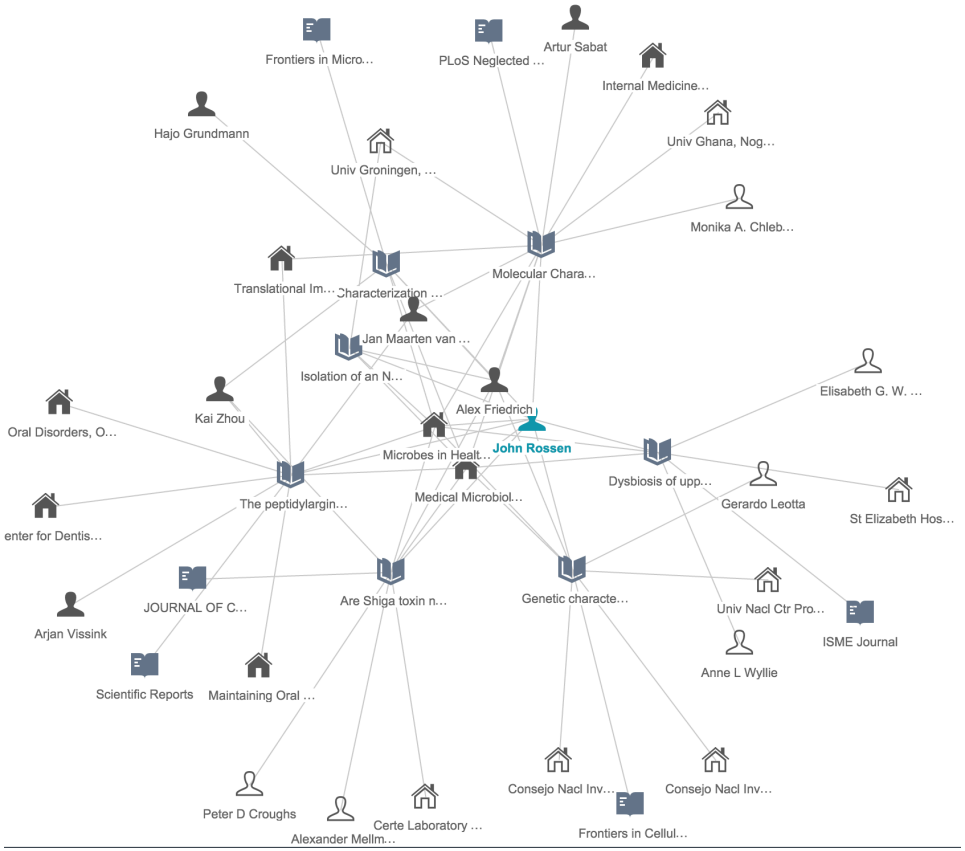
Trace and control the regional expansion of extended-spectrum β-Lactamase producing ST15 Klebsiella pneumoniae



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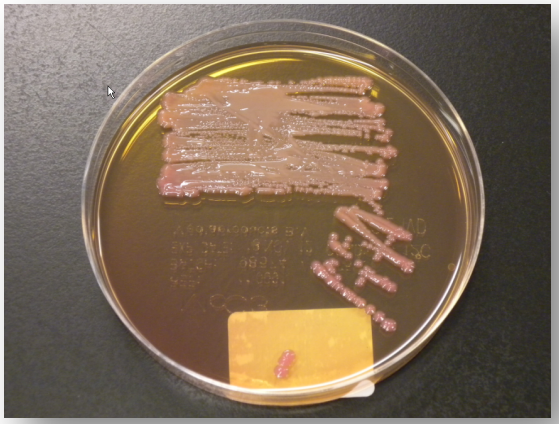
Disclosure of speaker's interests

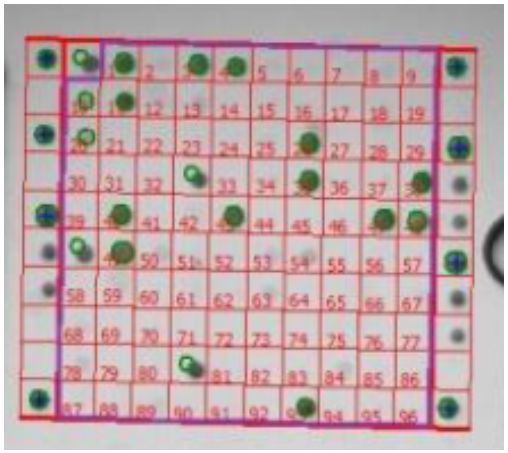
(Potential) conflict of interest	None
Potentially relevant company relationships in connection with event	None
Sponsorship or research funding	Several National and European Grants

Klebsiella pneumoniae epi-event

- September 2012
- ESBL-producing *K. pneumoniae* (CTX-M-15)



