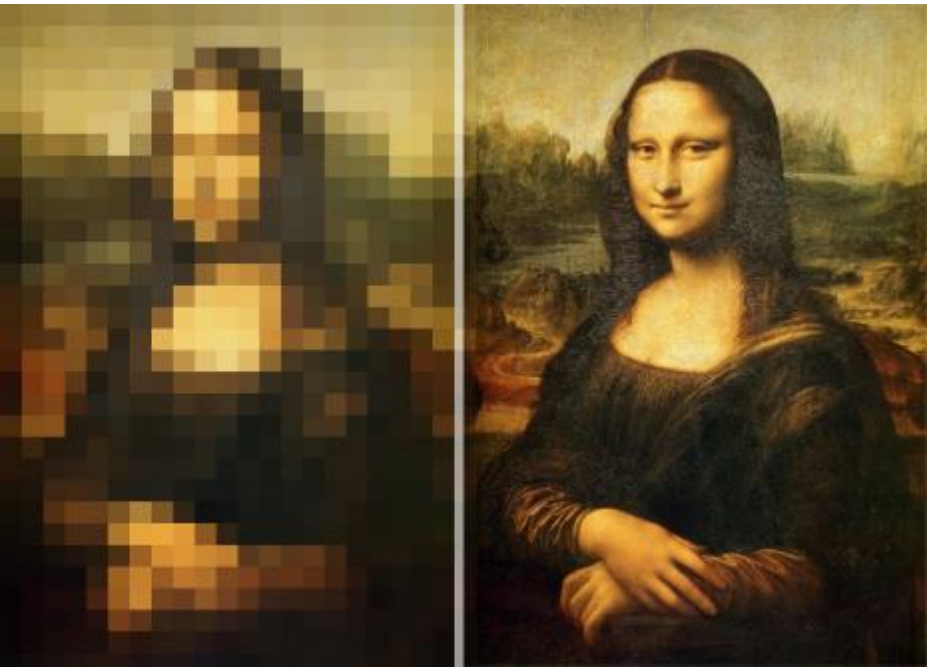
Third International Conference on Clinical Metagenomics

Hôpitaux Universitaires Genève

University of Geneva Hospitals
and Faculty of Medicine, Geneva, Switzerland

WHO Collaborating Centre
on Patient Safety
Infection Control & Improving Practices



How can WGS help in nosocomial outbreaks? The point of view of the hospital epidemiologist

S. Harbarth & R. Martischang

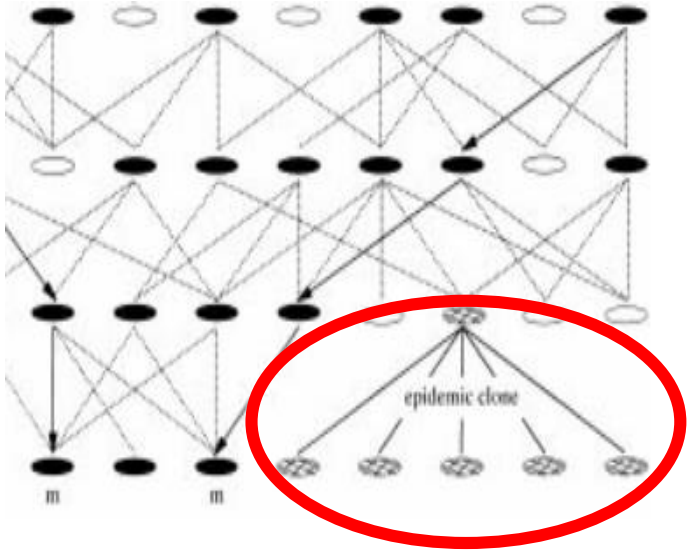
Geneva, 19 October 2018

Infection Control Programme, University of Geneva Hospitals and Faculty of Medicine, Geneva, Switzerland

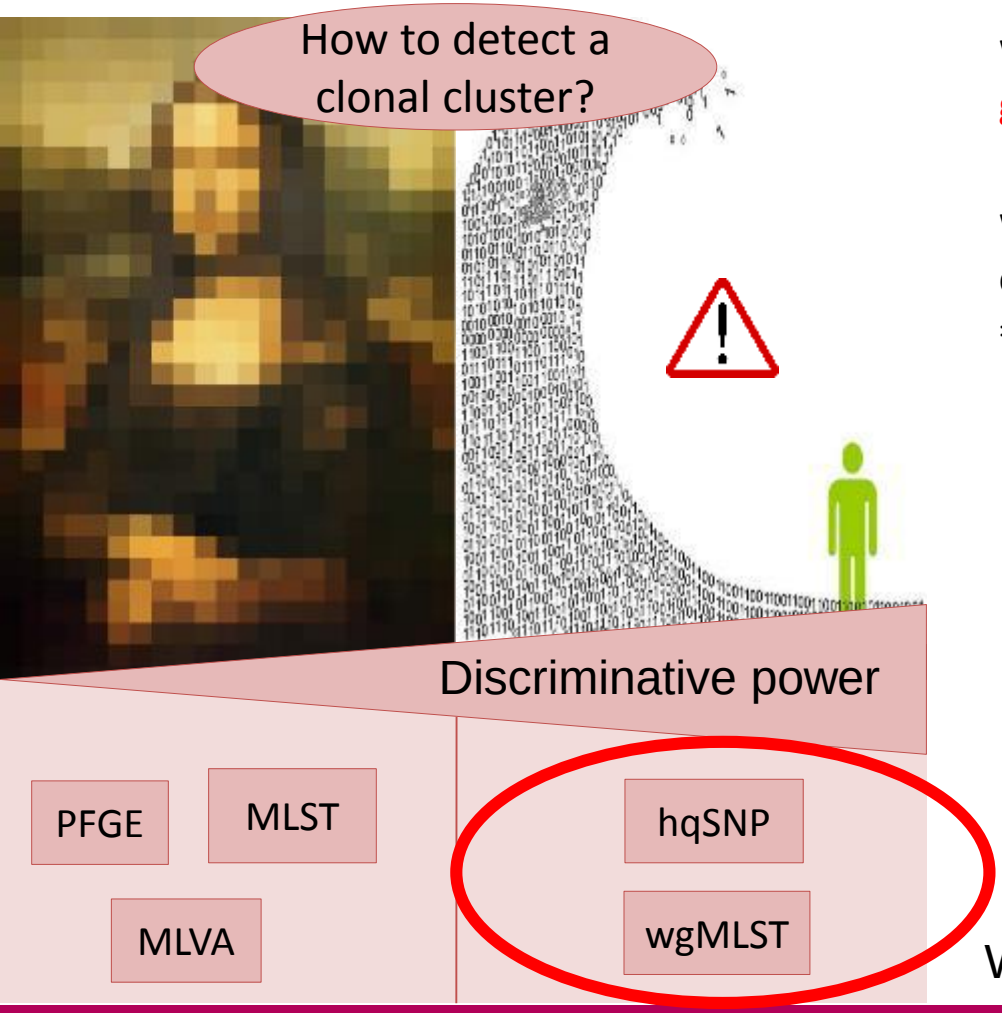
Making epidemiological inferences based on molecular data

We expect epidemiologically linked isolates to be genetically identical or similar, therefore:

We expect the bacterial population to have a clonal structure
=> Detection of monoclonal clusters of isolates.

