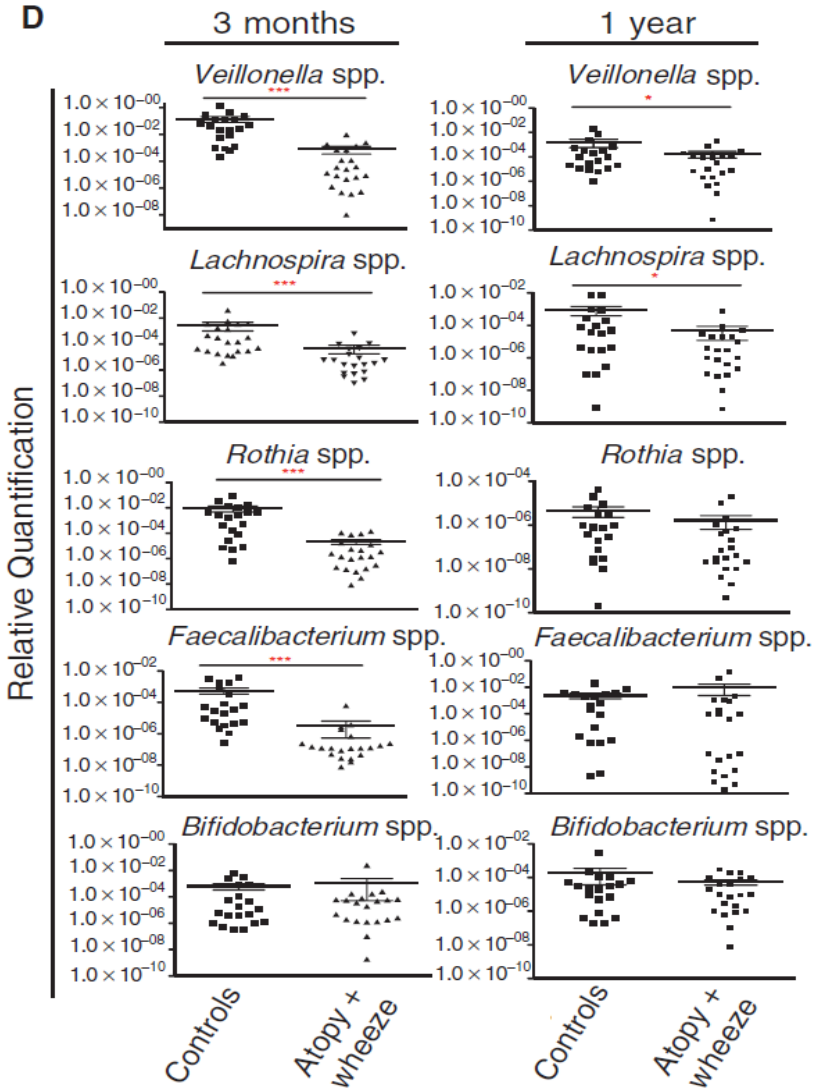
Infant antibiotic exposures and early-life body mass

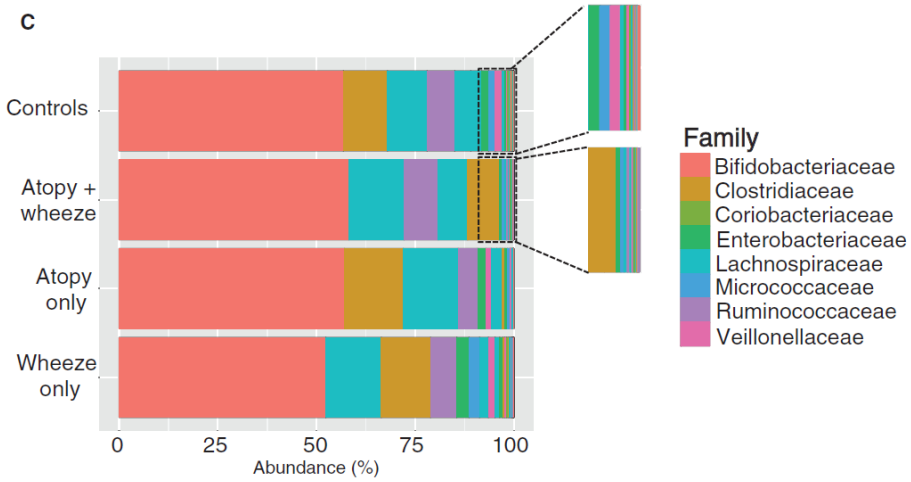
L Trasande[1,2,3], **J Blustein**[3,4], **M Liu**[2], **E Corwin**[3], **LM Cox**[5], and **MJ Blaser**[4,5]

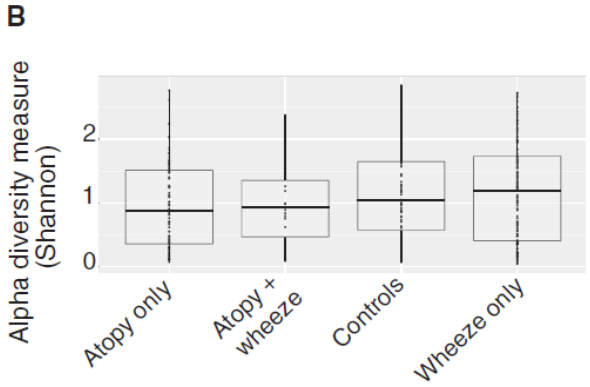
Int J Obes (Lond). 2013 January ; 37(1): 16–23. doi:10.1038/ijo.2012.132.

CONCLUSIONS—Exposure to antibiotics during the first 6 months of life is associated with consistent increases in body mass from 10 to 38 months. Exposures later in infancy (6–14 months, 15–23 months) are not consistently associated with increased body mass. Although effects of early exposures are modest at the individual level, they could have substantial consequences for population health. Given the prevalence of antibiotic exposures in infants, and in light of the growing concerns about childhood obesity, further studies are needed to isolate effects and define life-course implications for body mass and cardiovascular risks.

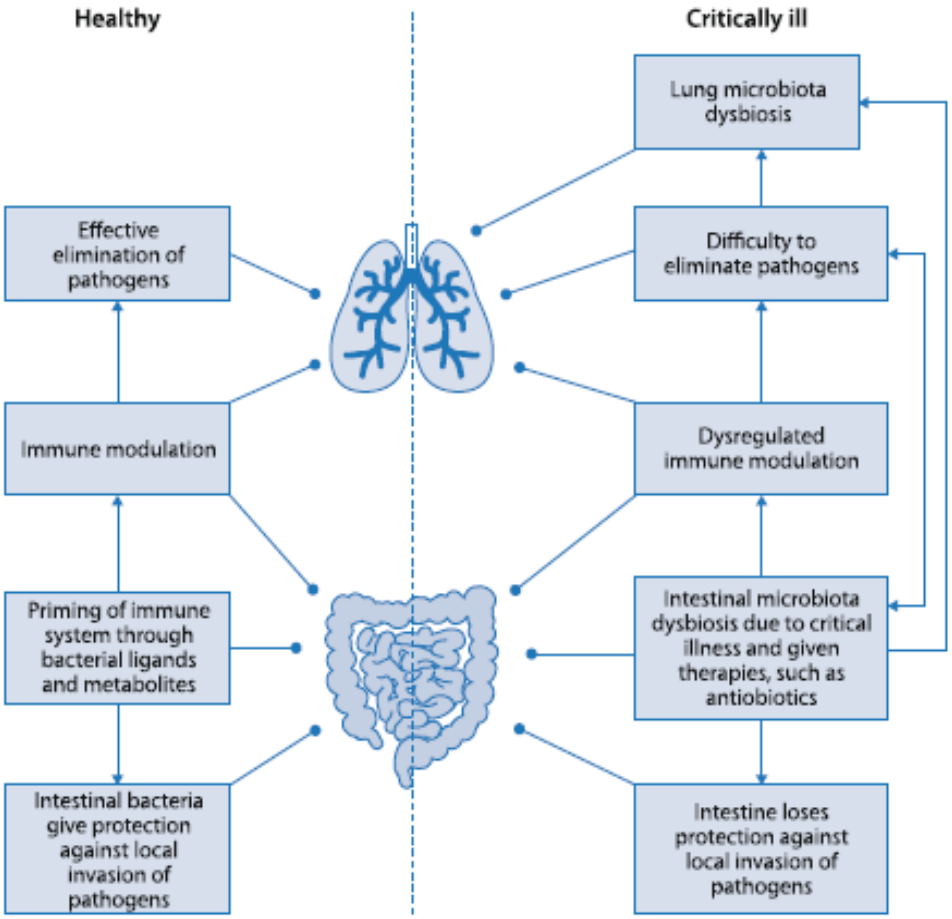
Early infancy microbial and metabolic alterations affect risk of childhood asthma

