



The Danish Surveillance System for pathogenic *E. coli* infections

November 2019



Flemming Scheutz

The International Centre for
Reference and Research on
Escherichia and *Klebsiella*

Foodborne Infections

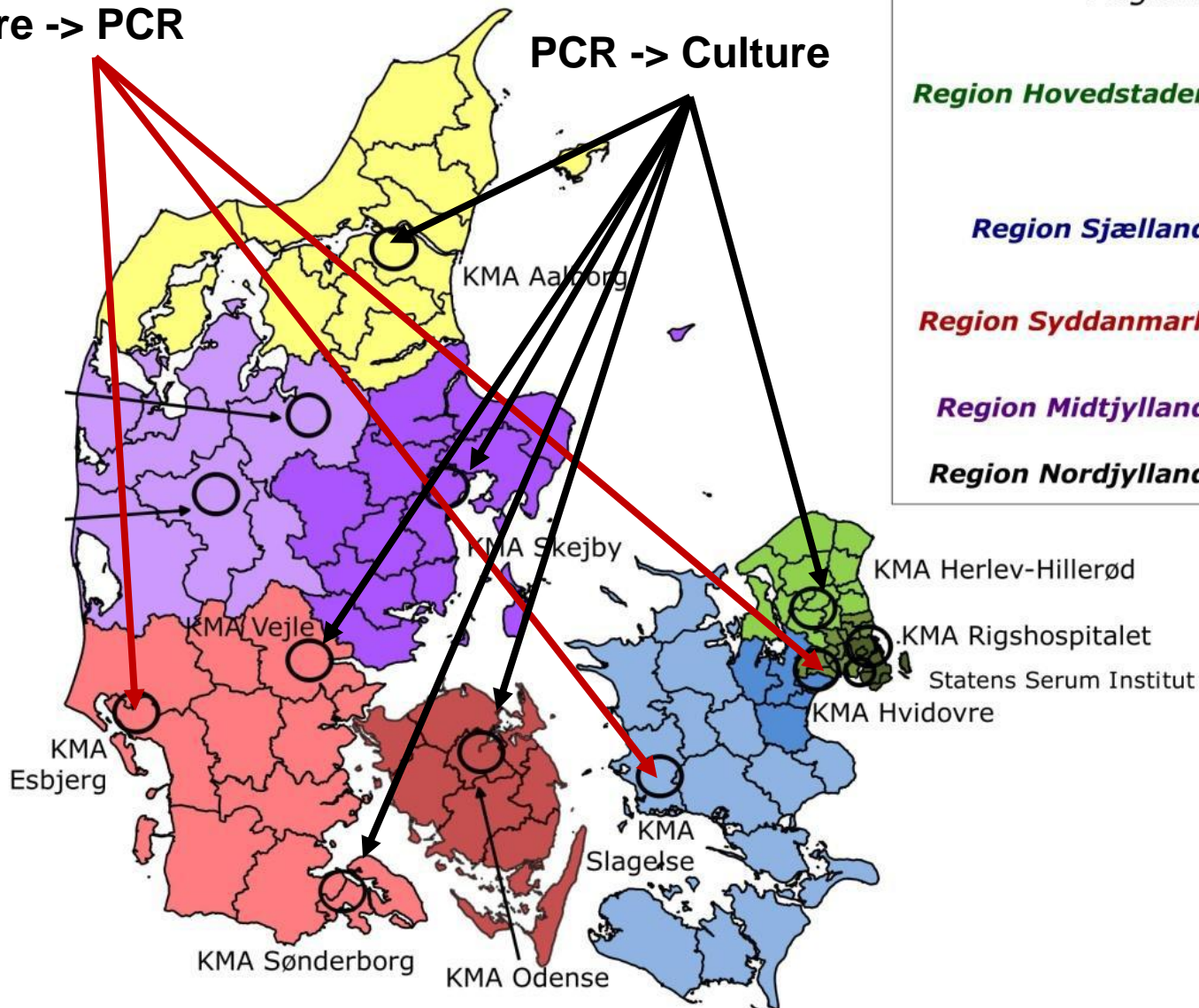
Department for Bacteria, Parasites &
Fungi

STATENS SERUM INSTITUT

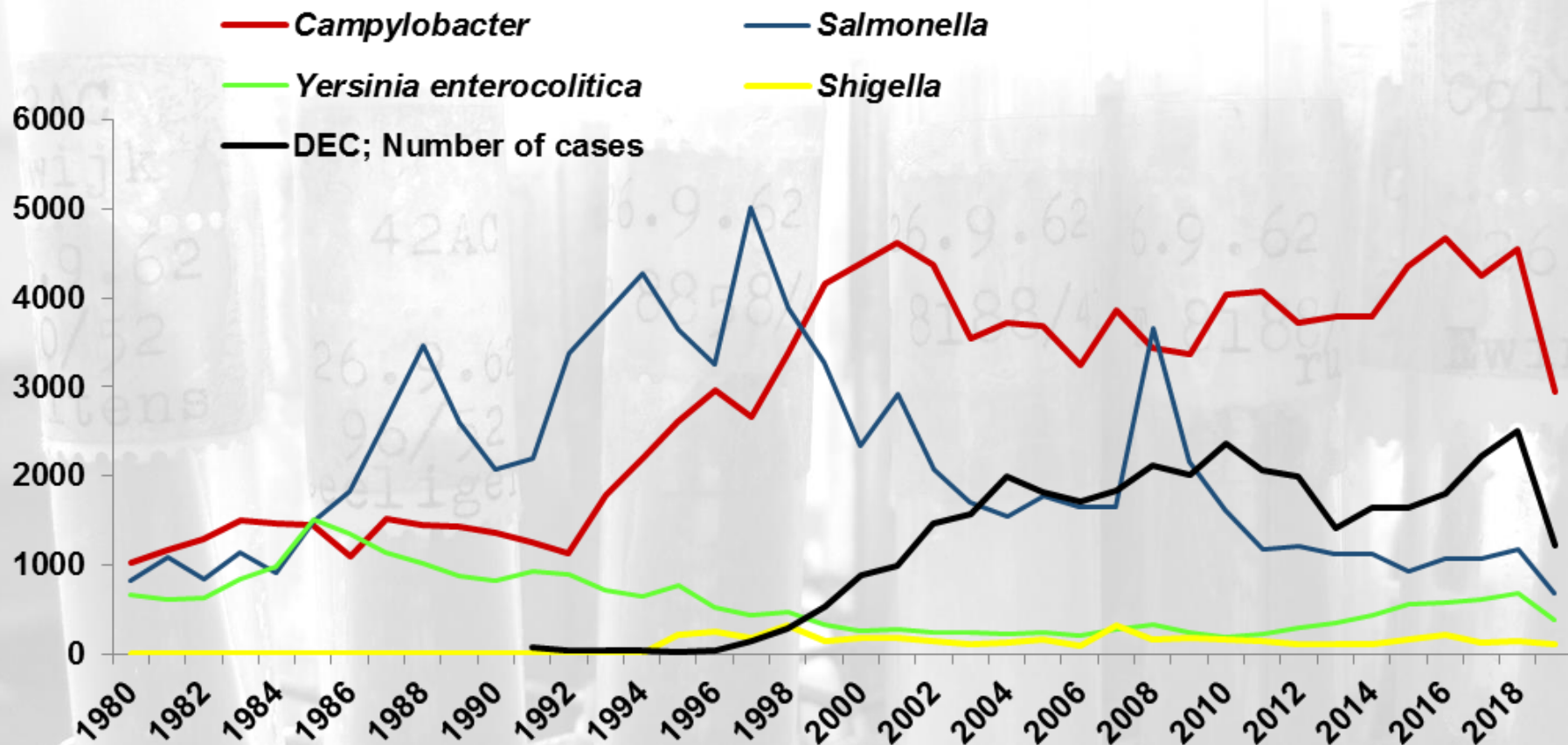


Culture -> PCR

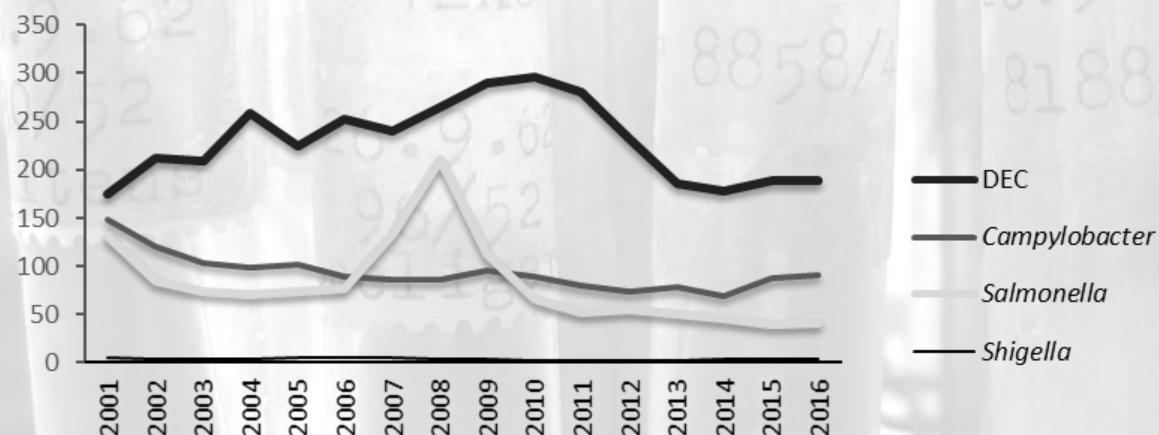
PCR -> Culture



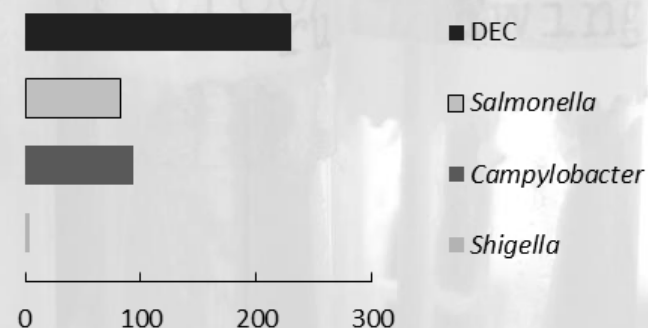
DEC in Denmark 1980- 2019



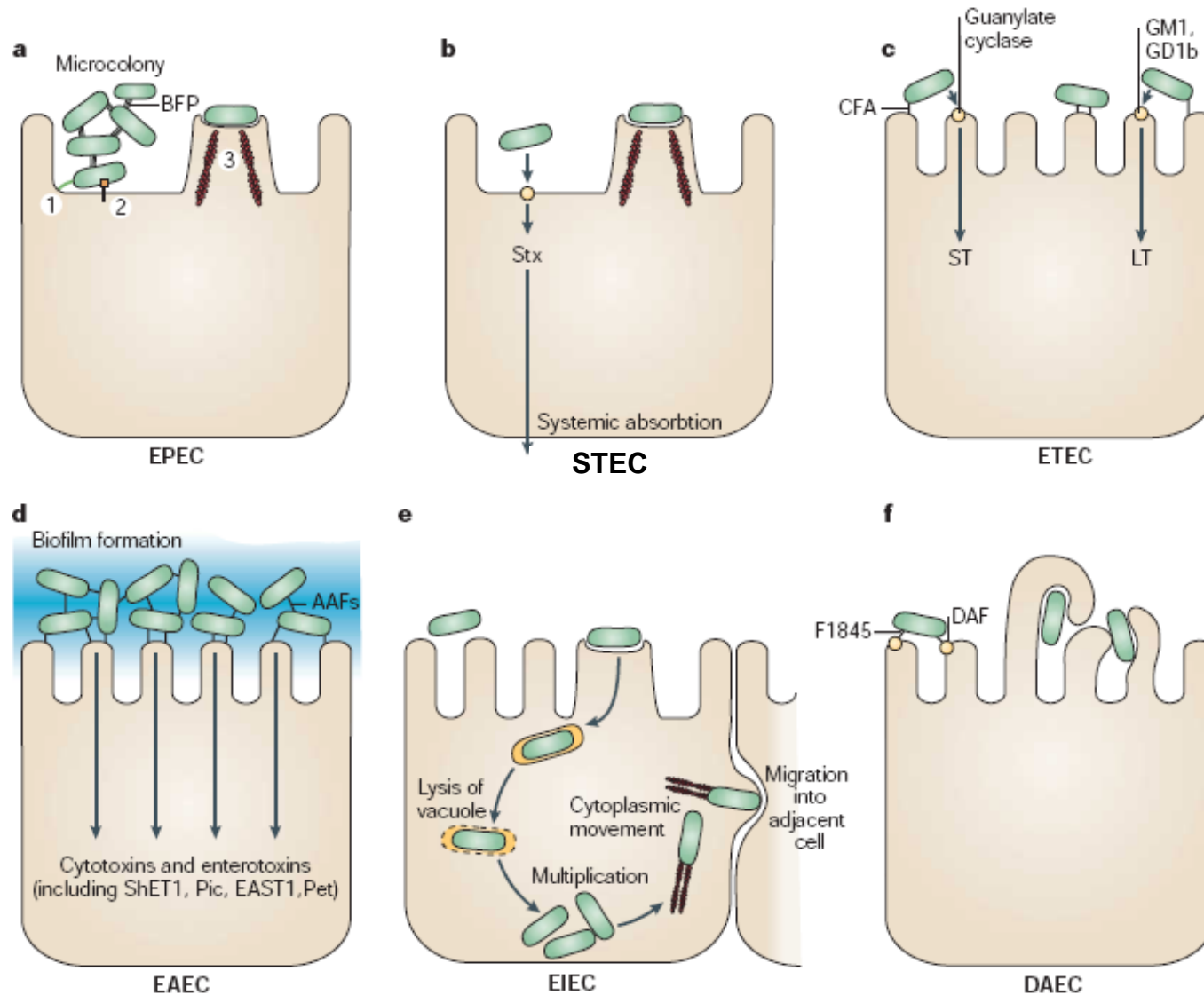
Reported incidence of the four most common enterpathogenic bacteria in Denmark, 2001 - 2016; less than 5 years



Average incidence of the four most common enterpathogenic bacteria 2001 – 2016; less than 5 years

