HELSE STAVANGER
Stavanger universitetssjukehus

Fem studier fra siste år

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1. Attributable mortality of infections caused by carbapenem-resistant Enterobacterales: results from a prospective, multinational case-control-control matched cohorts study (EURECA)

- Paniagua-García M, Bravo-Ferrer JM, Pérez-Galera S, Kostyanev T, de Kraker MEA, Feifel J, Palacios-Baena ZR, Schotsman J, Cantón R, Daikos GL, Carevic B, Dragovac G, Tan LK, Raka L, Hristea A, Viale P, Akova M, Cano Á, Reguera JM, Bartoloni A, Florescu SA, Benea S, Bukarica L, Asensio Á, Korten V, Grundmann H, Goossens H, Bonten MJ, Gutiérrez-Gutiérrez B, Rodríguez-Baño J; COMBACTE-CARE-EURECA team. Attributable mortality of infections caused by carbapenem-resistant Enterobacterales: results from a prospective, multinational case-control-control matched cohorts study (EURECA).
- Clin Microbiol Infect. 2024 Feb;30(2):223-230. doi: 10.1016/j.cmi.2023.11.008. PMID: 38267096.
- https://doi.org/10.1016/j.cmi.2023.11.008

PICOT

Population	50 sykehus i Europa 235 pasienter med CRE-infeksjon, 235 med CSE-infeksjon,	
Intervention	Case –control observasjonsstudie, ingen intervensjoner. Pasientene har UVI; Pneumoni, intraabdominal infeksjon eller blodbaneinfeksjon med påvist mikrobe.	
Control	705 uten infeksjon, matchede kontroller basert på samtidig opphold i samme sengepost.	
Outcome	Betydelig høyere mortalitet hos CRE-infeksjoner. 23,8 vs 10,6 vs 8,4%	
Time	2016-2018 – i tiden før tilgjengelige kombinasjonsmedikamenter	

Table 1
Baseline characteristics of patients with infections caused by carbapenem-resistant Enterobacterales, carbapenem-susceptible Enterobacterales, and non-infected patients. Data are no. of patients (percentage) except where specified

Characteristic	CRE group (n = 235)	CSE group (n = 235)	p[a]	Non-infected group (n = 705)	p[b]
Demographics[c]					
Median age (y) (IQR)	73 (62–82)	70 (59–79)	0.081	67 (53–77)	<0.001
Male sex	134 (57.4)	126 (53.6)	0.42	412 (58.4)	0.69
Chronic underlying conditions[c]					
Median Charlson index (IQR)	3 (2–4)	2 (1–4)	0.008	2 (0–3.5)	<0.001
Diabetes mellitus	70 (29.8)	66 (28.1)	0.66	170 (24.1)	0.083
Chronic pulmonary disease	44 (18.7)	36 (15.3)	0.31	109 (15.5)	0.22
Chronic heart failure (NYHA ≥2)	44 (18.7)	28 (11.9)	0.038	84 (11.9)	0.005
Dementia	37 (15.7)	22 (9.4)	0.025	34 (4.8)	<0.001
Chronic liver disease	15 (6.4)	14 (6.0)	0.83	64 (9.1)	0.63
Chronic renal failure (grades 3 or 4)	65 (27.7)	33 (14)	<0.001	88 (12.5)	<0.001
Solid organ cancer	64 (27.2)	57 (24.3)	0.41	143 (20.3)	0.014
Haematologic cancer	12 (5.1)	12 (5.1)	1.00	35 (5.0)	0.90
Bone marrow/stem cell transplantation	1 (0.4)	1 (0.4)	1.00	10 (1.4)	0.17
Neutropenia (<500 cells/μL)	13 (5.8)	8 (3.4)	0.23	27 (3.8)	0.13
Solid organ transplantation	16 (6.8)	13 (5.5)	0.53	28 (4)	0.028
HIV infection	1 (0.4)	2 (0.9)	0.57	14 (2)	0.14
Immunosuppressive drugs (last 3 months)	59 (25.1)	52 (22.1)	0.40	121 (17.2)	0.002
Invasive procedures[c]					
Central venous catheter (last week)	78 (33.2)	60 (25.5)	0.020	152 (21.6)	<0.001
Urinary catheter (last week)	153 (65.1)	120 (51.1)	0.001	216 (30.6)	<0.001
Mechanical ventilation (last week)	42 (17.9)	45 (19.1)	0.58	96 (13.6)	0.013
Surgery (last month)	71 (30.2)	65 (27.7)	0.41	133 (18.9)	<0.001
Acute severity of disease/infection					
Median Pitt score at day 0 (IQR)	1 (0–3)	0 (0–2)	0.096	0 (0–1)	<0.001
Median SOFA score at day 0, median (IQR)	3 (1–5)	2 (1–4)	0.013	1 (0–3)	<0.001
SOFA ≥2 at day 0	162 (68.9)	143 (60.9)	0.066	313 (44.4)	<0.001
Severe sepsis or septic shock at day 0	40 (17.0)	27 (11.4)	0.086	NA	NA
Bacteraemia, any source	90 (38.3)	85 (36.2)	0.70	NA	NA
Etiology					
Klebsiella spp.	208 (88.5)	74 (31.4)	<0.001	NA	NA
Enterobacter spp.	11 (4.7)	17 (7.2)	0.23	NA	NA
Escherichia coli	7 (3.0)	113 (48.5)	<0.001	NA	NA
Proteus mirabilis	6 (2.6)	13 (5.5)	0.10	NA	NA
Serratia spp.	1 (0.4)	6 (2.6)	0.06	NA	NA
Citrobacter spp.	2 (0.9)	4 (1.7)	0.41	NA	NA
Morganella morganii	0	2 (0.9)	0.16	NA	NA
Other Enterobacterales	0	6 (2.6)	0.008	NA	NA