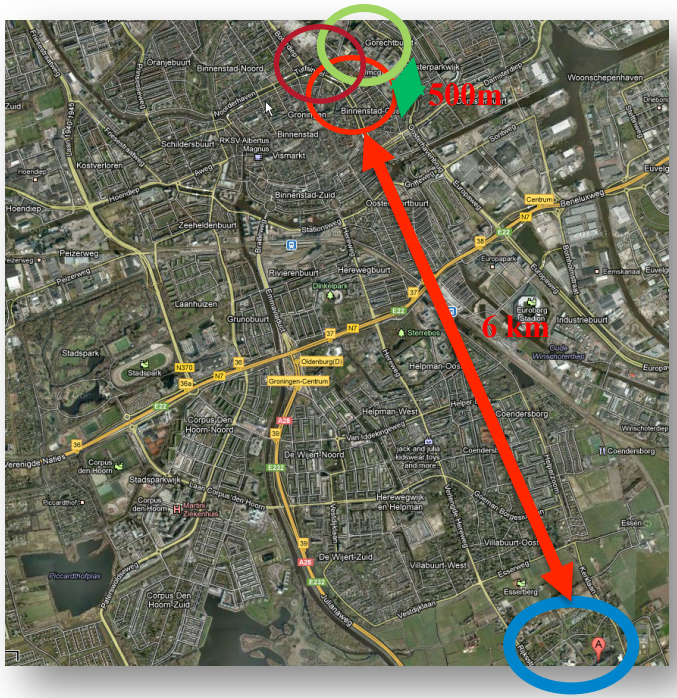
		4-MIC
AMOXICILLINE	R	> 32
AMOX.+CLAVZ.	R	16
CEFUROXIM	R	> 64
CEFOTAXIME	R	> 64
CEFTAZIDIME	R	16
IMIPENEM	S	<0.250#
GENTAMICINE	R	> 16
TOBRAMYCINE	R	> 16
TRIMETHOPRIM	R	> 16
CO-TRIMOXAZO	R	> 320
NITROFURANTO	R	64#
NORFLOXACIN	R	> 16#
CIPROFLOXACI	R	> 4
POLYMYXINE	S	<0.500
CEFOXITIN	S	< 4#
CEFEPIME	R	2
MEROPENEM	S	<0.250
PIPERA+TAZOB	R	32

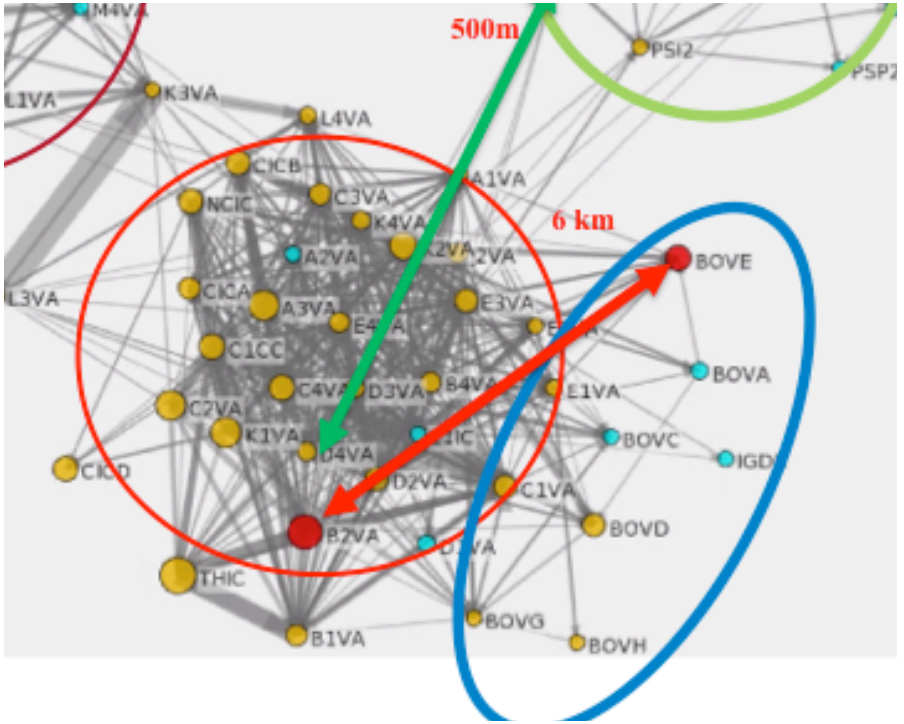


Zhou et al. Front Microbiol. 2015 6:1250; Sci Rep. 2016;6:20840

Klebsiella pneumoniae outbreak

- May - September 2012
- ESBL-producing *K. pneumoniae* (CTX-M-15)
- Hospital and rehabilitation center (n=12*)





