# VRE in Switzerland: from first cases to the national spread

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2) National Center for Infection Control / Switzerland

3) IAME, DeSCID team, INSERM, Université Paris Diderot and Sorbonne Paris Cité / France

# CONTENT

1) **OUTBREAK DESCRIPTION: BERN UNIVERSITY HOSPITALS AND REGION**

2) NATIONAL OUTBREAK INVESTIGATIONS

3) LOCAL MANAGEMENT STRATEGIES

4) SWISS RECOMMENDATIONS

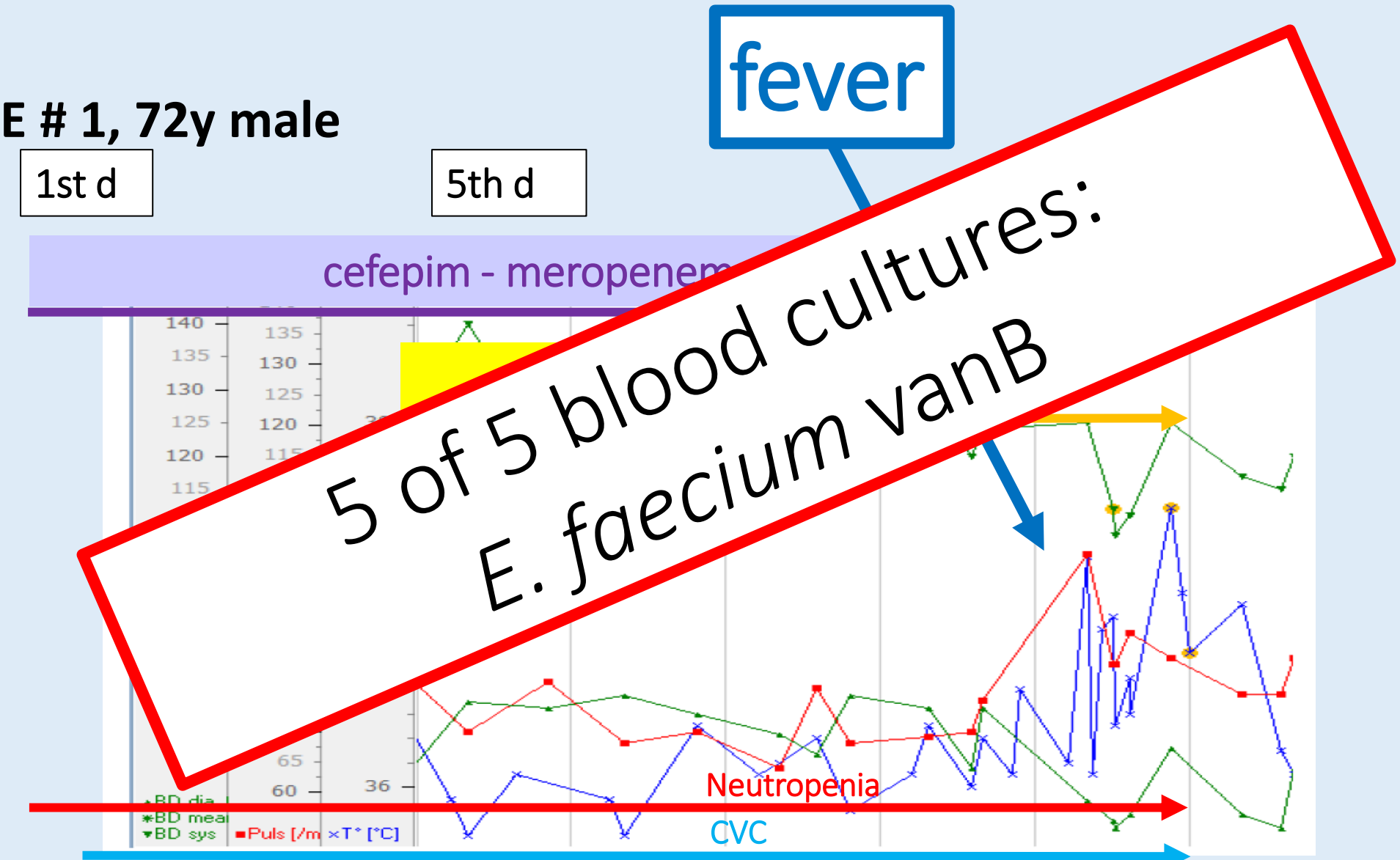
# 1. OUTBREAK DESCRIPTION – BERN/REGION

**CASE # 1**

- **72y, male**
- **Ischemic cardiopathy** with left heart failure (NYHA III-IV) and PM implantation (Apr 2014)
- **B-Cell-Non-Hodgkin Lymphoma**, Stadium IV E pulmonary (Dg: Jan 2017 → more chemotherapies administered → relapse → Blinatumomab on Dec 22nd 2017)
- Pulmonal invasive aspergillosis (Dg May 2017 → under Voriconazol) Myastenia gravis. **Neutropenia** start December 3rd 2017 (multifactorial)
- Emergency department 17th December: Fever, cough.
  - blood cultures
  - Abdominal and pulm. CT: unchanged neoplasia
  - Start cefepim/metronidazol (in the course switch on meropenem)

# 1. OUTBREAK DESCRIPTION – BERN/REGION

**CASE # 1, 72y male**



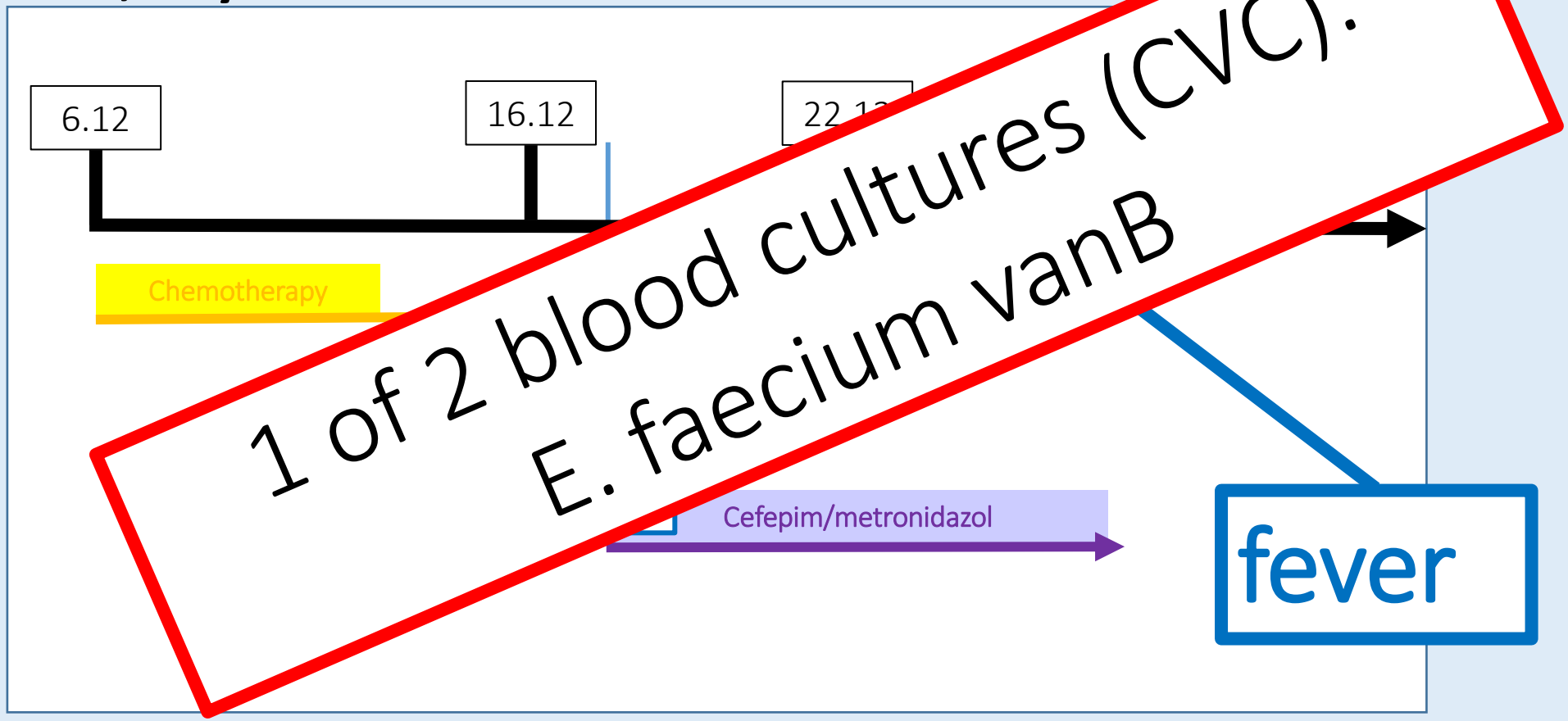
# 1. OUTBREAK DESCRIPTION – BERN/REGION

**CASE # 2**

- **70y, male**
- **Ischemic cardiopathy** with left heart failure (NYHA II-III)
- **Multiple myeloma, Stadium III** (Dg July 2017) → chemotherapy Aug-Nov 2017 → planned autologous hematopoietic cell transplantation (HCT) Dec 2017