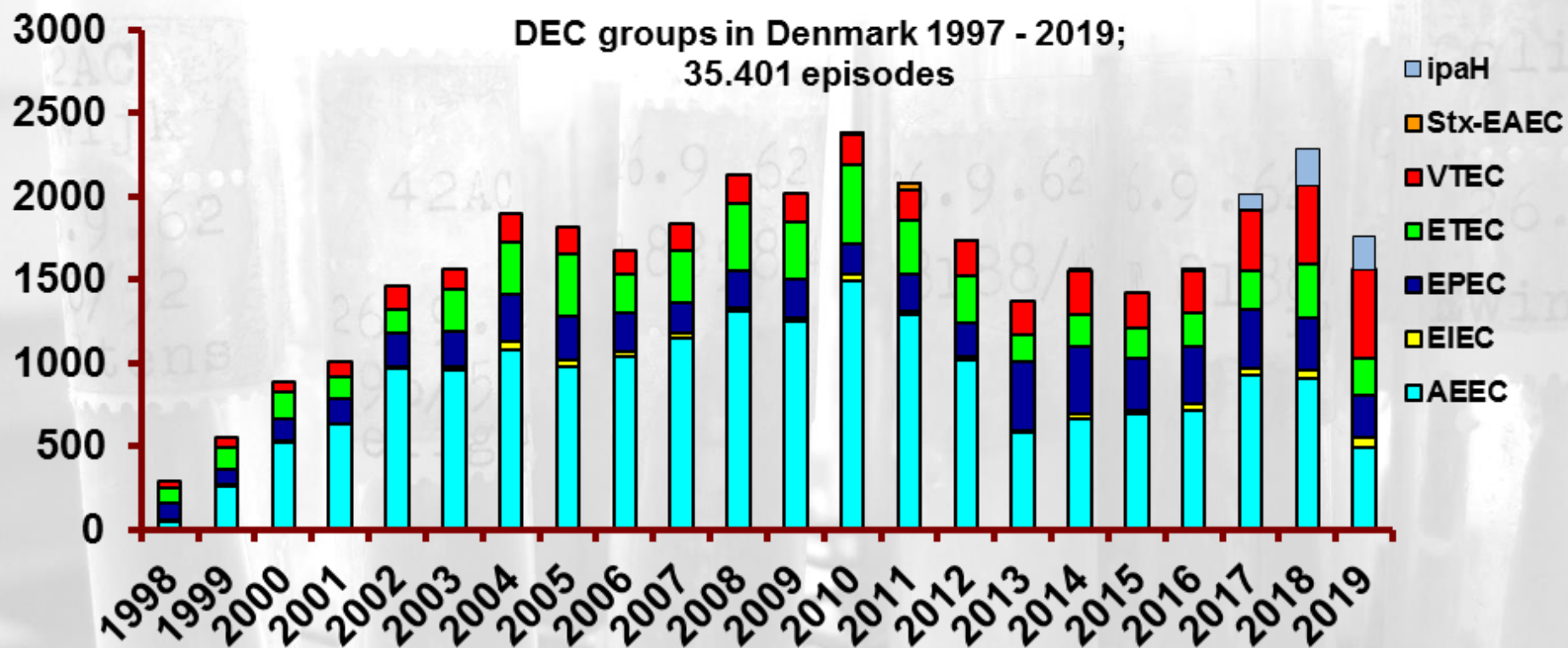


Diarrhoeagenic *E. coli* DEC

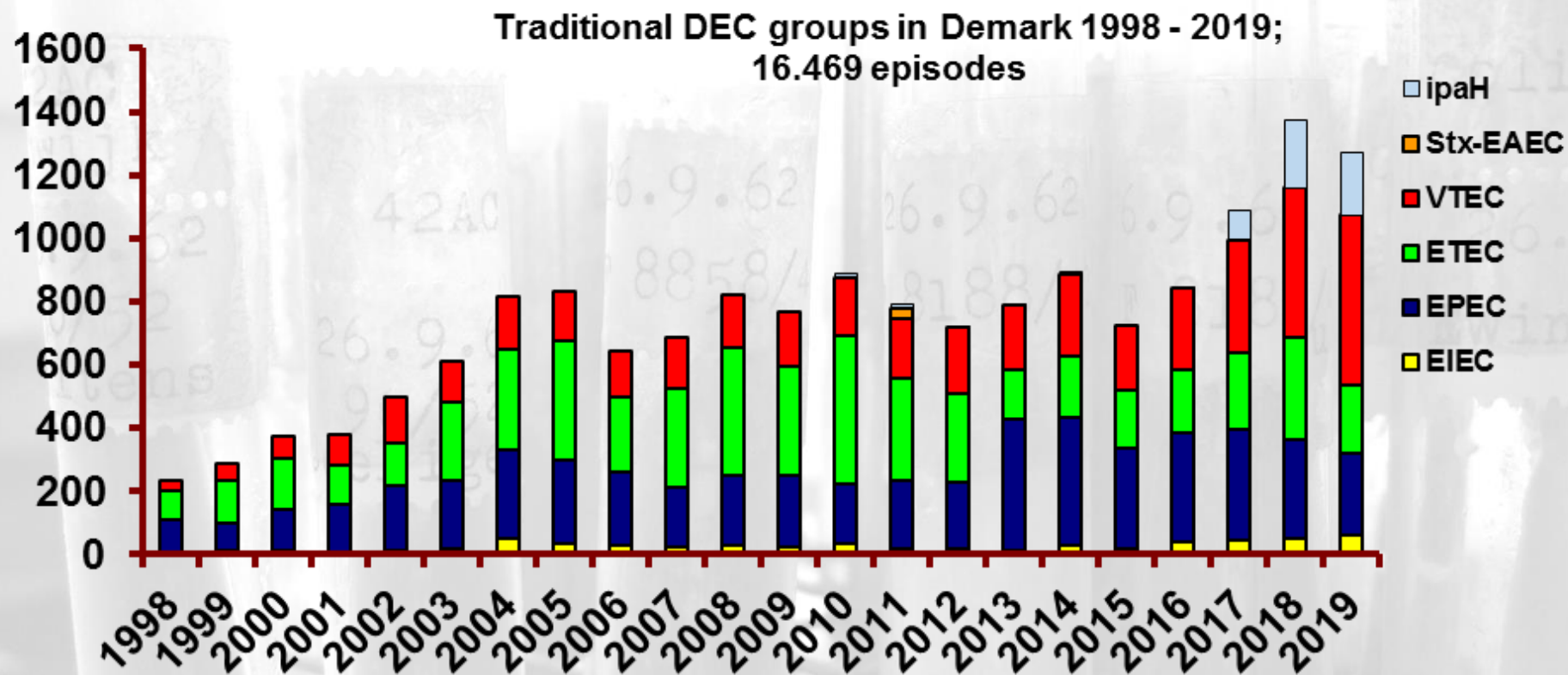


Kaper *et al*,
Nature
Reviews;
Microbiology
2004

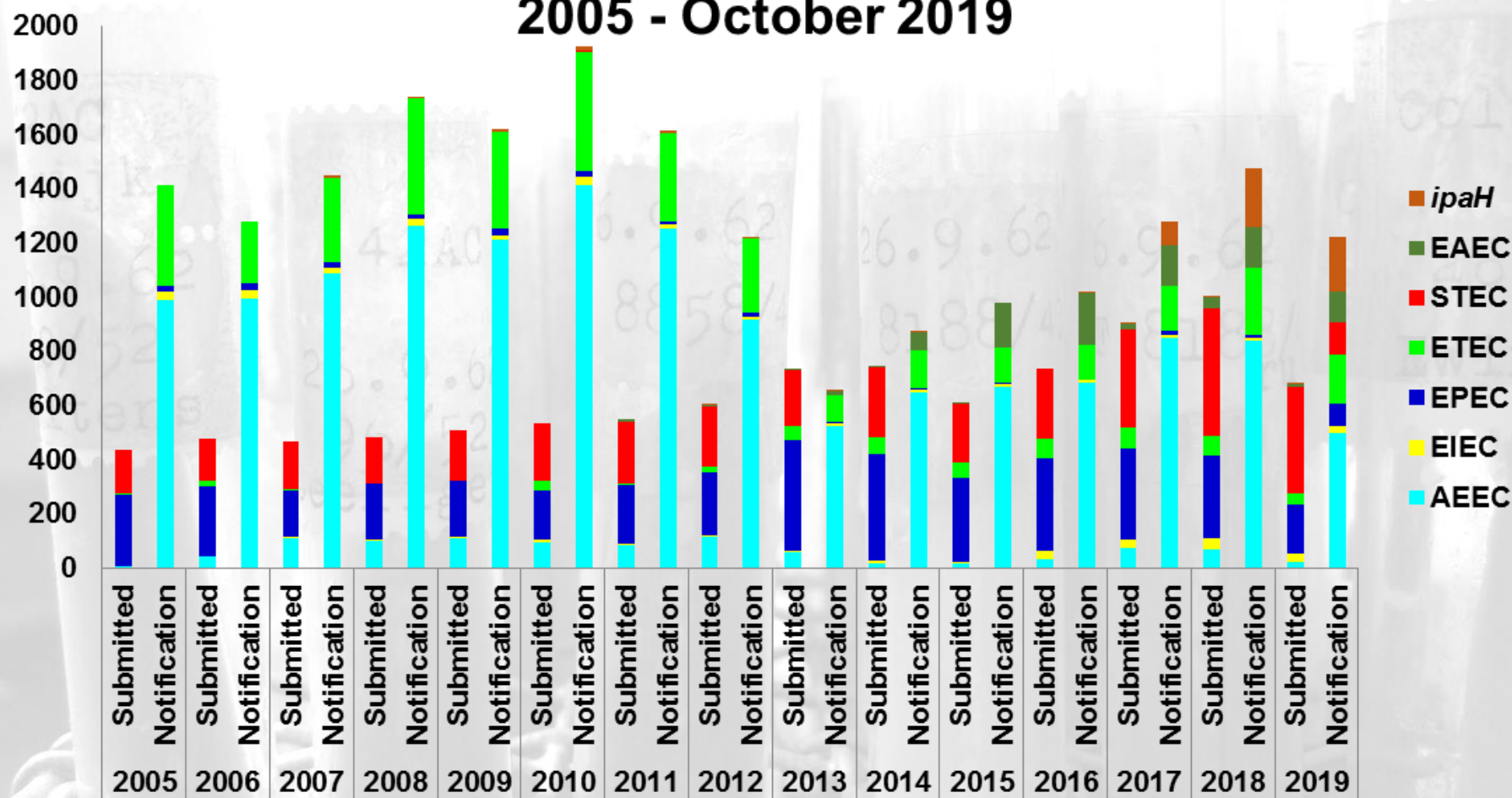
DEC in Denmark



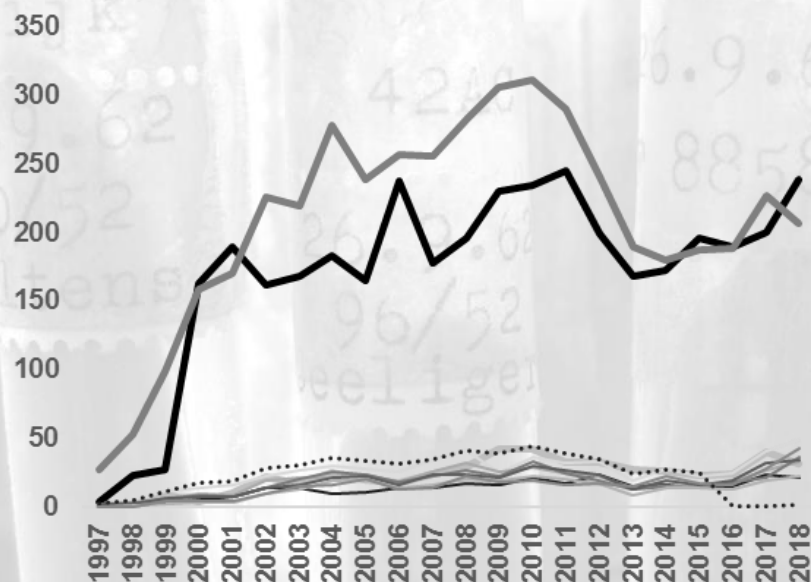
DEC in Denmark



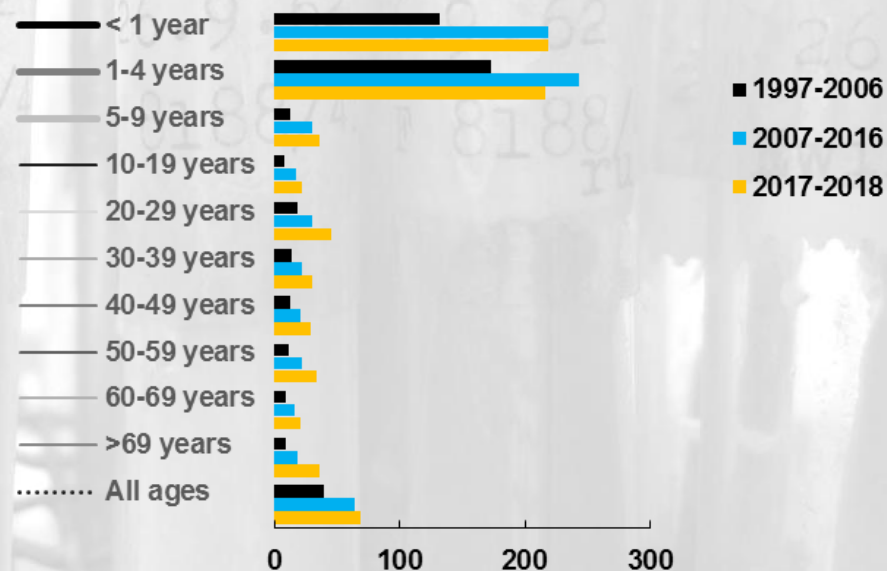
Submitted versus notified DEC groups 2005 - October 2019



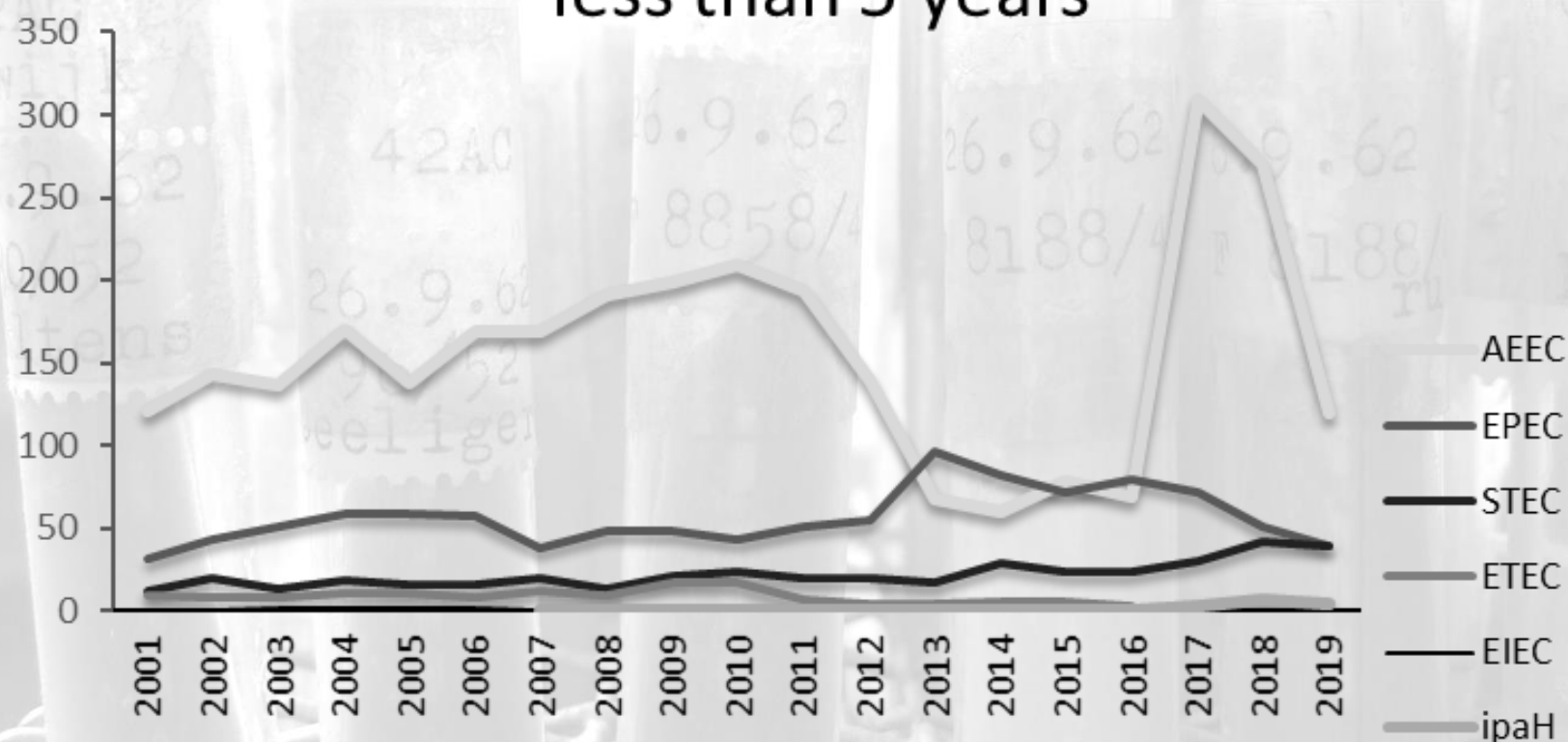
Reported incidence of DEC in Denmark, 1997 - 2018 by age group



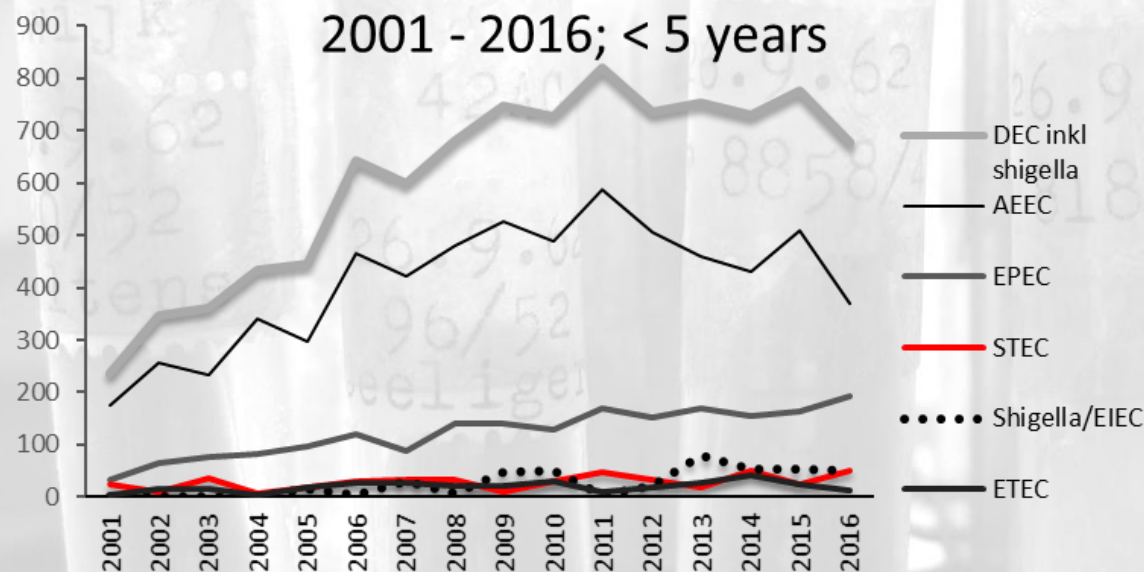
Average incidence of DEC 1997 - 2006, 2007 - 2016 and 2017-2018 by age group



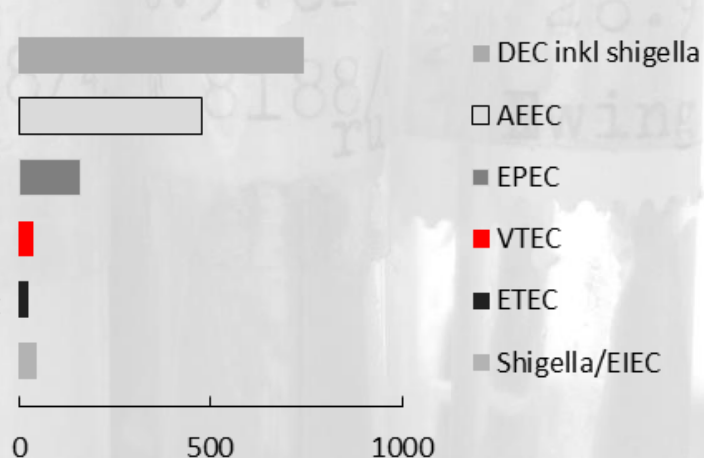
Reported incidence of five diarrhoeagenic *E. coli* (DEC) pathotypes in Denmark, 2001 - 2019; less than 5 years



Reported incidence of five diarrhoeagenic *E. coli* (DEC) pathotypes on Funen 2001 - 2016; < 5 years

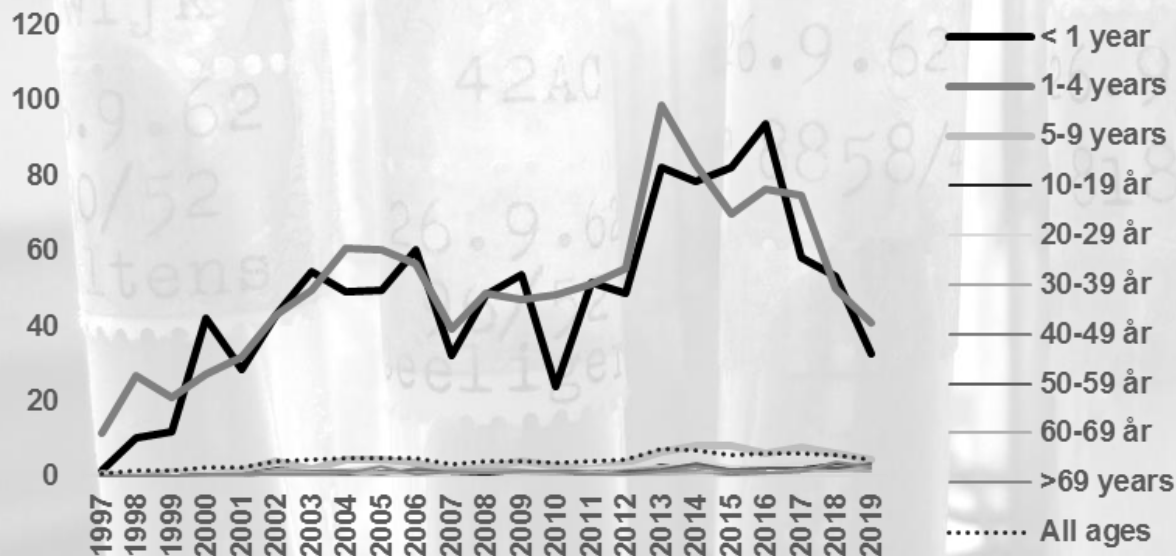


Average incidence of five diarrhoeagenic *E. coli* (DEC) pathotypes on Funen 2010 – 2016; less than 5 years

