Investigation and pathogenomic analysis of Shiga toxin−producing *Escherichia coli* (STEC) from patients in Region Jönköping County

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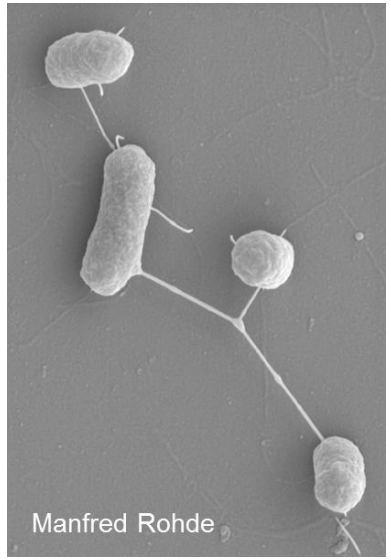
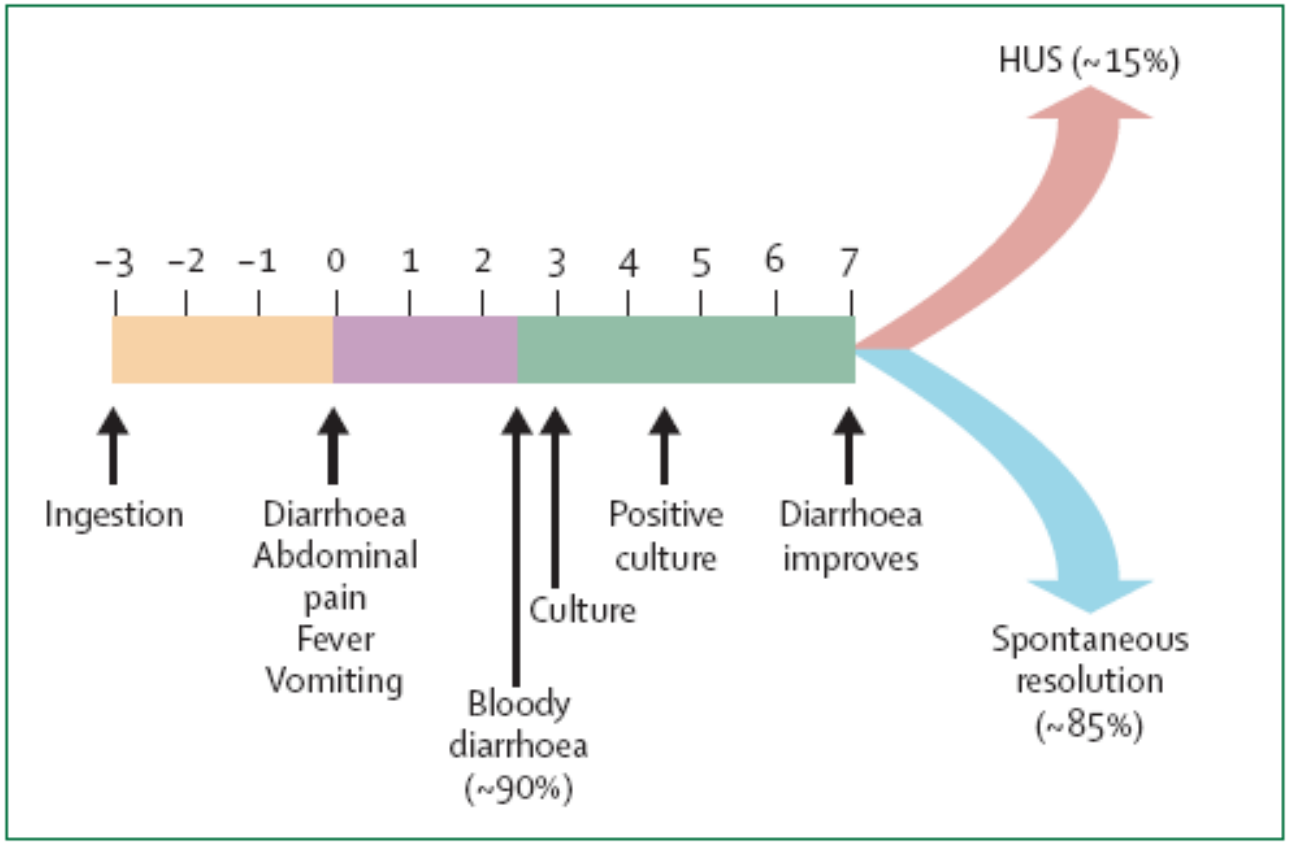
Course of disease