# 1. OUTBREAK DESCRIPTION – BERN/REGION

**CASE # 2, 70y male**



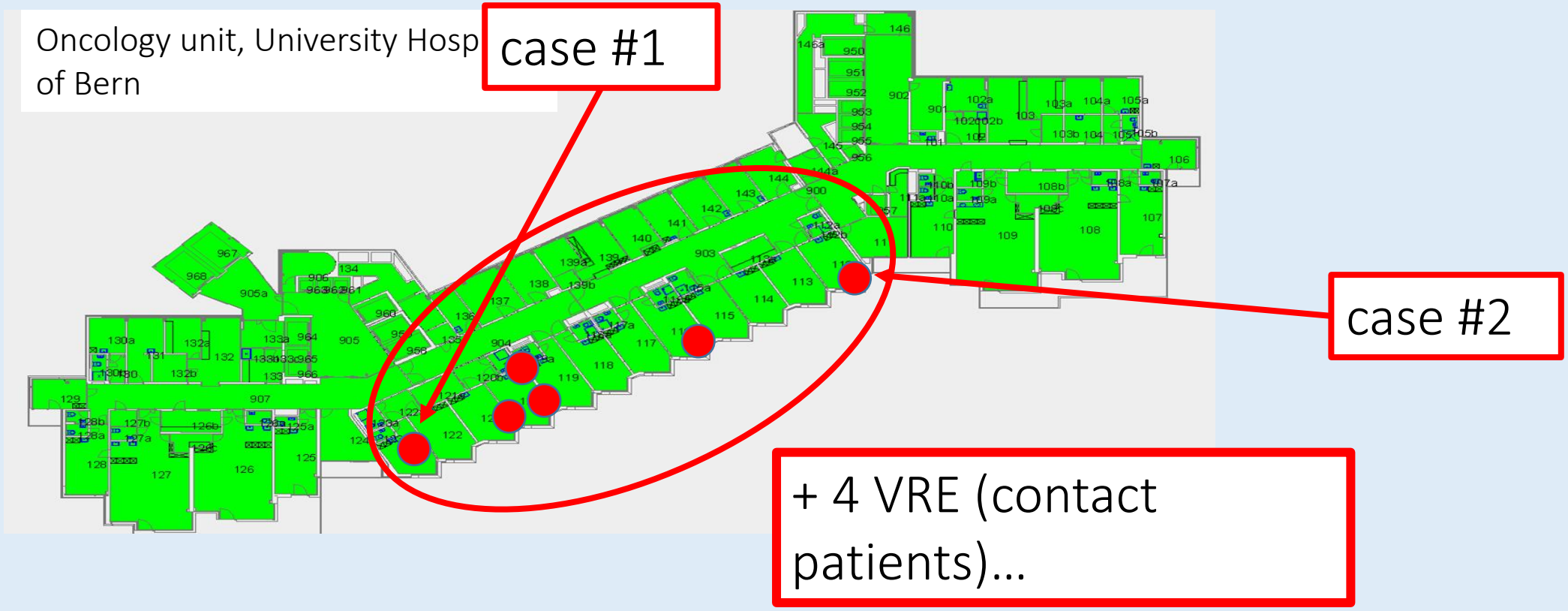

1 of 2 blood cultures (CVC):
E. faecium vanB

# 1. OUTBREAK DESCRIPTION – BERN/REGION

**CASE # 1 and CASE # 2**

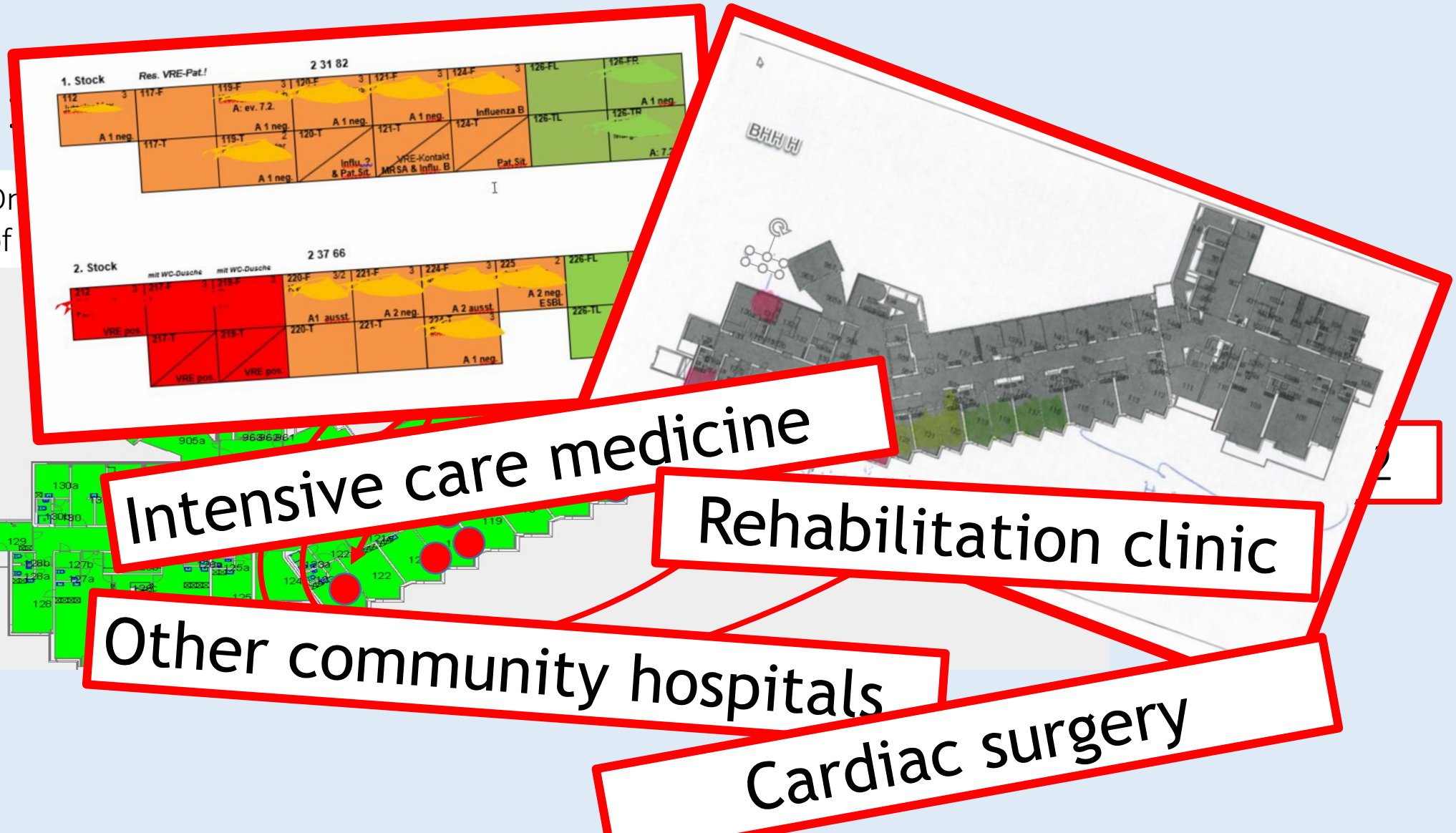
# 1. OUTBREAK DESCRIPTION – BERN/REGION

**CASE # 1 and CASE # 2**



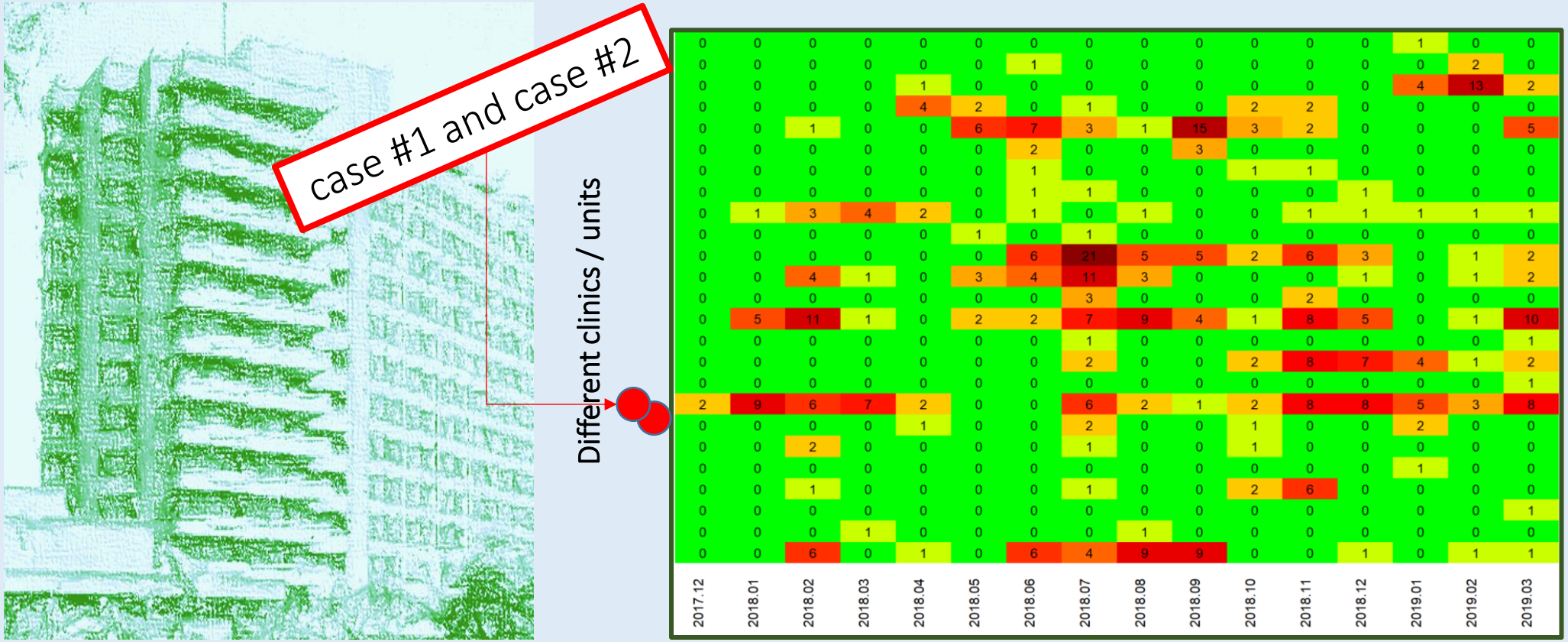
# 1. OUTBREAK DESCRIPTION – BERN/REGION

CASE # :



# 1. OUTBREAK DESCRIPTION – BERN/REGION

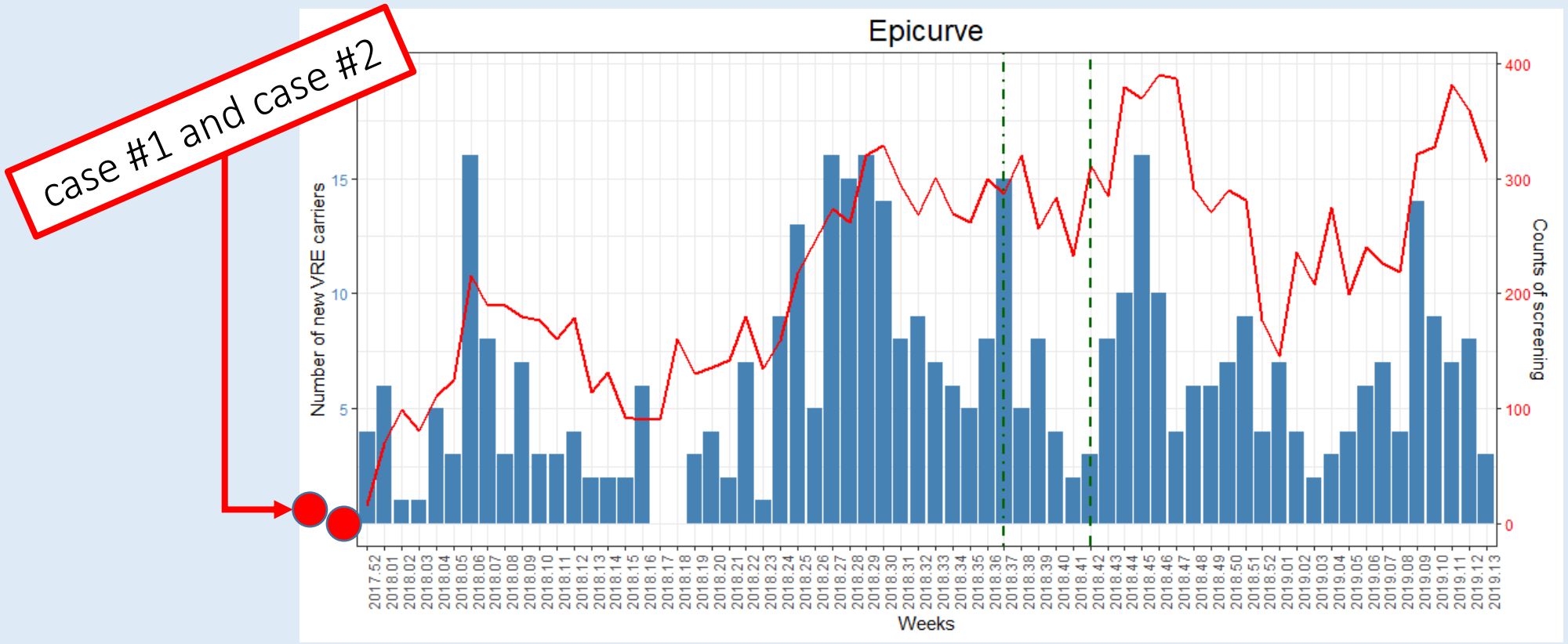
## BERN UNIVERSITY HOSPITALS – OUTBREAK DESCRIPTION 2017 – 3/2019




Adapted from Wassilew *et al.* Oral presentation. ECCMID Amsterdam, Apr 2019

