NZ dairy cattle – a reservoir for antimicrobial resistant Enterobacteriaceae?

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Antimicrobial Resistance: A Global Issue

Overview

- Source of extended spectrum β-lactamase producing Enterobacteriacae (ESBL-E)
- Definition of ESBL
- One Health Approach
- ESBLs in dairy cattle
- Manawatu pilot study

Where do you find ESBL producing Enterobacteriaceae?

Why ESBL-E?

WHO: These 12 bacteria pose greatest risk to human health

Priority 1: CRITICAL

1. *Acinetobacter baumannii*, carbapenem-resistant
2. *Pseudomonas aeruginosa*, carbapenem-resistant
3. *Enterobacteriaceae*, carbapenem-resistant, ESBL-producing

In New Zealand:

- National rate 95.5 per 100,000 people with ESBL-E infection in 2014 (Dyet et al. 2014)

- Approximately 40% of ESBL-E infections are urinary tract infections in the community

What are ESBL-E?

Definition - Rubin and Pitout (2014):

"ESBLs …. **enzymes** evolved from narrow spectrum parent enzymes or which have hydrolytic activity against the **extended spectrum cephalosporins** (3rd GC) the penicillins but not the cephamycins (cefoxitin) or carbapenems, and are inhibited by β-lactamase inhibitors including clavulanic acid "

A broader definition of ESBLs includes enzymes acquired through mobilisation of chromosomal β-lactamase coding genes with similar activity

β-lactamases

β-lactamase group	Examples	Resistance range
Penicillinases	TEM, SHV	Pen, 1GC
ESBLs	Common: CTX-M, TEM & SHV (Not parent type) Rare: FONA (Chr), SFO-1, BES-1	Pen, 1GC, 3GC
AmpC	CMY-2 (Plasmid) AmpC (Chr)	Pen, 1GC, 2GC, 3GC
Carbapenemases	OXA KPC Metallo β-lactamases (NDM)	Pen, 1GC, 2GC, 3GC Pen, 1GC, 2GC, 3GC, 4GC, Carbapenems

GC: Generation Cephalosporin

Table adapted from Irendell et al. 2010. BMJ 351:h6240

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mEpiLab: AMR Research: ESBL-E in the community

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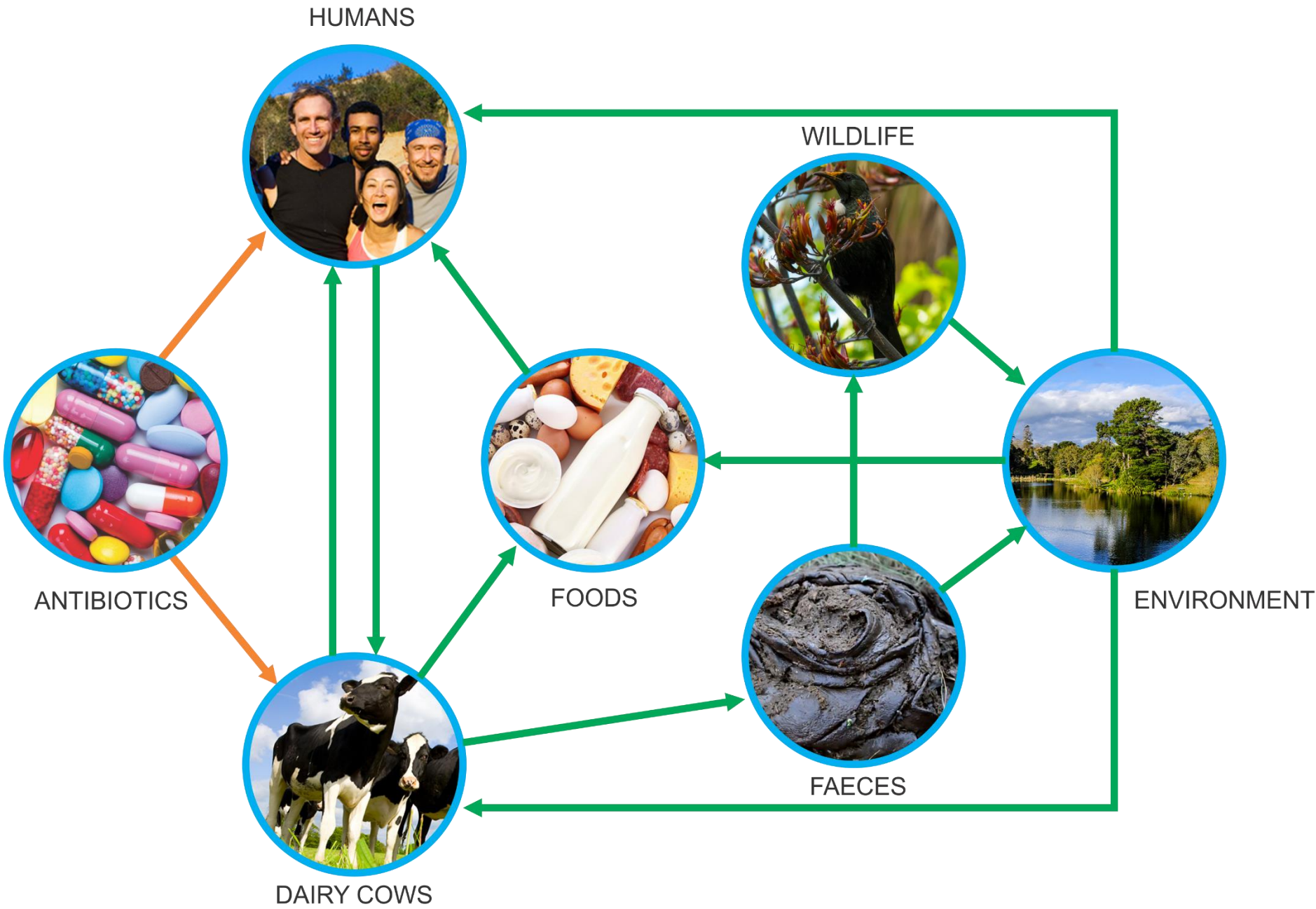
Overarching question

What evidence is there for the transmission of ESBL-E between humans, animals and the environment?

