One Health in Focus
Advancing Solutions To Antimicrobial Resistance ("AS2AMR") & 2nd Bacteriocin International Conference (3BIC")
Brussels, 25-28 May 2025

Decolonization strategies against multidrug resistant organisms in the ICU

Stijn BLOT

Internal Medicine & Pediatrics
Faculty of Medicine & Health Science
Ghent University, Ghent, Flanders (Belgium)

~

UQ Centre for Clinical Research, Faculty of Medicine
The University of Queensland, Brisbane, Queensland (Australia)

Introduction

- Multidrug Resistance = global concern
- ICU = epicenter
- Determinants of the epidemiology of MDR

Import of MDR strains (colonized HCWs, LTCF residents, …)

Development of MDR strains (mutation, genetic transfer)

Selection of MDR strains (pre-existing MDR flora)

Dissemination of MDR strains (failure of infection control)

- Regional variation +++

Bonten & Maccini. Intensive Care Med 2003
Blot S, Ruppe E, Harbarth S, et al. Intensive Crit Care Nurs 2022

Objective

- Practical recommendations
  - Screening
  - Decolonization strategies
    - Nasal
    - Oropharyngeal
    - Skin

Screening

- Screening purpose
  - Identify MDRO colonization at an early stage
  - Monitor trends (e.g., outbreaks)
  - Enhance contact precautions (isolation, cohorting, elimination of reservoirs)
- ICU
  - Heterogenous case-mix → variation in risk profile
- Screening approach
  - Universally (all patients)
  - Targeted ~risk profile: Recent hospitalization, AB exposure, nursing home resident, …, prediction scores (?)

Screening

- Detection techniques
  - Surveillance cultures
  - PCR: Faster (turn around time approx. 2 hrs.) but expensive (3-4 fold)
- Positive test results
  - Immediate communication to staf
  - Track patient's whereabouts & contacts
- (!) MDRO colonization = dynamic process
  - Detection, spontaneous clearance, and infection
- Suggested approach
  - Screening on admission
  - Thereafter: once (or twice) weekly

Nasal decolonization

- Focus: *S. aureus*
  - Risk factor for post-operative surgical site infection & bloodstream infection

- Pre-operative decolonization of MSSA or MRSA
  - Nasal mupirocin (bid, 5 days)

Nasal decolonization

- Focus: *S. aureus*
  - Risk factor for post-operative surgical site infection & bloodstream infection
- Pre-operative decolonization of MSSA or MRSA
  - Nasal mupirocin (bid, 5 days)
- Problem: literature blurred
  - Applying targeted (screen positive) or universal decolonization (all patients)
  - Or combined with other strategies (e.g., CHG bathing)

Povoa P, Ramirez P, Blot S. Intensive Care Med 2024

Nasal decolonization

- **Health technology assessment**
  - ➢ Targeted or Universal nasal mupirocin ➜ little-to-no effect
  - ➢ (!) Nasal mupirocin + CHG bathing
    - ➜ likely to reduce SSI risk (MSSA & MRSA)
    - ➜ Cardio-thoracic, vascular, orthopedic, gastrointestinal, general surgery

