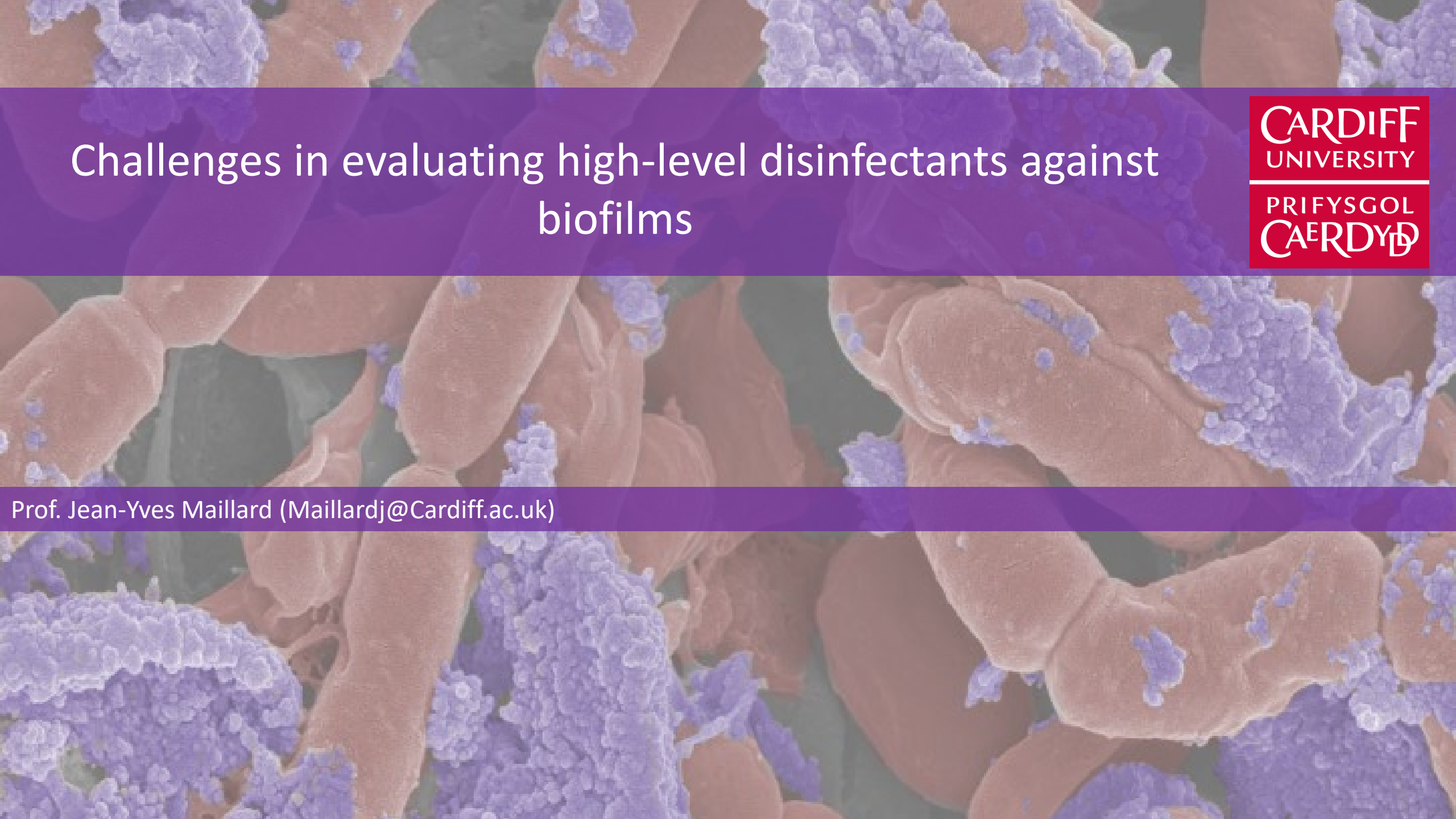
Challenges in evaluating high-level disinfectants against biofilms



Prof. Jean-Yves Maillard (Maillardj@Cardiff.ac.uk)

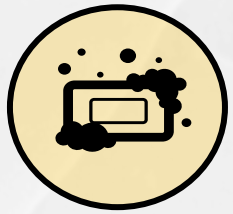
Transparency declaration

Director of Biocide Consult ltd

Chief Editor, Journal of Infection Prevention

– nothing pertinent to this presentation to declare

Cleaning *vs.* disinfection



CLEANING

- Removal of dirt
- Not designed to kill pathogens
- Might (and probably will) remove pathogens

DISINFECTION

- Killing pathogens – a “cidal” activity
- Different levels of disinfection
- Delivery (applicator) plays a role

It is not possible to ‘sterilise’ surfaces of equipment/ patient environment using disinfection; only to temporarily reduce the number of microbes present.

Revised Spaulding Classification

Spaulding classification

CRITICAL DEVICES
In contact with sterile tissue or vascular system

Sterilisation required
- Physical sterilisation (heat)
- Radiation sterilisation
- Chemical disinfectant (ethylene oxide, hydrogen peroxide

High-level disinfection (may be acceptable)
- PAA, H_2O_2, ClO_2, GTA, OPA,

SEMI-CRITICAL DEVICES
In contact with intact mucous membrane

High-level disinfection required
- Heat
- Glutaraldehyde
- Peracetic acid
- Chlorine dioxide
- Hydrogen peroxide
- Chlorine releasing agents

NON-CRITICAL
Not in contact with patient/ contact with intact skin

Low-level disinfection required
- Alcohols
- QACs
- Biguanides

Cleaning or disinfection
- Cleaning and drying
- Disinfection in case of contaminated spillage

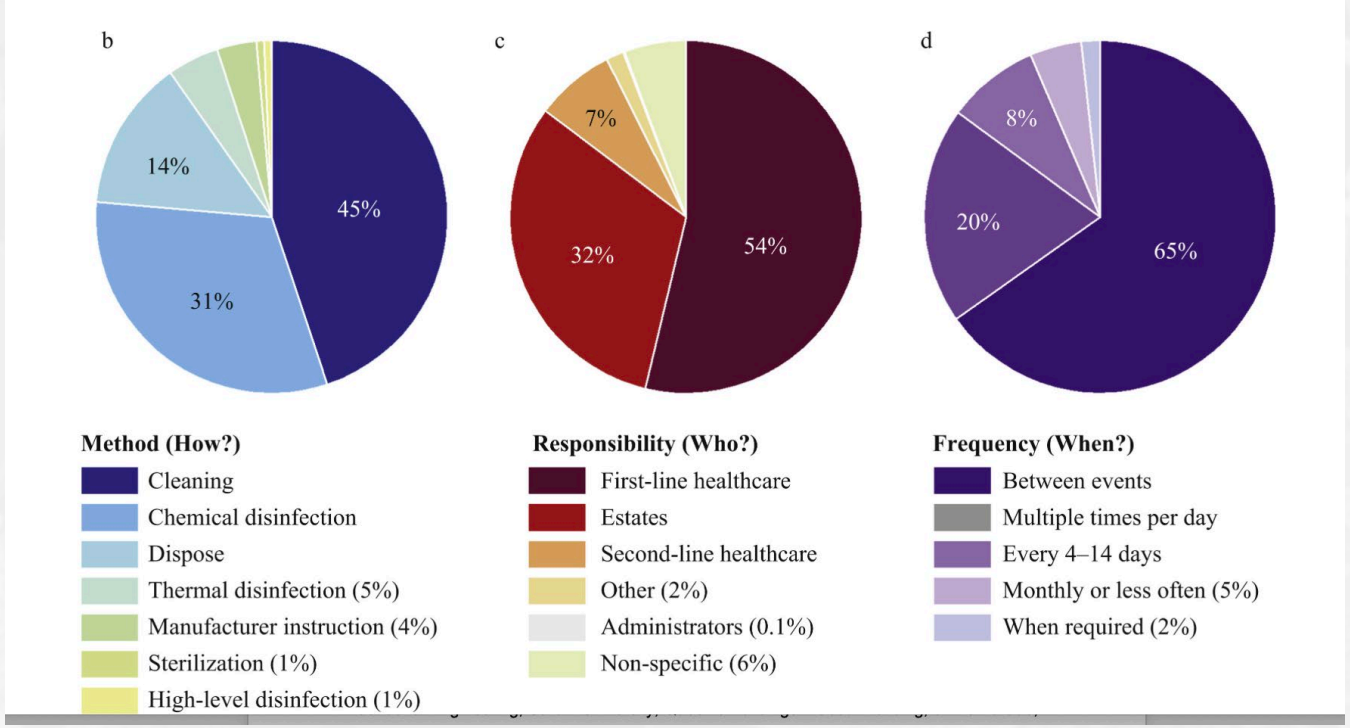
Decontamination protocols for shared non-critical objects

- The lack of clear indications regarding the person responsible for the decontamination process put at risk the ability of policies to serve as guidance

Castelli *et al. J Hosp Infect* 2022;120:65-72.