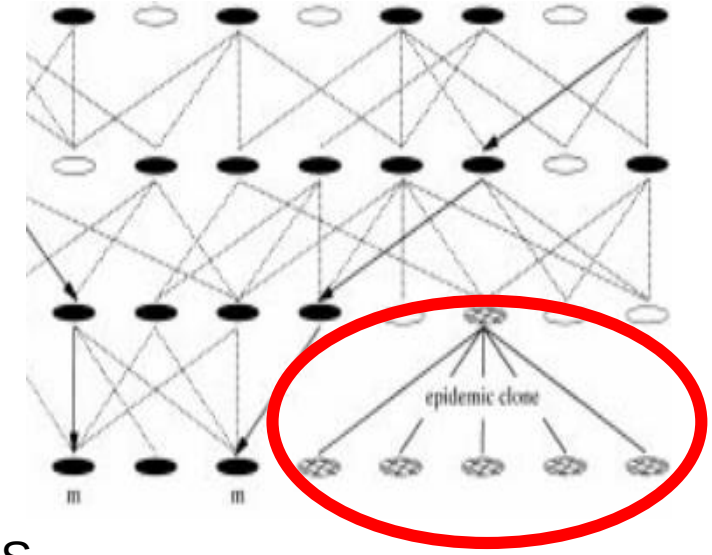


Making epidemiological inferences based on molecular data

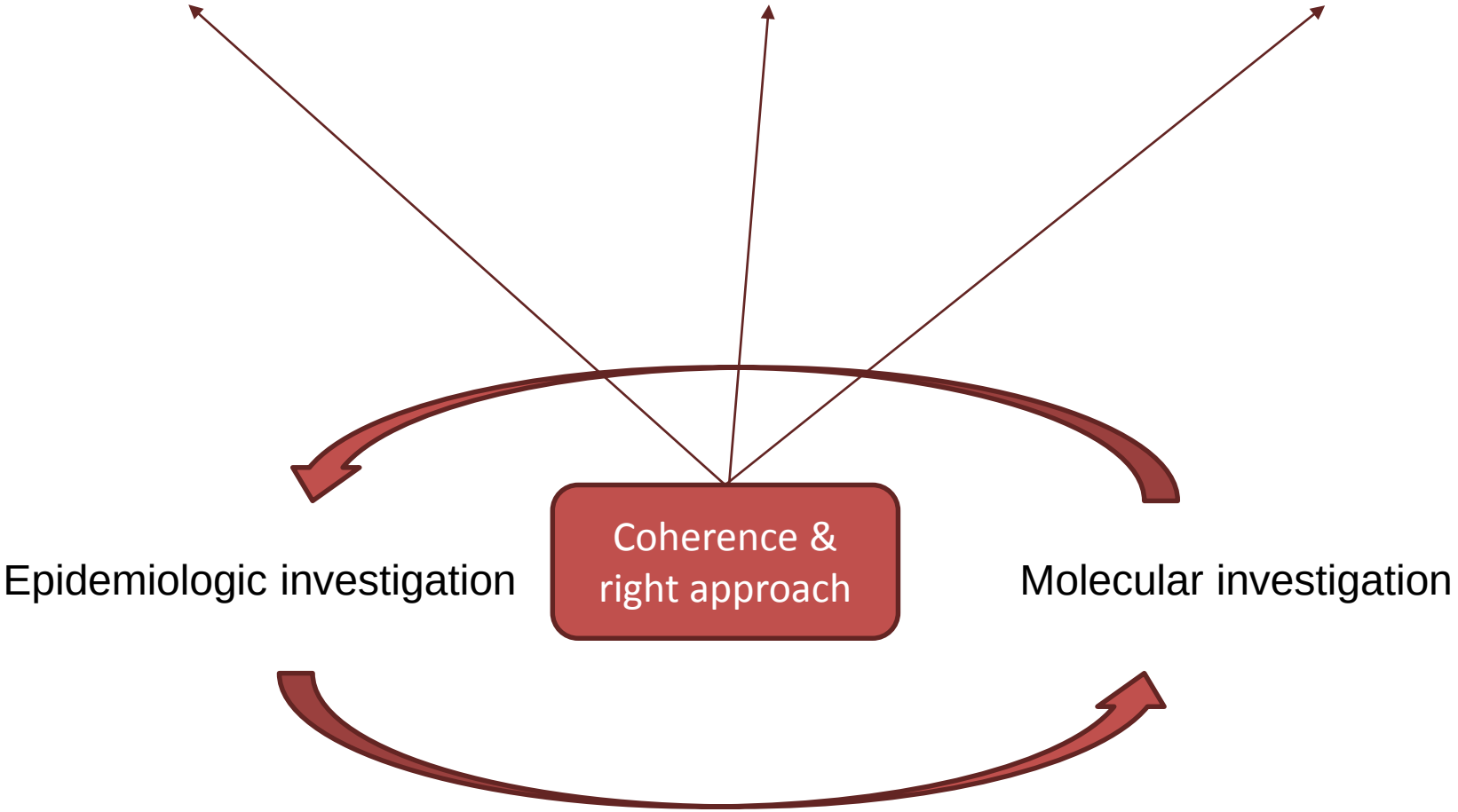


We expect epidemiologically linked isolates to be genetically identical or similar, therefore:

We expect the bacterial population to have a clonal structure
=> Detection of monoclonal clusters of isolates.



WGS


Epidemiologic investigation
Coherence & right approach
Molecular investigation

Indication for molecular typing?

- Do I have an epidemiologic hypothesis ?

➔ **Molecular fishing expedition?**

Indication for molecular typing?

- Do I have an epidemiologic hypothesis ?

➔ **Molecular fishing expedition?**

- Do I expect any impact on infection control interventions ? Or futile academic exercise ?

➔ **Priority action item for changing preventive measures?**

Clinical Infectious Diseases

MAJOR ARTICLE

Genomic Surveillance Reveals Diversity of Multidrug-Resistant Organism Colonization and Infection: A Prospective Cohort Study in Liver Transplant Recipients

Nenad Macesic,[1,2] Angela Gomez-Simmonds,[1] Sean B. Sullivan,[1,3] Marla J. Giddins,[1,3] Samantha A. Ferguson,[1] Gautam Korakavi,[1] David Leeds,[1] Sarah Park,[1] Kevin Shim,[1] Madeleine G. Sowash,[1] Melanie Hofbauer,[1] Ryan Finkel,[1] Yue Hu,[1] Jared West,[1] Nora C. Toussaint,[4,a] William G. Greendyke,[1] Benjamin A. Miko,[1] Marcus R. Pereira,[1] Susan Whittier,[5] Elizabeth C. Verna,[6] and Anne-Catrin Uhlemann[1,3]

Results. We collected 998 stool samples and 119 rectal swabs from 128 patients. MDRO colonization was detected in 86 (67%) patients at least once and was significantly associated with subsequent MDRO infection (0 vs 19.8%, $P = .002$). Child-Turcotte-Pugh score at LT and duration of post-LT hospitalization were independent predictors of both MDRO colonization and infection. Temporal dynamics differed between MDROs with respect to onset of colonization, clearance, and infections. We detected an unexpected diversity of CRE colonizing isolates and previously unrecognized transmission that spanned Ceph-RE and CRE phenotypes, as well as a cluster of *mcr-1*–producing isolates.

Conclusions. Active surveillance and WGS showed that MDRO colonization is a highly dynamic and complex process after LT. Understanding that complexity is crucial for informing decisions regarding MDRO infection control, use of therapeutic decolonization, and empiric treatment regimens.

Infection control measures in high-quality CPE control studies

-- Systematic WHO review & meta-analysis --

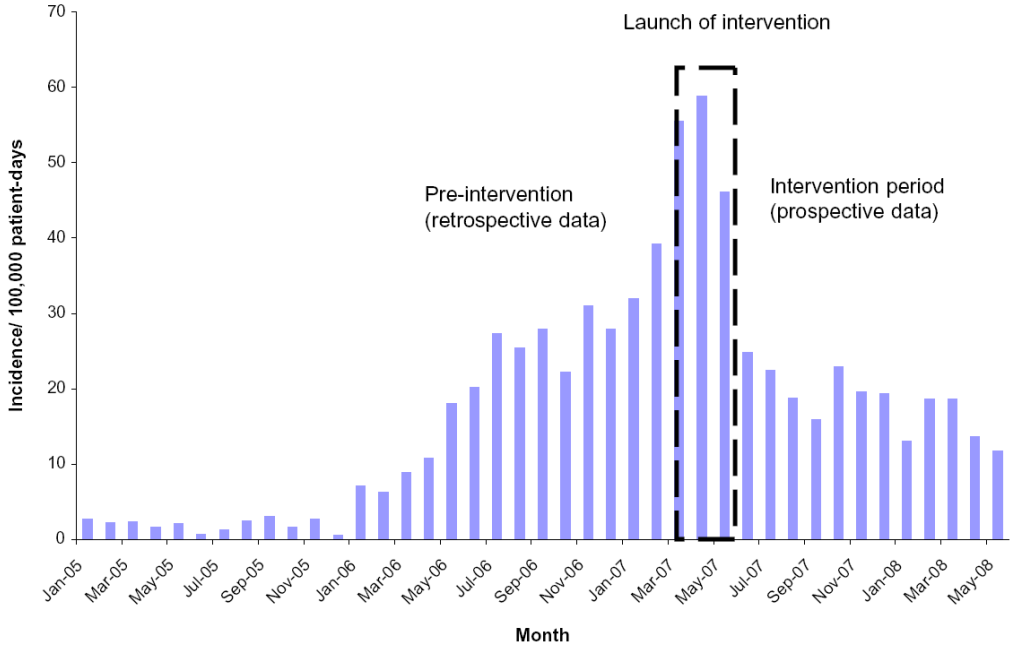
Intervention	EPOC studies
Active surveillance	10/11
Contact precautions	10/11
Cohorting	9/11
Monitoring, audit and feedback	9/11
Patient isolation	9/11
Hand hygiene education & monitoring	6/11
Education	4/11
Antibiotic stewardship	4/11
Enhanced environmental cleaning	3/11
Daily chlorhexidine gluconate baths	3/11
Flagging positive patients in medical record (alerts)	3/11
Environmental surveillance	1/11
Temporary ward closure	1/11

Tomczyk S et al. Clin Infect Dis 2019 (in press)

Containment of a Country-wide Outbreak of Carbapenem-Resistant *Klebsiella pneumoniae* in Israeli Hospitals via a Nationally Implemented Intervention

Clinical Infectious Diseases 2011;52(7):1–8

Mitchell J. Schwaber,[1] Boaz Lev,[2] Avi Israeli,[2] Ester Solter,[1] Gill Smollan,[1] Bina Rubinovitch,[1] Itamar Shalit,[1] Yehuda Carmeli,[1] and the Israel Carbapenem-Resistant Enterobacteriaceae Working Group[a]



Stalking a lethal superbug by whole-genome sequencing and phylogenetics: Influence on unraveling a major hospital outbreak of carbapenem-resistant *Klebsiella pneumoniae*

Thorsten Kaiser MD [a], Knut Finstermeier PhD [a], Madlen Häntzsch MSc [a], Sarah Faucheux MD [b], Martin Kaase MD [c], Tim Eckmanns MD [d], Sven Bercker MD, PhD [e], Udo X. Kaisers MD, PhD [e], Norman Lippmann MD [f,g], Arne C. Rodloff MD, PhD [f,g], Joachim Thiery MD, PhD [a], Christoph Lübbert MD, PhD, DTM&H [g,h,*]

- **34-month outbreak in Leipzig University Hospital**
- **84/105 KPC-2-*kp* (ST258) available**
- **Index case transferred from Rhodes, Greece**
- **19 wards affected**

Am J Infect Control 2018; 46: 54-59

WGS & Spread of KPC-2

- Positioning pillow to maintain patient prone in ICU, might have been the link
- Additional cases after screening
- 34 median number of single nucleotide variants

Epidemiology	WGS
Pathways explained for 11 (12.4%) patients	Pathways explained for 15 extra patients & confirmed 5 of epidemiology

- Exact mode of transmission unknown for 63 (71%) patients

Indication for molecular typing?