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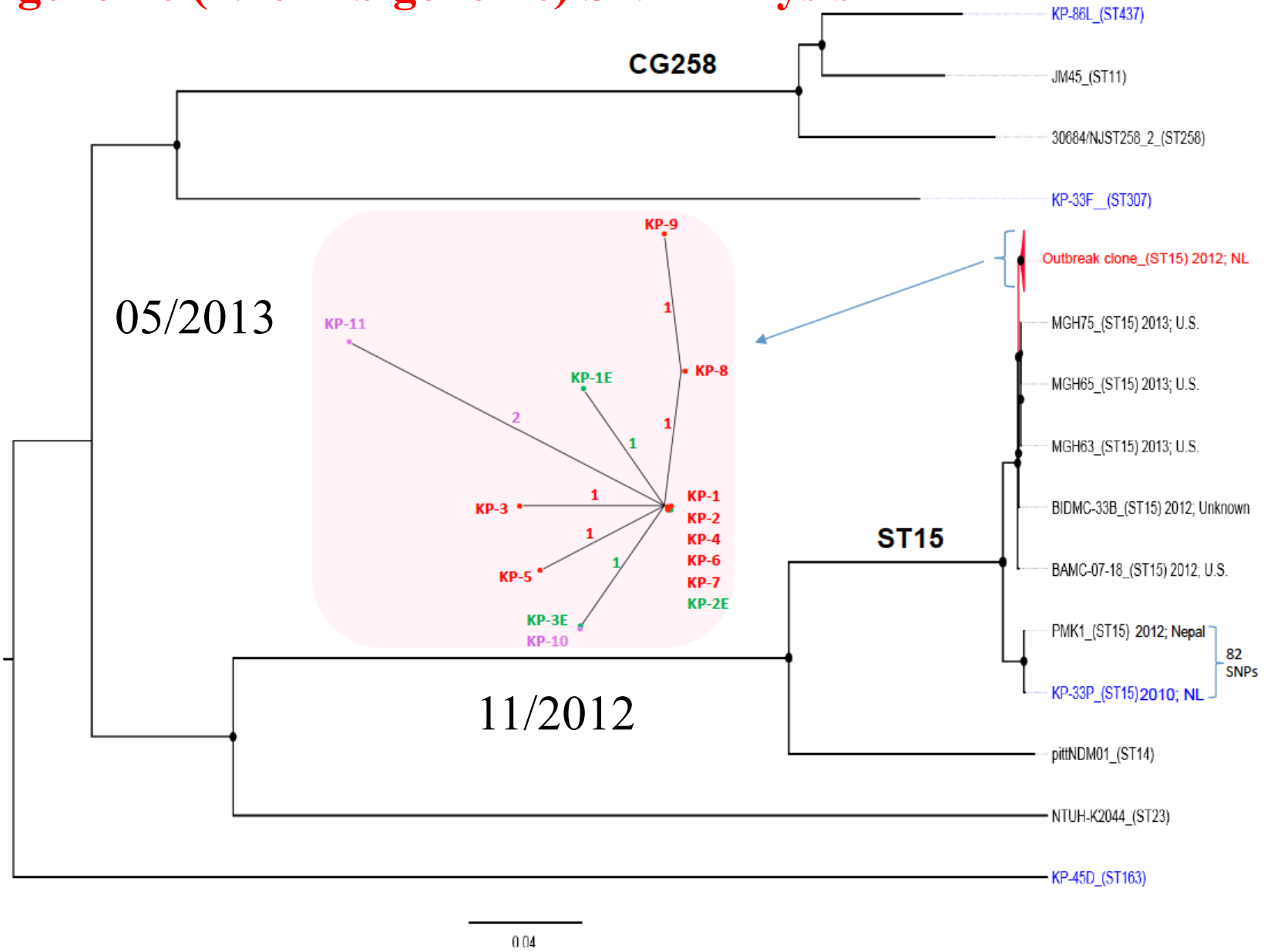
Core genome (4.47 Mb genome) SNP analysis



10/57 environmental samples pos

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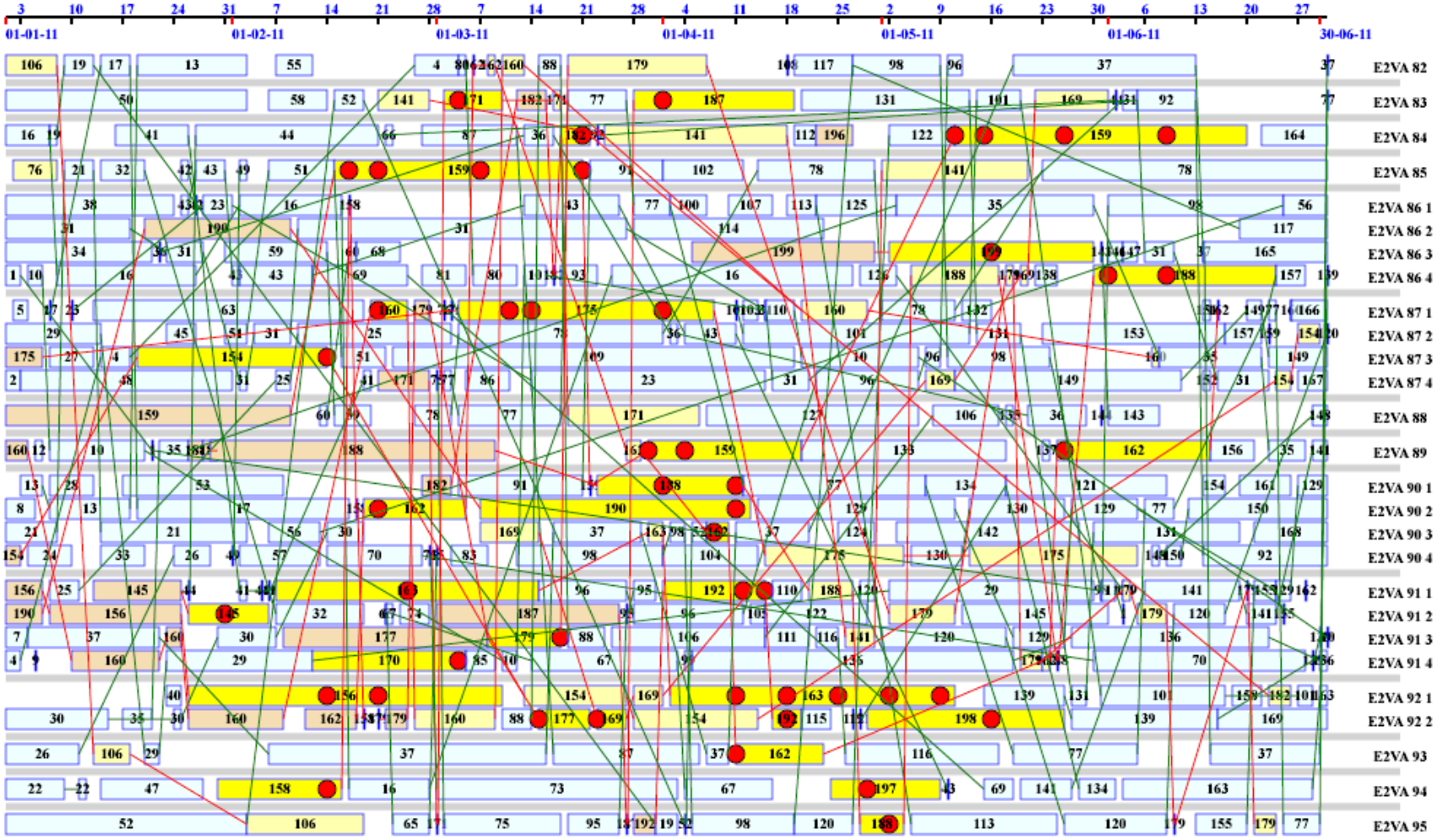