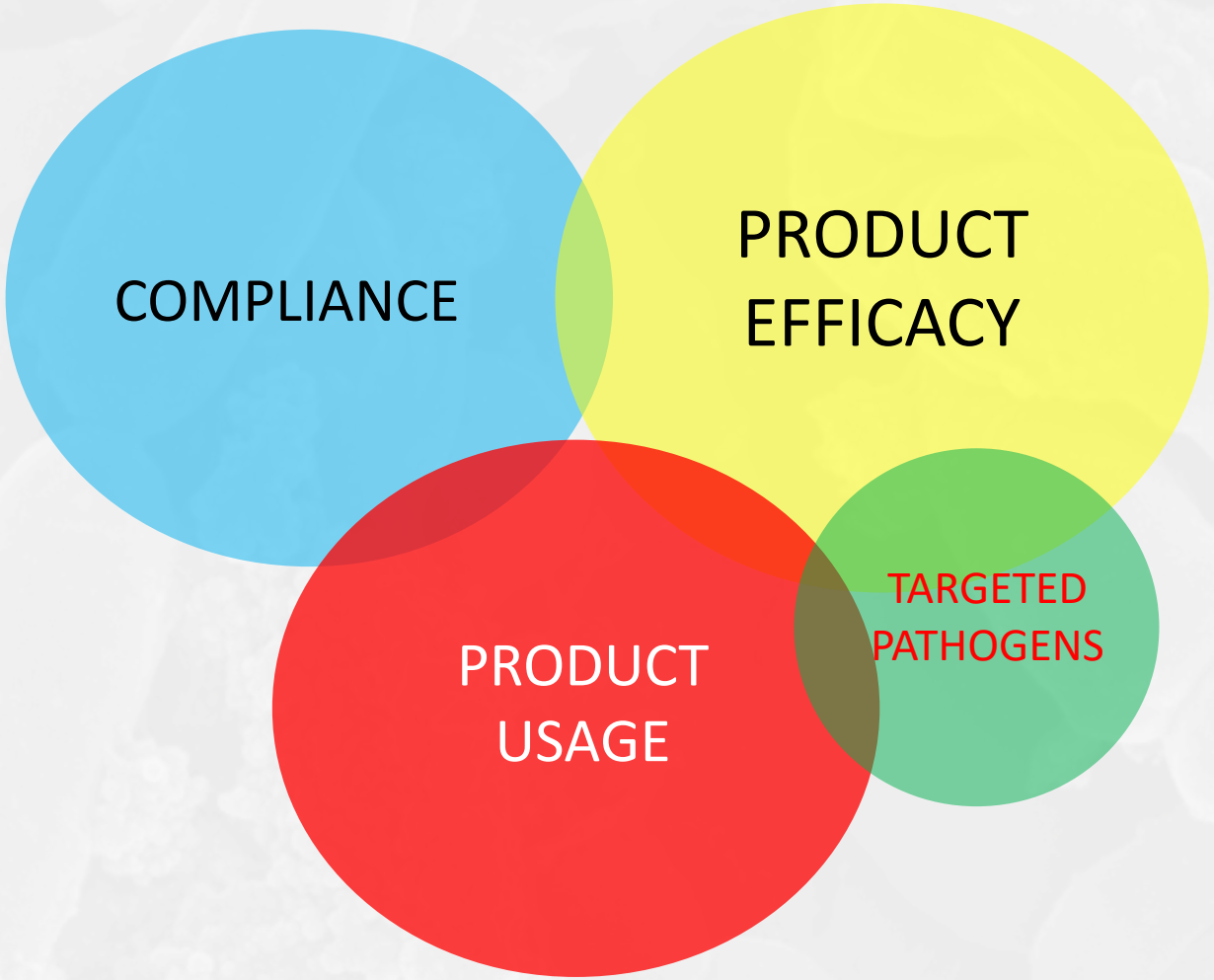
- 35 NHS Acute Care Organisations
- 1279 decontamination protocols regarding 283 different shared non-critical objects were retrieved.

- 689 (54%) did not indicate the person responsible for decontamination
- Only 425 (33%) were complete, giving indications for (a) decontamination method, (b) responsibility and (c) frequency
- Only 2.5% (32/1279) of decontamination protocols were complete and identical in two policies



Summarized indications retrieved for the decontamination method (b), responsibility (c) and frequency (d).

Factors impacting Disinfectant efficacy



Factors impacting Disinfectant efficacy

FACTORS INHERENT TO THE PRODUCT

- Concentration
- Formulation
- Delivery system

FACTORS INHERENT TO THE APPLICATION OF THE PRODUCT

- Surface
- Organic load (soiling)
- Contact time
- Temperature
- Humidity

FACTORS INHERENT TO THE MICRO-ORGANISMS

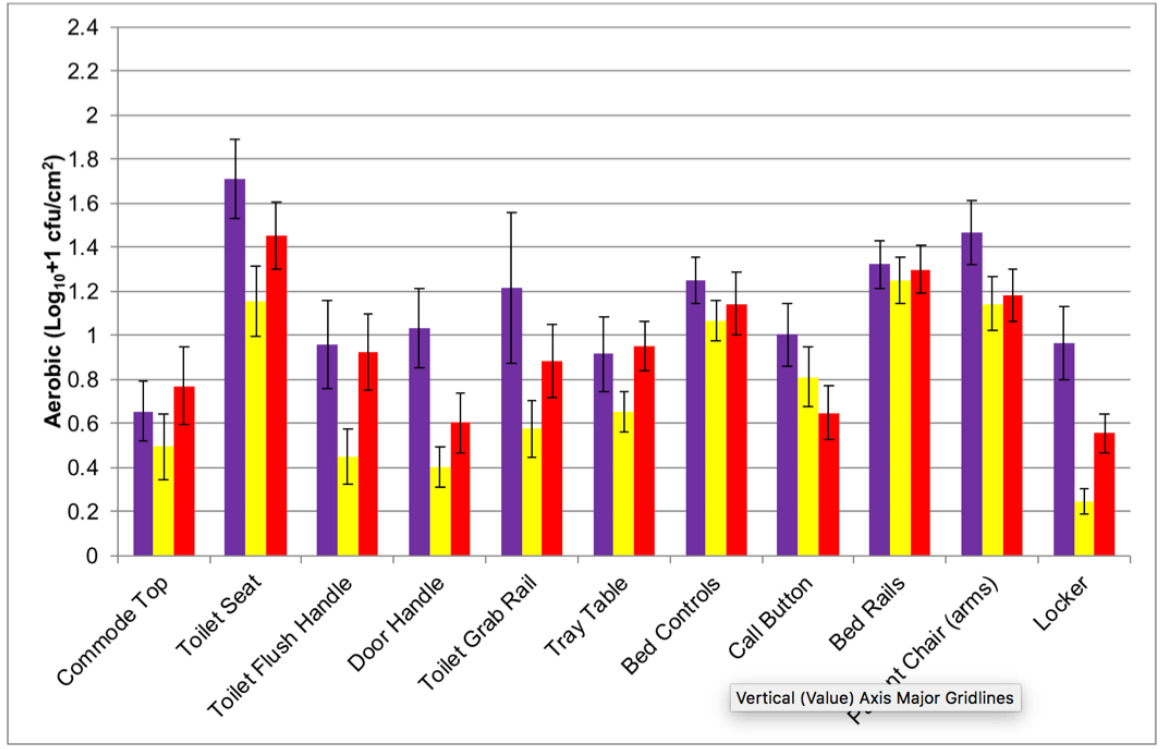
- Type
- Number
- Association (biofilms)

Factors impacting Disinfectant efficacy

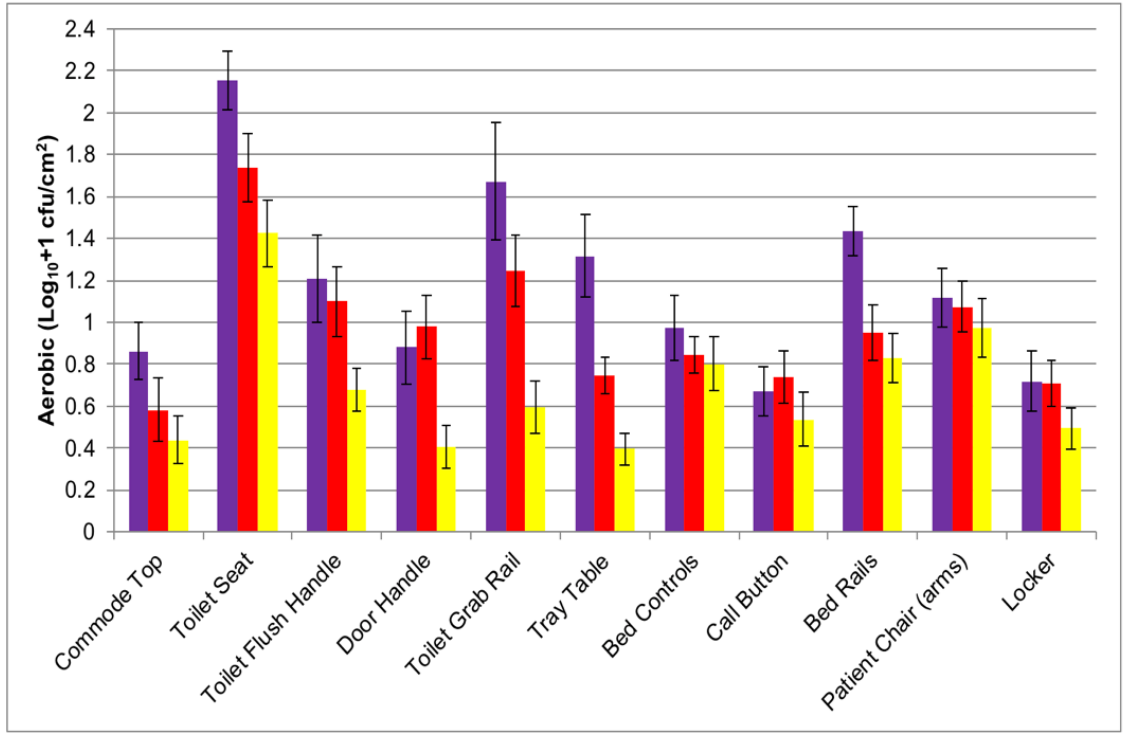
Delivery – preformulated wipe *vs.* bucket & cloth

Siani *et al. Am J Infect Control* 2018 46;1180-7

Double-crossover study was performed on 2 different surgical and cardiovascular wards in a 1,000-bed teaching hospital over 29 weeks.



