TRAINING SEMINAR

Towards higher patient safety in EU hospitals

Innovation in hygiene & sanification to reduce healthcare associated infections and antimicrobial resistance.

The case history of the innovative sanitation system PCHS®

4th February 2019 - 15:00-18:00
Thon Hotel EU, Brussels

E. Caselli
Dept. Medical Sciences – University of Ferrara

UNIVERSITÀ DEGLI STUDI DI FERRARA
- EX LABORE FRUCTUS -
CICS

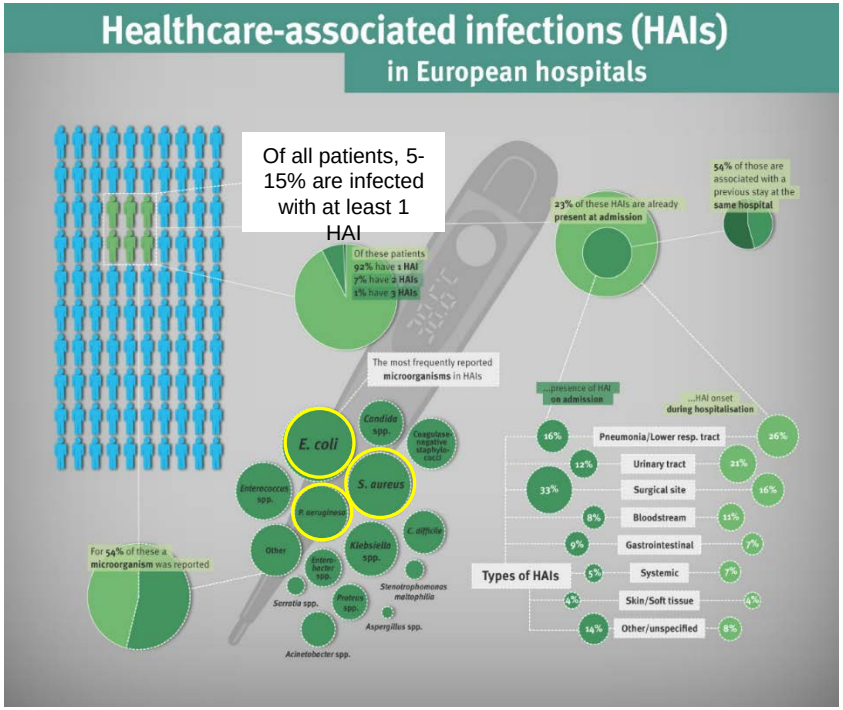
ACTIVE CITIZENSHIP NETWORK
CITTADINANZATTIVA

BACKGROUND

Healthcare associated infection (HAI) are a global concern (5-15% patients): over **4 millions patients** with HAI in EU every year. About **37000 deaths** as a direct HAI consequence.

Major causes:

- **<u>Persistent microbial contamination</u>** on hospital surface
- **<u>Drug resistance (AMR</u>**): often if not always HAI-associated pathogens are MDR or even panDR



WHO «dirty dozen» : critical, high & medium priority (MRSA, ESBL, KPC, Colistin…)

World Health Organization

Priority 1: CRITICAL

- ***Acinetobacter baumannii***, carbapenem-resistant
- ***Pseudomonas aeruginosa***, carbapenem-resistant
- ***Enterobacteriaceae***, carbapenem-resistant, 3rd generation cephalosporin-resistant

Priority 2: HIGH

- ***Enterococcus faecium***, vancomycin-resistant
- ***Staphylococcus aureus***, methicillin-resistant, vancomycin intermediate and resistant
- ***Helicobacter pylori***, clarithromycin-resistant
- ***Campylobacter***, fluoroquinolone-resistant
- ***Salmonella spp.***, fluoroquinolone-resistant
- ***Neisseria gonorrhoeae***, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

- ***Streptococcus pneumoniae***, penicillin-non-susceptible
- ***Haemophilus influenzae***, ampicillin-resistant
- ***Shigella spp.***, fluoroquinolone-resistant

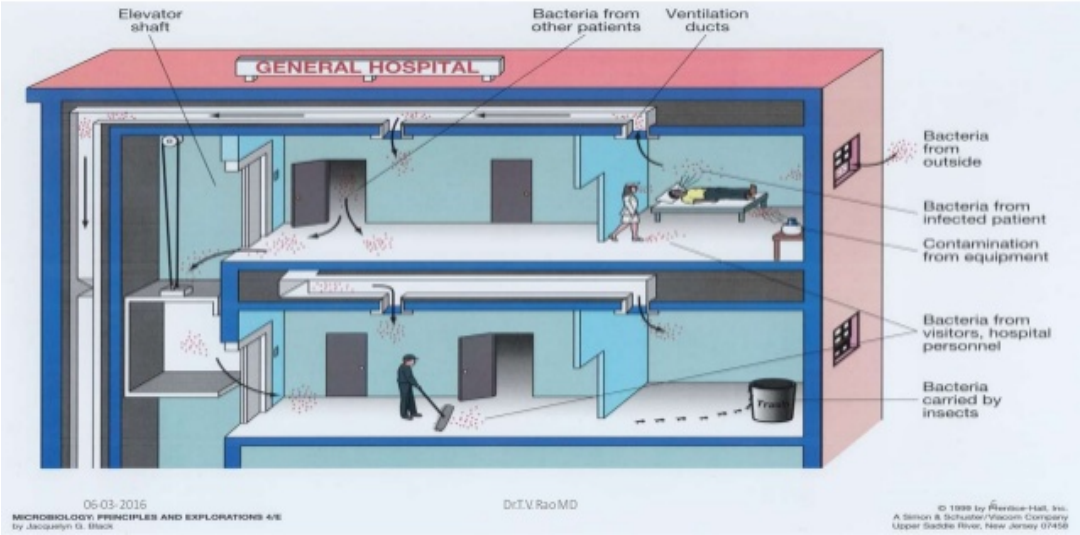
BACKGROUND

EU:
- with the current rapidity of diffusion, in 2050 AMR might cause more deaths than tumors…
- within the next 20 years even banal infections might become deadly, and therapies like transplant (bone marrow, staminal cells) or chemotherapy, etc might result impossible in the absence of effective antibiotics to prevent infections