Anonymous. Ont Health Technol Assess Ser 2022

Nasal decolonization

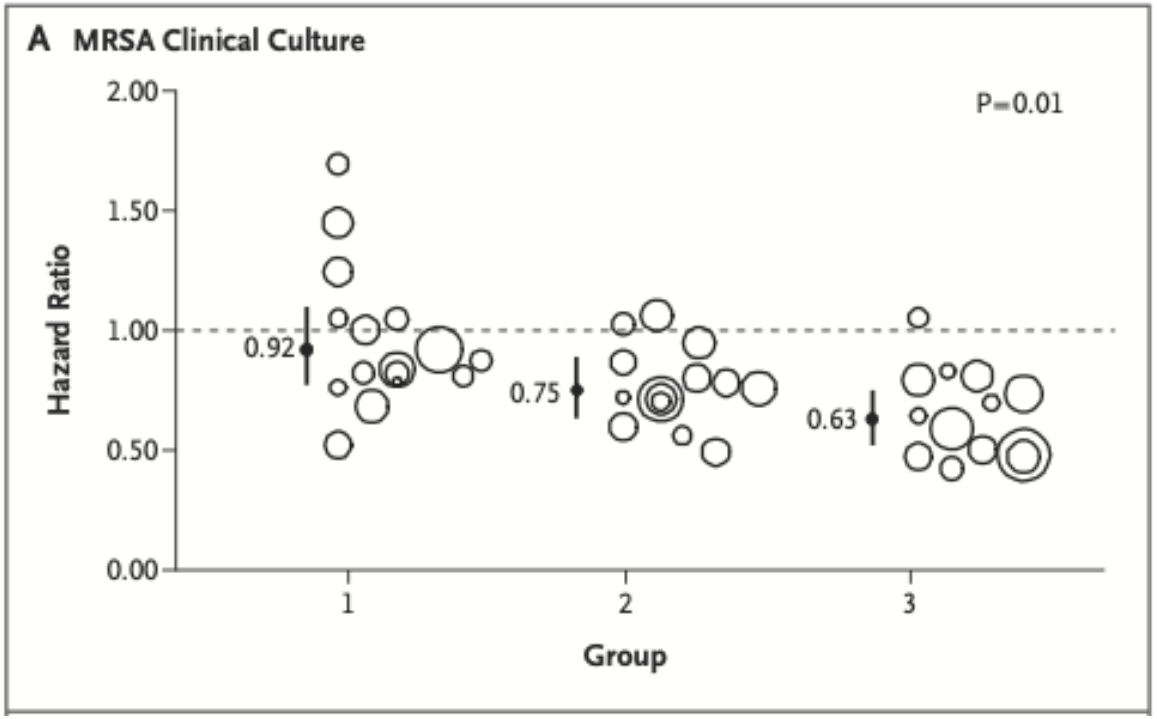
- **Cluster-randomized trial**
  - Assigned hospitals (n=43) → three strategies
    - Targeted-1: screening & isolation (no decolonization)
    - Targeted-2: screening, isolation, nasal decolonization, CHG bathing
    - Universal (all patients): nasal decontamination & CHG bathing