p values calculated by conditional logistic regression.
NA, not applicable.
[a] p value for CRE vs. CSE groups.
[b] p value for CRE vs. non-infected groups.
[c] Already published data (ref. 11), shown here for understanding of the analyses.

Diskusjon

- Antibiotikaresistens fører til?

- Mange forbehold
  - CRE-kohort er sykere, har mer komorbiditet og får ikke adekvat behandling
  - Når man justerer for disse faktorer blir hazard-ratio lavere og ikke sikkert signifikant økt.
  - Friske kontroller er nok vanskelig å matche i denne studien. Vanskelig å sammenlikne pasienter

- Uansett er konklusjonen valid:
  - CRE-infeksjoner er assosiert med betydelig tilskrivbar dødelighet. Underliggende pasientkarakteristika og forsinkelse i adekvat behandling og støttebehandling ser ut til å spille en viktig rolle i CRE-dødelighet.
  - Resultatene understreker viktigheten av å gi raske resistenssvar, tilgjengelighet av aktive legemidler mot CRE og av forebygging av CRE-infeksjoner.

- Støtter begrunnelsen om at resistente mikrober fører til økt sykelighet og dødelighet, men konkrete estimater på omfang er usikre. Disse infeksjonene rammer de sykeste pasientene.


359
Urent läger

2.

Investigating the effect of enhanced cleaning and disinfection of shared medical equipment on health-care-associated infections in Australia (CLEEN): a stepped-wedge, cluster randomised, controlled trial

- Browne K, White NM, Russo PL, Cheng AC, Stewardson AJ, Matterson G, Tehan PE, Graham K, Amin M, Northcote M, Kiernan M, King J, Brain D, Mitchell BG. Investigating the effect of enhanced cleaning and disinfection of shared medical equipment on health-care-associated infections in Australia (CLEEN): a stepped-wedge, cluster randomised, controlled trial.

- Lancet Infect Dis. 2024 Aug 13:S1473-3099(24)00399-2. doi: 10.1016/S1473-3099(24)00399-2. Epub ahead of print. PMID: 39151440.

- 10.1016/S1473-3099(24)00399-2

CLEEN –studie 2024

Population	Akutt sykehus i Australia, ca 500 senger. 10 sengeposter, voksne pasienter, Kluster randomisert, Trappetrinnsdesign.	
Intervention	Økt rengjøringsressurs i avdelinger. 3 timer/dag Dedikert til rengjøring av pasientnært utstyr, inkludert nattbord. Audit med feedback til rengjøring	
Control	Avdelinger fases inn suksessivt. PPS hver 2. uke jfr. ECDC-kriterier. HAI-vurdering blindet	
Outcome	Signifikant reduksjon i forekomst av HAI, både alle HAI, HAI utenom COVID OR 0,62 og 0,59	
Time	Gjennomført ila. 36 uker	