One Health Approach



Why dairy cattle?

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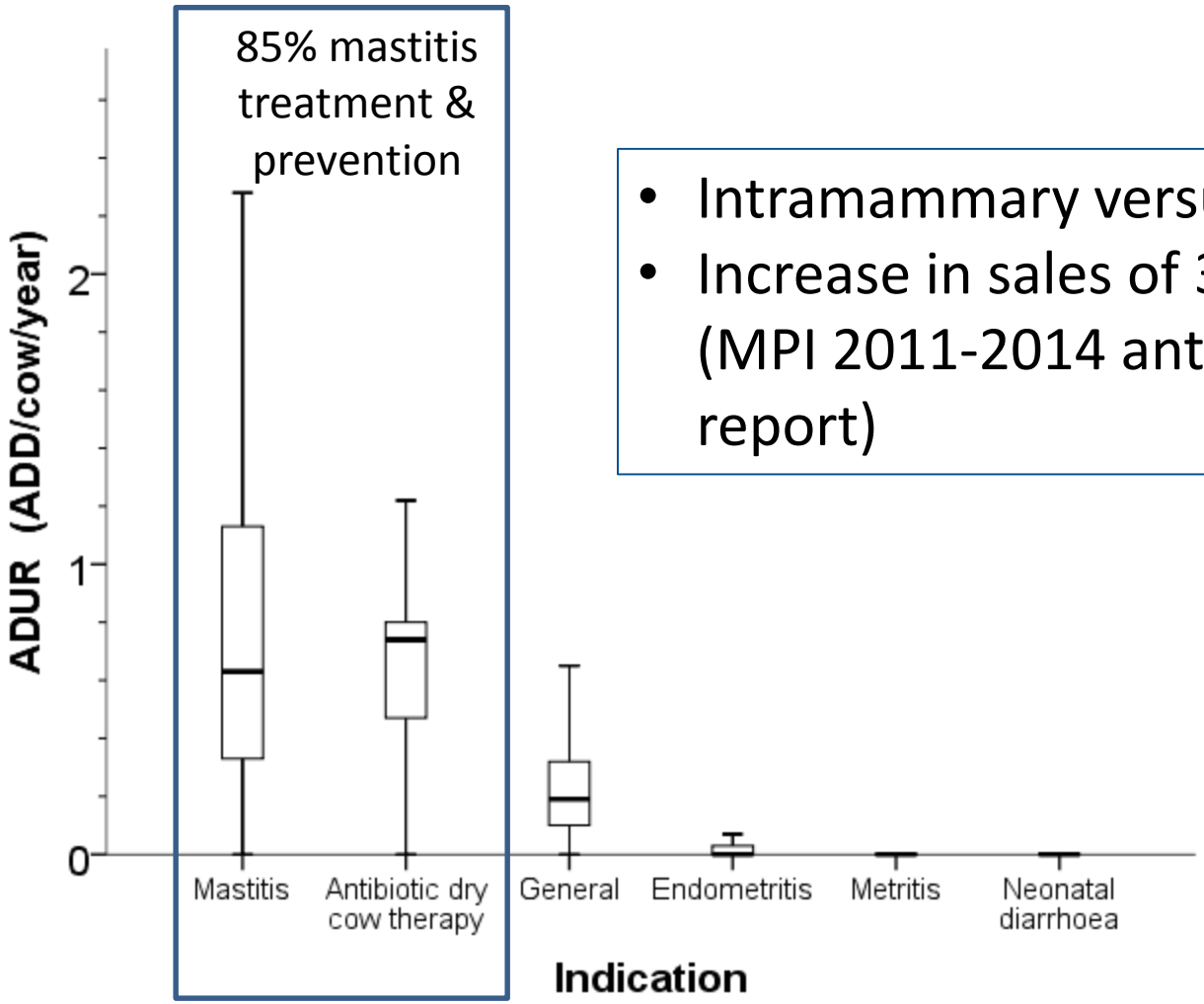
Does the presence of ESBL-E in livestock have implications for human health?

- Dairy cattle as an exemplar:
  - For NZ 2:1 dairy cattle to human ratio
  - Contact with animals
  - Large amount of faecal matter