Tarr et al. Lancet 2005; 365: 1073–86

STEC background

- STEC 0157:H7 is the most common serotype worldwide
- WHO recognize non-0157 STEC as emerging pathogens
- Specific genetic lineages prone to cause severe disease (e.g clade 8 of O157)
- Shiga toxin (Stx) is the most important virulence factor; Stx1 & Stx2
- Stx1 & Stx2 are further categorized into several subtypes
- Outer membrane protein intimin (*eae*)

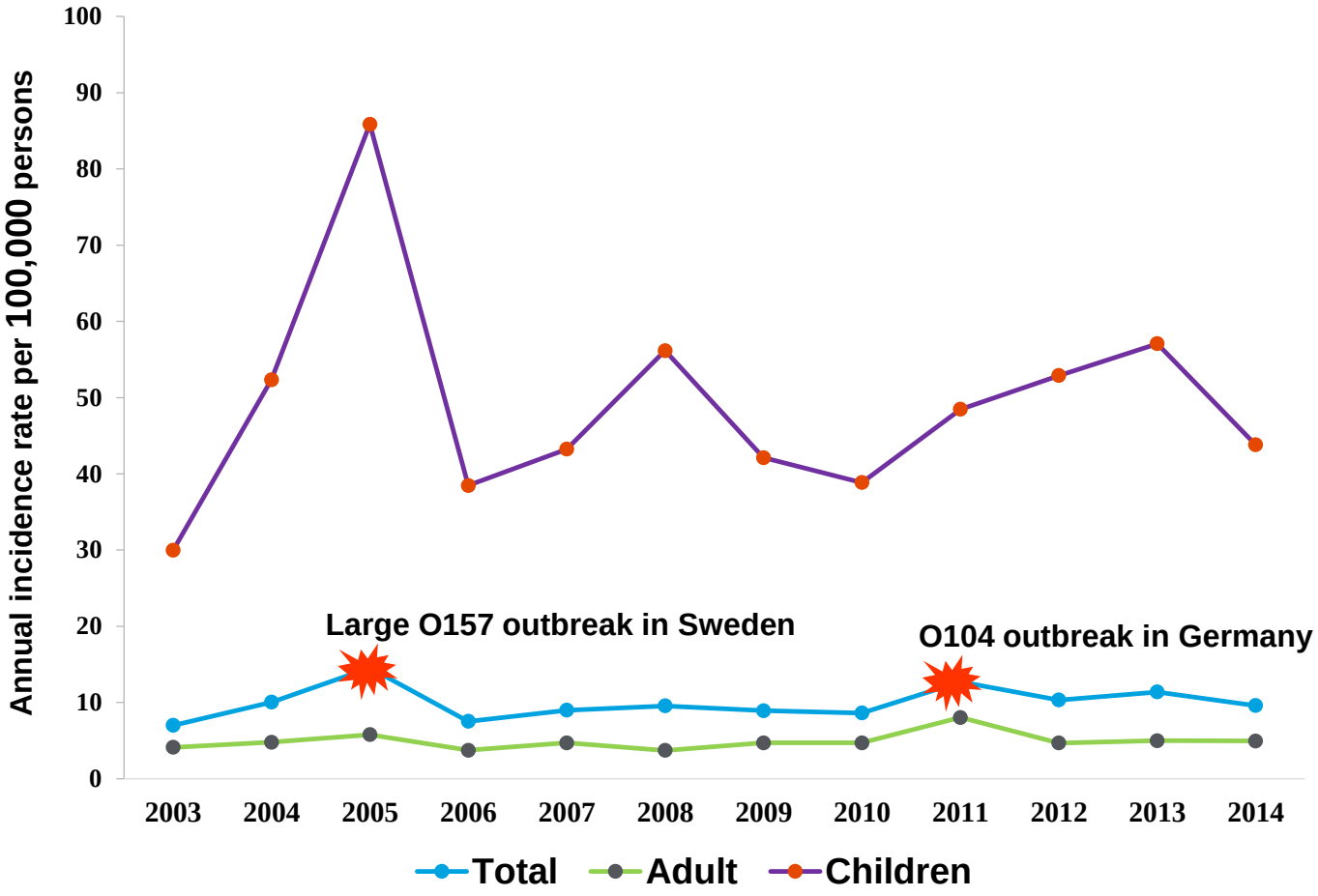
Objectives

- Evaluate incidence & molecular characteristics of STEC in patients over a 12 year period in Region Jönköping County
- Reveal insights into genetic markers in correlation with clinical symptoms & STEC shedding