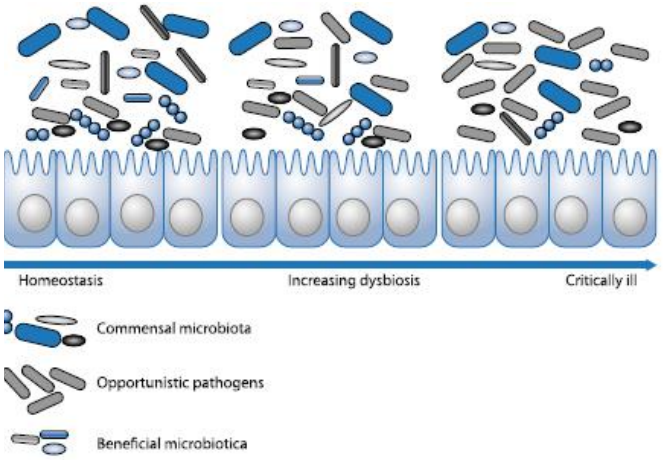






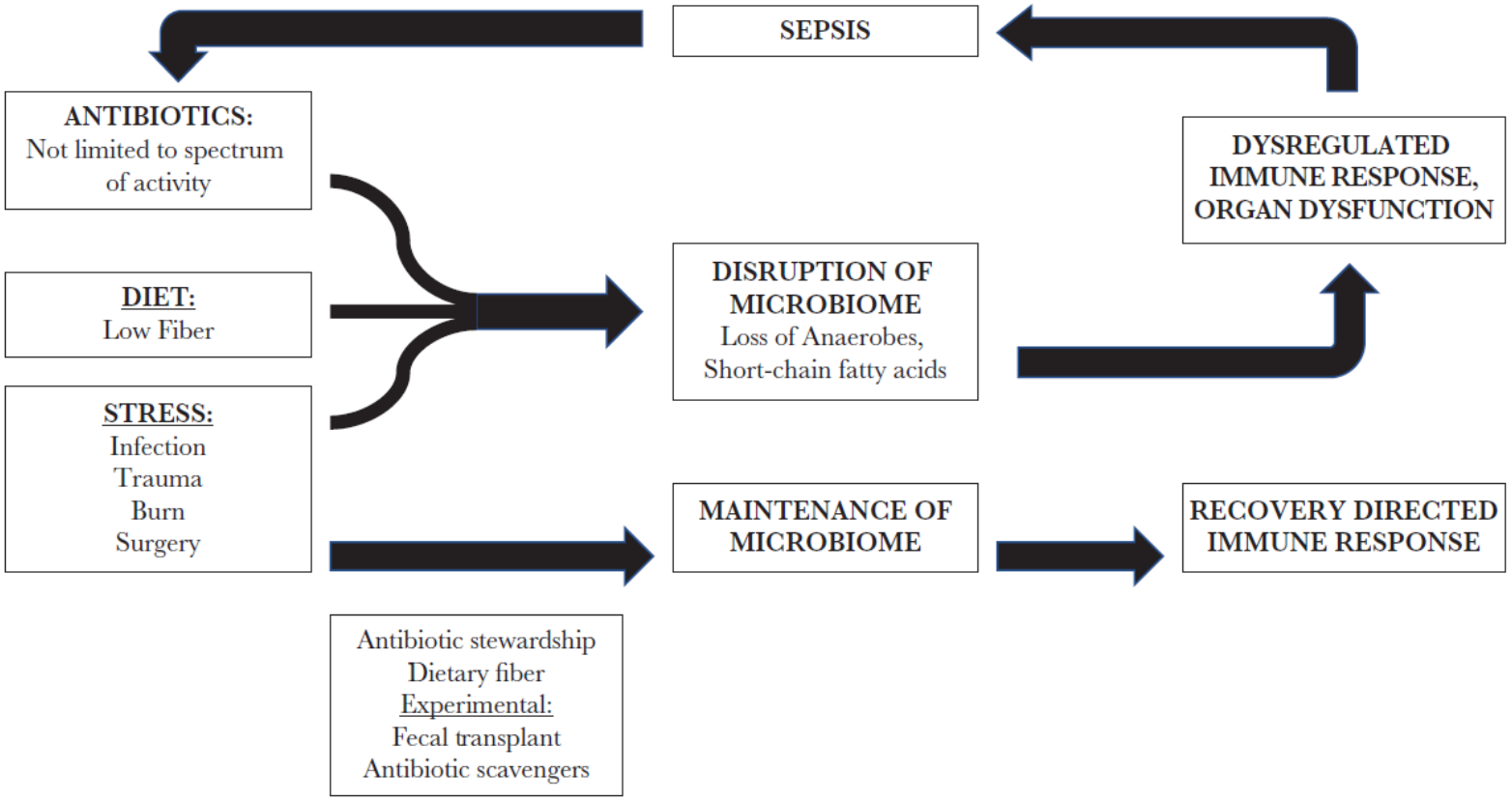
The emerging role of the microbiota in the ICU





Wolff *et al. Critical Care* (2018) 22:78

Microbiome et sepsis



Miller W.D JID 2021:223 (suppl 3)

