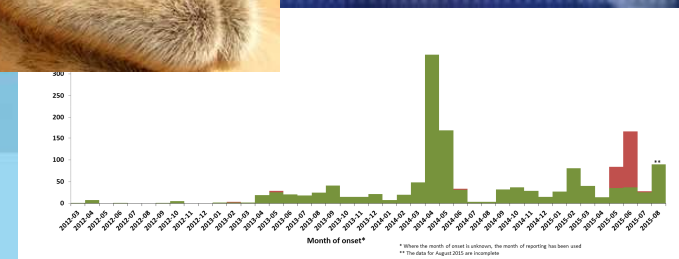




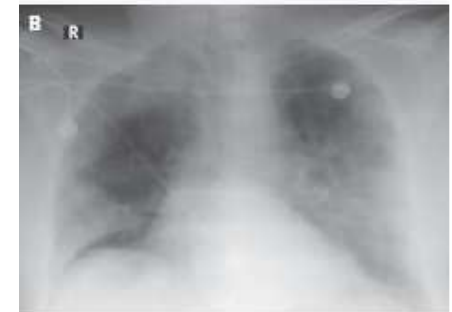
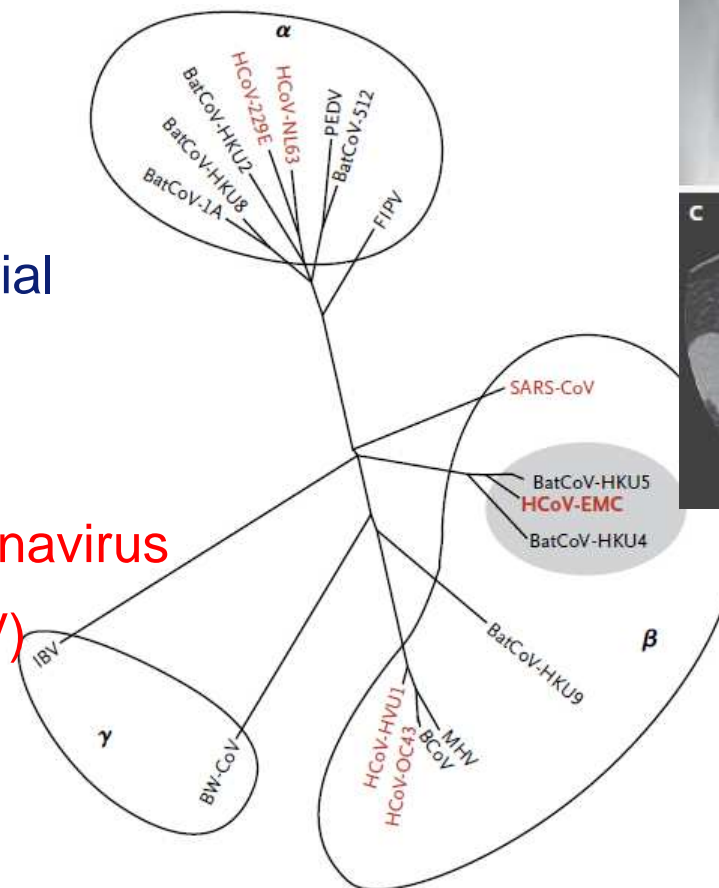
MERS-CoV, current knowledge



Case report (sept 2012)