EU, 18 november: European Antibiotic Awareness Day

European Committee: june 2017 the new Plan to fight AMR
(One Health Action Plan against Antimicrobial Resistance) →
for the first time included also hygienic conditions in hospital environment

EXOGENOUS SOURCES OF INFECTION



So far, control of contamination addressed by conventional **chemical-based sanitation:**

- cannot prevent **recontamination**
- high **environmental impact**
- can favour **selection of resistance** (i.e. chlorexidin induction of ColR in KPC)

Urgent need for new effective methods:

- STABLE abatement of contamination
- Devoid of «side effects» (AMR, environmental impact)

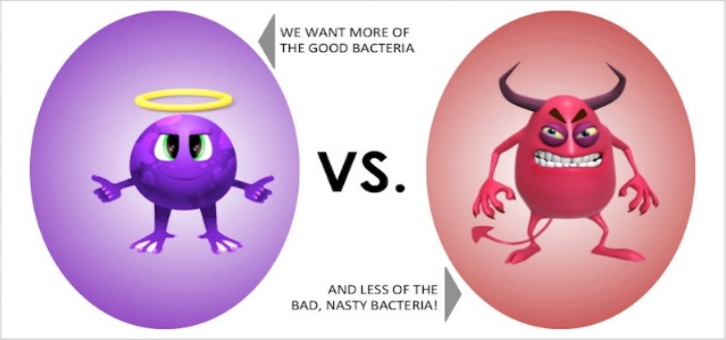
PCHS: Probiotic Cleaning Hygiene System

HUMAN MICROBIOME PROJECT

Environmental health = Human body health

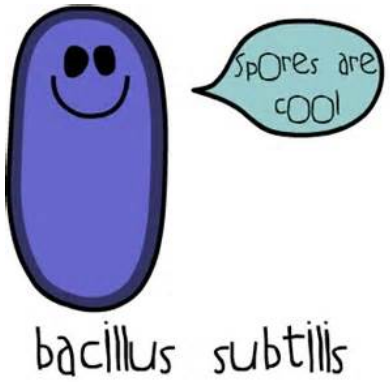
<u>Microbiome project</u>:
Good bacteria are important to preserve health, as they fight and replace bads ones

<u>COMPETITIVE ANTAGONISM</u>



Eco-sustainable detergents additioned with **spores** of **probiotic** bacteria of the ***Bacillus*** genus: *B. Subtilis*, *B. Pumilus*, *B. megaterium*.

***Bacillus* genus:** ubiquitous bacteria, detected in soil, water, human and animal gut. NON PATHOGENIC (except 2).
All produce SPORES.



Bacillus spores have a long history of safe use in humans

SPORES: dormant forms, resistant to adverse environmental conditions (chemical-physical factors); very suitable for addition to detergent withou loss of activity.

Food preparation: Natto, Doenjang traditional japanese and corean foods), produced by soy fermentation with *B. subtilis*, variant *natto*. Final product contains up to 10^8 bacilli/gr!

Use in agriculture: biofungicide (es. Serenade, Bayer)

Therapeutic use: for prevention of GI diseases or restoration of GI flora after antibiotic treatment (Enterogermina, Bactisubtil, Biocult, Biosporin, Bispan, Fora-balance, ecc).

Use in farm animals: food additives to prevent diseases and increase livestocks wellness.

Experimental use: in 1966 USA Army released billions of *B. subtilis* spores in the NY subways, to simulate a bacteriological attack, and no cases of infections were reported.

AIM of RESEARCH

Effectiveness of PCHS against hospital pathogens

EFFECTIVENESS ***in vitro***

EFFECTIVENESS ***on field***

SAFETY of use

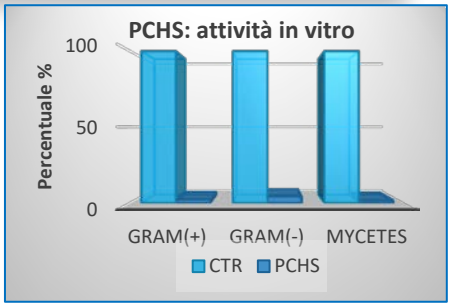
EFFECTIVENESS on HAI incidence

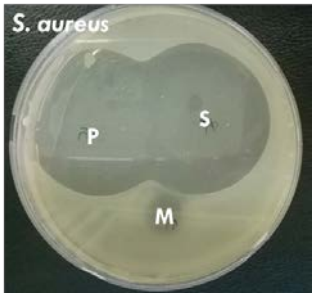
(*) Set up of rapid and reliable methods of analysis, able to <u>MONITOR</u> all microbiota variations and all associated effects.