Respiratory mirobiome in mechanically ventilated patients
A narrative review

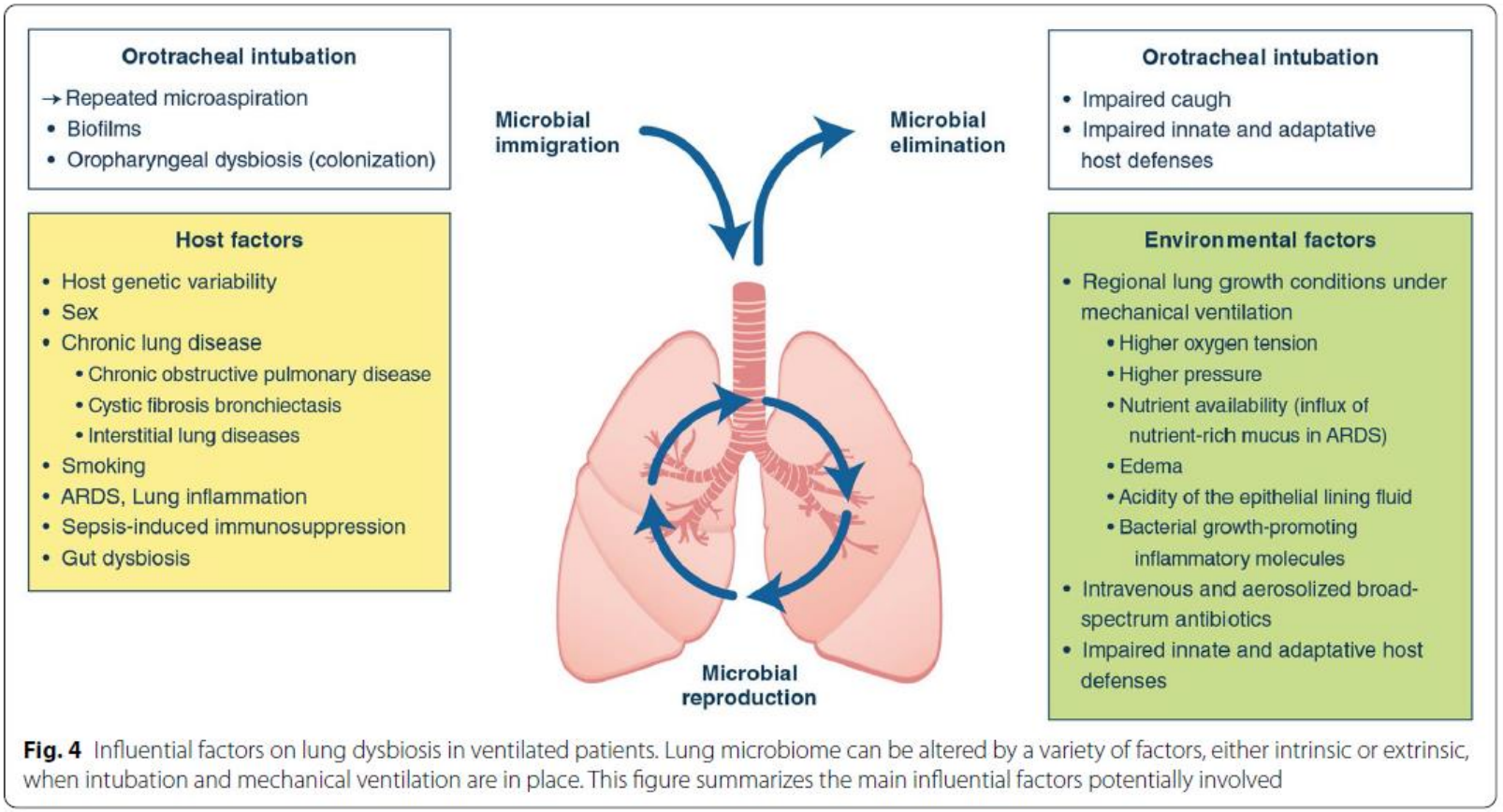
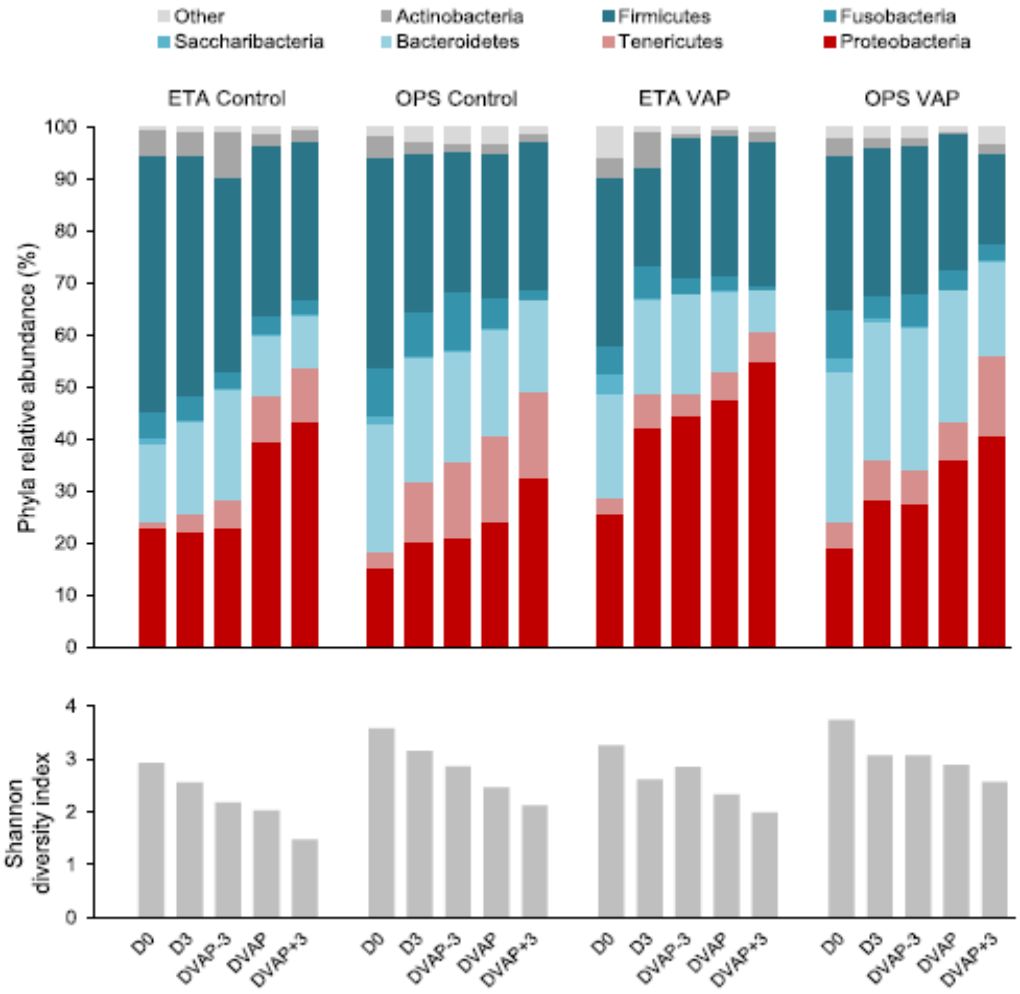


Fig. 4 Influential factors on lung dysbiosis in ventilated patients. Lung microbiome can be altered by a variety of factors, either intrinsic or extrinsic, when intubation and mechanical ventilation are in place. This figure summarizes the main influential factors potentially involved

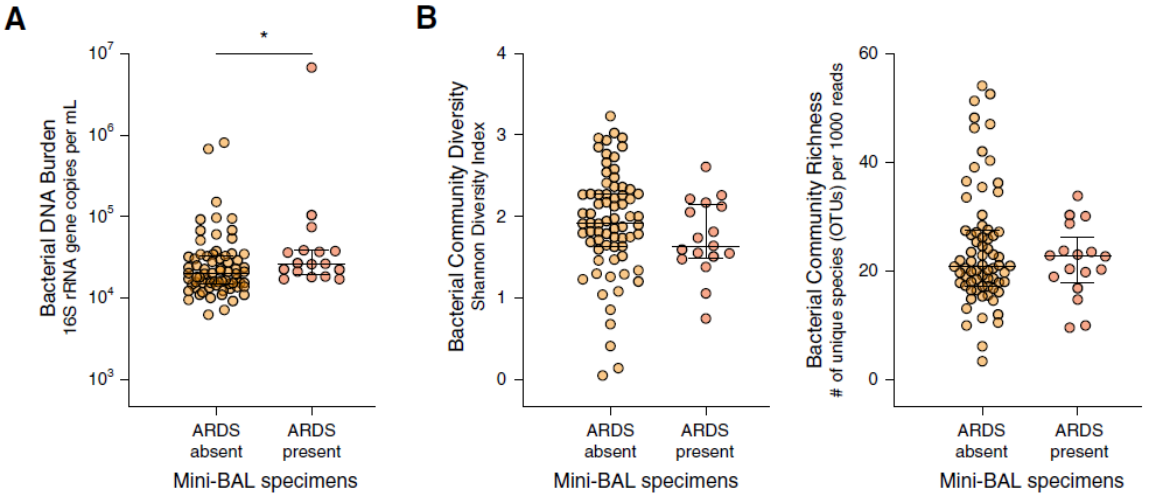
Fromentin M Intensive Care Med (2021)47 : 292-306

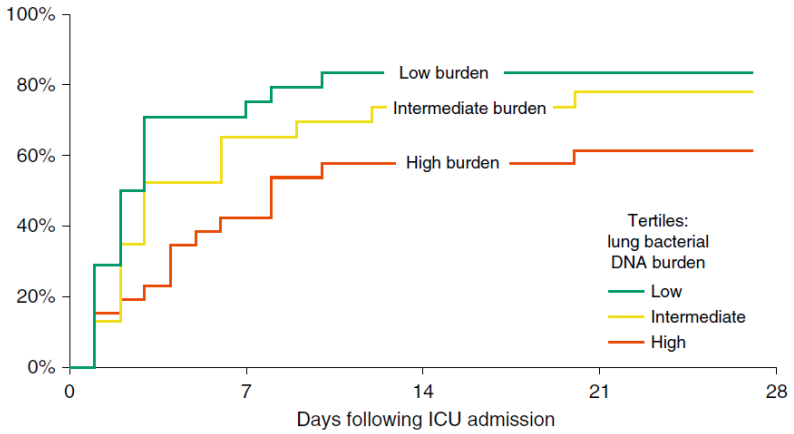
Identification of respiratory microbiota markers in ventilator-associated pneumonia