# 1. OUTBREAK DESCRIPTION – BERN/REGION

## BERN UNIVERSITY HOSPITALS – EPIDEMIC CURVE Dec 2017 – March 2019




Adapted from Wassilew *et al.* Oral presentation. ECCMID Amsterdam, Apr 2019

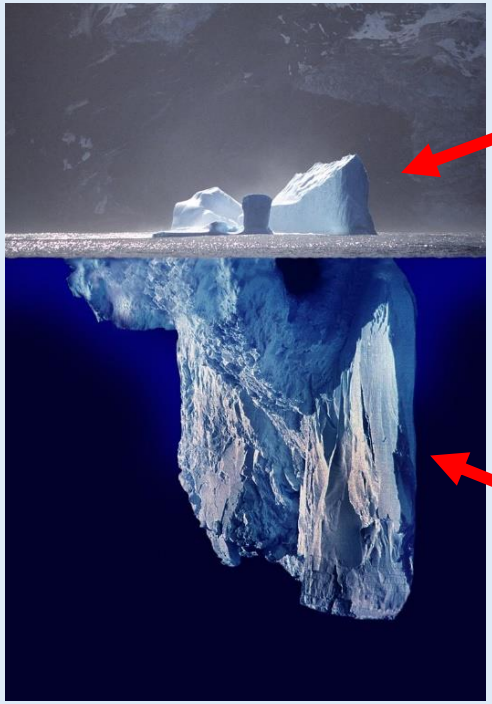
Courtesy Prof. Marschall, Bern University Hospital, Apr 2019

# 1. OUTBREAK DESCRIPTION – BERN/REGION

## BERN UNIVERSITY HOSPITALS – OUTBREAK DESCRIPTION 2017 – 3/2019

- Total: 424 VRE positive patients
- Mean age: 68
- Female: 158 (37,3%)
- Resistance type vanB: 407 (96%)
- BSI: 8 (1.9%)
- Other Infections: 10 (2.3%)
- Screening samples >16’000