PCHS: results

1. EFFECTIVENESS *in vitro*

<u>>90% INHIBITION</u> pathogen growth





2a. EFFECTIVENESS *on field*

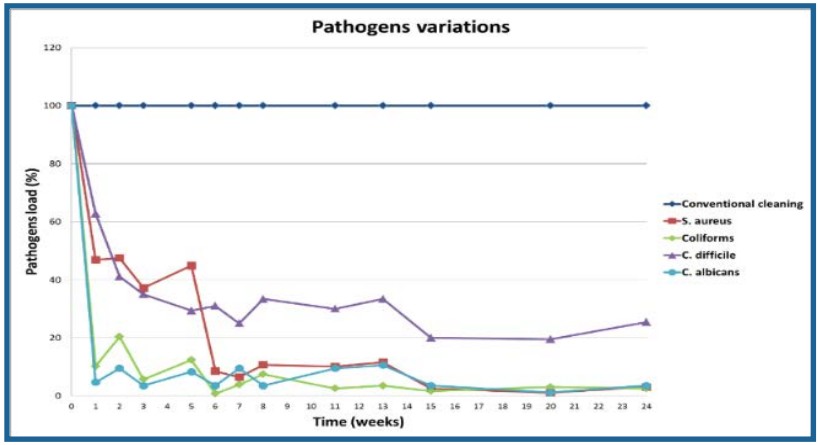
<u>~80% STABLE DECREASE</u> of pathogen load on treated surfaces compared to conventional cleaning

OPEN ACCESS Freely available online PLOS | ONE

Hard Surface Biocontrol in Hospitals Using Microbial-Based Cleaning Products

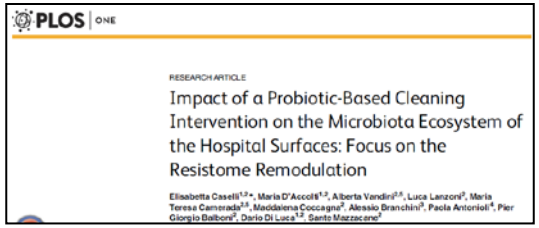
Alberta Vandini[1], Robin Temmerman[2,3], Alessia Frabetti[1], Elisabetta Caselli[4], Paola Antonioli[5], Pier Giorgio Balboni[6], Daniela Platano[6], Alessio Branchini[7], Sante Mazzacane[1*]

1 CIAS Laboratory, Centre for the Study of physical, chemical and microbiological Contamination of Highly Sterile Environments, Department of Architecture, University of Ferrara, Ferrara, Italy, 2 Laboratory of Microbial Ecology and Technology, Ghent University, Ghent, Belgium, 3 Chrisal R & D Department, Lommel, Belgium, 4 Department of Medical Sciences, Microbiology Section, University of Ferrara, Ferrara, Italy, 5 Department of Infection Prevention Control and Risk Management, Ferrara University Hospital, Ferrara, Italy, 6 Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy, 7 Department of Life Sciences and Biotechnology, University of Ferrara, Ferrara, Italy



2b. AMR selection?

NO AMR selection, but rather a DECREASE of resistant strains up to -90%.

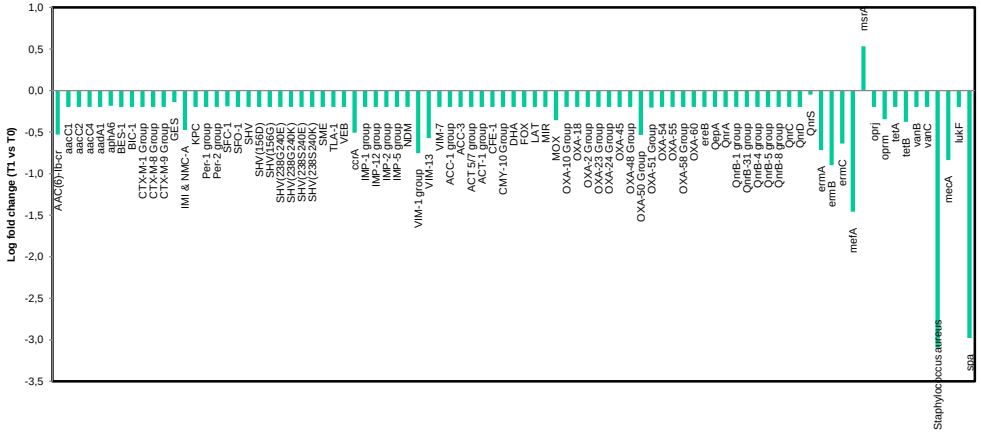


PLOS | ONE

RESEARCH ARTICLE

Impact of a Probiotic-Based Cleaning Intervention on the Microbiota Ecosystem of the Hospital Surfaces: Focus on the Resistome Remodulation

Elisabetta Caselli[1,2*], Maria D'Accolti[1,2], Alberta Vandini[2,3], Luca Lanzoni[2], Maria Teresa Camerada[1,3], Maddalena Coccagna[2], Alessio Branchini[2], Paola Antonioli[4], Pier Giorgio Balboni[5], Dario Di Luca[1,2], Sante Mazzacane[2]



3. SAFETY of use

(Caselli E. et al., JHI 2016)

Can PCHS-*Bacillus* acquire R genes from surrounding pathogens?

Can PCHS-*Bacillus* themselves be dangerous for hospital inpatients?