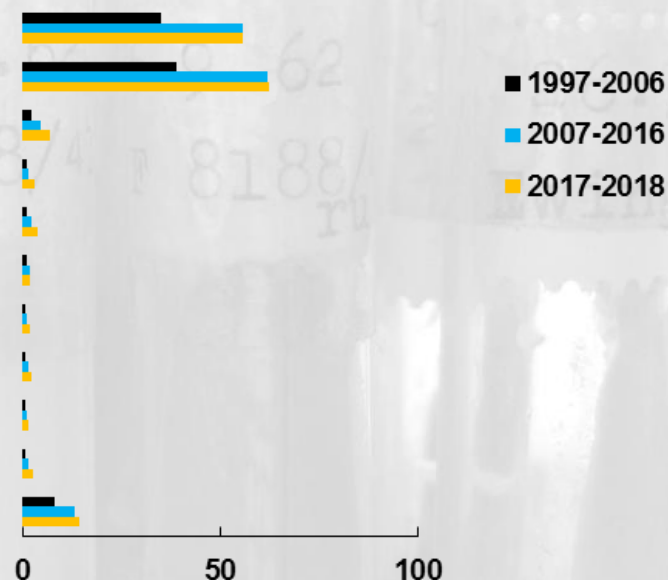


EPEC in Denmark

Reported incidence of EPEC in Denmark, 1997 - 2019 by age group

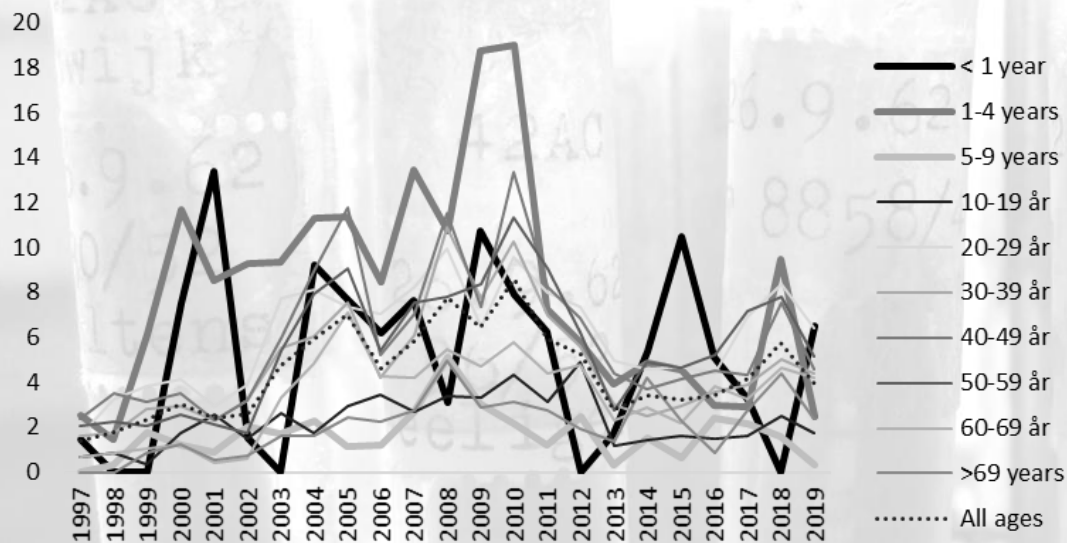


Average incidence of EPEC 1997 - 2006, 2007 - 2016 and 2017-2018 by age group

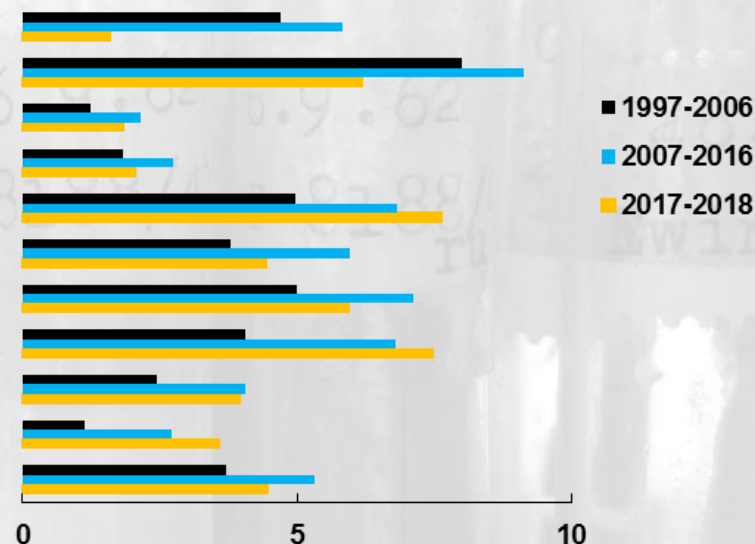


ETEC in Denmark

Reported incidence of ETEC in Denmark, 1997 - 2019 by age group



Average incidence of ETEC 1997 - 2006, 2007 - 2016 and 2017-2018 by age group

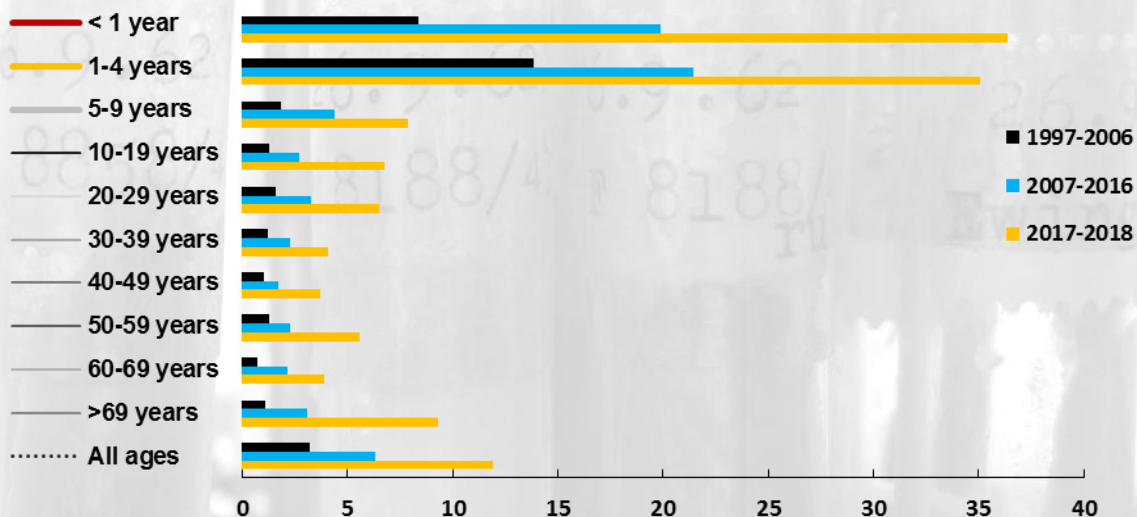


STEC in Denmark

Reported incidence of STEC in Denmark, 1997 - 2018 by age group

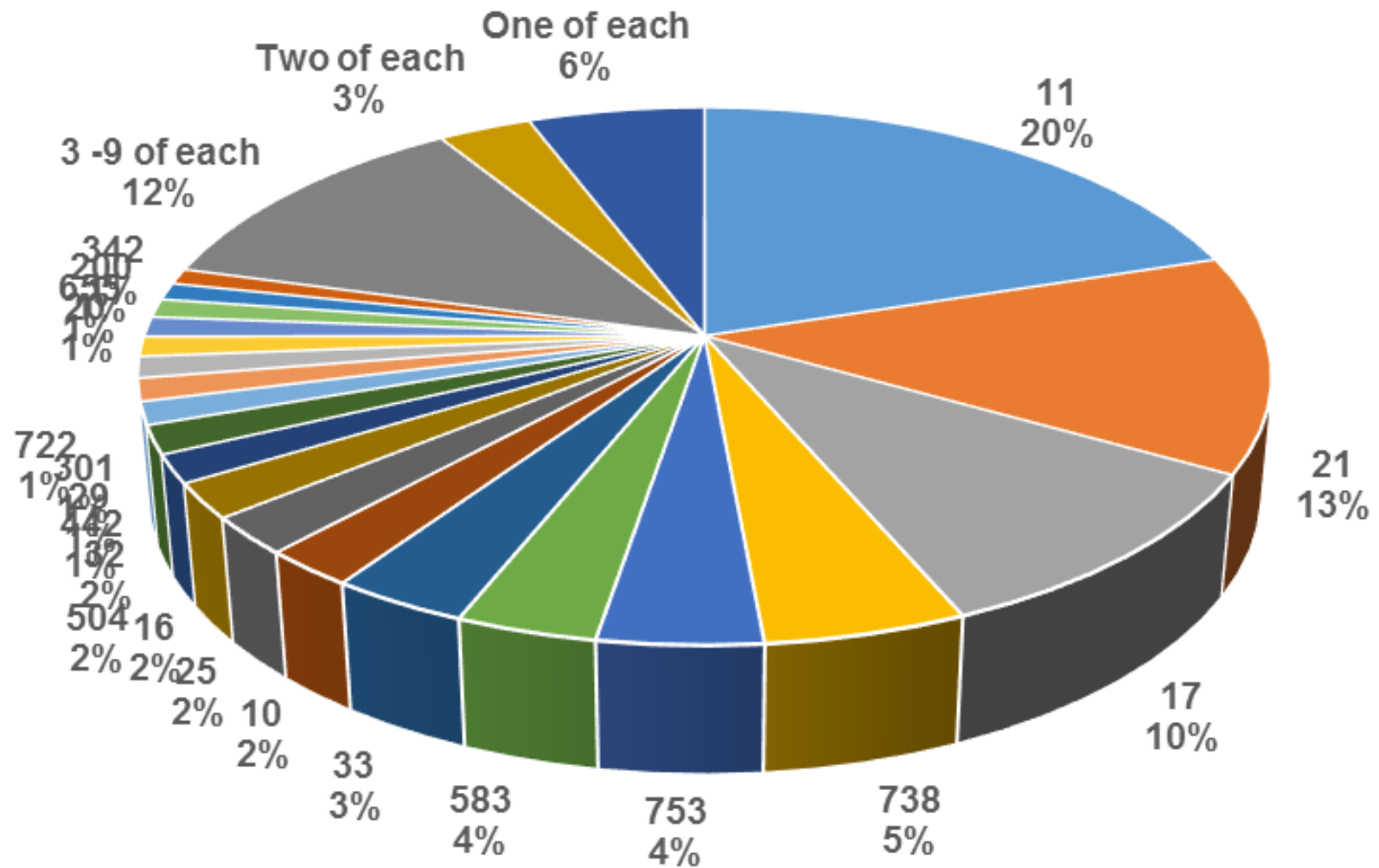


Average incidence of STEC 1997 - 2006, 2007 - 2016 and 2017-2018 by age group

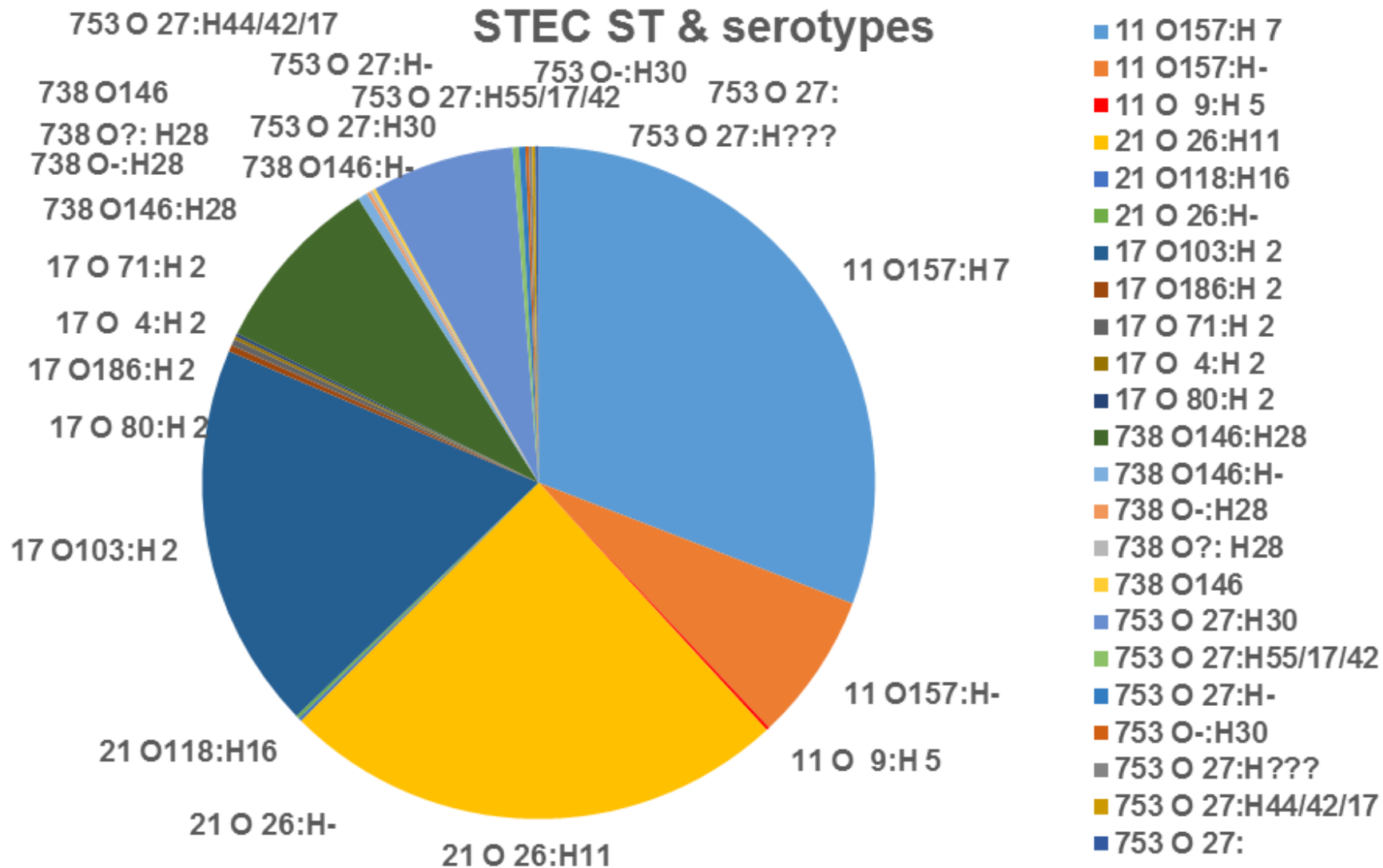




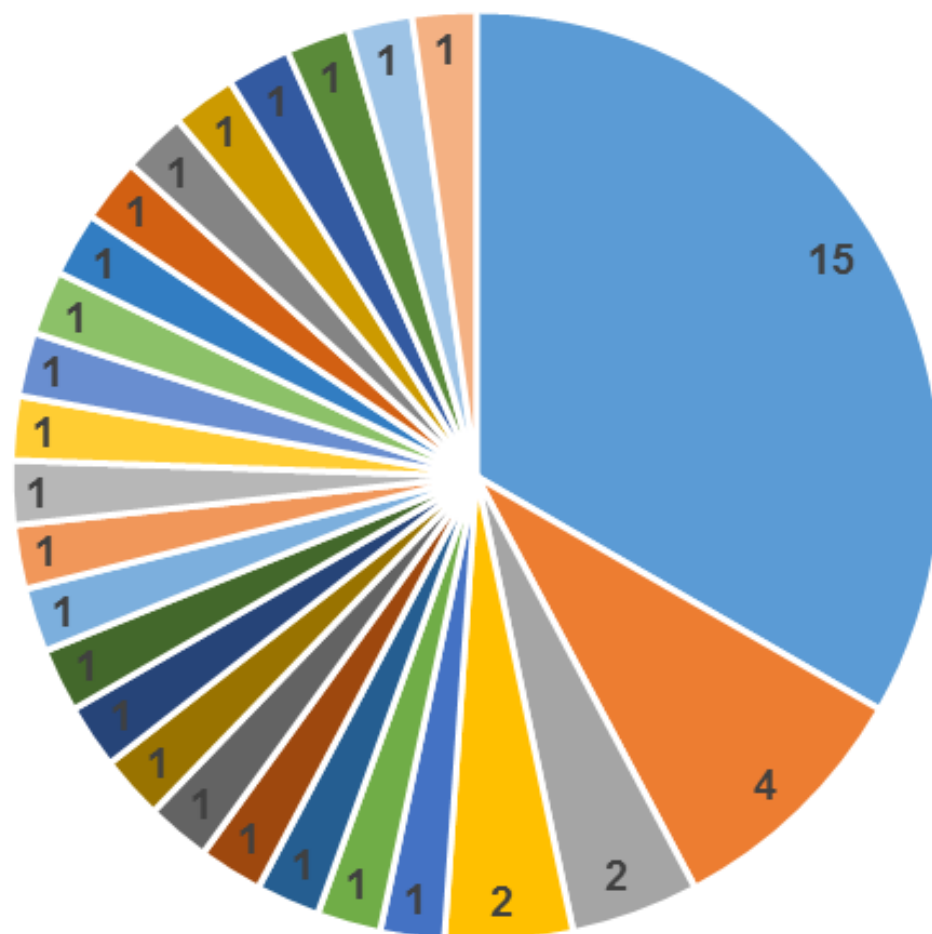
STEC ST types by WGS



STEC ST & serotypes

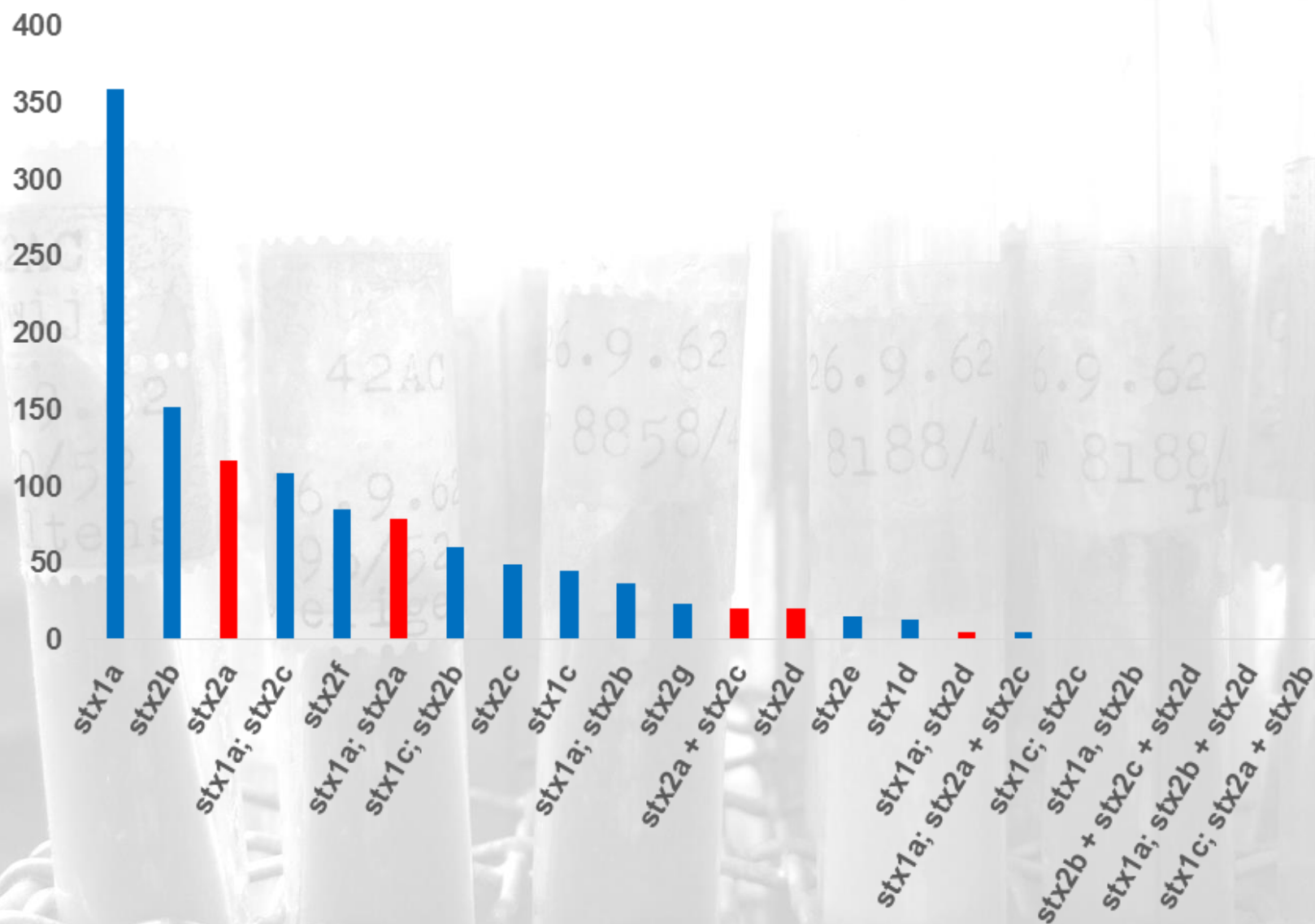


STEC ST10 & SEROTYPES

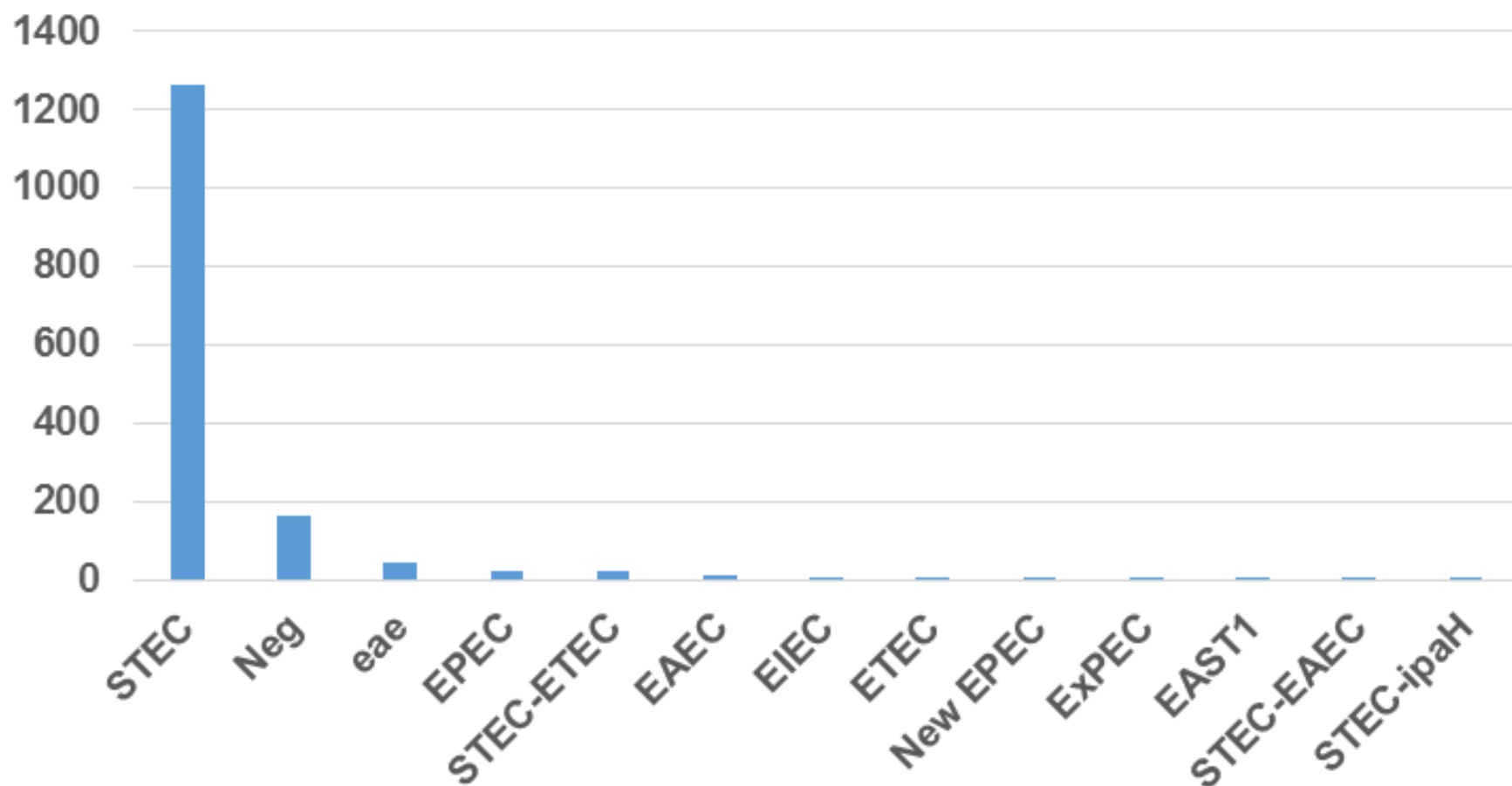


- 10 O113:H 4
- 10 O 38:H26
- 10 O156:H 4
- 10 O 89:H 9
- 10 O162:H10
- 10 O113:H 4/H17
- 10 O-:H40
- 10 O 36:H19
- 10 O126:H 2
- 10 O 9a:H 9
- 10 Oru:H 4
- 10 O 45:H 4
- 10 O 19:H 4
- 10 O128:H10
- 10 O117:H10
- 10 O145:H40
- 10 O 26:H32
- 10 O 16:H48
- 10 O154:H19
- 10 O 90/O127:H40
- 10 O157:H16
- 10 O 99:H 4/H17
- 10 O181():K 26:
- 10 O-:H 4
- 10 :H10
- 10 O-:H16

stx subtypes in Denmark (1206 isolates)



Pathotypes using WGS (1548)



Definition of *hybrid*



1: an offspring of two animals or plants of different races, breeds, varieties, species, or genera a *hybrid* of two roses

2: a person whose background is a blend of two diverse cultures or traditions

3a: something heterogeneous in origin or composition : COMPOSITE

hybrids of complementary DNA and RNA strands

a *hybrid* of medieval and Renaissance styles

3b: something (such as a power plant, vehicle, or electronic circuit) that has two different types of components performing essentially the same function
drives a *hybrid* that gets really good mileage



Crossovers

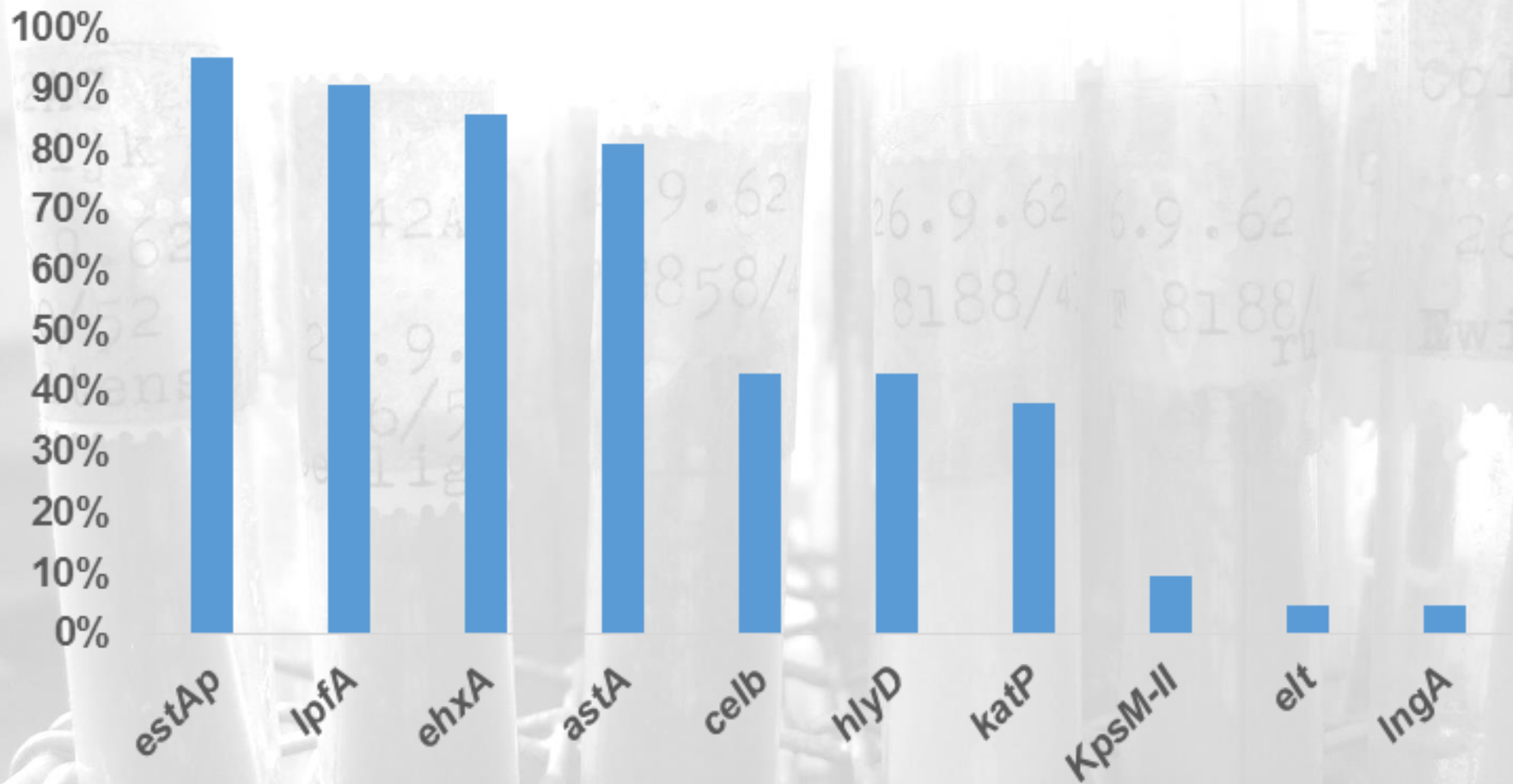
GROUP	MLS T ST	SEROTYPE	stx_sub	Enterotoxin	Total
STEC-ETEC	200	O187:H28	stx2g	estap	12
STEC-ETEC	5822	H 7	stx2g	estap	2
STEC-ETEC	5822	Orough:H 7	stx2g	estap	2
STEC-ETEC	5822	O?:H 7	stx2g	estap	1
STEC-ETEC	58	O 8:H 9	stx2e	estap	1
STEC-ETEC	325	O 15:H16	stx2g	estap	1
STEC-ETEC	2353	O 6:H16	stx1a	elt	1
STEC-ETEC	8880	O 13:H23	stx2d	estap	1
STEC-ipaH		<i>Shigella flexneri</i> 2a	stx1a		1
STEC-EAEC		O104:H 4	stx2a	pic, sigA	1
Total					23

E. albertii eae, stx2f 1

21 STEC-ETEC in Denmark



Virulence genes in STEC-ETEC





OPEN

Molecular Characterization and Comparative Genomics of Clinical Hybrid Shiga Toxin-Producing and Enterotoxigenic *Escherichia coli* (STEC/ETEC) Strains in Sweden

Xiangning Bai^{1,2}, Ji Zhang³, Anoop Ambikan¹, Cecilia Jernberg⁴, Ralf Ehricht^{5,6}, Flemming Scheutz⁷, Yanwen Xiong² & Andreas Matussek^{1,8,9}

Received: 11 January 2019

Accepted: 21 March 2019

Published online: 04 April 2019

Strain	Serotype	<i>stx</i> subtype	<i>sta</i> subtype	ST	Sampling year	Clinical symptom	Duration of <i>stx</i> shedding (day)	Age of patients (year)
SE572	O187:H28	<i>stx2g</i>	<i>sta4</i> , <i>sta5</i>	200	2005	D	11	1
SE573	O15:H16	<i>stx2g</i>	<i>sta4</i>	325	2009	D, AP, F	16	56
SE574	O136:H12	<i>stx2a</i>	<i>sta4</i> , <i>sta4</i> , <i>sta5</i>	329	2014	N	18	10
SE575	O100:H30	<i>stx2e</i>	<i>sta1</i>	993	2017	D	—	82

Table 1. Characteristics of STEC/ETEC hybrid strains in this study. D: Diarrhea. AP: Abdominal pain. F: Fever. N: No symptoms, individual was sampled due to contact tracing around an index case. -: Unavailable.