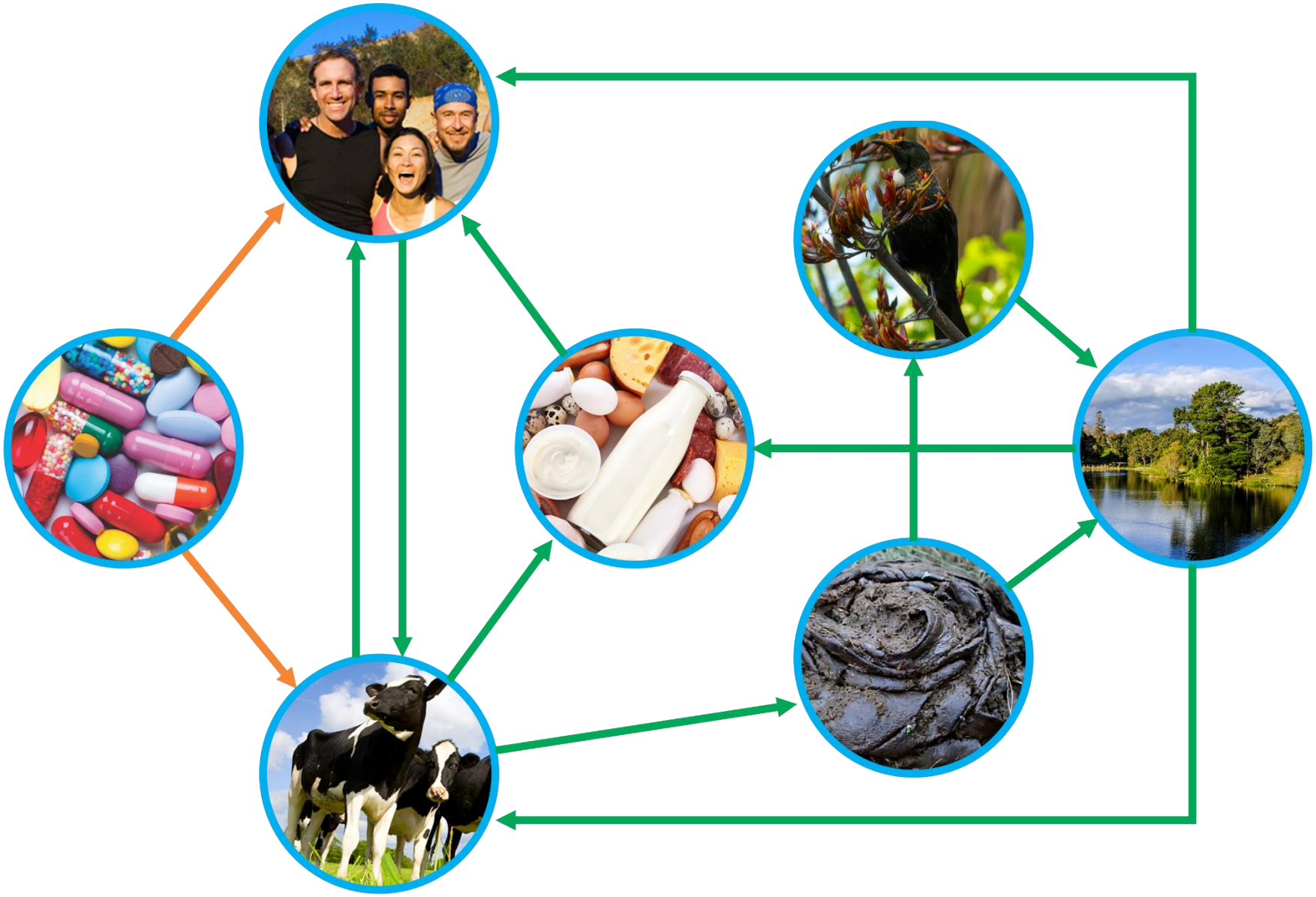
Antimicrobial use in dairy cattle



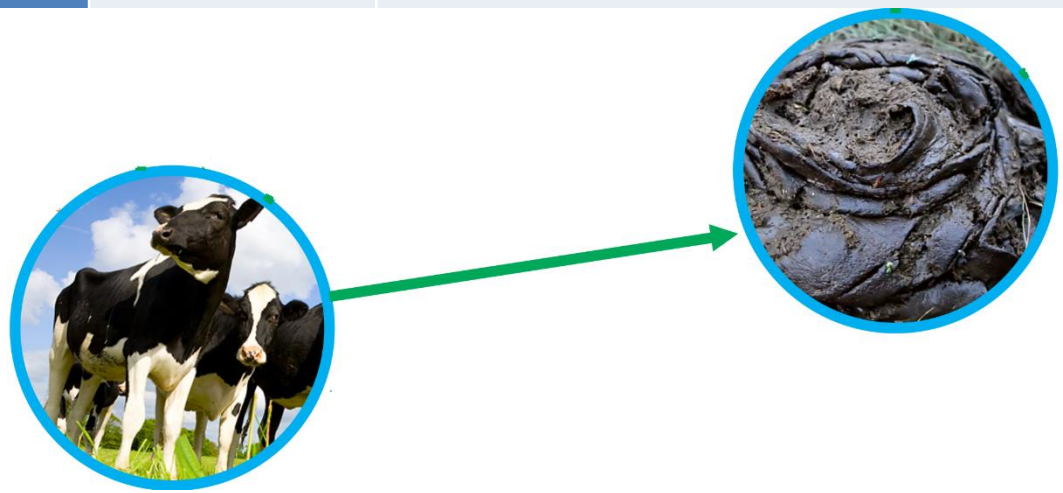
- Intramammary versus systemic
- Increase in sales of 3rd and 4th GC (MPI 2011-2014 antibiotic sales report)

