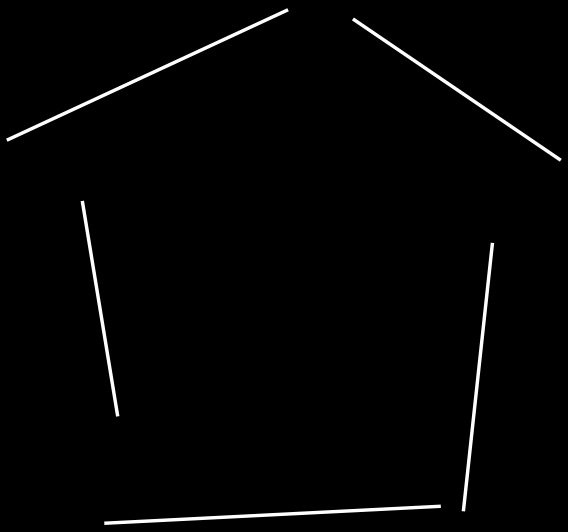
Prof Hugo Sax, MD, Department of Infectious Diseases, Bern University Hospital, University of Bern, saxhealthdesign.com Switzerland

Hospital transmission networks

What do we know?

www.webbertraining.com December 8, 2022

Chapter 1. How we see things.



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Mental models.

4

https://jamesclear.com/mental-models

Mental models.

Mental models are the thinking tools to understand life, make decisions, and solve problems.
They are imperfect, fluid, and fuzzy but useful.
They are unconscious, which makes them treacherous.

https://jamesclear.com/mental-models

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Transmission?

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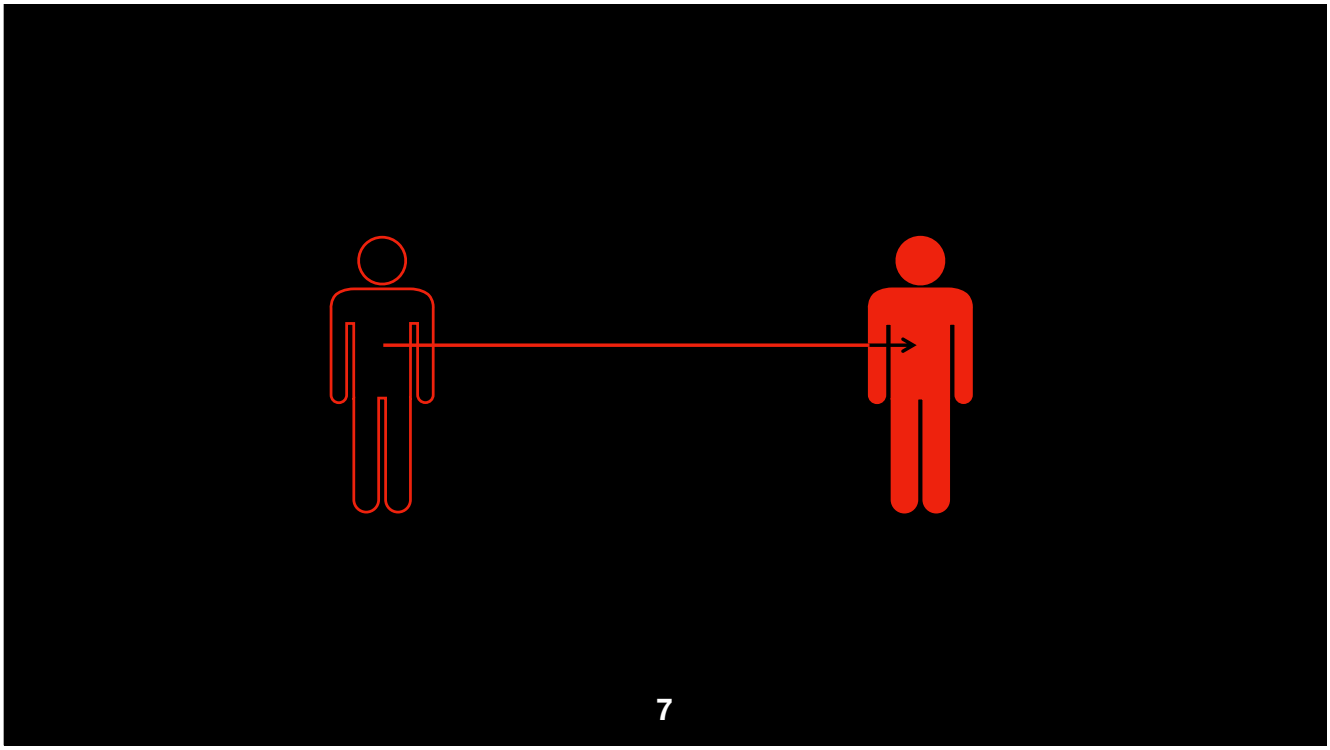

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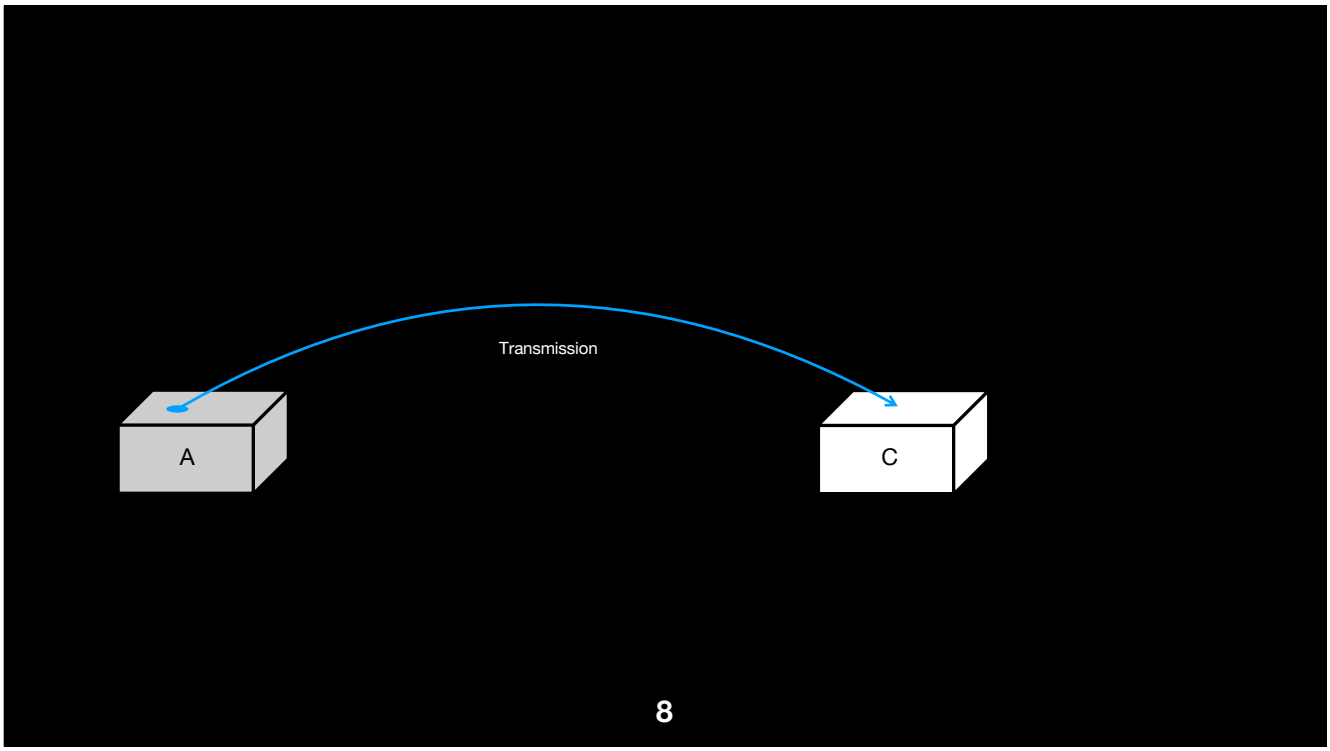