Enterohemorrhagic *Escherichia coli* Hybrid Pathotype O80:H2 as a New Therapeutic Challenge

Nurcan Soysal, Patricia Mariani-Kurkdjian, Yasmine Smail, Sandrine Liguori, Malika Gouali, Estelle Loukiadis, Patrick Fach, Mathias Bruyand, Jorge Blanco, Philippe Bidet, Stéphane Bonacorsi

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 22, No. 9, September 2016

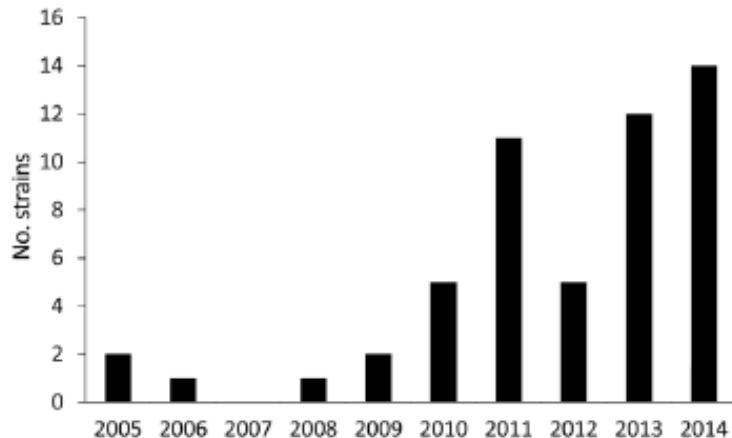


Figure 1. Number of enterohemorrhagic *Escherichia coli* O80:H2 strains detected annually, France, January 2005–October 2014.

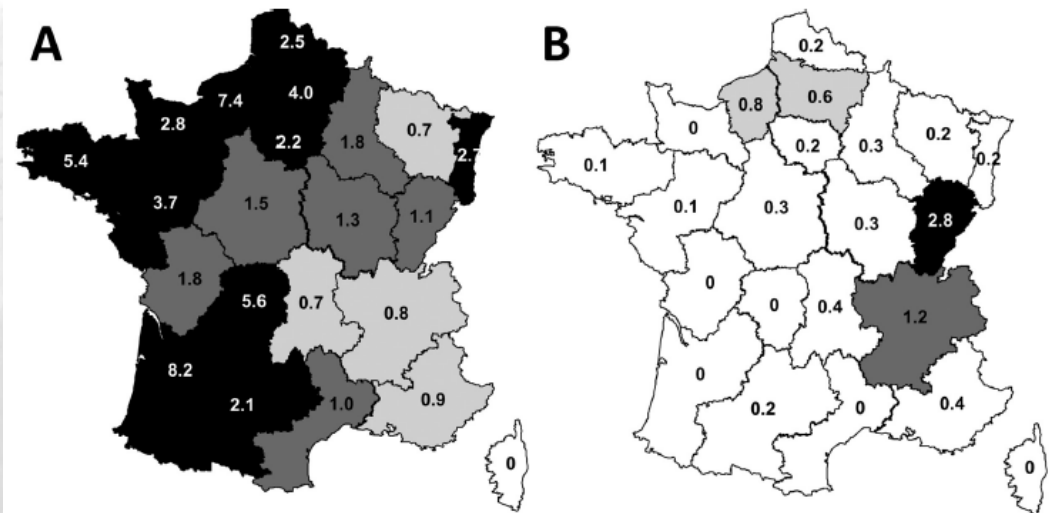


Figure 2. Regional 10-year cumulative incidence rates of hemolytic uremic syndrome cases caused by enterohemorrhagic *Escherichia coli* serotypes O157:H7 and O80:H2, France, January 2005–October 2014. A) Serotype O157:H7. B) Serotype O80:H2. White, <0.5 cases/100,000 children; light gray shading, 0.5–0.7 cases/100,000 children; medium gray shading, 0.8–0.9 cases/100,000 children; dark gray shading, 1–2 cases/100,000 children; black, >2 cases/100,000 children.

48/53 (91%) had HUS; Median age for these 48 patients was 1.2 years



Characteristics of 57 STEC-ExPEC O80:H2

69% combination af *stx2* subtypes:

***stx2c/2d* (62%)**

***stx2a/2d* (7%)**

31% only one subtype:

***stx2a* (22%)**

***stx2d* (9%)**

All *eae-ξ*

87% enterohaemolysin *ehxA*

All 57 isolates: ≥ 4 genes from pS88 plasmid: *sitA*, *cia*, *hlyF*, *ompT*

98% *iss* og *iroN* genes

96% *cvaA* gene

61% *iucC* og *etsC*



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Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Research note

K. De Raauw et al. / Clinical Microbiology and Infection 25 (2019) 111.e5–111.e8

111.e7

Table 1

Characteristics, conventional virulence genes, extraintestinal pathogenic *Escherichia coli* plasmid pS88-related genes and extended-spectrum β -lactamase production of the studied Belgian *E. coli* O80:H2

Strain	Source	Year	Patient characteristics ^b					Virulence genes			pS88 related genes										ESBL ^c
			Sex	Age	Prov.	HUS	GI	<i>stx</i>	<i>eae</i>	<i>ehecA</i>	<i>cia</i>	<i>cvaA</i>	<i>eitB</i>	<i>etsC</i>	<i>hlyF</i>	<i>iroN</i>	<i>iss</i>	<i>iucC</i>	<i>ompT</i>	<i>sitA</i>	
EH1752	Human	2008	F	1 y	FB	N	D	<i>stx2d</i>	<i>eae</i> ₂	+	+	+	–	+	+	+	+	+	+	+	–
EH1764		2008	F	72 y	UNK	N	D	<i>stx2d</i>	<i>eae</i> ₂	+	+	+	–	+	+	+	+	+	–	+	–
EH2262		2013	F	49 y	FB	N	D	<i>stx2a</i>	<i>eae</i> ₂	+	+	+	–	+	+	+	+	+	+	+	–
EH2400		2014	F	61 y	WF	N	D	<i>stx2d</i>	<i>eae</i> ₂	+	+	+	–	+	+	+	+	+	+	+	–
EH2436		2014	F	78 y	WB	UNK	UNK	<i>stx2d</i>	<i>eae</i> ₂	–	+	+	–	+	+	+	+	+	+	+	–
EH2549		2015	F	60 y	A	N	BD	<i>stx1a</i>	<i>eae</i> ₂	+	+	+	–	–	–	–	+	–	–	–	+
EH2644		2015	F	11 m	WB	Y	D	<i>stx2d</i>	<i>eae</i> ₂	+	+	+	–	+	+	+	+	+	+	+	–
EH2786		2016	F	2 y	BCR	UNK	UNK	<i>stx2a</i>	<i>eae</i> ₂	+	+	+	–	–	+	+	+	–	+	+	–
EH2808		2016	F	61 y	N	Y	UNK	<i>stx2d</i>	<i>eae</i> ₂	+	+	+	–	+	+	+	+	+	+	+	–
FMV 36819_3 ^a	Calf	1987	UNK	2.5 m	WB	NR	D	<i>stx1a</i>	<i>eae</i> ₂	+	+	+	–	–	+	+	+	–	+	+	–
FMV 36819_5 ^a		1987	UNK	2.5 m	WB		D	<i>stx1a</i>	<i>eae</i> ₂	–	–	+	–	–	–	–	–	–	–	–	–
ARSIA 22		2009	UNK	UNK	L		D	/	<i>eae</i> ₂	+	+	+	–	–	+	+	+	–	+	+	–
ARSIA 23		2009	UNK	UNK	N		D	/	<i>eae</i> ₂	+	–	+	–	–	+	+	+	–	+	+	–
ARSIA 94		2010	M	1 m	Lu		D	/	<i>eae</i> ₂	+	+	+	–	+	+	+	+	+	+	+	–
ARSIA 150		2012	M	6.5 m	L		D	/	<i>eae</i> ₂	+	+	+	–	–	+	+	+	–	+	+	–
ARSIA 212		2013	F	4.5 m	L		D	/	<i>eae</i> ₂	+	+	+	–	–	+	+	+	–	–	+	–
ARSIA 3042		2014	M	16 d	L		D	/	<i>eae</i> ₂	+	+	+	–	–	+	+	+	–	+	+	–
ARSIA 3088		2015	M	17 d	Lu		D	/	<i>eae</i> ₂	+	+	+	–	–	+	+	+	–	–	+	+

^a Strains FMV 36849_3 and FMV 36819_5 originate from the same calf.

