Public health action and management of patients with VTEC infection: the Danish approach

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STATENS SERUM INSTITUT

Public health

Disease prevention

- Prevent onset of disease
- Minimize the risk of progression of the disease in individuals or transmission of illness
- Rehabilitation in order to prevent the worsening of an individual's health

Principles of Public Health Practice
F. Douglas Scutchfield,C. William Keck
2nd edition; Delmar Learning

Three primary issues:

- Risk of severe disease and prognosis
- Quarantine of infected individuals
- Treatment with antibiotics – especially with long-term otherwise healthy carriers

DETECTION and NOTIFICATION

Public Health guidance and regulations:

”All patients, including children, with bloody diarrhoea, and suspected infection should be examined for VTEC”

and notified …

HUS: VTEC positive or seropositive

VTEC detected or isolated

All isolates should be sent to NPHRL (=SSI)

HUSEC

GUIDANCE FOR PATIENTS INFECTED WITH HUS ASSOCIATED VTEC = HUSEC:

1. *child in institution*
2. *person associated to nursing home or similar*
3. *hospitalised patients*
4. *employee at hospital, institution, nursing home or similar*
5. *employee in food industry or similar (restaurants, cafés, cantinas etc)*

PRECAUTIONS & MANAGEMENT …1

- local public health officer (MD) is notified
- information on hygiene
- contacts in institution or household with diarrhoea (one week prior to onset in index patients) should be examined for VTEC
- all patients are quarantined until clinically well and two separate VTEC negative stools have been obtained

PRECAUTIONS & MANAGEMENT …2

- **if employee in food industry or similar the local (or national) food authorities must be notified**

LOW RISK VTEC

PRECAUTIONS & MANAGEMENT …3

- Usual procedures related to infectious diarrhoea
- no control stools needed
- can return to work/institution when clinically well and without diarrhoea

The Danish cohort: HUS cases in the period 1983-2012 among Danish patients with VTEC infection stratified according to virulence types and age

Virulence type	< 5 years	6-14 years	>14 years
eae + vtx2	34/180 (19%)	7/49 (14%)	4/120 (3%)
eae + vtx1 + vtx2	6/95 (6%)	3/38 (8%)	2/110 (2%)
eae + vtx1	3/332 (1%) a)	1/51 (2%) c)	0/169
vtx2	0/36	1/25 (4%) d)	8/233 (3%) e)
vtx1 + vtx2	0/22	0/31	0/187
vtx1	1/33 (3%) b)	0/35	0/255

a)

- O103:H2 was treated with mecillinam due to suspicion of a urinary tract infection
- O104:H7 was probably nosocomially infected when hospitalised with nephrotic syndrome
- part of an outbreak with two VTEC O157 types and several non-VTEC types

b)

- O55:H12 was initially treated with two antibiotics (Cetriaxon and Penicillin) which after two days was changed to three other antibiotics (Ampicillin, Gentamicin and Meronem).

c)

- Patient with a double VTEC infection who also had O157:H7 (*eae* + *vtx1* + *vtx2*)

d)

- O13,O73:K1:H18 (*vtx2d*)

e)

- Eight of 25 (32%) patients with culture confirmed EAggEC-VTEC O104:H4 (*vtx2a*) developed HUS and were part of the German outbreak in 2011

BASIC & PRIMARY DEFINITION OF HUSEC FOR *first line* PUBLIC HEALTH ACTION:

- ***vtx2*** **in a background of** ***eae*****,** ***aggR*** **is HUS-associated**
- **“on hold” until** ***vtx*** **subtyped**

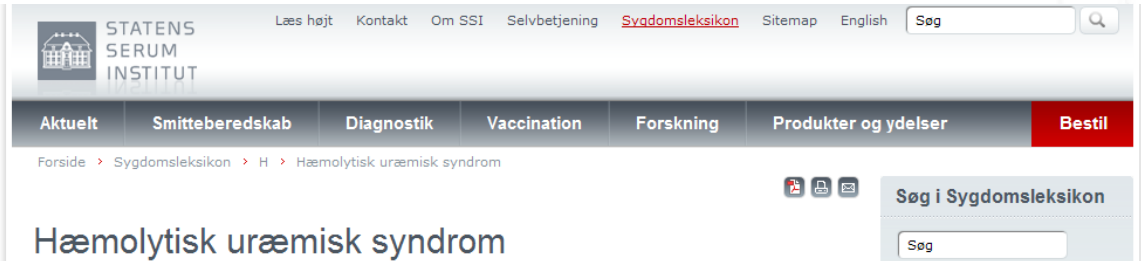
Consequences using the HUSEC paradigm

Using these criteria 71% (1454/2046) of Danish patients would have been informed that they had a ”low risk VTEC” infection

Twenty-nine percent (552/2046) would be informed that they might have an HUSEC infection

If *vtx2f* = *vtx2* then an additional 55 (3%)

Risk assesment of VTEC



HUS associated VTEC = HUSEC

…

These virulence profiles have clinical relevant association with HUS:

1. *vtx1* and *eae* and O103:H2
2. *vtx1* and *vtx2* and *eae*
3. *vtx2* and *eae*
4. *vtx2* in an enteroaggregative *E. coli* (EAggEC)