Compton & McDougall 2014

One Health Approach

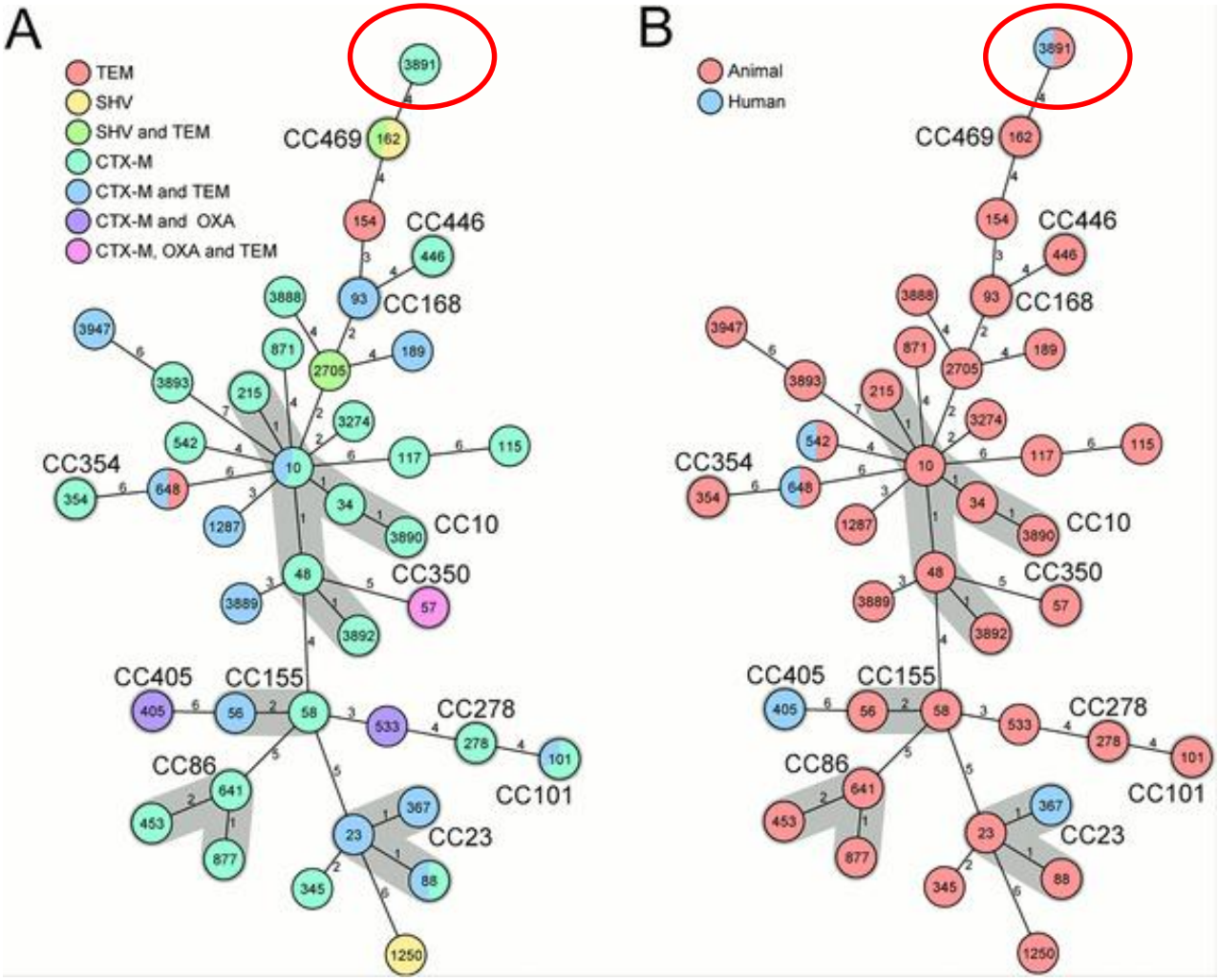


Sample type	Country	Prevalence	Reference
Cow slurry samples	Netherlands	**41 %** (41/100) **farms** positive for ESBL producing ***E. coli***	Gonggrijp, et al.
Ground faecal samples from	United Kingdom	**35.4 %** (17/48) **farms** positive for ESBL producing ***E. coli***	Snow, et al.
Faecal, dust and boot swab samples	Germany	**93.3 %** (28/30) **farms** positive for ESBL producing ***E. coli***, **41.1 %** (37/90) **cow faecal samples** positive for ESBL producing ***E. coli***	Schmid, et al.