4.2%




Wassilew *et al.* Oral presentation. ECCMID Amsterdam, Apr 2019

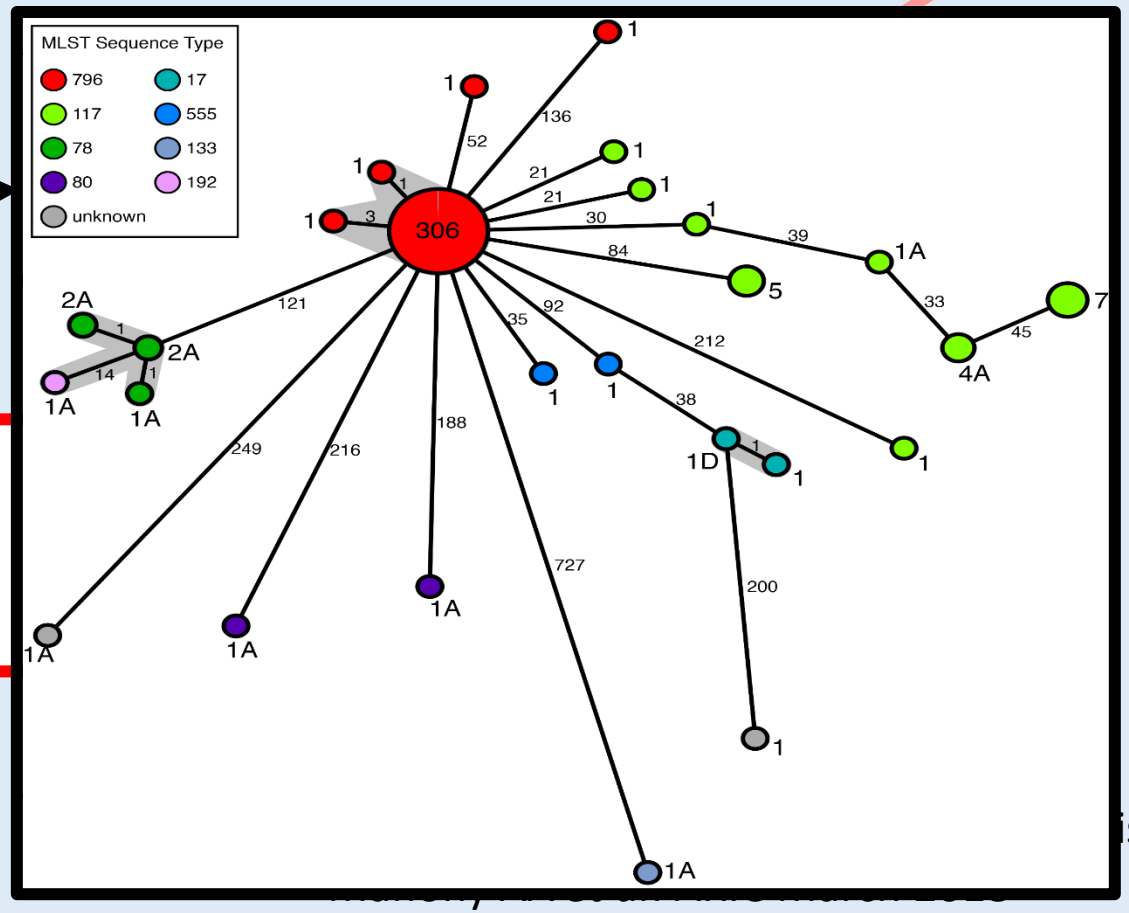
# 1. OUTBREAK DESCRIPTION – BERN/REGION

## CANTON OF BERN – A NEW CLONE: ST796

PINK: Australian isolates

Updated figure:
**ST769: 310/328 (95%)**

RED: Swiss isolates




- First recognized in Australia in 2011

- Rapid dissemination appears to continue in hospital of several Australian states as well New Zealand

-First description of VRE ST796 clonal dissemination across several hospitals in Switzerland

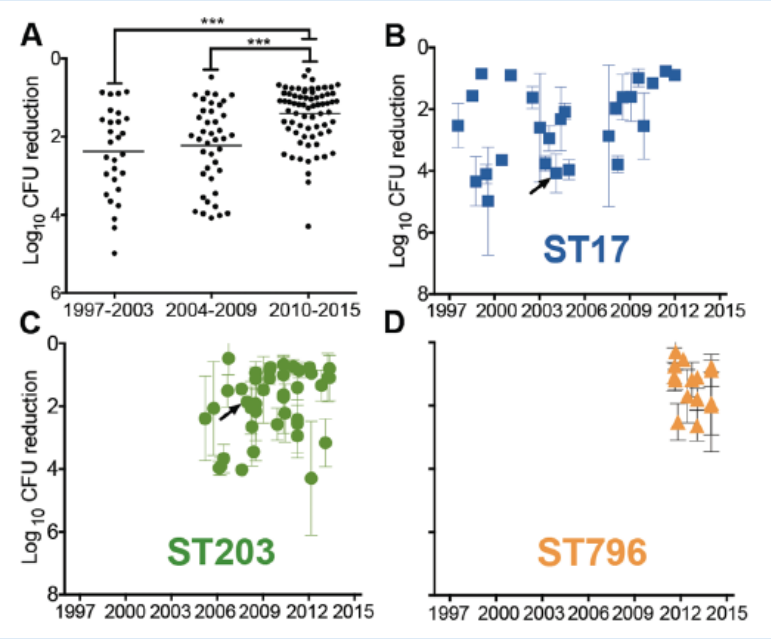
isco 2018

Wassilew *et al.* Oral presentation. ECCMID Amsterdam Apr 2019

# 1. OUTBREAK DESCRIPTION – BERN/REGION

## A NEW CLONE: ST796 – ISOPROPANOL RESISTANCE?

- The description of alcohol tolerance among Australian *Enterococcus faecium* strains to 23% isopropanol was recently described




Moreover, the tolerant strains were shown to resist a standard 70% isopropanol surface disinfection → greater mouse gut colonization compared to isopropanol-sensitive *E. faecium*.

Pidot S *et al*. Sci Transl Med, Aug 2018

# 1. OUTBREAK DESCRIPTION – BERN/REGION

## A NEW CLONE: ST796 – ISOPROPANOL RESISTANCE?

| Test strains | Concentration of isopropanol (v/v) | Exposure times | Mean $\log_{10}$ reduction |
|---|---|---|---|
| *E. faecium* ATCC 6057 | 23% | 5 min | 0.99 ± 0.27* |
| | | | 0.82 ± 0.29** |
| | | 15 min | 0.86 ± 0.11* |
| | 60% | 15 s | 5.56 ± 0.29** |
| | | | 5.47 ± 0.37*** |
| | | 30 s | 5.91 ± 0.02** |
| | | | 5.80 ± 0.21*** |
| | | 60 s | 5.91 ± 0.02** |
| | | | 5.96 ± 0.20*** |
| | 70% | 15 s | 5.89 ± 0.10** |
| | | | 5.90 ± 0.13*** |
| | | 30 s | 5.89 ± 0.10** |
| | | | 5.96 ± 0.11*** |
| | | 60 s | 5.89 ± 0.10** |
| | | | 5.86 ± 0.12*** |
| *E. faecium* ST 796 (Australia) | 23% | 5 min | 0.84 ± 0.09** |
| | | | 0.91 ± 0.27* |
| | | 15 min | 1.62 ± 0.31* |
| | 60% | 15 s | 5.45 ± 0.19** |
| | | | 5.57 ± 0.30*** |
| | | 30 s | 6.13 ± 0.03** |
| | | | 6.04 ± 0.04*** |
| | | 60 s | 6.13 ± 0.03** |
| | | | 6.04 ± 0.04*** |
| | 70% | 15 s | 5.38 ± 0.69** |
| | | | 5.65 ± 0.20*** |
| | | 30 s | 6.14 ± 0.23** |
| | | | 5.84 ± 0.01*** |
| | | 60 s | 6.14 ± 0.23** |
| | | | 5.84 ± 0.01*** |

| Test strains | Concentration of isopropanol (v/v) | Exposure times | Mean $\log_{10}$ reduction |
|---|---|---|---|
| | | | [illegible] |
| *E. faecium* ST 796 (Switzerland) | 23% | 5 min | 0.79 ± 0.20** |
| | | | 0.77 ± 0.06* |
| | | 15 min | 0.80 ± 0.12* |
| | 60% | 15 s | 5.65 ± 0.53** |
| | | | 5.92 ± 0.02*** |
| | | 30 s | 5.94 ± 0.03** |
| | | | 5.92 ± 0.02*** |
| | | 60 s | 5.94 ± 0.03** |
| | | | 5.92 ± 0.02*** |
| | 70% | 15 s | 5.95 ± 0.02** |
| | | | 5.83 ± 0.02*** |
| | | 30 s | 5.95 ± 0.02** |
| | | | 5.83 ± 0.02*** |
| | | 60 s | 5.95 ± 0.02** |
| | | | 5.83 ± 0.02*** |
| *E. hirae* ATCC 10541 | 60% | 15 s | 5.99 ± 0.03** |
| | | | 5.67 ± 0.44*** |
| | | 30 s | 5.83 ± 0.29** |
| | | | 6.02 ± 0.02*** |
| | | 60 s | 5.99 ± 0.03** |
| | | | 6.02 ± 0.02*** |
| | 70% | 15 s | 5.95 ± 0.03** |
| | | | 5.56 ± 0.45*** |