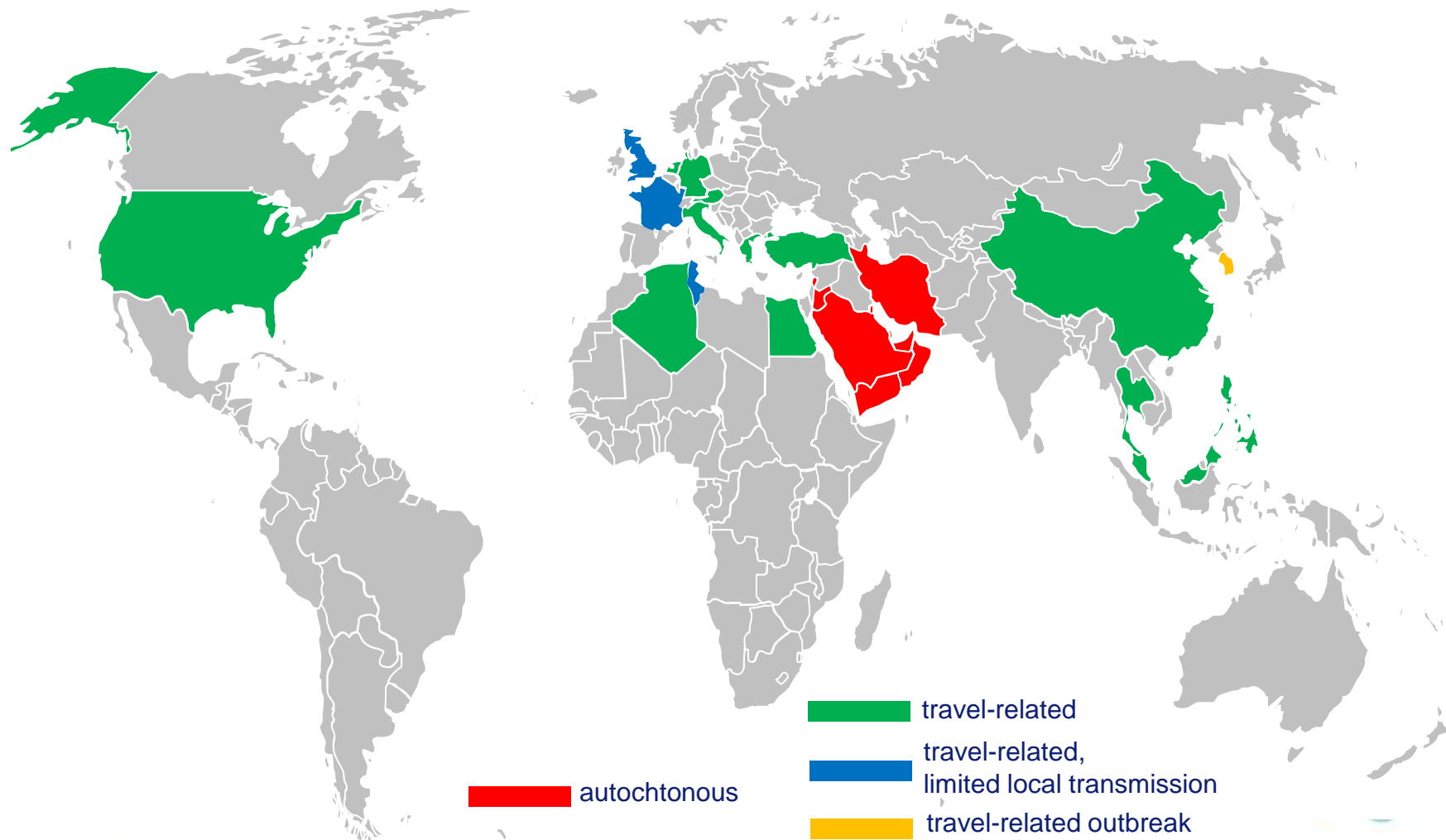
- 60 year-old Saudi male
- Fever, cough, expectoration, shortness of breath
- Body temperature 38,3 °C
- Pneumonia
- Impairment of renal function
- Co-morbidities including bacterial infections

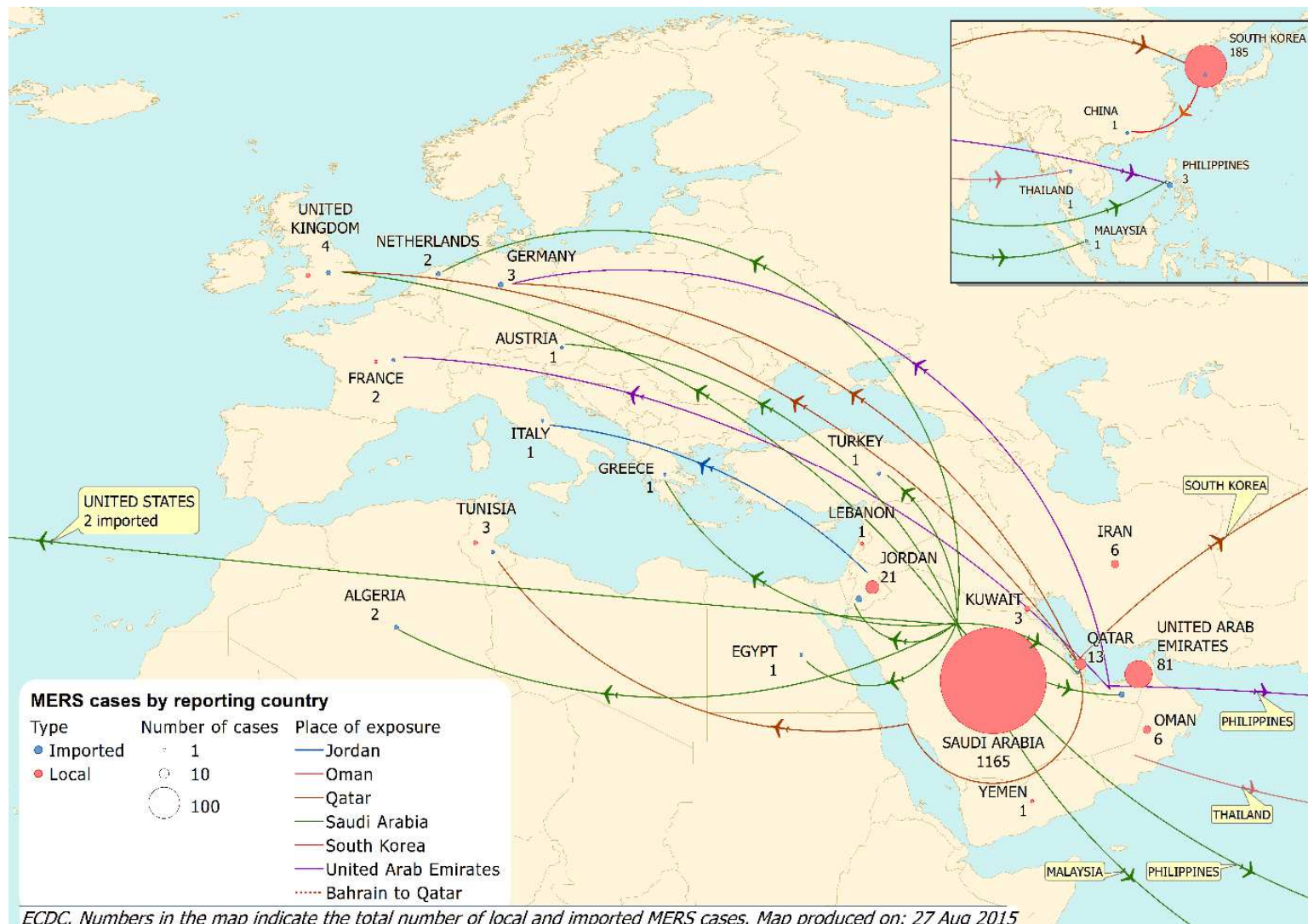
Identification novel human β -coronavirus
MERS-CoV (hCoV-EMC, nCoV)