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

HIGH GENETIC STABILITY

Analyses performed in ~8 years:

NO acquisition of any new R gene

NO INFECTIOUS RISK

Microbiological surveillance in all hospital using PCHS:

- **NO infections** caused by PCHS-*Bacilli*
- PCHS-*Bacilli* **NEVER** detected in > 60,000 biological samples

Journal of Hospital Infection 94 (2016) 193–208

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin

ELSEVIER

Letters to the Editor

Safety of probiotics used for hospital environmental sanitation

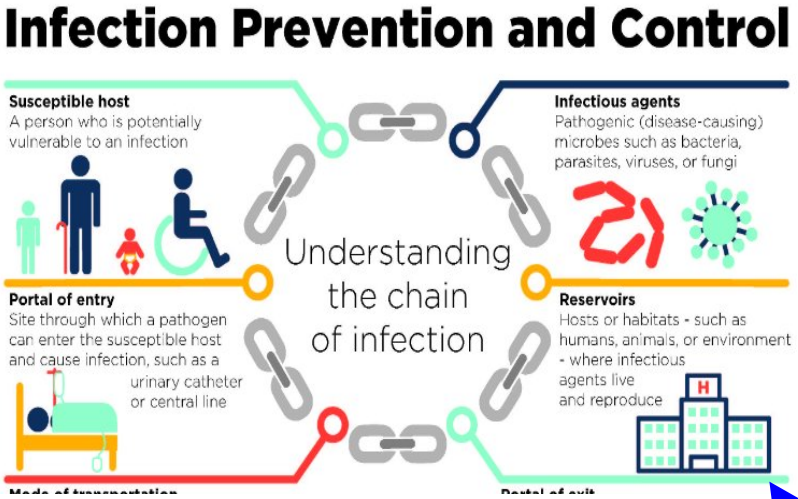
E. Caselli[a,b,*]
P. Antoniolli[c]
S. Mazzacane[b]

4. EFFECTIVENESS on HAI incidence

Can PCHS-sanitation have an impact on HAI occurrence?

<u>SAN-ICA</u> study

The Inanimate Environment Can Facilitate Transmission



RESERVOIR

SAN-ICA: *involved 6 Italian public hospitals and 5 Universities*

Ospedale Roma
Filippo Berloco
Francesca Trozzi

Ospedale Ferrara
Paola Antonioli
Silvano Nola

Ospedale Tolmezzo
Nelso Trua

Ospedale Foggia
Giovanni Villone
Ermelinda Del Buono

Ospedali Pavia-Vigevano
Antonella Mastretti
Francesca Campanella

Ospedale Feltre
Lorenzo Tognon
Paolo Grotto

Ferrara: Sante Mazzacane
Elisabetta Caselli

Udine: Silvio Brusaferro
Luca Arnoldo

Pavia: Gabriele Pelissero

Messina: Vincenza La Fauci

Università Bocconi-CERGAS
Rosanna Tarricone
Carla Rognoni

Multicentre
Pre-post interventional study
18 months
Internal Medicine wards

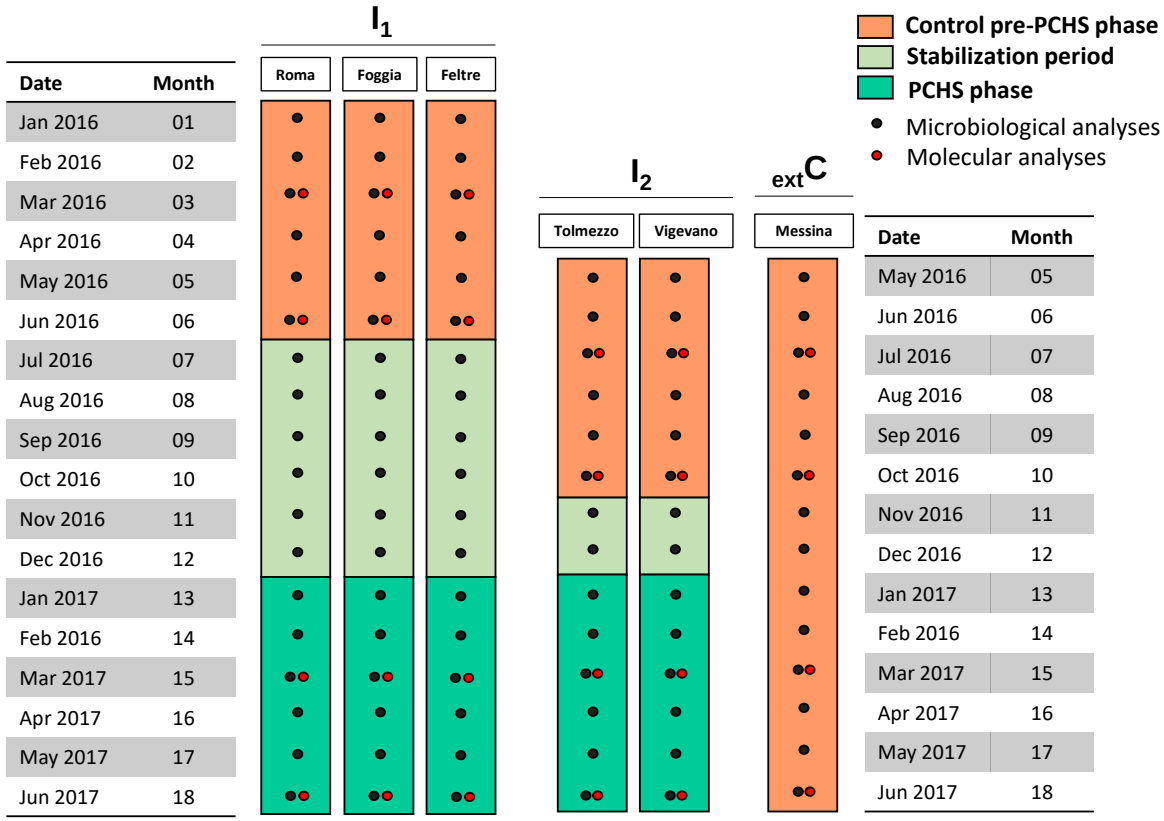
Simultaneous and continuous analysis of:

1. **Surface bioburden**
2. **HAI incidence**

Intervention: PCHS substituted conventional chemical sanitation

Hospitals located in different **geographic** regions, and subdivided in groups entering the study in different **periods** to minimize seasonality bias.
All hospitals were evaluated in a 6 month **pre-PCHS phase** (conventional sanitation) and in a 6 month **PCHS phase.**

STUDY DESIGN



Date	Month
Jan 2016	01
Feb 2016	02
Mar 2016	03
Apr 2016	04
May 2016	05
Jun 2016	06
Jul 2016	07
Aug 2016	08
Sep 2016	09
Oct 2016	10
Nov 2016	11
Dec 2016	12
Jan 2017	13
Feb 2016	14
Mar 2017	15
Apr 2017	16
May 2017	17
Jun 2017	18

Date	Month
May 2016	05
Jun 2016	06
Jul 2016	07
Aug 2016	08
Sep 2016	09
Oct 2016	10
Nov 2016	11
Dec 2016	12
Jan 2017	13
Feb 2016	14
Mar 2017	15
Apr 2017	16
May 2017	17
Jun 2017	18

One hospital was not subjected to intervention (external control), to check the effect due to mere «participating to a study» (***Hawthorn effect***).

PCHS introduction was the only intervention.

Hospital staff was not aware of the changing sanitation (as the procedures are similar, no change in professionals doing cleaning, etc.).

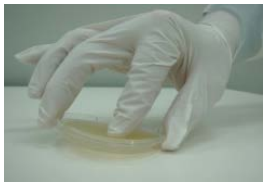
Microbiological analyses

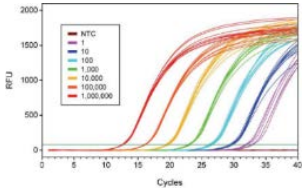
1. Conventional microbiology: 6 pathogens, Rodac plates (CFU counts); antibiograms on all *Staphylococcus aureus* isolates.

2. Molecular analyses: total bacterial load, % *Bacillus*, microbiota resistome, *Bacillus* resistome.

Tested surfaces: floor, bed footboard and sink (in duplicate).
3-6 randomized rooms per ward (depending on the bed number < or > 100 beds)

>32,000 environmental samples





HAI analyses

Analysis ***in continuum*** (INCIDENCE), made by independent sanitary professionals:

- Specific software for digital recording of data (anonymized) in a central database

-Record S1 (at admission): all patient's characteristics
-Record S2 (only in HAI): HAI characteristics (type, location, therapy, etiological agent, time of duration, outcome, etc), and patient's characteristics (risk factors)

HAI definition: ECDC criteria.

>12,000 patients

MICROBIOTA RESULTS

(Caselli E. et al., PLOS One 2018)

STABLE MICROBIOTA REMODULATION

Tot CFU for the 6 tested pathogens.

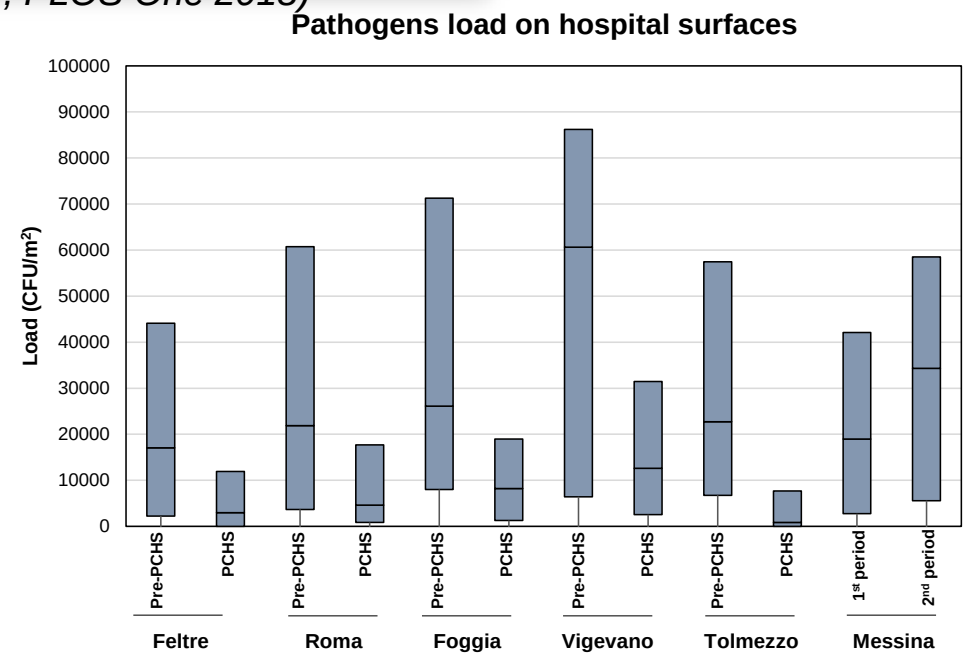
Median values (6 sampling) of pre-PCHS and PCHS phases.