Huang SS et al. N Engl J Med 2013

Nasal decolonization

MRSA clinical isolates

Results intervention compared with baseline period

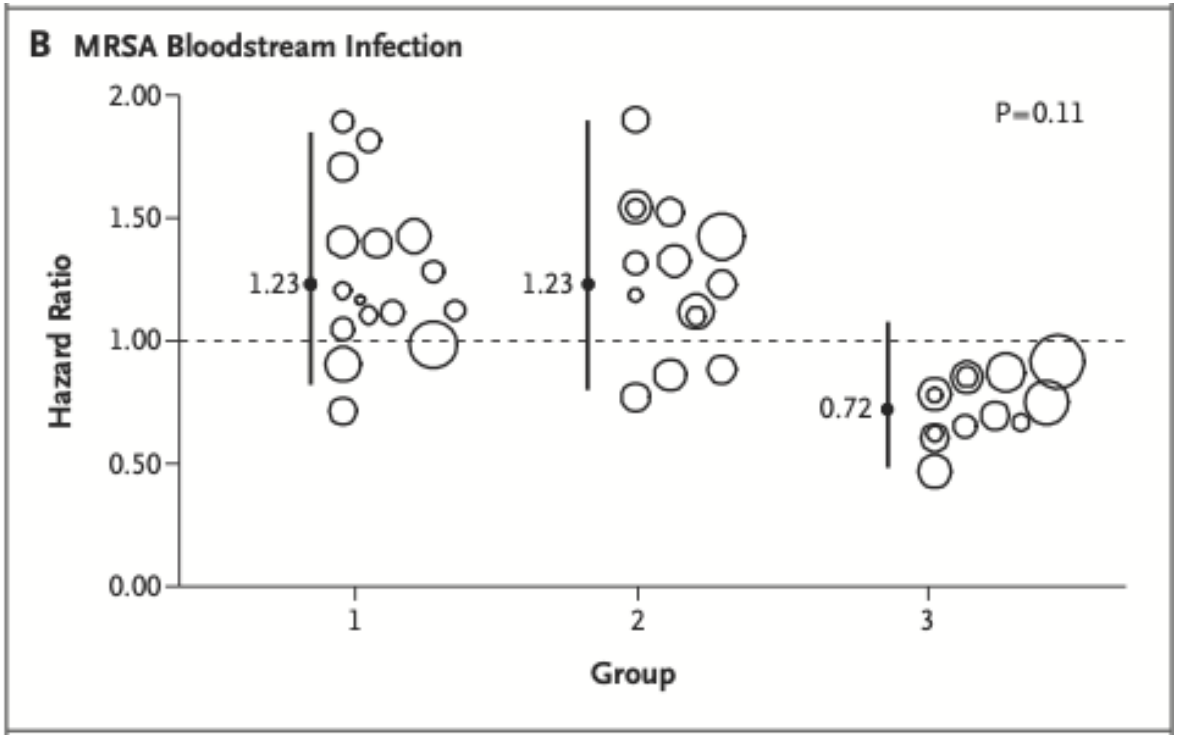


Huang SS et al. N Engl J Med 2013

Nasal decolonization

MRSA Bloodstream infection

Results intervention compared with baseline period

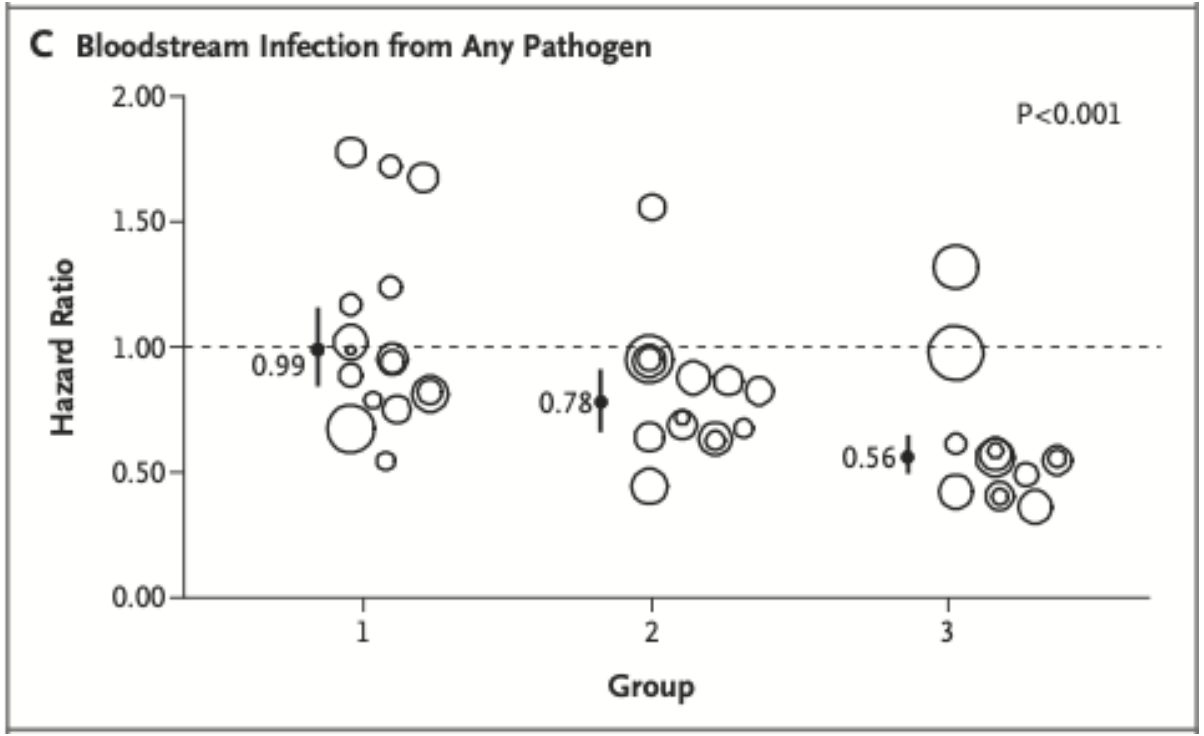


Huang SS et al. N Engl J Med 2013

Nasal decolonization

Results intervention compared with baseline perio

Bloodstream Infection Any pathogen



Huang SS et al. N Engl J Med 2013

Nasal decolonization

(!) Mupirocin resistance

- Prefer targeted over universal approach
- Without CHG bathing: little-to-no effect
- Alternative: povidone-iodine nasal decontamination

  → inferior in preventing *S. aureus* & MRSA clinical cultures

Huang SS et al. N Engl J Med 2013
Huang SS et al. JAMA 2023

Skin decolonization

- **Agent: CHG 2%** (liquid bathing or impregnated washcloths)
- **Broad antimicrobial action & residual effect**
- **Potential to prevent**
  - HAIs (> CLABSI)
  - Eliminate MDRO colonization

Skin decolonization & HABSI risk

- **Systematic review & meta-analysis**
  - **Pooling results of 4 randomized crossover trials**
  - **Including 25 ICUs, n=22,850**
  - **Results:**
    - Total HABSI risk: OR 0.74 (95% CI, 0.60 – 0.90)
    - CLABSI risk: OR 0.50 (95% CI, 0.35 – 0.71)
    - Non-CLABSI HABSI OR 0.82 (95% CI, 0.70 – 0.97)