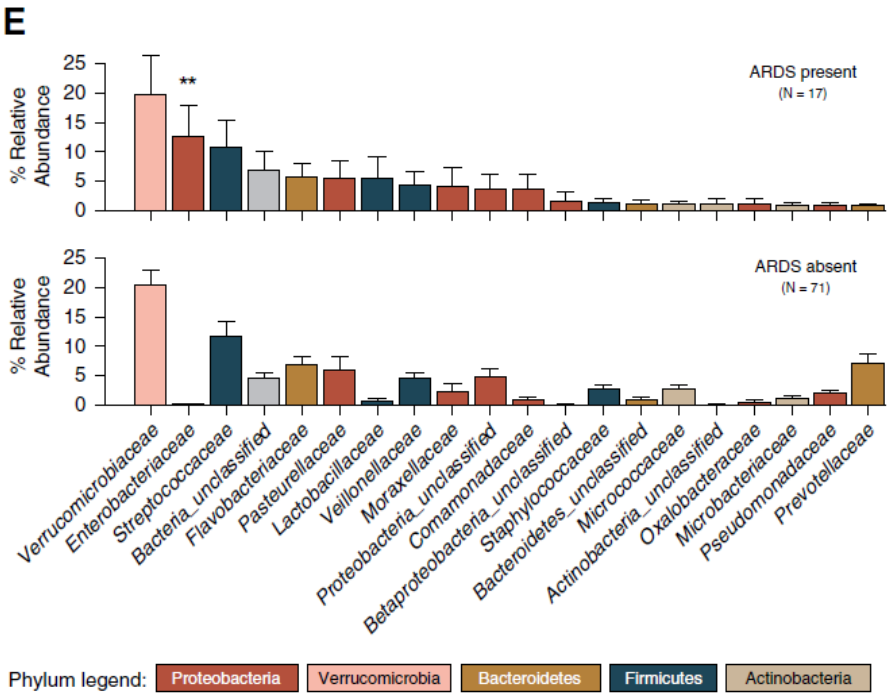


Emonet S Intensive Care Med (2019) 45 : 1082-1092

Lung Microbiota Predict Clinical Outcomes in Critically Ill Patients

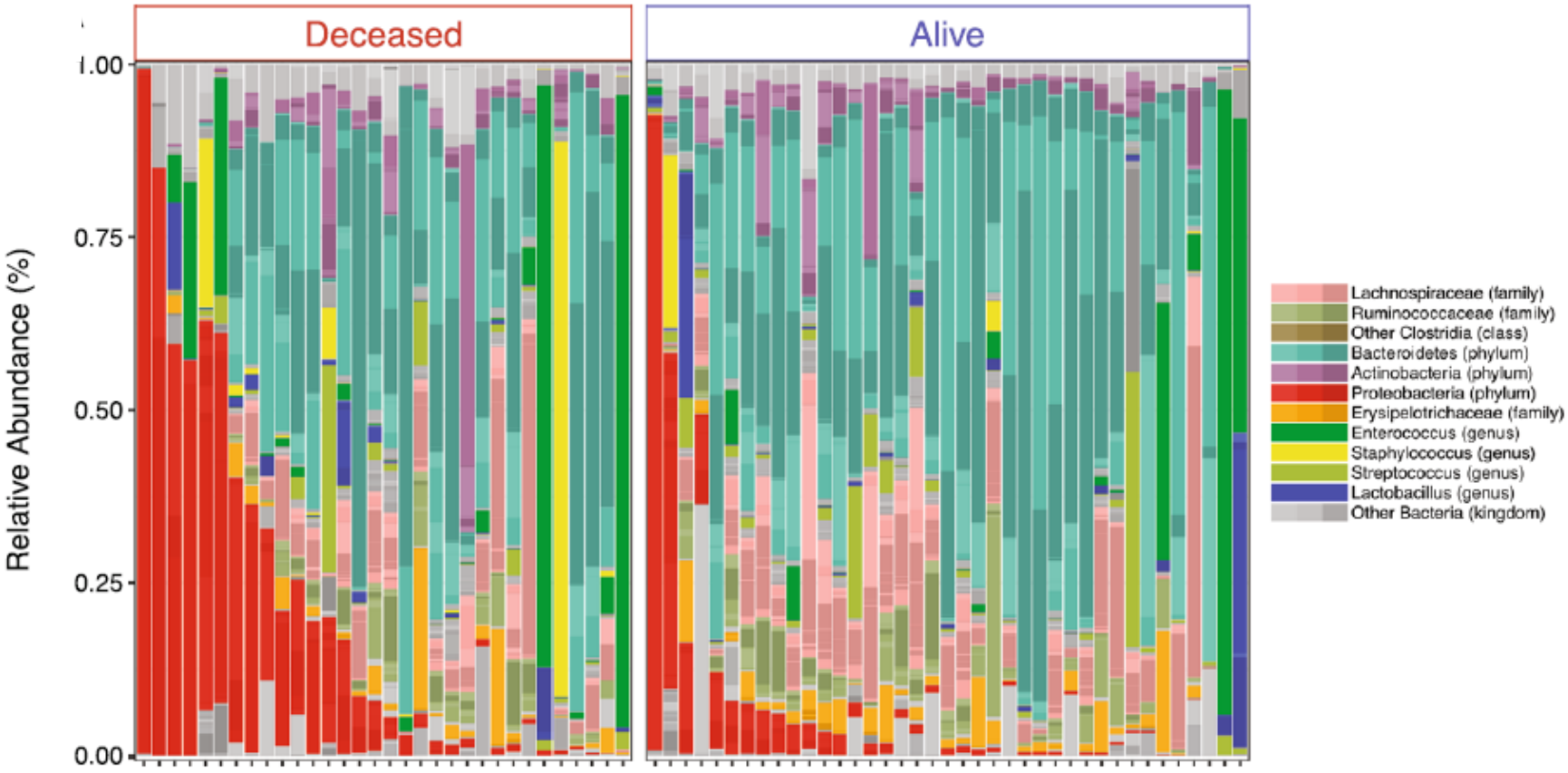






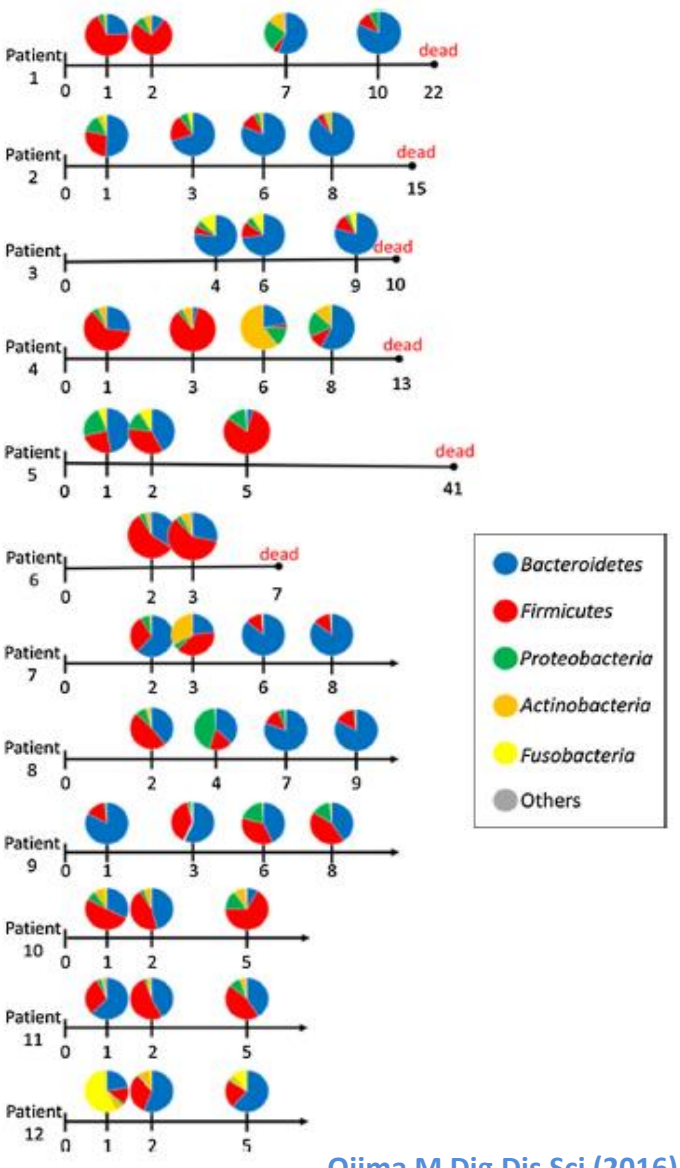
R.P Dickson AJRCCM vol 201, 5, March1 2020