Faecal samples from dairy cattle	Japan	**5.2 %** (20/381) **farms** positive for ESBL producing Enterobacteriaceae	Ohnishi, et al.
Faecal samples from calves	Switzerland	**13.7 %** (17/124) **calf faecal samples** positive for ESBL producing Enterobacteriaceae – **98% *E. coli***	Geser, et al.



ESBLs in Dutch dairy herds

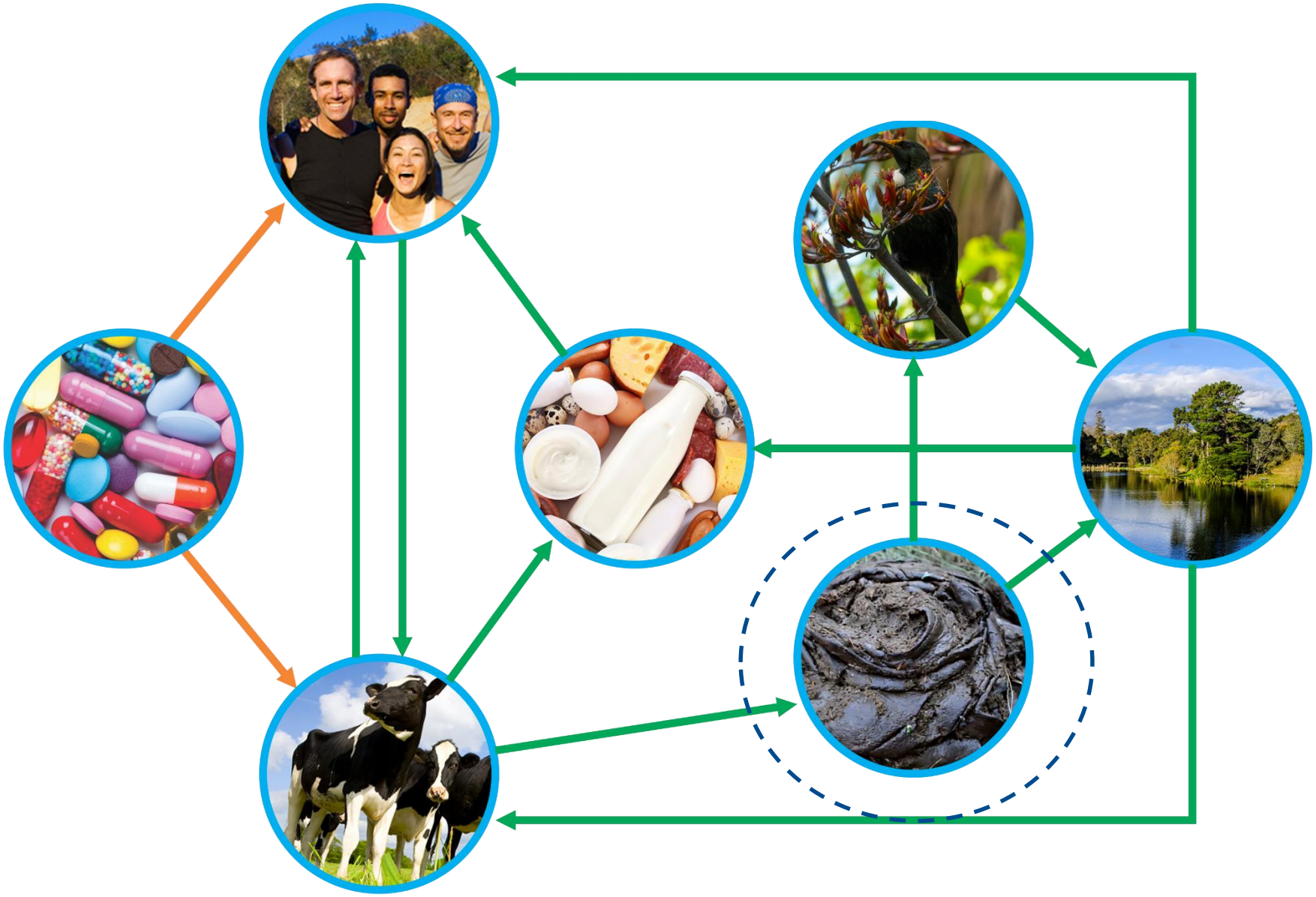
- Gonggrijp et al (2016):
- 41/100 dairy herds positive ESBL producing *E. coli*
- Total antimicrobial use not significantly different between ESBL+ve vs ESBL-ve herds
- Average daily usage rate of 3rd/4th GC significantly different for ESBL+ve *vs* ESBL-ve herds