- Do I have an epidemiologic hypothesis ?

➔ **Molecular fishing expedition?**

- Do I expect any impact on infection control interventions ? Or simply academic exercise ?

➔ **Priority action item for modified preventive measures?**

Sampling?

- Do I have a strong, robust sampling strategy ? (Who, How, When)

➔ **Avoid detection & selection & misclassification bias**

- Adequate screening for asymptomatic carriers
- If possible, select the right colonies by selective cultures (multiresistant organisms).
- How many morphologically similar isolates to sample from the same clinical culture ?

Multiple Variants of *Klebsiella pneumoniae* Producing Carbapenemase in One Patient

Michael R. Mulvey, Ph.D.
National Microbiology Laboratory
Winnipeg, MB, Canada
michael.mulvey@phac-aspc.gc.ca

Louis-Patrick Haraoui, M.D.
McGill University Health Centre
Montreal, QC, Canada

Yves Longtin, M.D.
Jewish General Hospital
Montreal, QC, Canada

- 82 yr man
- Admitted to the same hospital 21 times (2011-2015)
- Often grouped with patients colonized with KPC-producing Enterobacteriaceae (KPE)
- Numerous antibiotic courses

Typing methods for outbreak investigations and epidemiologic surveillance

PFGE
MLVA

Various targets

POS: Established method
CONS: Little discriminatory power, cannot establish exact transmission routes

Monocentric outbreak

MLST

Selected loci

POS: Robust, reproducible method; allows to observe longterm trends
CONS: Little discriminatory power

Long-term Surveillance / Multicenter outbreaks

Outbreak of vancomycin-resistant *Enterococcus faecium* clone ST796, Switzerland, December 2017 to April 2018

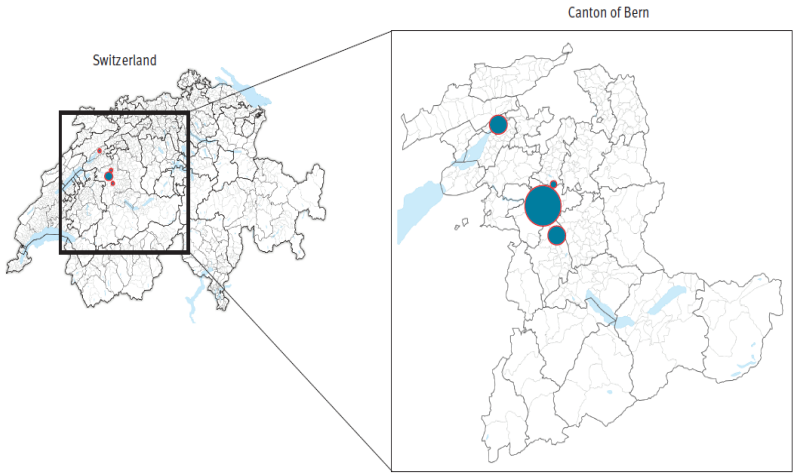
Nasstasja Wassilew[1], Helena MB Seth-Smith[2,3], Eveline Rolli[1], Yvonne Fietze[1], Carlo Casanova[4], Urs Führer[5], Adrian Egli[2,3], Jonas Marschall[1], Niccolò Buetti[1]

1. Department of Infectious Diseases, University Hospital Bern, Bern, Switzerland
2. Division of Clinical Microbiology, University Hospital Basel, Basel, Switzerland
3. Applied Microbiology Research, Department of Biomedicine, University of Basel, Basel, Switzerland
4. Institute for Infectious Diseases, University of Bern, Bern, Switzerland
5. Infectious Diseases Department, Biel Hospital, Biel, Switzerland

Correspondence: Niccolò Buetti (niccolo.buetti@gmail.com)

FIGURE 1

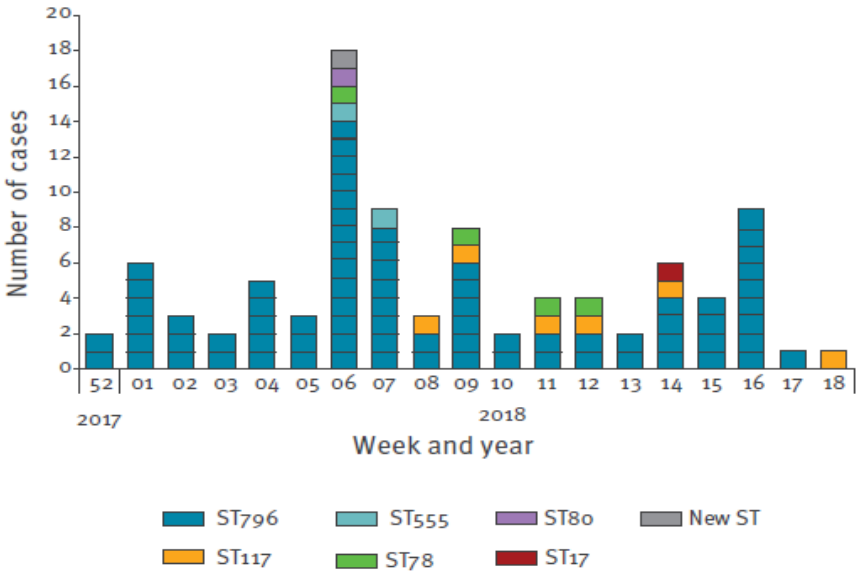
Distribution of vancomycin-resistant *Enterococcus faecium* ST796 in four different hospitals, Canton of Bern, Switzerland, 30 December 2017 to 30 April 2018 (n = 89)



The largest outbreak at University hospital is shown by the largest circle.

FIGURE 3

Epidemic curve of vancomycin-resistant enterococci (VRE) cases by sequence type, Canton of Bern outbreak, Switzerland, December 2017–April 2018 (n = 89)



Typing methods for outbreak investigations and epidemiologic surveillance

PFGE MLVA

Various targets

POS: Established method
CONS: Little discriminatory power, cannot establish exact transmission routes

Monocentric outbreak

MLST

Selected loci

POS: Robust, reproducible method; allows to observe longterm trends
CONS: Little discriminatory power

Long-term Surveillance / Multicenter outbreaks

WGS

Core genome

POS: High discriminatory power
CONS: Still expensive and requires special analytical skills

Outbreaks or epidemiologic surveillance

nature microbiology

ARTICLES

https://doi.org/10.1038/s41564-018-0230-7

Global spread of three multidrug-resistant lineages of *Staphylococcus epidermidis*

Jean Y. H. Lee[1], Ian R. Monk[1], Anders Gonçalves da Silva[2,3], Torsten Seemann[3,4], Kyra Y. L. Chua[5], Angela Kearns[6], Robert Hill[6], Neil Woodford[6], Mette D. Bartels[7], Birgit Strommenger[8], Frederic Laurent[9], Magali Dodémont[10], Ariane Deplano[10], Robin Patel[11], Anders R. Larsen[12], Tony M. Korman[13], Timothy P. Stinear[1,3,15] and Benjamin P. Howden[2,3,14,15]*

➔ Uncovered the previously unrecognized international spread of a near pandrug-resistant nosocomial pathogen, identifiable by a rifampicin-resistant phenotype.

A *Candida auris* Outbreak and Its Control in an Intensive Care Setting

David W. Eyre, D.Phil., Anna E. Sheppard, Ph.D., Hilary Madder, F.A.N.Z.C.A., Ian Moir, Ruth Moroney, M.Sc., T. Phuong Quan, M.Sc., David Griffiths, B.Sc., Sophie George, M.Sc., Lisa Butcher, M.Sc., Marcus Morgan, M.Sc., Robert Newnham, Mary Sunderland, B.Sc., Tiphanie Clarke, B.A., Dona Foster, Ph.D., Peter Hoffman, B.Sc., Andrew M. Borman, Ph.D., Elizabeth M. Johnson, Ph.D., Ginny Moore, Ph.D., Colin S. Brown, F.R.C.Path., A. Sarah Walker, Ph.D., Tim E.A. Peto, F.R.C.P., Derrick W. Crook, F.R.C.Path., and Katie J.M. Jeffery, Ph.D.

➔The transmission of *C. auris* was found to be linked to reusable axillary temperature probes, indicating that this emerging pathogen can persist in the environment and be transmitted in health care settings.

N Engl J Med 2018;379:1322-31.

Analytic (sequencing)

Bias during the process

Storage → Extraction → Library preparation → Sequencing

Storage parameters:
T°C, time, media, UV, container

Extraction parameters:
enzymatic, mechanical (fav. GPB)

Size selection:
gels (melting~dec. AT-rich sequences)

Library preparation:
PCR approaches (heterogeneous affinities)

The right platform

Illumina	Accurate Takes time(days)
454, **Ion torrent**	! False positive variant calling
PacBio, **MinION**	! False positive variant calling

«Next-generation sequencing technologies and their application to the study and control of bacterial infections», J.Besser, CMI, 2018
Prof. SCHRENZEL Jacques
«Library preparation methods for next generation sequencing: Tone down the bias», E.L. van Dijk, Exp Cell Research, 2014

What is close enough ?