- Isopropanol at 60% and 70% were effective in 15 s against all strains but 23% isopropanol was not.

Conclusion: Healthcare workers can be reassured that 60% and 70% isopropanol with an appropriate volume are effective against *E. faecium*.

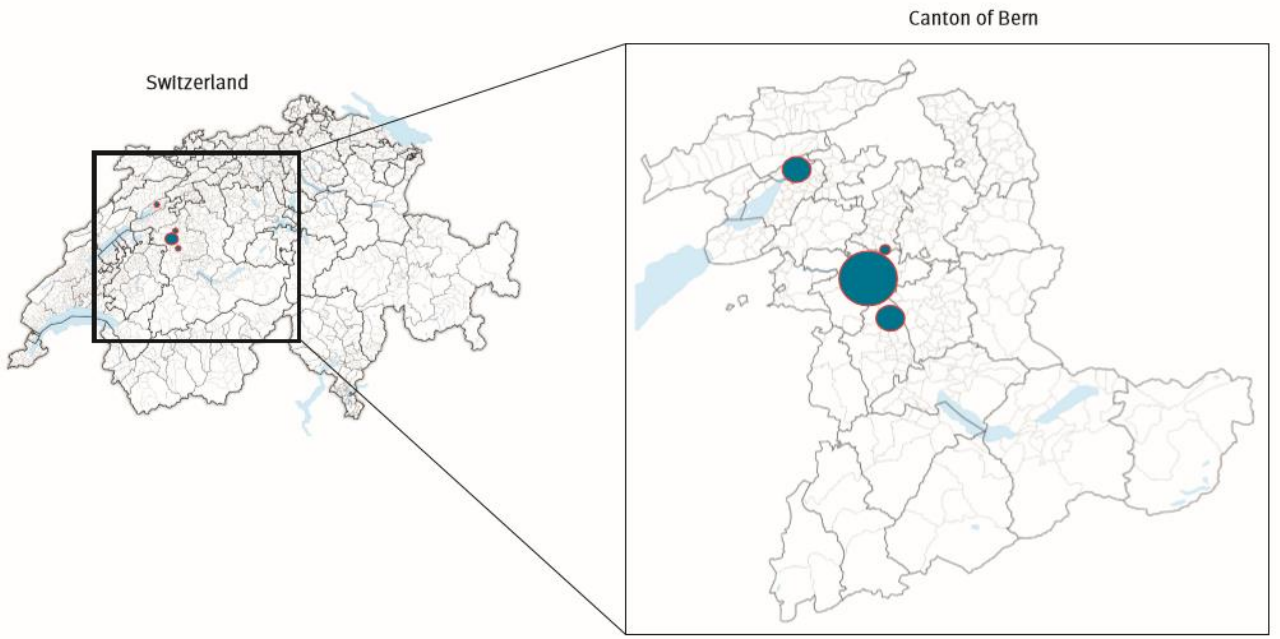
Gebel J *et al*. Journal of Hospital Infection, Jan 2019

# 1. OUTBREAK DESCRIPTION – BERN/REGION

## CANTON OF BERN – the first 4 months…

**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)




Wassilew *et al.* Eurosurveillance, July 2018

**Update 2019 Canton of Bern:**
- Detected in at least 7 hospitals (community hospitals and long-term facility)

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**2) NATIONAL OUTBREAK INVESTIGATIONS**

3) LOCAL MANAGEMENT STRATEGIES

4) SWISS RECOMMENDATIONS

# 2. NATIONAL OUTBREAK INVESTIGATIONS

MAIN STEPS OF INVESTIGATIONS:

- Nation-wide Survey
- Information National Center for Infection Control (Swissnoso) and VRE task-force
- Collaboration with Swiss Centre for Antibiotic Resistance (ANRESIS)

# 2. NATIONAL OUTBREAK INVESTIGATIONS

## NATION-WIDE SURVEY ON THE EPIDEMIOLOGY OF VRE (2015 – Mar 2018):

- 205 potential institutions asked → 70% response rate → 142 institutions included

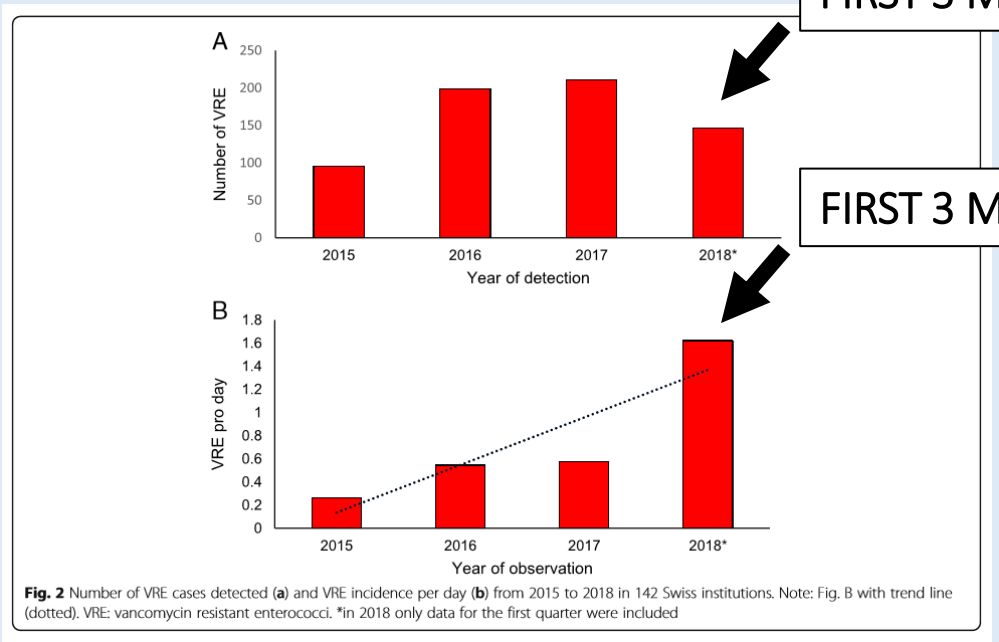



**Fig. 2** Number of VRE cases detected (**a**) and VRE incidence per day (**b**) from 2015 to 2018 in 142 Swiss institutions. Note: Fig. B with trend line (dotted). VRE: vancomycin resistant enterococci. *in 2018 only data for the first quarter were included

- Incidence rate increased from 0.26 cases/day in 2015 to 1.58 in 2018
- 1st Jan 2018 - April 2018 five outbreaks were observed
- Heterogeneity regarding the management of VRE outbreaks

Buetti N *et al*. ARIC, Jan 2019

# 2. NATIONAL OUTBREAK INVESTIGATIONS

## SWISSNOSO AND VRE TASK-FORCE

**The VRE task force:**

1. No existing mandatory reporting for VRE (outbreaks)
2. ANRESIS originally not designed for outbreak detection
3. Many institutions without established screening policy

- ✓ Infection prevention and control
- ✓ Microbiology
- ✓ epidemiology and public health

Courtesy of Dr. Vuichard-Gysin D. Presentation «Club de pathologie». Bern, Feb 2019.
Martischang R *et al.* ARIC, Jan 2019

Good for description of resistant microorganisms and including >70% laboratories in Switzerland BUT…