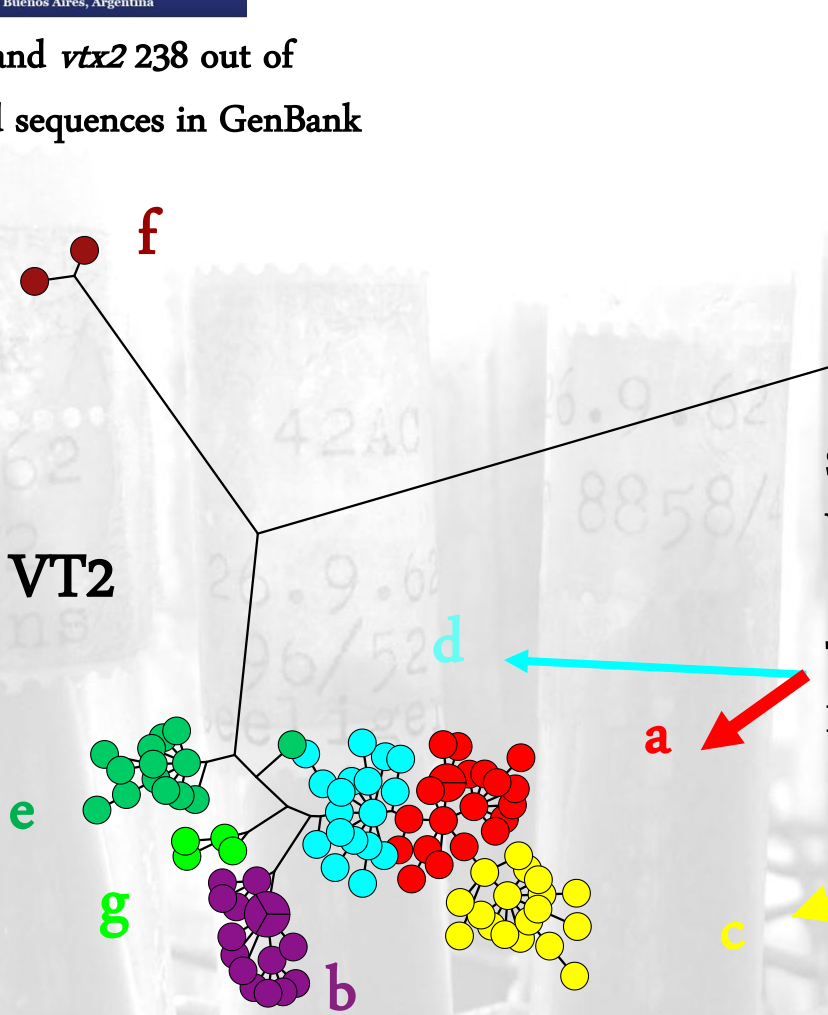
   eg. O104 or O111
5. *vtx2d* in *eae* negative VTEC

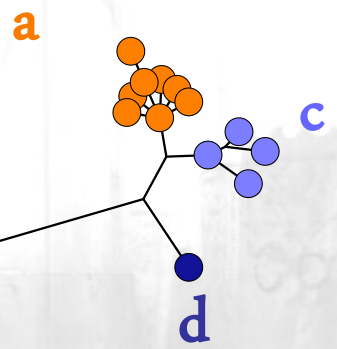
Sidst redigeret 1. september 2011

Stx subtypes and variants

47 *vtx1* and *vtx2* 238 out of

285 valid sequences in GenBank





Stx/VT1: 3 subtypes; 13 variants

VT2: 7 subtypes; 93 variants

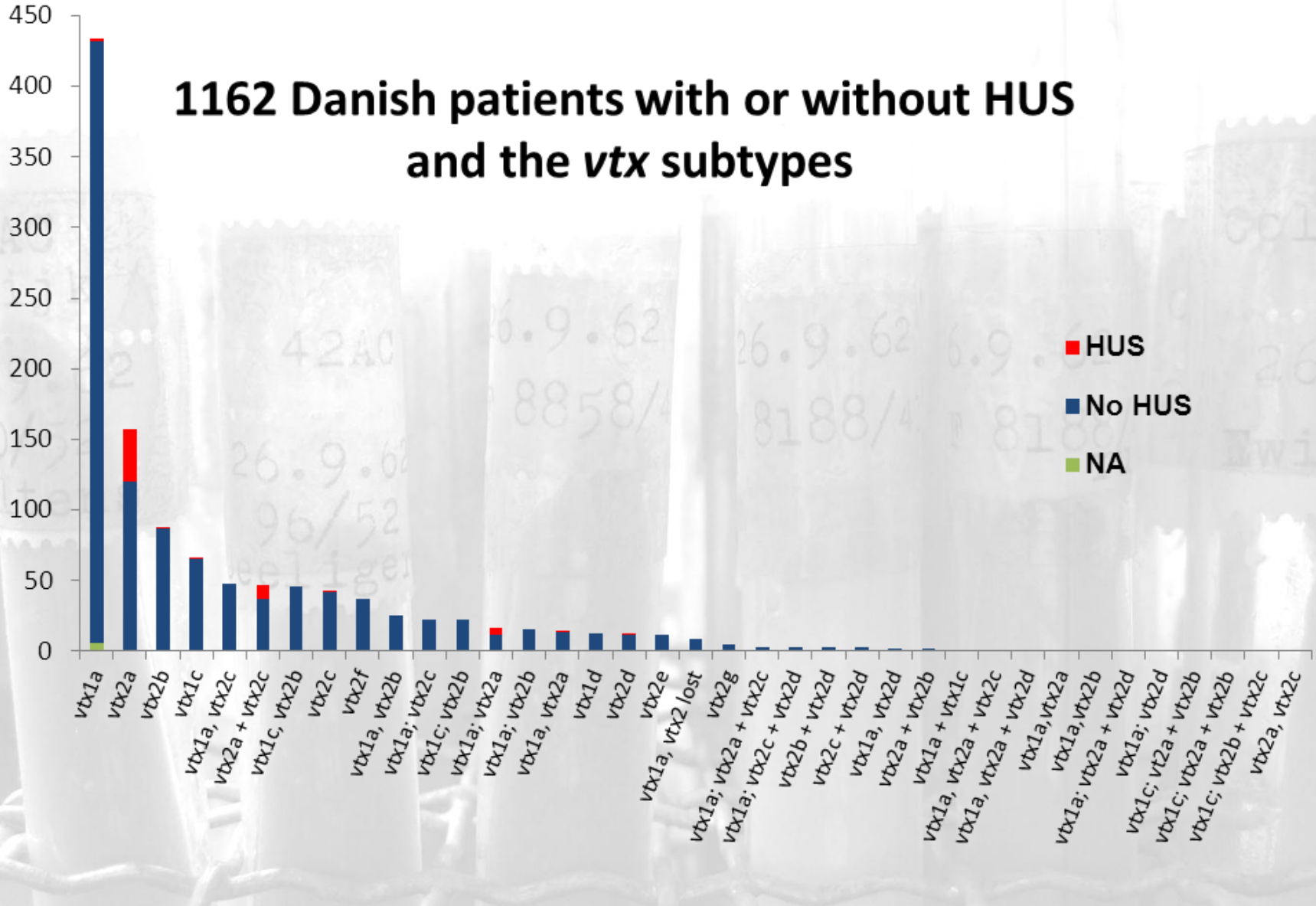
Two subtypes associated with serious complications:

HUS

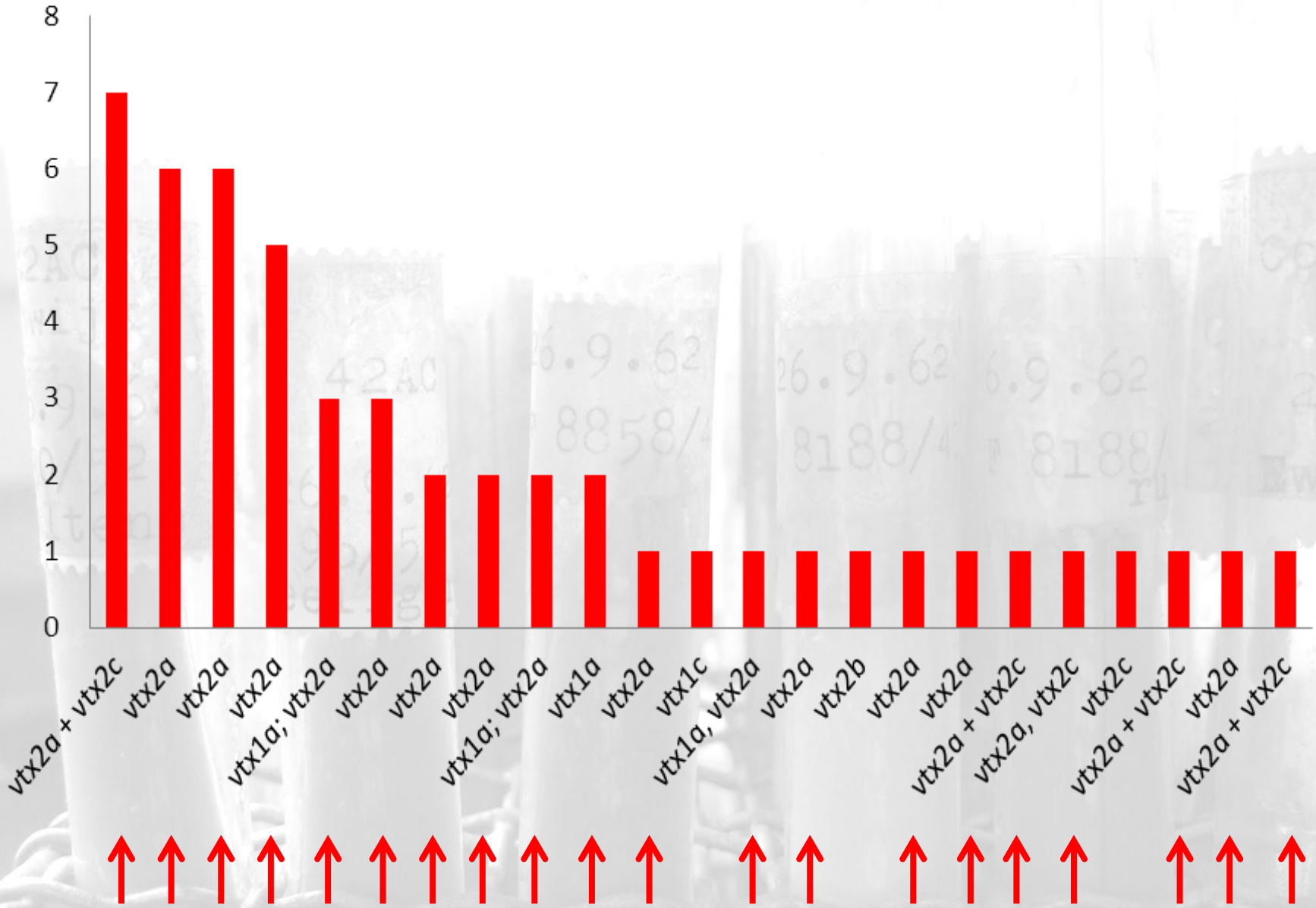
Possible association?