Baseline
Sporicidal wipe
Cleaning and use of chlorine 1,000 ppm (bucket)



Baseline
Cleaning and use of chlorine 1,000 ppm (bucket)
Sporicidal wipe

Factors impacting Disinfectant efficacy

Delivery – preformulated wipe *vs.* bucket & cloth

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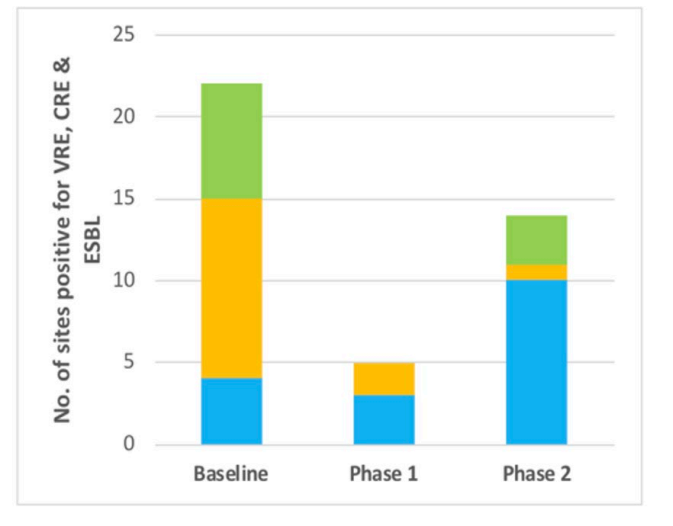
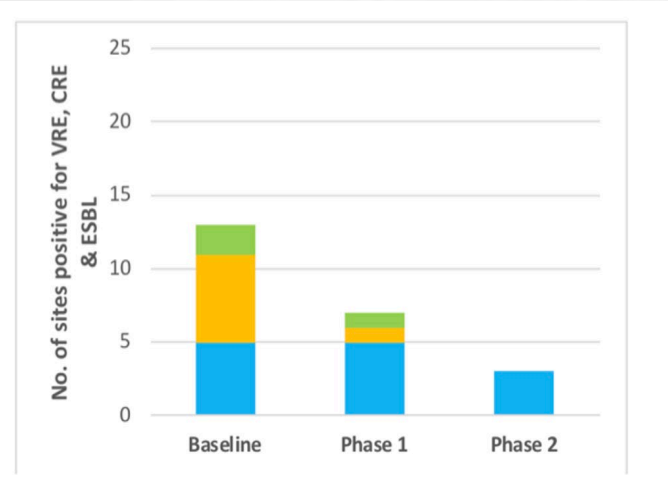


Ward 1

- Phase 1: Sporicidal wipe
- Phase 2 Cleaning and use of chlorine 1,000 ppm (bucket)



Ward 2

- Phase 1: Cleaning and use of chlorine 1,000 ppm (bucket)
- Phase 2: Sporicidal wipe

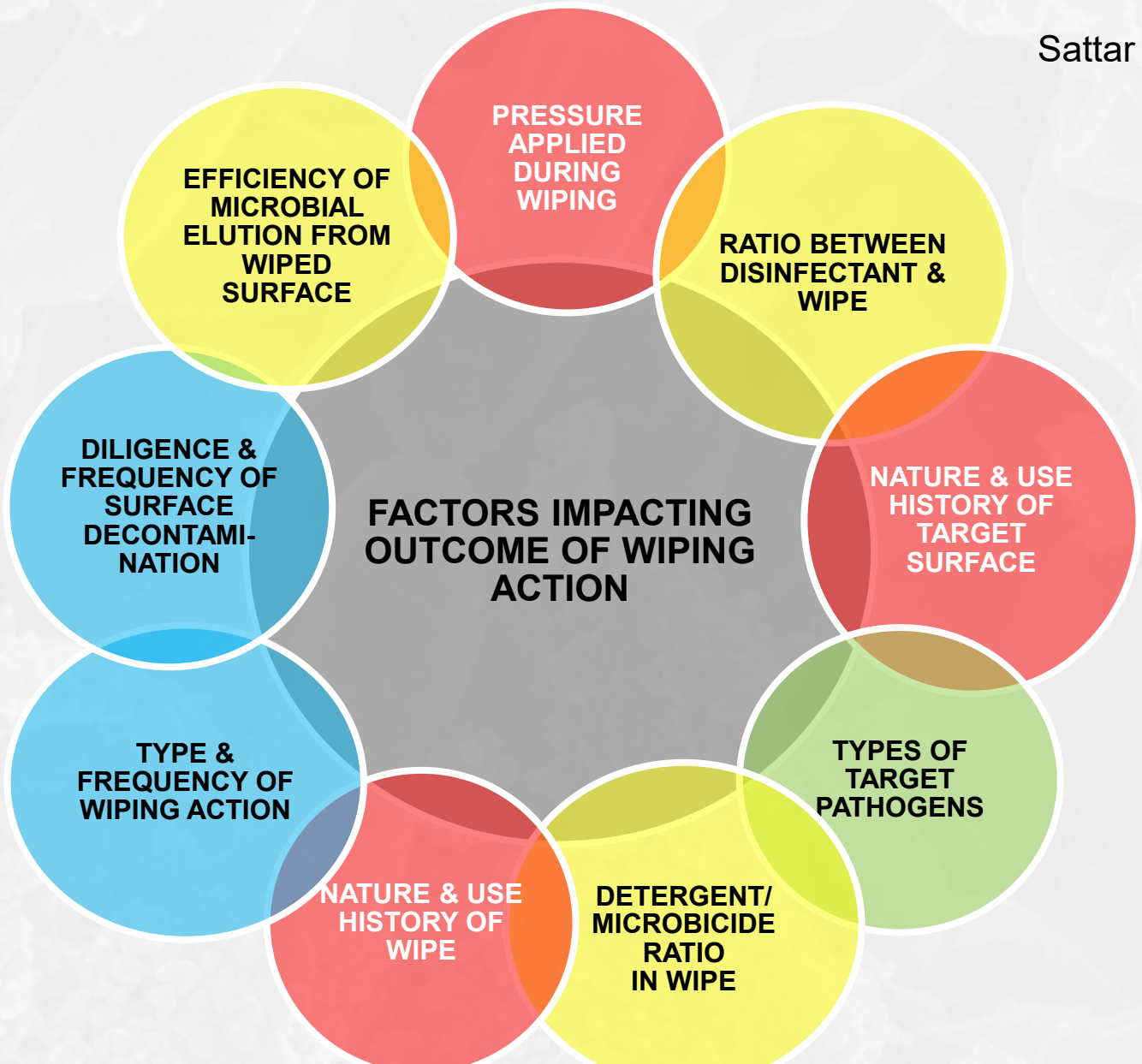
Extended-spectrum beta lactamases Enterobacteriaceae (ESBL)

Carbapenem-resistant Enterobacteriaceae (CRE)

Vancomycin-resistant enterococci (VRE).

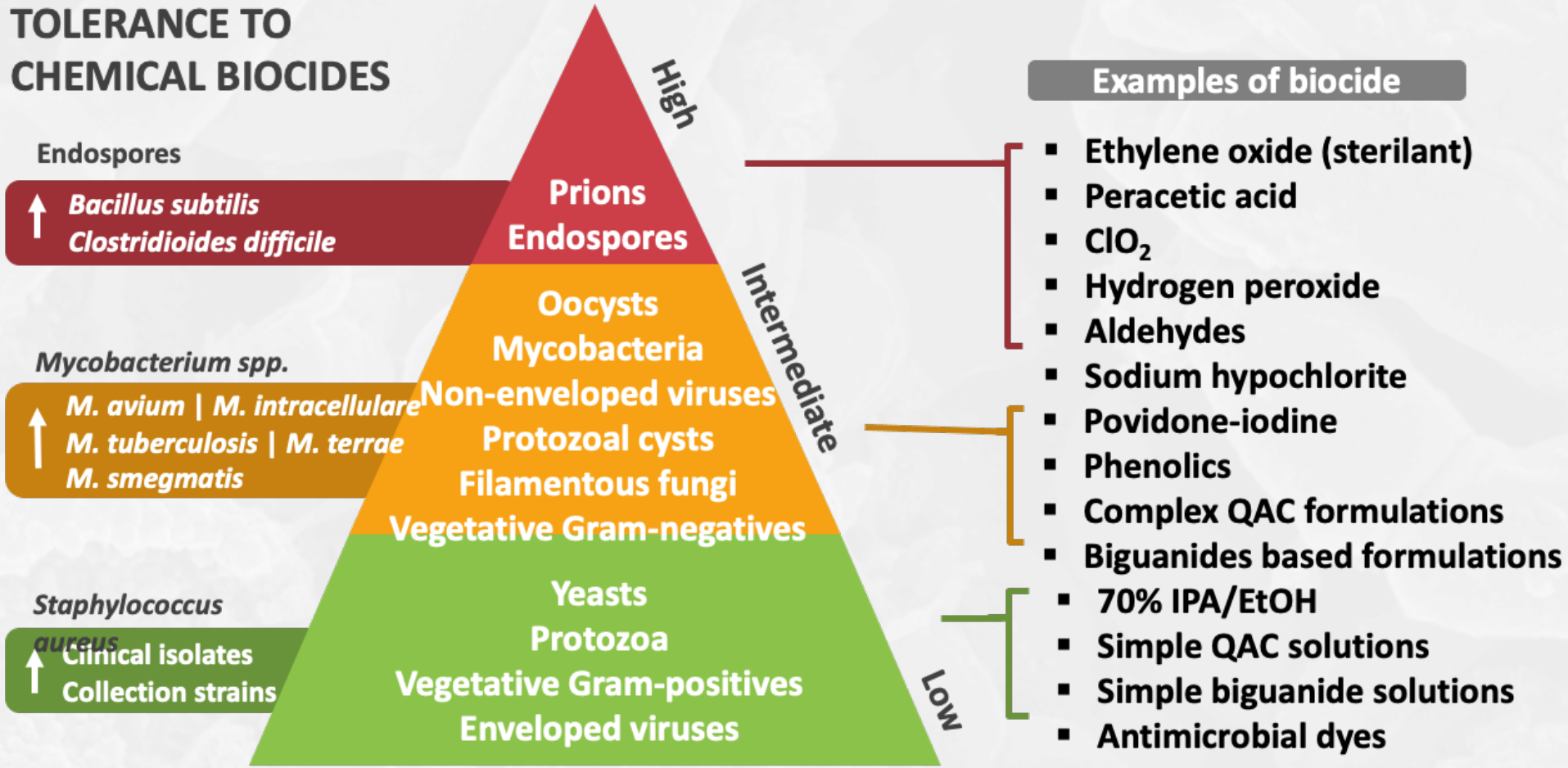
Factors impacting Disinfectant efficacy

Sattar & Maillard *Am J Infect Control* 2013 41;S97-S104



Factors impacting Disinfectant efficacy

Maillard & Pascoe. *Nature Rev Microbiol* 2023: doi.org/10.1038/s41579-023-00958-3