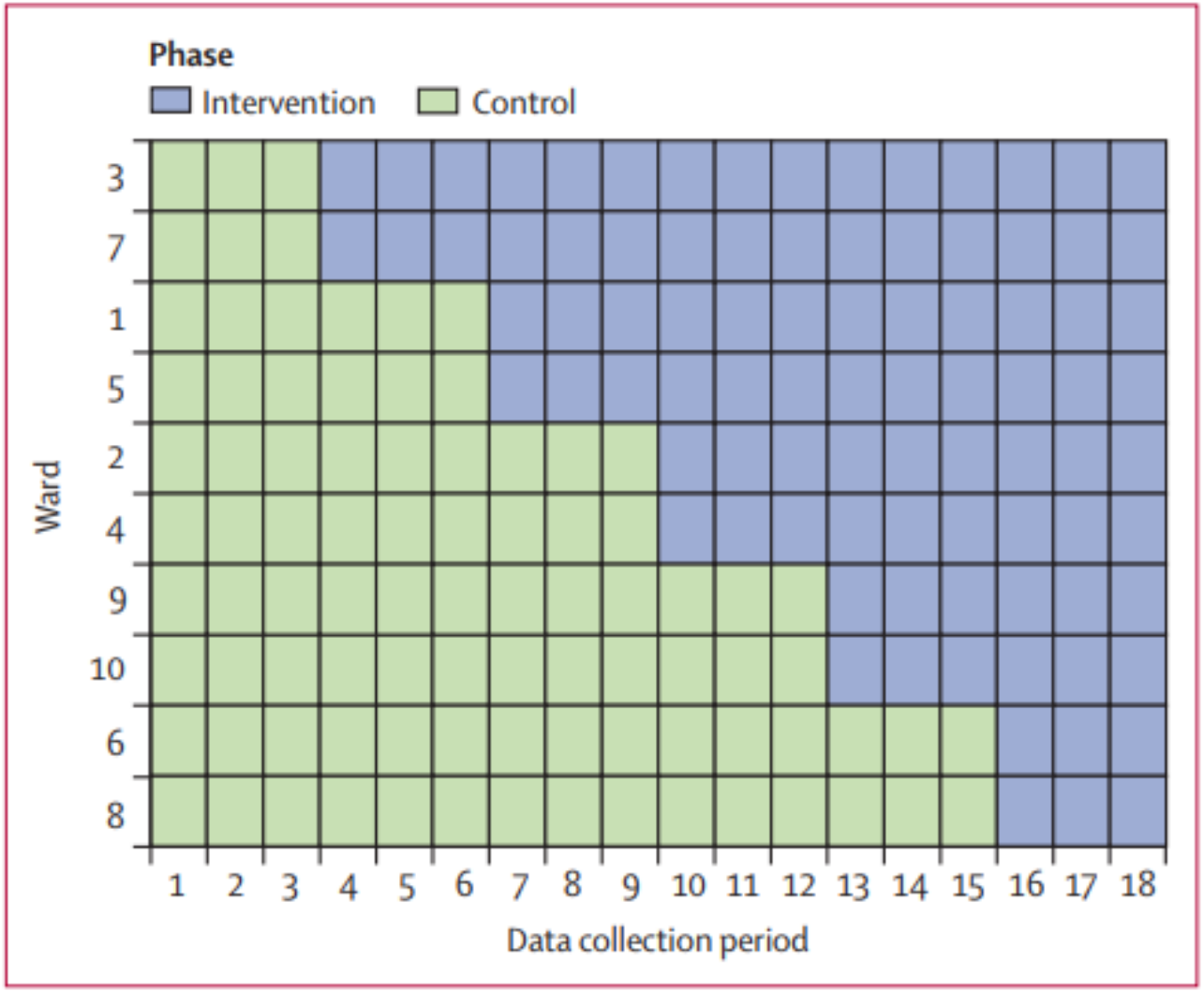
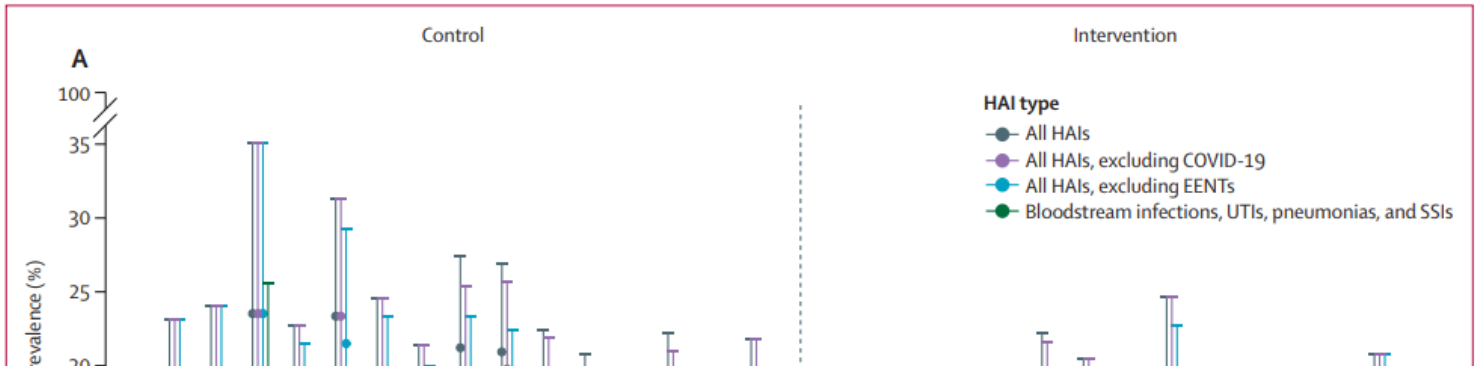