Positieve patienten: (n=26; overplaatsingen: n=84; ratio=3,2; gemiddelde ligduur=46,4 dg)

Pos. patient

pat.vnr Opname nadat patient pos. was

Neg. patient

Opname voordat patient pos. wordt

enfmvb

negatief MO

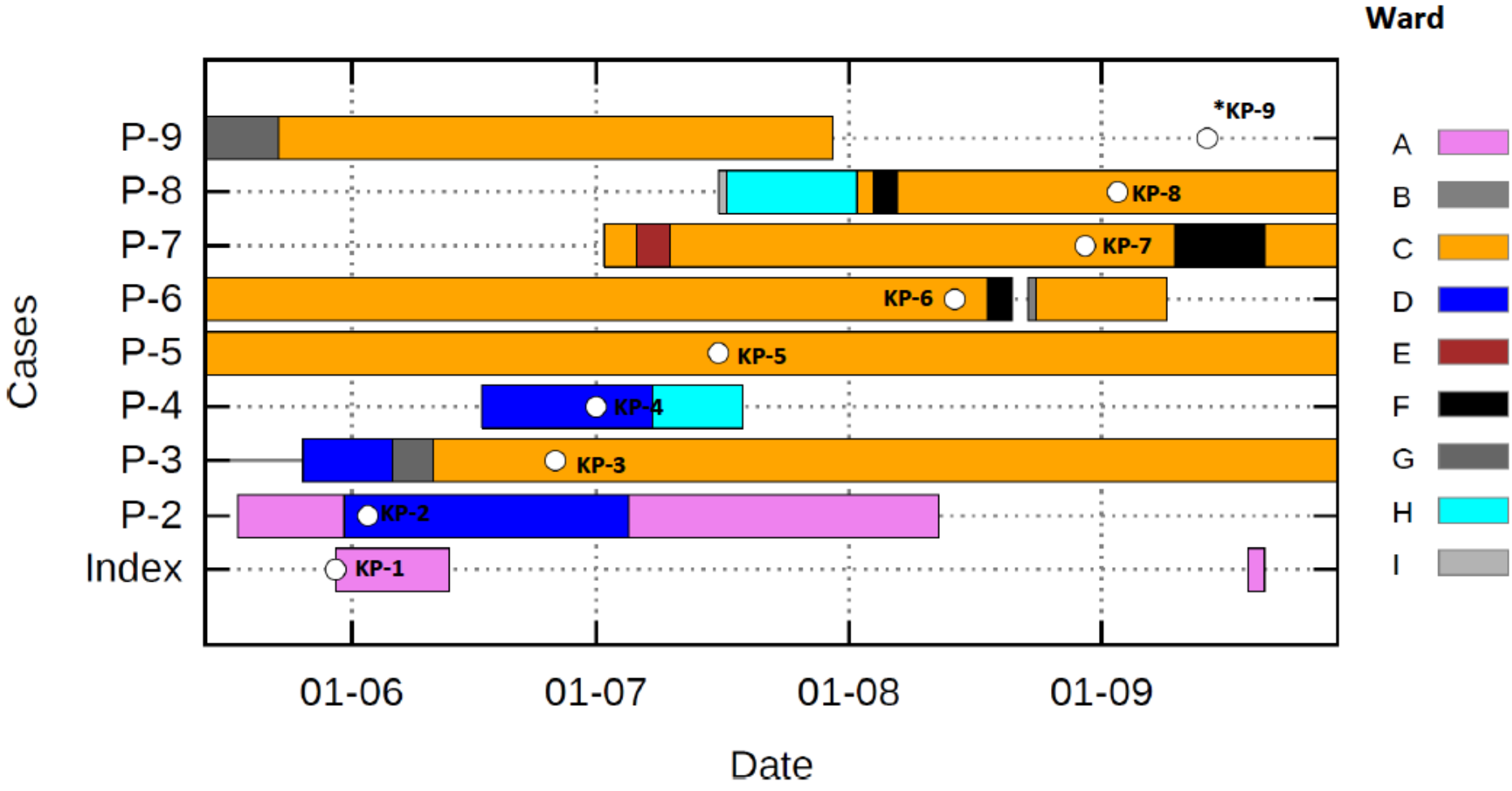
Verbindingslijn neg. pat.

Verbindingslijn pos. pat.