TARGETED PATHOGENS

Factors impacting Disinfectant efficacy

SPORICIDAL ACTIVITY

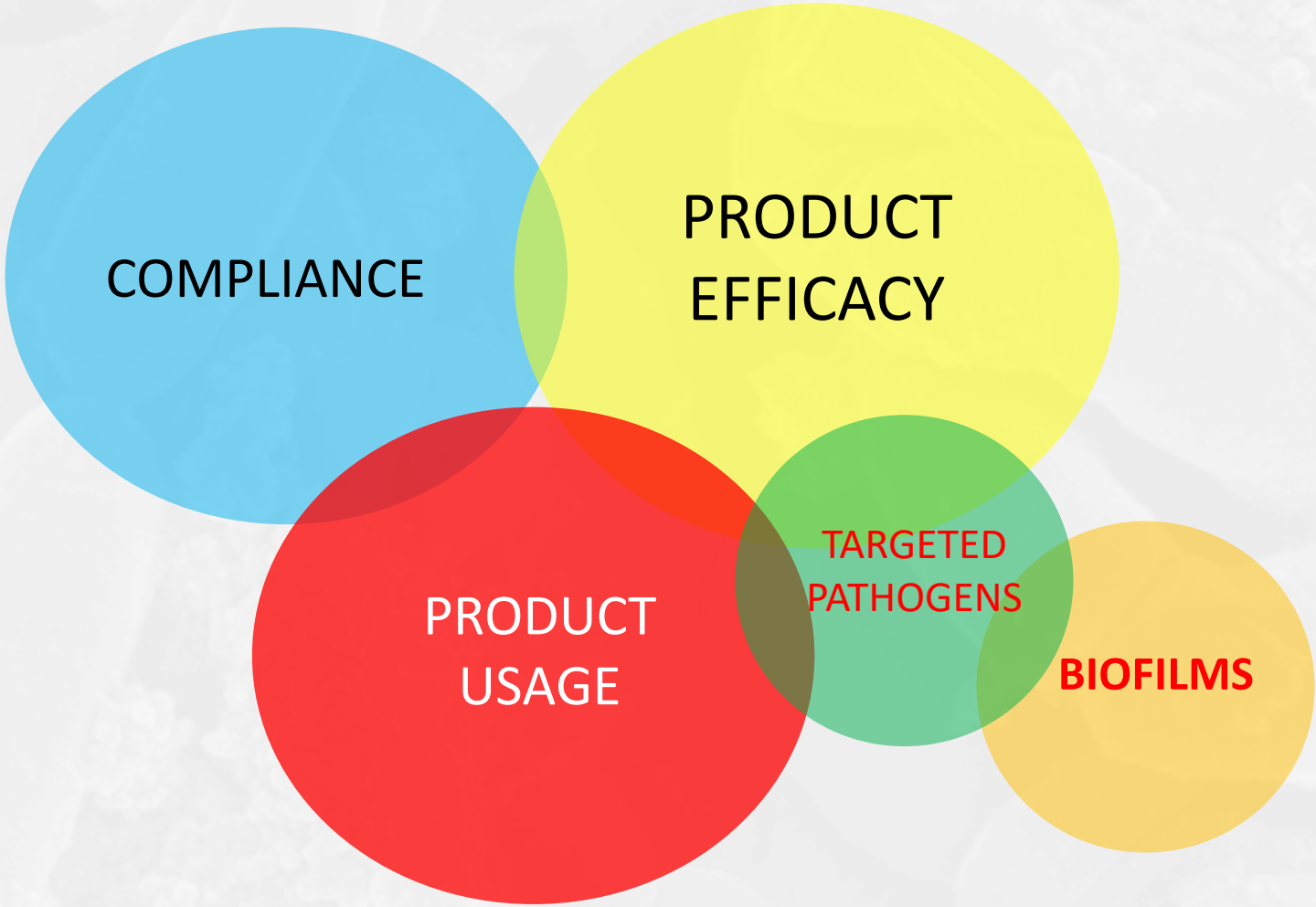
Russell AD. Clin Microbiol Rev 1990;3:99-119.

- Hydrogen peroxide
- Peracetic acid
- Chlorine dioxide
- Ozone
- Sodium hypochlorite
- Sodium dichlororisocyanurate (?)
- Chloramine-T
- Calcium hypochlorite
- Iodine and iodophors
- Ethylene oxide
- Glutaraldehyde
- Formaldehyde
- *ortho*-phthalaldehyde

NOT SPORICIDAL

- Phenols and cresols
- Quaternary ammonium compounds
- Biguanides
- Organic acids and esters
- Alcohols

Factors impacting Disinfectant efficacy



Importance of biofilm in healthcare settings

Centeleghe et al. Infect Prev Pract 2024;6:100357

Isabella Centeleghe

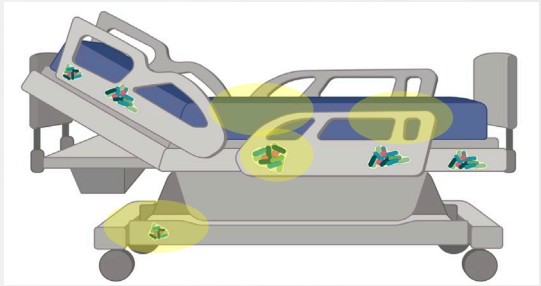
- 137 healthcare professionals completed the online survey
- 87.6% of all participants had heard of the term biofilm
- 83.9% knew what the term biofilm means.
  - Medical device (86.1%)
  - Drain biofilm (76.5%)
  - 39.1% knew about dry surface biofilms

Biofilms-related parameters to consider

Drain Biofilms

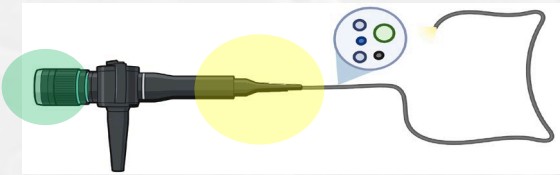
- Reduced microbicidal effect
- Decreasing biofilm biomass
- Regrowth post-intervention

Dry Surface Biofilms



- Reduced microbicidal effect
- Preventing transfer – ensuring the surface is safe
- Detection