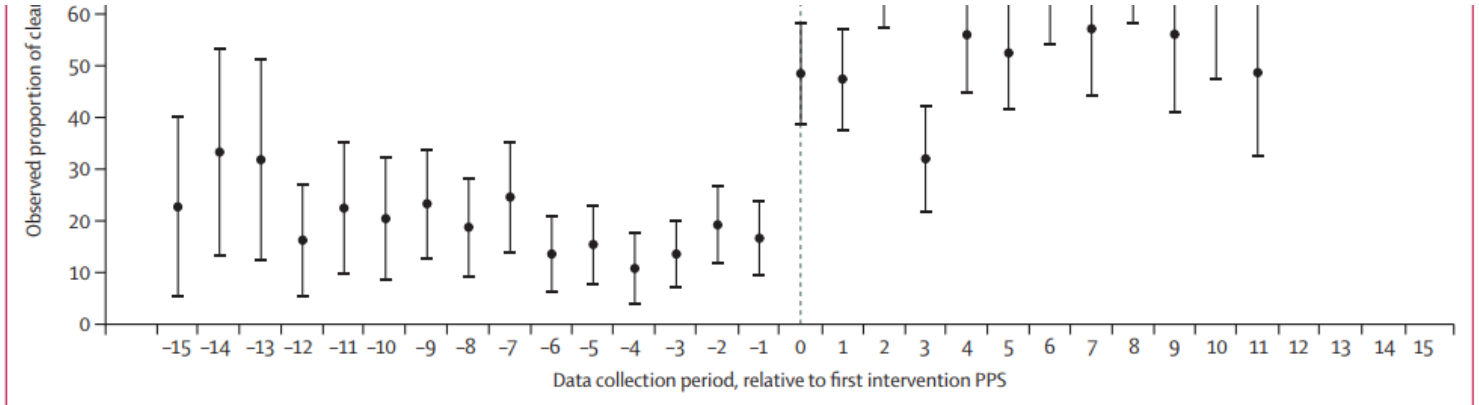
Figure 1: **Stepped-wedge trial design**
Each data collection period represents a 2-week period.



	HAI point prevalence in the control phase, % (95% CI)	HAI point prevalence in the intervention phase, % (95% CI)	Absolute difference, percentage points (95% CI)	Relative difference, percentage points (95% CI)	OR (95% CI)	p value for OR
All HAIs	14·9% (10·4 to 19·4)	9·8% (6·1 to 14·1)	−5·2 (−8·2 to −2·3)	−34·5 (−50·3 to −17·5)	0·62 (0·45 to 0·80)	0·0006
Bloodstream infections, pneumonias, UTIs, and SSIs	6·3% (3·3 to 9·6)	4·0% (1·9 to 6·8)	−2·3 (−4·3 to −0·7)	−36·2 (−56·1 to −12·8)	0·62 (0·42 to 0·86)	0·013
All HAIs, excluding COVID-19	14·4% (10·2 to 19·0)	9·0% (5·7 to 13·4)	−5·3 (−8·1 to −2·7)	−37·2 (−51·3 to −19·5)	0·59 (0·45 to 0·77)	0·0002
All HAIs, excluding EENTs	13·0% (8·6 to 17·4)	8·3% (4·9 to 12·0)	−4·8 (−7·6 to −2·1)	−36·7 (−51·7 to −17·4)	0·60 (0·45 to 0·81)	0·0008

Model-based bootstrap results, showing predicted outcomes by study phase and absolute and relative differences in prevalence (intervention – control), after accounting for clustering and secular time trends. EENT=ear, eye, nose, throat, and mouth infection. HAI=health-care-associated infection. OR=odds ratio. SSI=surgical site infection. UTI=urinary tract infection.