Overige patienten: (n=143; overplaatsingen n=165; ratio=1,2; gemiddelde ligduur=19,2 dg)

Courtesy: Patient transfer during HRMO-outbreak, Jan Arends, UMCG, Groningen (NL)

Movements of patients



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Zhou et al. Sci Rep. 2016;6:20840

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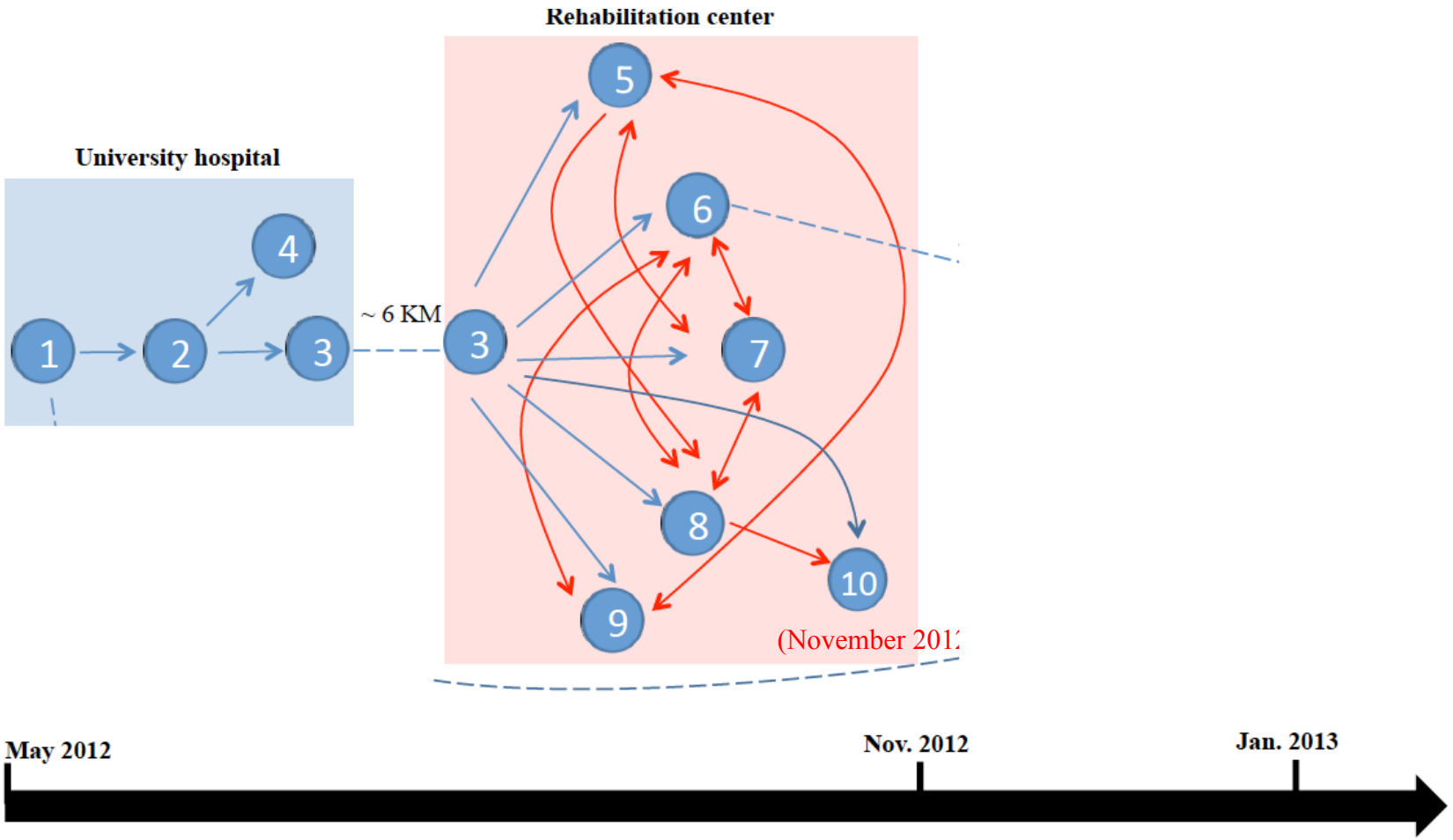
Putative transmission route of the regional outbreak

combining epi- and genetic-data



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> 120 patients were screened