Afonso E et al. Eurosurveillance 2016

Skin decolonization & HABSI risk

- **Systematic review & meta-analysis**
  - **Sensitivity analyses:**
    - Gram-positive HABSI risk:

      OR 0.55 (95% CI, 0.31 – 0.99)
    - Gram-negative HABSI risk:

      OR 0.83 (95% CI, 0.59 – 1.17)

Afonso E et al. Eurosurveillance 2016

Skin decolonization & HABSI risk

- **Cluster RCT** (72 ICUs, n=76,815)
- Intervention: antiseptic bathing with CHG or octenidine
- Control: routine care
- **Results**:
  - CHG bathing: Adjusted iRR 0.69 (95% CI, 0.37 – 1.22)
  - Octenidine: Adjusted iRR 1.22 (95% CI, 0.54 – 2.75)

Denkel LA et al. Clin Microbiol Infect 2022

Skin decolonization & HABSI risk

- **Cluster RCT** (72 ICUs, n=76,815) **Post hoc analysis**
- CHG or Octenidine bathing vs. Baseline period
- **Results**:
  - Octenidine: Adjusted iRR 0.98 (95% CI, 0.60 – 1.58)
  - CHG bathing: Adjusted iRR 0.63 (95% CI, 0.46 – 0.87)

    (!) Reduction limited to Gram-positive CLABSI

Denkel LA et al. Antimicrob Resist Infect Control 2023

Skin decolonization & MDRO risk

- **Systematic review**
  - 16 ICU studies (9 excluded)
  - Remaining studies: important differences
- **Results**:
  - MRSA acquisition reduced in 3 studies (primary endpoint)
  - MRSA infection reduced in only 1 on 5 studies
  - VRE carriage & BSI reduced in 1 study (primary endpoint)
  - Hardly any evidence for reduction in Gram-negative MDRO

Derde L et al. Intensive Care Med 2012

Skin decolonization: concerns

- **Universal CHG bathing → excessive CHG exposure**
- **Concerns:**
  - Hypersensitivy
  - CHG-resistance
- **Recommendation: selective use**
  - Outbreaks
  - Problematic high CLABSI rates despite high standard of care

Oropharyngeal decolonization: SOD

- **Selective Oral Decontamination (SOD)**
  - **What?** Colistin, tobramycin & nystatin ➜ target Gram-negatives
  - **Multicenter RCT** in patients ventilated >48 hrs.
  - **Objective**: reduction in ICU-acq. Gram-negative bacteremia
  - **Results**:
    - Absolute risk reduction: 0.6% (95% CI, -0.2% to 1.4%)
    - Adjusted HR: 0.89 (95% CI, 0.55 – 1.45)

Wittekamp BH et al. JAMA 2018

Oropharyngeal decolonization: CHG

- **CHG oral care**
  - Systematic review & meta-analysis
  - **Pneumonia risk** (16 RCTs)…
    - Cardiac surgery: RR 0.56 (95% CI, 0.41 – 0.77)
    - Non-cardiac surgery: RR 0.88 (95% CI, 0.66 – 1.16)
  - **Mortality risk** (12 RCTs)…
    - All ICU patients RR 1.13 (95% CI, **0.99** – 1.28)

Klompas M et al. JAMA Intern Med 2014

Oropharyngeal decolonization: CHG

- **CHG oral care**
  - Network meta-analysis of 29 studies (11 CHG)
  - Intervention: SDD, SOD, CHG oral care
  - ICU patients (n=3630), with excl. of specialized populations such as cardiac surgery or LTx
  - Outcomes: **Mortality associated with CHG oral care**
    - ➢ **OR 1.25 (1.05 – 1.55)**