Summary geographic situation human MERS.

Status as of August 27, 2015: 1511 confirmed with 574 deaths





Source: ECDC.
Data until August 27, 2015

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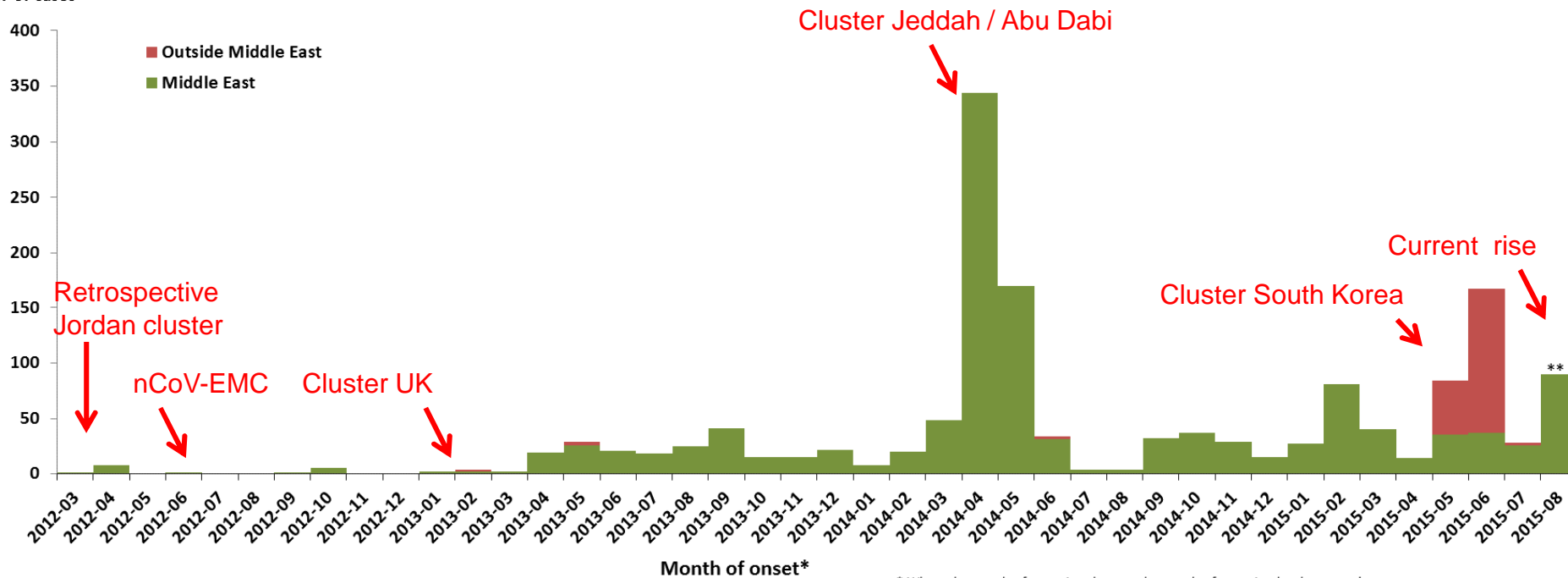


Monthly distribution MERS cases.

Period March 2012 – 27 August 2015



Number of cases



* Where the month of onset is unknown, the month of reporting has been used

** The data for August 2015 are incomplete

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Source: ECDC.

Data until August 27, 2015

Peak spring 2014?

- increased surveillance? Change case definition
- increased nosocomial transmission?
- increased virus transmissibility?
- diagnostic lab artifact?
- increased zoonotic transmission

(increase primary cases/seasonality effect)?



WHO mission 2014: severe lack/breach IPC measures

Drosten et al., CID 2015.

No evidence for contamination in Jeddah laboratory.

