Screening for vancomycin-resistant enterococci (VRE) Why bother?

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Hosted by Suzanne Rhodenizer-Rose
Nova Scotia Health Authority

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Declarations

The views expressed are in a professional but personal context & are not necessarily those of the RCSI & Beaumont Hospital, Dublin.

I have recently received research funding from Pfizer & Astellas. I have also provided professional advice & or education for Novartis, AstraZeneca & Cepheid

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Outline

1. Clinical impact of VRE
2. Different surveillance approaches
3. Laboratory detection
4. Conclusions

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Clinical Impact of VRE

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Enterococci

- Part of the normal bowel flora
- Cause urinary, bloodstream & abdominal infections
- Probably not as virulent as *Staphylococcus aureus* & most Enterobacteriaceae such as *Escherichia coli*
- *Enterococcus faecalis* & *Enterococcus faecium,* the two most important species
- *E. faecium* (EFm) more associated with vancomycin-resistance

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Vancomycin-Resistance

- Originally described in 1980s in renal patients
- Different genetic determinants of which *vanA* & *vanB* the most common
- Bloodstream infection (BSI) monitored as part of EARS-Net (European surveillance)
- Alternatives available to treat infections in last 10-15 years such as linezolid & daptomycin

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Impact - Overview

A. Enterococci are the 2nd most common cause of HCAIs in the USA after *S. aureus* & 89% of EFm associated with central-line-associated BSI are VRE

Infect Control Hosp Epidemiol, 2013

B. VRE are bacteria of serious concern which require prompt & substantial action

CDC, 2013

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Hospital-Onset BSI

- Retrospective study over 5 years in Detroit, USA
- Pitt bacteraemic score to quantify severity of illness
- Time to appropriate treatment calculated from when cultures taken & 1st dose of appropriate treatment

Results

190 patients

62.6% VRE

linezolid (32%), daptomycin (31%) & ampicillin (26%)

Clin Infect Dis, 2016

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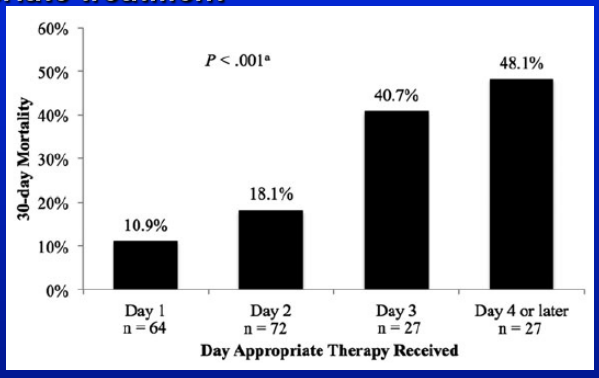
Hospital-Onset BSI

- 30-day mortality was 14.6% if initial appropriate therapy compared to 45.3% if > 48h delay
- Longer duration of BSI if delayed & vancomycin-resistant phenotype associated with delayed appropriate treatment



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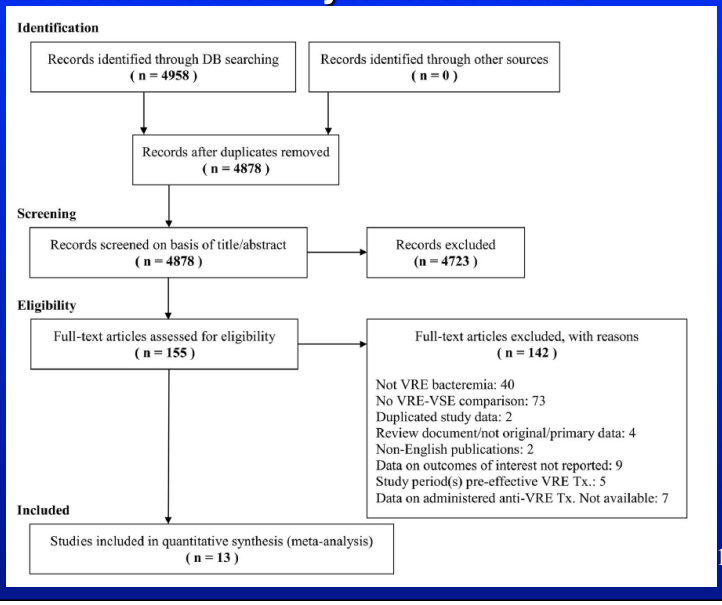
VRE *versus* VSE BSI