Price R et al. BMJ 2014

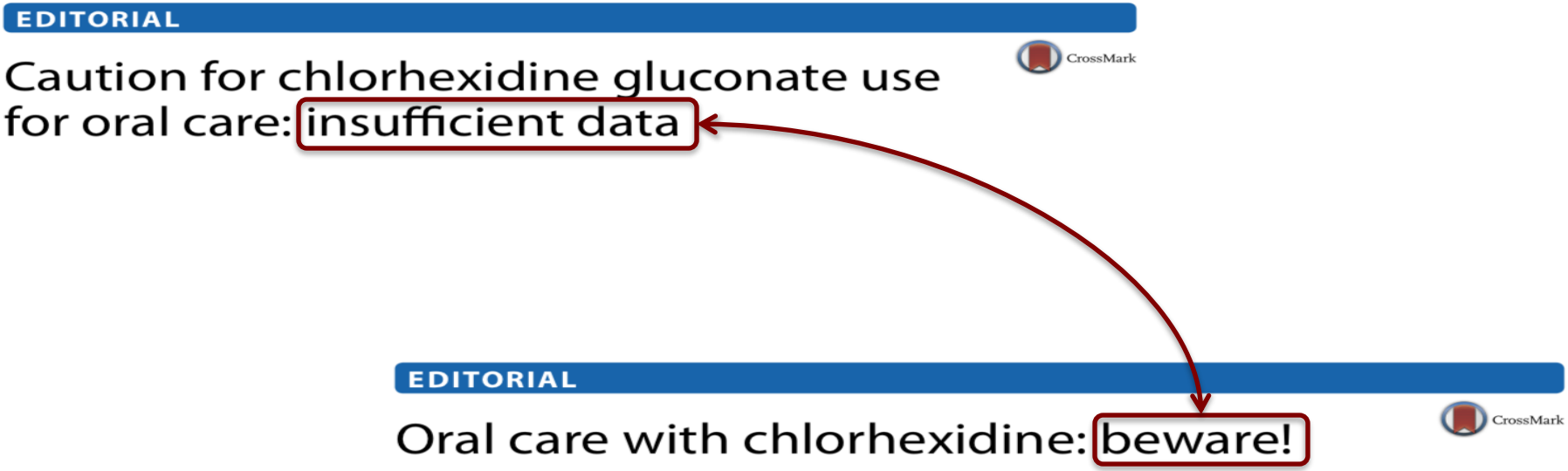
Oropharyngeal decolonization: CHG

- **CHG oral care**
  - Accumulation of evidence
  - CHG oral care ➜ associated with increased mortality risk
  - Large cohort studies (ICU & hospital-wide)
  - Lack of pathogenic mechanism ➜ Controversy!

Klompas M et al. JAMA Internal Med 2016
Deschepper M et al. Intensive Care Med 2018
Parreco J et al. Surg Infect 2020

Controversial viewpoints

Should CHG oral care be abandoned?



Klompas & Bouadma. Intensive care Med 2018
Ricard & Lisboa. Intensive Care Med 2018

Pathogenic mechanism linking CHG oral care with mortality

Hypothesis

- Antiseptic mouthwash
  → disturbance of NO homeostasis
  (i.e., decreased NO bio-availability)

Blot S. Intensive Care Med 2021

The role of NO in human physiology

Key messenger molecule in multiple physiological processes:

- Flow-mediated vasodilatation
- Decreased arterial blood pressure
- Platelet aggregation inhibition
- Antibacterial properties
- Increased circulation angiogenic cells
- Skeletal muscles: reduced oxygen cost
- Increased mucosal blood flow
- Increased mucosal thickness
- Increased cerebral blood flow
- …

In case of NO deficit, risk of…

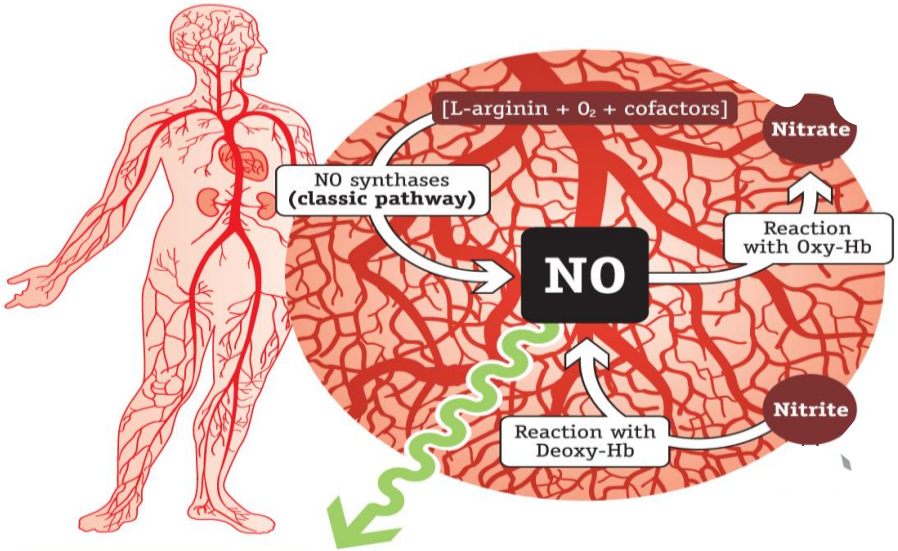
Flow-mediated vasodilatation + Decreased arterial blood pressure → Increased art. blood pressure… ischemic heart events