Relatedness thresholds

SNPs: nb of SNPs differences
MLST: nb of alleles variations

Table 1
Examples of relatedness criteria for wg/cgMLST and SNP typing schemes of representative clinically relevant bacteria

Organism	Relatedness threshold[a]		References
	wg/cgMLST (allele) SNPs		
Acinetobacter baumannii	≤8	≤3	[25,26]
Brucella spp.	Epidemiologic validation in progress[b]		http://www.applied-maths.com/applications/wgmlst
Campylobacter coli, C. jejuni	≤14	≤15	[27,28]
Cronobacter spp.	Epidemiologic validation in progress[b]		http://www.applied-maths.com/applications/wgmlst
Clostridium difficile	Epidemiologic validation in progress[b]	≤4	[29], http://www.cgmlst.org/ncs, http://www.applied-maths.com/applications/wgmlst
Enterococcus faecium	≤20	≤16	[30]
Enterococcus raffinosus	Epidemiologic validation in progress[b]		http://www.applied-maths.com/applications/wgmlst
Escherichia coli	≤10	≤10	[31,32], https://enterobase.warwick.ac.uk/
Francisella tularensis	≤1	≤2	[33,34]
Klebsiella oxytoca	Epidemiologic validation in progress[b]		http://www.applied-maths.com/applications/wgmlst
Klebsiella pneumonia	≤10	≤18	[35,36]
Legionella pneumophila	≤4	≤15	[37]
Listeria monocytogenes	≤10	≤3	[38,39]
Mycobacterium abscessus		≤30	[40]
Mycobacterium tuberculosis	≤12	≤12	[41]
Neisseria gonorrhoeae	Epidemiologic validation in progress[b]	≤14	[42], http://www.applied-maths.com/applications/wgmlst
Neisseria meningitidis	Epidemiologic validation in progress[b]		http://www.cgmlst.org/ncs
Pseudomonas aeruginosa	≤14	≤37	[31,43]
Salmonella dublin	Epidemiologic validation in progress[b]	≤13	[44], https://enterobase.warwick.ac.uk/
Salmonella enterica	Epidemiologic validation in progress[b]	≤4	[45], http://www.cgmlst.org/ncs, http://www.applied-maths.com/applications/wgmlst, https://enterobase.warwick.ac.uk/
Salmonella typhimurium	Epidemiologic validation in progress[b]	≤2	[46], https://enterobase.warwick.ac.uk/
Staphylococcus aureus	≤24	≤15	[47,48]
Streptococcus suis		≤21	[49]
Vibrio parahaemolyticus	≤10		[50]
Yersinia spp.	0		[51]

cg, core genome; MLST, multilocus sequence typing; SNP, single nucleotide polymorphism; wg, whole genome.
[a] Data often represent single studies that can be used to begin formulation of species-specific interpretation criteria. Thus, these data should be coupled with newly published similar studies to ensure that resulting values are not atypical and can be generally applied.
[b] Proposed wg/cgMLST schemes are available online (http://www.cgmlst.org/ncs, http://www.applied-maths.com/applications/wgmlst, https://enterobase.warwick.ac.uk/) but as yet have not been epidemiologically validated.

BUT

- Intra-individual variation
- Genetic recombination events
- Clock speed is different among pathogens

THUS

- Consider suggested thresholds more as a guideline

➔ Interprete epidemiological links on a case by case basis

➔ Interprete organism by organism (specific population genetics)

Outbreak investigations from Geneva

MRSA

CPE

VRE

Serratia

Friday, June 30

Phone rings:

„Hello...! We have a problem down here at the NICU – can you help us ?“

"Do you want to speak to the man in charge or the nurse who knows what's going on?

Veni vidi … (vici ?)

Julius Caesar, De Bello Gallico

You go in there and have a look…

- **What?** — MRSA outbreak
- **Who?** — 11 neonates, 2 mothers
- **Where?** — NICU & nursery
- **When?** — Over the last 3 months
- **Severe?** — No – mostly carriage

What would you recommend for the next week – priority action items except?

A. Isolate or cohort MRSA carriers
B. Reinforce hand hygiene
C. Screening of all hospitalized neonates
D. Implement active MRSA surveillance for all new admissions
E. Molecular typing of MRSA isolates

What would you recommend for the next week – priority action items except?

A. Isolate or cohort MRSA carriers

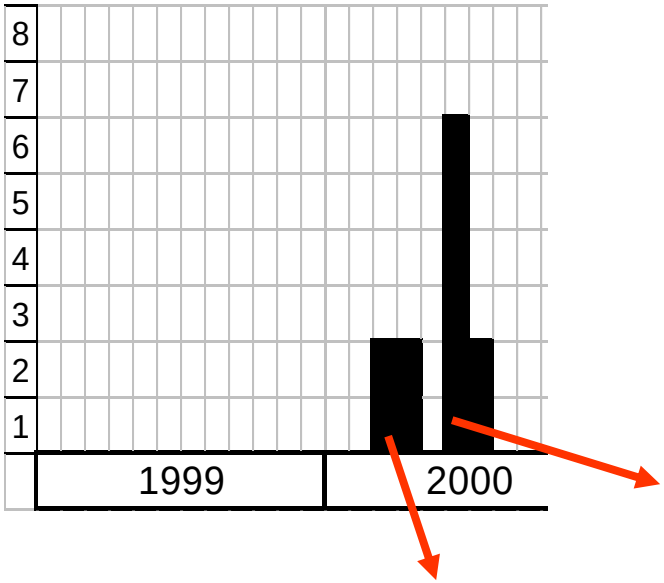
B. Reinforce hand hygiene

C. Screening of all hospitalized neonates

D. Implement active MRSA surveillance for all new admissions

E. **Molecular typing of MRSA isolates**

Epidemic curve
MRSA outbreak, NICU (HUG)



ANTIBIOGRAMMES	(1)x1 SCN. Interpré.	(2)x3 MRSAe Interpré.
Penicilline G	RESIST	RESIST
Flucloxacilline	RESIST	RESIST
Amikacine	RESIST	RESIST
Gentamicine	S	RESIST
Norfloxacine	RESIST	RESIST
Ciprofloxacine	RESIST	RESIST
Clindamycine	S	RESIST
Erythromycine	RESIST	RESIST
Acide fusidique	INTERM	S
Co-trimoxazole	RESIST	S
Fosfomycine		S
Rifampicine	S	S
Vancomycine	S	S
Teicoplanine	S	S

MBOMA+ 16 UU25
16/U//UU U8HUU trottis inguinal
MBOMA+ 18 U145
18/U//UU 12HU5 urine poche a urines
MBOMA+ 25 U13U
25/U//UU 1UH55 trottis de nez
MBOMA+ 25 U151
25/U//UU 1UH55 trottis inguinal
MBOMA+ 25 U155
25/U//UU 11HUU trottis ombilic

Meticilline-resistant (1) T 25.U7
1UE5 Flore mixte T 21.U7
1UE4 Staph. aureus Meticilline-resistant T 21.U7
ABS Staph. aureus Meticilline-resistant T 28.U7
PRES Staph. aureus Meticilline-resistant (1) T U2.U8
PRES Staph. aureus Meticilline-resistant (1) T U2.U8

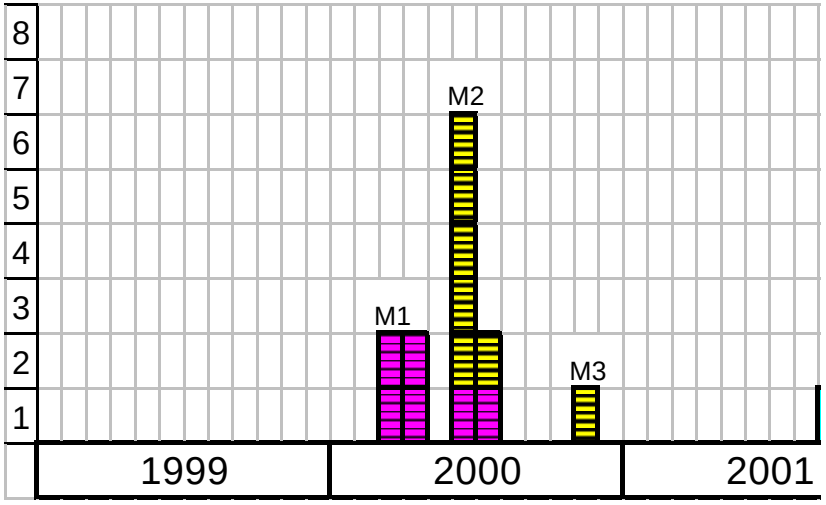
E = En cours. T = Terminé.

QUANTIFICATION: le chiffre (1UE4 = 1U'UL prélèvement ou par cm de cathéter.
ABS = absence de, PRES = présence de, Mit, POS = positif, + = rare,
++ = nombreux, +++ = très nombreux.