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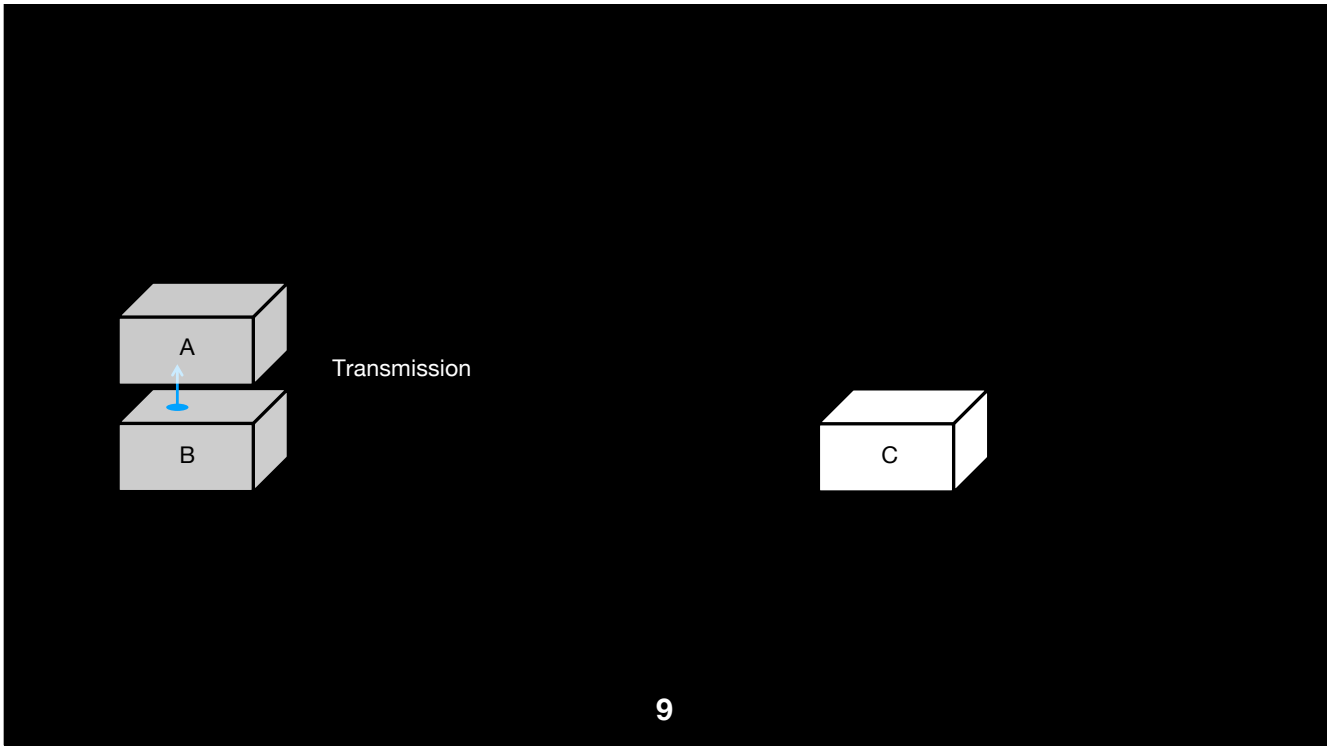
A
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Transmission
C
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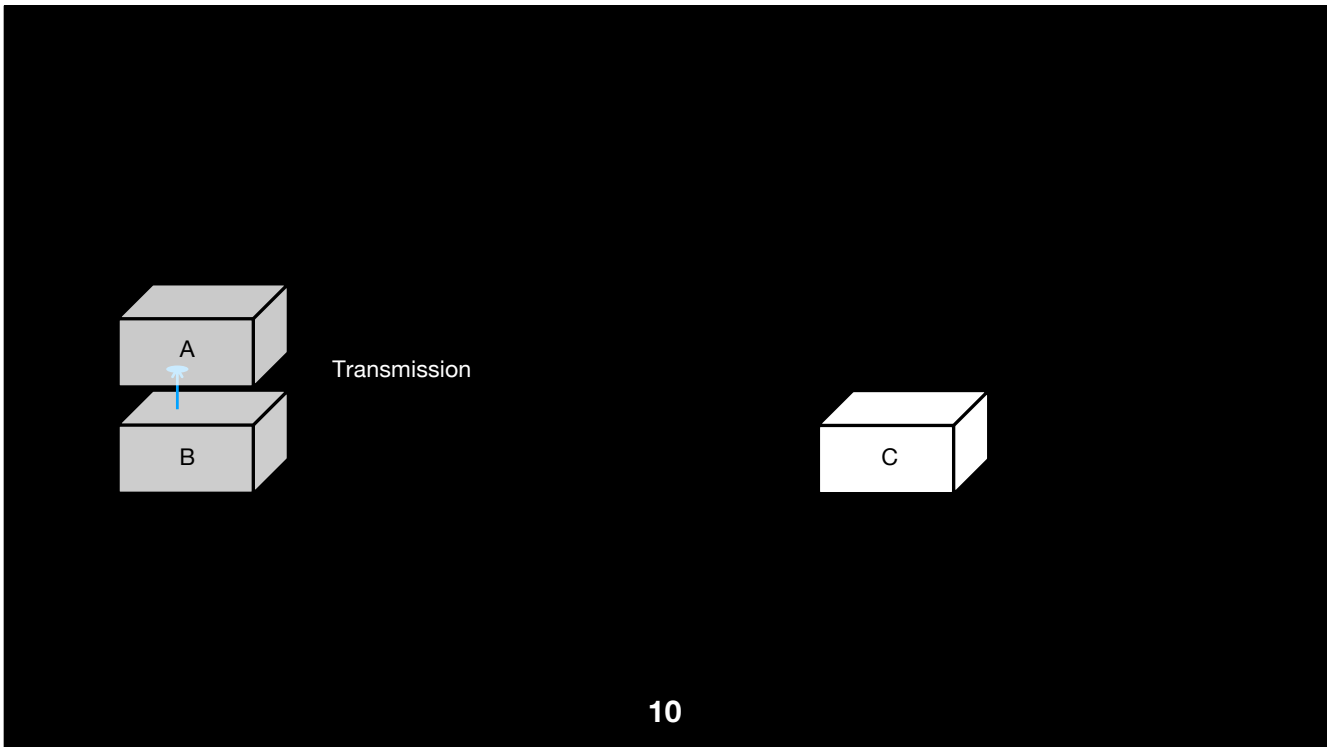
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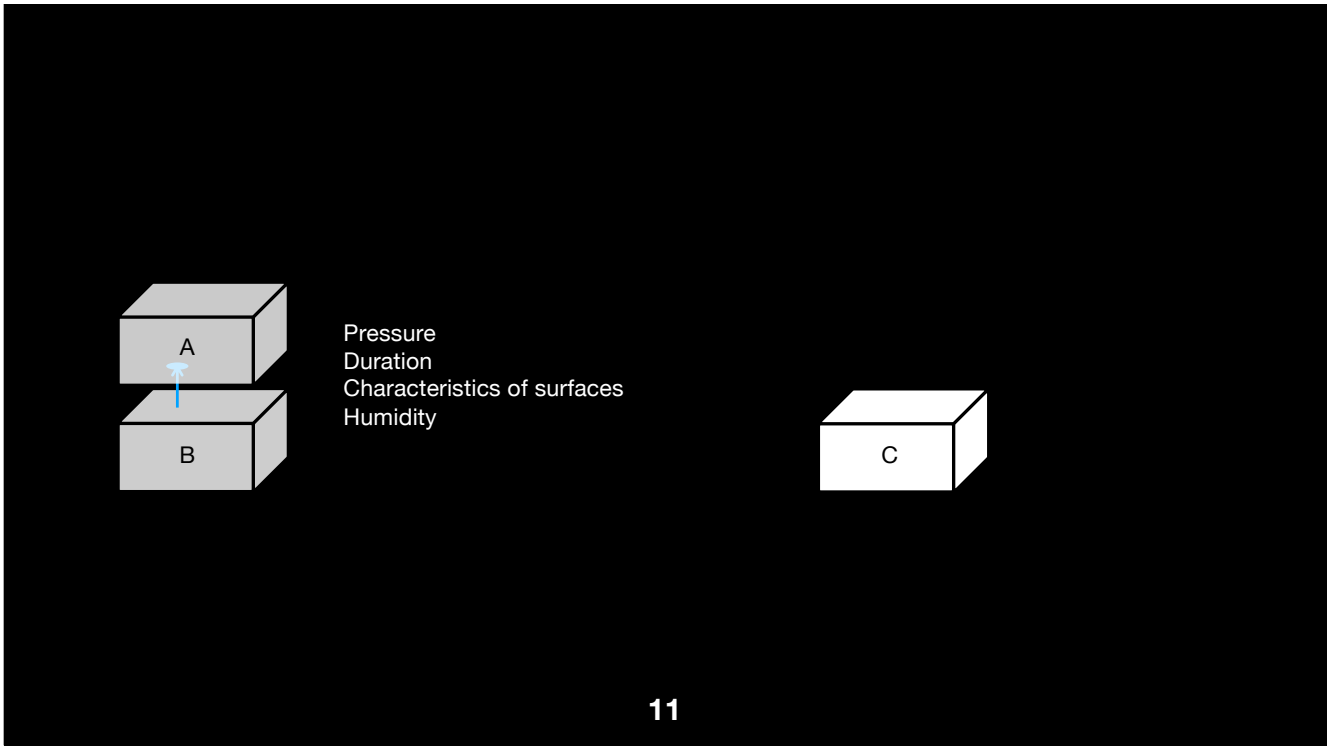
A
B
Pressure
Duration
Characteristics of surfaces
Humidity
C
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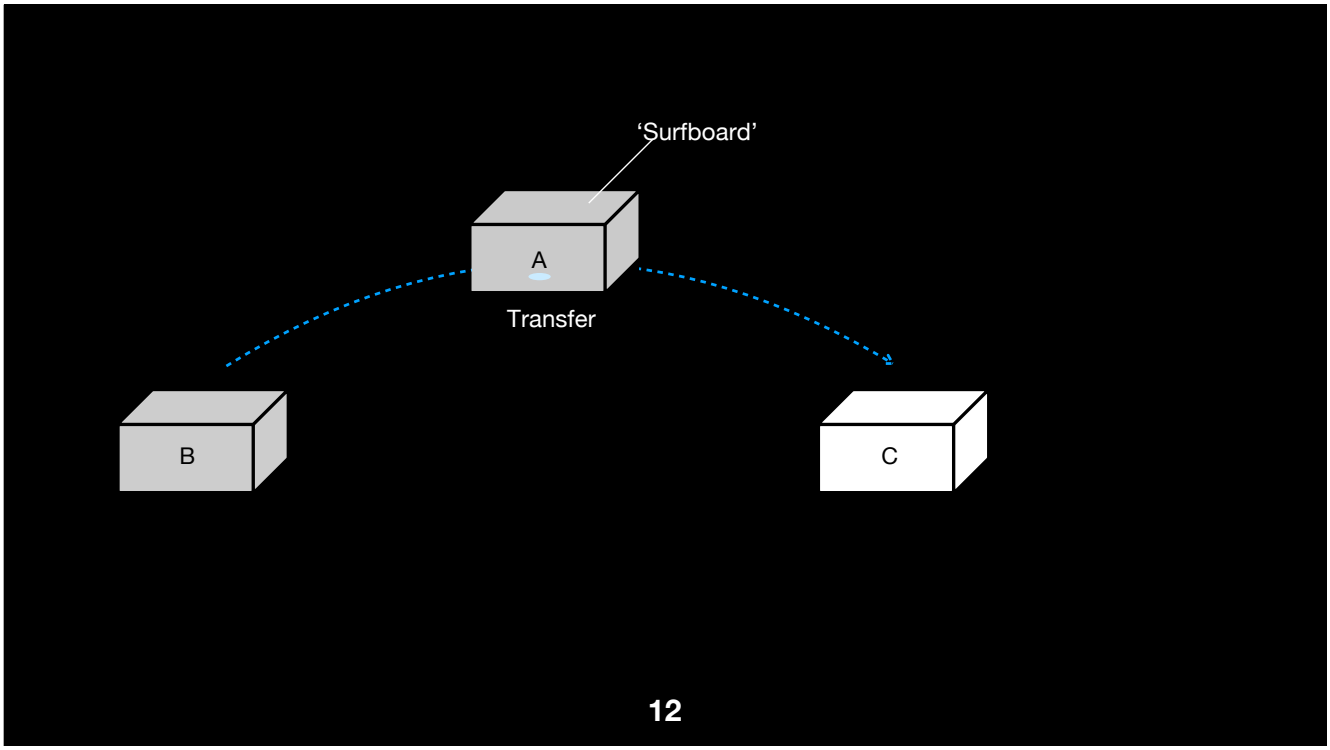
'Surfboard'
A
Transfer
B
C
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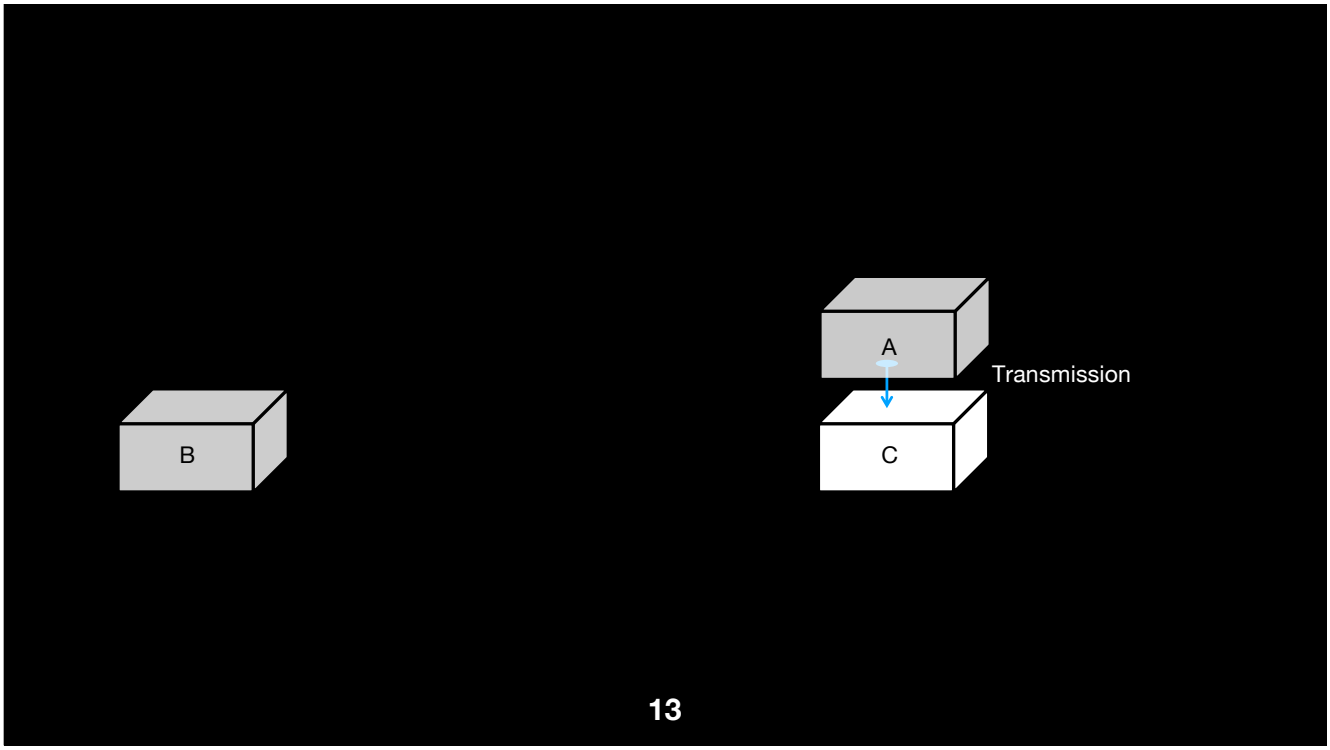
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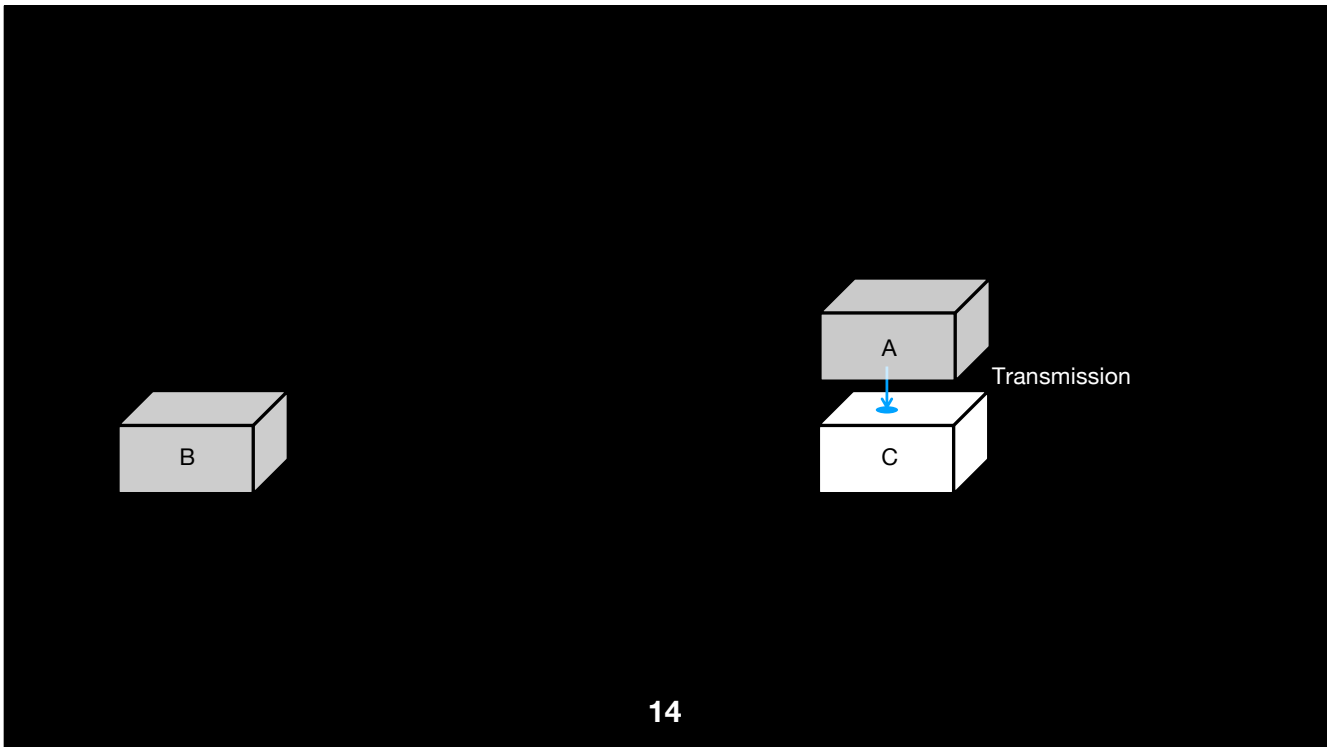
A
Transmission
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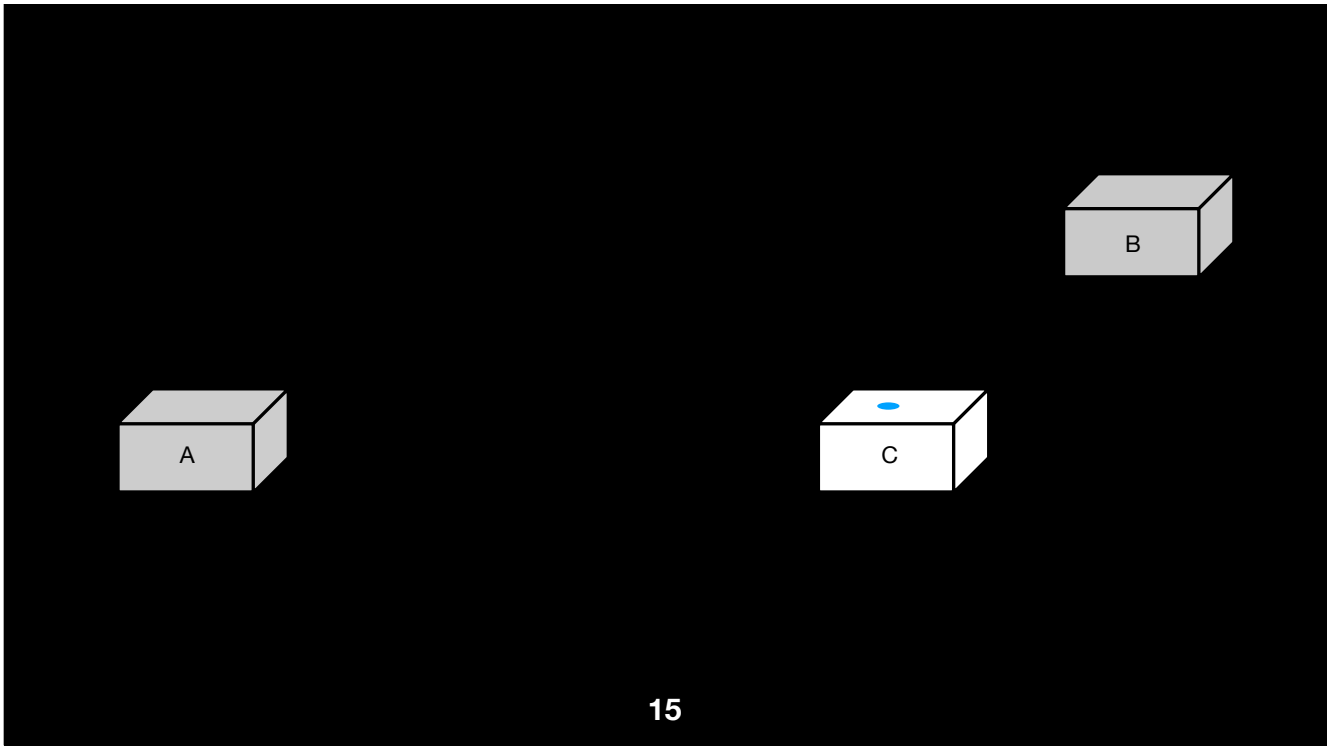