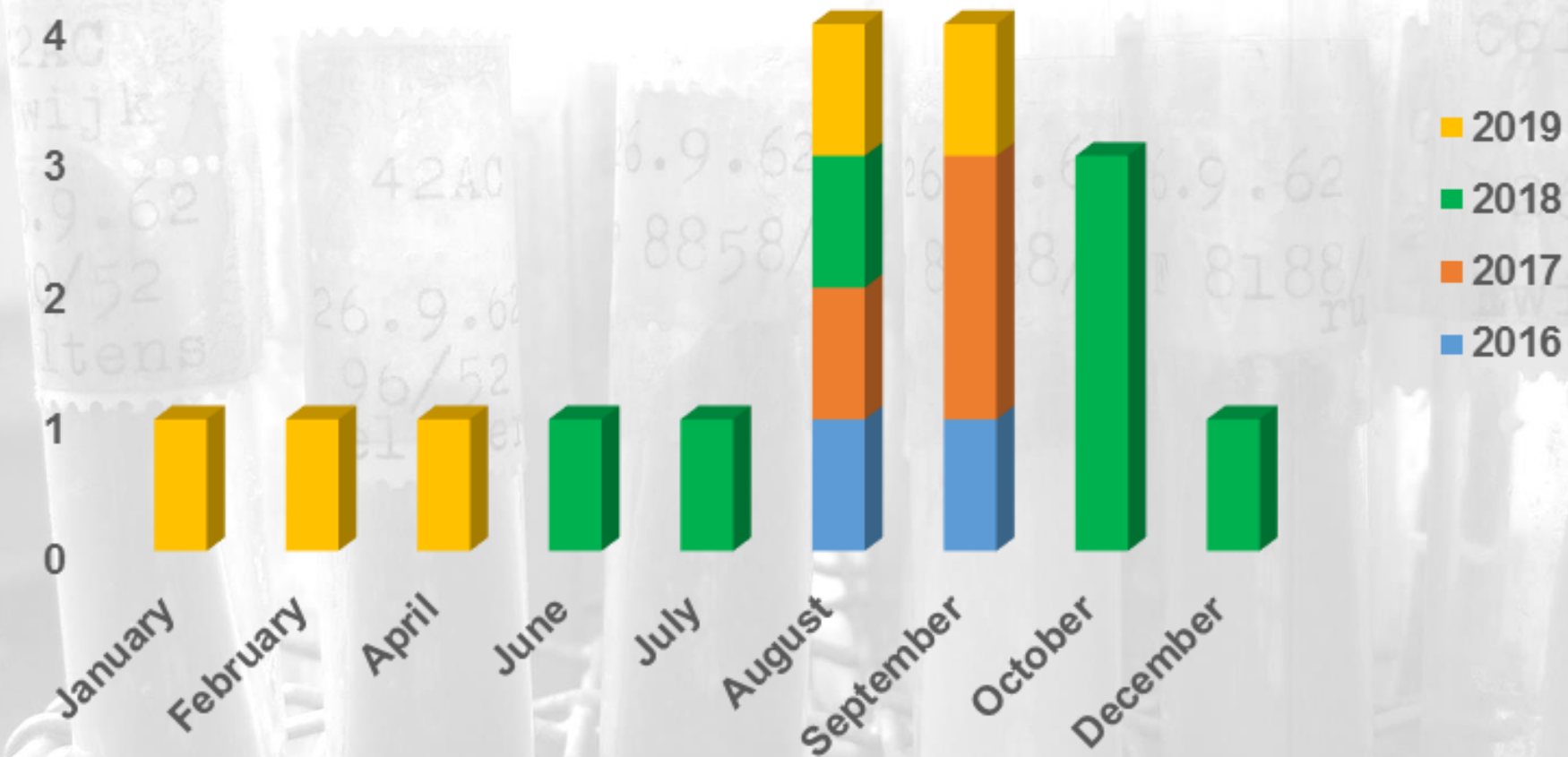
^b F, female; M, male; UNK, unknown; yr, years; m, months; d, days; Prov., Province of residence; FB, Flemish Brabant; WF, West Flanders; WB, Walloon Brabant; A, Antwerp; BCR, Brussels Capital Region; N, Namur; L, Liège; Lu, Luxembourg; HUS, haemolytic uraemic syndrome; N, no; UNK, unknown; Y, yes; NR, not relevant; GI, gastrointestinal symptoms; D, diarrhoea; UNK, unknown; BD, bloody diarrhoea.

^c ESBL, extended spectrum β -lactamase production.

STEC-ExPEC O80:H2 in Denmark?



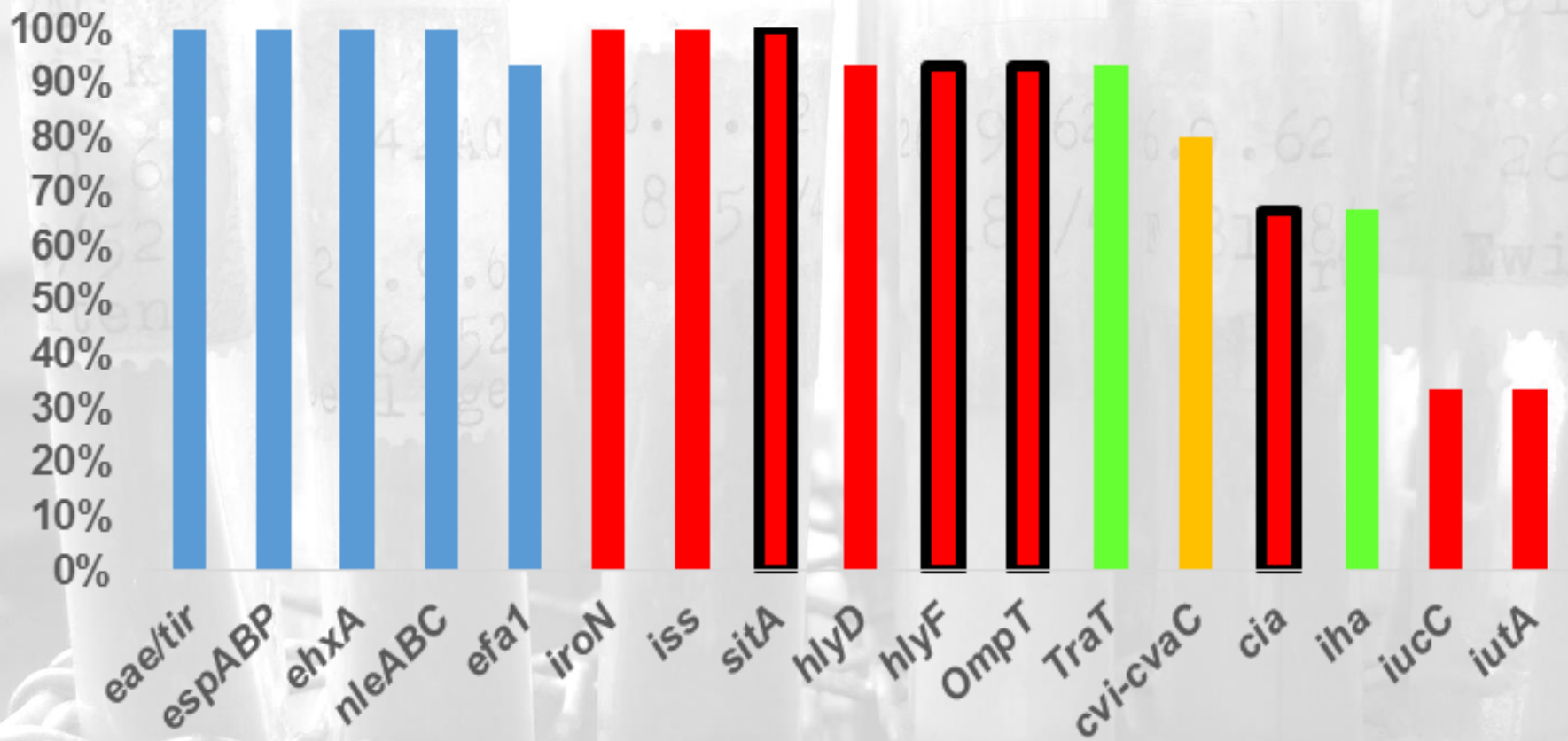
16 isolates O80:H2 - seasonal variation





STEC-ExPEC O80:H2 in Denmark

Prevalence of **ExPEC** and **DEC** associated virulence genes



Whole-Genome Characterization and Strain Comparison of VT2f-Producing *Escherichia coli* Causing Hemolytic Uremic Syndrome

Laura Grande, Valeria Michelacci, Roslen Bondi, Federica Gigliucci, Eelco Franz, Mahdi Askari Badouei, Sabine Schlager, Fabio Minelli, Rosangela Tozzoli, Alfredo Caprioli, Stefano Morabito



Table 2. Characteristics of VT2f-producing *Escherichia coli* investigated in a comparative analysis of the virulence profile of strains isolated from humans with mild and severe disease and from the animal reservoir*

Source and strain	Year isolated	Serotype	Phylotype	MLST	LEE	adfO	efa1	cif	nleA	nleB	nleC	Hly	katP	espP	Intimin type
Human diarrhea															
M856	2008	ONT:H6	B2	ST583	+	+	-	+	-	+	+	-	-	-	α-2
M858	2008	O125:H6	B2	ST583	+	+	-	+	-	+	-	-	-	-	α-2
M859	2009	O113:H6	B2	ST121	+	+	-	+	-	-	-	-	-	-	α-2
M884	2011	O96:H7	B2	ST28	+	+	-	+	+	+	-	-	-	-	β-2
M885	2011	O132:H34	B2	ST582	+	+	-	-	-	+	+	-	-	-	β-2
M900	2012	O145:H34	B2	ST722	+	+	-	-	-	+	-	-	-	-	α
BCW5711	2012	O63:H6	B2	ST583	+	+	-	+	+	-	+	-	-	-	α-2
BCW5746	2012	O63:H6	B2	ST583	+	+	-	+	-	-	+	-	-	-	α-2
BCW5743	2012	O63:H6	B2	ST583	+	+	-	+	-	-	+	-	-	-	α-2
BCW5739	2012	O63:H6	B2	ST583	+	+	-	+	-	-	+	-	-	-	α-2
BCW5717	2012	O63:H6	B2	ST583	+	+	-	+	-	-	+	-	-	-	α-2
Pigeon															
ED360	1997	O45:H2	B1	ST20	+	+	-	+	+	+	+	-	-	-	β
ED361	1997	O75:H2	B1	ST20	+	+	-	+	+	+	+	-	-	-	β
ED363	1997	O4:H2	B1	UNK	+	+	-	+	+	+	+	-	-	-	β
ED366	1997	ONT:H2	B1	ST2685	+	+	-	+	+	+	+	-	-	-	β
ED369	1997	O45:H2	B1	ST20	+	+	-	+	+	+	+	-	-	-	β
ED377	1997	O4:H2	B1	UNK	+	+	-	+	+	+	+	-	-	-	β
ED430	2000	O45:H2	B1	ST20	+	+	-	+	+	+	+	-	-	-	β
ED444	2000	O128:H2	B1	ST20	+	+	-	+	+	+	+	-	-	-	β
HUS															
EF453	2013	O80:H2	B1	ST301	+	+	+	-	+	+	+	+	-	+	ξ
EF467	2013	O26:H11	B1	ST21	+	+	+	+	+	+	+	+	+	+	β
EF476	2014	O55:H9	B1	ST301	+	+	+	-	+	+	+	+	-	+	ξ

*Human samples were diarrheal or fecal samples from HUS cases and pigeon samples were feces from asymptomatic birds. LEE, locus of enterocyte effacement; MLST, multilocus sequence type; UNK, unknown; +, positive; -, negative.

Heteropathogenic virulence and phylogeny reveal phased pathogenic metamorphosis in *Escherichia coli* O2:H6

Martina Bielaszewska^{1,†}, Roswitha Schiller^{1,2,†}, Lydia Lammers¹, Andreas Bauwens¹, Angelika Fruth³, Barbara Middendorf², M Alexander Schmidt⁴, Phillip I Tarr⁵, Ulrich Dobrindt^{1,2}, Helge Karch¹ & Alexander Mellmann^{1,*}

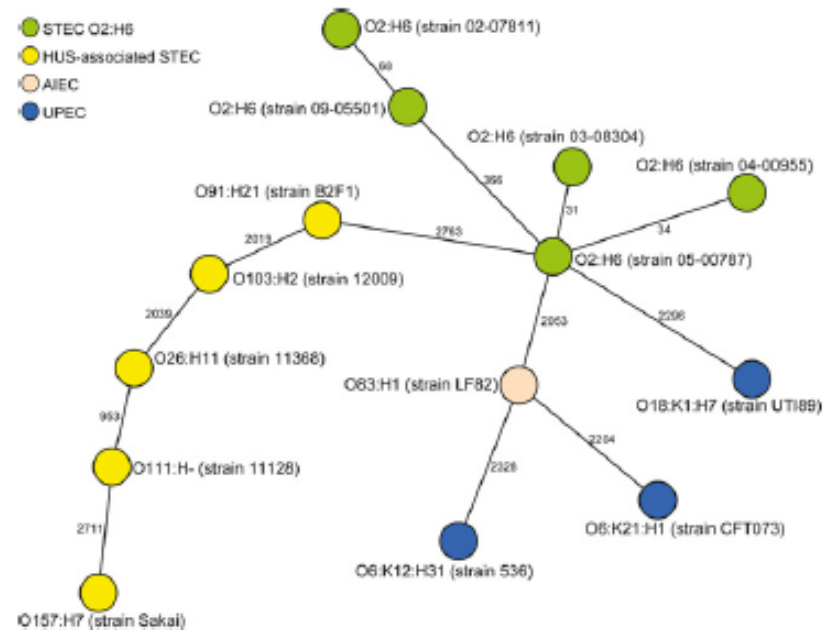
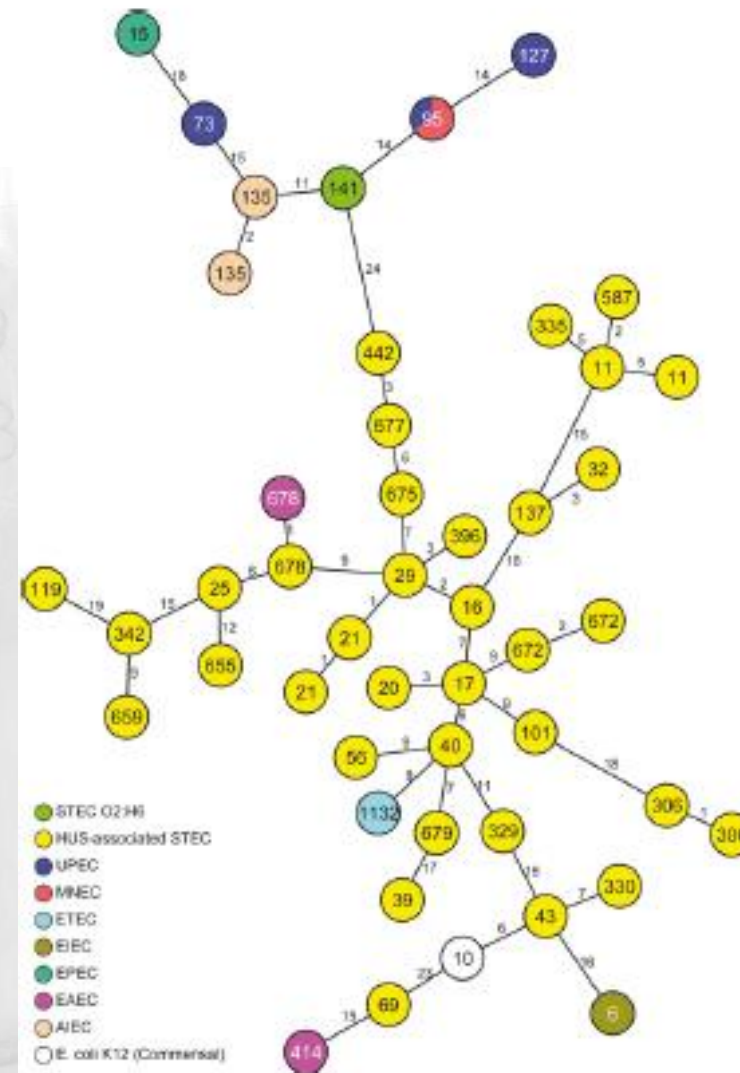
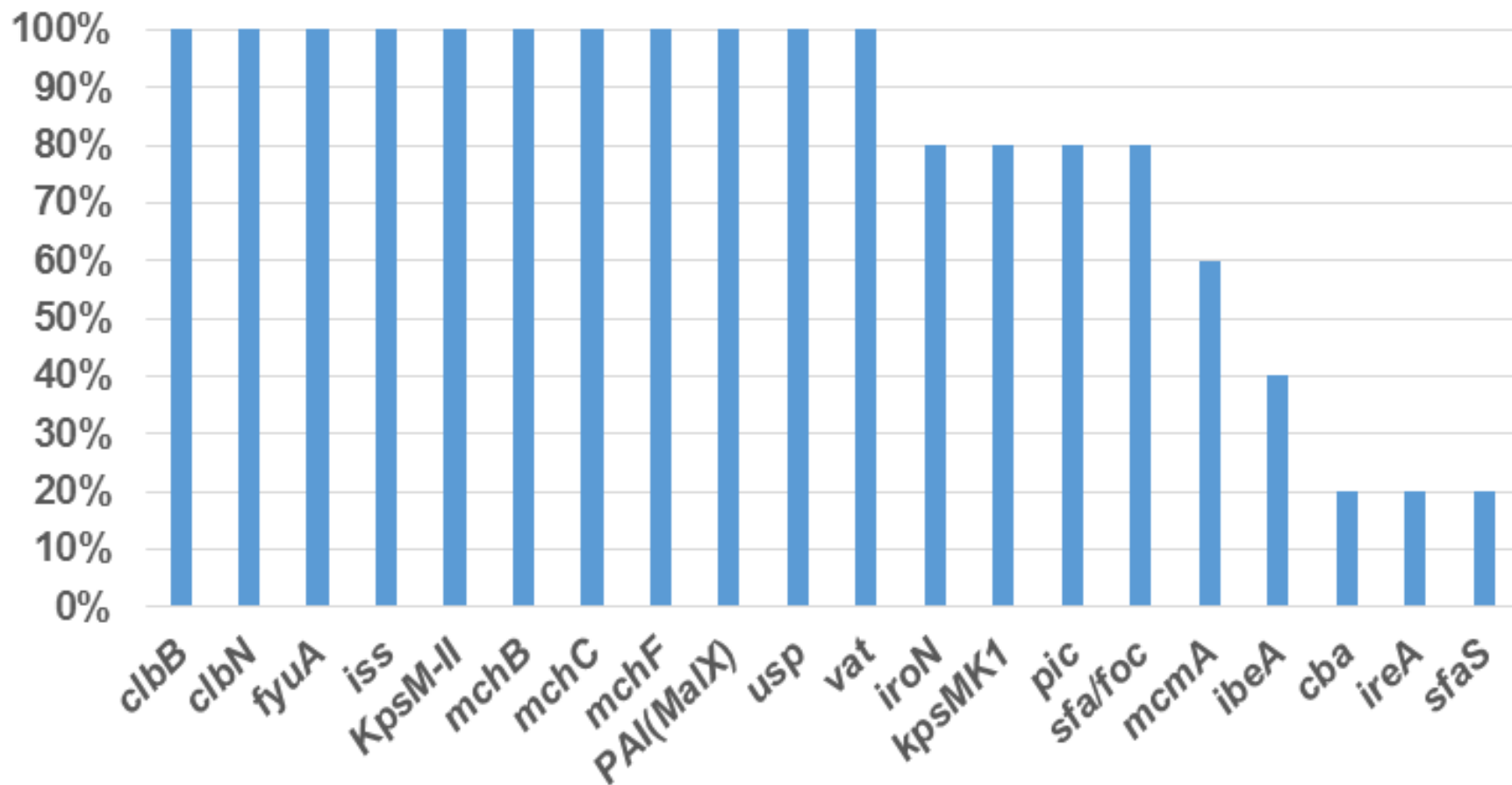