ANTIBIOGRAMME	(1)x8 MRSAe Interpré.
Penicilline G	RESIST
Flucloxacilline	RESIST
Amikacine	S
Gentamicine	S
Norfloxacine	S
Ciprofloxacine	S
Clindamycine	S
Erythromycine	S
Acide fusidique	RESIST
Co-trimoxazole	S
Fosfomycine	S
Rifampicine	S
Vancomycine	S
Teicoplanine	S

Sax et al. J Hosp Infect 2006; 63: 93-100

Control measures
MRSA outbreak, NICU (HUG)



A. Isolate or cohort MRSA carriers

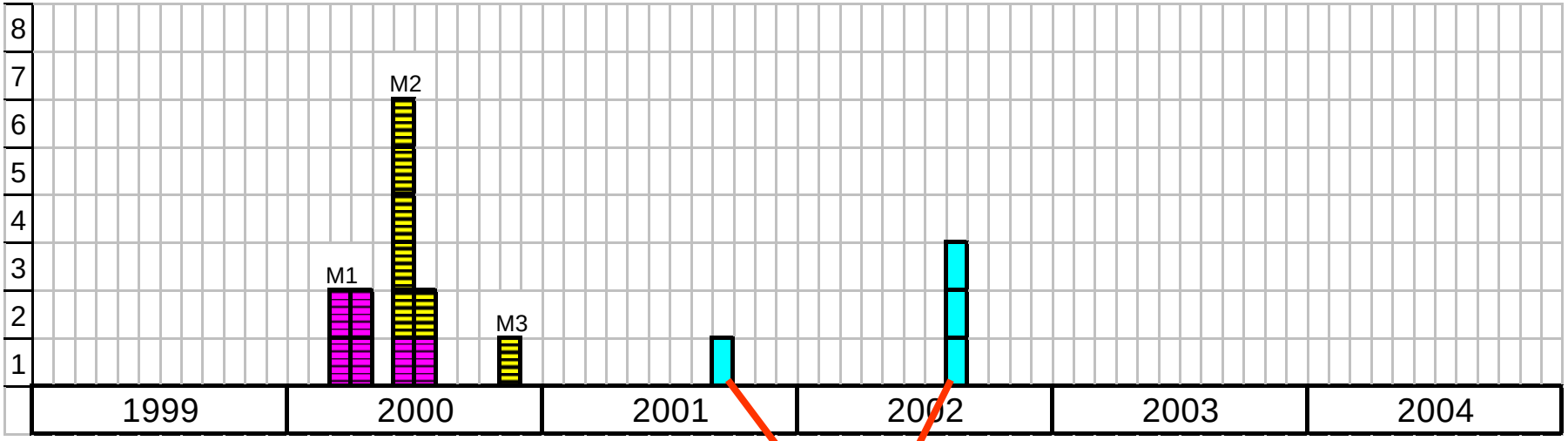
B. Reinforce hand hygiene

C. Screening of all neonates & mothers

D. Implement active MRSA surveillance (admission & discharge)

Sax et al. J Hosp Infect 2006; 63: 93-100

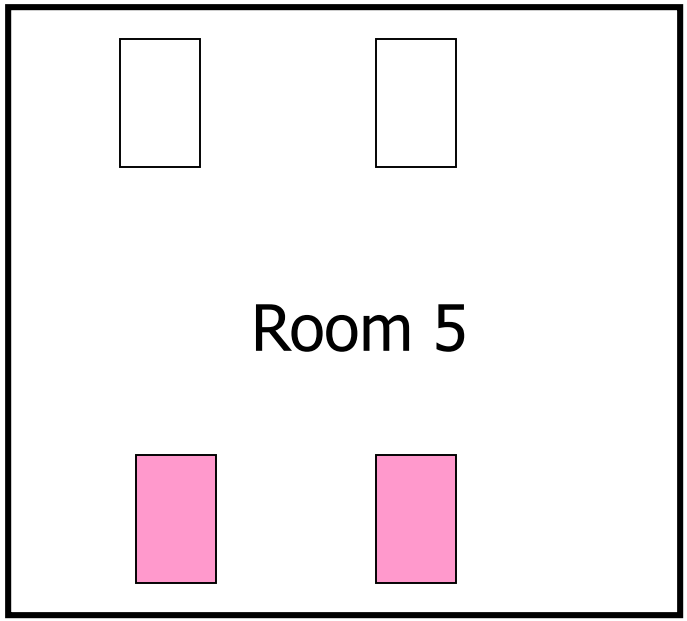
Epidemic curve
MRSA outbreak, NICU (HUG)

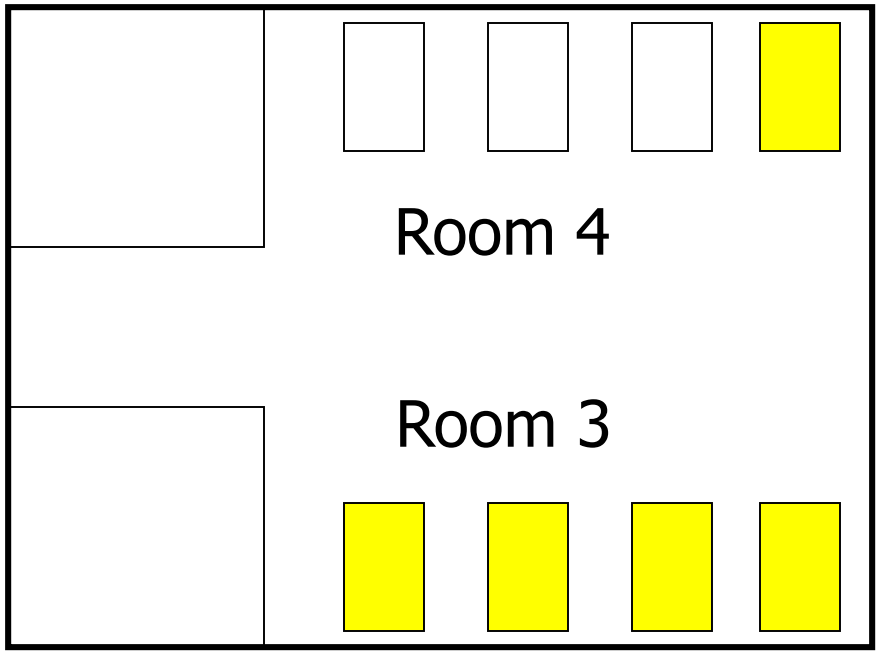


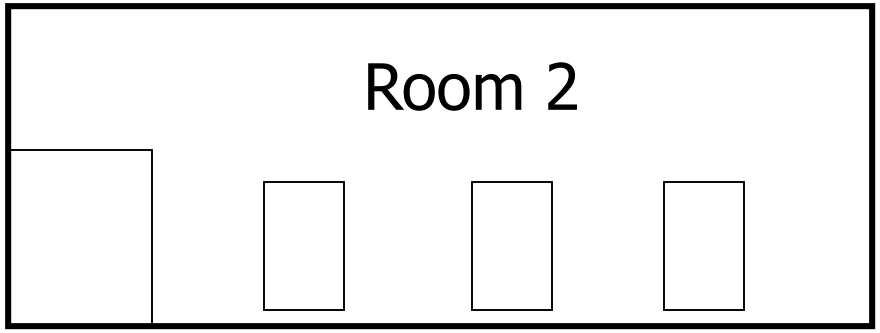
ANTIBIOGRAMME	(1)x1 MRSA Interpré.
Penicilline G	RESIST
Flucloxacilline	RESIST
Gentamicine	S
Norfloxacine	RESIST
Ciprofloxacine	RESIST
Clindamycine	RESIST
Erythromycine	RESIST
Acide fusidique	S
Co-trimoxazole	S
Rifampicine	S
Vancomycine	S
Teicoplanine	S

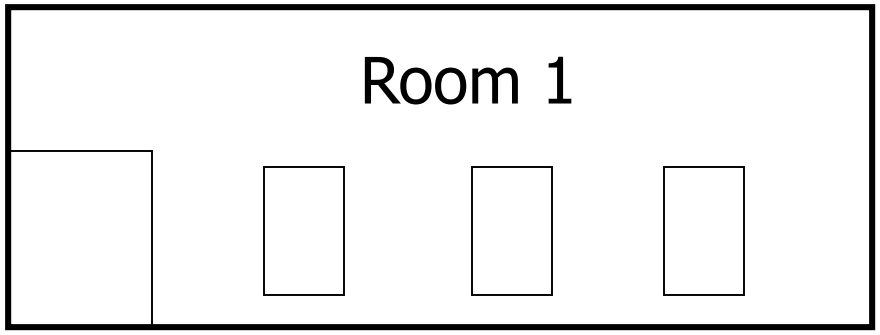
Sax et al. J Hosp Infect 2006; 63: 93-100