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Colonisation or infection?

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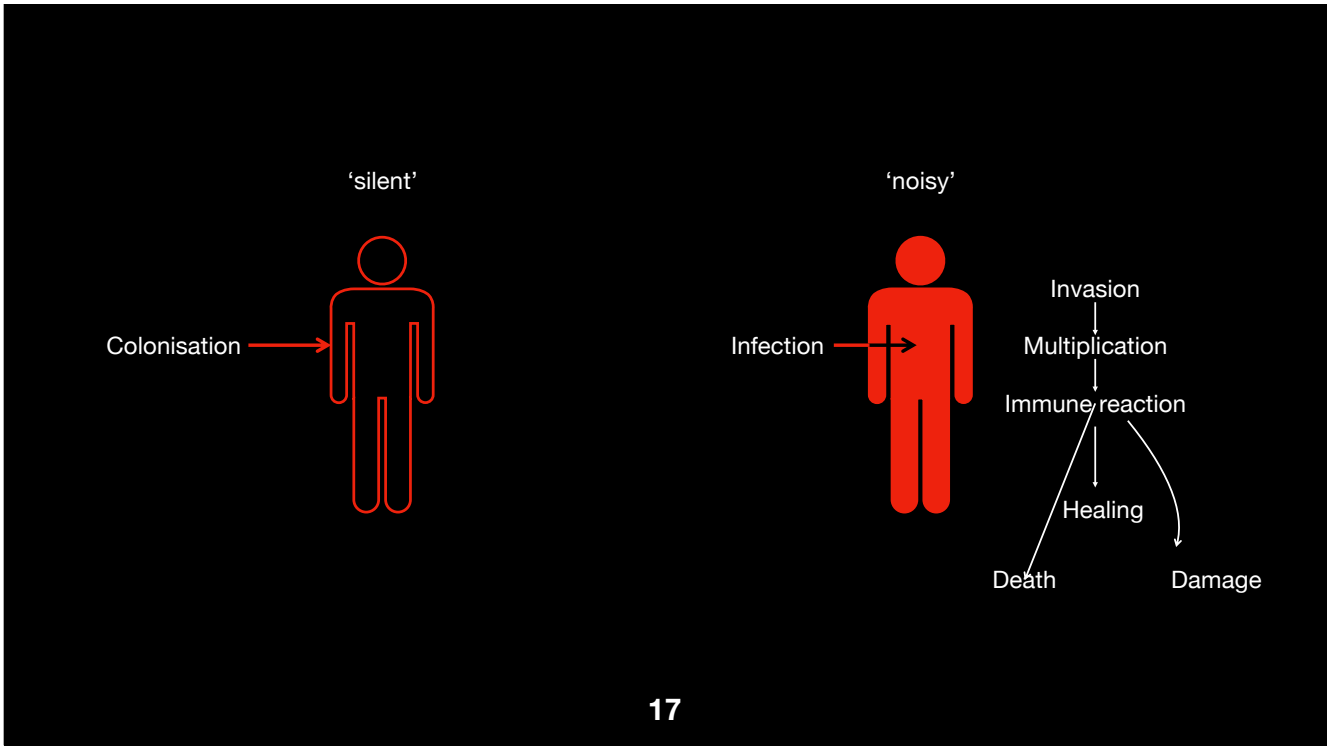
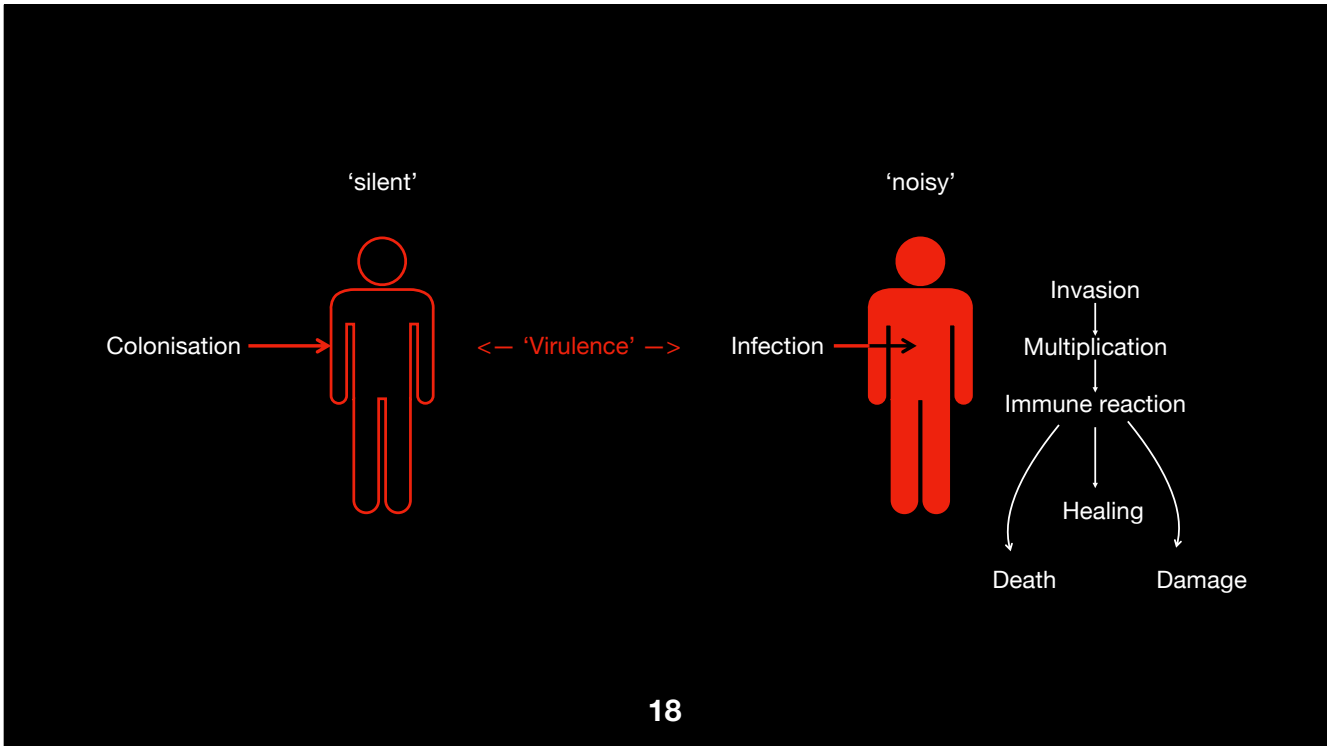

'silent'
'noisy'
Colonisation
Infection
Invasion
Multiplication
Immune reaction
Healing
Death
Damage
17


'silent'
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Colonisation
<— 'Virulence' —>
Infection
Invasion
Multiplication
Immune reaction
Healing
Death
Damage
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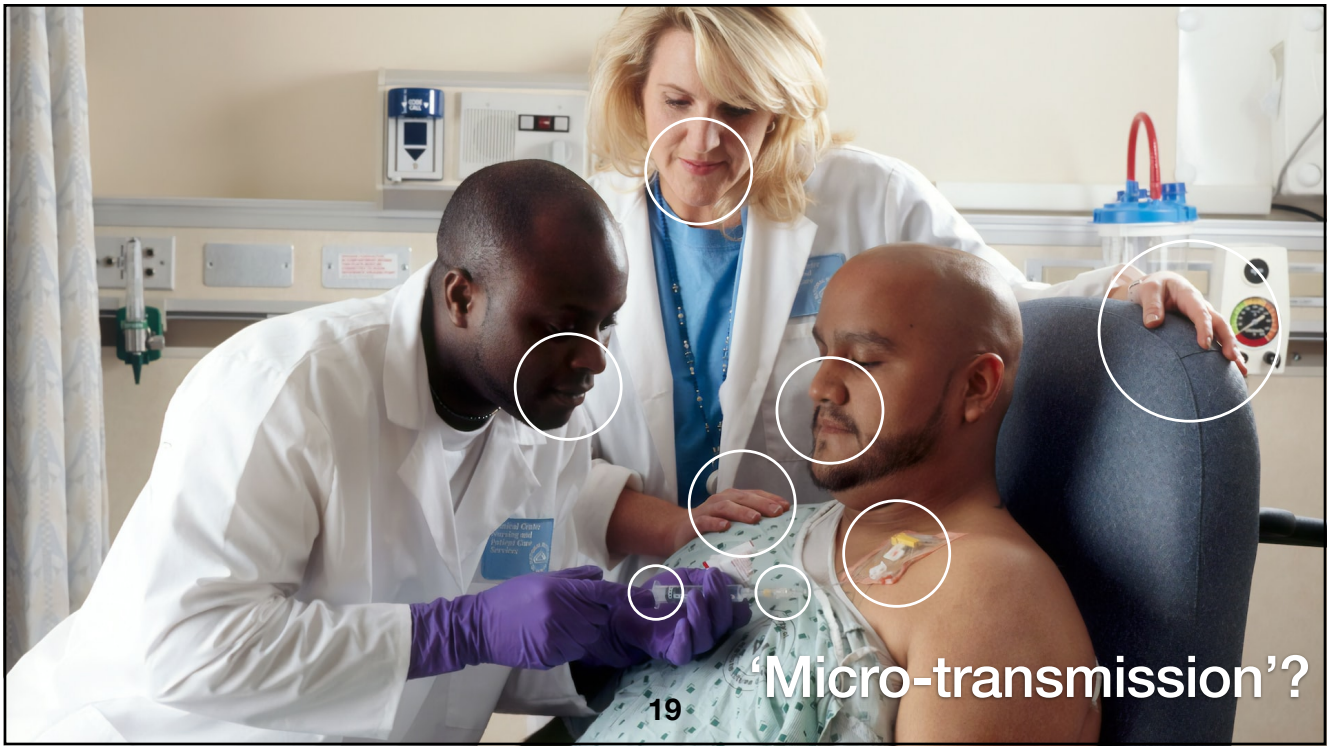

How do we imagine infections?