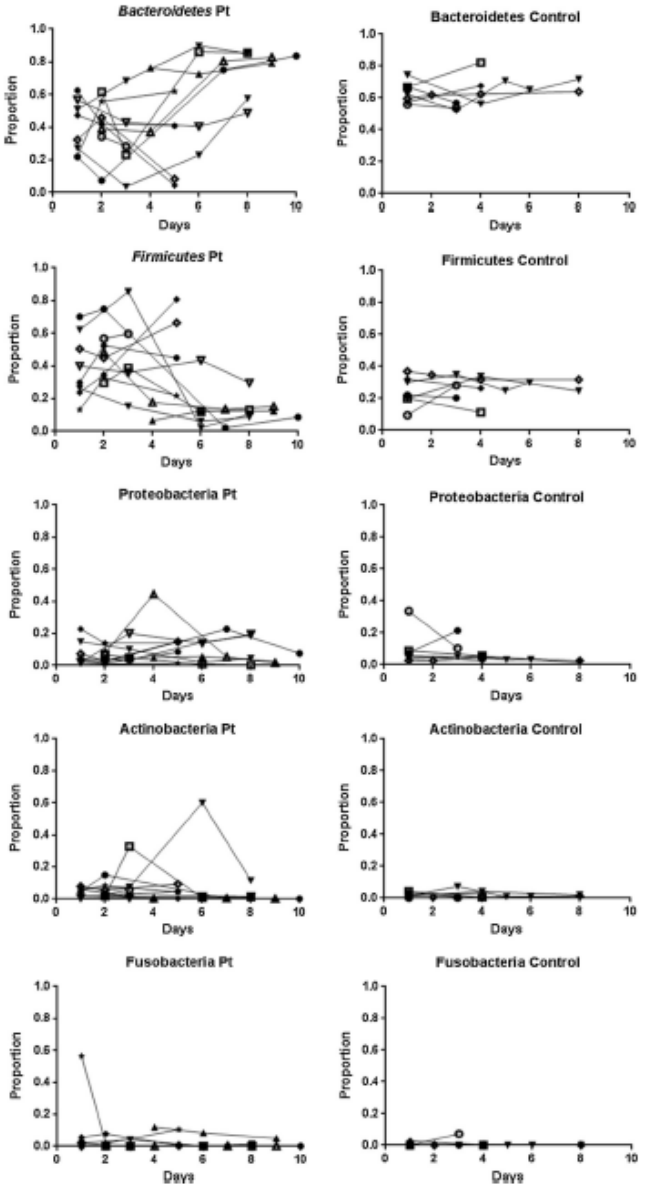
Immunomodulatory fecal metabolites are associated with mortality in COVID-19 patients with respiratory failure



Stutz MR Nature Communications (2022) 13 :6615

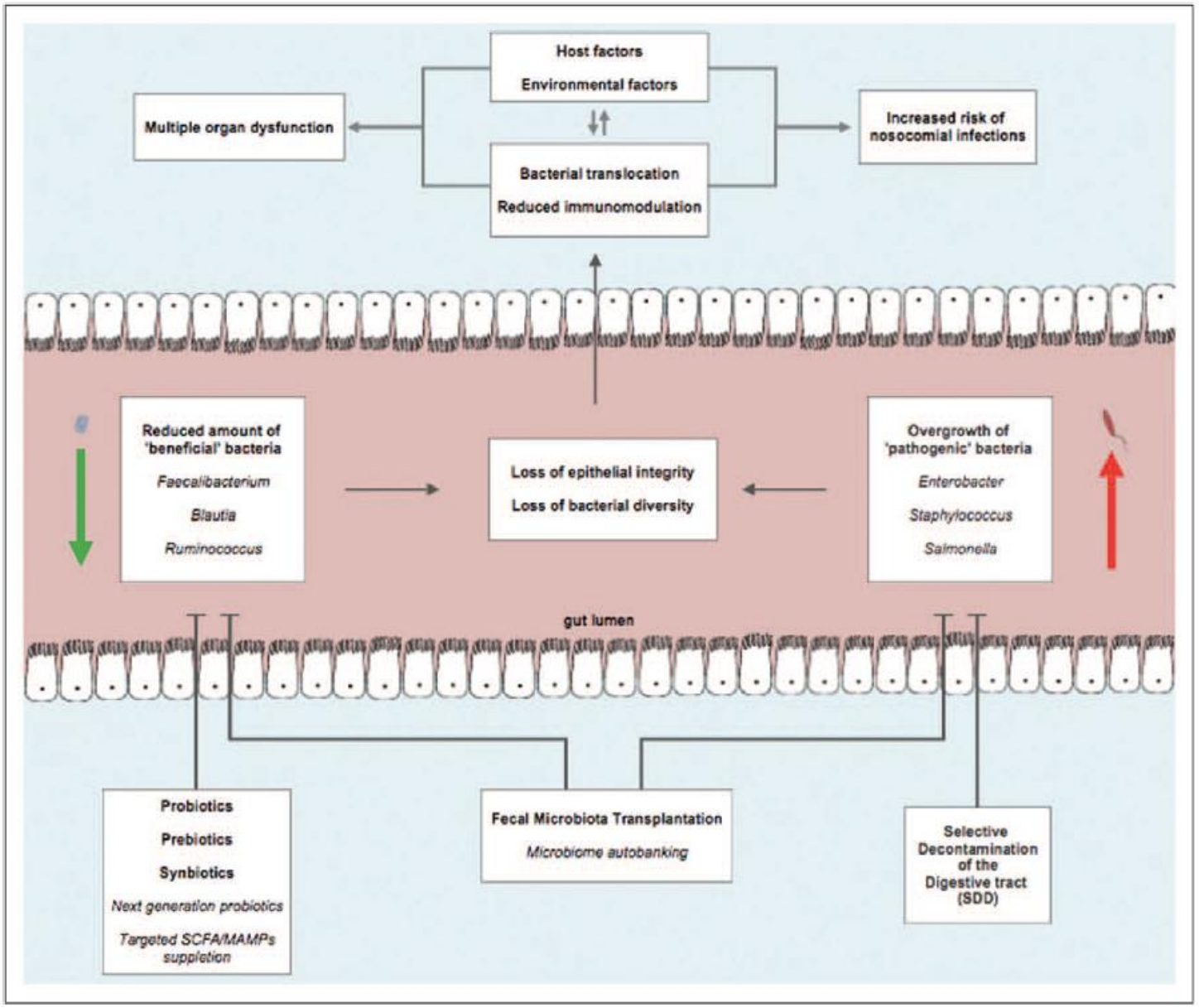
Metagenomic Analysis Reveals Dynamic Changes of Whole Gut Microbiota in the Acute Phase of Intensive Care Unit Patients