- Systemic review & meta-analysis of outcomes



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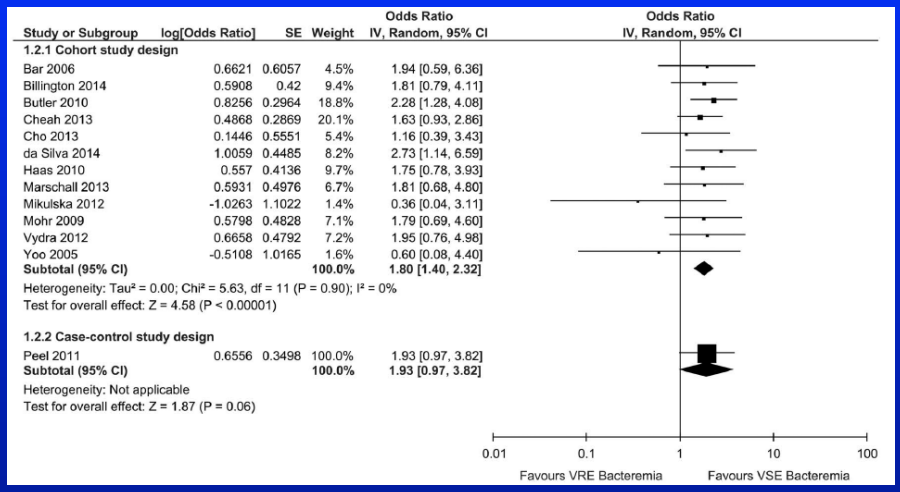
VRE *versus* VSE BSI



Infect Control Hosp Epidemiol 2016; 37: 26-35

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VRE & Renal Dialysis Patients

- Meta-analysis from 1982-2014 of prevalence, risk factors & significance
- 23 studies from 100 dialysis centres involving 4,842 patients
- Prevalence, 6.2% (5.2% North America)
- Risk of infection increases x 21.6 if VRE +ve
- Heterogeneity may reflect differences in infection prevention & control practices & use of antibiotics

Am J Kidney Dis 2015; 65: 88-97

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Different Surveillance Approaches

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Surveillance for VRE

Passive

- Only check isolates causing infection to guide therapy
- Occasional prevalence surveys of enterococcal isolates

Active

- Selective, e.g. admission & weekly in ICU
- Universal, all patients in certain clinical units on admission, weekly & on discharge

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Risk Factors

Intrinsic	Comment
Immunosuppression	Haematology/Oncology, SOT
Renal dialysis	Healthcare contact
Antibiotics	3GC, FQ, vanc, B-L/B-L inhibitors
Underlying diseases	Healthcare contact
Extrinsic	**Comment**
ICU	Most studies
LTCF	? Underlying disease or lack of prevention
Single room	Inadequate cleaning
Prior hospitalisation	Studies in tertiary centres

J Hosp Infect 2014; 88: 191-198 15

Studies on Screening

- Mixed & sub-optimal in large part due to
  - Differences in centres
  - Sampling & laboratory methodology
  - Patient populations
  - Design, retrospective, prospective, case-controlled
  - Some are mathematical modelling

Despite this, there is at least a suggestion that active screening reduces prevalence due to possible increased awareness, indirect measures +/- direct preventative measures

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Examples of Screening/Interventions

Setting / Design	Screening	Outcome	Comments
Japan, observational	All hospital admissions	Initial ↑ prevalence but then fell	Improved hand hygiene
US, retrospective	BSI in 2 hospitals, one that screens	Higher BSI rate & cohort in non-screening hospital	Hospitals, similar but not controlled
US, multicentre retrospective	Admission & weekly ICU screen	↑ detection	-
US, oncology unit Historical controls	Admission & weekly screening	Reduced BSI rates & costs	Single centre
Europe 13 ICUs cluster randomised	Frequent screening	Improved hand hygiene & chlorhexidine bathing most important	Some patients not screened