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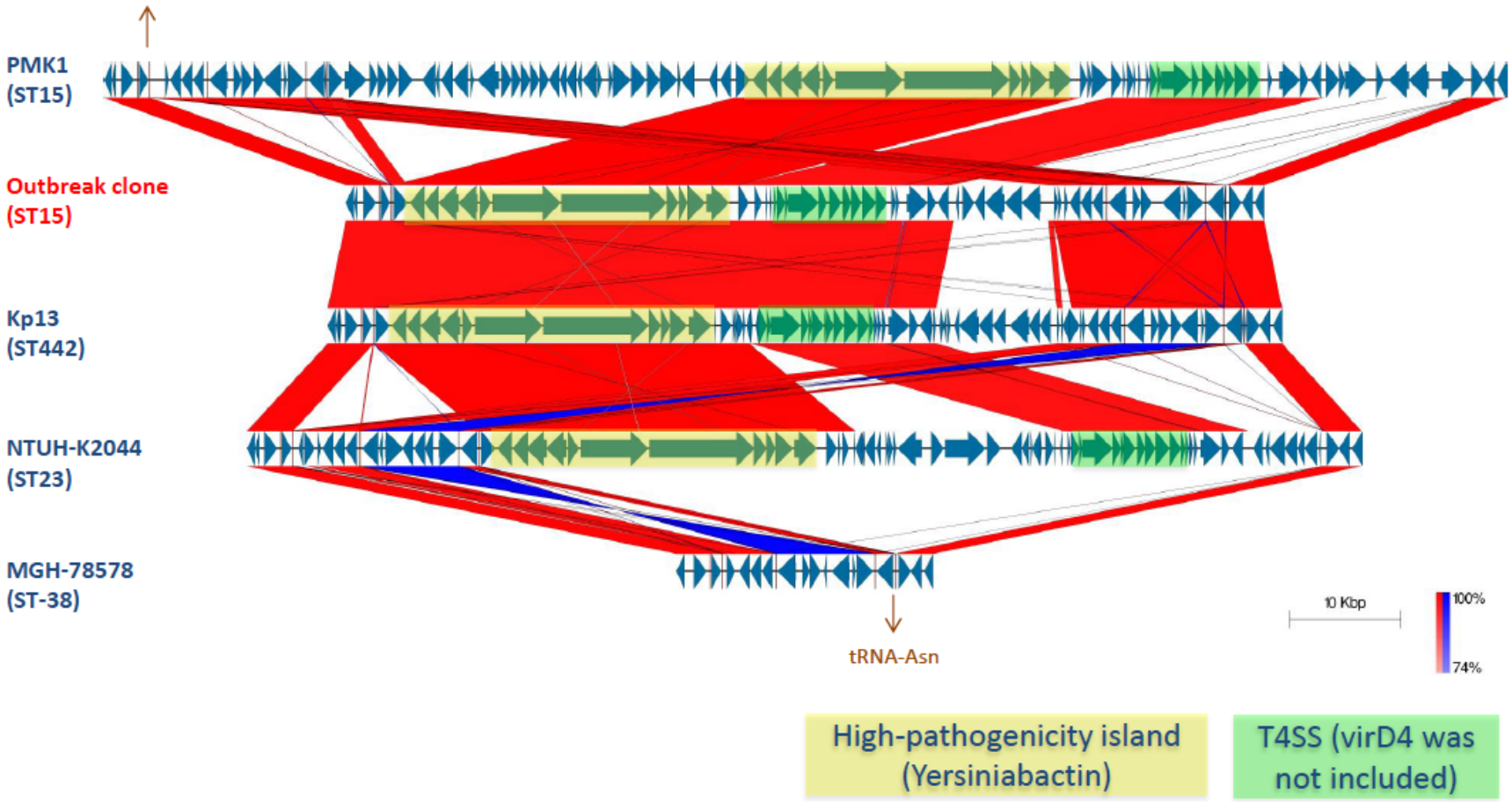
WGS more than epi-typing



All outbreak isolates shared the same resistance genes

essential to become an effective respiratory pathogen

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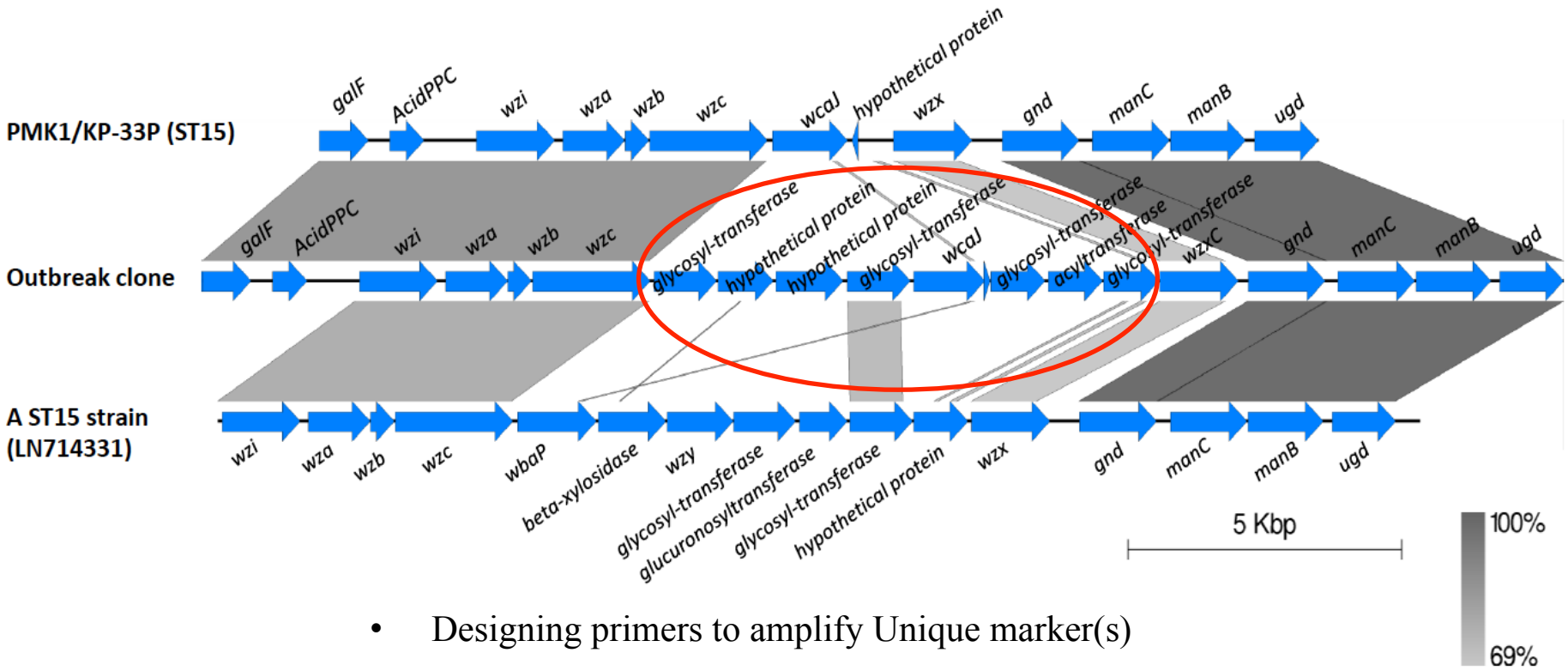
Identification of unique regions in the capsular polysaccharide synthesis (*cps*) region of the outbreak clone