Figure 2. Phylogenetic relationships of STEC O2:H6 to prototypic UPEC, AIEC and most closely related and prototypic HUS-associated STEC based on whole genome sequencing. Minimum spanning tree is based on allelic profiles of 2827 genes present in all strains investigated (see supplementary Table S1). The different pathotypes are distinguished by colors of the circles and the serotypes and strain numbers (in parentheses) are given.

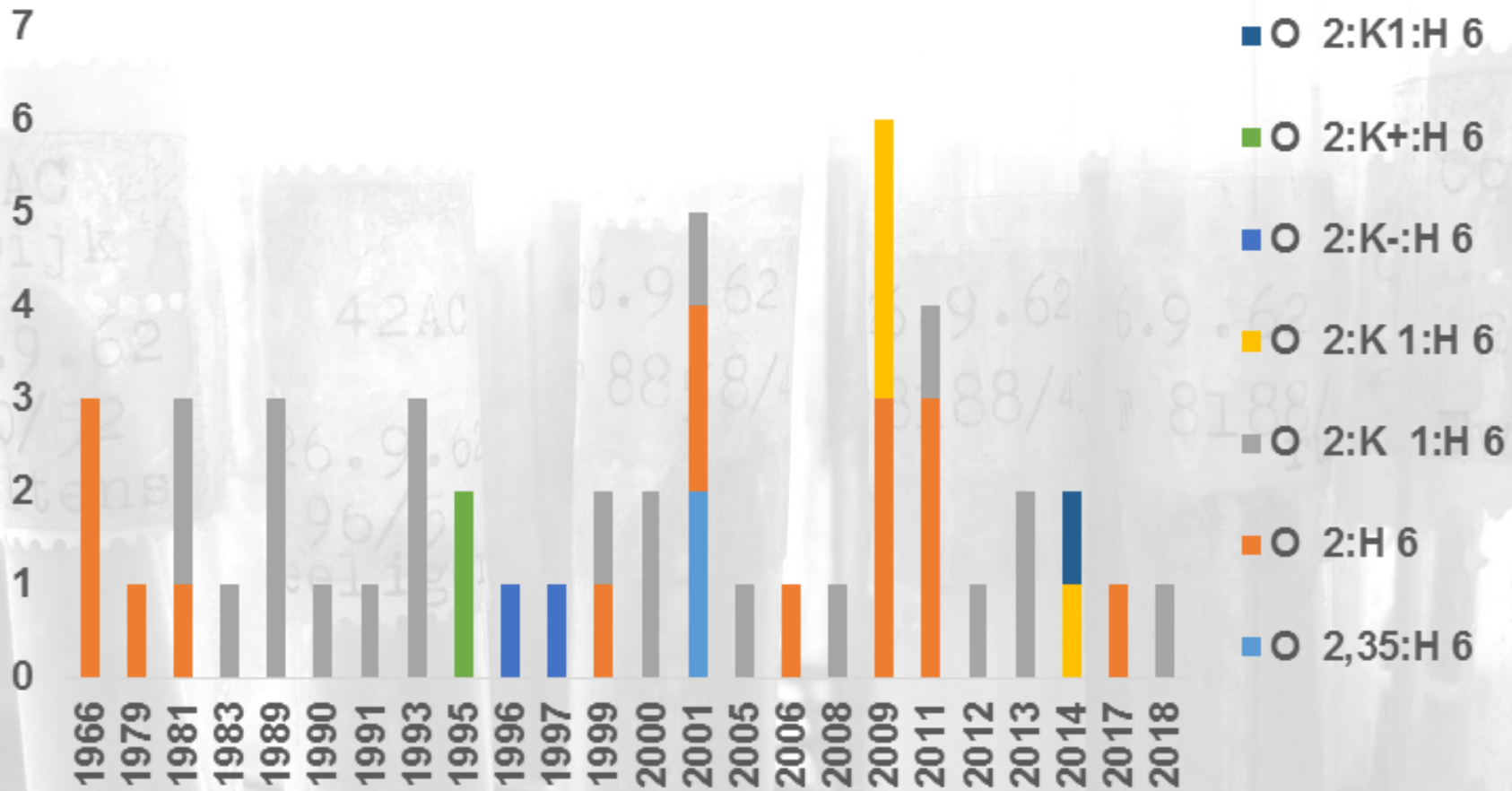


5 STEC-ExPEC O2:H6





49 patients with O2:(K1:)H6





49 patients with O2:(K1:)H6

NA	15
D	13
Bacteraemia	9
UTI	3
BD	3
Meningitis	1
Bacteraemia, recurrent; second	1
PD	1
Bacteraemia, recurrent; index	1
Endocardit	1
BD; Long term carrier	1



Extraintestinal pathogenic *E. coli* ExPEC Groups

***E. coli* associated with extraintestinal infections in humans**

- **ExPEC: Extraintestinal pathogenic *E. coli***
- **UPEC: Uropathogenic *E. coli***
- **MNEC: Meningitis *E. coli* (Neonatal)**
- **APEC: Avian pathogenic *E. coli***

Gene, strain, or replicon	% of prevalence relative to the total no. of isolates (n)			Statistical significance of prevalence			
	UPIC (531)	NMEC (61)	APIC (452)	APIC vs human APIC	APIC vs UPIC	APIC vs NMEC	UPIC vs NMEC
<i>ast</i>	67.8	85.6	78.1	+	—	—	—
<i>aid</i>	83.4	95.6	80.6	—	—	—	—
<i>ica4</i>	46.4	77.8	30.8	++	++	—	+
<i>idjF</i>	5.6	38.0	75.4	++	++	—	++
<i>entA</i>	6.0	61.1	67.0	++	++	—	++
<i>entB</i>	6.0	58.9	66.8	++	++	—	++
<i>ompT</i> ^{qpi}	5.6	64.4	81.6	++	++	—	++
<i>icaE</i> ^{qpi}	26.6	55.6	82.7	++	++	++	++
<i>antV</i>	34.8	63.3	87.4	++	++	++	++
<i>icaA</i>	23.4	68.9	77.4	++	++	—	++
<i>icaB</i> ²	24.1	65.6	77.4	++	++	—	++
<i>icaB</i> ³	22.0	61.1	68.1	++	++	—	++
<i>icaC</i>	5.6	54.4	67.5	++	++	—	++
<i>icaD</i>	3.8	4.4	24.6	++	++	++	—
<i>icaE</i>	4.0	21.1	34.3	++	++	—	++
<i>ak</i>	2.6	31.1	52.7	++	++	+	++
<i>icaF</i>	4.3	5.6	37.2	++	++	++	—
<i>icaH</i>	4.5	5.6	37.2	++	++	++	—
U11095	0.4	2.2	26.5	++	++	++	—
U11024	2.4	5.6	19.7	++	++	—	—
<i>icaB</i>	2.4	5.6	19.7	++	++	—	—
<i>icaC</i>	2.2	5.6	19.7	++	++	—	—
<i>icaE</i>	2.1	0.0	0.2	—	—	—	—
<i>icaA</i>	54.8	28.9	7.5	—	++	++	++
<i>icaC</i>	59.7	35.6	40.5	++	++	—	+
<i>icaB</i> ²	55.4	32.2	39.2	++	++	—	+
<i>icaG</i>	0.6	6.7	1.5	—	—	+	++
<i>icaG</i> ²	42.9	22.2	40.7	++	—	+	++
<i>icaG</i> ³	20.2	4.4	0.7	—	++	—	++
<i>icaI</i>	39.2	70.0	15.7	++	++	++	++
<i>icaJ</i>	78.5	85.6	25.0	++	++	++	—
<i>icaK</i>	4.0	2.2	1.8	—	++	++	—
<i>icaL</i>	68.2	56.7	15.0	++	++	—	—
<i>icaM</i>	26.0	17.8	48.0	++	++	++	—
<i>icaN</i>	19.2	58.9	14.2	++	—	++	++
<i>icaO</i>	22.6	56.7	8.8	++	++	++	++
<i>icaP</i>	62.3	74.4	33.4	++	++	++	—
<i>icaQ</i>	23.4	4.4	1.3	++	++	—	++
<i>icaR</i>	80.6	68.9	58.2	++	++	—	—
<i>icaS</i>	8.7	35.6	1.1	++	++	++	++
<i>icaT</i>	1.3	2.2	0.4	—	—	—	—
<i>icaU</i>	26.4	51.1	4.4	++	++	++	++
<i>icaV</i>	34.1	3.3	0.9	++	++	—	++
<i>icaW</i>	5.3	4.4	0.4	++	—	—	—
<i>ompT</i> chrom	81.5	31.1	70.4	—	+	++	++
<i>icaX</i>	16.0	47.8	4.6	++	++	++	++
<i>icaY</i>	14.3	2.2	0.0	++	++	—	++
<i>icaZ</i>	39.2	26.7	3.5	++	++	++	—
<i>icaA</i>	12.6	25.6	8.2	—	—	++	+
<i>icaB</i>	14.1	46.7	40.0	++	++	++	++
icaBVO replicon	14.5	36.9	17.9	—	—	++	++
icaBVC replicon	1.1	3.3	12.4	++	++	—	—
icaBVC replicon	0.6	0.0	3.3	++	—	—	—
icaBVC replicon	0.8	8.9	21.7	++	++	—	+
icaBVC replicon	0.0	0.0	0.9	—	—	—	—
icaBVC replicon	0.0	2.2	1.5	—	—	—	—
icaBVC replicon	0.2	0.0	34.3	—	—	—	—
icaBVC replicon	3.0	1.1	24.3	++	++	++	—

* Values shown for results of genotyping are given in percentages. Two-way comparisons were performed for each gene, strain, or replicon studied between the different groups examined, using Fisher's exact test. For each comparison, a *P* value of <0.05 (+) was considered statistically significant, and a *P* value of <0.01 (++) was also considered statistically significant, while a *P* value of >0.05 (-) was not considered statistically significant. epi, episome; chron, chromosome; Phyo, phytotoxin.

Criteria for extraintestinal pathogenic *E. coli* (ExPEC)

- exhibits ≥ 2
- *pap* (P fimbriae)
- *sfa/foc* (S/F1C fimbriae)
- *afa/dra* (Dr binding adhesins),
- *iutA* (aerobactin receptor)
- *kpsMT II* (group 2 capsule synthesis)

Johnson, J. R., A. C. Murray, A. Gajewski, M. Sullivan, P. Snippes, M. A. Kuskowski, and K. E. Smith. 2003. Isolation and molecular characterization of nalidixic acid-resistant extraintestinal pathogenic *Escherichia coli* from retail chicken products. Antimicrob. Agents Chemother. **47**:2161-2168

Alternative definition for extraintestinal pathogenic *E. coli* (UPEC)

- presence of ≥ 3
- *chuA* (heme binding)
- *fyuA* (yersiniabactin receptor)
- *vat* (vacuolating toxin)
- *yfcV* (putative fimbrial subunit)

Spurbeck, R. R., P. C. Dinh, Jr., S. T. Walk, A. E. Stapleton, T. M. Hooton, L. K. Nolan, K. S. Kim, J. R. Johnson, and H. L. Mobley. 2012. *Escherichia coli* isolates that carry *vat*, *fyuA*, *chuA*, and *yfcV* efficiently colonize the urinary tract. *Infect.Immun.* **80**:4115-4122.

Whole genome sequence (WGS)-based prediction of antimicrobial resistance in clinical *Escherichia coli* from one day in Denmark

Non-biased snapshot of the *E. coli* available from that day (January 2018) in the clinical settings in Denmark.

170 isolates:

- **148 (87.1%) urine**
- **8 (4.7%) blood**
- **14 (8.2%) other sources including urethral and tracheal swabs, pus, faeces and abscess**

Findings:

- **ST-73 (n=22; 12.9%)**
- **ST-69 (n=19; 11.2%)**
- **ST-131 (n=13; 7.6%)**
- **ST-95 (n=10; 5.9%)**
- **other STs represented by six or less isolates each**

Whole genome sequence (WGS)-based prediction of antimicrobial resistance in clinical *Escherichia coli* from one day in Denmark

- All ST-131 (n=13) serotype O25:H4
- 7 (53.8%) were resistant to 3rd generation cephalosporins, attributed either to *bla*CTX-M-15 (n=5) or *bla*CTX-M-27 (n=2)
- These isolates correspond to 70% of all 3rd generation cephalosporin-resistant isolates observed in this study (n=10).



Figure 8.0.1 Distribution of species from invasive isolates, 2017, Denmark

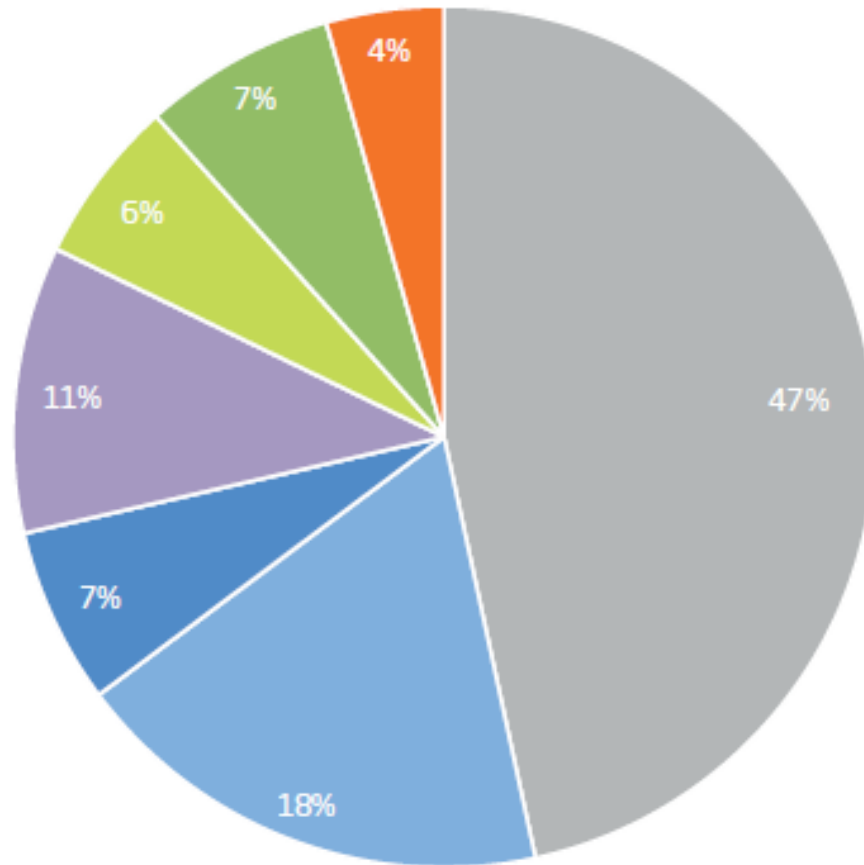
DANMAP 2017

DANMAP 2017

DANMAP 2017 - Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark



Statens Serum Institut
National Veterinary Institute, Technical University of Denmark
National Food Institute, Technical University of Denmark



■ *E. coli*; 47%

■ *S. aureus*; 18%

■ *S. pneumoniae*; 7%

■ *K. pneumoniae*; 11%

■ *E. faecalis*; 6%

■ *E. faecium*; 7%

■ *P. aeruginosa*; 4%



Figure 8.0.2 Number of submitted invasive isolates (from 2009 to 2017) for each of the species under surveillance.