J Hosp Infect 2014; 88: 191-198

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Laboratory Detection

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General Issues

Samples	Rectal swabs or stools
Culture	Direct, enrichment, chromogenic media
Molecular	Resistance detection, species, clones

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Sensitivity & Specificity

CHROM agar 99% sensitive, 94.8% specific

Molecular

Light cycler	poor predictive value for *vanB*
Cepheid	positive prediction value of 54%

Excludes VRE being present, & highly specific for *vanA*

J Hosp Infect 2014; 88: 191-198

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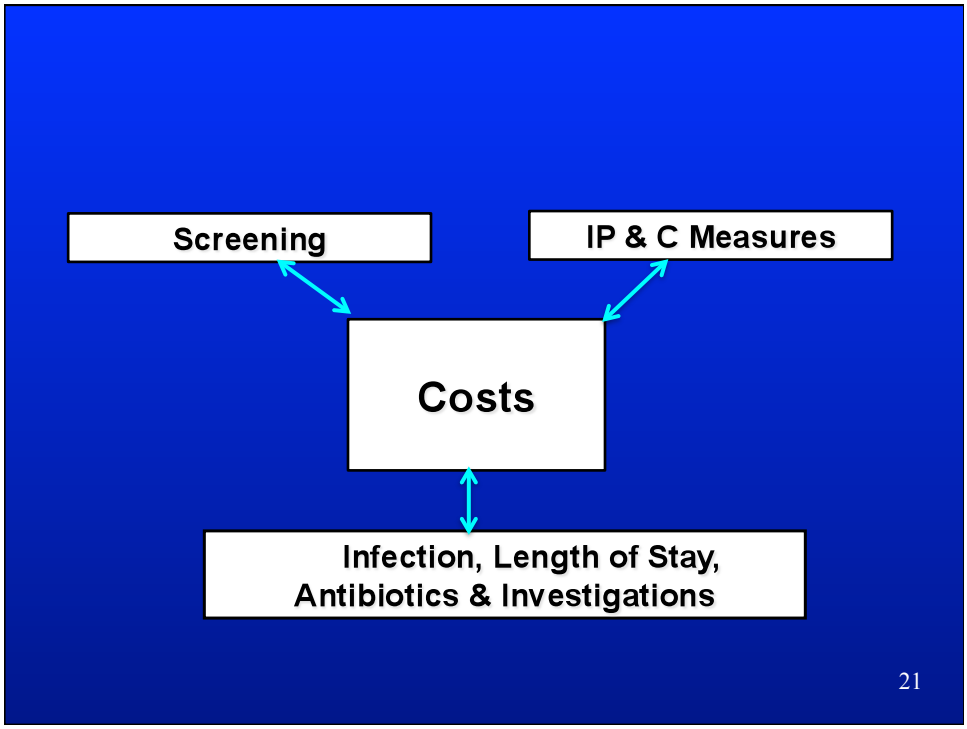

Trade Off in Costs

Peri-rectal cultures taken

1 case of VRE BSI ⟶ 19 days of hospitalisation

28 cases of VRE BSI ≡ $761,320

VRE IP&C measures ≡ $253,097

Infect Control Hosp Epidemiol 2002; 23: 429-435

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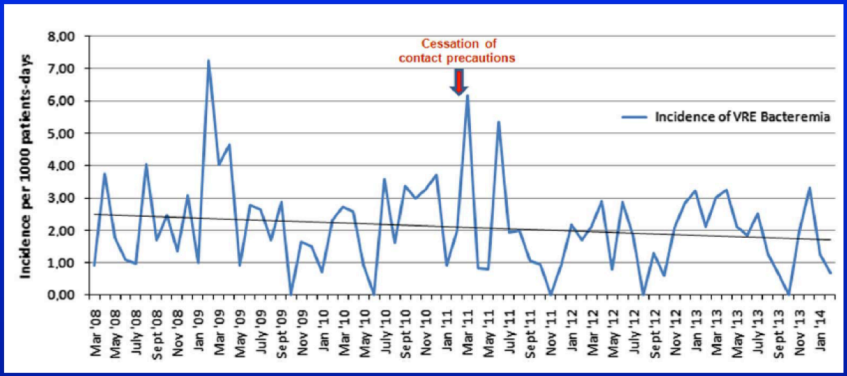
What happens when you stop surveillance & contact precautions?