Phylogenetic and phenotypic analysis Jeddah and Riyadh circulating strains

⇒ biologically unchanged viruses

⇒ Jeddah: vast majority nosocomial transmission

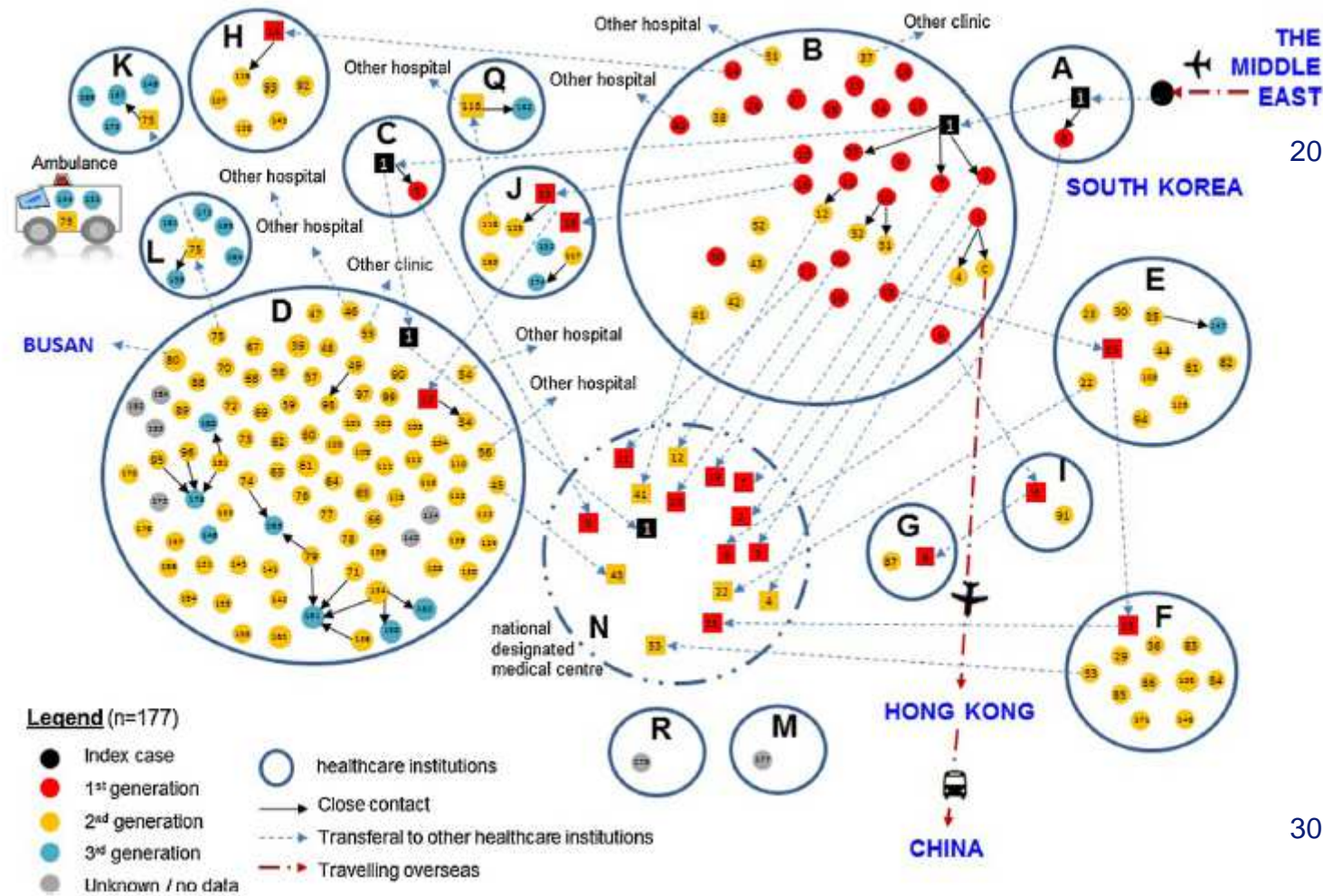
⇒ Riyadh: multiple independent sources (zoonotic, human import other regions, nosocomial)

Oboho et al., NEJM 2015

⇒ H2H transmission, amplification in health care facilities

⇒ No evidence for sudden increase in primary cases; exposure to animals was not assessed in this study!

South Korea



20 May 2015

Index case

30 June 2015

186 cases

South Korea

- increased surveillance?
- increased nosocomial transmission?
- increased virus transmissibility?
- diagnostic lab artifact?
- increased zoonotic transmission (increase primary cases)?

- No evidence for changed properties virus
- After onset of illness index case : 9 days before diagnosis
- Tradition: Doctor shopping
- Overcrowded ER, hospital rooms
- Risk procedures in crowded rooms
- Tradition: Family and friends



This picture was tweeted by @HeyyltsJmo

186 confirmed cases
36 death
16,693 quarantine/isolation

Cluster Riyadh



3 sept 2015, IHR emergency committee on MERS-CoV:

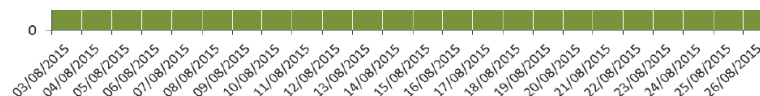
*“insufficient awareness about the urgent dangers posed by this virus,
insufficient engagement by all relevant sectors,
insufficient implementation of scalable infection control measures,
especially in health care settings such as emergency departments”*

“progress is not yet sufficient to control this threat ”

“The Committee further noted that its advice has not been completely followed. Asymptomatic cases that have tested positive for the virus are not always being reported as required. Timely sharing of detailed information of public health importance.....remains limited and has fallen short of expectations.