Ojima M Dig Dis Sci (2016) 61: 1628-1634

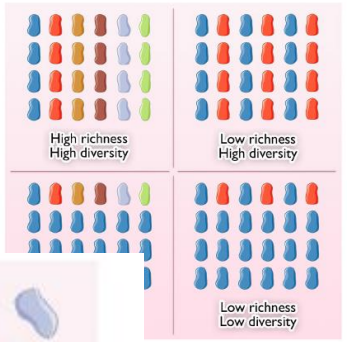
Microbiota targeted therapies in ICU

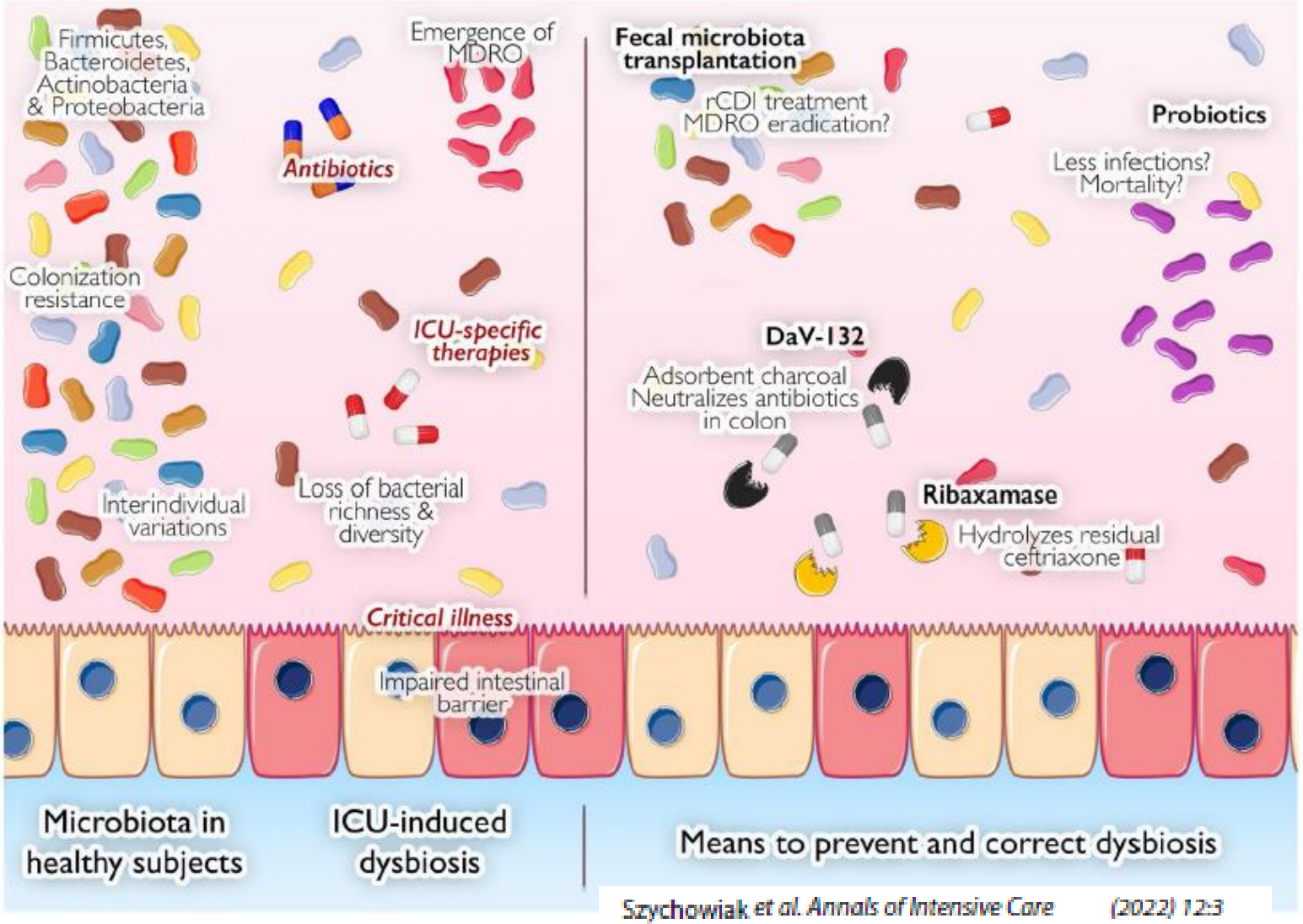


Haak B.W curr Opin crit Care 2017, 23: 167-174

The role of the microbiota in the management of intensive care patients

Piotr Szychowiak[1,2], Khanh Villageois-Tran[1,3], Juliette Patrier[1,4], Jean-François Timsit[1,4] and Étienne Ruppé[1,5*]



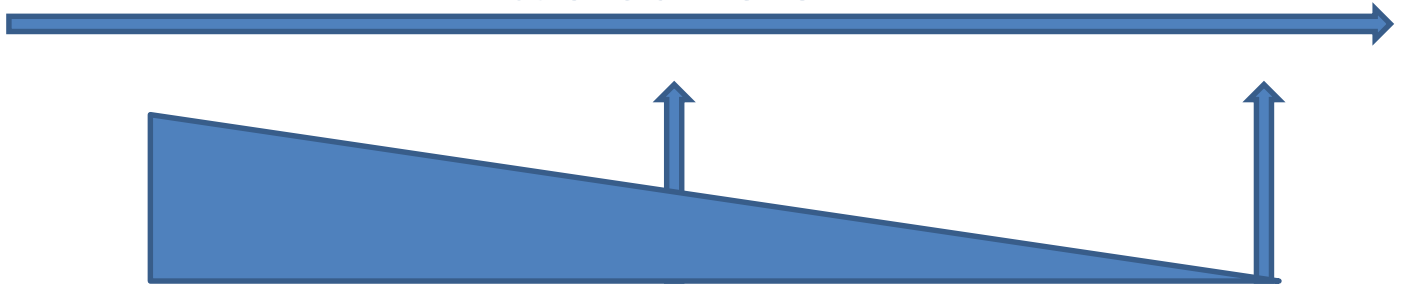


Szychowiak et al. Annals of Intensive Care (2022) 12:3

Le Microbiote, comment l'inclure dans nos pratiques

- Évolution du microbiote: causes ou conséquences
- Indicateur de suivi: gravité , pronostic en fonction de son évolution
- **Symbiose ⟶ Dysbiose ⟶ Restauration**

Actions à mener



Avant sa modification

Restoration mineure

Restoration majeure

Microbiota-targeted therapies in inflammation resolution

Bon usage des Antibiotiques

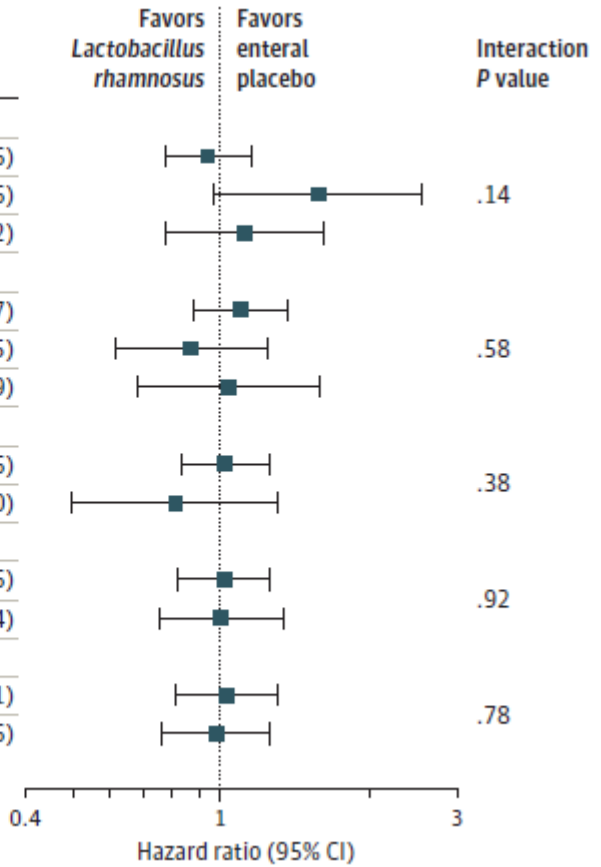
- Tests diagnostics
  - Meilleure sensibilité
  - Plus rapide
- Spectre étroit autant que possible
- Moindre impact sur le tube digestif
- Désescalade
- Durée de traitement

List of microbiota-modulating tools in animal models and patients affected by infective diseases.

Type of infection	Microbiota modulation tool	Studies in animal models	Studies in patients
Clostridium difficile	Antibiotics	Vancomycin; Fidaxomycin [27]	Vancomycin; Fidaxomycin [27] (28, 29, reviewed in 30)
	FMT	–	Fatal adverse events in two cases (*Escherichia coli* contaminated FMT [32]
	Microbiota-based products	–	RBX2660 (31, PUNCHCD3, NCT03244644) Oral capsule: CP101 (NCT03110133) RBX7455 (NCT02981316) SER-109 (33, 34, NCT03183128) Multi-strain probiotics consortium [35] SER-262 (NCT02830542) VE303 (NCT03788434)
Mycobacterium tuberculosis	Combinatory therapies with probiotics	–	Antibiotics or vitamins plus probiotics (*Bifidobacterium* spp. and *Lactobacillus* spp,) [44,45]
	Next-generation probiotics	–	*Bifidobacterium adolescentis* resistant to anti-TB drugs [46]
	FMT	[47]	–
	Postbiotics	Indolepropionic acid [38,39] Bacteria-derived AMPs [42,43]	–
Sars-Cov2	FMT	–	Pre-COVID19 as preventive setting [50, 51] Post-COVID19 as therapeutic for the cytokine storm (NCT04824222)

Effect of Probiotics on Incident Ventilator-Associated Pneumonia in Critically Ill Patients

Subgroup	No./total patients: *Lactobacillus rhamnosus*	No./total patients: Enteral placebo	Hazard ratio (95% CI)	Interaction *P* value
Admission type				
Medical	184/1006	199/1021	0.94 (0.77-1.16)	
Surgical	44/141	29/129	1.58 (0.97-2.56)	.14
Trauma	61/171	56/182	1.12 (0.77-1.62)	
Age, y				
<65	173/752	168/767	1.10 (0.88-1.37)	
65-75	69/335	66/319	0.87 (0.61-1.25)	.58
>75	47/231	50/246	1.04 (0.68-1.59)	
Clinical frailty score				
≤4	188/844	191/866	1.02 (0.83-1.26)	.38
≥5	37/240	40/232	0.81 (0.50-1.30)	
Received antibiotics on day of randomization and 2 preceding days				
No	193/766	181/739	1.02 (0.82-1.26)	.92
Yes	96/552	103/593	1.00 (0.75-1.34)	
Prevalent pneumonia as primary diagnosis or comorbid infection				
No	168/542	151/532	1.03 (0.81-1.31)	.78
Yes	121/776	133/800	0.98 (0.76-1.26)	