Scheutz *et al.* A Multi-center evaluation of a sequence-based protocol to subtype Shiga toxins and standardize Stx nomenclature Submitted

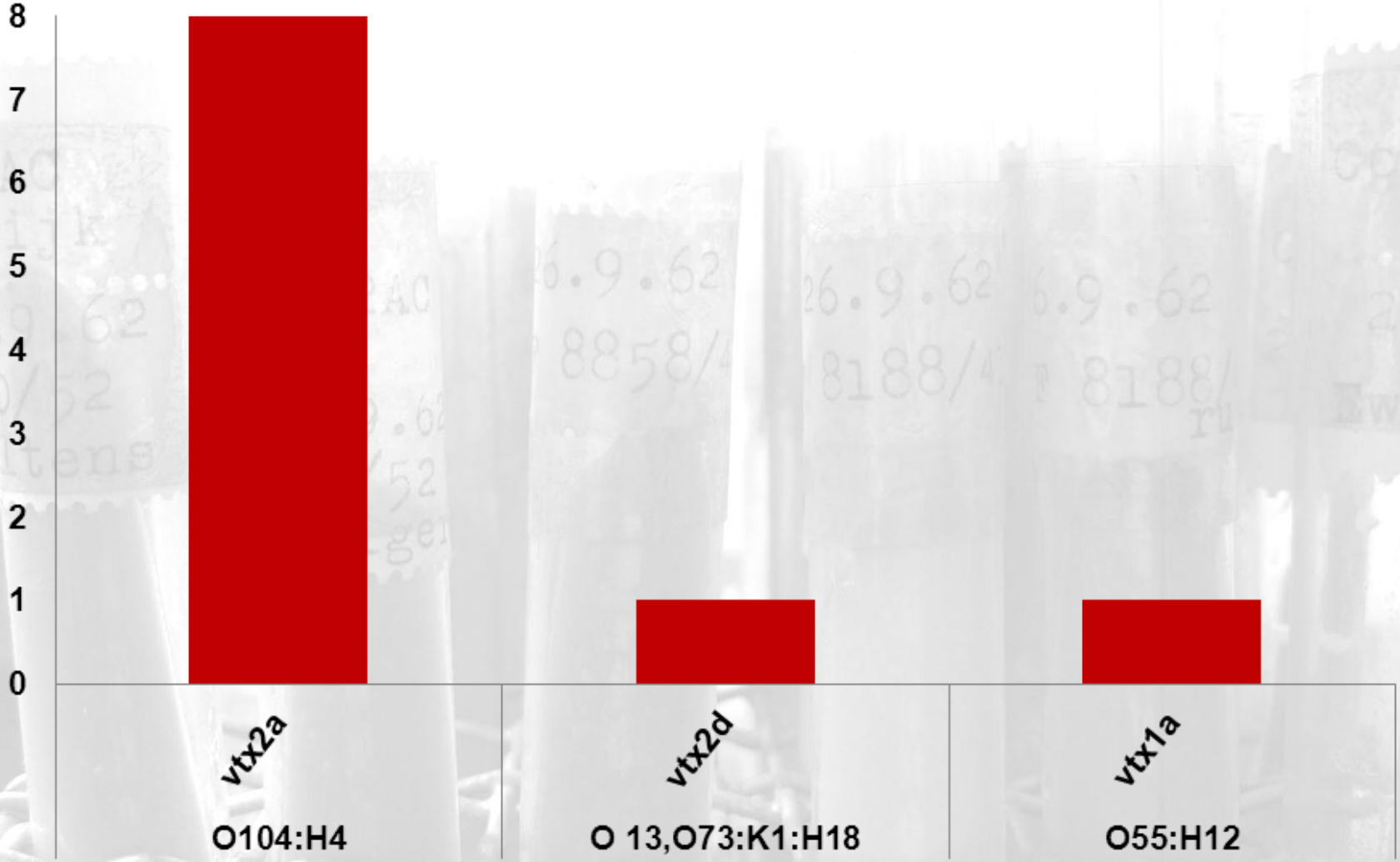
HUS & *vtx* subtypes



vtx subtypes; all *eae* positives



Sero- & *vtx* subtypes; all *eae* negatives



Consequences using the HUSEC paradigm and *vtx* subtyping

Recall that:

71% had a ”low risk VTEC” infection

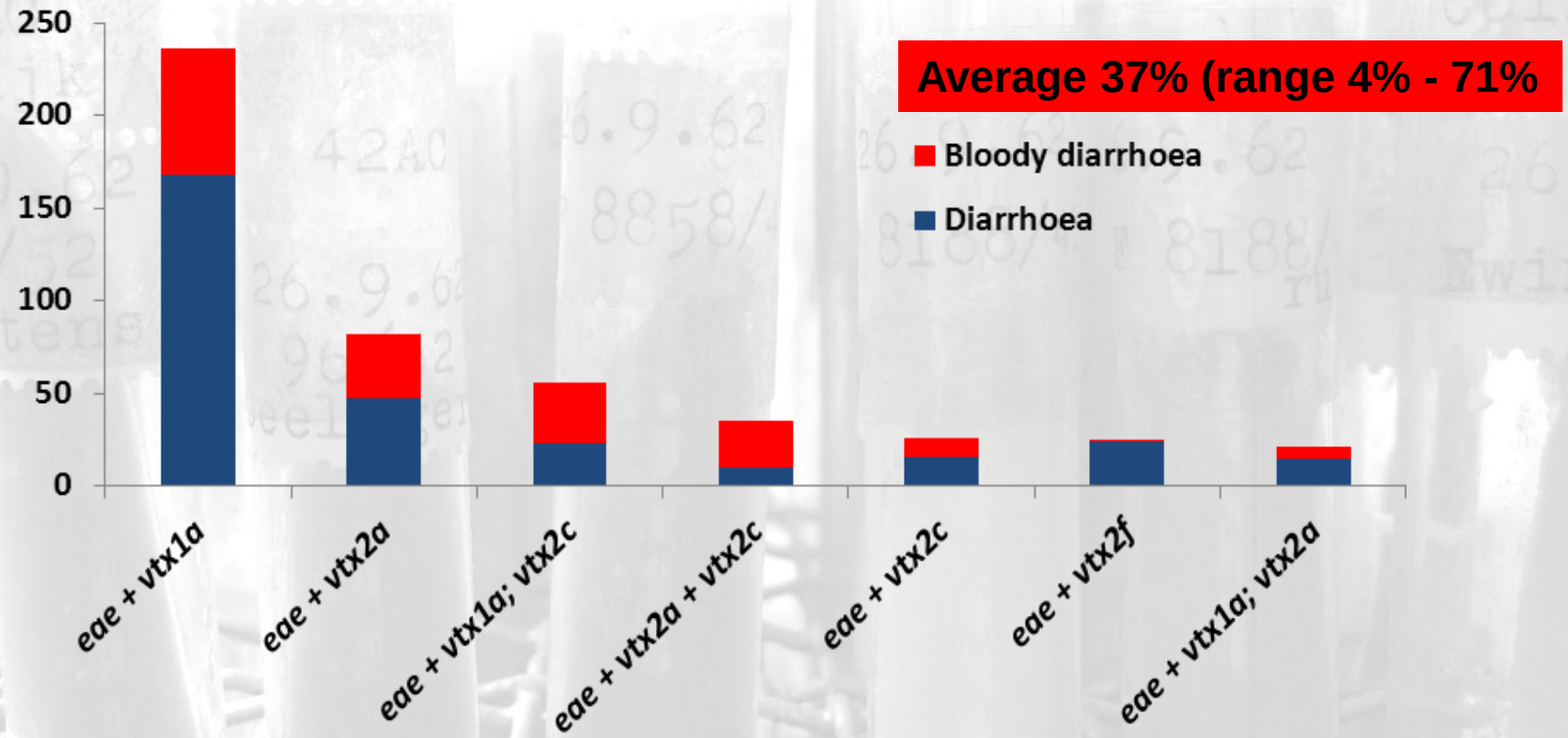
29% might have an HUSEC infection

***vtx* subtyping would reduce this to ~11% (224/2062)**

eae positive VTEC and bloody diarrhoea (BD)

581 *eae* positive VTEC

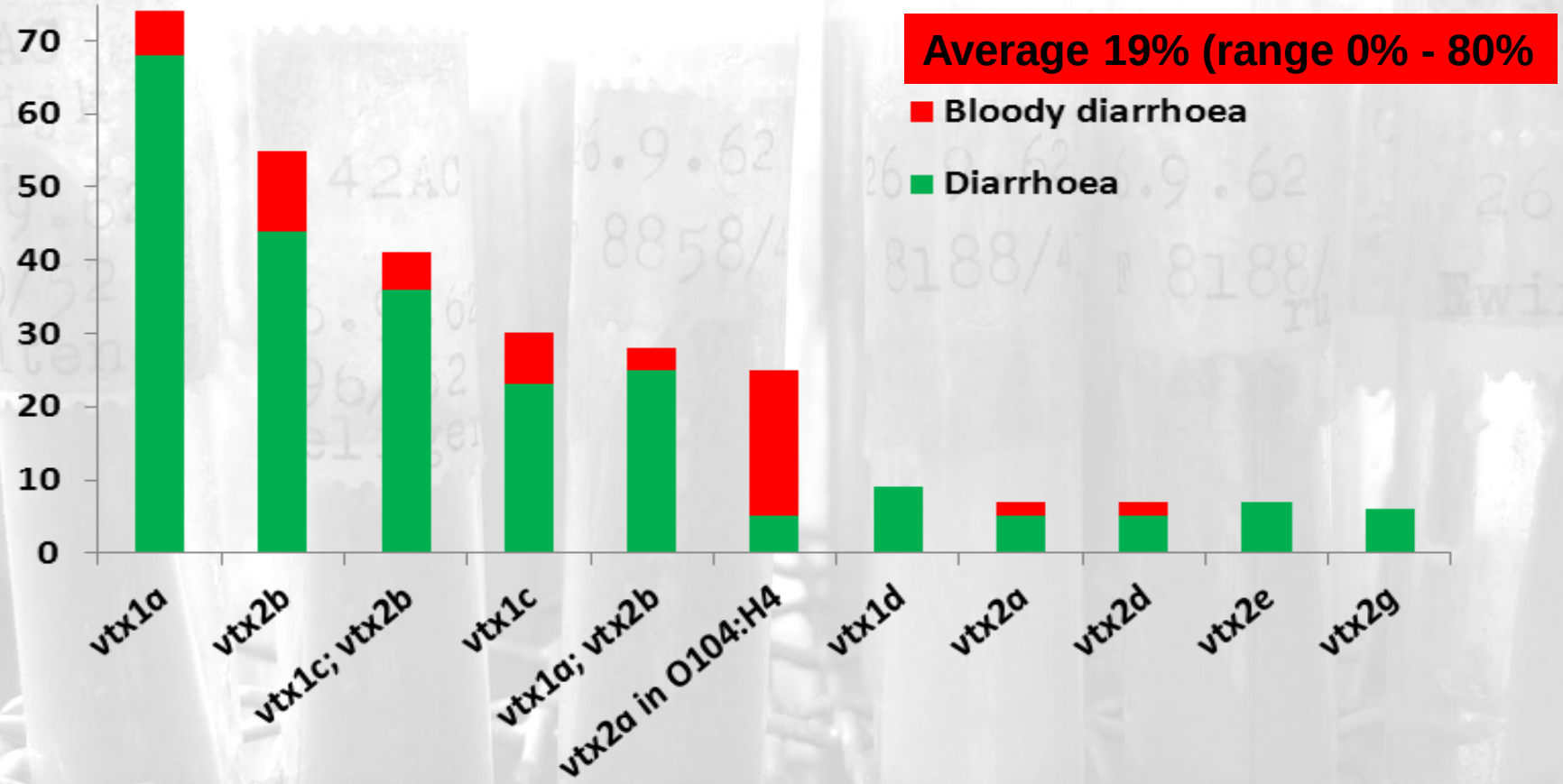
178 BD patients & 303 patients without BD