Medical device biofilms



- Effective elimination of all microorganisms in all the medical device parts

  Regrowth post-intervention

Importance of biofilm in healthcare settings

Adapted from Otter *et al. J Hosp Infect* 2015; 89:16e27

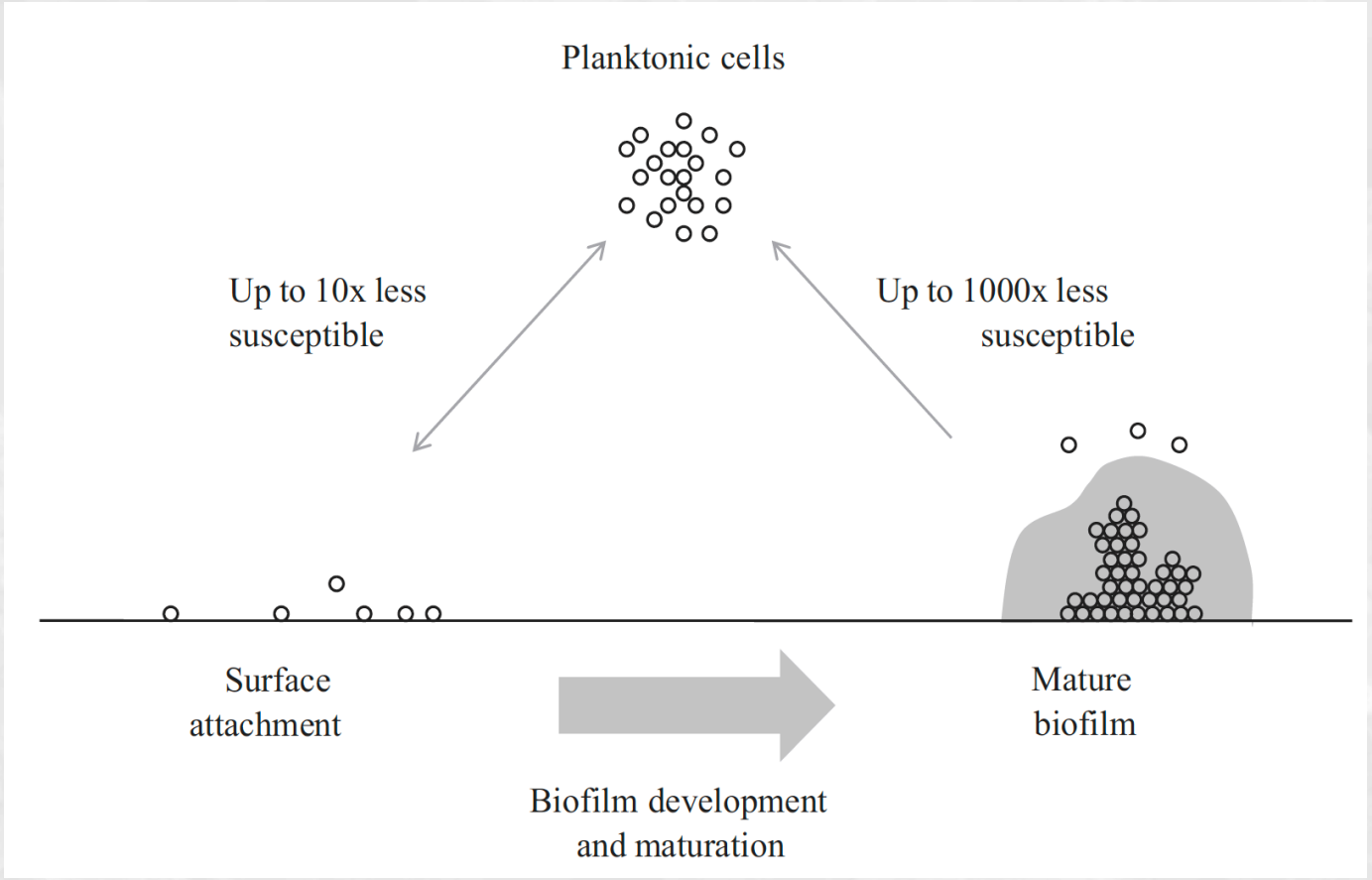
Susceptibility to disinfection

Planktonic suspension

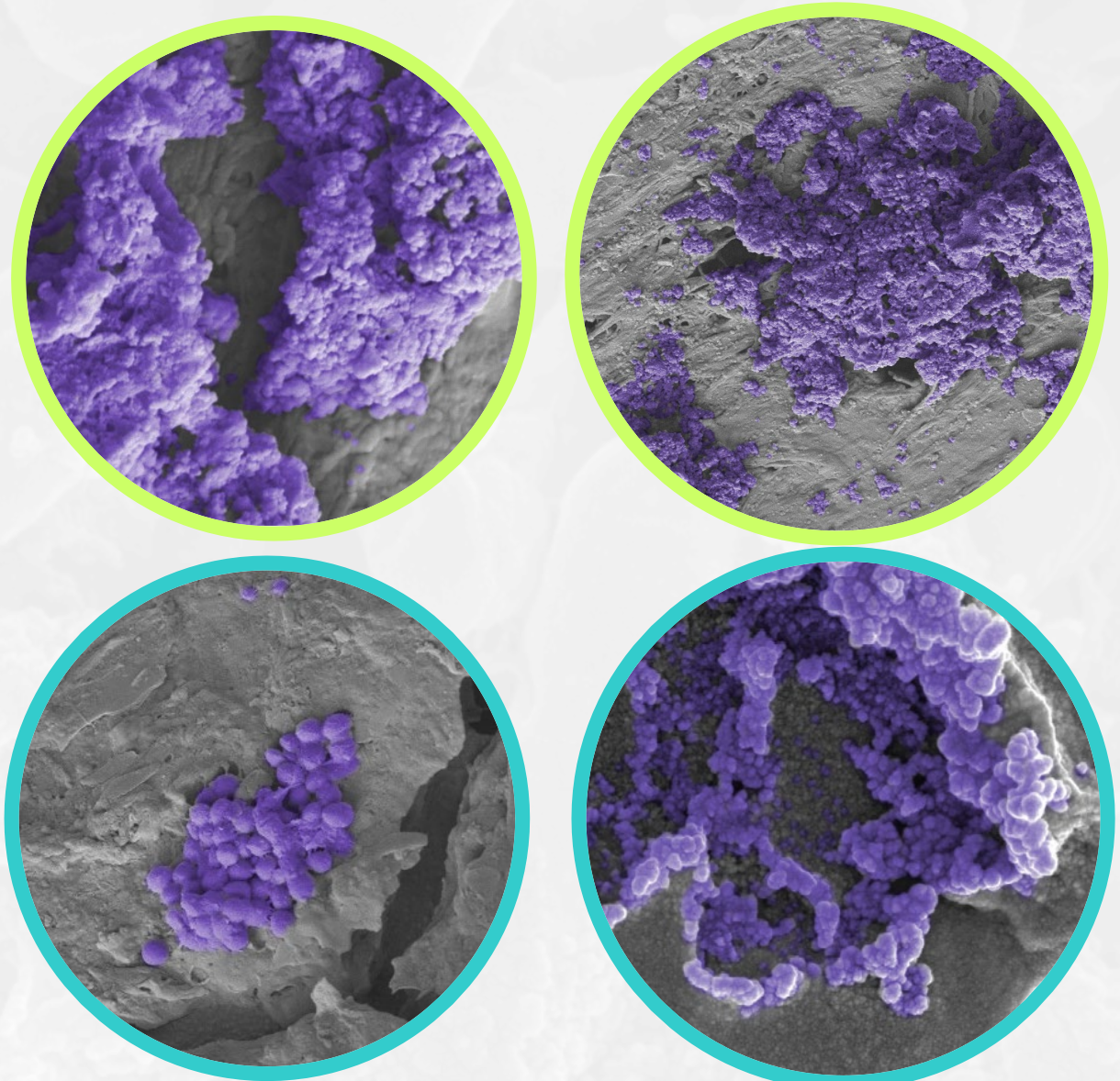
Planktonic dried on surfaces

Hydrated biofilms

Dry surface biofilms



DSB in healthcare settings



Ledwoch et al. J Hosp Infect 2018;100:3:e47-e56

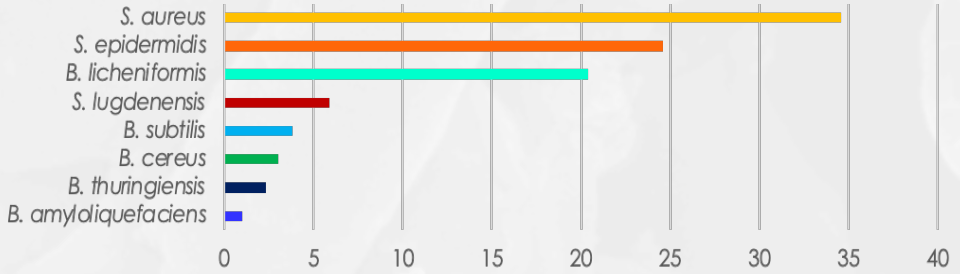
- Dry surface biofilms are **widespread** on surfaces in hospitals (**90-95 % surfaces sampled**)
- DSB contribute to pathogens survival **despite cleaning and disinfection**
- DSB **cannot be detected** by swabbing or contact plates when surfaces are dried

DSB composition

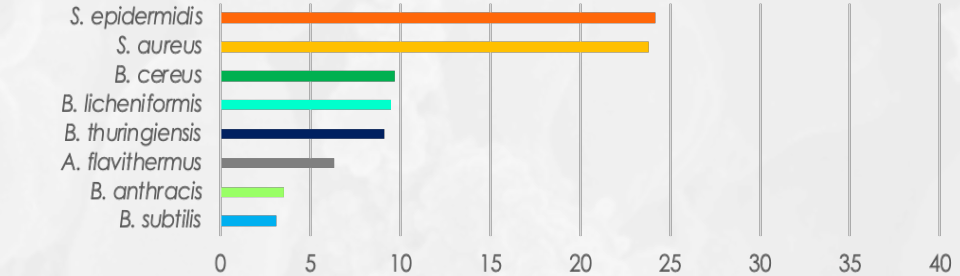
Ledwoch et al. J Hosp Infect 2018;100:3:e47-e56

Next Generation Sequencing (16s rRNA)

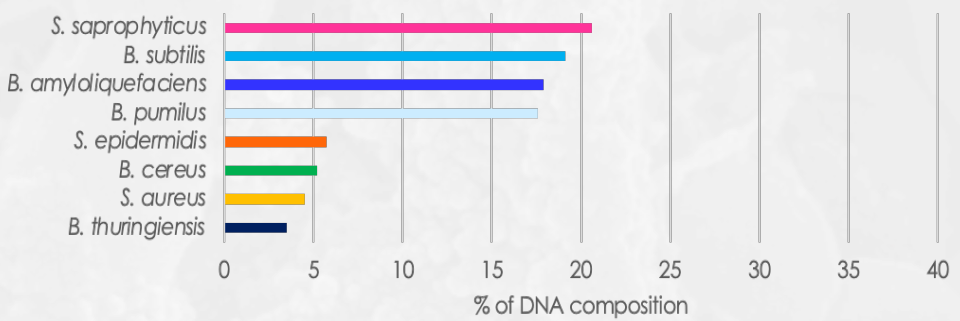
A



B

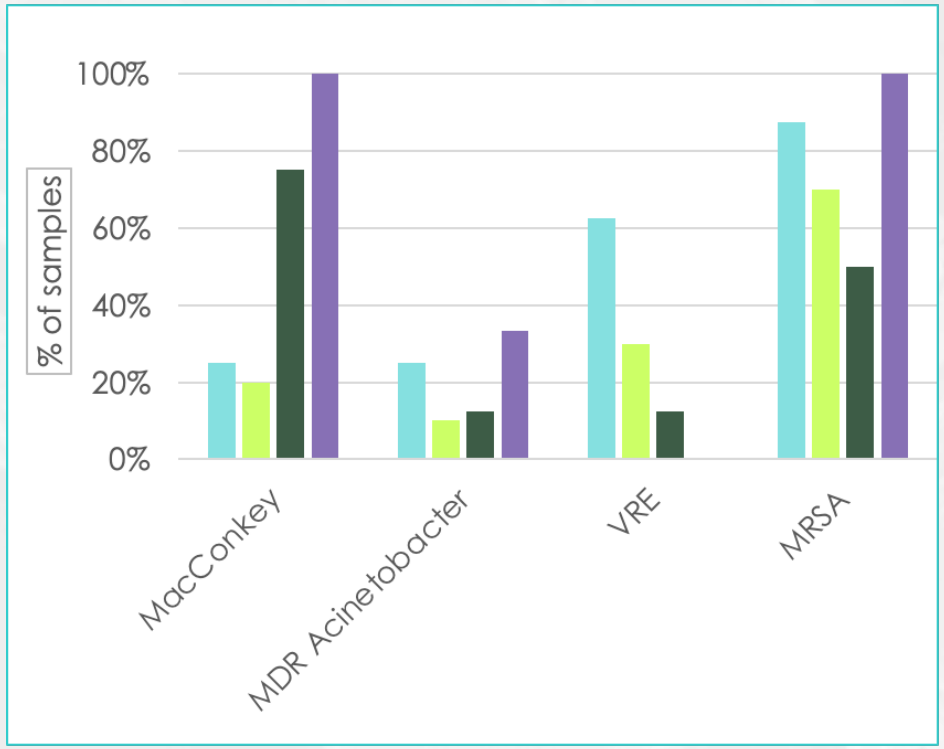


C



Ledwoch et al. J Hosp Infect 2021;112:3:31-6

Selective agar



Keyboard samples from:
- WH - Welsh Hospital
- SH - Scottish Hospital
- EH - English Hospital
- SD - Scottish Dental practice