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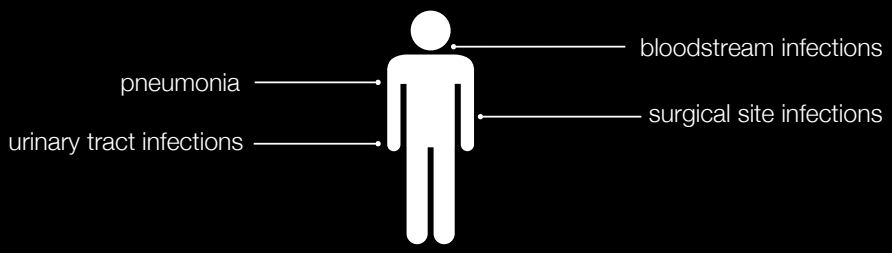
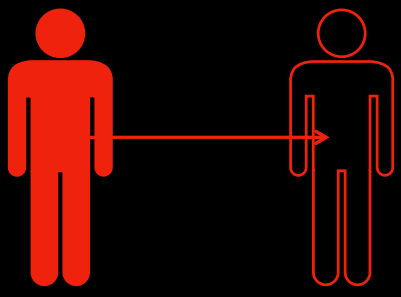


~85% of all healthcare-associated infections



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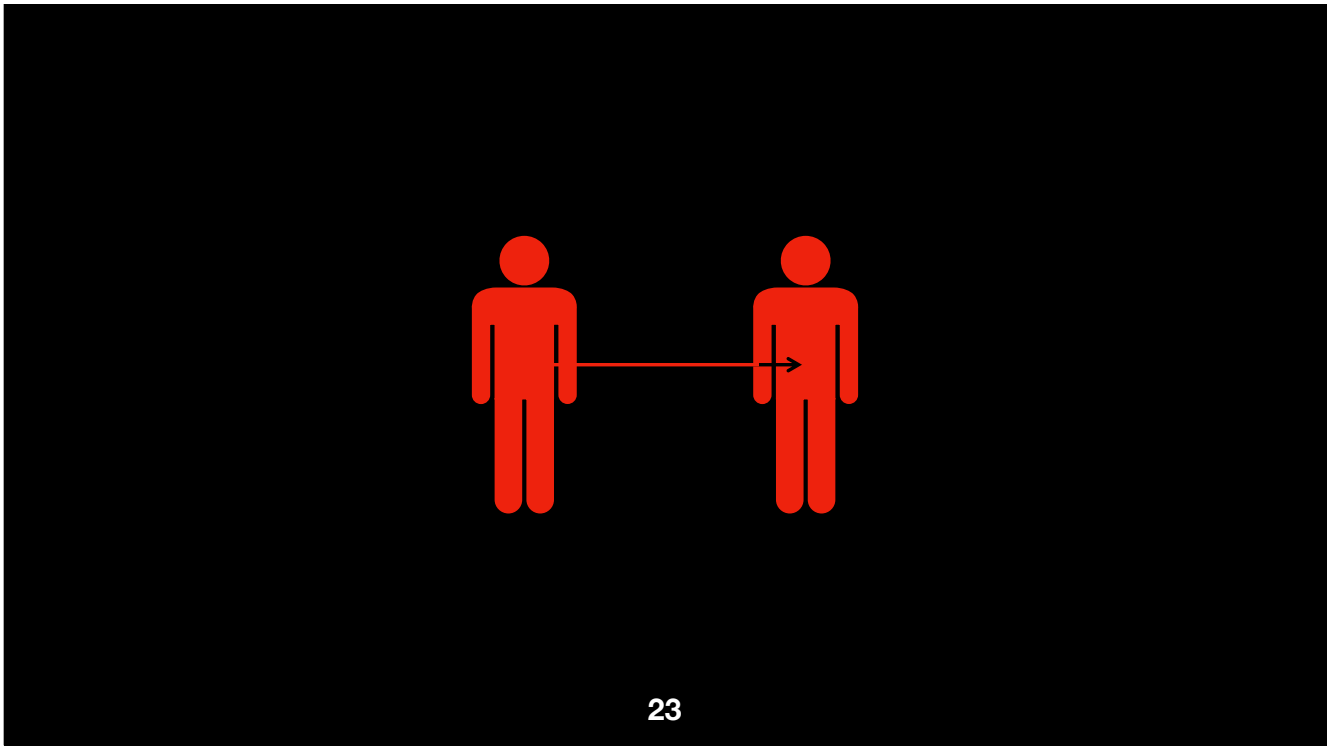

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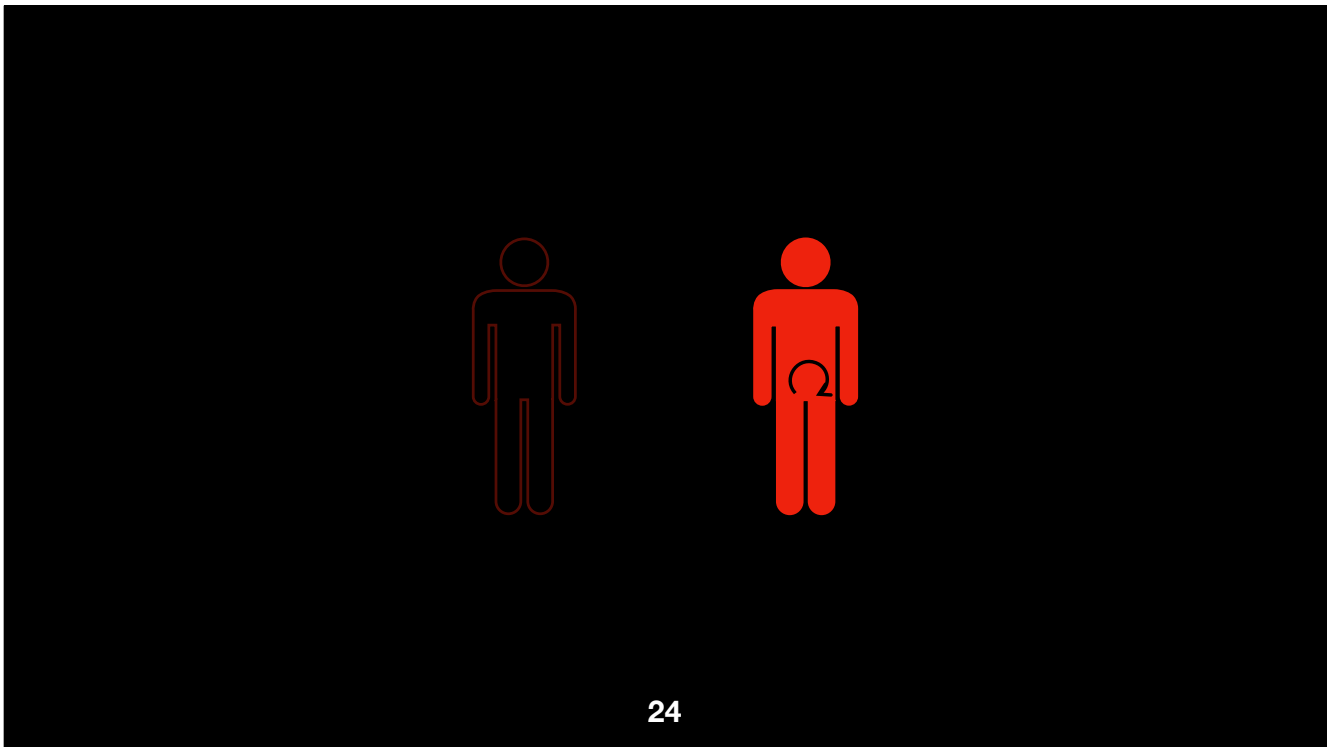

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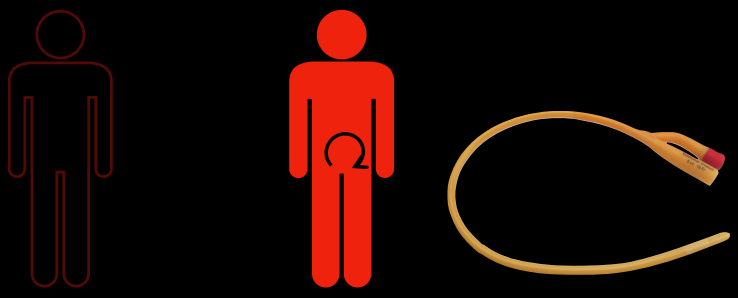

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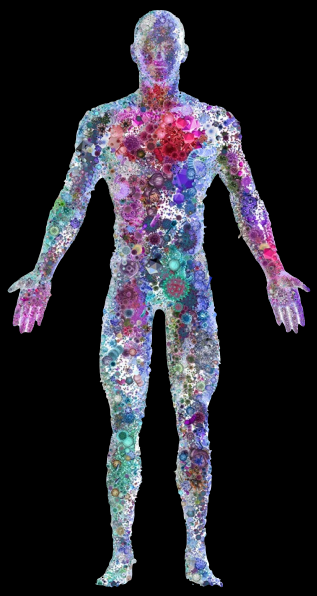
Where are the ‘germs’?

26



40 trillion bacteria
30 trillion human cells

27

Ron Sender, Shai Fuchs, Ron Milo: Are We Really Vastly Outnumbered? Revisiting the Ratio of Bacterial to Host Cells in Humans, in: Cell 164, January 28, 2016 | Luckey, T.D.: Am. J. Clin. Nutr. 25, 1292–1294 (1972).

https://dirt.asla.org/2018/06/25/designing-cities-for-healthier-human-microbiomes/microbiome/