Pre-PCHS = 11,737 CFU/m^2

PCHS = 4,632 CFU/m^2

Whole decrease = **-83.0% (70-96.3%)**

No reduction in control not-treated hospital.



PCHS-*Bacillus* replace pathogens

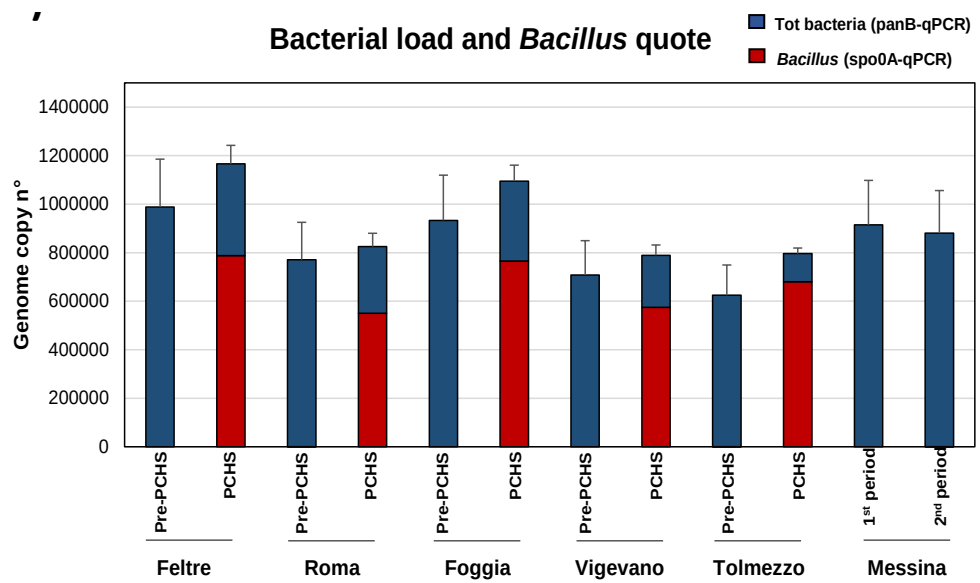
PCHS *Bacillus* %

Median values (6 sampling) of pre-PCHS and PCHS phases.

Pre-PCHS = 0%

PCHS = **70% (40-87%)**

No variation in control not-treated hospital.



«AMR» RESULTS

(Caselli E. et al., PLOS One 2018)