eae negative VTEC and bloody diarrhoea (BD)

289 *eae* negative VTEC

56 BD patients & 233 patients without BD



Criteria for antibiotic treatment of patients infected with VTEC

- **Relevant clinical or social indication**
- **Absence of clinical or biochemical indication of acute or chronic kidney disease or other relevant disease**
- **Patient well hydrated at the beginning of treatment**
- **Confirmed presence of LOW-RISK VTEC:**
  - ***vtx1***
  - ***vtx1* and *eae*, except VTEC O103:H2 ***
  - ***vtx2***
  - ***vtx1* and *vtx2***
- **No isolation of HUSEC**
- **>2 weeks since the first isolation of VTEC in a faecal specimen from the patient**
- **Isolation of identical types of VTEC (based on presence of virulence genes and serotype) found in 2 separate specimens**
- **Detailed characterisation of VTEC strain's virulence profile and serotype**

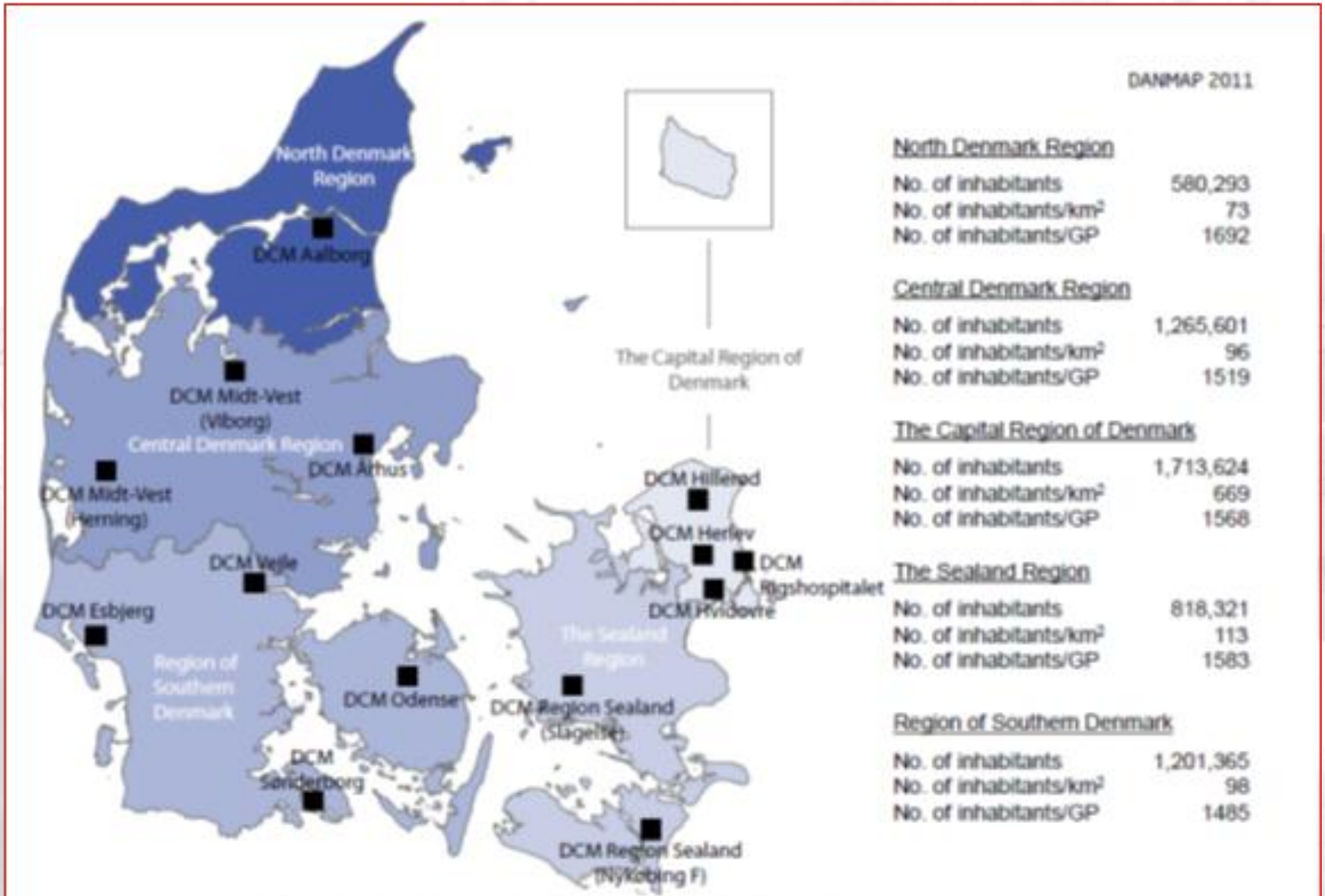


Figure 1 – The five health care regions and 14 Departments of Clinical Microbiology of Denmark

VTEC 2000-2003

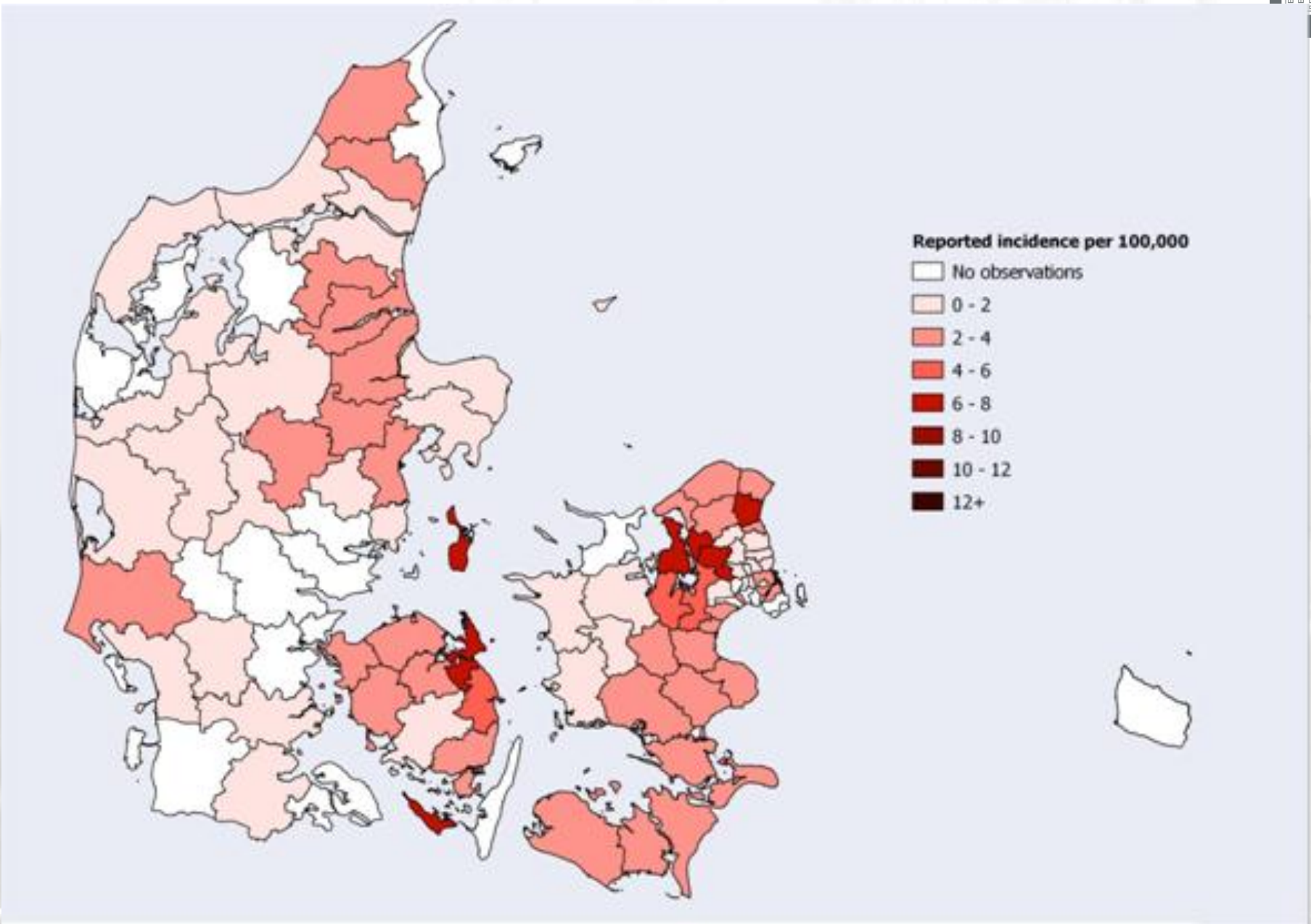


Figure 1 - Average yearly reported incidence of VTEC in Denmark from 2000-2003, by municipality