- Comparison of different time periods & effect on BSI



But, single centre, malignant haematology patients, no details on hand hygiene & cleaning, & all admissions in single rooms

Infect Control Hosp Epidemiol 2016; 37: 398-403 23

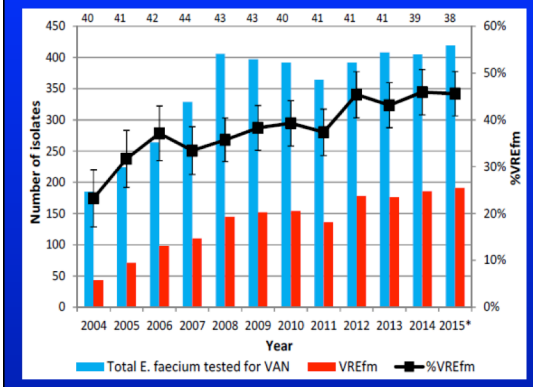
Interventions to reduce colonisation and transmission of antimicrobial-resistant bacteria in intensive care units: an interrupted time series study and cluster randomised trial

- Phase 1 – baseline data
- Phase 2 – hand hygiene
- Phase 3- screening (molecular & culture) & if +ve, contact precautions
- 15-22% of patients in single rooms; more than % carriers

At ICUs using rapid screening	n=983	n=906	n=2351
Any (%)	12·3% (10·4–14·5)	11·0% (9·2–13·2)	14·1% (12·7–15·5)
MRSA (%)	3·3% (2·3–4·6)	4·6% (3·5–6·2)	3·3% (2·6–4·1)
VRE (%)	3·5% (2·5–4·8)	2·2% (1·4–3·4)	5·8% (4·9–6·8)
HRE			
Total (%)	7·0% (5·6–8·8)	5·7% (4·4–7·5)	7·7% (6·7–8·8)

Lancet Infect Dis 2014; 14: 31–39

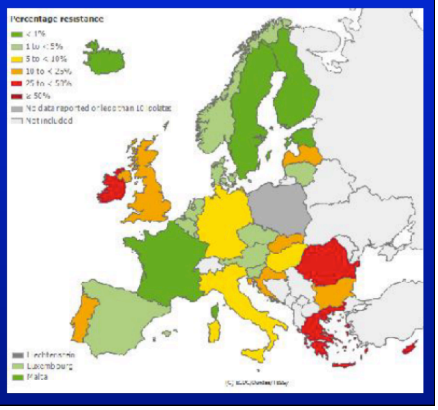
VRE & Ireland



VREFm BSI

EARS-Net & Health Protection Surveillance Centre (Ireland)

Ireland & Europe



Why the higher rates in Ireland?

- Dominant & widespread clones different to elsewhere?
- Antibiotic use?
- Animal-human antibiotic chain?
- Greater patient vulnerability?
- Inadequate facilities & health resources?

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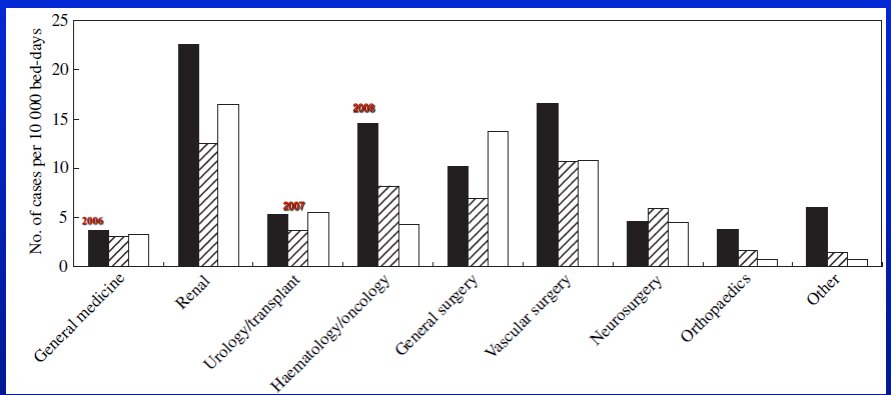
VRE BSI in Tertiary Care Hospital

1. 75 patients, mainly intra-abdominal source for BSI
2. 52% *vanA*
3. Clonal relatedness with environmental isolates
4. Similar STs & virulence factors to those in Europe
5. High EFm in Ireland?