J Johnstone

JAMA September 21, 2021 Volume 326, Number 11

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 31, 2013 VOL. 368 NO. 5

Duodenal Infusion of Donor Feces for Recurrent *Clostridium difficile*

Els van Nood N Engl J Med 2013;368:407-15.
DOI: 10.1056/NEJMoa1205037

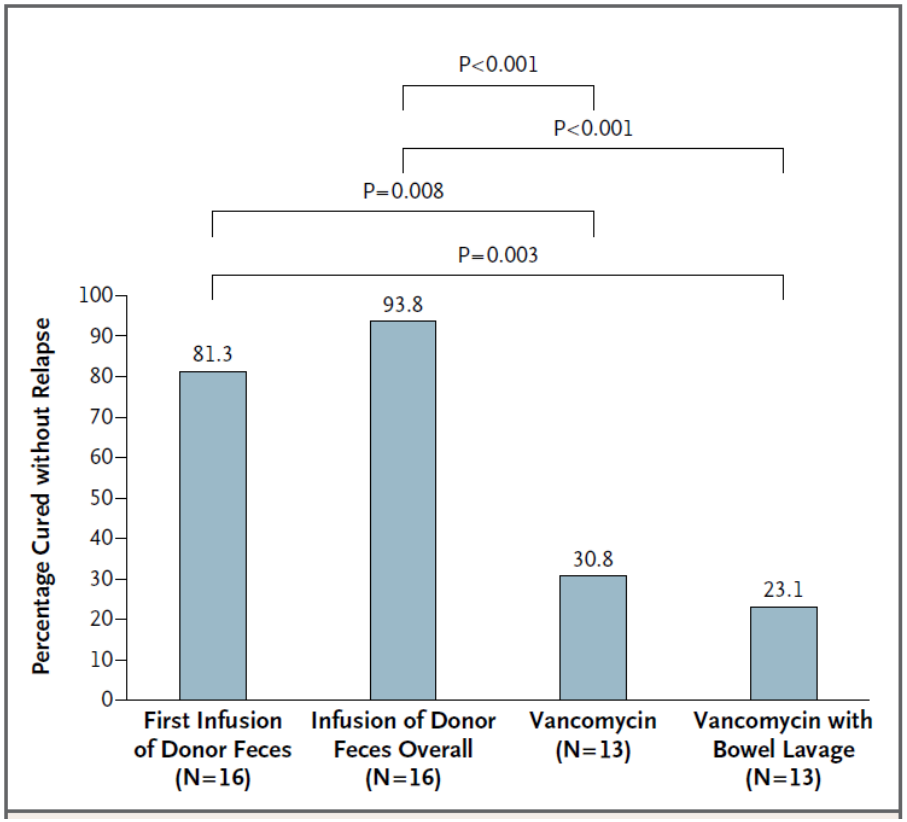


Table 2. Adverse Events in 16 Patients in the Infusion Group.*

Adverse Event	On Day of Infusion of Donor Feces	During Follow-up
	no. of events	
Belching	3	0
Nausea	1	0
Vomiting	0	0
Abdominal cramps	5	0
Diarrhea	15	0
Constipation	0	3
Abdominal pain	2 (associated with cramping)	0
Infection	0	2†
Hospital admission	NA	1‡
Death	0	0
Other adverse event	1§	1‡

Microbiota-targeted therapies in inflammation resolution

List of microbiota-modulating tools in animal models and patients in immune-compromised conditions.

Immune compromised condition	Microbiota modulation tool	Studies in animal models	Studies in patients
Cancer therapies-associated Mucositis and Colitis	Probiotics	[63]	(Reviewed in 64)
	FMT	[65,66,67,68,69, 70], *Bifidobacterium* spp. and *Enterococcus gallinarum* [69,72]	(71, NCT03772899; NCT03637803)
HSCT and GvHD	Probiotics	*L. rhamnosus* GG [79]	*L. rhamnosus* GG [80] was inefficient
	Prebiotics	–	(NCT027630331, NCT02805075, 81)
	FMT	–	(83–86, NCT02269150; NCT03359980; NCT03492502; NCT03549676; NCT03720392)
HIV and AIDS	Probiotics	–	[100,101,102]
	FMT	In SIV infected primates [103]	(104, 105, NCT03008941)

List of microbiota-modulating tools in animal models and patients having dysbiosis-induced inflammation in CNS disorders.

CNS disorders	Microbiota modulation tool	Studies in animal models	Studies in patients
Multiple Sclerosis	Probiotics	PSA+ *B. fragilis* or *Bifidobacterium* [122]	Multi-strain probiotics consortium [124]
	FMT	[120,123]	(125, NCT04150549; NCT03975413 and NCT03183869)
Parkinson's disease	Probiotics	*Bifidobacterium* spp., *Lactobacillus* spp. and *Lactococcus* spp. [133]	Planned clinical trials with; MRx0005 (*Parabacteroides distasonis*) and MRx0029 (*Megasphaera massiliensis*)
Alzheimer's Disease	Antibiotics	[140]	–
	Probiotics	Human isolates of *Bifidobacterium longum* [142]	*Lactobacillus* and *Bifidobacterium* multistrain probiotic [143,144]
	FMT	Transplant from diseased mice into GM one [139]	–

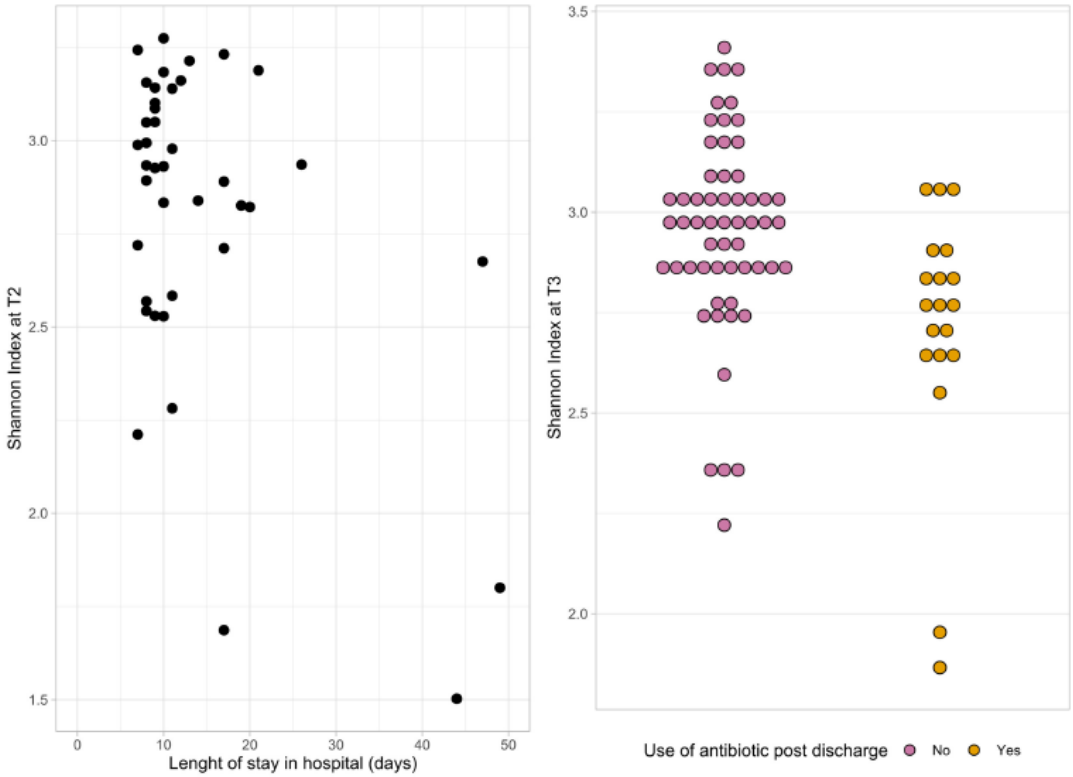
Strati F Seminars in Immunology 59 (2022) 101599

Microbiota-targeted therapies in inflammation resolution

List of microbiota-modulating tools in animal models and patients suffering from cardiovascular diseases.