Dahms et al. (2015):

"One human isolate shared an identical MLST sequence type (ST)
3891 and CTX-M allele to the isolate found in the cattle fecal sample from the same farm,
indicating a zoonotic transfer."

One Health Approach



Manawatu pilot study

+ 1mg/L ceftazidime

+ 1mg/L cefotaxime

- 15 dairy cattle and 15 sheep farms sampled
- Two sampling rounds: Spring 2016 and Autumn 2017

Freezer

MALDI-TOF MS

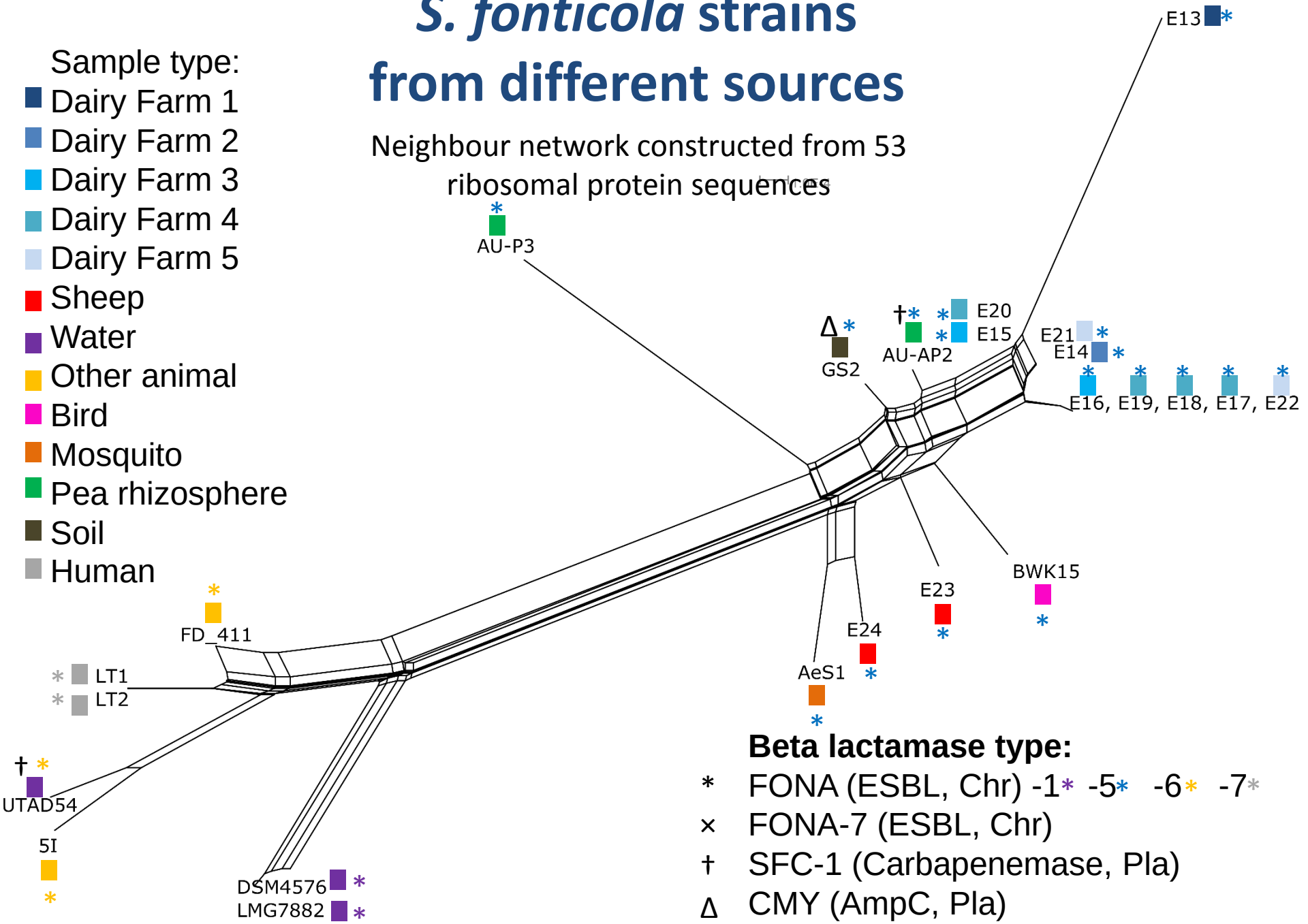
Antibiotic Susceptibility testing

Results – Autumn sampling round

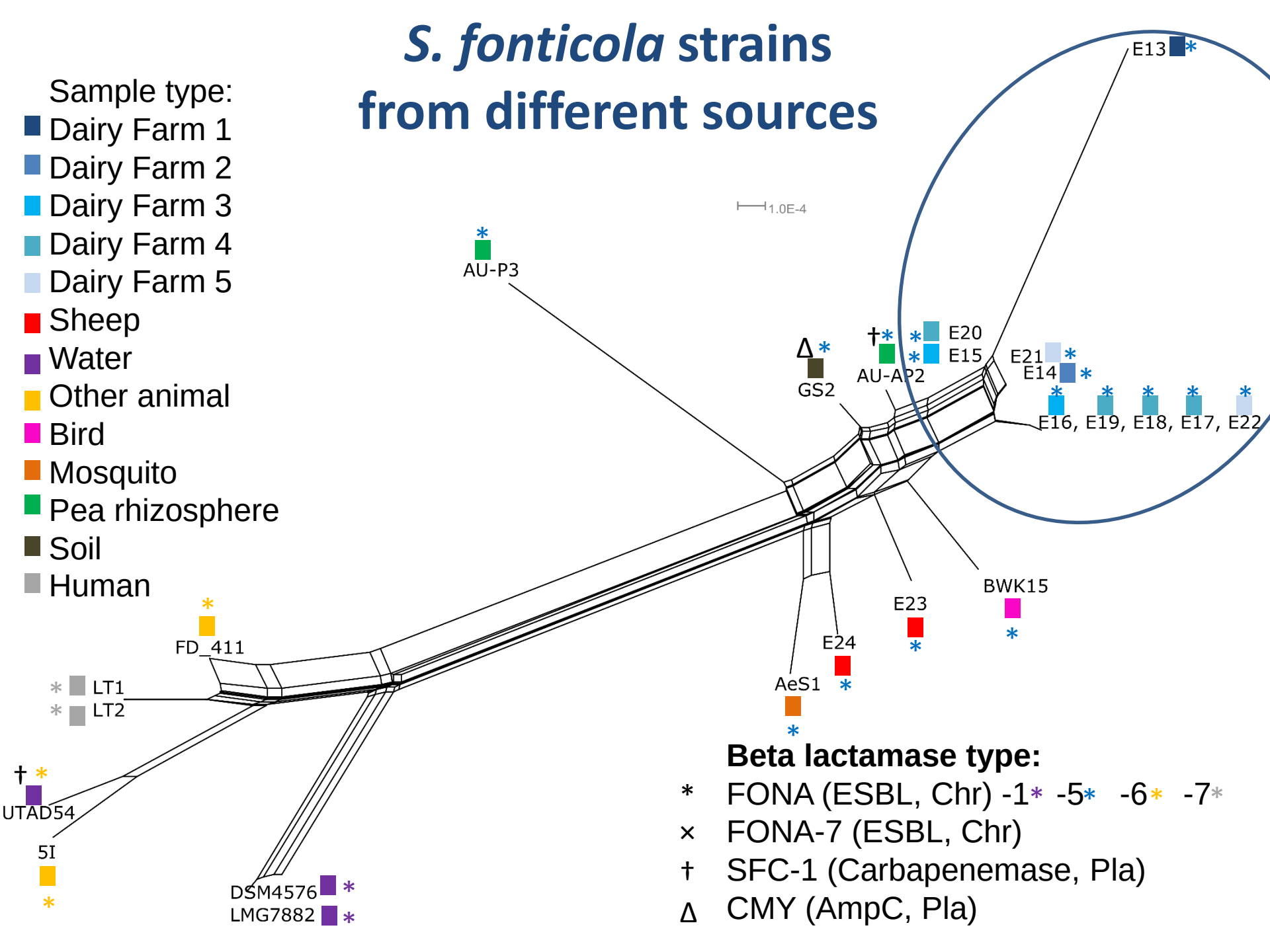
Dairy cattle	Sheep
10/15 farms 'ESBL positive'	15/15 farms 'ESBL positive'
222 Enterobacteriaceae isolates	270 Enterobacteriaceae isolates
16% (36/222) ESBL producers	11% (31/270) ESBL producers
97% ESBL-E *Serratia fonticola*	84% ESBL-E *Serratia fonticola*