Study design & methods

- Diarrheal specimens from patients
  I. ≤10 years from 2003 to 2013 (n=10342)
  II. >10 years from 2003 to 2015 (n=14550)
- Direct detection of *stx* by PCR
- Culture & whole genome sequencing (WGS)
- Repeated weekly samplings
- Reviewing medical records & questionnaire

STEC incidence



STEC cases (n=399)

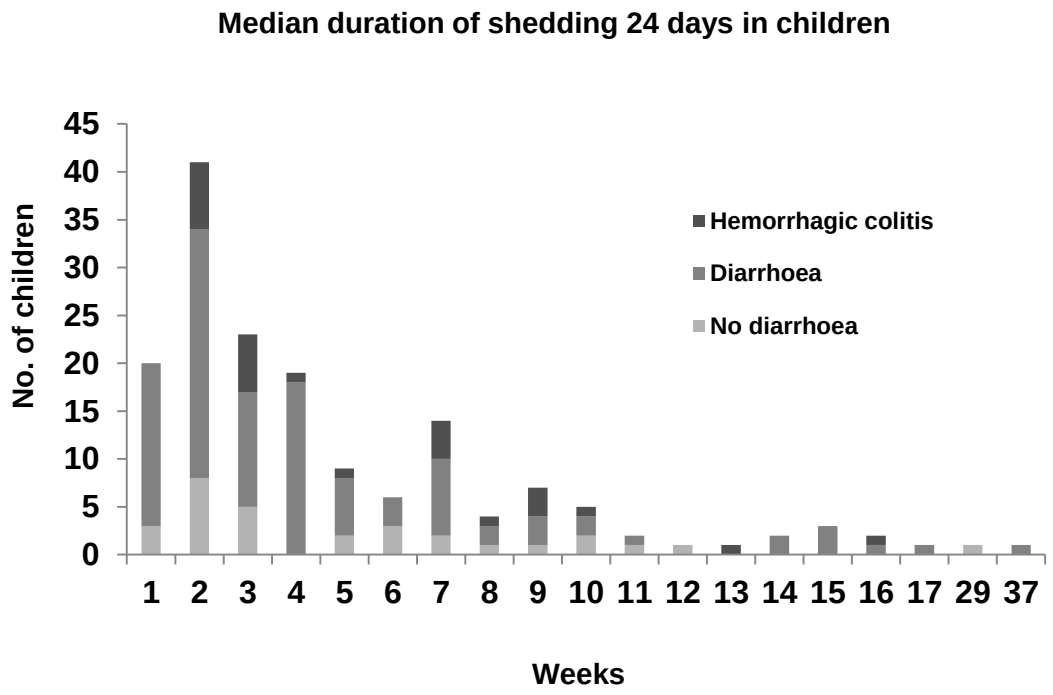
Children (n=224)

Adults (n=175)

Culture rate (43%)