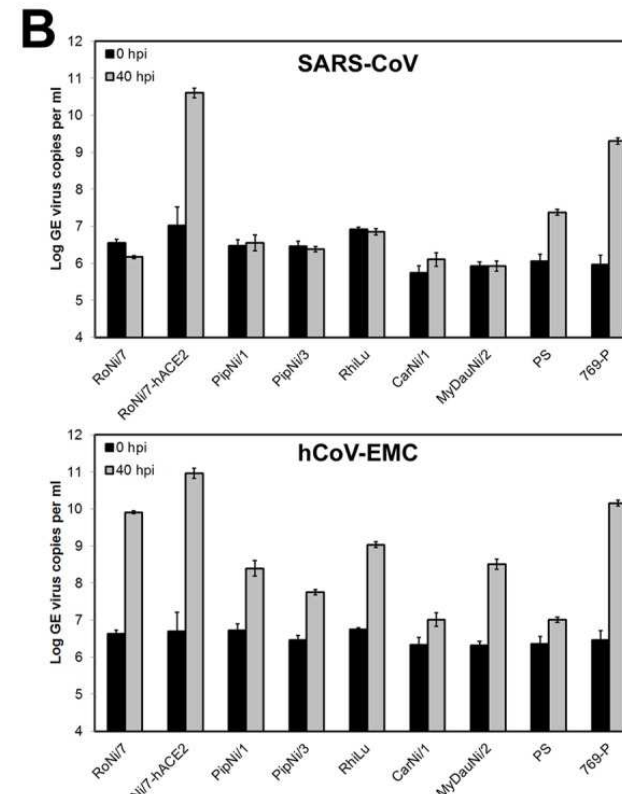
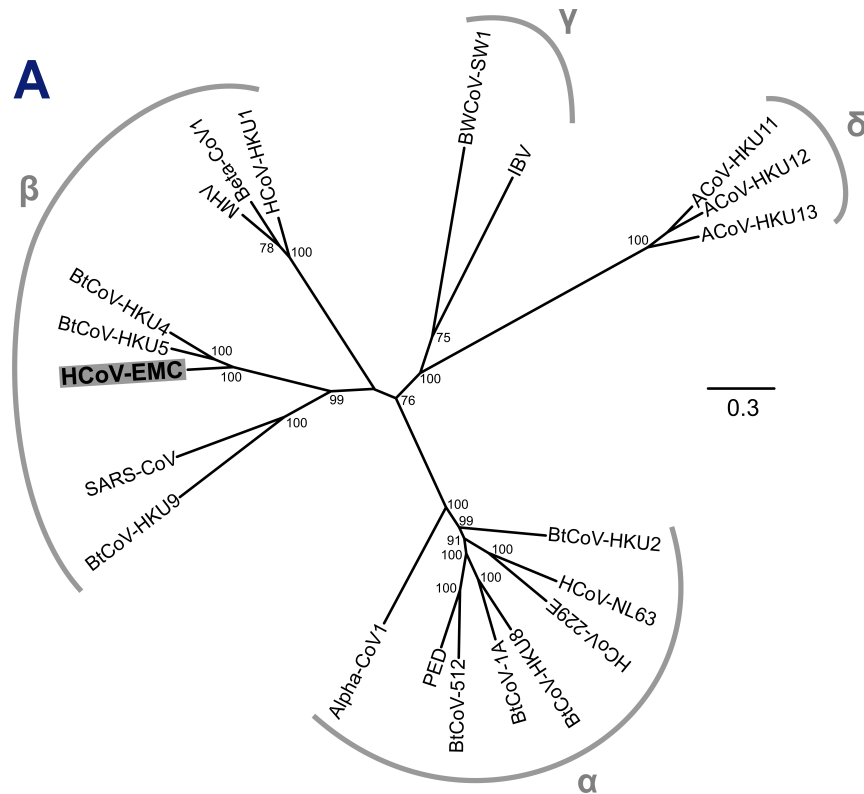
Inadequate progress has been made.....

The Committee was disappointed at the lack of information from the animal sector. ”



Source: ECDC

MERS-CoV zoonotic transmission from bats?