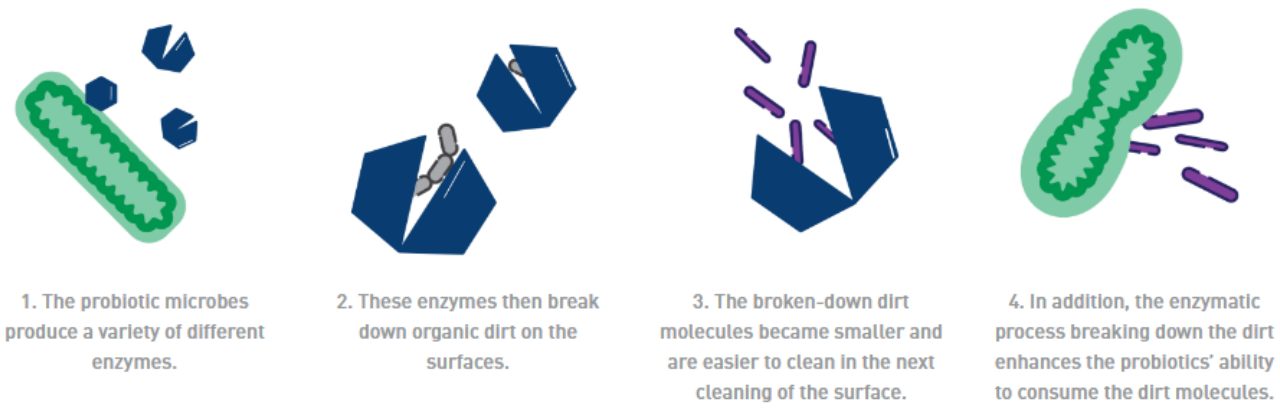
Table 3: **Estimated changes in HAI point prevalence attributable to the intervention**



Diskusjon

- Viktig studie som dokumenterer effekt av god rengjøring av pasientnært utstyr for å forebygge HAI.
- Rengjøring vs. Desinfeksjon – hva har størst betydning? Her benyttes en klut med både desinfeksjon og såpe samtidig. Tensider og QA
- Invitert flere sykehus, hvorfor bare ett deltakende sykehus?
- Høye HAI-forekomster sammenliknet med norske forhold, men kanskje reelt ved grundig gjennomgang slik det gjøres her?

- Kan probiotika erstatte desinfeksjonsmidler



[Probiotic cleaning - Kiilto]

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Lancet eClinical Medicine – mai 2023

Articles

Environmental cleaning to prevent hospital-acquired infections on non-intensive care units: a pragmatic, single-centre, cluster randomized controlled, crossover trial comparing soap-based, disinfection and probiotic cleaning

Rasmus Leistner,[a,b,] Britta Kohlmorgen,[a] Annika Brodzinski,[a] Frank Schwab,[a] Elke Lemke,[a] Gregor Zakonsky,[c] and Petra Gastmeier[a]*

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[b]Division of Gastroenterology, Infectious Diseases and Rheumatology, Medical Department, Charité–Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin and Berlin Institute of Health, Berlin, Germany
[c]Charité CFM Facility Management GmbH, Berlin, Germany