Platelet aggregation inhibition → Thrombotic events

Antibacterial properties → Septic events

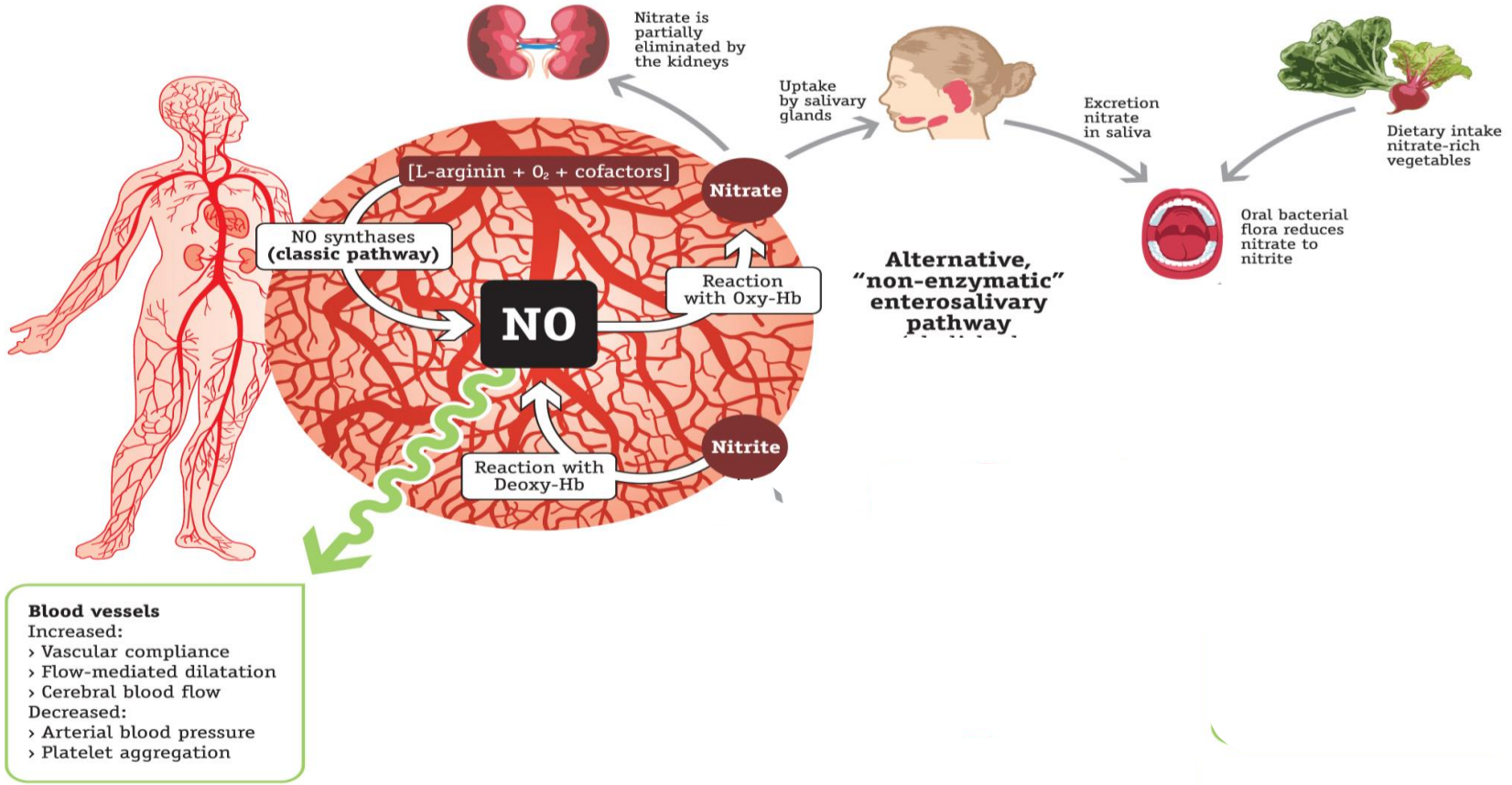
Generation of nitric oxide (NO)