# IAL OUTBREAK INVESTIGATIONS

ONLY FOR CPE

D VRE TASK-FORCE

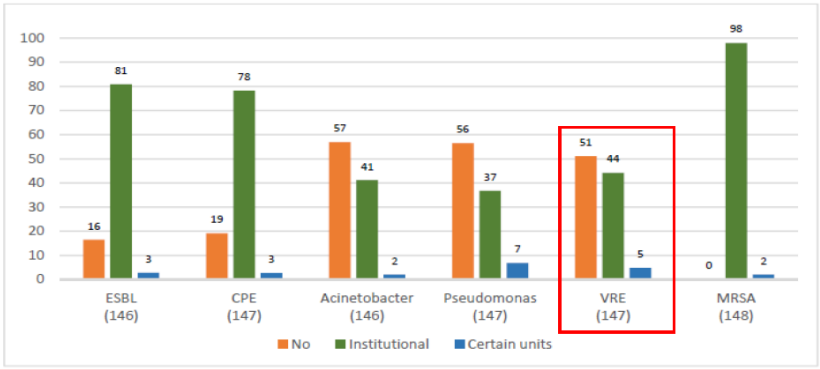
**The VRE task force:**

1. No existing mandatory reporting for VRE (outbreaks)
2. ANRESIS originally not designed for outbreak detection

s without established screening policy

- ✓ Microbiology
- ✓ epidemiology and public health

Targeted admission screening (%) for each pathogen (n)

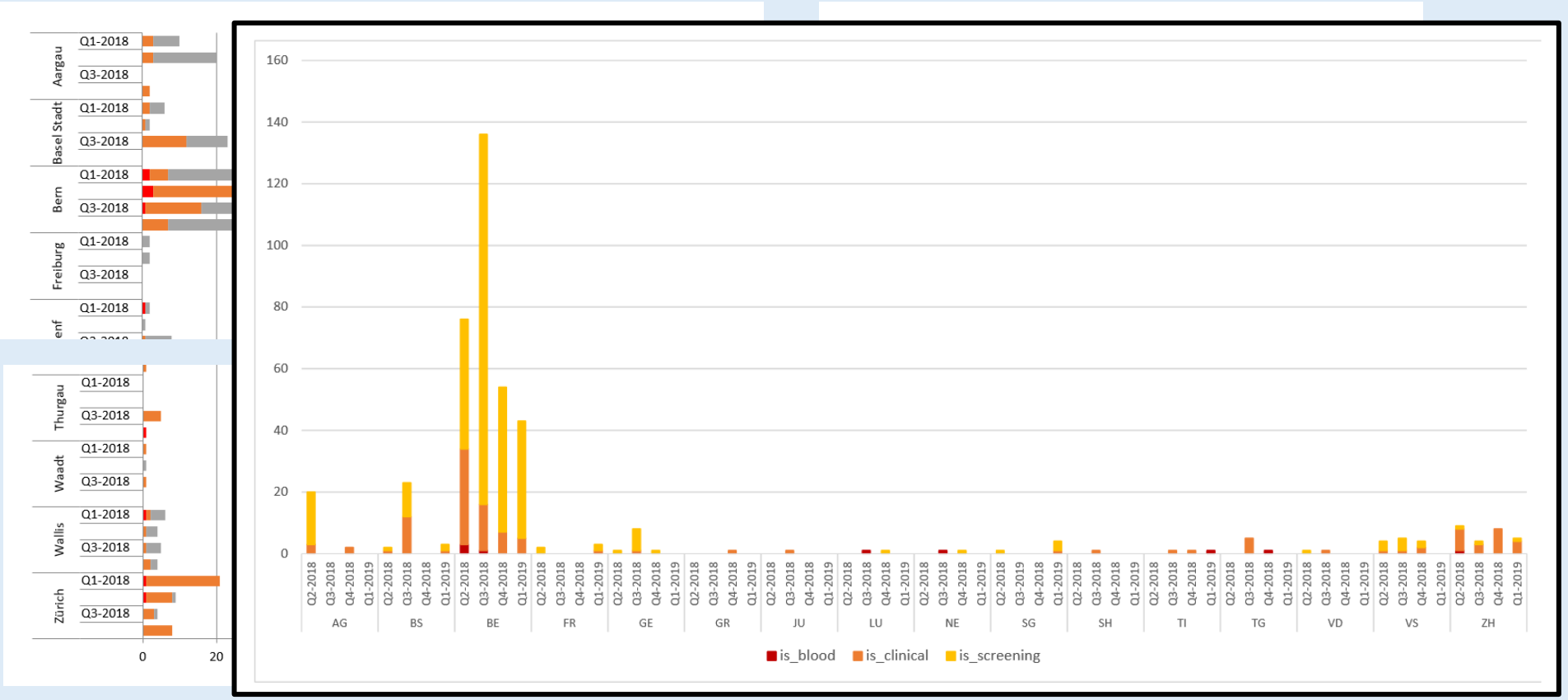



-Gysin D. Presentation «Club de pathologie». Bern, Feb 2019.