DANMAP 2017

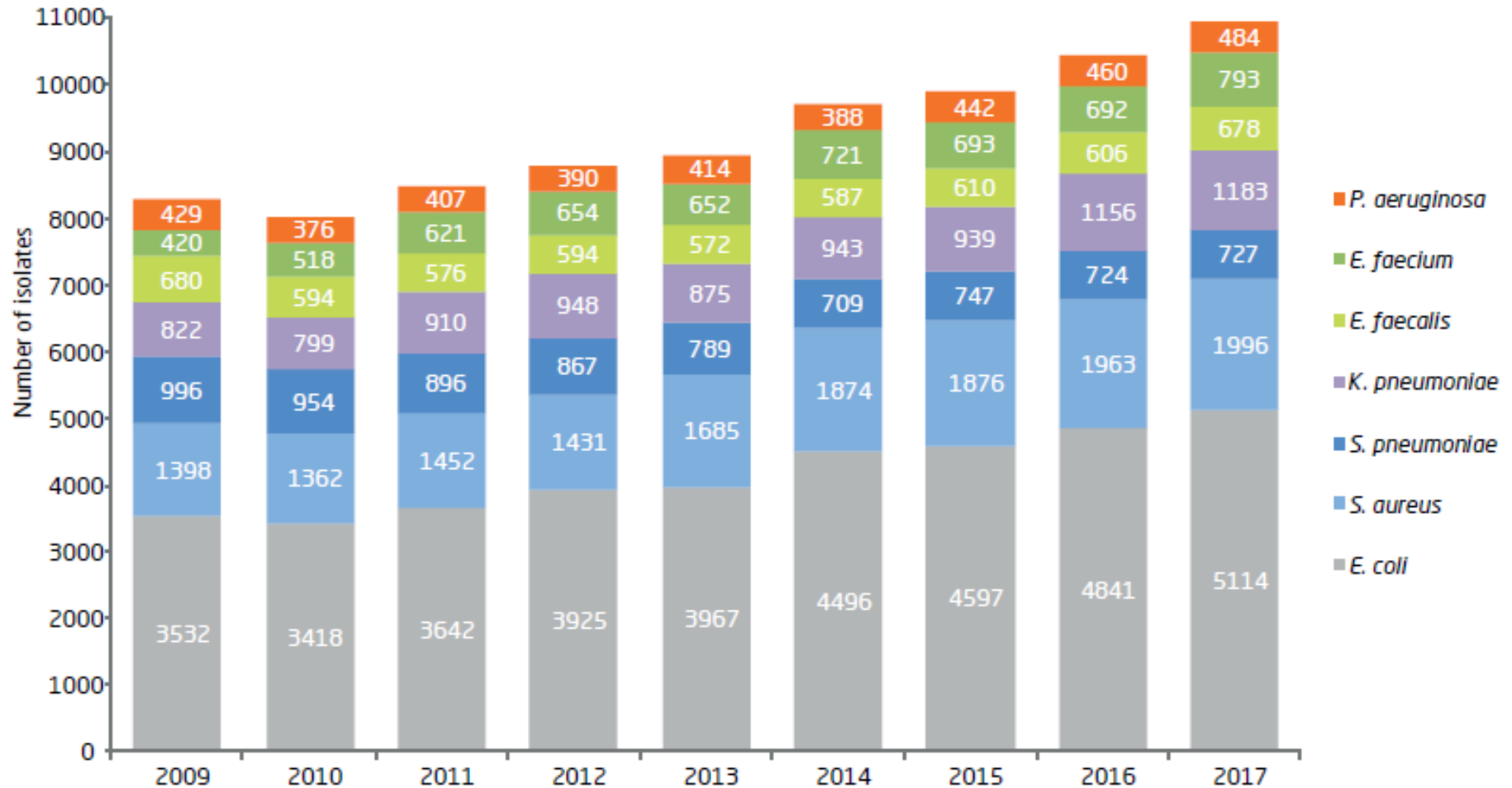


Figure 8.1.2 Resistance (%) in *Escherichia coli* urine isolates from humans in hospitals, Denmark
DANMAP 2017

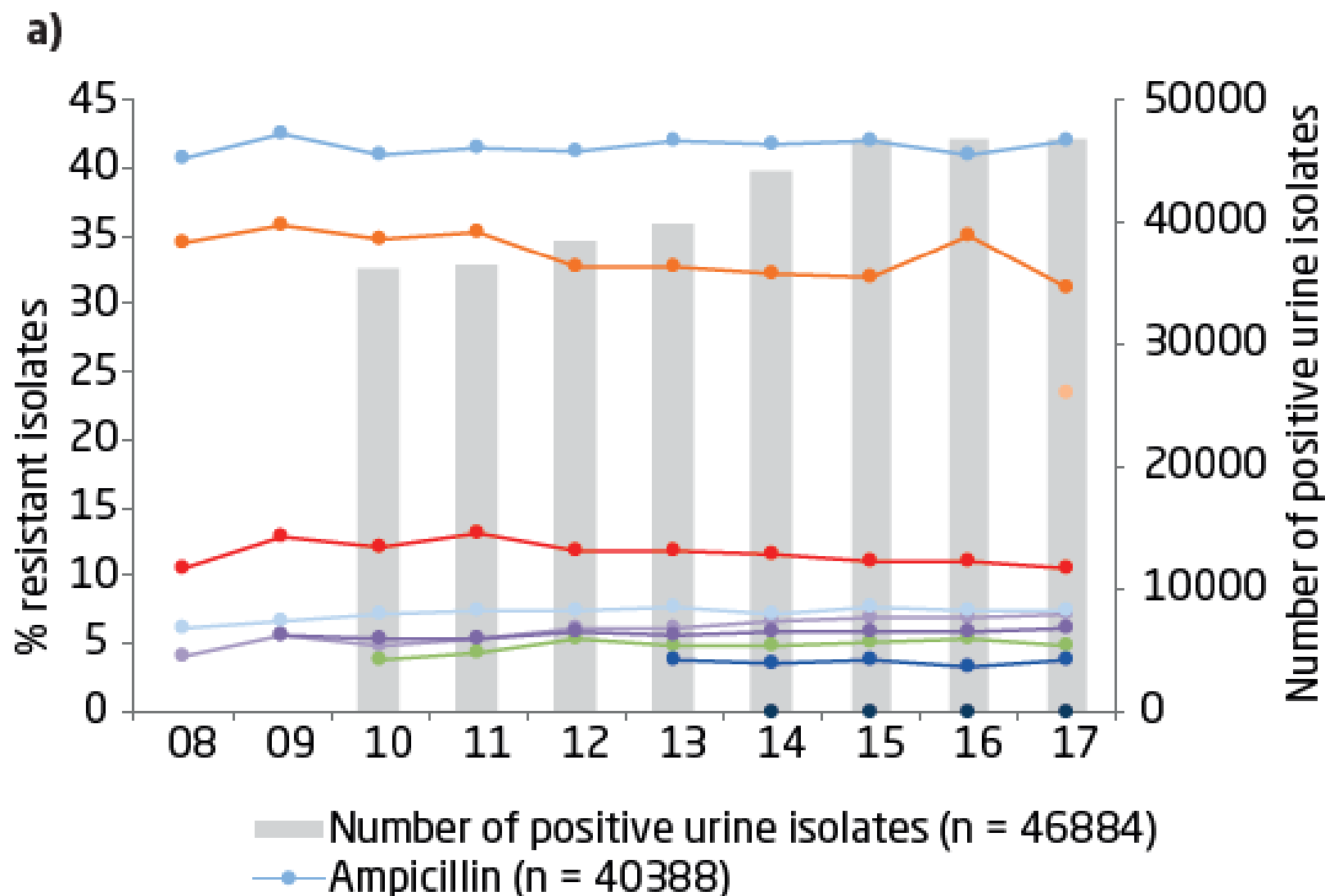
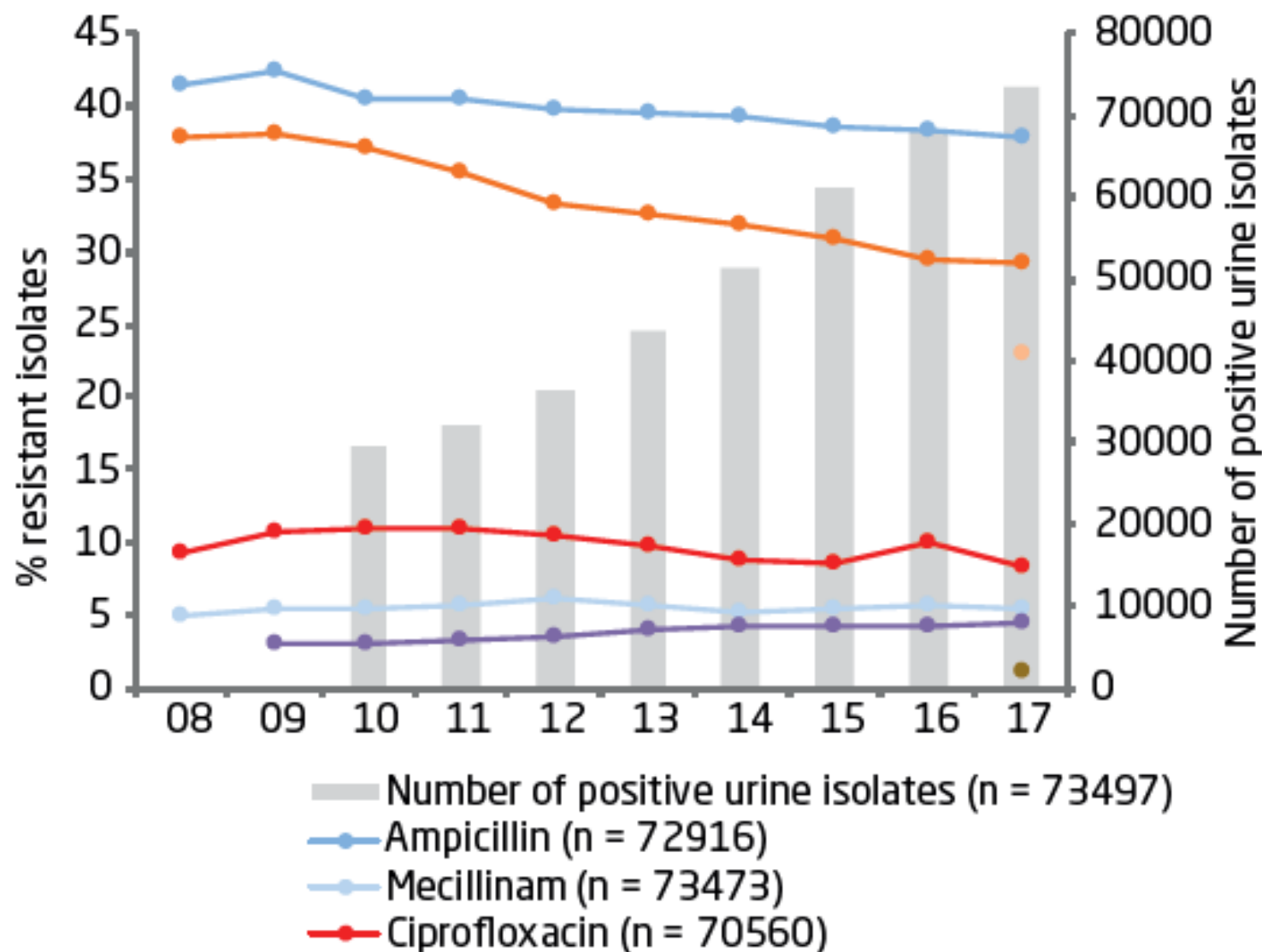


Figure 8.1.3 Resistance (%) in *Escherichia coli* urine isolates from humans in primary health care, Denmark DANMAP 2017

a)



Sharing of Virulent *Escherichia coli* Clones among Household Members of a Woman with Acute Cystitis


Clinical Infectious Diseases 2006;43:e101-8


























James R. Johnson and Connie Clabots

*  O1:K1:H7

*  O6:K2:H1

*  O1:K1:H7

*  O2;F10,F48

Host	Specimen	Sample Week 1	Sample Week 2	Sample Week 3
Mother	Urine			NG
	Feces	 		 
Father	Feces	 		
Daughter 1	Feces			 
Daughter 2	Feces		•	 
Son	Feces			
Dog	Feces			 
Sample Week		1	2	3
		1	3	7-9

* No. of Virulence Factor (VFs) scores: ExPEC ≥ 10

pap sfa/foc focG iha hlyD sat iroN fyuA ireA iutA kpsM II K1 traT ompT iss usp malX H7

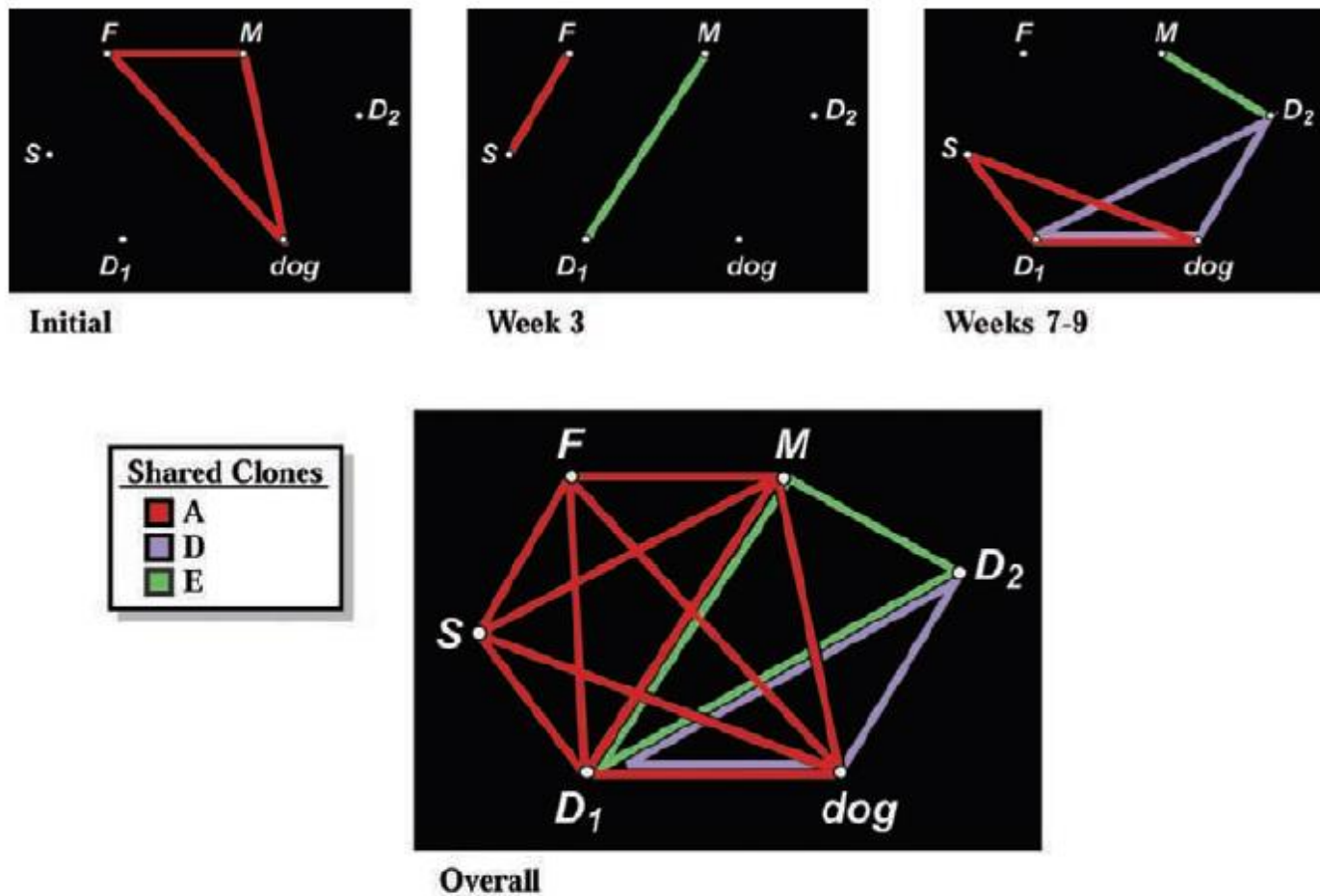


Figure 3. Clone-sharing relationships among 6 household members at 3 individual sampling points (*top*) and overall (*bottom*). Colored lines indicate presence of indicated clone (A, red; D, purple; E, green) in both members of a particular host pair, either at the same sampling point (*top*) or overall (*bottom*). More clone-sharing pairs are evident in the bottom panel than in the 3 top panels combined.

WGS-based surveillance of third-generation cephalosporin-resistant *Escherichia coli* from bloodstream infections in Denmark

Louise Roer^{1*}, Frank Hansen¹, Martin Christen Frølund Thomsen², Jenny Dahl Knudsen³, Dennis Schrøder Hansen⁴, Mikala Wang⁵, Jurgita Samulionienė⁶, Ulrik Stenz Justesen⁷, Bent L. Røder⁸, Helga Schumacher⁹, Claus Østergaard⁹, Leif Percival Andersen¹⁰, Esad Dzajic¹¹, Turid Snekloth Søndergaard¹², Marc Stegger¹, Anette M. Hammer¹ and Henrik Hasman¹

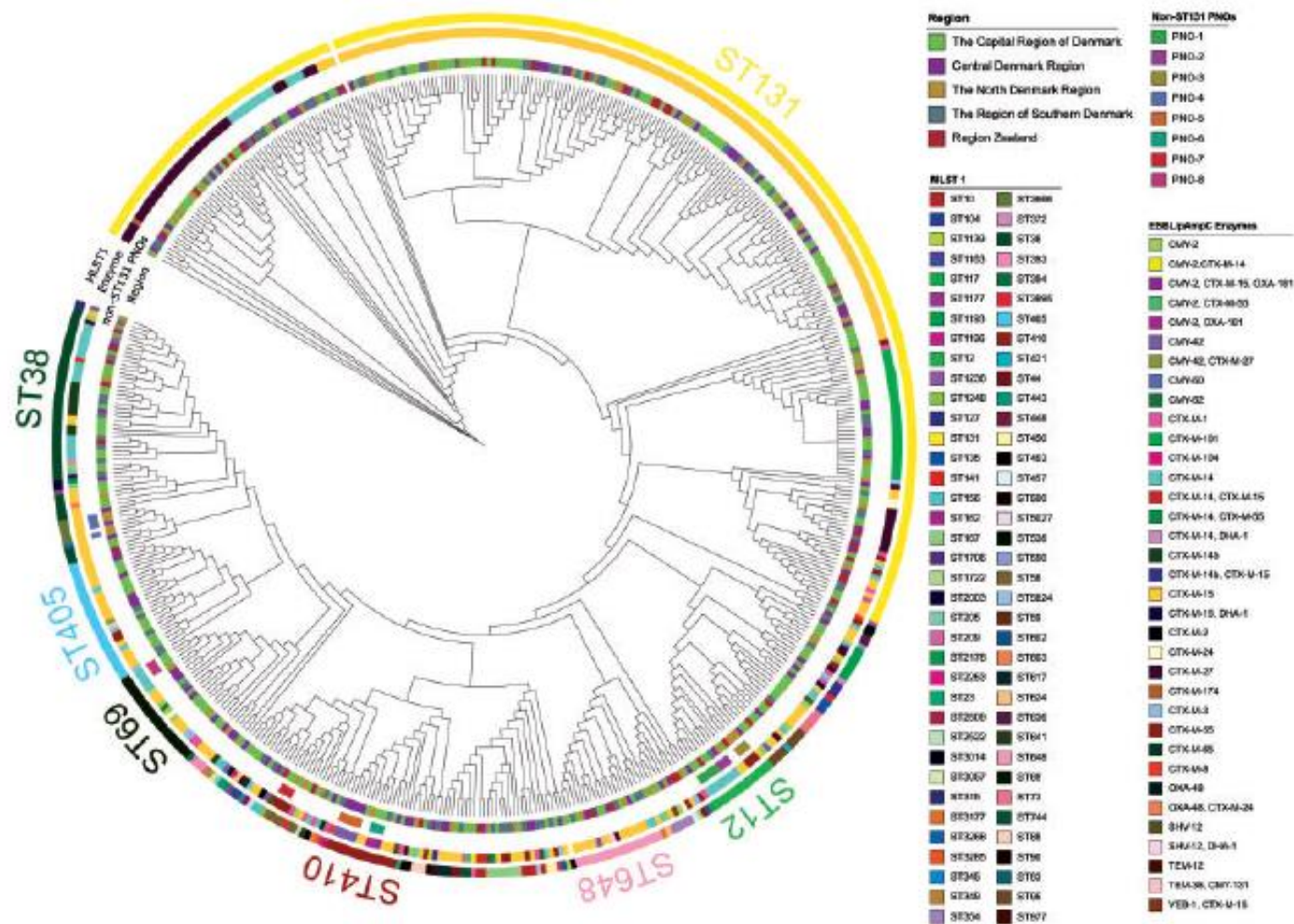


Figure 1. Phylogenetic analysis of 3GC-R *Ec* isolates from bloodstream infections in Danish patients. Phylogenetic tree of the 518 ESBL, carbapenemase and pAmpC isolates, constructed from 191623 SNPs, and represented as a cladogram. PNOs for ST131 are presented in Figure 2. This figure appears in colour in the online version of JAC and in black and white in the print version of JAC.