Introduction to the nitrate-nitrite-NO pathway…

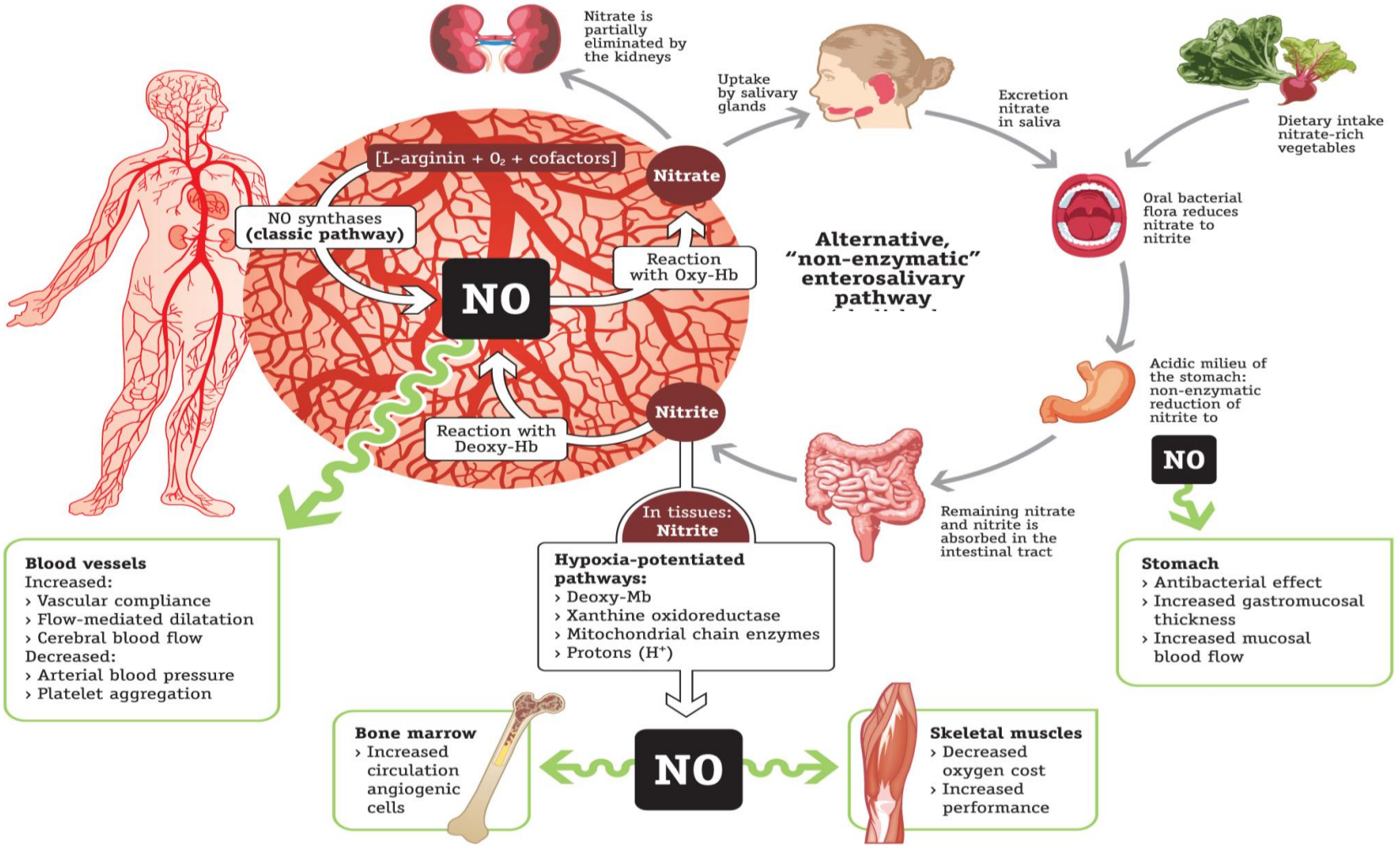


Blood vessels
Increased:
› Vascular compliance
› Flow-mediated dilatation
› Cerebral blood flow
Decreased:
› Arterial blood pressure
› Platelet aggregation