S. fonticola strains from different sources

Neighbour network constructed from 53 ribosomal protein sequences



S. fonticola strains from different sources



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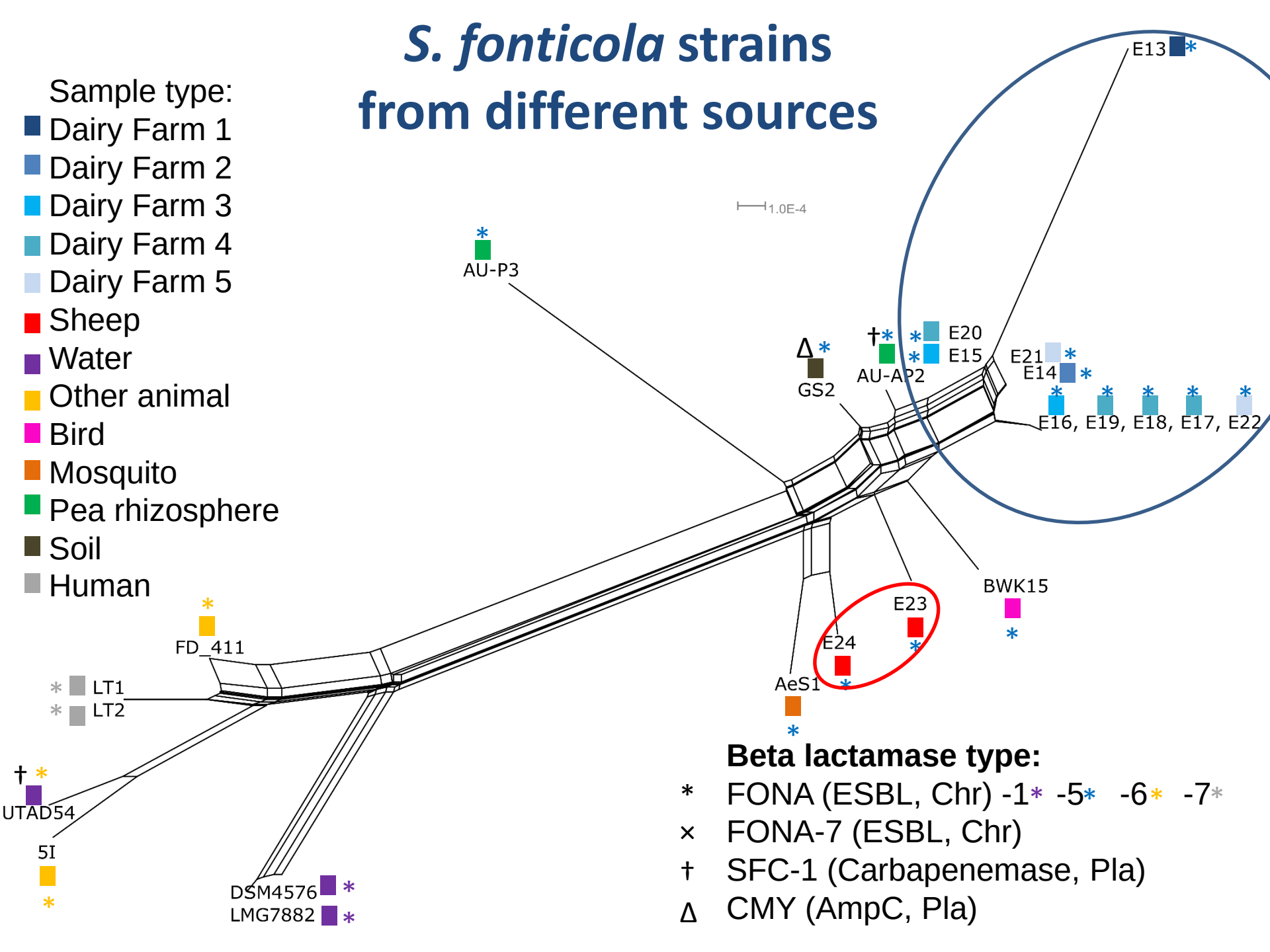
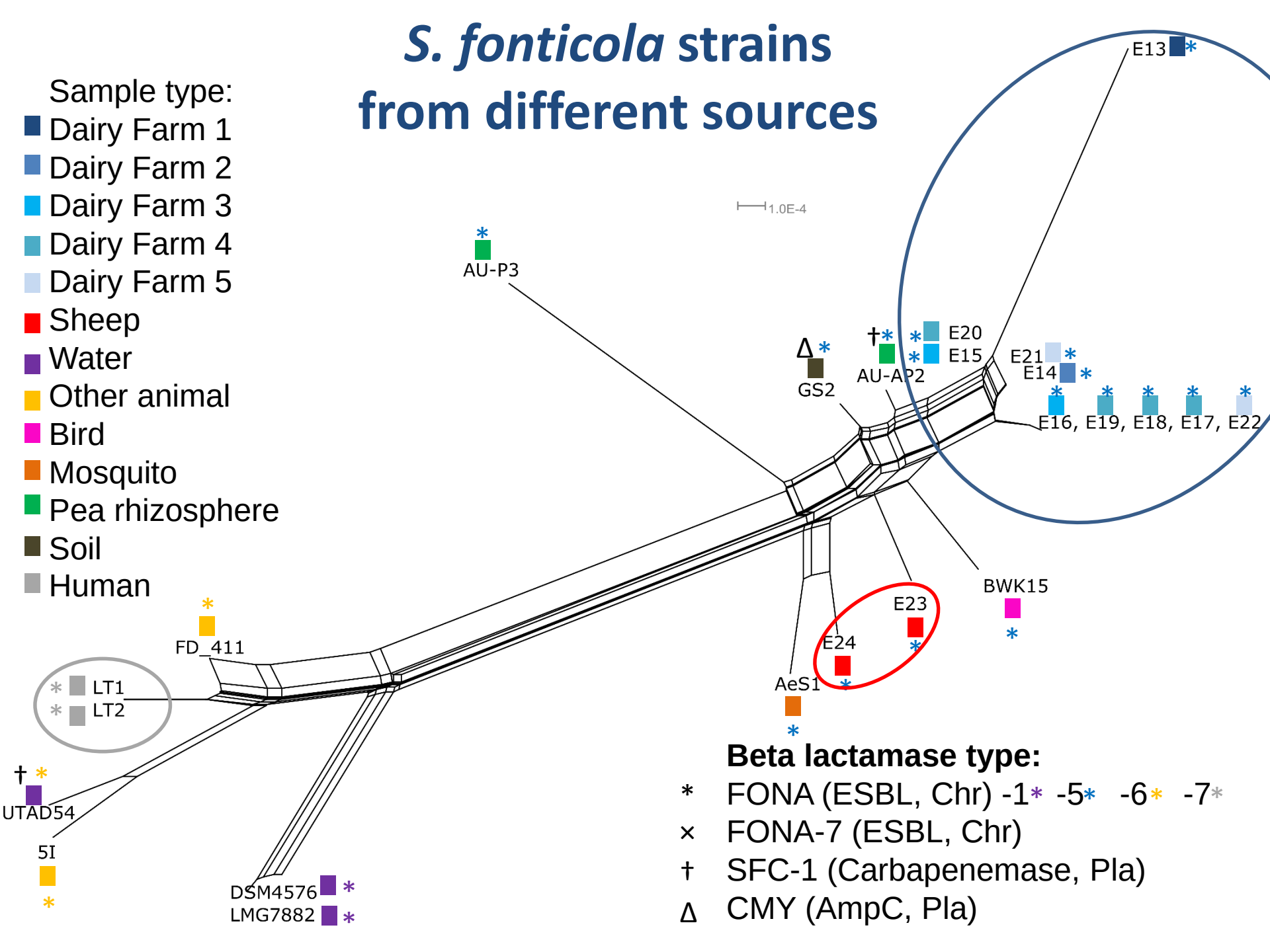
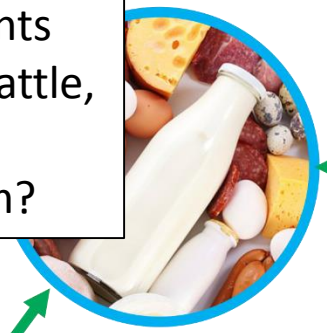


S. fonticola strains from different sources



Where to next?

Are ESBL-E and their resistance determinants shared between dairy cattle, humans and the environment on farm?