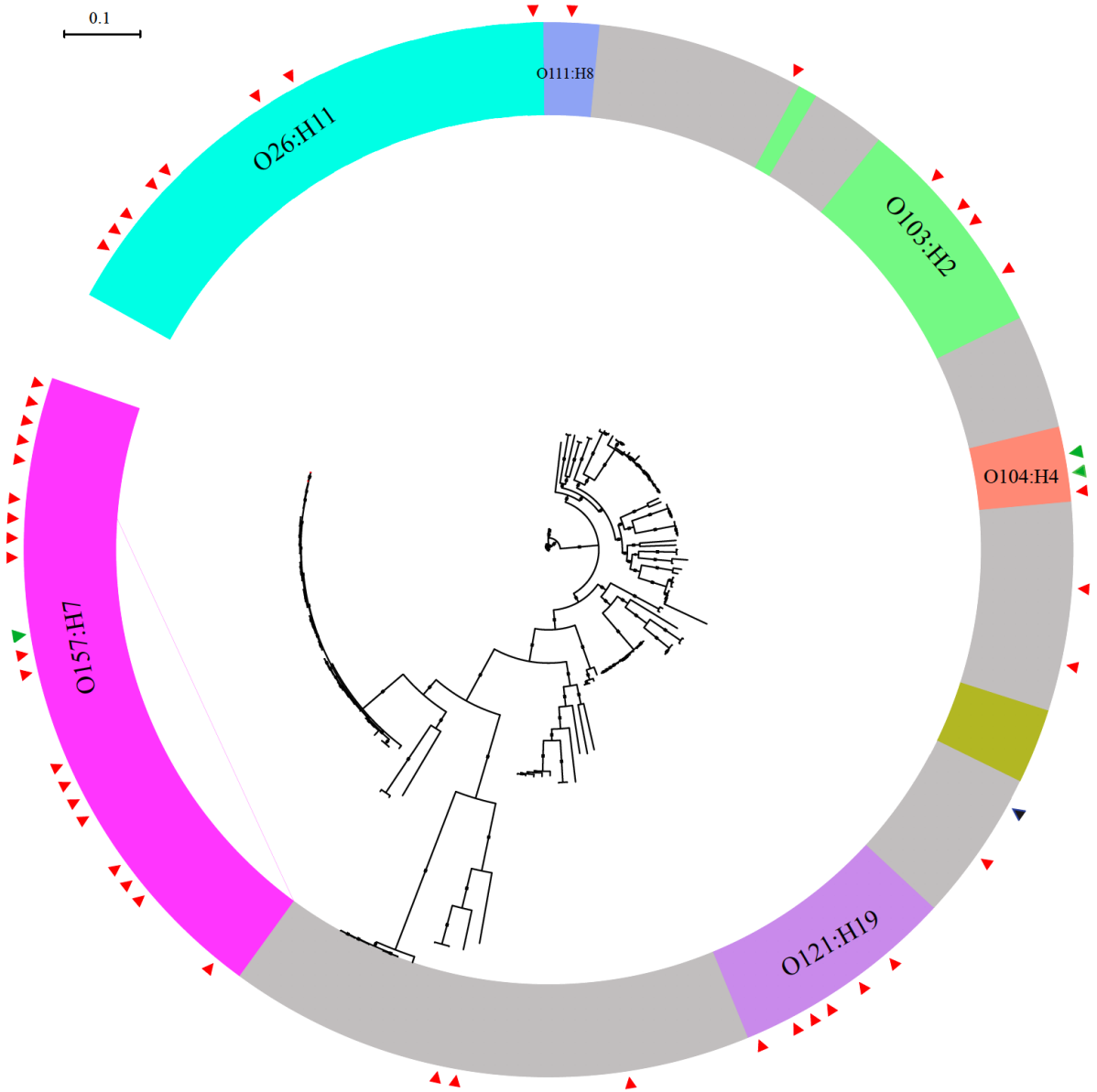
Clinical symptoms & duration of shedding

Symptoms/duration of shedding	All cases	BD	NBD
No. (%)	399	91 (22.8)	308 (77.2)
Median age of patients	7 (0-89)	23 (0-89)	6 (0-82)
Median duration of shedding, days	20 (0-294)	21 (5-197)	20 (0-294)
Abdominal pain (%)	150 (37.6)	58 (63.7)	92 (29.9)
Fever (%)	59 (14.8)	15 (16.5)	44 (14.3)
Vomiting (%)	50 (4.0)	10 (11.0)	40 (13.0)
HUS (%)	13 (3.3)	5 (5.5)	8 (2.6)