MERS-CoV is phylogenetically related to bat CoVs (A) and replicates in a range of bat cell lines (B), in contrast to SARS-CoV

(Van Boheemen et al., mBio 2012; Muller et al., MBio 2014)

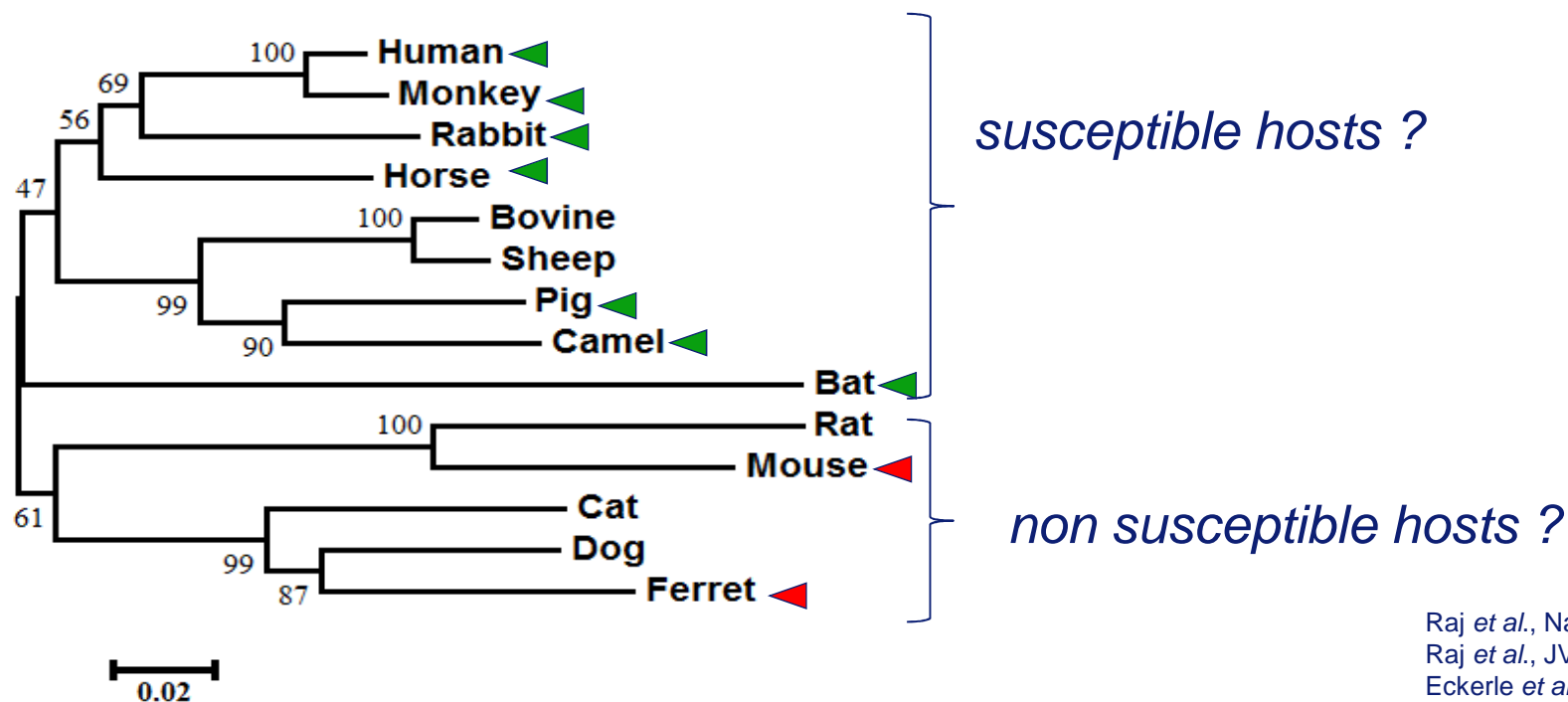
Deeper virus origins

Unlikely that bats are the immediate contact for the human cases as human contacts with bats occurs with relatively low frequency.

Plausible a spillover from bats to humans through intermediated species (e.g. domesticated animals or livestock).

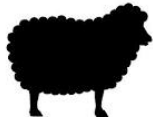


MERS-CoV binding region of DPP4



Raj *et al.*, Nature 2013
Raj *et al.*, JV 2014
Eckerle *et al.*, EID, 2014
v. Doremalen *et al.*, J. Virol 2014
Haagmans *et al.*, JV 2015