DSB in healthcare settings

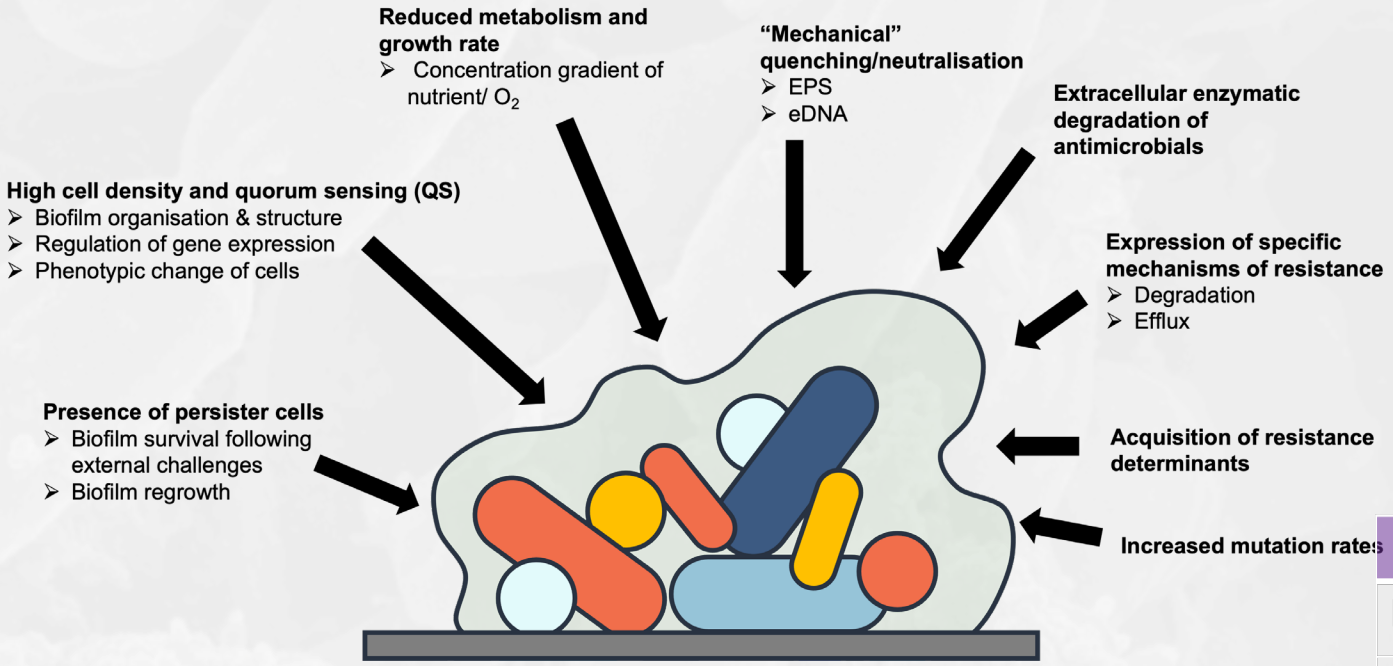
Ledwoch et al. J Hosp Infect 2021;112:31-36.

Keyboard sample number	Origin	Healthcare facility	Bacteria from DSB detected (+) / not detected (-)	
			Transfer test after wiping with sterile water[2]	Transfer test after wiping with NaOCl 1,000 ppm[2]
1	Wales	1,000-bed hospital	+	+
2			+	-
3			-	-
4			-	-
5	Scotland	500-bed hospital	+	-
6			+	+
7			-	+
8			+	-
9	England	1,700-bed hospital	-	+
10			+	+
11			+	-
12	Scotland	Dental practice	+	+
13			+	+
Total			9/13	7/13

- Pathogens from 69% of samples could be transferred following wet wiping with sterile water.
- 54% of samples continued to transfer bacteria following 1,000 ppm NaOCl treatment.

Dry surface biofilm *vs*. hydrated biofilms

Maillard & Centeleghe. *Antimicrob Res Infect Control* 2023;12:95.



TARGETED PATHOGENS

	DSB	Hydrated biofilms
EPS	✓	✓
eDNA	?	✓
Depth (gradients)	✗	✓
Desiccation	✓	✗
Reduced metabolism	✓	✓
Persister cells	?	✓

Efficacy of disinfectants against hydrated biofilms

Hydrated biofilms

- Complex microbial communities formed and grown in wet /semi-wet habitats.
- Colonize various surfaces (drain, medical equipment)
- Clean + mechanical action + disinfection

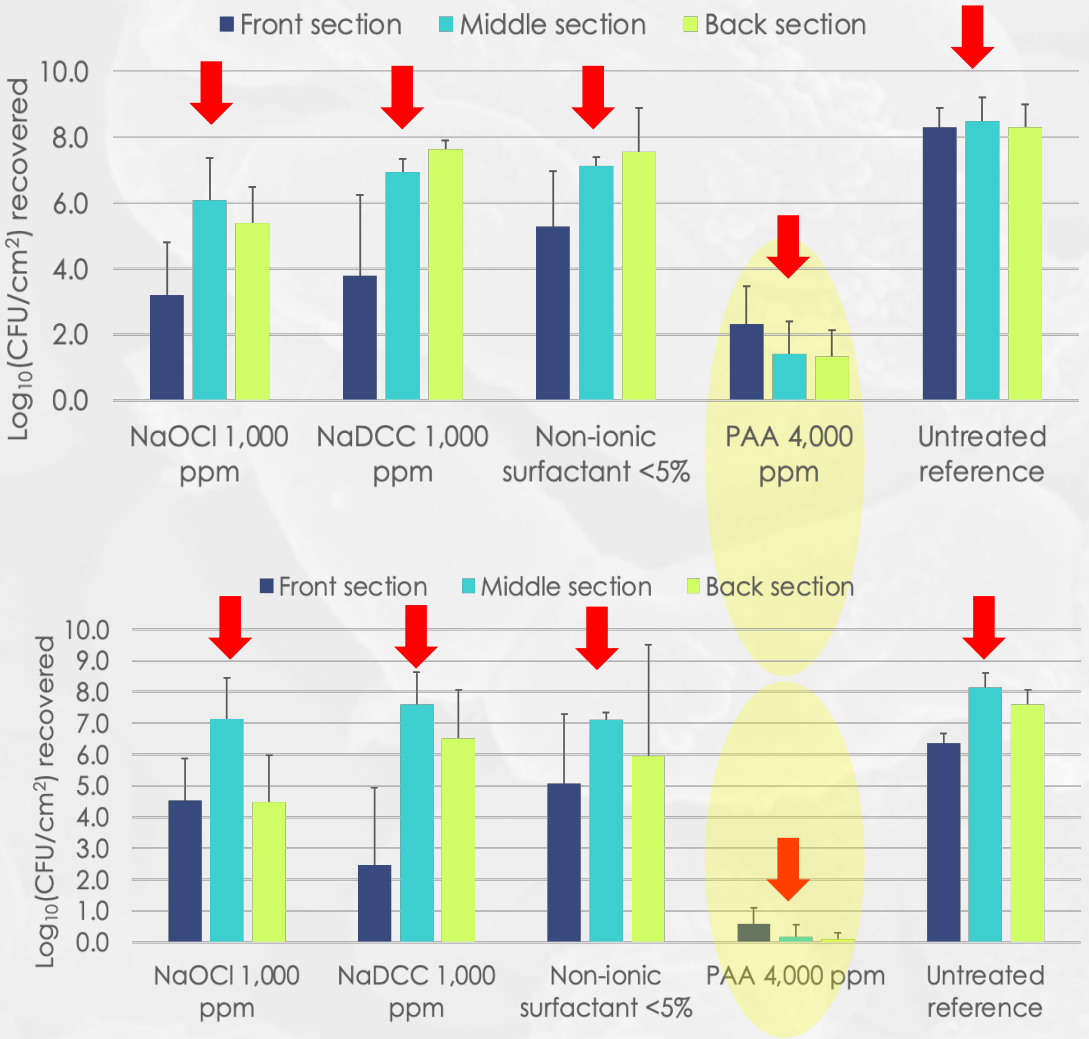
Disinfection

- Product treatment: 3 x 15 min doses

Regrowth test

- Drain biofilm bacteria recovered 4 days after product treatment

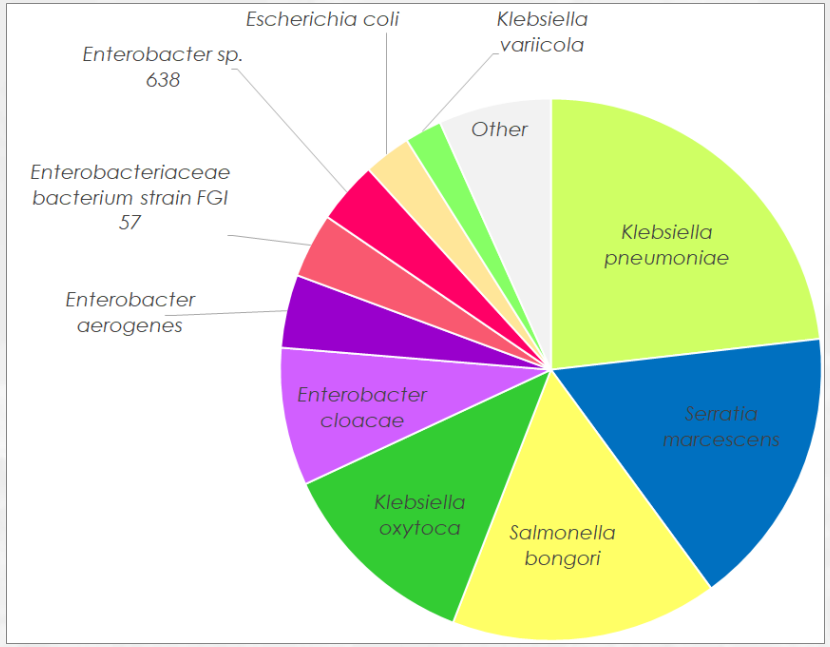
Ledwoch *et al. J Hosp Infect* 2020 106;757-764.