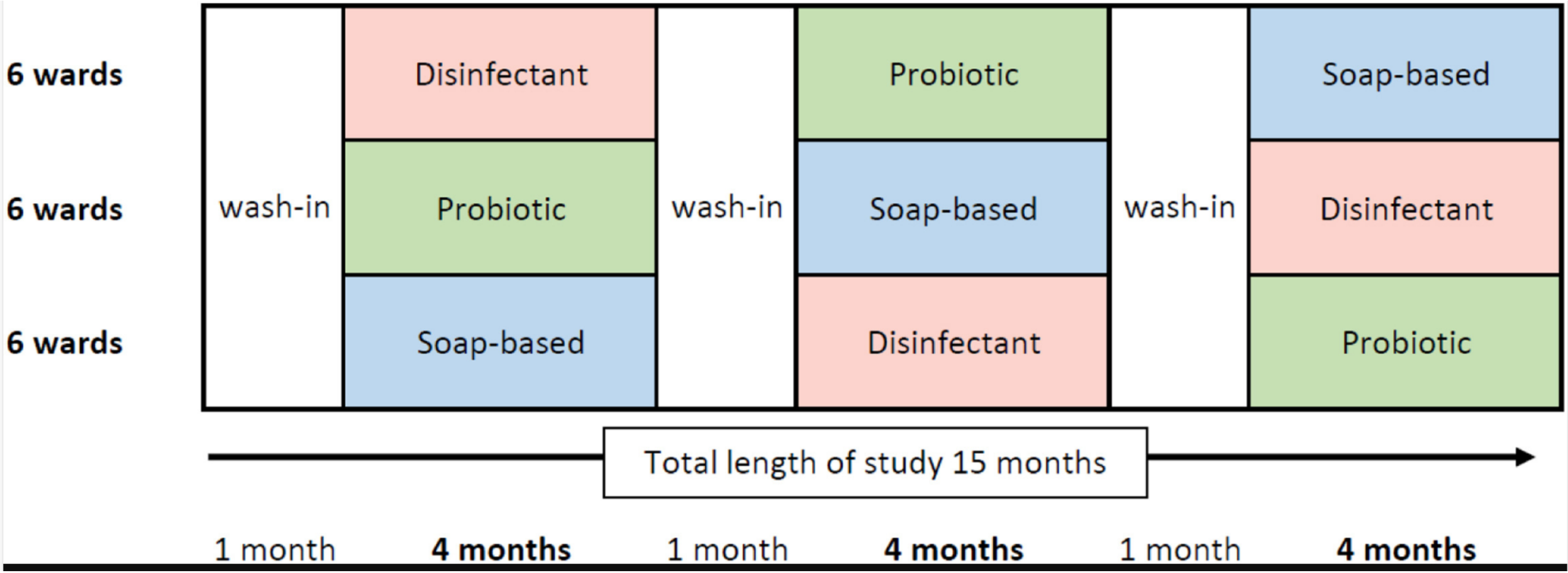
3. Environmental cleaning to prevent hospital-acquired infections on non-intensive care units: a pragmatic, single-centre, cluster randomized controlled, crossover trial comparing soap-based, disinfection and probiotic cleaning

- Leistner R, Kohlmorgen B, Brodzinski A, Schwab F, Lemke E, Zakonsky G, Gastmeier P. Environmental cleaning to prevent hospital-acquired infections on non-intensive care units: a pragmatic, single-centre, cluster randomized controlled, crossover trial comparing soap-based, disinfection and probiotic cleaning.

- EClinicalMedicine. 2023 Apr 6;59:101958. doi: 10.1016/j.eclinm.2023.101958. PMID: 37089619; PMCID: PMC10113752.

- 10.1016/j.eclinm.2023.101958

Population	18 sengeposter ved Charite – Berlin. (8 medisinske, 10 kirurgiske sengeposter)	
Intervention	Crossover trial – single center, Rengjøringsmiddel vs. Desinfeksjonsmiddel (Incidin – Kvartært immunium salt) vs. Probiotic 1% konsentrasjon av diverse bacillus species. Daglig renhold og «terminal cleaning»	
Control	Crossover trial Ved kjent smitte ble desinfeksjonsmidler benyttet	
Outcome	Primær: Incidens – forekomst av HAI – beregnet fra nasjonal prevalens (3,6%), 14.000 innleggelser/12 måneder Sekundær: Mottak av MDRO 222 HAI hos 219 pasienter (1,59 pr. 100 innlagte pasienter)	
Time	2017-18 12 måneder	


6 wards
6 wards
6 wards
wash-in
Disinfectant
Probiotic
Soap-based
wash-in
Probiotic
Soap-based
Disinfectant
wash-in
Soap-based
Disinfectant
Probiotic
Total length of study 15 months
1 month
4 months
1 month
4 months
1 month
4 months

Diskusjon

- Ingen endring i forekomst av HAI i de forskjellige fasene
- Bacillus ikke funnet i kliniske infeksjoner
- Lav forekomst av enterokokker og E.coli i miljøprøver
-
- Hvordan måle effekt?
  - HAI prevalens vs HAI incidens – her er det lavere verdier enn i den australske studien.
  - Sammenliknbare med vår punktprevalens
  - Illustrerer hvor stor populasjon som behøves for å få effekt?

- Er probiotika fremtiden?