Livestock



N = 346; Egypt, Jordan, KSA, UAE



N = 244; Egypt, Jordan, KSA



N = 84; Egypt, Jordan, KSA



N = 8; Egypt



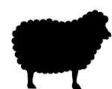
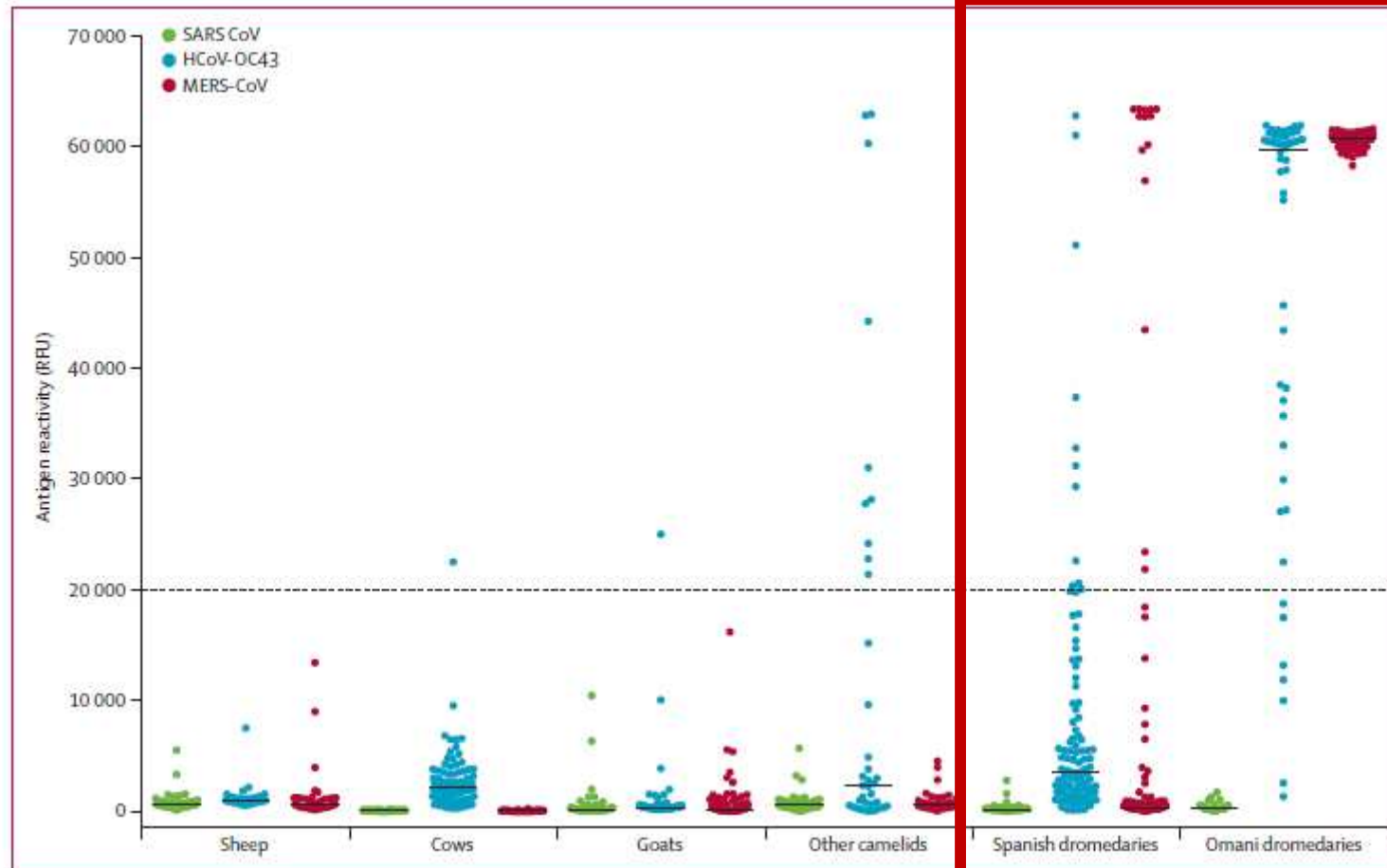
N = 192; UAE



N = 240; KSA

No evidence for MERS-CoV

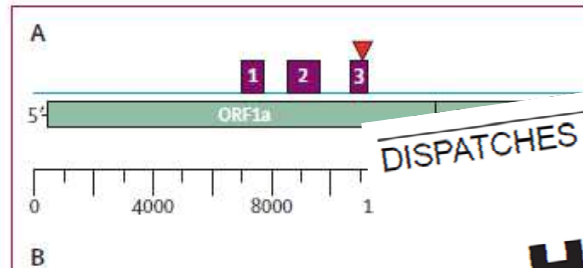
Reusken *et al.*, Eurosurveillance 2013
Hemida *et al.*, Eurosurveillance 2013
Perera *et al.*, Eurosurveillance 2013
Alexandersen *et al.*, Transbound Emerg. Dis, 2014
Alagaili *et al.*, Mbio, 2014
Meyer *et al.*, EID, 2015



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MERS-CoV outbreak human and camels same barn Qatar