ed from Martischang R *et al.* ARIC, Jan 2019

# 2. NATIONAL OUTBREAK INVESTIGATIONS

## COLLABORATION WITH ANRESIS (Swiss Center of Antibiotic Resistance)

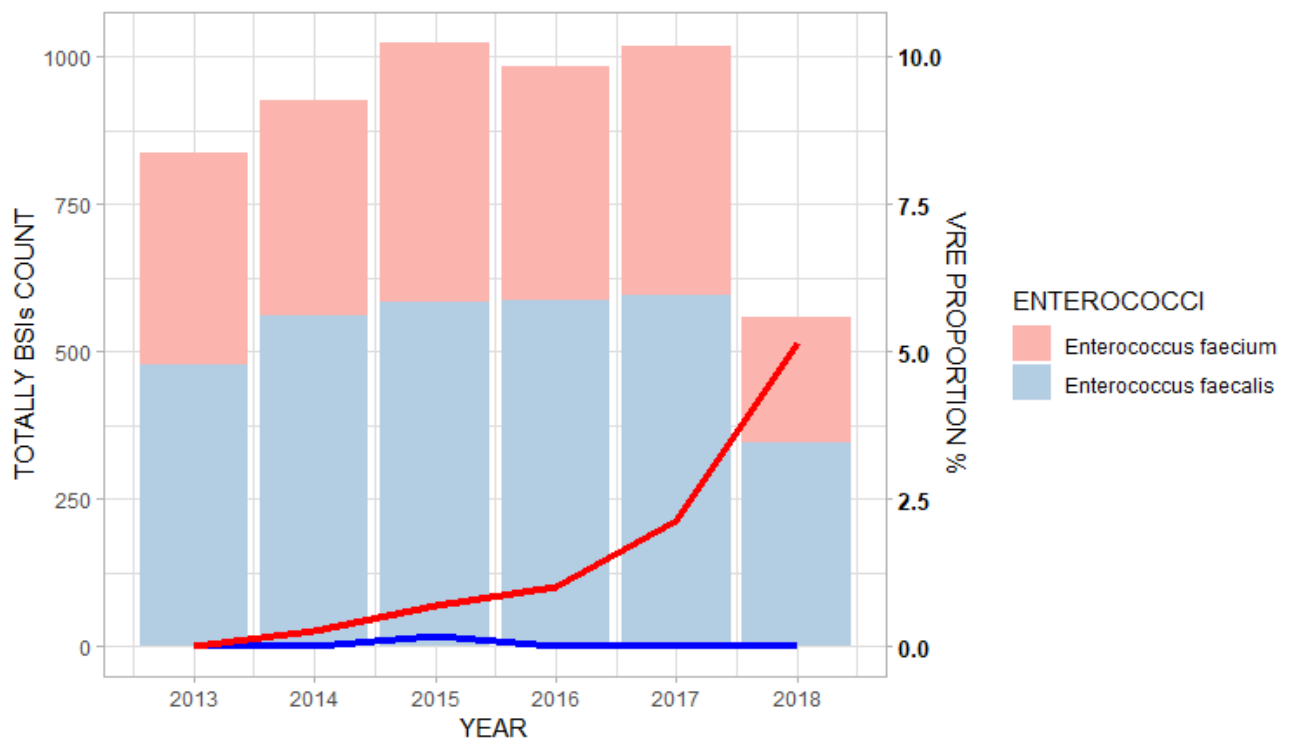



www.anresis.ch and www.swissnoso.ch

Courtesy of PD Dr. A. Kronenberg, Apr 2019

# 2. NATIONAL OUTBREAK INVESTIGATIONS

## COLLABORATION WITH ANRESIS (Swiss Center of Antibiotic Resistance)



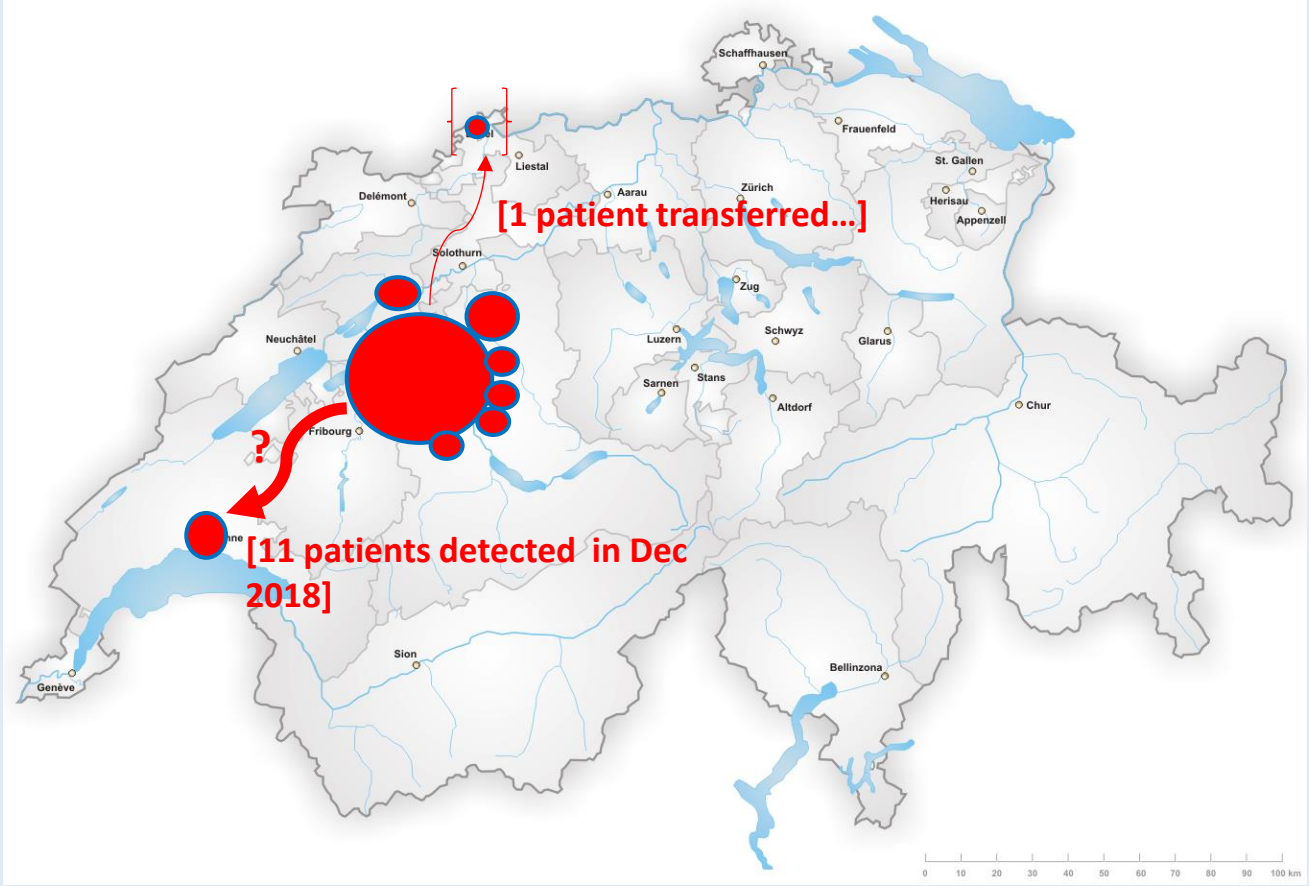

- Absolute numbers of enterococcal BSIs from January 2013 to October 2018.
- **The lines represent the proportion of BSIs due to VRE** (red for *E. faecium* and blue for *E. faecalis).*

Piezzi *et al.* Preliminary data (abstract submission planned [ICPIC, Sept 2019 Geneva])

# 2. NATIONAL OUTBREAK INVESTIGATIONS

## SWITZERLAND - ST796

Bullets' size doesn't represent the magnitude of the different outbeaks




Unofficial data.

Personal communications: Prof. Dr. J Marschall (Bern), PD Dr. L. Senn (Lausanne), Prof Dr. A. Widmer (Basel), VRE task force

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# 3. LOCAL MANAGEMENT STRATEGIES - BERN

- Temporary admission stop on affected wards
- Contact precautions for and cohorting of VRE and contact patients
- Staff cohorting
- Extensive contact tracing and screening
- Weekly screening of affected wards
- Targeted cross-sectional screenings of certain wards
- Enhanced disinfectant cleaning
- Enhanced infection prevention measures

Discontinuation of preemptive contact precautions

- Isolation management transferred to wards
- Hospital wide disinfectant cleaning in stages
- UV-C room disinfection upon patient discharge
- Automated signal of VRE status in patient chart
- Screen saver on hand hygiene indications
- Chlorhexidine bathing ICU
- In-house PCR
- Hospital wide screening
- Screening prior to transfer
- Outpatient Screening

Management - Strategy - 1

Management – Strategy - 2

6 months

From July 2018

Adapted from Wassilew *et al.* oral presentation ECCMID Amsterdam, Apr 2019

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# 4. SWISS RECOMMENDATIONS

**CLINICAL IMPLICATIONS OF VRE SPREAD**

- Treatment failure due to wrong choi
- Use of more toxic, more ex… necessary
- Risk of explosive o… tient populations
  - Enhanced…
  - Hi… …gs

… resistance genes clusters

→ Expert opinions…
→ similar to France guidelines and canton of Vaud guidelines…

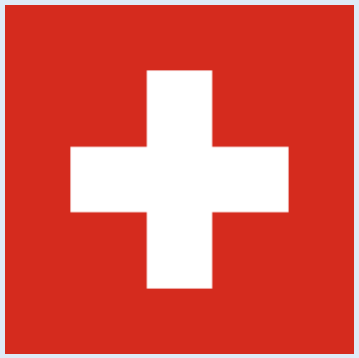
Arias et al. Nature Reviews Microbiology 2012
Mahony et al. ARIC 2018
Melo-Cristino et al. Lancet 2013
slide adapted from Prof. S. Harbarth, Geneva and Dr D. Vuichard-Gysin, Basel

# 4. SWISS RECOMMENDATIONS

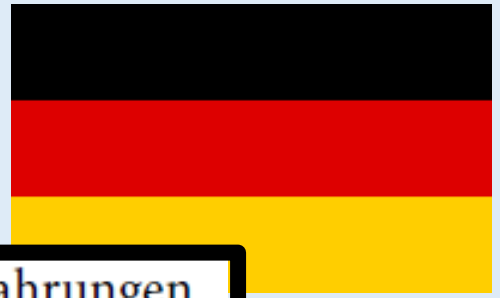
**MORTALITY ?**

- «*Die Sterblichkeit bei VRE-Sepsis beträgt 20–50 % und ist nach vorliegenden Meta-Analysen höher als bei VSE Sepsis, wobei aktuell nicht sicher geklärt ist, ob hierbei Unterschiede in der verursachenden Spezies (E. faecium vs. E. faecalis) eine Rolle spielen. Ob die Vancomycin-Resistenz unter den aktuellen Therapieregimen mit einer zusätzlichen erhöhten Sterblichkeit verbunden ist, bedarf weiterer Studien.*»
- Study ARIC 2018: "*data indicates that in-hospital mortality and infection-attributed hospital stay in enterococci BSI might rather be influenced by Enterococcus species and underlying diseases than by vancomycin resistance.*"