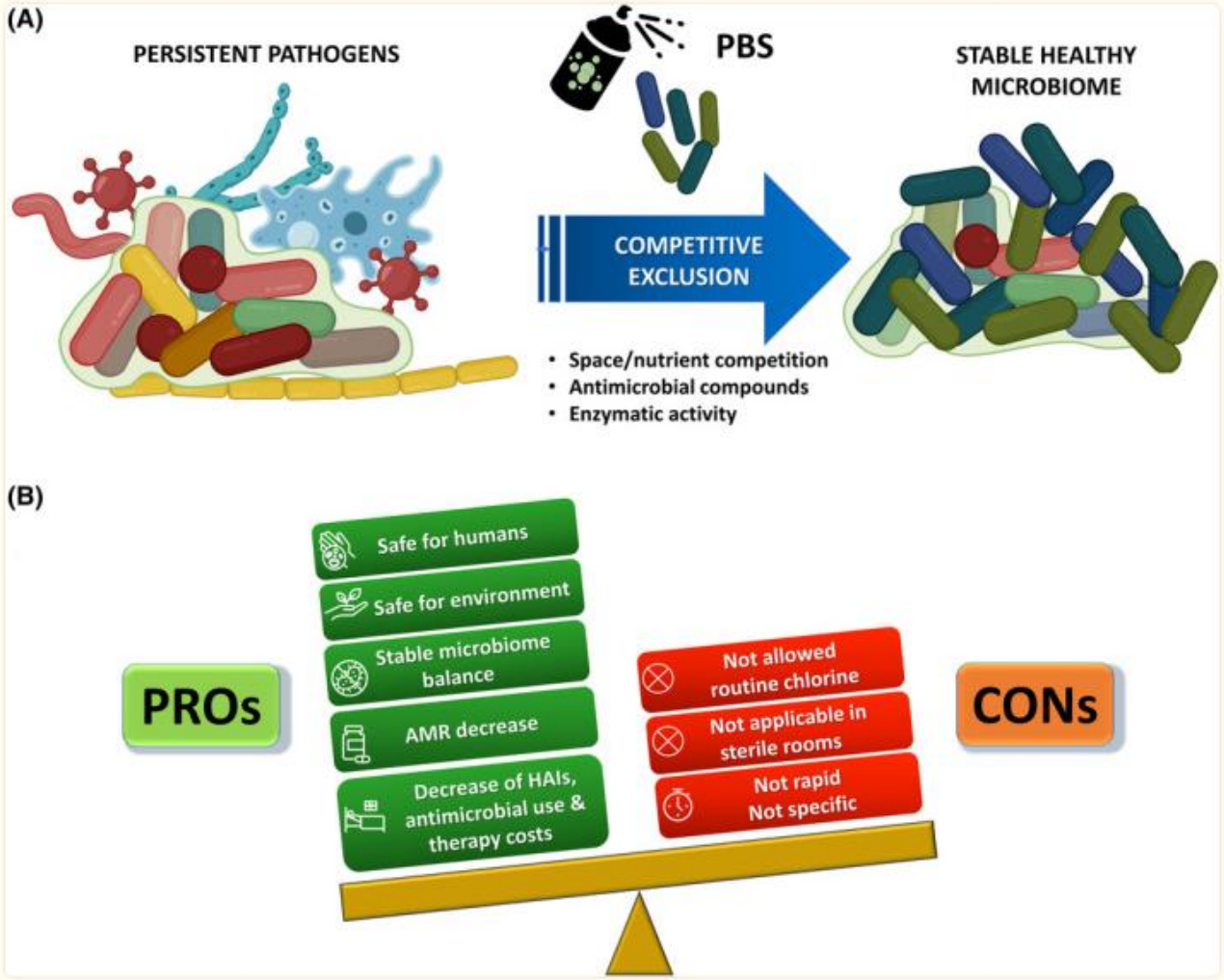


FIGURE 4

PBS strengths and weaknesses. (A) Known mechanisms of action of PBS: Germinated probiotics replace pathogens by competitive exclusion, including space and nutrient competition, production of antimicrobial compounds (bacteriocins) and enzymatic activity (lipases, proteases). (B) PBS strengths (PROs) and weaknesses (CONs) based on currently available published data.

D'Accolti M, Soffritti I, Bini F, Mazziga E, Caselli E. Tackling transmission of infectious diseases: A probiotic-based system as a remedy for the spread of pathogenic and resistant microbes. Microb Biotechnol. 2024 Jul;17(7):e14529. doi: 10.1111/1751-7915.14529. PMID: 39045894; PMCID: PMC11267305.

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Betyr enerom noe for smittevern?

Helse- og omsorgsminister Jan Christian Vestre delte tirsdag nyheten om at Stavanger universitetssjukehus får lån til første fase av videre utbygging på Ullandhaug.

Foto: Kari Nessa Nordtun, Jan Christian Vestre, Geir Pollestad og Lisa Marie Klungland.