- Designing primers to amplify Unique marker(s)
  - 2 CDS for hypothetical proteins
  - 1 within capsule biosynthesis region -> glycosyltransferase-encoding gene
- Screen patient isolates

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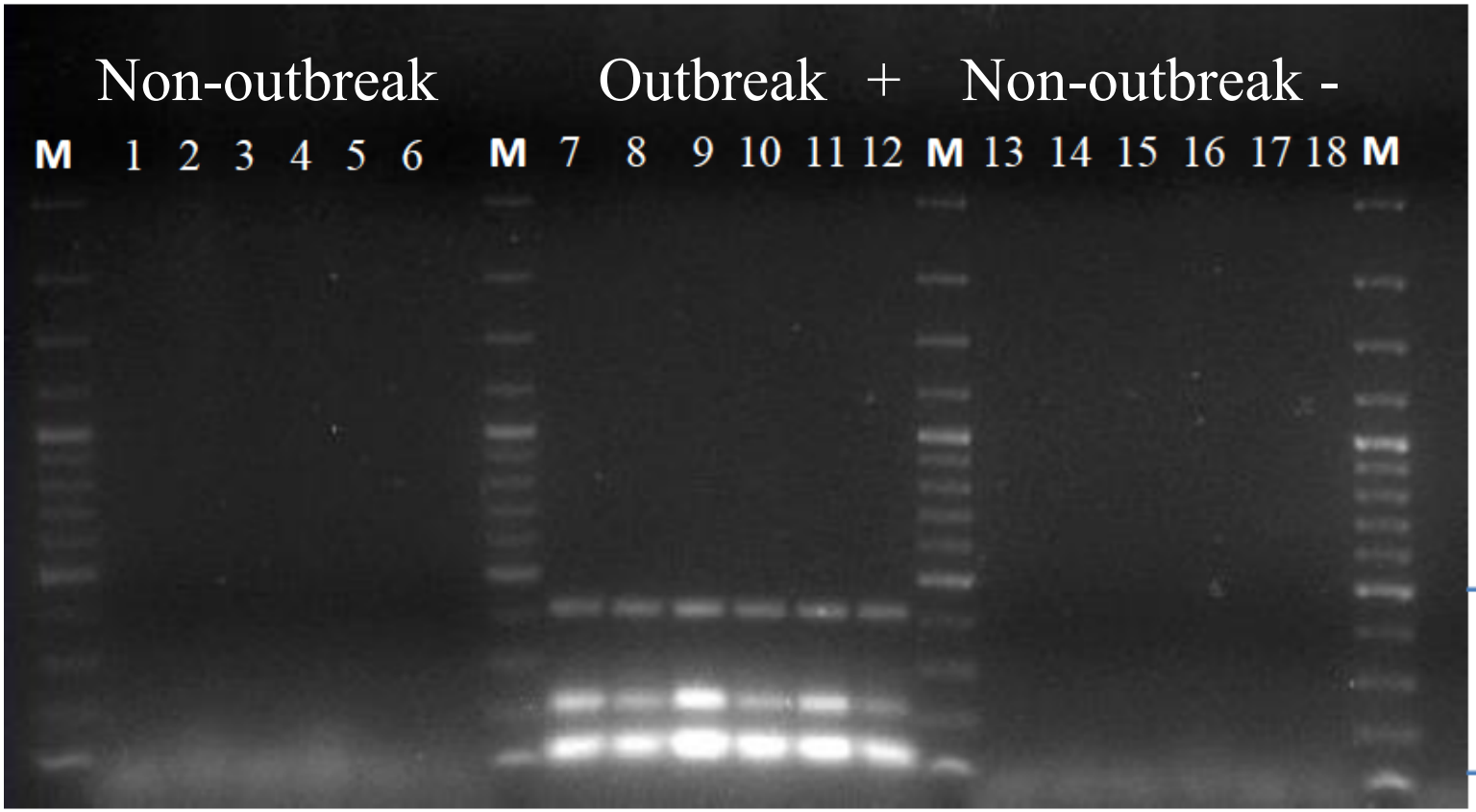
Validation of the outbreak-specific multiplex PCR