Microbiome / Microbiota

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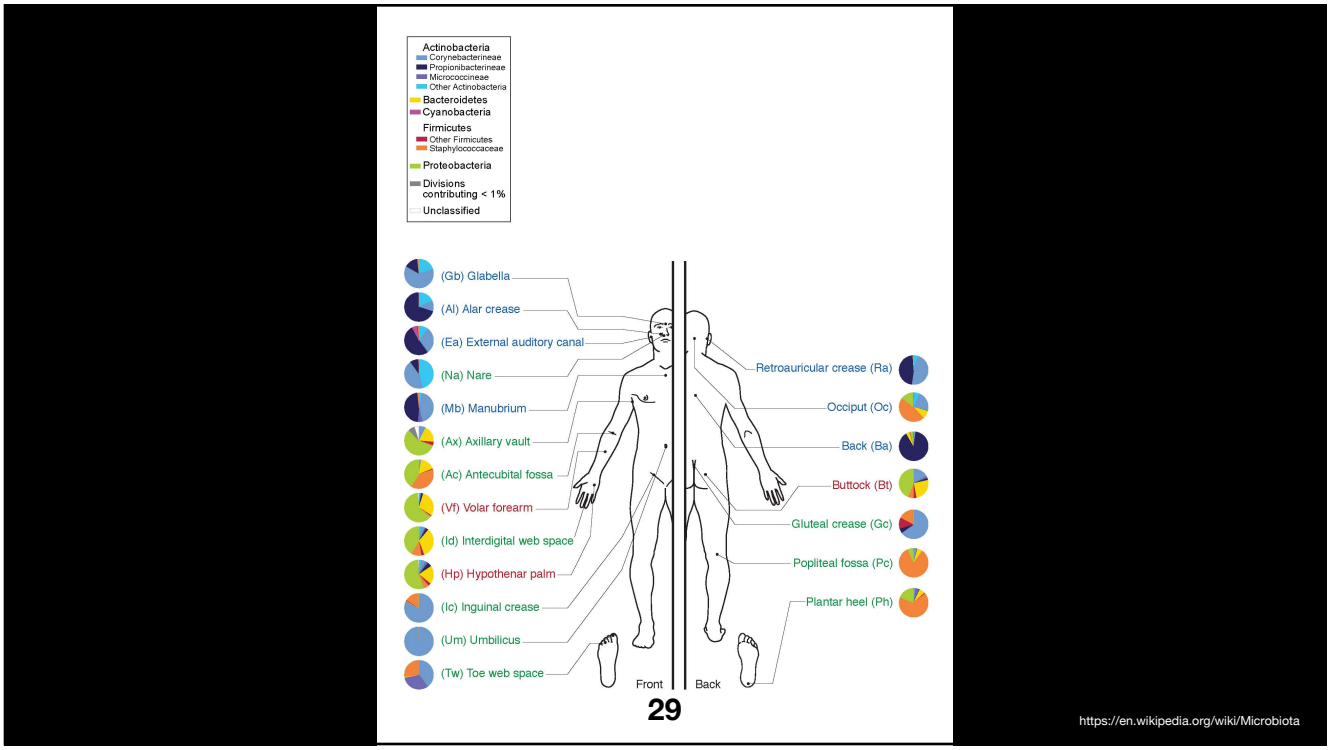
Actinobacteria
Corynebacterineae
Propionibacterineae
Micrococcineae
Other Actinobacteria
Bacteroidetes
Cyanobacteria
Firmicutes
Other Firmicutes
Staphylococcaceae
Proteobacteria
Divisions contributing < 1%
Unclassified
(Gb) Glabella
(Al) Alar crease
(Ea) External auditory canal
(Na) Nare
(Mb) Manubrium
(Ax) Axillary vault
(Ac) Antecubital fossa
(Vf) Volar forearm
(Id) Interdigital web space
(Hp) Hypothenar palm
(Ic) Inguinal crease
(Um) Umbilicus
(Tw) Toe web space
Retroauricular crease (Ra)
Occiput (Oc)
Back (Ba)
Buttock (Bt)
Gluteal crease (Gc)
Popliteal fossa (Pc)
Plantar heel (Ph)
Front
Back
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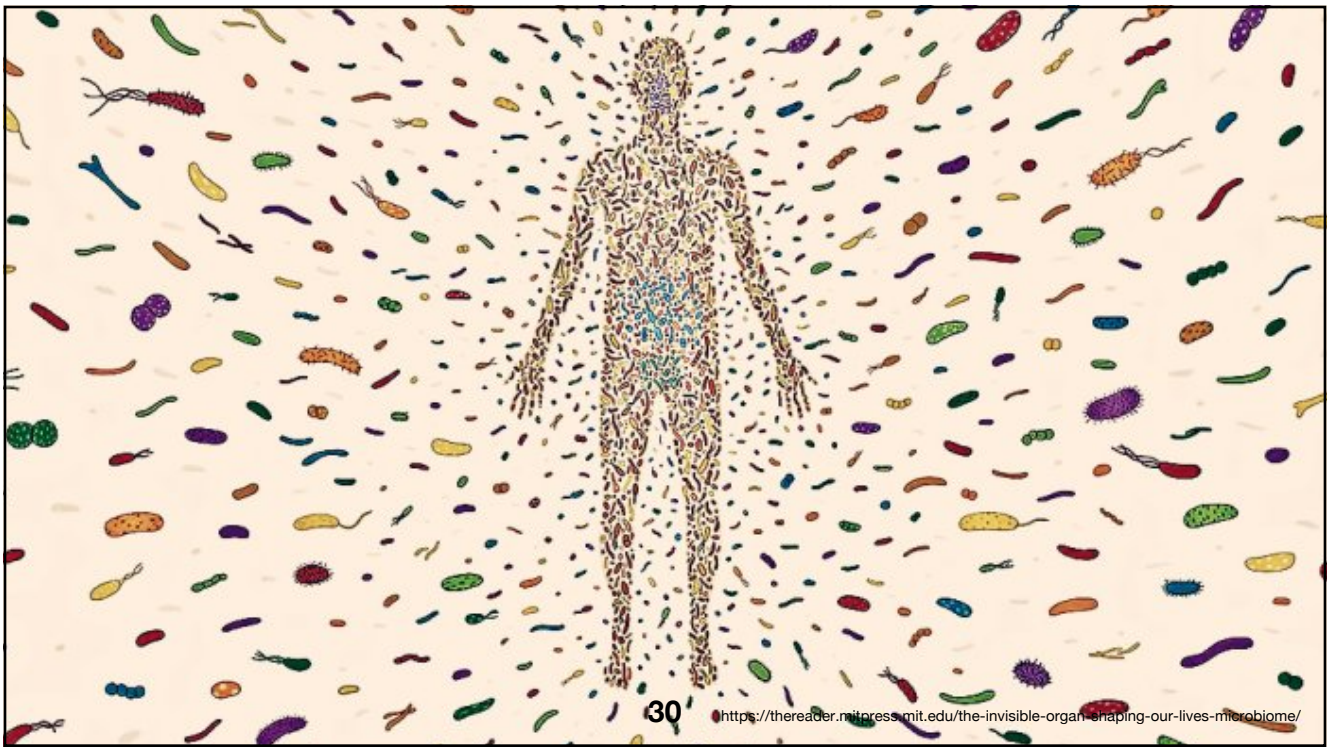
https://en.wikipedia.org/wiki/Microbiota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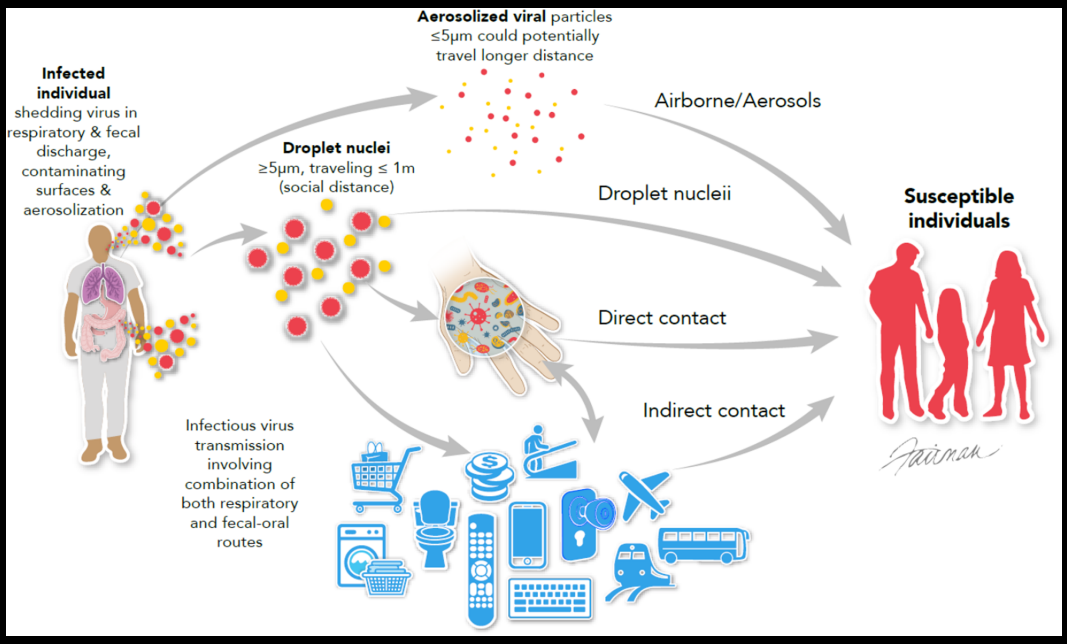
https://thereader.mitpress.mit.edu/the-invisible-organ-shaping-our-lives-microbiome/



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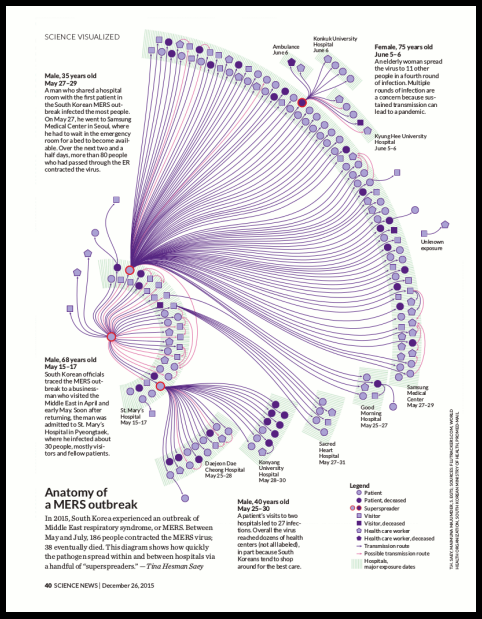
How do we imagine spread?

32

MERS-CoV Outbreak

2015 South Korea
186 infected, 38 died
—> Superspreading



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Chapter 2. So what do we know?

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Microbiology I. In the ICU

35

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Are HAI transmissible?

- 5 ICUs, 18 months, genetic typing of all strains of 10 pathogens, daily chart review, 9-day time window for same strains between patients = transmission
- 28,498 patient days, 278 (431) infections, **41 (14.5%) were** associated with transmission.

Table 6. Ascertained transmission episodes and transmission-associated nosocomial infections related to indicator organisms in five intensive care units (Jan 2000 to July 2001)

Intensive Care Unit	Transmissions, n	Transmissions per 1,000 Patient Days (95% CI)	Average Waiting Time Between Transmission in Days (95% CI)	Nosocomial Infections Caused by Indicator Organisms, n	Proportion of Transmission-Associated Nosocomial Infections (%)
A	57	5.9 (4.5–7.7)	9.6 (12.6–7.4)[a]	111	21
B	21	6.8 (4.2–10.4)	26.0 (41.9–16.9)[a]	28	3
C	33	5.0 (2.2–5.3)	16.5 (37.9–15.7)[a]	40	9
D	12	2.8 (1.4–4.9)	45.4 (90.3–25.8)[a]	17	2
E	18	3.7 (2.2–5.8)	30.3 (50.2–19.1)[a]	82	6
Total	141	5.0 (4.2–5.8)	23.2 (27.3–19.8)[b]	278	41 (14.5)

Grundmann H, Bärwolff S, Tami A, et al. How many infections are caused by patient-to-patient transmission in intensive care units? Crit Care Med 2005, 33:946–951. https://journals.lww.com/ccmjournal/fulltext/2005/05000/how_many_infections_are_caused_by.5.aspx

Microbiology II. Literature review

37

38

How and how often do pathogens travel?

A systematic literature review 2018

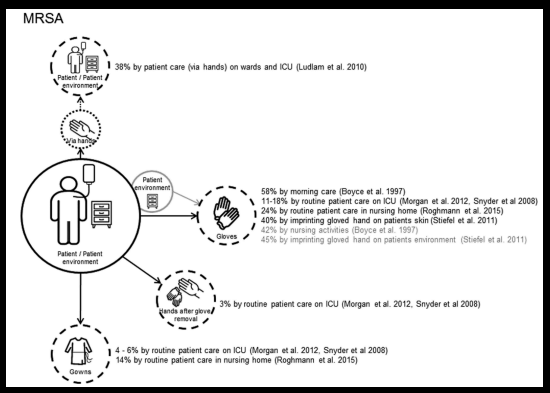
32 of 13,121 articles included

84% examined transfer **from patients —>HCWs**

Transfer frequency from the patient or their environment
—>hands 33%
—>gloves 30%
—>gowns 10%

Only two studies investigate transfer **HCW —>patients**.

Increased risk:
- moist body sites (n=7)
- longer duration of care (n=5)
- patients with an invasive device (n=3)



Wolfensberger, A. Clack L, Kuster SP, Passerini S, Mody L Chopra V, Mann J, Sax H. Transfer of pathogens to and from patients, healthcare providers, and medical devices during care activity-a systematic review and meta-analysis. Infect Control Hosp Epidemiology 39, 1–15 (2018). https://doi.org/10.1017/ice.2018.168

Microbiology III. Stopcocks

39

Sources of stopcock contamination in anesthesia.

Swabs from:
- anaesthesiologists (hands)
- patient (nose, axilla)
- environment (anesthesia dials)
- stopcock

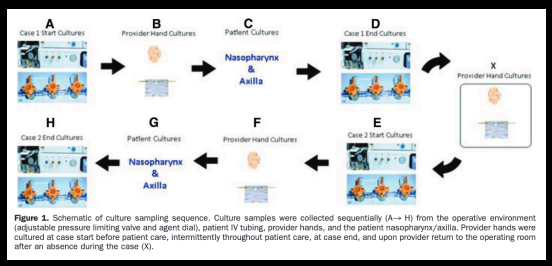
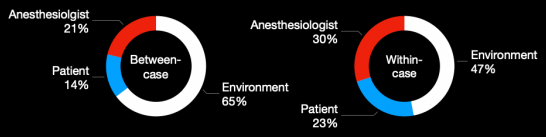


Figure 1. Schematic of culture sampling sequence. Culture samples were collected sequentially (A→ H) from the operative environment (adjustable pressure limiting valve and agent dial), patient IV tubing, provider hands, and the patient nasopharynx/axilla. Provider hands were cultured at case start before patient care, intermittently throughout patient care, at case end, and upon provider return to the operating room after an absence during the case (X).

Source of stopcock contamination



Overall **23%** of stopcocks (126/548 cases)

Density of hand hygiene per hour was not associated with stopcock contamination.

Anesthesiologists' hands proven transmission in 27%.

No bloodstream infection occurred but 40 other HAI.

"Thus, these results do **not** suggest that anesthesia providers are the major reservoir for intra-operative bacterial transmission. Instead, we observed that the surrounding patient environment was a more likely source."

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Microbiology IV. Microbiota

41

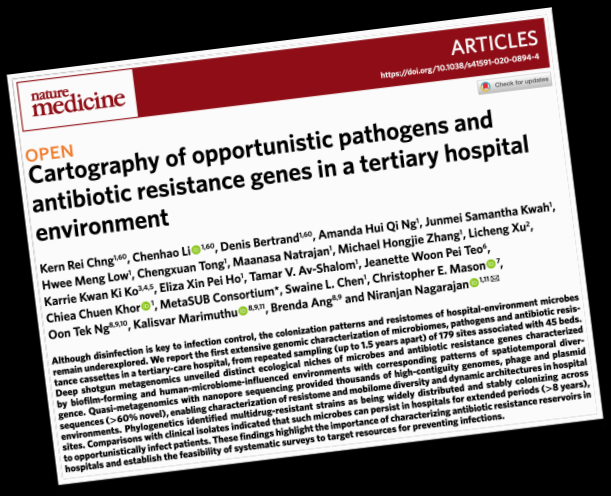
Distinct ecological niches define dynamic architecture of hospital resistome and mobilome.