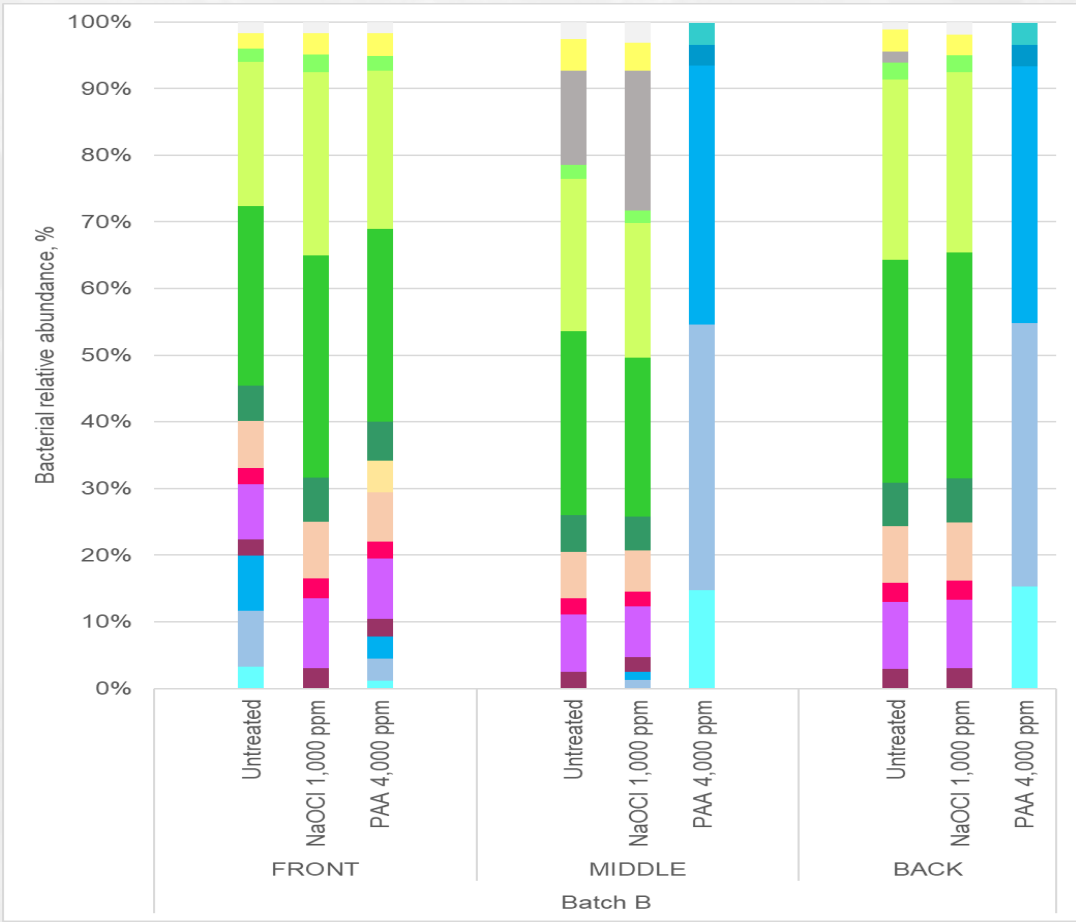
Efficacy of disinfectants against hydrated biofilms

Drain biofilms

- Complex microbial communities formed and grown in drain.
- Can migrate to sink and disperse around the sink (2 m)
- Associated with HAIs



Biofilm composition from the small-scale drain model after treatment & regrowth



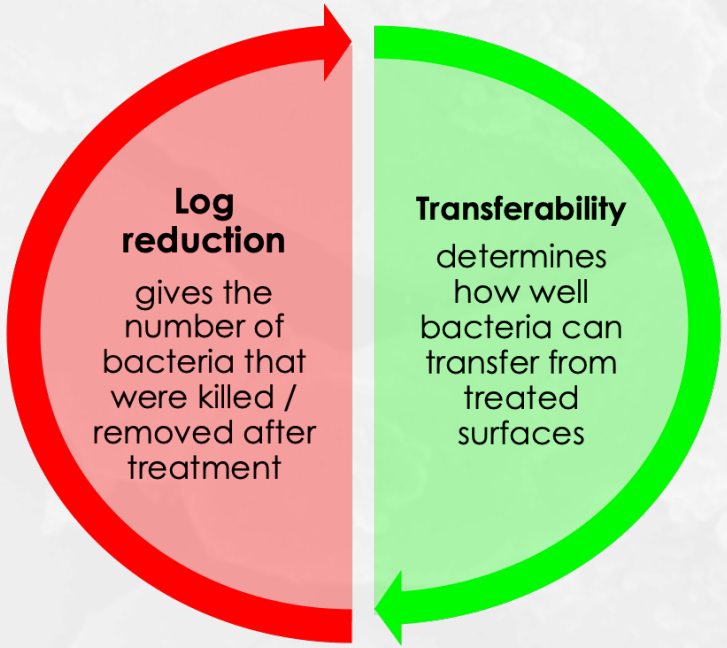
Efficacy of disinfectants against DSB

Ledwoch *et al. J Hosp Infect* 2021;112:31-36.

Treatment: 10 sec wiping (500 g)
+ 2 min residual time post wiping
ATM2967-15 "Wiperator test"

S. aureus NCTC10788 dry surface biofilm			Log_{10} reduction	Direct transferability
			log_{10}(CFU/ml)	no of contacts positive for bacterial growth
Treatment	**Concentration /power**	**pH**	■≥4, ■<4	■<2, ■>2
BZK	< 0.5%	5.41	4.9 ± 2.4	0.0 ± 0.0
ClO_2	1,000 ppm	4.31	3.0 ± 0.3	31.0 ± 8.7
NaOCl-Ref	1,000 ppm	11.31	4.3 ± 1.3	33.3 ± 3.1
NaOCl-2	1,000 ppm	13.13	2.9 ± 0.4	2.7 ± 4.6
PAA-1	3,500 ppm	8.82	6.3 ± 0.8	0.7 ± 1.2
PAA-2	250 ppm	7.74	6.1 ± 1.5	36.0 ± 0.0
VHP	7% hydrogen peroxide 5% acetic acid 0.4% peracetic acid	n/a	0.8 ± 0.7	36.0 ± 0.0
CAP	$P_{discharge}$ = 34.5 W	n/a	0.8 ± 0.0	36.0 ± 0.0
Water	n/a	6.99	2.3 ± 0.4	36.0 ± 0.0
No treatment		n/a	n/a	36.0 ± 0.0

Wipe



Efficacy of disinfectants against DSB

Ledwoch et al. ICHE 2021;2:1-7.

S. aureus NCTC10788 dry surface biofilm			Cross transferability (nitrile gloves) no of contacts positive for bacterial growth	Cross transferability (latex gloves) no of contacts positive for bacterial growth
Treatment	**Concentration /power**	**pH**	■<2, ■>2	■<2, ■>2
BZK	< 0.5%	5.41	4.3 ± 1.5	2.7 ± 2.5
ClO_2	1,000 ppm	4.31	2.3 ± 2.1	1.3 ± 1.2
PAA-1	3,500 ppm	8.82	0.7 ± 0.6	0.0 ± 0.0
PAA-2	250 ppm	7.74	0.0 ± 0.0	0.3 ± 0.6
APG	<1%	5.30	2.3 ± 1.2	4.7 ± 1.5
CP	0.2-0.5%	6.41	1.3 ± 0.6	2.7 ± 2.1
LDAO	0.5%	5.87	0.0 ± 0.0	2.3 ± 3.2
NIS	<5%	7.05	2.0 ± 2.0	2.0 ± 2.6
Water	n/a	6.99	3.0 ± 1.0	6.7 ± 1.5
No treatment		n/a	10 ± 3.0	7.0 ± 1.7

APG: Alkyl polyglucoside, CP: Capryl glucoside, LDAO: Lauryldimethylamine oxide, NIS: Non-ionic Surfactant

Treatment: 10 sec wiping (500 g)
+ 2 min residual time post wiping

- High transfer rates using gloves following the use of surfactants.
- Type of gloves matter with latex gloves performing worse than nitrile ones.

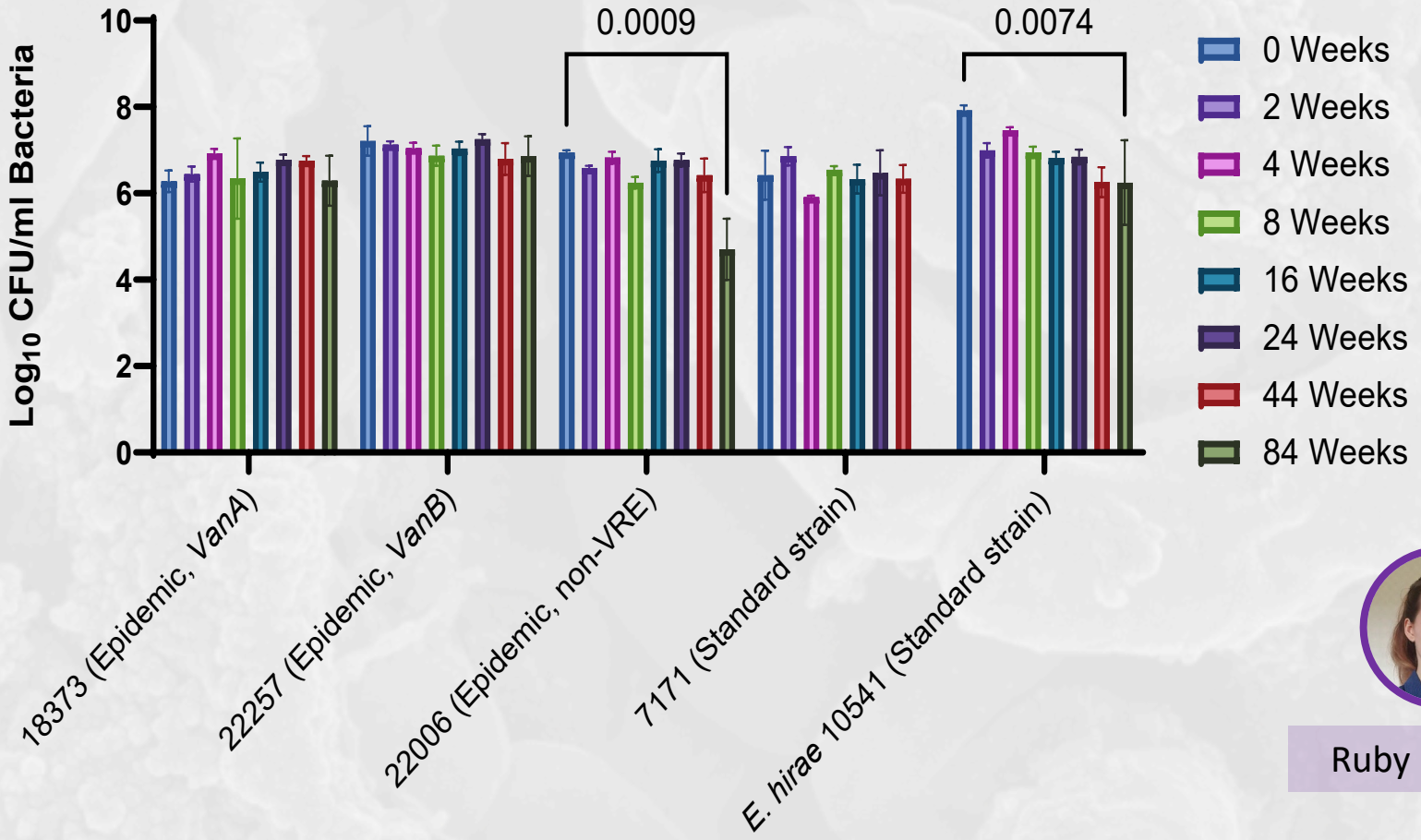
Persistence of DSB on surfaces

Harsent *et al. J Hosp Infect* ; under review

- *Enterococcus faecium* DSB & *E. hirae* on stainless steel disks

➢ > 84 weeks (20ºC; 55% RH)

➢ >6 Log_{10} recovered



Ruby Harsent

Clinical implication of DSB?