NICU at HUG
June/July 2000









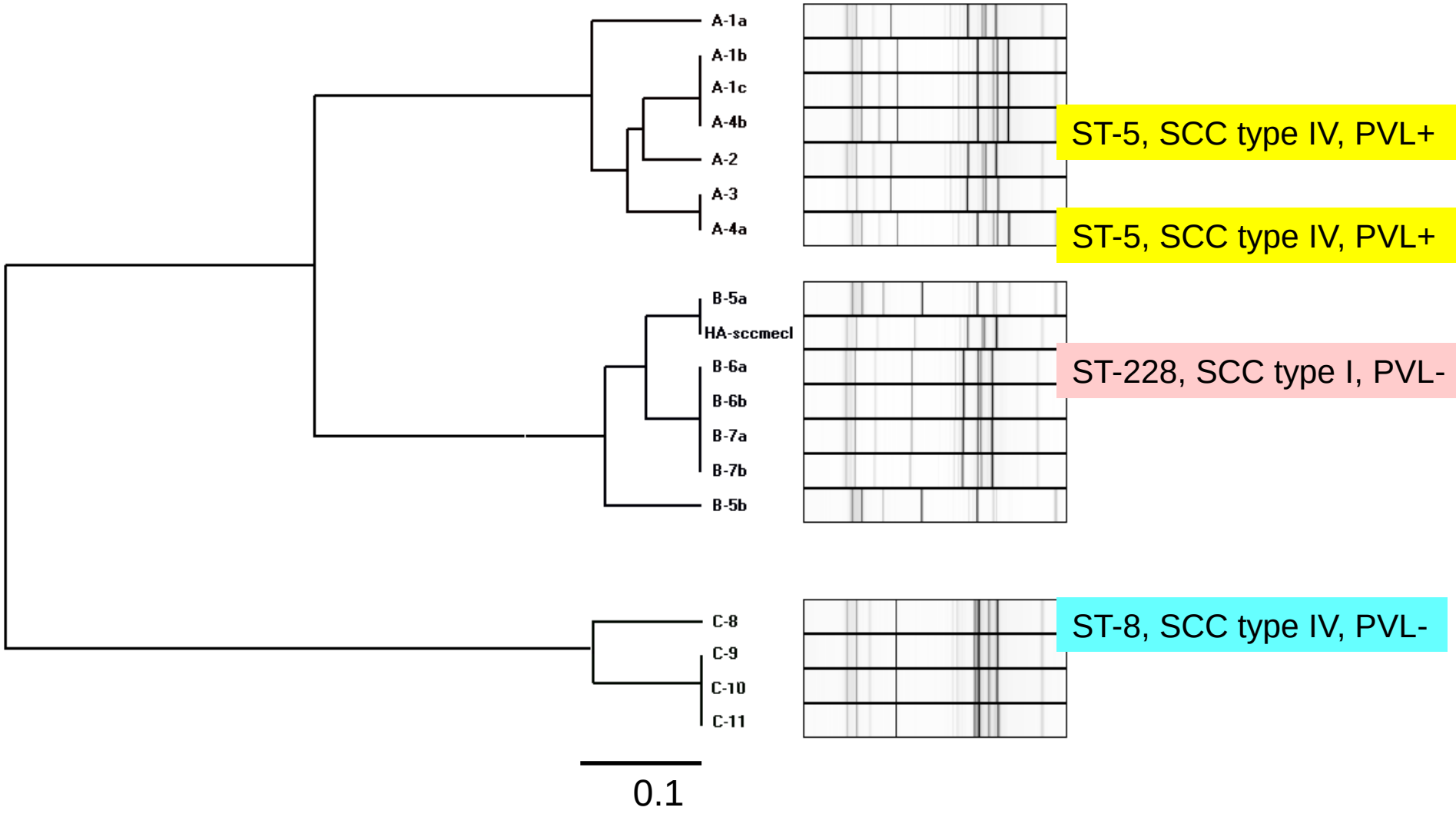
Legend

PVL+ CA-MRSA strain

Multi-R strain (endemic at HUG)

Sax et al. J Hosp Infect, 2006.

Molecular Epidemiology



Sax et al. J Hosp Infect 2006; 63: 93-100

General internal medicine ward, Geneva

Sporadic, imported CPE
(OXA-48 cluster in 2011)

KPC outbreak in Geneva, 2015

- Mr CV, Italian origin, known KPC carrier since 2012
- Admitted in January 2015 for severe KPC urosepsis
- Control measures were applied (private room)

Courtesy: F. Olearo, D. Pires

voir sous MS-Excel	06/03/2015 10:25:00	04/03/2015 11:45:00	04/03/2015 11:45:00	27/02/2015 19:00:00	27/02/2015 19:00:00	20/02/2015 17:00:00	19/02/2015 10:55:00
	Klebsiella pneumoniae	Klebsiella pneumoniae	Proteus mirabilis	Klebsiella pneumoniae	Proteus mirabilis	Klebsiella pneumoniae	Klebsiella pneumoniae
	sgv ponction	frot. plaie prof.	frot. plaie prof.	frot.	frot.	liqu.	liqu.
Penicilline G							
Flucloxacilline							
Amoxicilline	R	R	R	R	R	R	R
Co-amoxiclav	R	R	S	R	S	R	R
Piperacilline	R	R	S	R	I	R	R
Piperac.+tazob	R	R	S	R	S	R	R
Cefalotine							
Cefoxitine	R	R	S	R	S	R	R
Cefuroxime	R	R	S	R	S	R	R
Cefuroxime axetil (oral)							
Ceftazidime	R	R	S	R	S	R	R
Ceftriaxone	R	R	S	R	S	R	R
Cefepime	R	R	S	R	S	R	R
Imipenem	(>32) R	R	S	(32) R	(0.500) S	R	(32) R
Meropeneme	(>32) R	R	S	(32) R	(0.032) S	R	(>32) R
Ertapènem	(>32) R	R	S	(32) R	(0.160) S	R	(>32) R
Aztreonam	R	R	S	R	S	R	R
Amikacine	R	R	S	R	S	R	I
Gentamicine	S	S	R	S	R	S	S
Tobramycine							
Norfloxacine	R	R	S	R	S	R	R
Ciprofloxacine	R	R	S	R	S	R	R
Levofloxacine							
Clindamycine							
Erythromycine							
Acide fusidique							
Co-trimoxazole	R	R	R	R	R	R	R
Fosfomycine	R	R	S	S	S	R	R
Rifampicine							
Tetracycline							
Tigécycline	S	S	R	S	R	S	S
Vancomycine							
Teicoplanine							
Linézolide							
Mupirocine							
Furanes	R	R	R	R	R	R	R
Colistine	(12) R	(4) R		(16) R			(0.750) S
Carbapénèmase-OXA48							A
Carbapénèmase-KPC							P

Case TC: KPC cross-transmission despite single room isolation of index patient

Sepsis due to Colistin-R KPC, HUG, March 2015

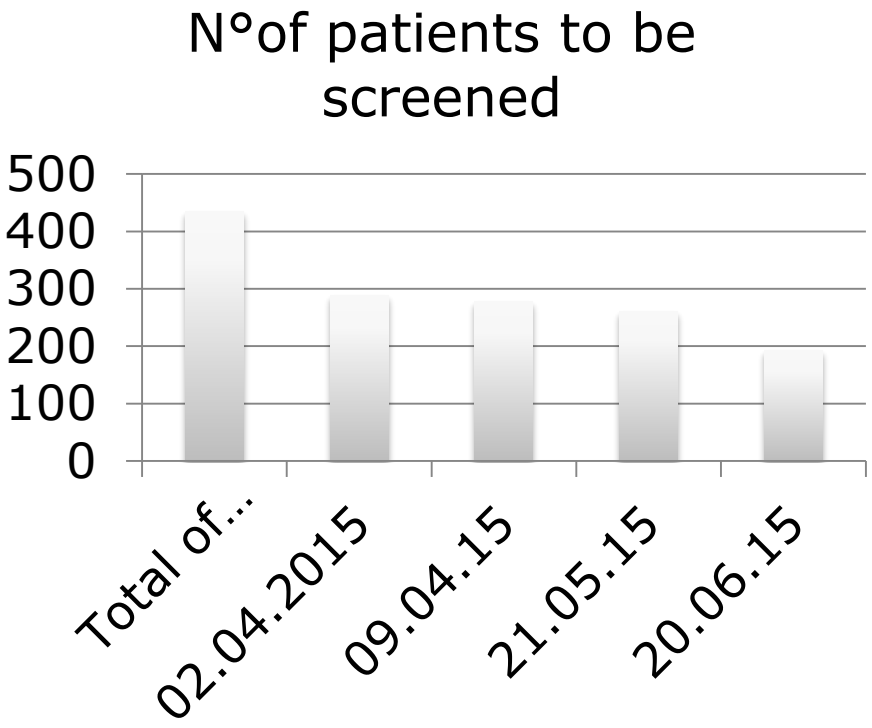
Total: 3 cases of KPC cross-transmission

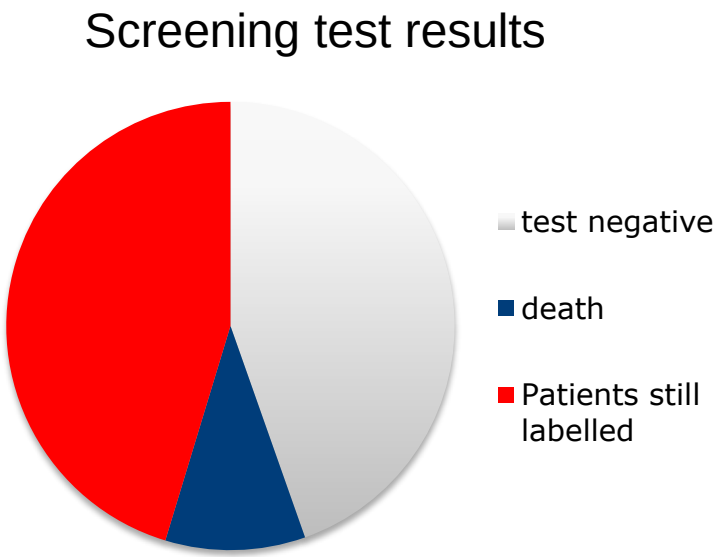
(2 clinical infections + 1 asymptomatic colonization)

Need of a bundled intervention

- Contact tracing with widespread screening
- Cohorting / strict contact precautions
- Electronic re-admission alert system
- Information (HCWs, patients, families)

Results of extensive screening





Not one single additional KPC case detected!