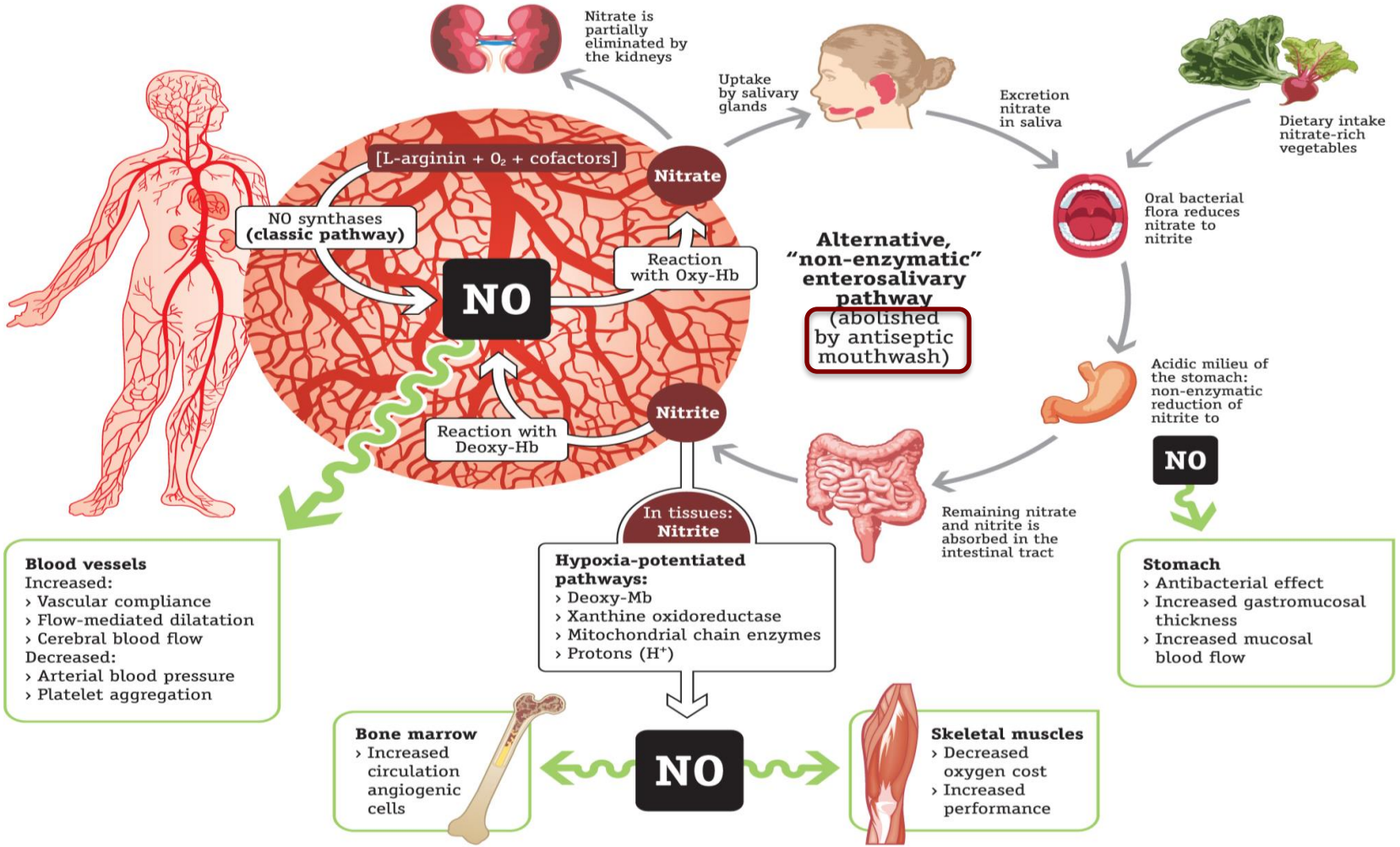
Blot S. Intensive Care Med 2021



Blot S. Intensive Care Med 2021



Blot S. Intensive Care Med 2021



Blot S. Intensive Care Med 2021

Oropharyngeal decolonization

- **CHG oral care and pneumonia prevention:** only evidence in cardiac surgery setting
- **CHG oral care and mortality:** Accumulating evidence of the association supported by meta-analysis of RCTs and large cohort studies
- **Presumed pathogenic mechanism:** disturbance of NO homeostasis resulting suboptimal bio-availability of NO

- **(!) Harmful effect = not CHG-specific**

- **(!) SHEA / IDSA / APIC practice recommendation:**
  - **advise against CHG oral care**
  - **Toothbrushing twice daily**

Conclusion: recommendations

- **Screening**
  - Universal
  - Nasal & rectal swabs on admission and ≥1 weekly

- **Nasal decolonization**
  - Nasal mupirocine: effect on SSI unlikely
  - Combined with CHG bathing: likely to reduce SSI risk
  - (!) Resistance concerns ➜ usage ∽ local conditions

- **Skin: CHG washcloths**
  - Reduce HABSI / CLABSI risk (> Gram-positives)
  - (!) Hypersensitivity & resistance ➜ selective use (e.g., outbreaks)

- **Oral decolonization**
  - No selective oral decontamination
  - No CHG mouthwashes

Thank you

Dept. of Internal Medicine and Pediatrics, Faculty of Medicine & Health Science, Ghent University
UQ Centre for Clinical Research, Faculty of Medicine, The University of Queensland, Brisbane, Australia
stijn.blot@UGent.be

Het is niet nodig te hopen om te ondernemen, noch te gelukken om te volharden