Cardiovascular disease	Microbiota modulation tool	Studies in animal models	Studies in patients
Atherosclerosis and coronary artery disease	Probiotics	*L. fermentum* MTCC:5898 [162] *S. thermophilis*, *L. acidophilus* LA-5 and *B. bifidum* BG-12 [163] *L. plantarum* DR7 or *L. plantarum* PH40 [165]	*Lactobacillus* and *Bifidobacterium* (NCT05095350)
	FMT	[151,166,167]	https://www.trialregister.nl/trial/4188, NTR4338 [168] (NCT04406129)
Chronic and acute heart failure	Diet	Choline-rich, TMAO-containing diet [174]	–
	Probiotic	–	*L. rhamnosus* GG [175] *L. acidophilus* (NCT03968549)
	FMT	[177]	–

Marked Changes in Gut Microbiota in Cardio-Surgical Intensive Care Patients: A Longitudinal Cohort Study



Aardema Frontiers in cellular and infection Microbiology , vol 9 , Jan 2020

The role of the microbiota in the management of intensive care patients

Piotr Szychowiak[1,2], Khanh Villageois-Tran[1,3], Juliette Patrier[1,4], Jean-François Timsit[1,4] and Étienne Ruppé[1,5*]

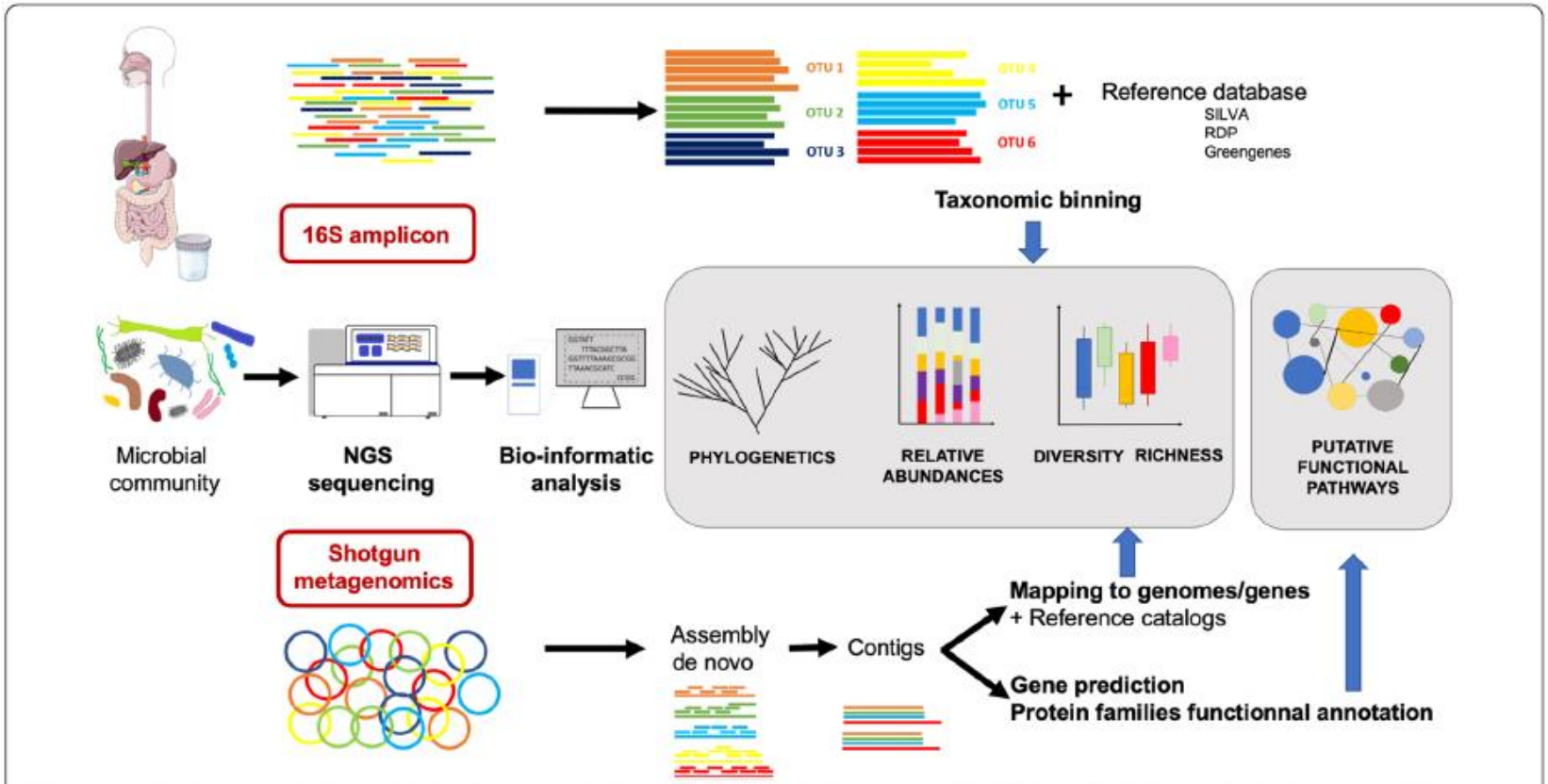
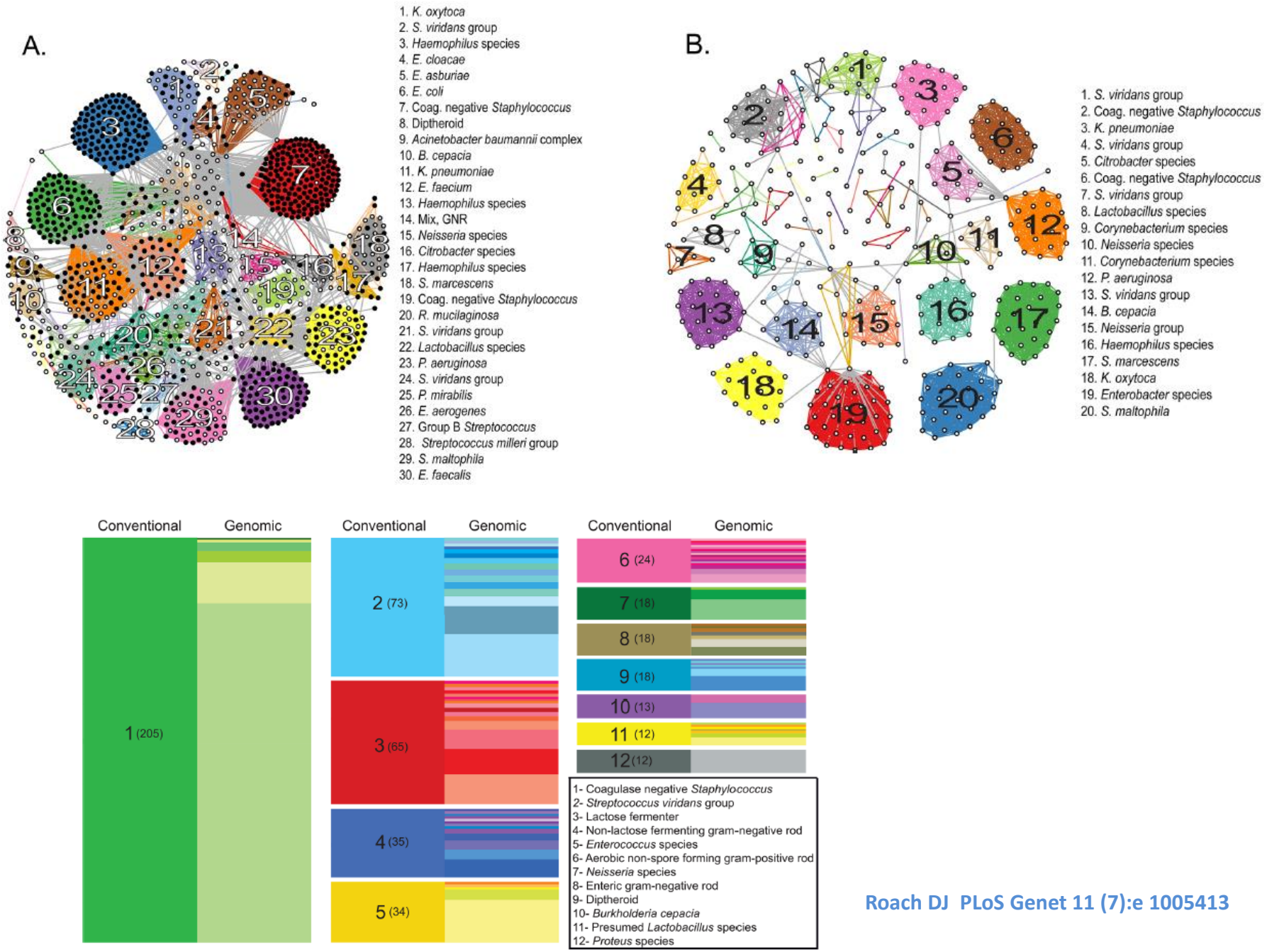
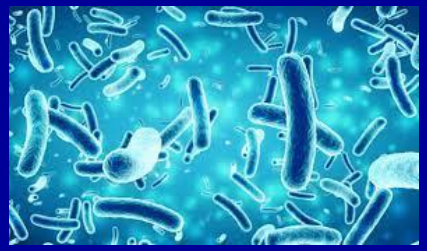


Fig. 2 Schematic representation of classically used next-generation sequencing methods. 16S rRNA coding gene amplification and shotgun metagenomics are well-used techniques for microbiota studies. OTU: operational taxonomic unit (an OTU being assumed to be a bacterial genus). NGS: next-generation sequencing



Roach DJ PLoS Genet 11 (7):e 1005413

Conclusion



On ne voit bien qu'avec le cœur. L'essentiel est invisible pour les yeux