SNVs analysis from whole common DNA

Whole genome analysis: KPN7 had 3 SNV differences with others, KPN10 has another SNV

➔ Index strain slightly different from the strains recovered from secondary cases, likely because prior long-term carriage (3 years) by the index patient allowed for genetic mutations over time with intra-individual strain variation

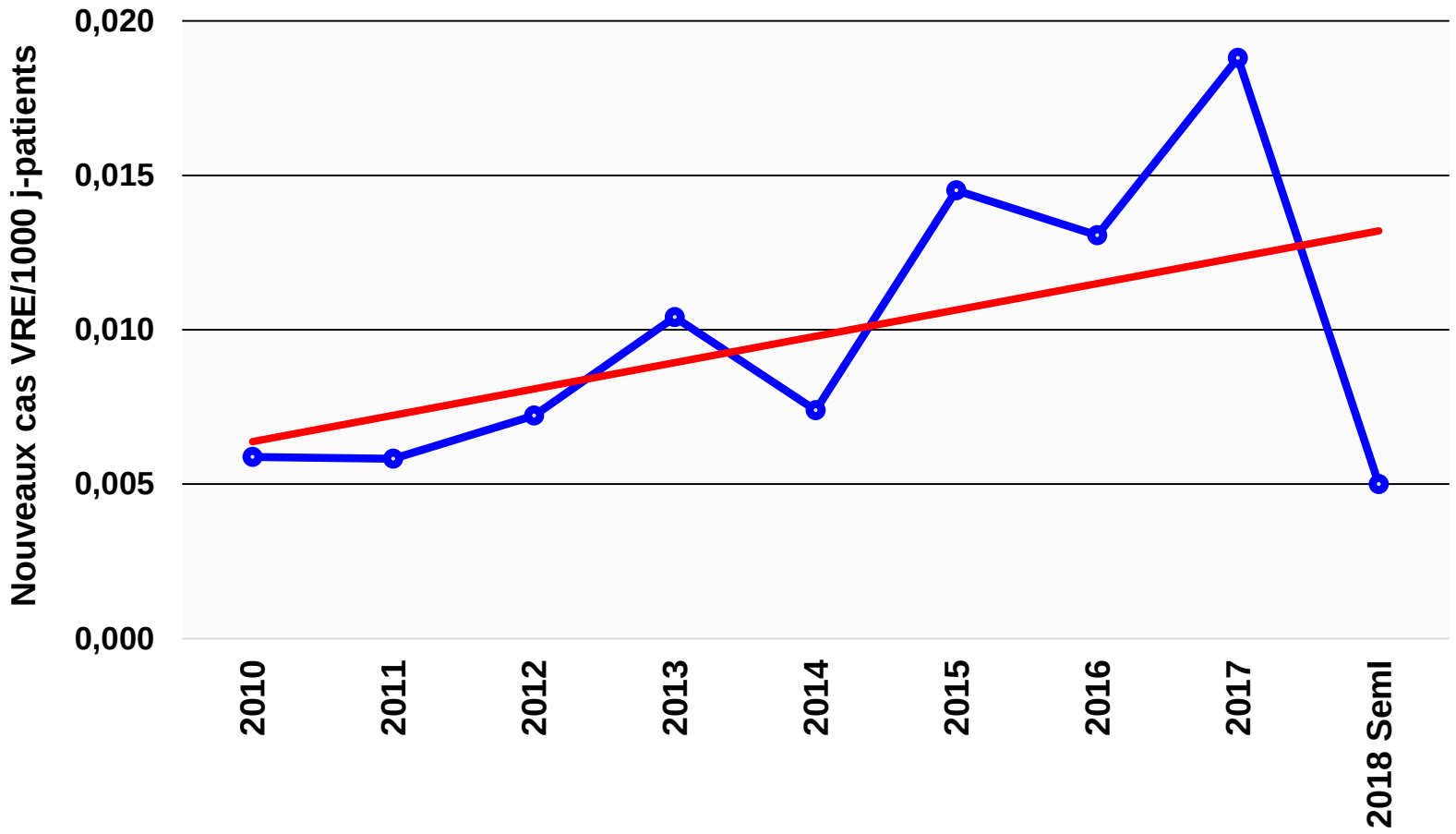
*ParSNP, all strains against strain KPN7 (index case)

E. Ruppé et al. Clin Micro Infect 2018

VRE outbreak

- Geneva,
  surgical unit

Incidence density of hospital-acquired VRE
HUG, January 2010 – June 2018



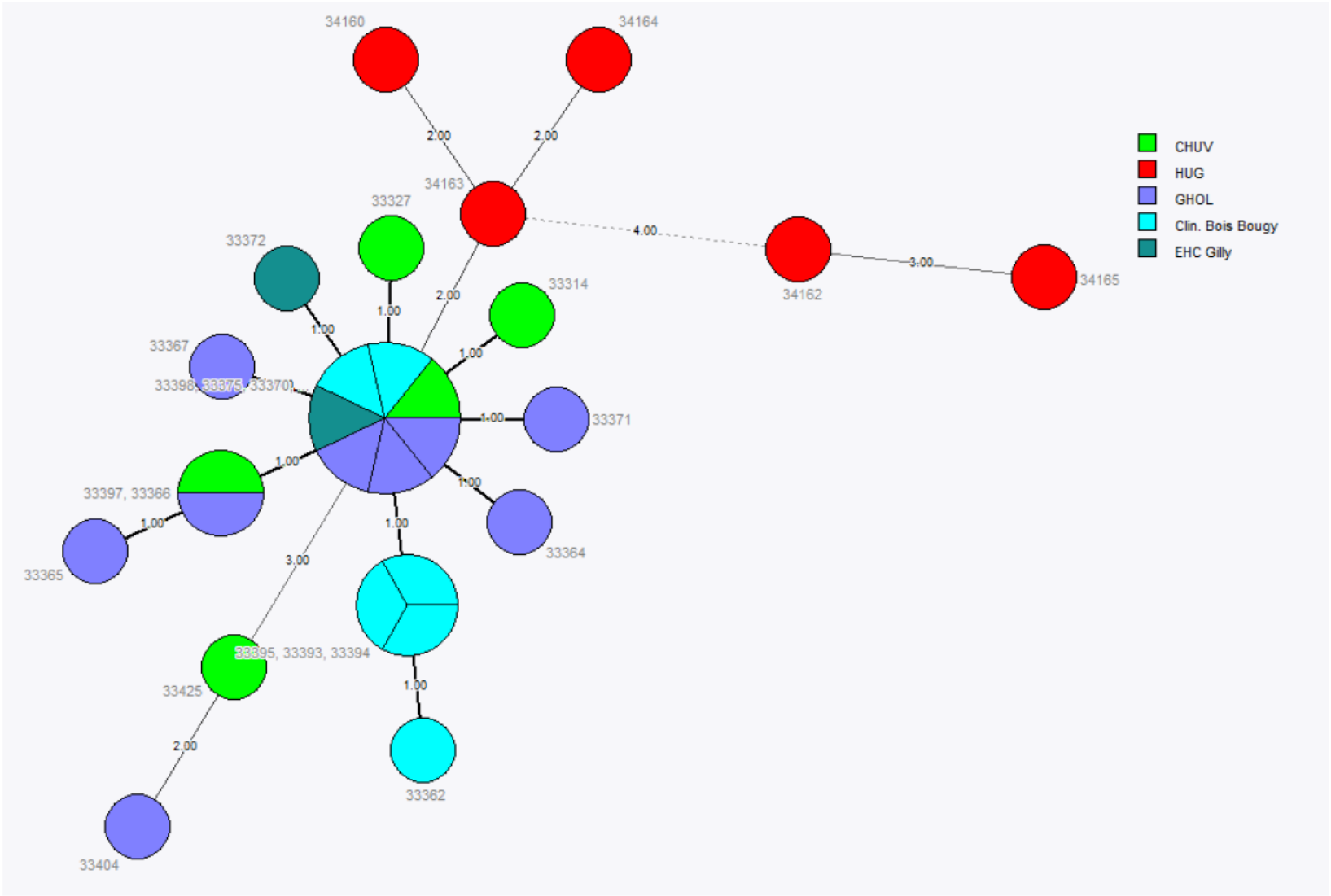


Figure 1. Arbre de maximum de parcimonie entre les souches du cluster ST117-B. La distance entre chaque souche indique le nombre de loci de différence.