Otter *et al. Am J Infect Control* 2013;41:S6-11

American Journal of Infection Control 41 (2013) S6-S11

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Original research article

Evidence that contaminated surfaces contribute to the transmission of hospital pathogens and an overview of strategies to address contaminated surfaces in hospital settings

Jonathan A. Otter PhD [a,b,*], Saber Yezli PhD [b], James A.G. Salkeld BSc [b], Gary L. French MD, FRCPath [a]

[a] Centre for Clinical Infection and Diagnostics Research (CIDR), Department of Infectious Diseases, King's College London & Guy's and St. Thomas' NHS Foundation Trust, London, UK
[b] Bioquell, Andover, Hampshire, UK

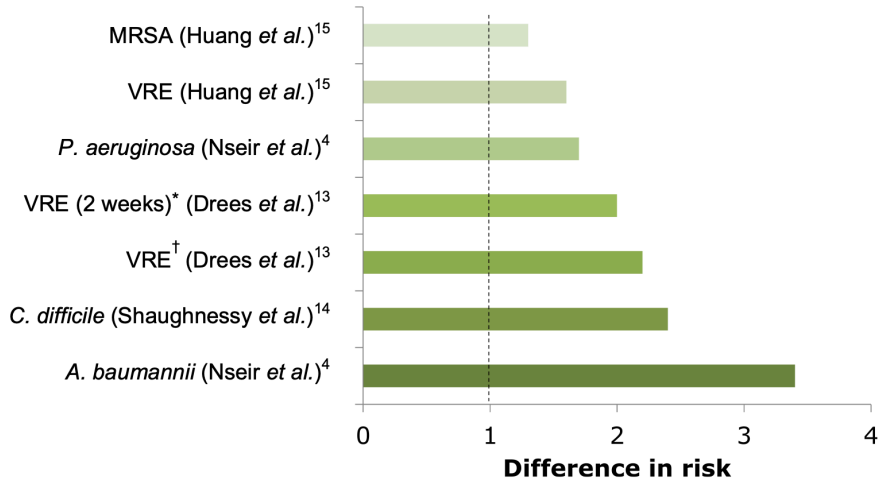


Fig 1. Chart showing the increased risk associated with the prior room occupant. The figures of difference in risk are unadjusted based on raw data. Several of the studies included adjusted measures of risk, but these were not included because of differences in study design. * Any patient infected or colonized with VRE in the two weeks prior to admission. † The immediate prior room occupant was known to be infected or colonized with VRE.

Mitchell *et al. Infect Dis Health* 2023;28:290-7.

Infection, Disease & Health xxx (xxxx) xxx

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ScienceDirect

journal homepage: http://www.journals.elsevier.com/infection-disease-and-health/

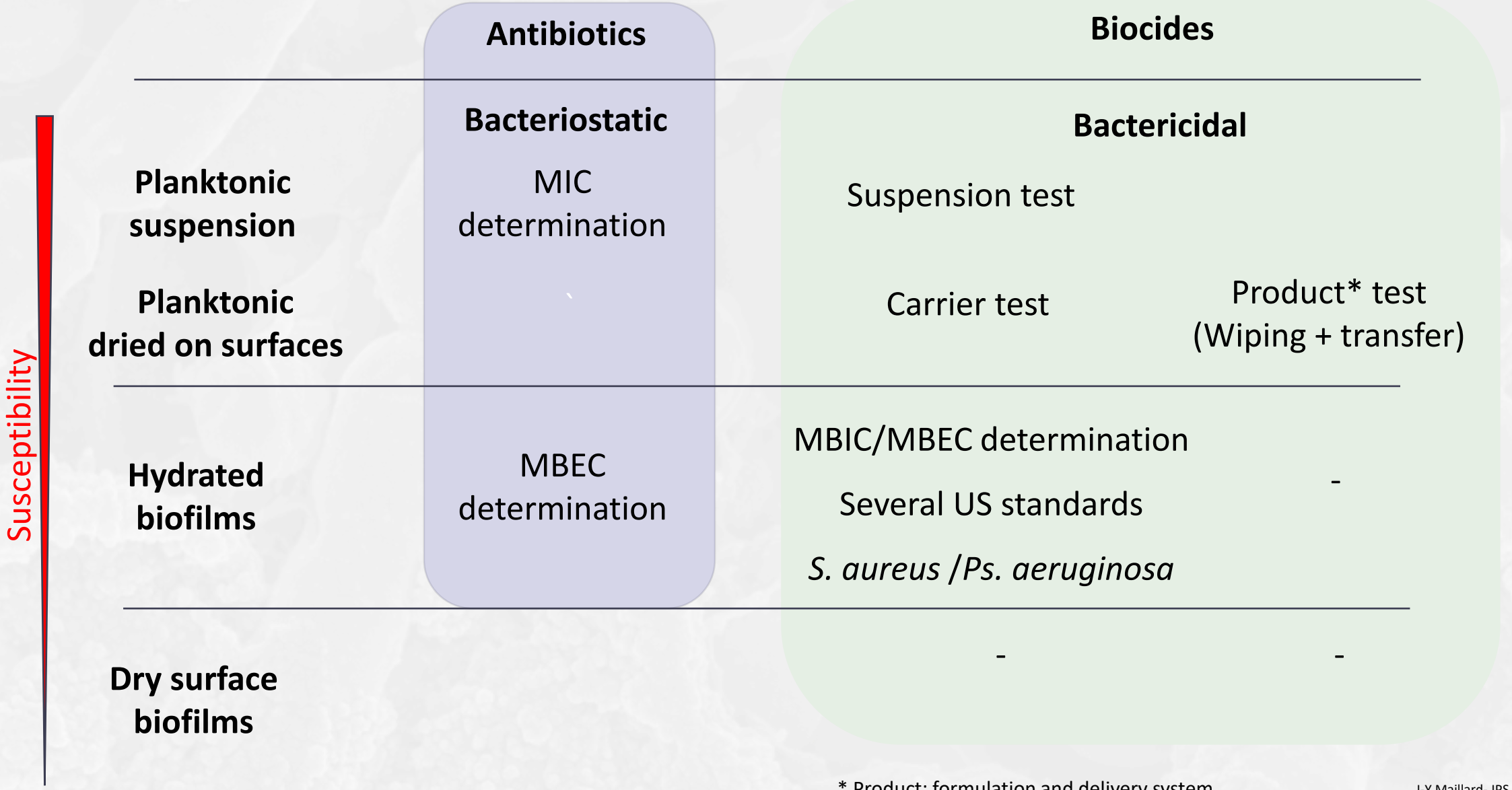
Review

Risk of organism acquisition from prior room occupants: An updated systematic review

Brett G. Mitchell [a,b,c,d,*], Julee McDonagh [e,f], Stephanie J. Dancer [g], Sindi Ford [h,i], Jenny Sim [j,k,l,m], Bismi Thottiyil Sultanmuhammed Abdul Khadar [d,k], Philip L. Russo [b,n,o], Jean-Yves Maillard [p], Helen Rawson [q], Katrina Browne [a,b], Martin Kiernan [b,r]

- The risk of pathogen acquisition remains high; pooled acquisition odds ratio for all the pathogens was 2.45 (95% CI: 1.53-3.93]
- Support the need for a clean environment to reduce the risk of healthcare associated infections.

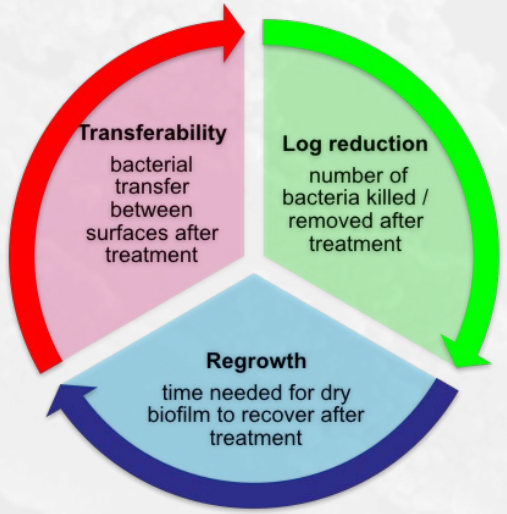
Biofilms susceptibility to disinfectants

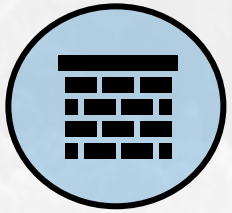


* Product: formulation and delivery system

Biofilms susceptibility to disinfectants

- No “wet” standard biofilm test protocol in Europe
  - Product claim? Ad hoc testing
  - Knowing the end points: **Reduction in viability + regrowth**
  - Review data but need to understand protocol





- No dry surface biofilm standard test protocol
  - Product claim? Ad hoc testing
  - Knowing the end points – **Reduction in viability + transfer**
  - Review data but need to understand protocol

Acknowledgments

Dr Katrina Duggan

Dr Katarzyna Ledwoch

Dr Isabella Centeleghe

Dr Ruby Harsent