Methods

- Repeated sampling of patients environment
- Combination of short-read **shotgun metagenomics** with **nanopore sequencing** of antibiotic-resistant mixed cultures
- Antibiotic resistance genes in microbial genomes, closed plasmid sequences

Conclusions

- MDROs **persist** in the hospital environment for **>8 years** and **infect** patients opportunistically
- Found >60% novel sequences



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Hospital Transmission Networks. What Do We Know?
Prof, Hugo Sax, University of Bern, Switzerland
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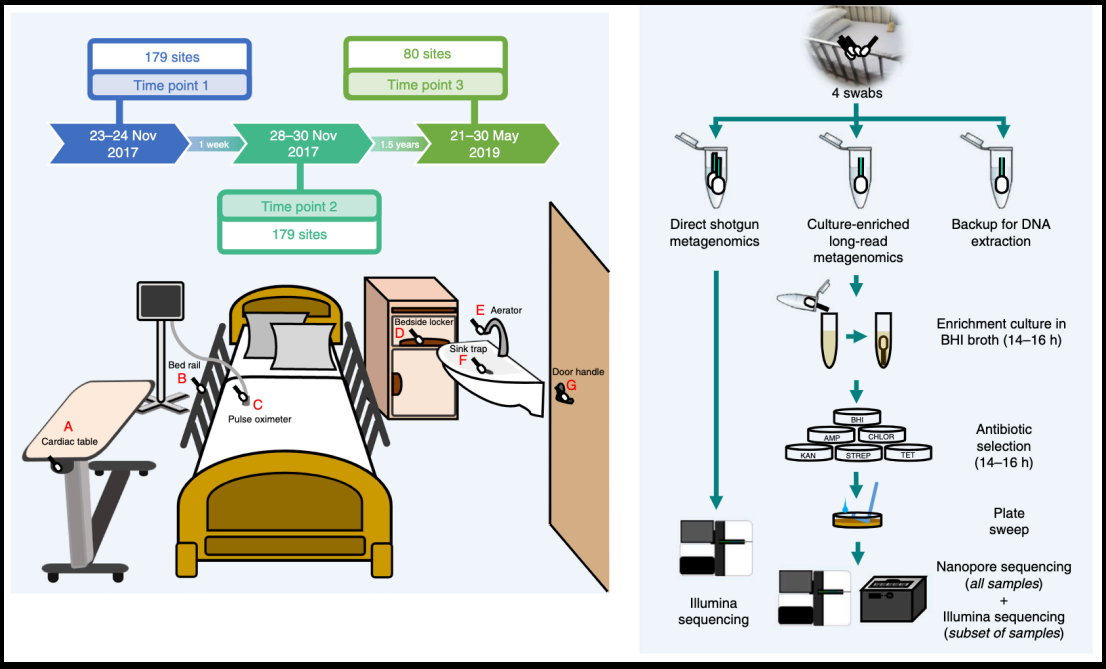

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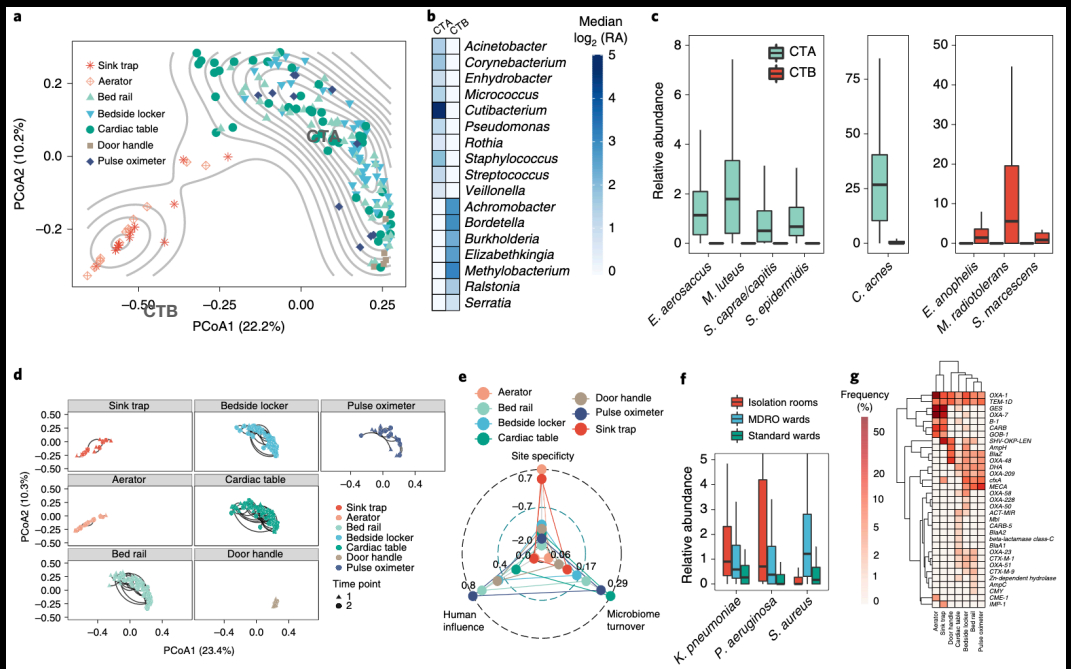

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Prof, Hugo Sax, University of Bern, Switzerland
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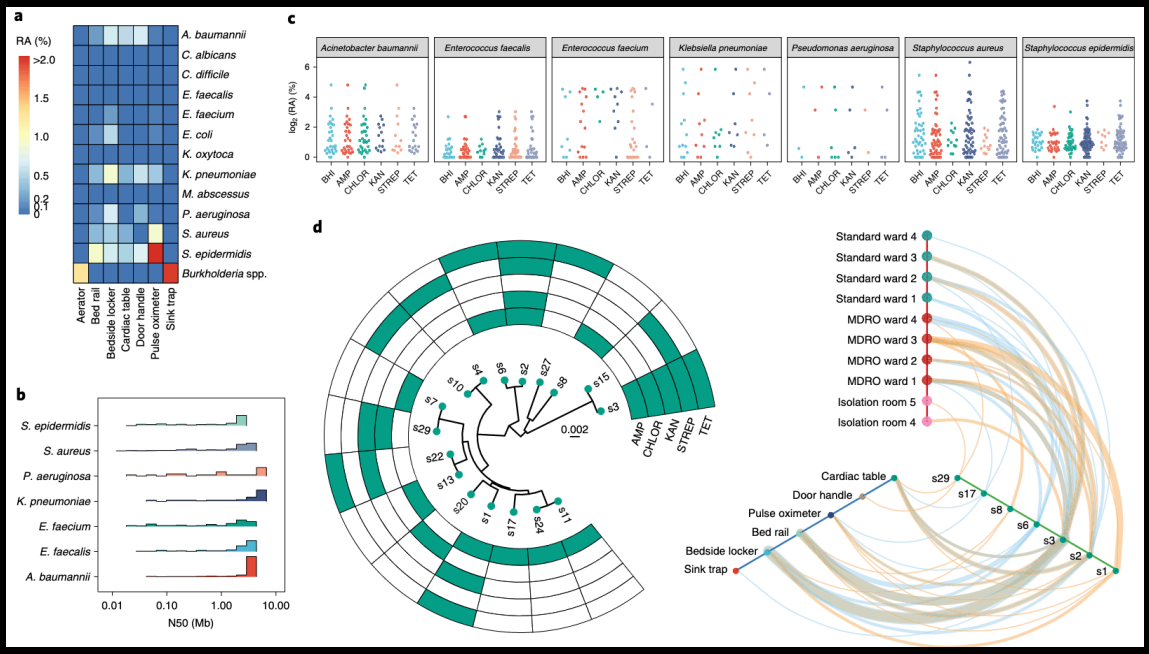

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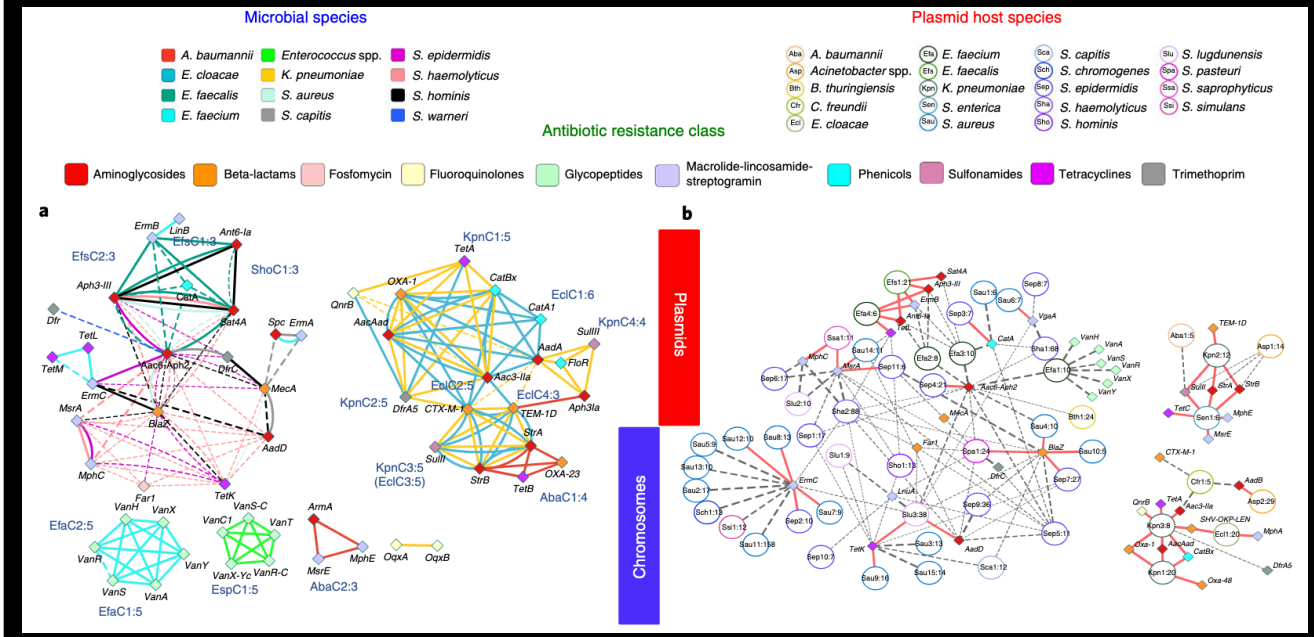

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Microbiology V. Surrogate tracers

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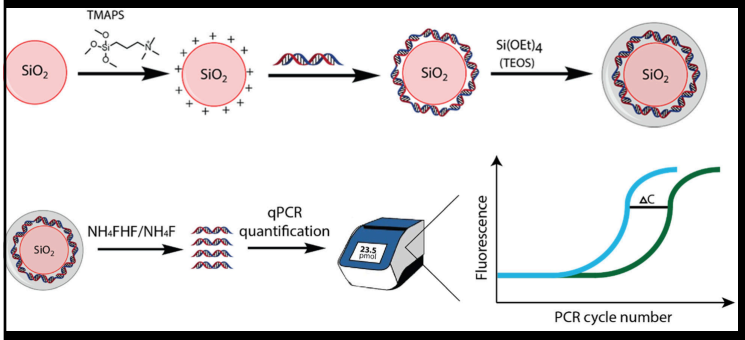
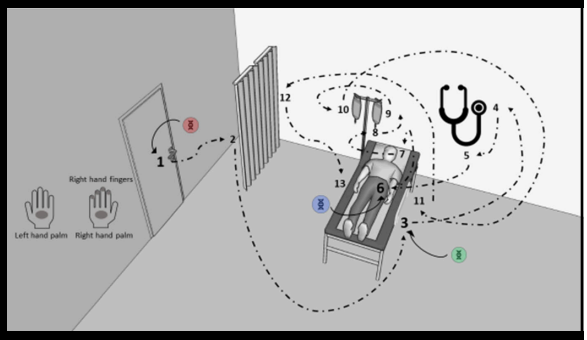
How and how often do pathogens travel?

Silica nanoparticles with encapsulated DNA (SPED)





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Scotoni M, Koch J, Clack, L, Pttal AK, Wolfensberger A, Grass R, Sax H. Silica nanoparticles with encapsulated DNA (SPED) – a novel surrogate tracer for microbial transmission in healthcare. Antimicrob Resist Infect Control 9, 152 (2020). https://doi.org/10.1186/s13756-020-00813-7

How and how often do pathogens travel?