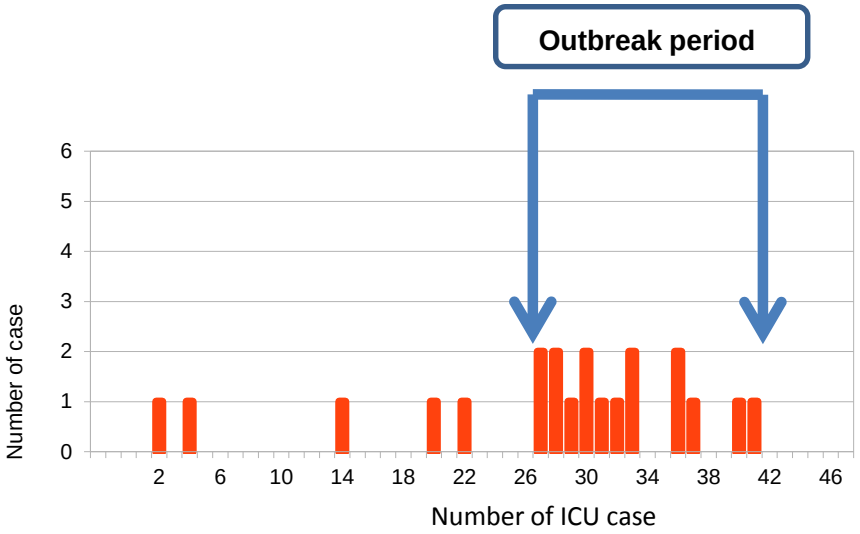
Courtesy: D. Blanc - CHUV

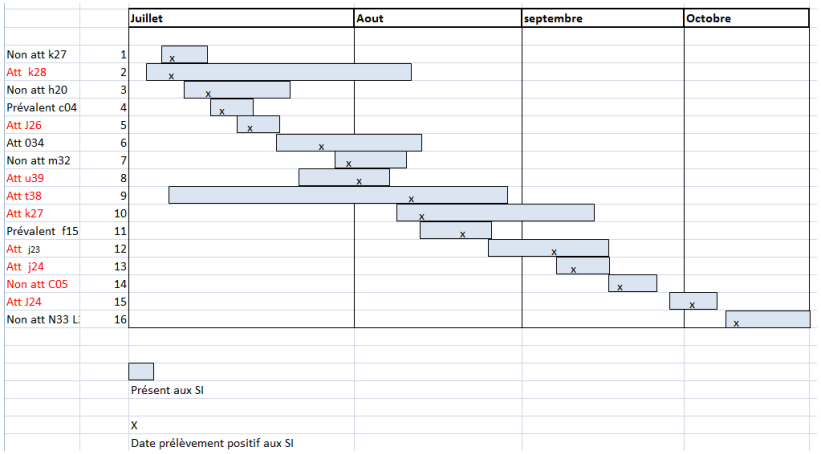
Serratia outbreak

Geneva ICU

Routine Serratia Surveillance => Epidemic curve in the ICU

Epidemiologic outbreak investigation => nosocomial transmission?

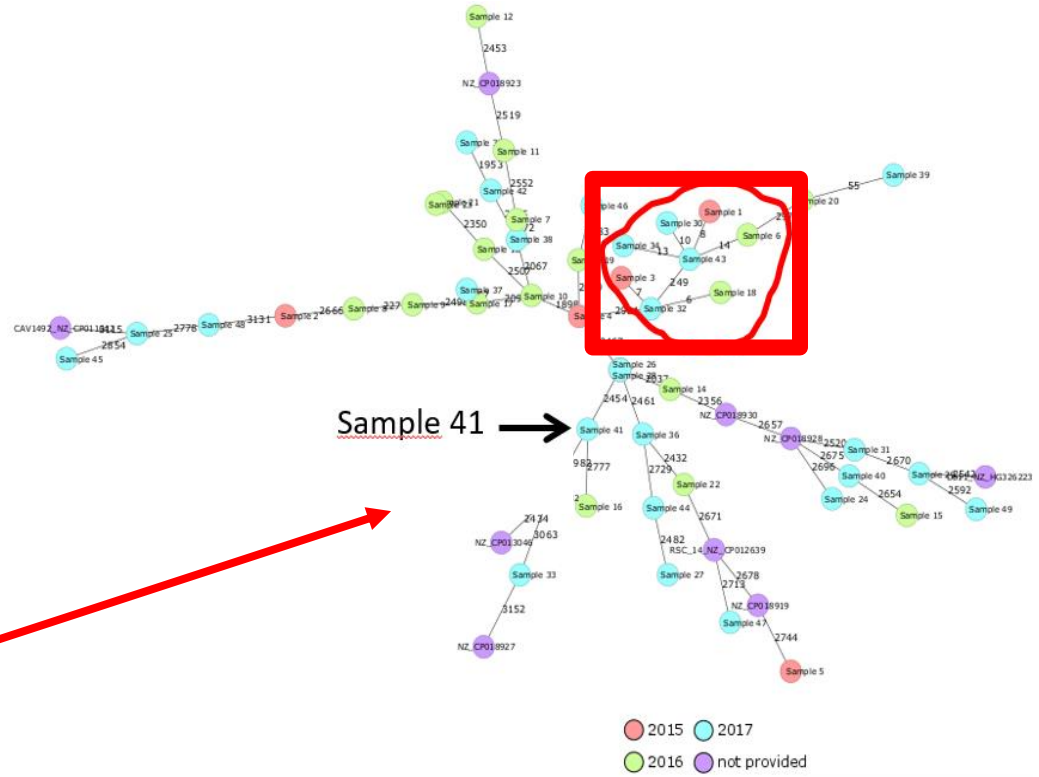




HH compliance: 66 % (1st semestre) to 52% (3d Trimestre)

Genomic investigation

-Selection and sequencing of multiple *S.marcescens* isolates (incl. outbreak strains) stored in the microbiological laboratory



GRL
[Genomic Research Lab]

Vladimir Lazarevic, PhD
Biologiste de recherche
CMU – Genomic Research Lab
Room C09.2141.A
Rue Michel Servet 1
CH - 1211 Genève 4
vladimir.lazarevic@genomic.ch
Tél. +41 22 379 41 25

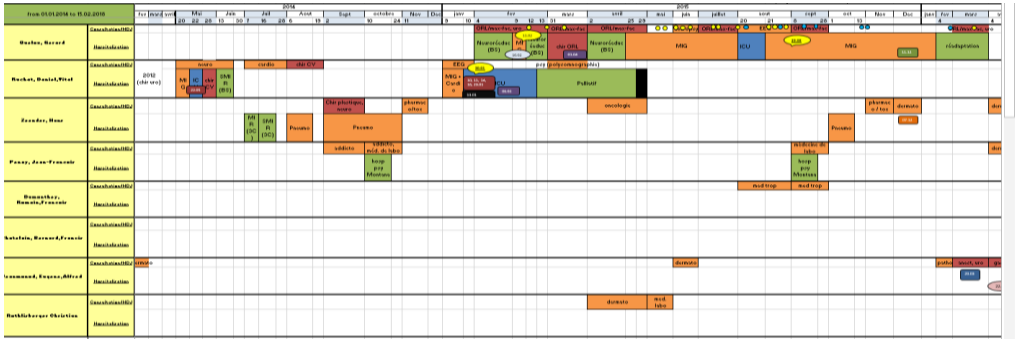
Cluster 26/28 : 2 isolats prélevés de différents patients mais dans un intervalle de 25 jours (4.7.2017, 29.7.2017). **Les profils cgMLST de ces deux souches sont identiques.**

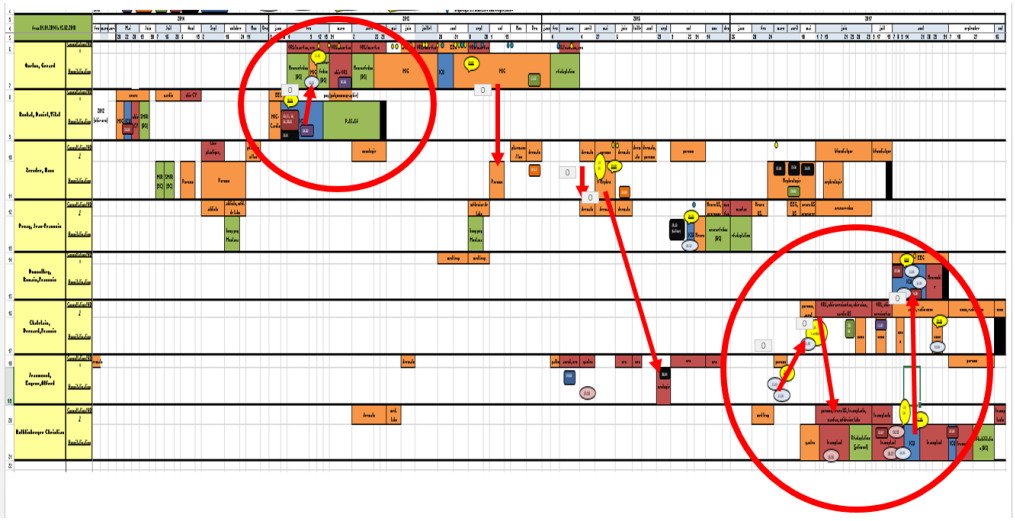
Cluster 1/3/6/18/30/32/34/43 : 8 isolats, tous provenant d'échantillons respiratoires mais de différents patients, prélevés dans un intervalle de deux ans (29.08.2015, 30.01.2015, 30.05.2016, 26.10.2016, 10.08.2017, 29.08.2017, 21.03.2017, 17.08.2017). Dans ce cluster, les cgSNPs ont été trouvés en 20 positions (sur un total de 1'485'517 positions), avec 0–8 cgSNPs dans les comparaisons par paires de souches (Table1). Le Neighbour-joining tree (cgSNP) est représenté dans la Figure 2. **Les profils cgMLST sont identiques pour les isolats 34 et 43.**

Epidemiologic investigation

-Data collection to retrieve epidemiological links based on genomic data (small monoclonal cluster from 2015 to 2017)

-Epidemiological investigation based on geospatial, microbiological and medical information (respiratory procedures, respiratory therapy, surgery etc…)





BUT

- Selection & detection bias (missing cases)
- Misclassification bias
- Information bias (retrospective study)

Conclusions

Future improvements to help hospital epidemiologists

WGS can reveal detailed spatial and temporal dynamics of nosocomial transmission events and MDRO evolution, <u>but we need</u>:

- Quality standards, proficiency testing for routine use
- Standard-operating procedures for sampling, data extraction…
- Agreements on data sharing practices (larger outbreaks)

- Shorter TAT
- Reduced costs
- Streamlined data analyses
- Thresholds to determine clustering and transmission events

- **<u>Most importantly</u>: demonstrate impact of WGS on preventive measures and clinical decision making (compared to less expensive tools)**

Thanks for your attention!