VTEC 2009-2012

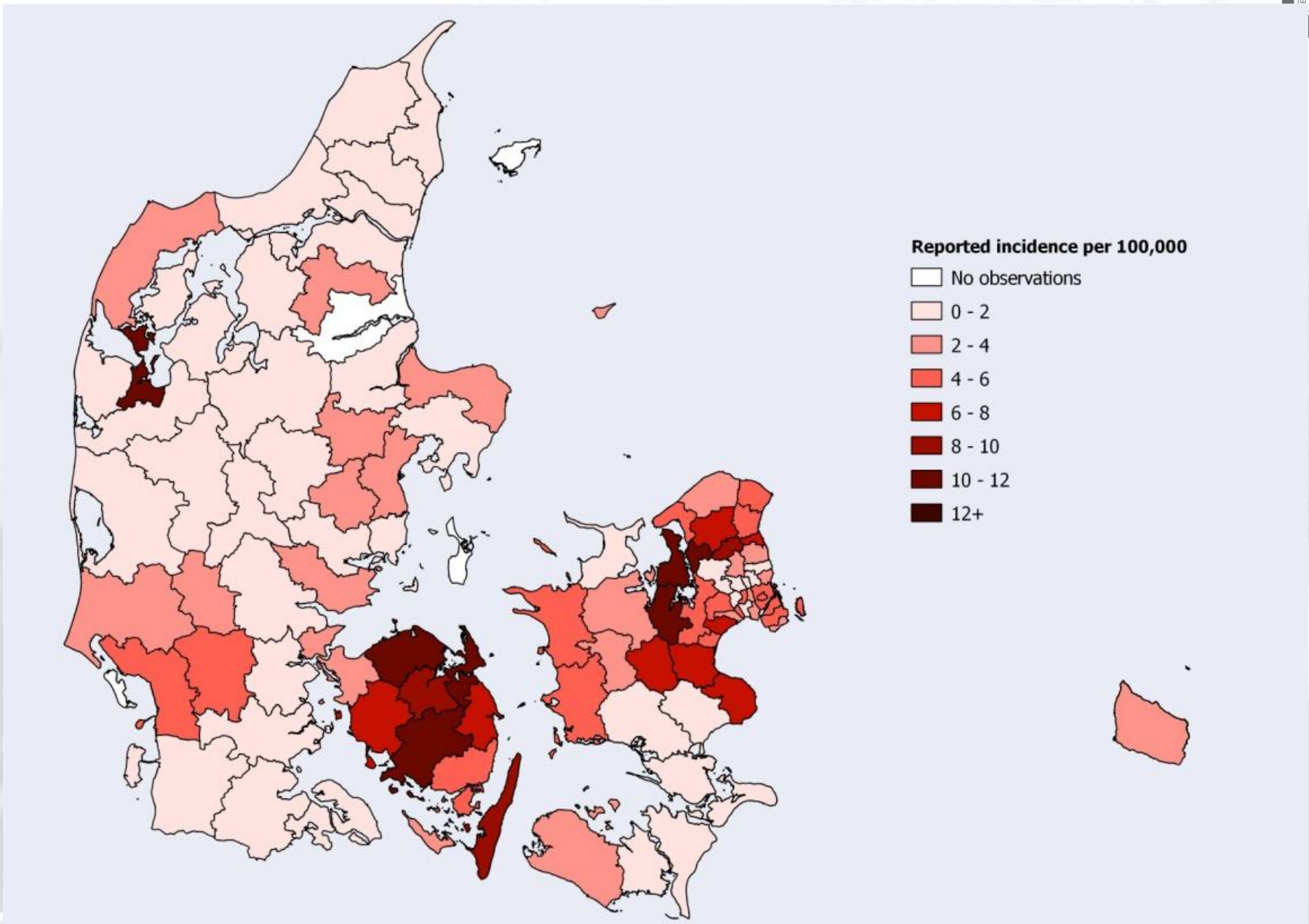


Figure 35 - Average yearly reported incidence of VTEC in Denmark from 2009-2012, by municipality

Extrapolating from a *landsdel* with high incidence

Table 9 - Number of reported cases of VTEC in 2012, extrapolated number of cases, and diagnostic benefit, by *landsdel*

VTEC	Inhabitants	Number of reported cases	Reported incidence per 100,000 inhabitants
Byen København	704,108	33	4.7
Københavns omegn	520,784	14	2.7
Nordsjælland	448,291	31	6.9
Bornholm	41,406	1	2.4
Østsjælland	236,429	10	4.2
Vest- og sydsjælland	581,478	23	4.0
Fyn	485,190	51	**10.5**
Sydjylland	716,152	14	2.0
Østjylland	839,710	12	1.4
Vestjylland	426,972	5	1.2
Nordjylland	579,996	3	0.5
Total		**197**	

Public health action in Denmark

vtx subtyping is used to

- Evaluate the risk of progression of the disease in individuals
- Minimize transmission of HUSEC associated to severe disease
- Rehabilitate individuals in order to prevent the worsening of an individual's health and the socio-economic impact on their families

Thank yous and acknowledgements !

The lab

Susanne Jespersen

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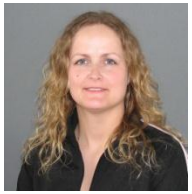
Charlotte Hoe



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Eva Møller Nielsen (The boss)

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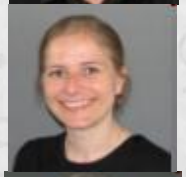
Antibiotic treatment recommendations

Andreas Munk Petersen

The epidemiologists

Steen Ethelberg



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