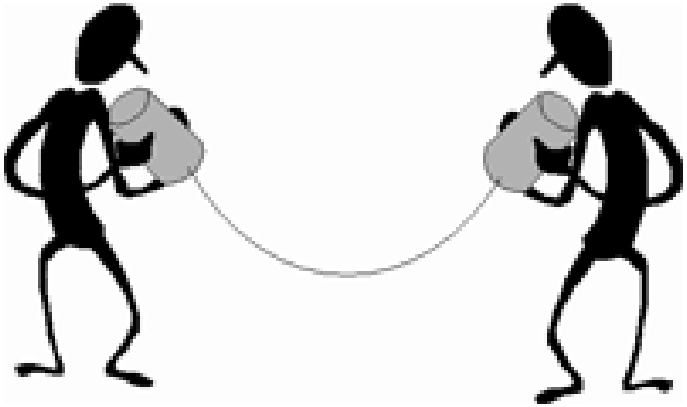
FAECES

Is there an association between antibiotic use and presence of ESBLS?

Can these AMR determinants spread to other environments?

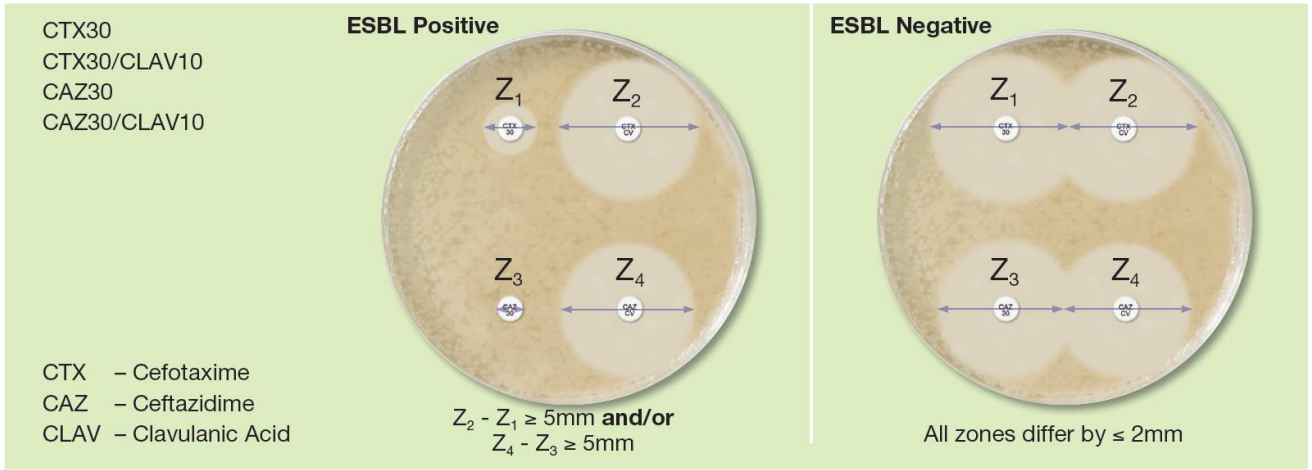
Other AMR determinants?

Spread the word

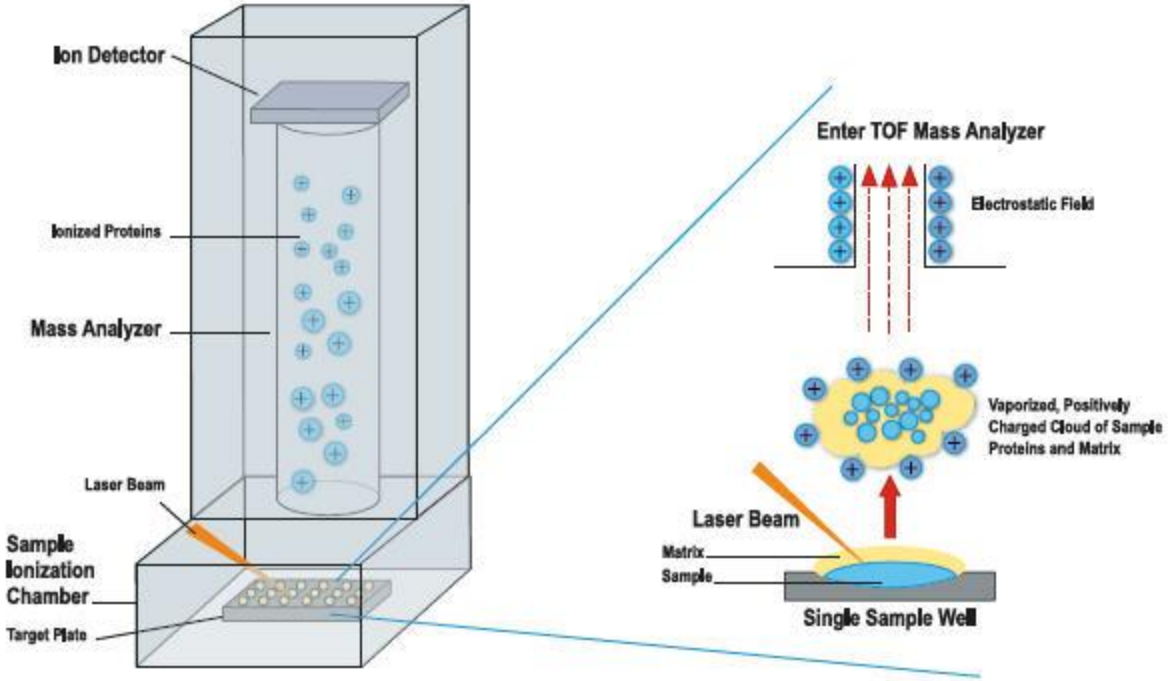


Additional slides at end to explain things if needed

ASTs



MALDI-TOF


Ion Detector
Ionized Proteins
Mass Analyzer
Laser Beam
Sample Ionization Chamber
Target Plate
Enter TOF Mass Analyzer
Electrostatic Field
Vaporized, Positively Charged Cloud of Sample Proteins and Matrix
Laser Beam
Matrix
Sample
Single Sample Well