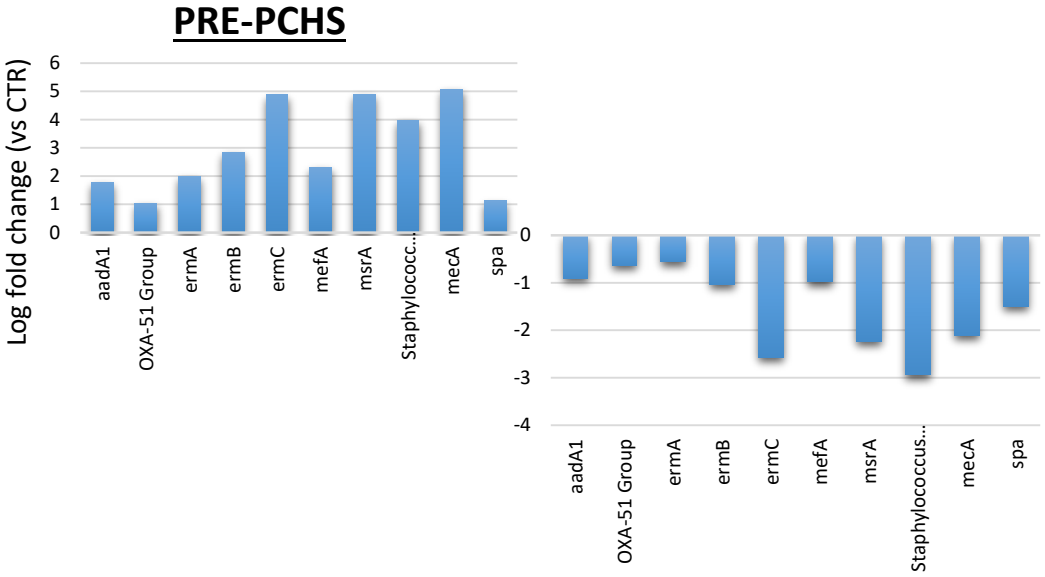
RESISTOME analysis

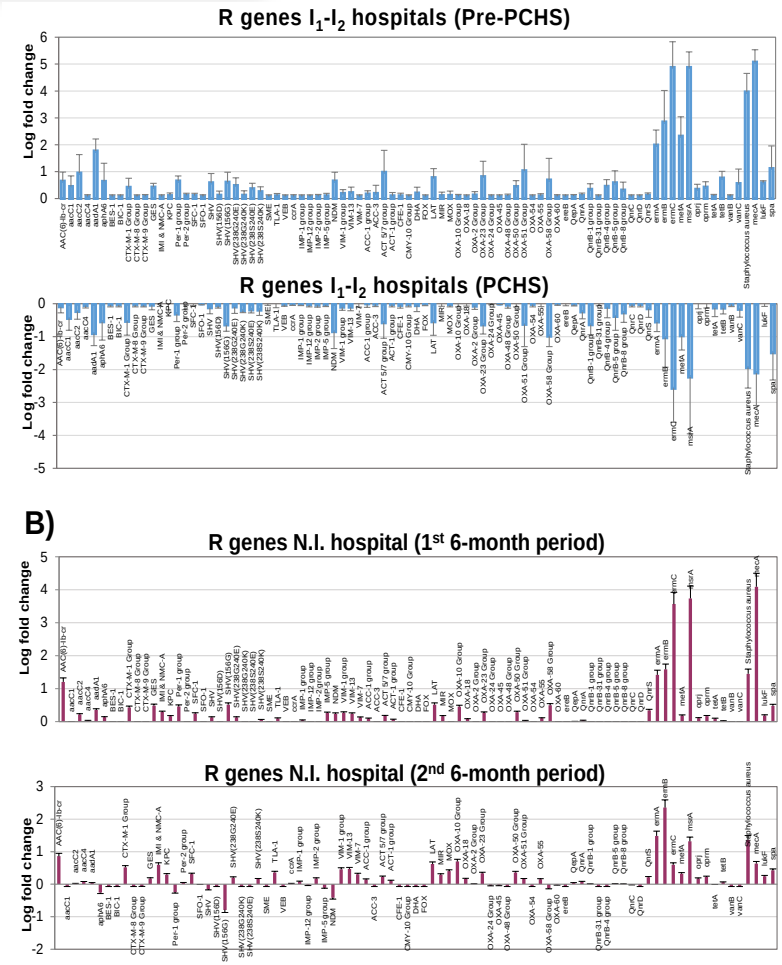
All R genes detected in the microbial population in the pre-PCHS phase resulted **REDUCED** up to **100-1000 folds** in PCHS phase.

No reduction in CTR hospital.

STABLE AMR DROP

Main R genes -67-99% (-72% colR *mcr-1*)

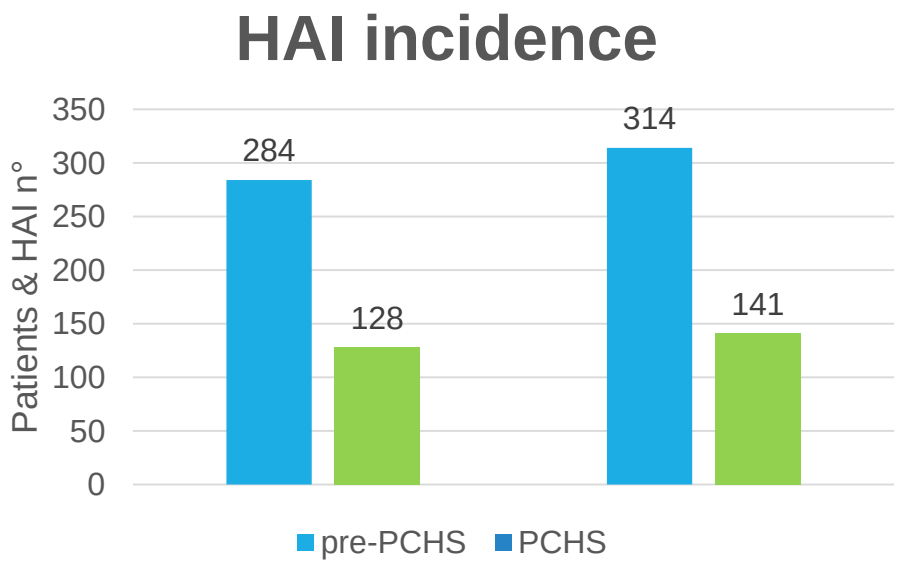




Data confirmed by antibiogram results (-72.4% MDR strains)

«HAI» RESULTS

(Caselli E. et al., PLOS One 2018)



GLOBAL REDUCTION
(patients with ay least 1 HAI): **-52.1%**

Tot HAI n°: **-55%**

Detected in all settings, independently of the initial value.

Most frequent HAI types:

- **UTI (57%): -60.9%**
- **BSI & Sepsi (24,2%): -60.1% (42.6-77.3%)**

Type of HAI	Pre-PCHS ($I_1 + I_2$) No. (%)	PCHS ($I_1 + I_2$) No. (%)	PCHS vs pre-PCHS
TOTAL	314* (100%)	141° (100%)	-55.0%
Urinary tract infections-UTI	179 (57.0%)	70 (49.6%)	**-60.9%**
Bloodstream infections-BSI	54 (17.2%)	31 (22.0%)	**-42.6%**
Systemic-clinical sepsis	22 (7.0%)	5 (3.5%)	**-77.3%**
Gastrointestinal-GI	17 (5.4%)	6 (4.3%)	-64.7%
Skin and soft tissue	15 (4.8%)	6 (4.3%)	-60.0%
Pneumonia	12 (3.8%)	8 (5.7%)	-33.3%
Lower respiratory tract	10 (3.2%)	6 (4.3%)	-40.0%
Reproductive tract	1 (0.3%)	-	-100%
Eye, ear, nose and throat or mouth EENT	1 (0.3%)	2 (1.4%)	+100%
Bone and joint	-	1 (0.7%)	+100%
Intra-abdominal	-	1 (0.7%)	+100%
Not specified	3 (1.0%)	5 (3.5%)	+66.7%

«HAI» RESULTS

(Caselli E. et al., PLOS One 2018)

Multivariate analysis: analysis of all risk factors significantly associated with HAIs