ST15

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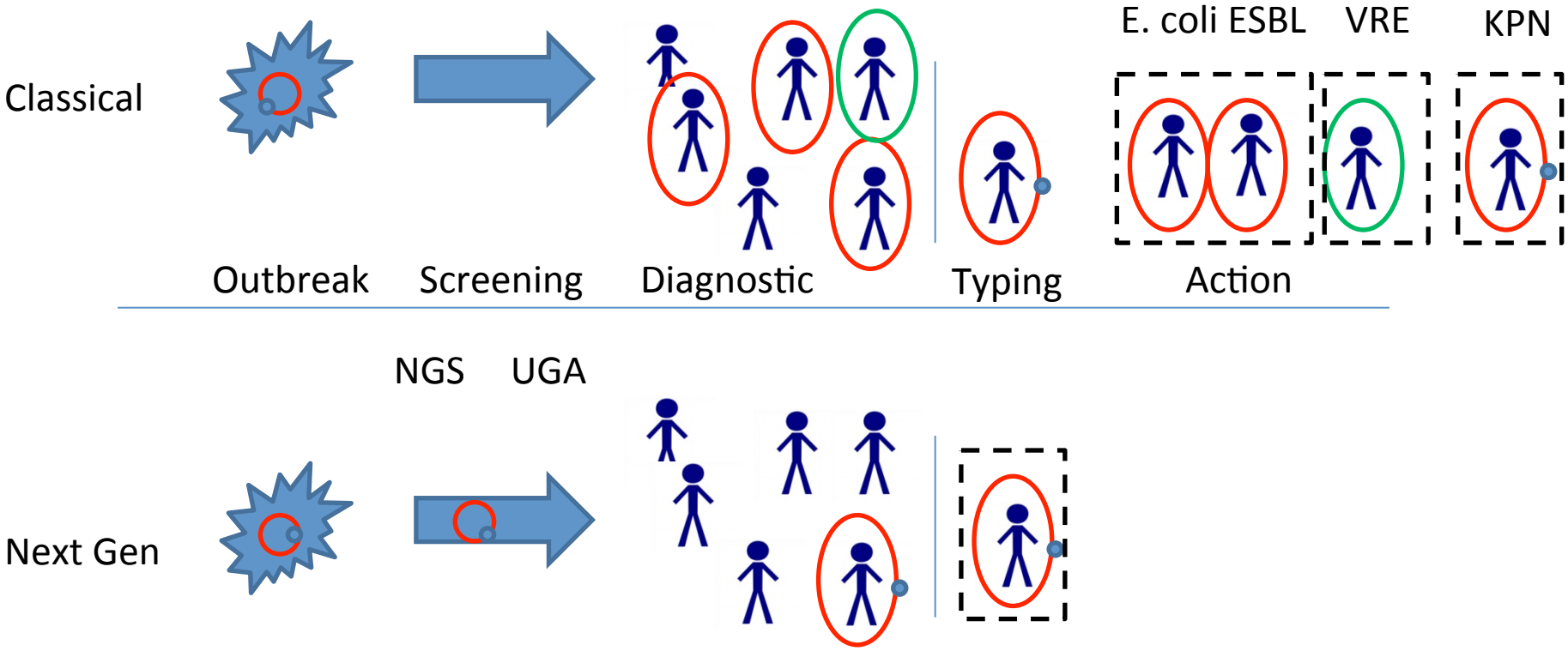
Tailor-made diagnostics

"Precised microbiology"



-> identified the 2013 strains

-> exclude 3 strains in 2015

Bacteria follow their hosts through the H[illegible]-network challenging IP

Donker *et al,* UMCG/Oxford

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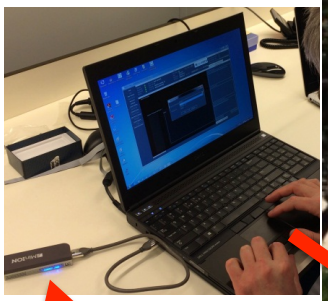
Unique marker in forensics



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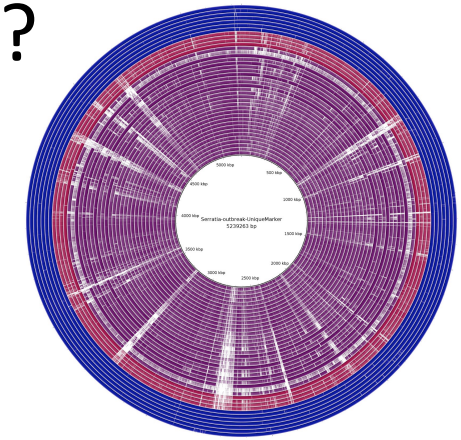
Forensic microbiology – to consider

- Sequence one or more isolates?
- How different is different?
- Unique marker approach to trace a specific clone?
- How common is a “unique” clone?



A. Internal quality control and validation

- SOP for internal quality control

B. External quality control

- Annual proficiency testing
- Continuous quality control

C. Curatorship for (Eu)regional NGS server

- Synchronization of typing data
- Study groups within NGS data server (Euregio study area, REMIS-study group)
- Local strain collection – central database

D. harmonize interpretation of NGS data

October, 12-14th 2016 Groningen

- how many SNPs/alleles are allowed for strains belonging to the same outbreak cluster
- help to define MLST+ sequence types and schemes

E. Capacity Building

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Alex W Friedrich

Erik Bathoorn

Sigrid Rosema

Erwin RaaNGS

Kai Zhou

Mariëtte Lokate

Monika Chlebowicz

The Wet Lab during a dry moment

Genomics for Infection Prevention

Molecular biologists
Medical microbiologists
Infection control practitioners
ID-doctors
E-lab technicians
Bioinformaticians

Ruud Deurenberg

Silvia Garcia Cobos

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Eyes for the Invisible !

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SAVE THE DATE

ONE HEALTH SYMPOSIUM
FOCUS ON GENOMICS OF PATHOGENIC ESCHERICHIA COLI

1 AND 2 DECEMBER 2016 / JAARBEURS, SUPERNOVA / UTRECHT, THE NETHERLANDS

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