J Antimicrob Chemother 2015; 70: 2718-2721 27

VRE – Local Experiences

- Endemic VRE
- ICU screening & all clinical isolates checked
- Inadequate numbers of single rooms



J Hosp Infect 2010: 75: 228-233 28

VRE – Clinical Impact

	2001	2003	2005	2007	2008
No. of screens	1344	1525	1121	1288	1220
+ ves	42	63	94	75	92
+ves/10,000 bed days (BD)	1.96	2.94	4.06	3.18	3.85
+ve blood cultures	2	11	18	8	11
VRE BSI/10,000 BD	0.09	0.51	0.78	0.34	0.46

J Hosp Infect 2010; 75: 228-233

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Conclusions

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i) VRE is endemic in many healthcare settings & the extent underestimated
ii) Predisposing factors are multiple & include healthcare & community factors
iii) Not as virulent as *S. aureus* or Enterobacteriaceae
iv) Control measures are worthwhile

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v) Invasive infections occur in vulnerable patients
vi) Studies on the value of screening & preventative measures are flawed
vii) Surveillance & the feeding back of data has positive effects
viii) Much unknown about reservoirs & environmental factors

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What you don't know, you can't solve

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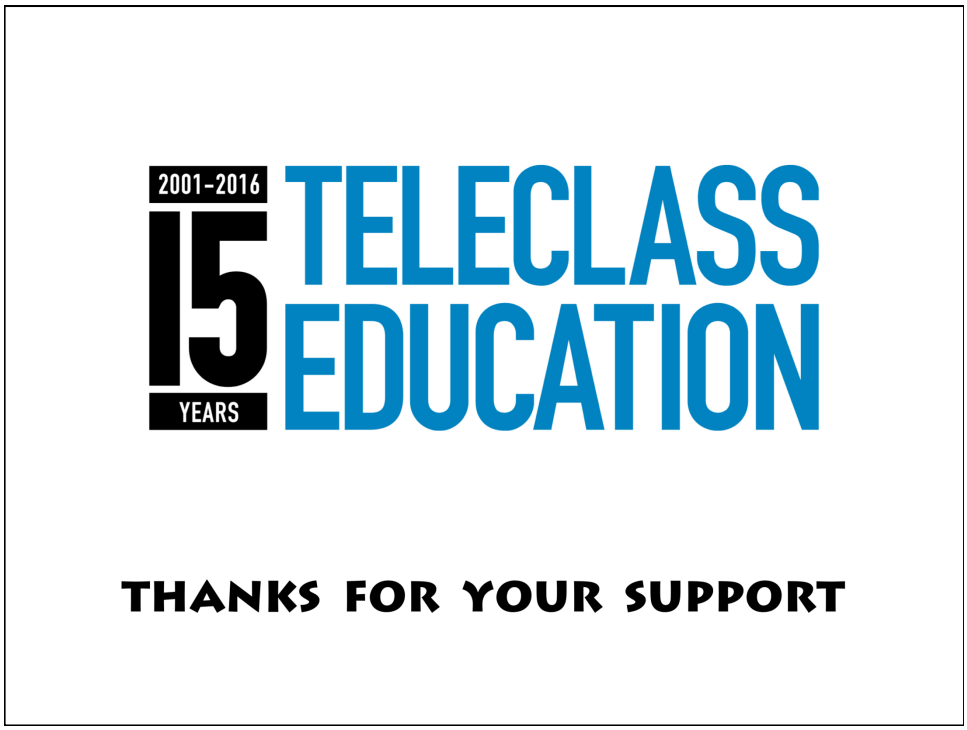
Prof. Hilary Humphreys, Royal College of Surgeons in Ireland, Dublin
A Webber Training Teleclass



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