PCHS emerges as an independent **protective factor: OR=0.44 → halved risk**

Variables	OR	95% CI	*P*
Male	0.78	0.63-0.96	0.01812
Age 65-74 vs Age <65	1.71	1.18-2.48	0.0047
Age 75-84 vs Age <65	1.88	1.33-2.67	0.0004
Age 85 or more vs Age <65	1.78	1.22-2.58	0.0026
Length of stay	1.08	1.07-1.09	p<0.0001
Incontinence	0.85	0.66-1.10	0.2253
Disorientation	1.37	1.05-1.76	0.0226
Self-sufficiency	0.92	0.69-1.43	0.5600
Pressure sores	0.99	0.69-1.44	0.9757
Ventilation	1.07	0.68-1.67	0.7702
ATB 2 week before	0.97	0.68-1.37	0.8479
MDRO at admission	0.86	0.47-1.57	0.6230
Urinary catheter (any type)	2.68	2.10-3.41	p<0.0001
CVC	1.99	1.40-2.82	0.0001
PCHS	**0.44**	0.35-0.54	p<0.0001

Antimicrobials consumption & costs

(Caselli E. et al., Infection & Drug resistance, in press)

-52% HAI reduction

Drug types	Molecules (n)	
	Pre-PCHS	PCHS
Beta-lactams*	126	75 (-40.5%)
Fluoroquinolones	111	20 (-82%)
Glycopeptides	43	18 (-58.1%)
Cephalosporins	43	22 (-48.8%)
Antifungals	31	6 (-80.6%)
Acid antibiotics	11	1 (-90.9%)
Polymixins	7	3 (-57.1%)
Sulphamides	6	1 (-83.3%)
Aminoglycosides	5	2 (-60.0%)
Others	16	9 (-43.7%)
Tot	403	160 (-60.3%)

-60%
HAI-associated antimicrobial drug consumption

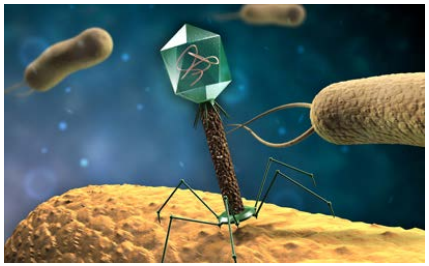
-75%
global reduction of HAI therapy costs

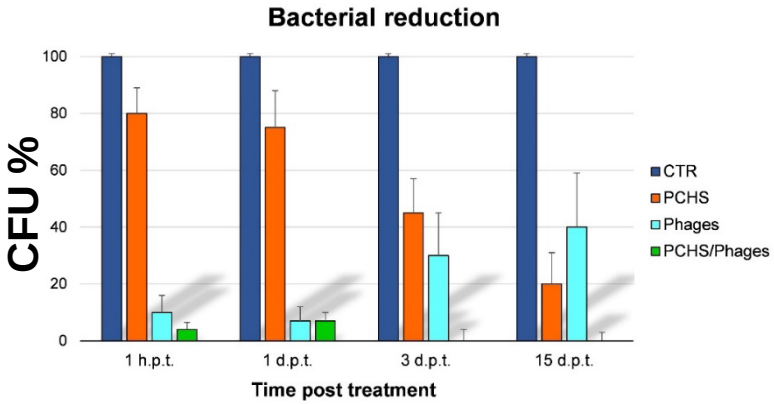
CONCLUSIONS

By stably modulating the microbiota of hospital surfaces, it is possible to impact significantly on AMR and HAIs.

It is important to monitor these phenomena!

**** The system might be further improved ….***
Work in progress on BACTERIOPHAGES
(the enemies of our enemies)

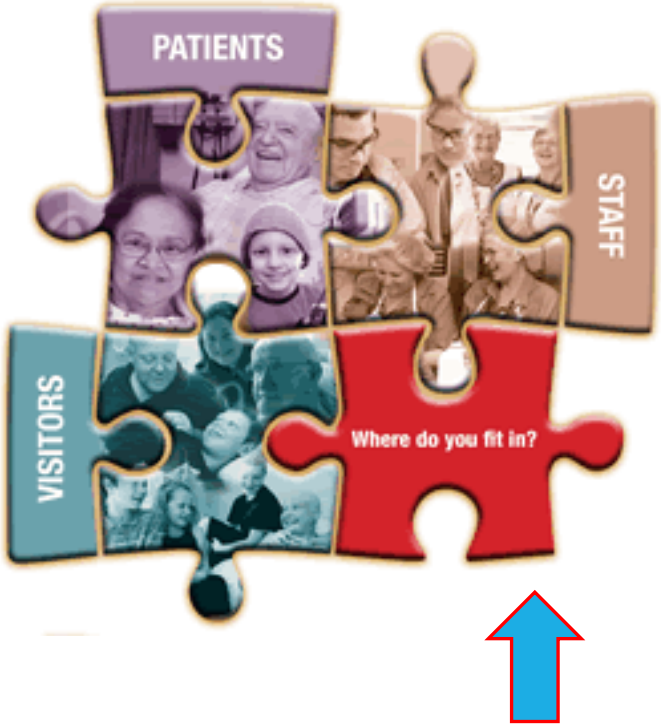




The combined use of probiotics+phages leads to <u>RAPID, SPECIFIC</u> & <u>STABLE</u> decontamination

(D'Accolti E. et al, Infection & Drug resistance, 2018)

THANK YOU!!!



It is possible to act also at the environmental level, as a part of IPC strategies

SAN-ICA Group