4. Impact of a new hospital with close to 100% single-occupancy rooms on environmental contamination and incidence of vancomycin-resistant Enterococcus faecium colonization or infection: a genomic surveillance study

5. Environmental contamination with highly resistant microorganisms after relocating to a new hospital building with 100% single-occupancy rooms: A prospective observational before-and-after study with a three-year follow-up

4. Blane B, Coll F, Raven K, Allen O, Kappeler ARM, Pai S, Floto RA, Peacock SJ, Gouliouris T. Impact of a new hospital with close to 100% single-occupancy rooms on environmental contamination and incidence of vancomycin-resistant Enterococcus faecium colonization or infection: a genomic surveillance study.

J Hosp Infect. 2023 Sep;139:192-200. doi: 10.1016/j.jhin.2023.06.025. Epub 2023 Jul 12. PMID: 37451408.
10.1016/j.jhin.2023.06.025

5. van der Schoor AS, Severin JA, Klaassen CHW, Gommers D, Bruno MJ, Hendriks JM, Voor In 't Holt AF, Vos MC. Environmental contamination with highly resistant microorganisms after relocating to a new hospital building with 100% single-occupancy rooms: A prospective observational before-and-after study with a three-year follow-up.

Int J Hyg Environ Health. 2023 Mar;248:114106. doi: 10.1016/j.ijheh.2022.114106. Epub 2023 Jan 6. PMID: 36621268.
10.1016/j.ijheh.2022.114106

2(3) studier, forskjellige resultater - observasjonsstudier

- **Nederland – stort universitetssykehus:**
  - 4500 Miljøprøver MDRO tydelig reduksjon i forekomst av MDRO 3,3% vs 0,1%
  - Obs kun kort observasjonstid før flytting, kun 750 prøver før flytting
  - Ikke sett effekt på reduksjon i opptak av MDRO hos pasienter
  - Obs – inn i pandemiperioden

- **UK – dedikert hjerte-lunge kirurgisk sykehus – 300 senger**
  - Omfattende miljøscreening inkludert skyllerom, toaletter – tastaturer og mus
  - VRE funnet i 29% av prøver vs. 1-6% i nytt sykehus
  - 53 kliniske funn med VRE i perioden, beregnet til en signifikant redusert rate pr. 10.000 liggedøgn ->10,9 vs 6,2

- Fullgenomsekvensering gjennomført og mange andre analyser

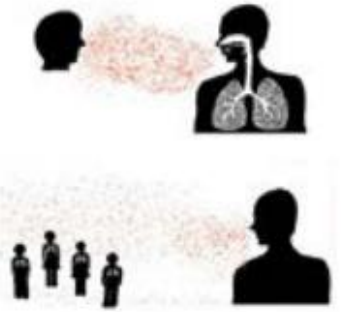
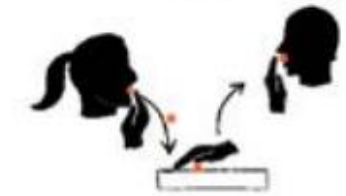
Diskusjon

- Vi bruker store summer på enerom for tiden. Er det rettferdiget smittevernmessig?
  - *Redusert forekomst av MDRO i miljø - JA*
  - *Redusert opptak av MDRO hos pasienter - ??*
  - *Redusert forekomst av HAI? – disse studiene svarer ikke på det.*

- Avhengig av bakgrunnsprevalens
- Omfattende studier – tid og ressurskrevende

- WHO april 2024

Table 1. Features of infectious respiratory particles and descriptors for modes of transmission[§]

Mode of transmission	Typical distance from the source	Route of transfer to another human	Respiratory tract entry mechanism	Respiratory tract entry portal	Schematic depiction
THROUGH THE AIR					
Airborne transmission/ inhalation	Any distance	Through the air (suspended in air or moving via air flows)	Inhalation	Anywhere along the respiratory tract	
Direct deposition	Short	Through the air (semi-ballistic trajectory)	Deposition on the mucosa	Mouth, nose or eyes*	
CONTACT[#]					
Direct contact	*Short*	*Not through the air*	*Direct transfer (via touch[°], usually with hands)*	*Mouth, nose or eyes**	
Indirect contact	*Any distance*	*Not through the air, although IRPs may reach an intermediate object through the air*	*Indirect transfer (via touching an intermediate object)*	*Mouth, nose or eyes**	

* Note that the mucosa of the eyes is not part of the human respiratory tract but are a portal of entry into the respiratory system.

[#] Note that this mode of transmission to another human does not involve a 'through the air' route but is included here for completeness. Depictions above assume the human(s) on the left is/are the infectious person(s) and the human on the right is the recipient of the IRP.

[°]Note that 'touch' is not through the air transmission but included for completeness and it does not include sharp injuries like needle prick.

[§]Source of figures: A. Manna and L. Bourouiba. Based on (*8, 12, 23*).

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