Region

- The Capital Region of Denmark
- Central Denmark Region
- The North Denmark Region
- The Region of Southern Denmark
- Region Zealand

ST131 PNOs

- PNO-9
- PNO-10
- PNO-11
- PNO-12
- PNO-13
- PNO-14
- PNO-15

MLST 2

- ST43
- ST506
- ST566
- ST9

ESBL Enzymes

- CTX-M-101
- CTX-M-14
- CTX-M-27
- TEM-12
- CTX-M-3
- CTX-M-55
- CTX-M-174
- CTX-M-1
- CTX-M-15
- CTX-M-24

***fimH* subtype**

- *fimH*22
- *fimH*27
- *fimH*30
- *fimH*30-like
- *fimH*35
- *fimH*41
- *fimH*89
- *fimH*99

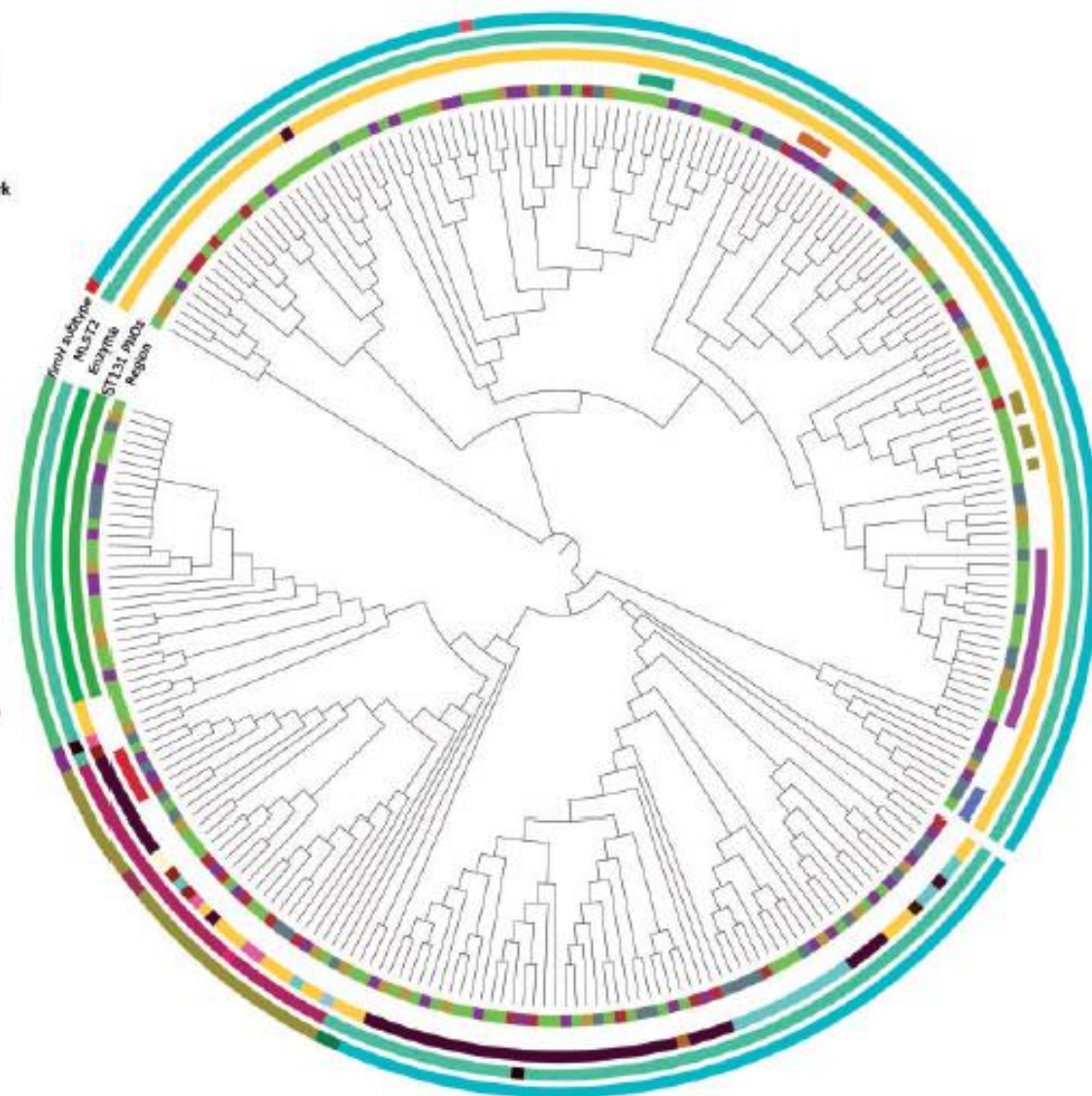


Figure 2. Phylogenetic analysis of ST131 ESBL *E. coli* isolates from bloodstream infections in Danish patients. Phylogenetic tree of the 258 ST131 ESBL isolates, constructed from 15050 SNPs, and represented as a cladogram. This figure appears in colour in the online version of JAC and in black and white in the print version of JAC.

DANMAP 2017

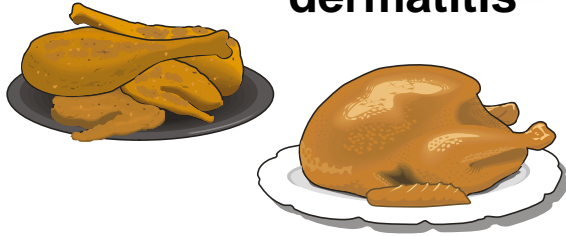
“The observation of close phylogenetic relations in ST131 CMY-2-producing *E. coli* and ST429 CMY-2-producing *E. coli* from animal origin and human bloodstream infections indicating a possible zoonotic spread should be noted. Occurrence and evolution of these ST/pAmpC combinations need to be monitored closely in the future.”

ExPEC as a zoonotic agent?

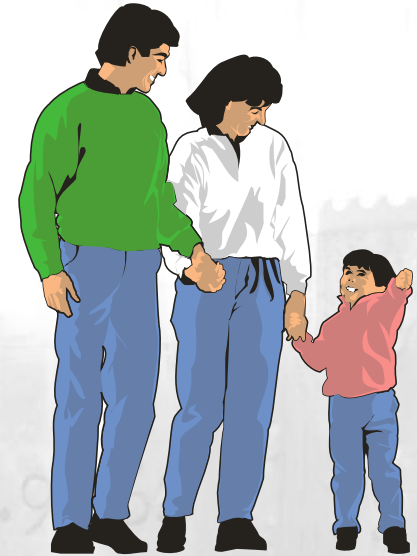
- 24% (396/1648) of foods samples *E. coli* positive:
- 9 % in miscellaneous foods (= "non-meat")
- 69% in beef / pork
- 92% in poultry

	ExPEC	AMR
■ Miscellaneous foods :	4%	27%
■ Beef / pork :	19%	85%
■ Poultry:	46%	94%

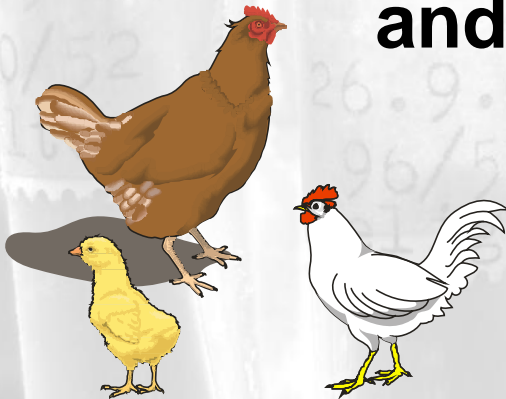
dermatitis



colonisation



***E. coli* O45:K1:H7
causing an outbreak
of neonatal meningitis
and sepsis in Germany**



septicaemia

**colonisation
septicaemia
meningitis**



Non-published data by Rita Prager, Helmut Tschäpe *et al.*



Poultry as reservoir for extraintestinal pathogenic *Escherichia coli* O45:K1:H7-B2-ST95 in humans



Azucena Mora ^{a,*}, Susana Viso ^a, Cecilia López ^a, María Pilar Alonso ^b,
Fernando García-Garrote ^b, Ghizlane Dabhi ^a, Rosalía Mamani ^a,
Alexandra Herrera ^a, Juan Marzoa ^a, Miguel Blanco ^a, Jesús E. Blanco ^a,
Maryvonne Moulin-Schouleur ^{c,d}, Catherine Schouler ^{c,d}, Jorge Blanco ^a

^a Department of Microbiology and Parasitology, Faculty of Veterinary Sciences, University of Santiago de Compostela, 27002 Lugo, Spain

^b Unit of Microbiology, Hospital Universitario Lucus Augusti, 27003 Lugo, Spain

^c Laboratoire de Pathogénie Bactérienne, INRA, UMRI 1282 Infectiologie et Santé Publique, F-37380 Nouzilly, France

...The most prevalent and highly pathogenic O45:K1:H7-B2-ST95 shows a successful persistence since the 90s to the present, with parallel evolution both in human and poultry ...

... In conclusion, poultry could be acting as a reservoir of O45:K1:H7-B2-ST95 and other pathogenic ST95 serotypes in humans

REVIEW ARTICLE

A systematic review of outbreak and non-outbreak studies of extraintestinal pathogenic *Escherichia coli* causing community-acquired infections

D. B. GEORGE AND A. R. MANGES*

Table 1. Reported outbreaks of community-acquired *Escherichia coli* causing human extraintestinal infections

Ref.	Location	Infection*	Observation period	Peak period	No. isolates	No. epidemic strain	Proportion (%)	Sex‡	Age (yr)	Serotype/sequence type (ST)
[13]	London, UK	UTI, PY, B	1986–1987	Oct. 1986–Apr. 1987	> 500			B	0–97	O15:K52:H1
[15]	Copenhagen, Denmark	UTI	1991–1992	Apr. 1991–Sept. 1991	72	19	26	B	0–87	O78:H10
[28]	Columbus, USA	UTI			101	16	16	F	≥ 18	O18:K1:H7
[27]	Barcelona, Spain		1994–1995		1871	25	1		0–83	O15:K52:H1
[16]	Berkeley, USA	UTI	1999–2000		255	28	11	F	18–45	O11/O17/O77:K52:H18
[14]	Calgary, Canada	UTI, PY, B	2000–2002	Oct.–Dec. 2000	232	67	29	B	1–92§	
[37]	UK	UTI, PY, B	2003–2004	Oct. 1986–Apr. 1987	291	110	38			O25
[35]	Zagreb, Croatia	U, UTI, PY	2004		2451	25	1	B	1–79	O4
[36]	UK	U, B	2004–2005		88	21	24			O25-ST131
[33]	Spain	UTI, B	2004–2005		525	103	20	B	≤ 14 to ≥ 65	
[34]	Portugal	U, B†	2004–2006		119	91	76	B		
[44]	Lugo, Spain	U	2006–2008		11 343	77	1			O25(b):H4-ST131

* B, Isolates recovered from blood samples, bacteraemia cases or sepsis cases; U, Isolates recovered from urine samples; UTI, isolates recovered from cases of cystitis or UTIs; PY, isolates recovered from pyelonephritis cases.

† *E. coli* was also recovered from wounds, ascitic fluid, sputum, gastric fluids, bronchioalveolar lavage and secretions.

‡ M, male; F, female; B, both male and female.

§ Dr J. Pitout, personal communication.

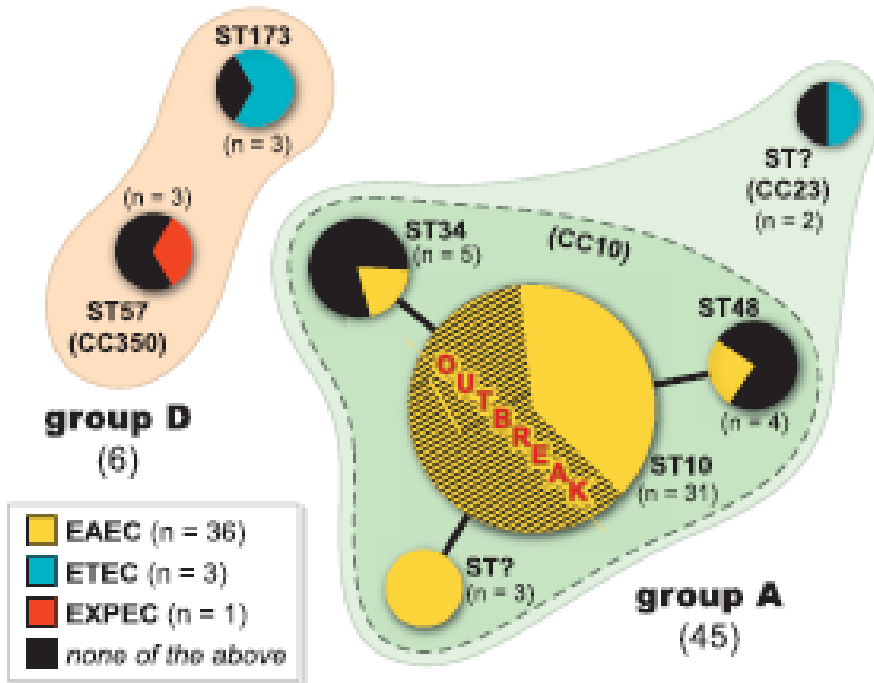
|| Indicates that the proportion is estimated based on a sub-sample of ESBL-producing *E. coli* and therefore does not reflect the overall proportion.

Crossovers



Enteroaggregative *Escherichia coli* O78:H10, the Cause of an Outbreak of Urinary Tract Infection

Bente Olesen,^{a,b} Flemming Scheutz,^b Rebecca L. Andersen,^a Megan Menard,^c Nadia Boisen,^d Brian Johnston,^c Dennis S. Hansen,^a Karen A. Krogfelt,^a James P. Nataro,^d and James R. Johnson^c



Genes present in >90% of outbreak isolates included *fimH* (type 1 fimbriae); *fyuA*, *traT*, and *iutA* (associated with ExPEC);

sat, *pic*, *aatA*, *aggR*, *aggA*, *aar*, *aaiC*, *aap*, and *ORF3* (associated with EAEC)



STATENS
SERUM
INSTITUT

Gene content of the
ExPEC database
downloaded from NCBI
and to be added to the
VirulenceFinder
database.

38 ExPEC specific genes

Gene	Description	No. from NCBI	No. in db
<i>afaA</i>	Transcriptional regulator	14	4
<i>afaB</i>	Periplasmic chaperone	12	6
<i>afaC</i>	Outer membrane usher protein	13	11
<i>afaD</i>	Afimbrial adhesin	62	37
<i>afaE</i>	Adhesin protein	42	30
<i>cea</i>	colicin E1	132	23
<i>chuA</i>	Outer membrane hemin receptor	423	79
<i>cia</i>	colicin ia	259	37
<i>cib</i>	colicin ib	24	6
<i>clbB</i>	Hybrid nonribosomal peptide / polyketide megasynthase	270	77
<i>cvaC</i>	microcin C	166	10
<i>etsC</i>	Putative type I secretion outer membrane protein	169	18
<i>focC</i>	S fimbrial/F1C minor subunit	710	2*
<i>focG</i>	F1C adhesin	9	2
<i>focI</i>	S fimbrial/F1C minor subunit	5	1
<i>fyuA</i>	Siderophore receptor	465	98
<i>hlyF</i>	Hemolysin F	287	21
<i>hra</i>	Heat-resistant agglutinin	132	8
<i>ibeA</i>	Invasin of brain endothelial cells;	369	66
<i>irp2</i>	High molecular weight protein 2 non ribosomal peptide synthetase	1033	346
<i>iucC</i>	Aerobactin synthetase	335	47
<i>iutA</i>	Ferric aerobactin receptor	350	71
<i>kpsE</i>	Capsule polysaccharide export inner-membrane protein	54	21
<i>kpsM</i>	Polysialic acid transport protein	94	82
<i>mcbA</i>	Bacteriocin microcin B17	949	2
<i>neuC</i>	Polysialic acid capsule biosynthesis protein	961	68
<i>ompT</i>	Outer membrane protease (protein protease 7)	3564	314
<i>papA</i>	Major pilin subunit	116	29
<i>papC</i>	Outer membrane usher P fimbriae	786	40
<i>sfaD</i>	S fimbrial/F1C minor subunit	18	10
<i>sfaE</i>	S fimbrial/F1C minor subunit	3	3*
<i>sfaS</i>	sialic acid-binding adhesin	54	2
<i>sitA</i>	Iron transport protein	369	56
<i>tcpC</i>	Tir domain-containing protein	24	3
<i>terC</i>	Tellurium ion resistance protein	126	25
<i>traT</i>	Outer membrane protein complement resistance	1386	200
<i>usp</i>	Uropathogenic specific protein	19	6
<i>yfcV</i>	Fimbrial protein	768	82
Total		14441	1929

*Two *sfaE* and *focC* alleles were 100% identical, and are called *focCsfaE* in the database

Conclusions

- **DEC are important causes of diarrhoea**
- ***eae* positive *E. coli* (EPEC, STEC, AEEC) are primarily affecting children < 5 years**
- **The ST and/or the serotype cannot be taken as a proxy for virulence potential**
- ***E. coli* crossover pathotypes poses diagnostic and clinical challenges**
- **ExPEC are the main cause of UTI and bacteraemia**
- **What is the zoonotic potential of APEC/ExPEC?**



"WE FINISHED THE GENOME MAP, NOW WE CAN'T FIGURE
OUT HOW TO FOLD IT!"

Thank you