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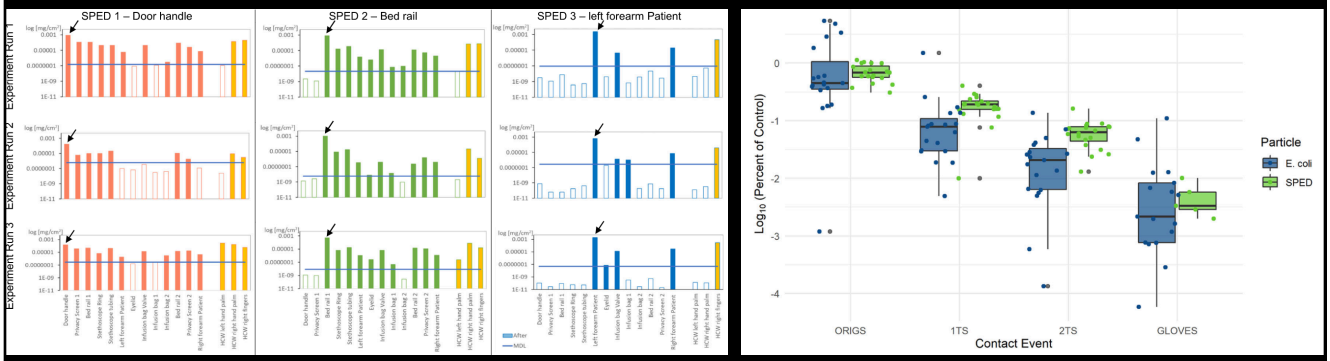

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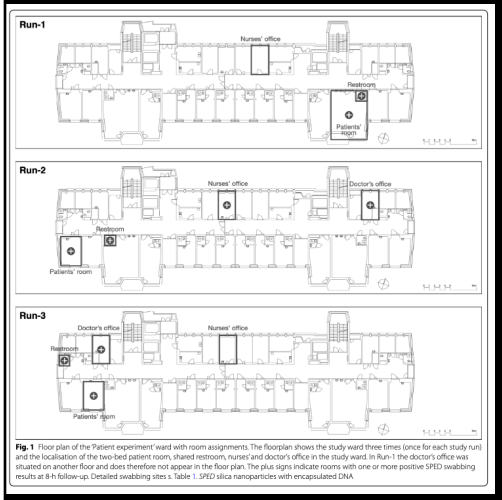
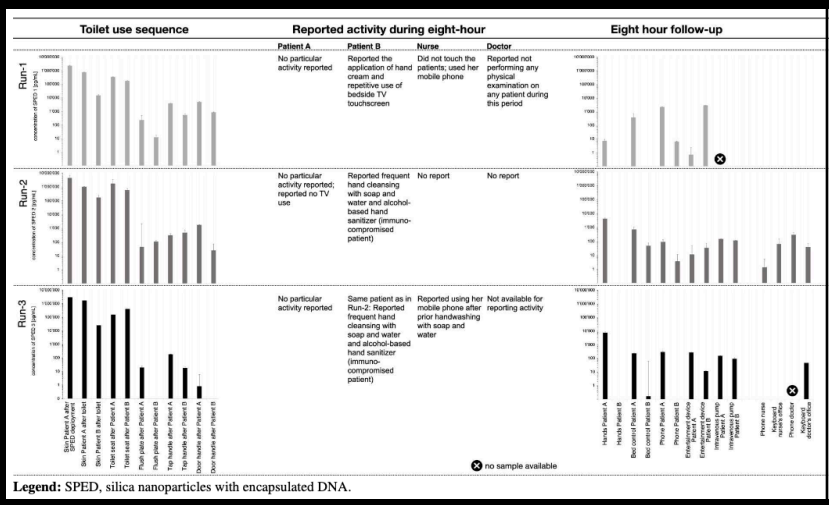


Fig. 1 Floor plan of the 'Patient experiment' ward with room assignments. The floorplan shows the study ward three times (once for each study run) and the localisation of the two-bed patient room, shared restroom, nurses'and doctor's office in the study ward. In Run-1 the doctor's office was situated on another floor and does therefore not appear in the floor plan. The plus signs indicate rooms with one or more positive SPED swabbing results at 8-h follow-up. Detailed swabbing sites s. Table 1. *SPED* silica nanoparticles with encapsulated DNA



Legend: SPED, silica nanoparticles with encapsulated DNA.

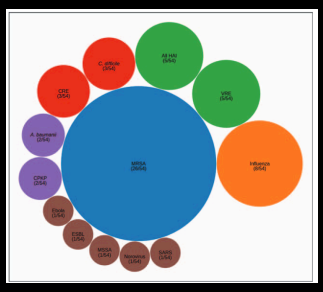
Ullrich, C., Luescher, A. M., Koch, J., Grass, R. N. & Sax, H. Silica Nanoparticles With Encapsulated DNA (SPED) to Trace the Spread of Pathogens in Healthcare. (2021) doi:10.21203/rs.3.rs-870804/v1

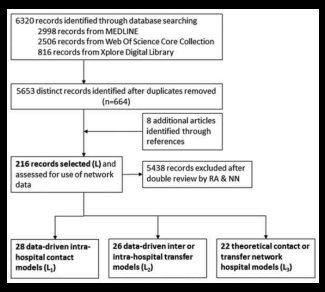
Mathematical modelling

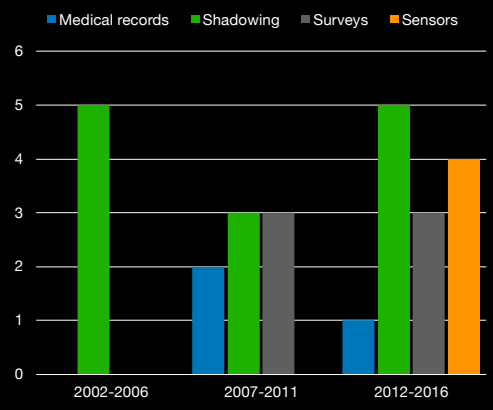
51

Mathematical models of infection transmission in healthcare settings.

A systematic review 2017







Conclusions

Models incorporating such data are limited to a small number of countries, settings, and pathogens, while there is a steady emergence of network graphs to study the contact and structure of patient movement and interactions with HCWs.

52

Assab, R. et al. Mathematical models of infection transmission in healthcare settings. Curr Opin Infect Dis 30, 410–418 (2017).

Agent-based model derived from sensor data.

Table 1. Model Parameters

Symbol	Definition	Range
P	Probability of transmission per 30 seconds of contact	0.0005–0.0050
D	Duration of pathogen colonization before treatment	10 days
λ	Hand hygiene efficacy	0.58 (soap), 0.83 (rub)
γ	Hand hygiene baseline compliance	$\mu = 0.25, 0.50, 0.75$ $\sigma = 0.10$
ε	Environmental contamination transmission rate	0.00–0.01

A contact was defined as a time period where both motes recorded each other's presence above a predefined minimal RSSI for at least 30 seconds.

We modeled the spread of nosocomial pathogens using an agent-based, discrete-event simulator of our own design that replays individual **HCW–HCW** and **HCW–patient contacts** and **hand hygiene opportunities** reconstructed from the data collected in the MICU.

Each 360-hour simulation is replicated 1000 times (using randomly chosen initial conditions), and aggregate results (eg, means, medians) are reported.

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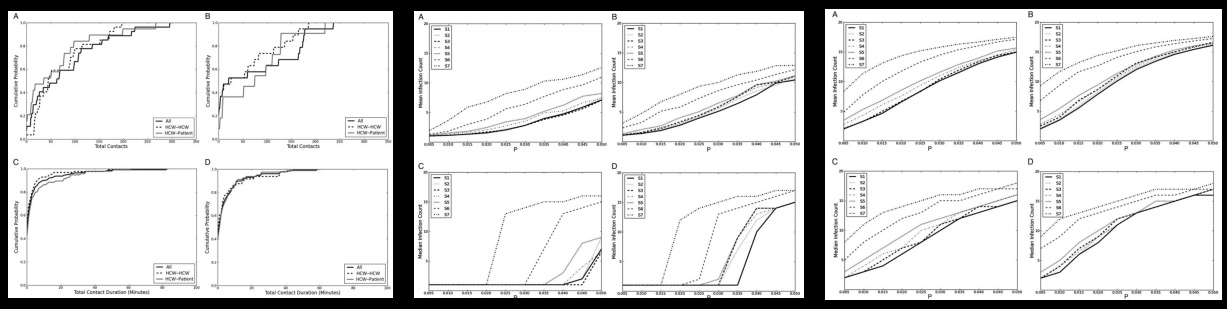
Hornbeck, T. et al. Using sensor networks to study the effect of peripatetic healthcare workers on the spread of hospital-associated infections. 206, 1549–1557 (2012).

Agent-based model derived from sensor data.

Day shift Night shift Day shift Night shift Day shift Night shift



Distribution of contacts Distribution of 'infectivity' Distribution of 'infectivity'

S1: All HCWs are equally compliant.
S2: The single least-connected HCW is noncompliant.
S3: The 2 least-connected HCWs are noncompliant.
S4: One randomly selected HCW is noncompliant.
S5: Two randomly selected HCWs are noncompliant.
S6: The single most-connected HCW is noncompliant.
S7: The 2 most-connected HCWs are noncompliant.

54

Hornbeck, T. et al. Using sensor networks to study the effect of peripatetic healthcare workers on the spread of hospital-associated infections. 206, 1549–1557 (2012).

Individual hand hygiene behaviour matters.

The PROHIBIT European central-line prevention study.

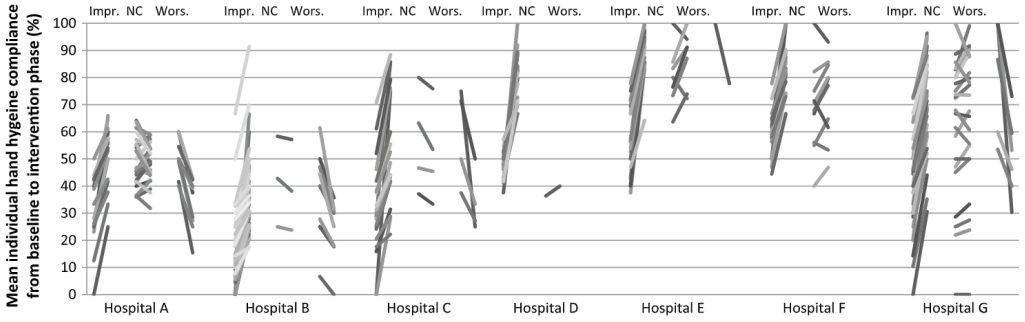


Fig. 1 Individual change of hand hygiene compliance, stratified by intensive care unit. Each line represents one HCW. Impr., improving healthcare workers; NC, Non-changing healthcare workers; Wors., Worsening healthcare workers

55

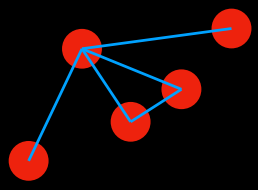
Kooi, T. van der et al. Hand hygiene improvement of individual healthcare workers: results of the multicentre PROHIBIT study. Antimicrob Resist Infect Control 11, 123 (2022).

Network analysis

56

Social network analysis

[Wikipedia]



Social network analysis characterizes **networked structures** in terms of **nodes** (individual actors, people, or things within the network) and the ties, **edges**, or links (relationships or interactions) that connect them.

Centrality assigns numbers or rankings to nodes within a graph corresponding to their network position. Applications include identifying the **most 'influential' person(s)** in a social network.

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Network analysis by HCW based on EMR data.

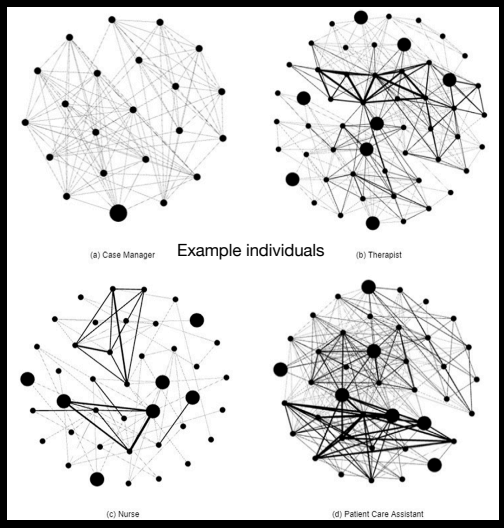
Table 1
Summary of measures for networks of 499 HCWs.

Provider type	Number of HCWs	Average degree centrality	Average clustering coefficient	Average network density
Nurses	279	5.15	0.79	0.72
Case manager	20	8.92	0.99	0.77
Patient care assistant	92	8.70	0.92	0.76
Therapist	74	8.94	0.88	0.58
Specialty technician	20	8.87	0.79	0.67
Other	14	6.75	0.79	0.69

Degree centrality is defined as the number of links incident upon a node (i.e., the number of ties that a node has).

Network density is the proportion of direct ties in a network relative to the total number possible.

Clustering coefficient is a measure of the likelihood that two associates of a node are also associates. A higher clustering coefficient indicates a greater 'cliquishness'.



Kang, H., Waselewski, M. E. & Lobo, J. M. Understanding provider-level properties that influence the transmission of healthcare associated infections using network analysis. Operations Res Heal Care 23, 100223 (2019).

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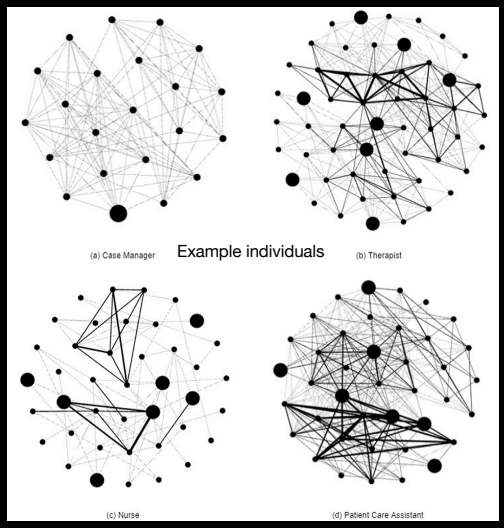
Network analysis by HCW based on EMR data.

Table 2
Poisson regression model results.

	Coefficient (β)	Robust standard error	Incident rate ratio [95% confidence interval]	p-value
Intercept	1.193	0.211	**3.296** [2.178,4.987]	<0.001
Role type (Nurses)				
Case manager	0.591	0.41	1.806 [0.809,4.033]	0.149
Patient care assistant	0.166	0.082	**1.18** [1.005,1.386]	0.043
Therapist	0.243	0.083	**1.275** [1.084,1.5]	0.003
Specialty technician	−0.179	0.244	0.836 [0.519,1.348]	0.463
Other	−0.229	0.178	0.795 [0.561,1.126]	0.197
Num_pts	−0.007	0.002	**0.993** [0.99,0.996]	<0.001
Avg_PPD	−0.066	0.03	**0.936** [0.883,0.993]	0.027
Work_days	0.019	0.003	**1.019** [1.012,1.026]	<0.001
Avg_deg	0.099	0.011	**1.104** [1.081,1.127]	<0.001
Avg_cls	0.506	0.273	1.658 [0.971,2.833]	0.064
Net_den	−3.29	0.245	**0.037** [0.023,0.060]	<0.001

Num_pts: total number of patients each provider saw during the two months; Avg_PPD: average patients each provider saw per day during LTACH workdays; Work_days: LTACH workdays; Avg_deg: average degree centrality; Avg_cls: average cluster coefficient; Net_den: network density.