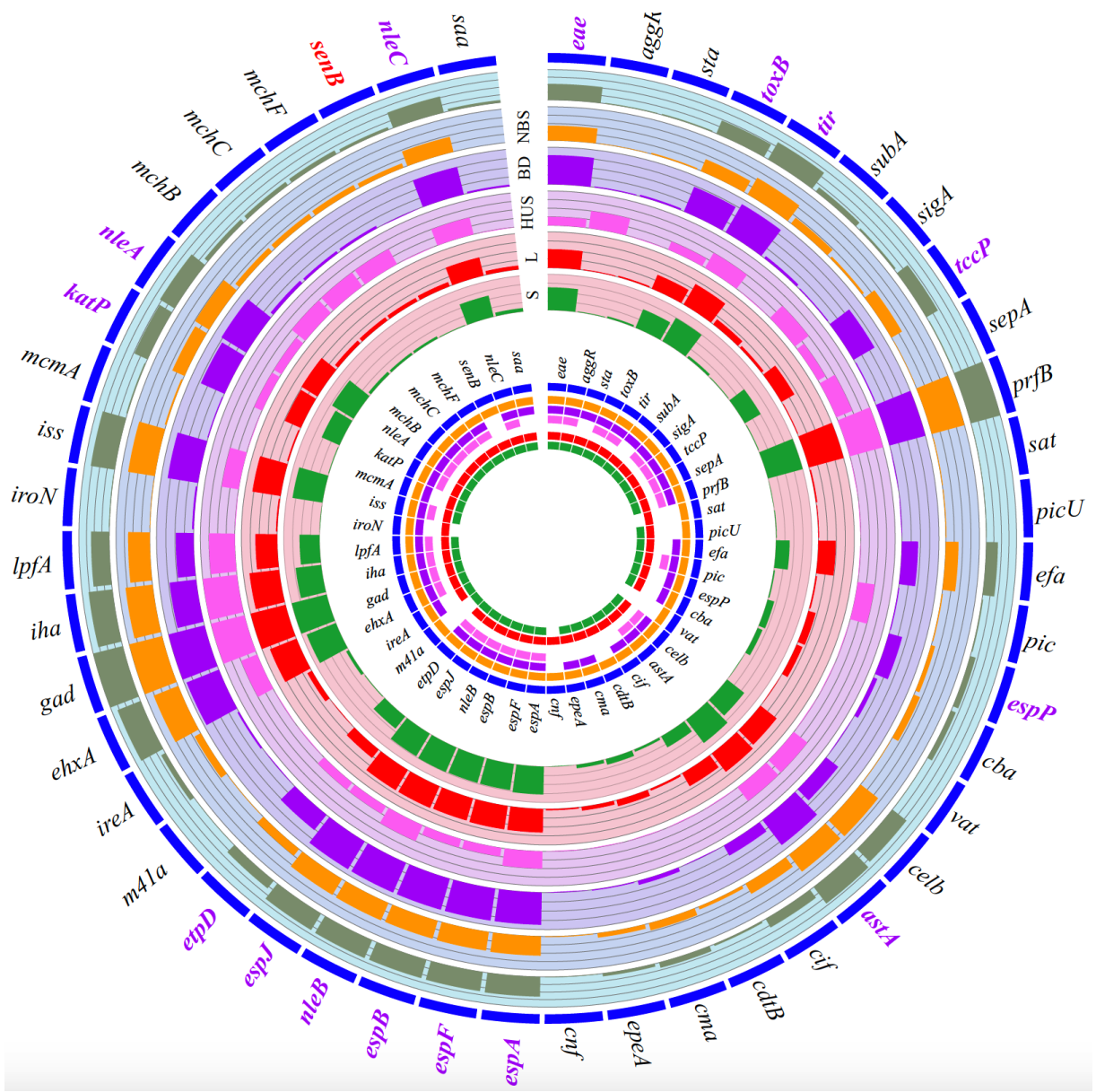
stx types & subtypes

- *stx1a* is most predominant, followed by *stx2a*, *stx2a+stx2c*, *stx2c*
- *stx2* is associated with BD; while *stx1* is associated with NBD
- *Stx2a & stx2a+stx2c* associated with BD; *stx1a* associated with NBD
- Four strains causing HUS carried *stx2a*, *stx2a+stx2c*, *stx1a*
- None of the *stx* types/subtypes correlated with duration of shedding



Predominant serotypes (O157:H7, O26:H11; O121:H19) are phylogenetically clustered together, and were more associated with BD

Phylogenomic diversity in STEC strains from similar clinical symptom



- ***VGs significantly associated with BD**

  Adhesion factors: *eae*, *toxB*, *tir*

  Secretion factors: *espA*, *espB*, *espF*, *espJ*, *espP*,*etpD, tccP, nleA*, *nleB*, *nleC*

  Toxins: *astA*,
  Plasmid-encoded: *katP*

- ***VGs associated with prolonged *stx* shedding**

  Toxin: *senB*

***virulence gene (VG)**

Conclusions

- STEC incidence highest among children
- Culture based methods needs improvement
- *stx2a* is associated with disease severity
- Specific serotypes & genes correlated with severity of disease
- Direct diagnostic algorithm could be of value to predict disease severity

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