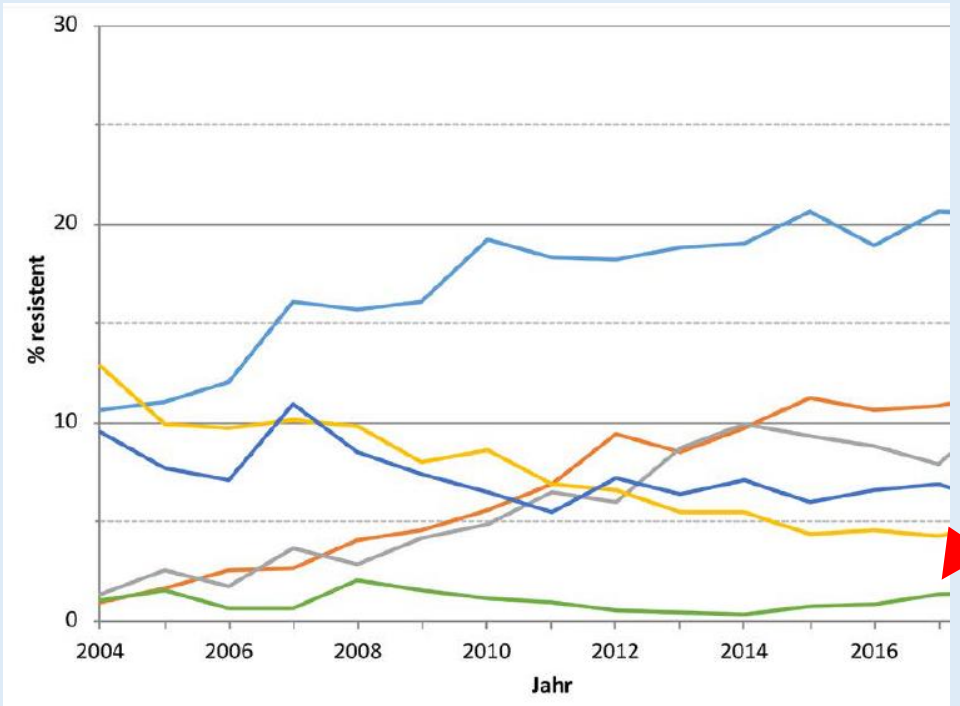
Bundesgesundheitsbl 2018 · 61:1310–1361
Siegfried Kramer T. *et al.* ARIC 2018



*versus*

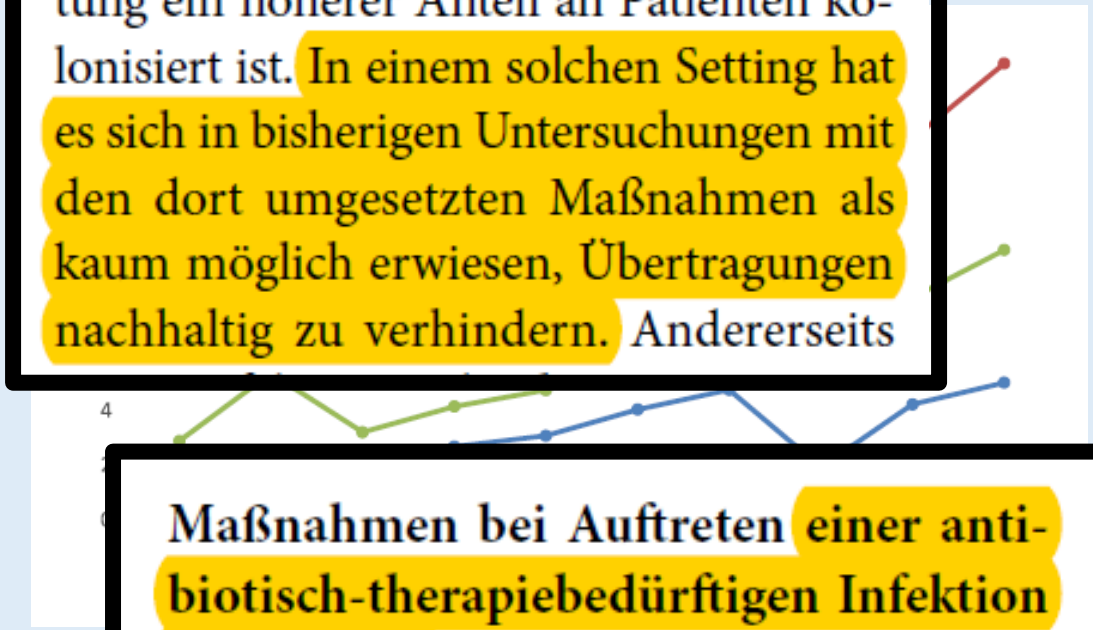



| Jahr | | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VRE | % | 1.0 | 1.5 | 0.6 | 0.6 | 2.0 | 1.5 | 1.1 | 0.9 | 0.5 | 0.4 | 0.3 | 0.7 | 0.8 | 1.3 | 1.4 |
| | n | 191 | 203 | 311 | 335 | 454 | 524 | 540 | 585 | 600 | 679 | 942 | 1061 | 954 | 1015 | 899 |




VRE

Demgegenüber stehen Erfahrungen und Berichte, dass in vielen Regionen Deutschlands bereits eine endemische Situation besteht, so dass schon bei der Aufnahme in die medizinische Einrichtung ein höherer Anteil an Patienten kolonisiert ist. In einem solchen Setting hat es sich in bisherigen Untersuchungen mit den dort umgesetzten Maßnahmen als kaum möglich erwiesen, Übertragungen nachhaltig zu verhindern. Andererseits




**Maßnahmen bei Auftreten einer antibiotisch-therapiebedürftigen Infektion durch VRE:**

Remschmidt C *et al.* ARIC 2018. Bundesgesu

www.anresis.ch ; BAG Bulletin 2019

# 4. SWISS RECOMMENDATIONS

**AIMS:**

Aims of this expert guidance document

- To contain the ongoing spread of VRE within and between health-care institutions
- To interrupt intra- and intercantonal VRE transmission
- To update hospital hygienists and infectious disease specialists on the core elements of successful VRE control

Vuichard-Gysin D *et al.* Temporary expert guidance for healthcare institutions to contain the spread of VRE in Switzerland. www.swissnoso.ch, Sept 2018

# 4. SWISS RECOMMENDATIONS

## CORE PRINCIPLES OF VRE CONTAINMENT:

1) **The iceberg tip principle**

Since the ratio colonization/infection is greatly unbalanced (>1/10), the first isolation of VRE in a clinical sample strongly suggests undetected VRE carriage

2) **The onion skin principle**

Detection of a VRE case should trigger screening of all contact patients according to a strategy of concentric circles

3) **The Speedy Gonzales principle**

Rapidity of detection and isolation of VRE patients and contacts is probably the most critical point

Vuichard-Gysin D *et al.* Temporary expert guidance for healthcare institutions to contain the spread of VRE in Switzerland. www.swissnoso.ch, Sept 2018

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# 4. SWISS RECOMMENDATIONS

Rules for discontinuations of CP

**DEFINITIONS:**

**Outbreak**

- ≥ 3 VRE cases with a possible epidemiological link on ward or institution level

**VRE case**

- Patient with a positive culture (clinical or screening sample) for *E. faecium* being resistant to amoxicillin and vancomycin (confirmed by pheno- or genotype).

**VRE contact**

- Patient is or has been hospitalized (going back to the entire stay of the index patient but max. 30 days) in the same room with a VRE patient

OR

- Patient on a ward where a VRE outbreak has been documented

***Possible*** **VRE contact**

- Patient from a hospital in Switzerland with known VRE outbreaks but not fulfilling the criteria above
- Patient transferred from a hospital outside Switzerland with a hospital stay of > 24 hours

Contact precautions (CP)

Pre-emptive CP!

If possible, pre-emptive CP!

-Stop admissions
-Patient flow
-Re-organize ward
-Environmental decontamination
-Antibiotic restriction
- …etc..

Vuichard-Gysin D *et al.* Temporary expert guidance for healthcare institutions to contain the spread of VRE in Switzerland. www.swissnoso.ch, Sept 2018

# CONCLUSIONS

- **Outbreak Bern University Hospitals: ongoing**
- **Outbreak Canton of Bern: probably ongoing**
- **National situation: probably under control but some questions remain open…**
- **Switzerland is a low VRE prevalence country → Impact on national VRE data**

# Thank you!

niccolo.buetti@gmail.com

**Inselspital and Region:**

- Die Spitalhygiene!
- Infektiologische Klinik
- Institut Mikrobiologie Bern (IFIK)
- Alle periphere Spitäler
- Die Patienten

**Nationale Empfehlungen/Abklärungen**

- Swissnoso
- VRE task force
- Bundesamt für Gesundheit
- SGM
- SGSH
- Anresis
- VKS