To understand **factors** associated with **provider contact frequency with CRE-positive patients** we built a Poisson regression model that includes provider-related characteristics and measures drawn from each provider's patient network.



Kang, H., Waselewski, M. E. & Lobo, J. M. Understanding provider-level properties that influence the transmission of healthcare associated infections using network analysis. Operations Res Heal Care 23, 100223 (2019).

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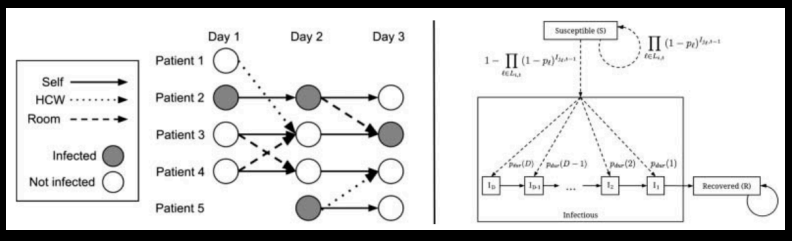
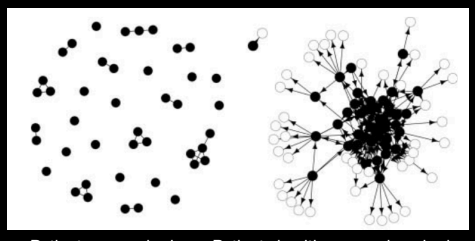
Network analysis by patient based on EMR data.





Patients room sharing Patients healthcare worker sharing

Cusumano-Towner, M., Li, D. Y., Tuo, S., Krishnan, G. & Maslove, D. M. A social network of hospital acquired infection built from electronic medical record data. J Am Med Inform Assn 20, 427–434 (2013).

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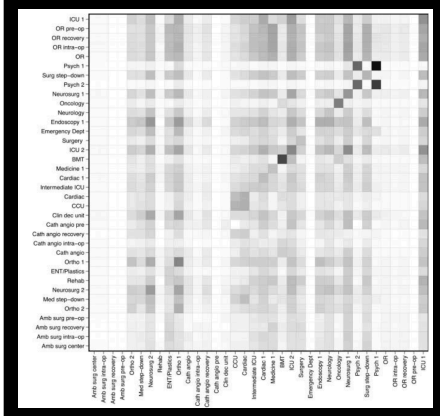
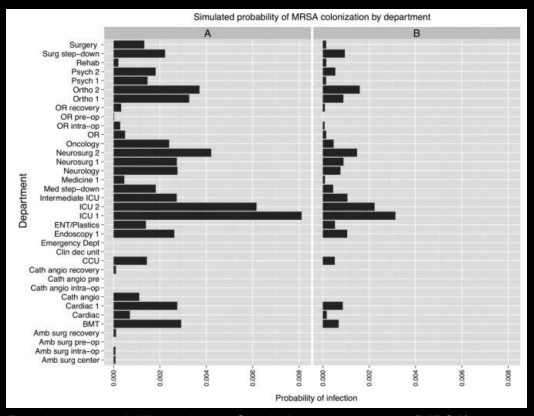
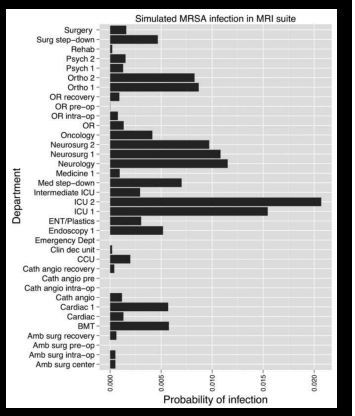
Network analysis by patient based on EMR data.



Matrix showing the probabilities for spread of influenza between wards.



Results of methicillin-resistant Staphylococcus aureus (MRSA) simulations conducted using a social network of hospital inpatients. A. One infected patient in step down unit. B. 50% increase in hand hygiene.



Results of methicillin-resistant Staphylococcus aureus (MRSA) simulation conducted using a social network of hospital inpatients, starting with one infection in the magnetic resonance imaging (MRI) department. The x-axis shows the probability of infection in each department at the end of 3 days and is based on room-sharing and healthcare worker-sharing links, as well as patient visits to the MRI suite.

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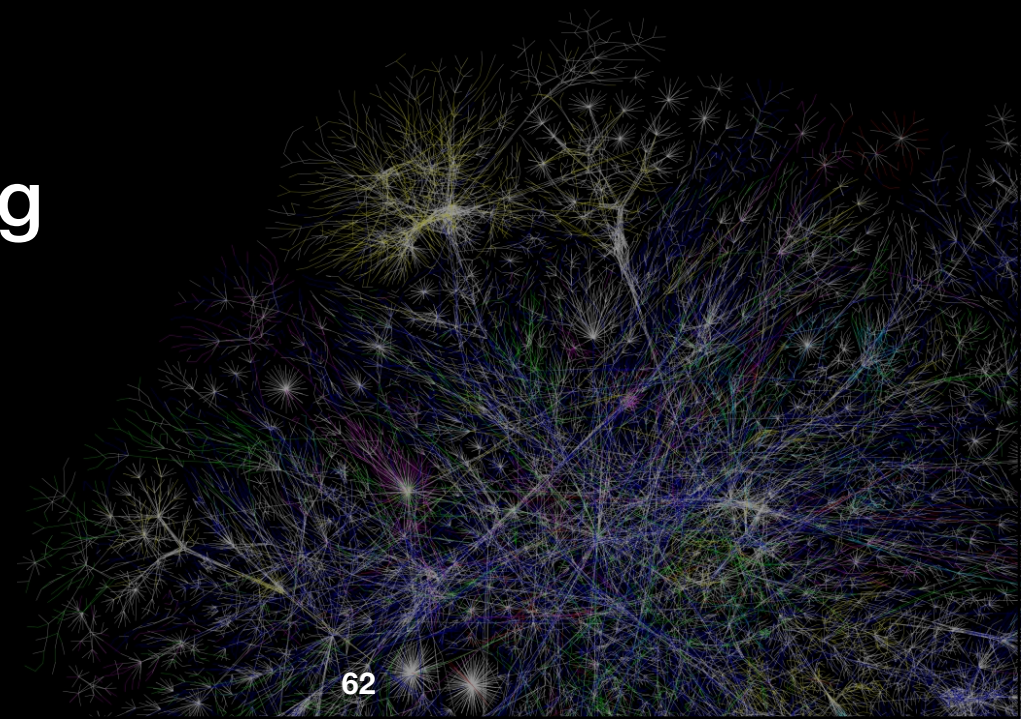
Cusumano-Towner, M., Li, D. Y., Tuo, S., Krishnan, G. & Maslove, D. M. A social network of hospital acquired infection built from electronic medical record data. J Am Med Inform Assn 20, 427–434 (2013).

Epilog



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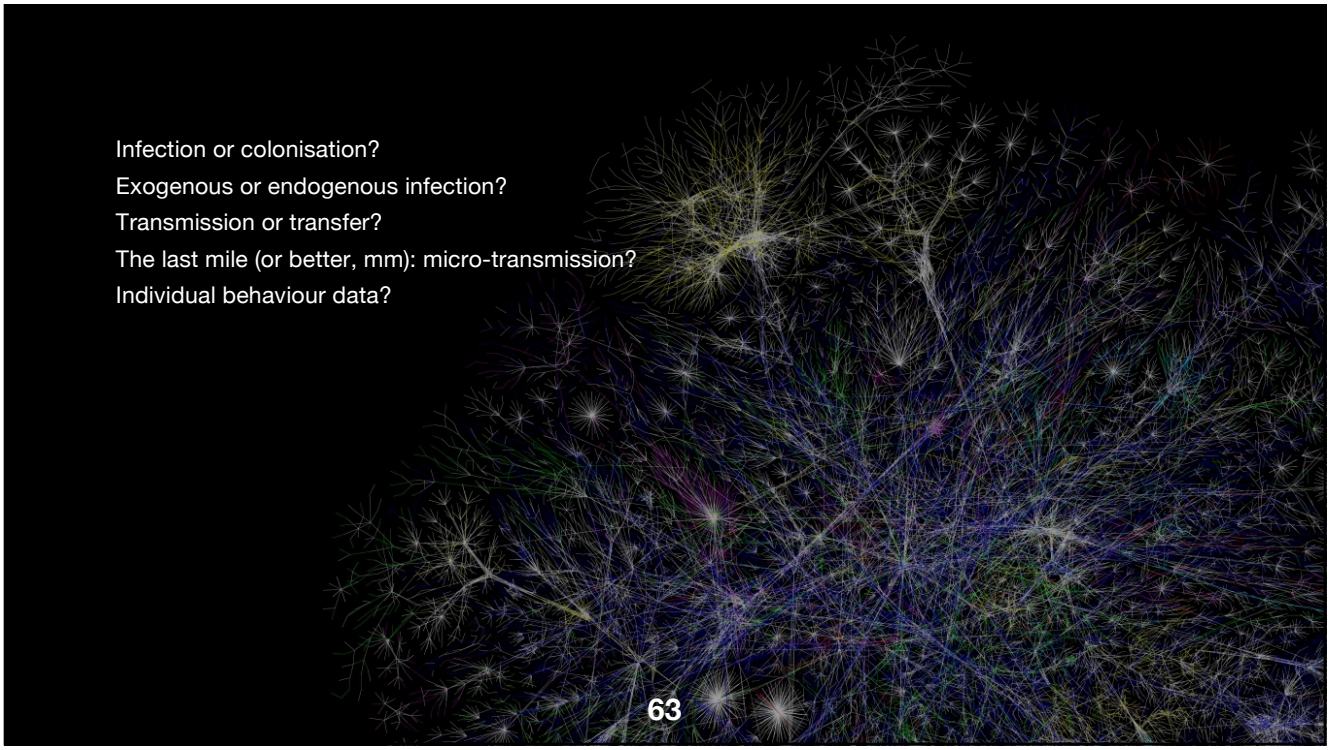
Infection or colonisation?
Exogenous or endogenous infection?
Transmission or transfer?
The last mile (or better, mm): micro-transmission?
Individual behaviour data?
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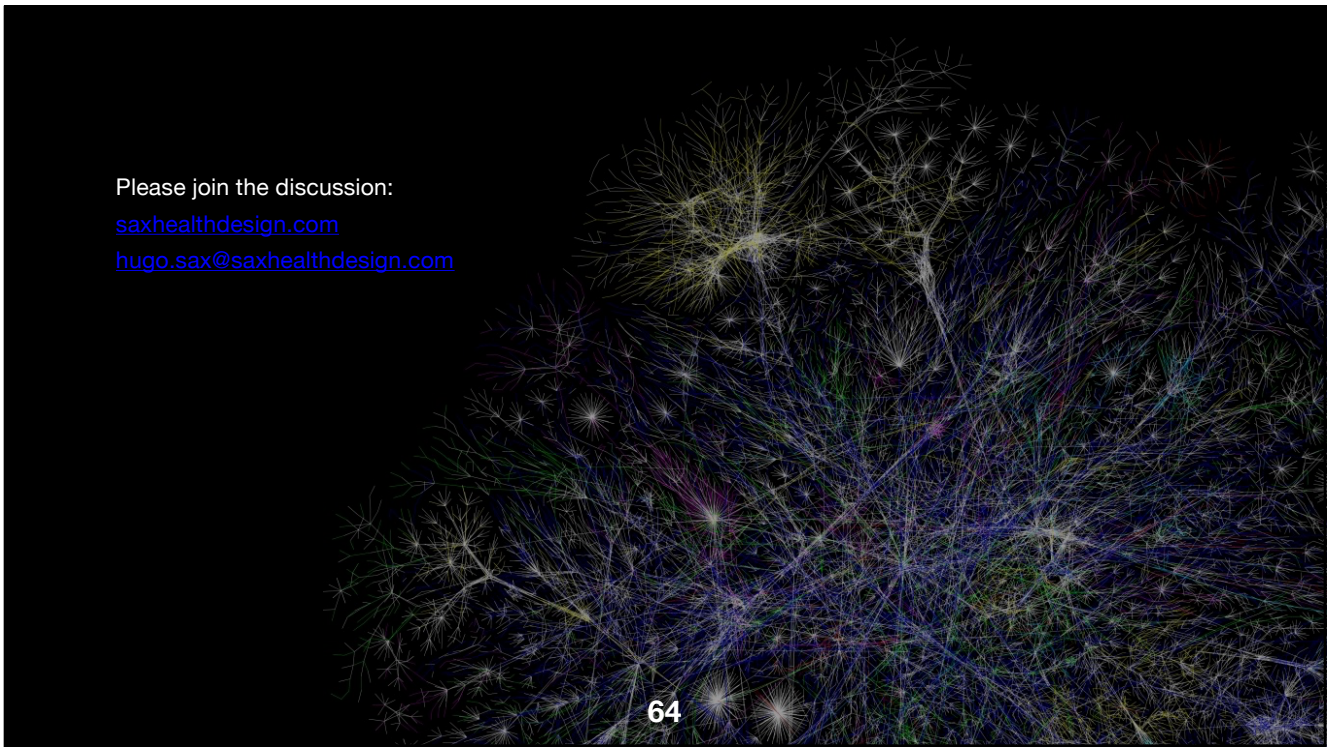
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