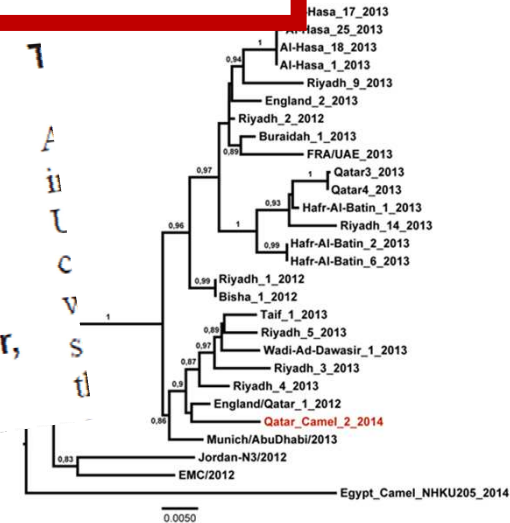
EID 2014

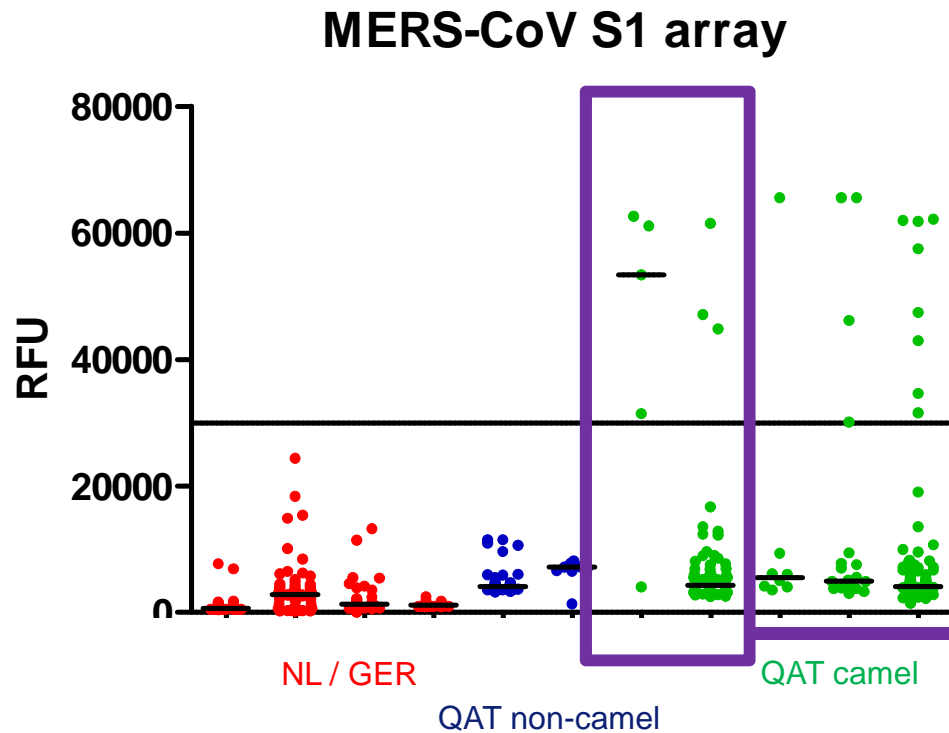
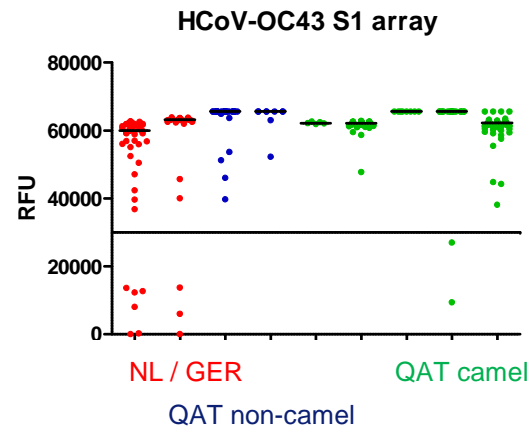
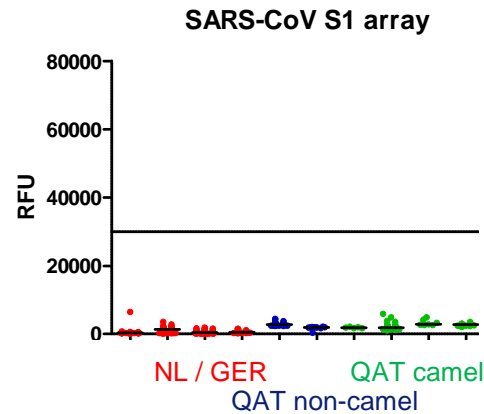
Human Infection with MERS after

Do people with daily exposure to camels/ camel products have a higher risk for MERS-CoV infection than people without camel contact?

Saudi Arabia, 2014

Ziad A. Memish, Matthew Cotten, Benjamin Meyer, Simon J. Watson, Abdullah J. Alsahafi, Abdullah A. Al Rabeeah, Victor Max Corman, Andrea Sieberg, Hatem Q. Makhdoom, Abdullah Assiri, Malaki Al Masri, Souhaib Aldabbagh, Berend-Jan Bosch, Martin Beer, Marcel A. Müller, Paul Kellam, and Christian Drosten





N=20 (20/294)
Confirmation 17/18 by
PRNT and/or IFA

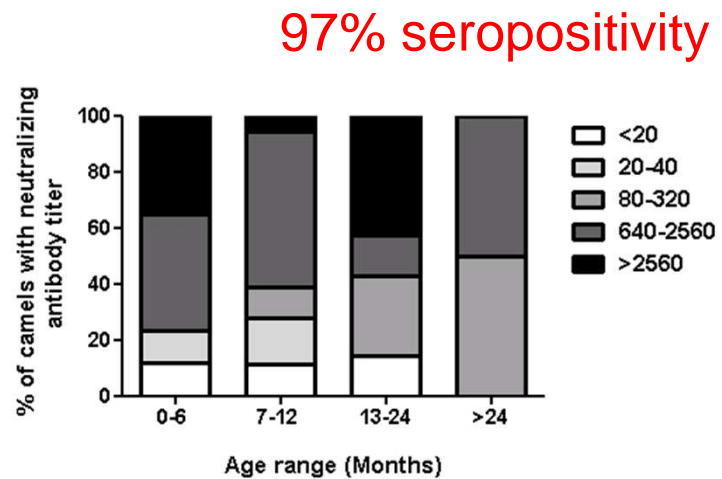
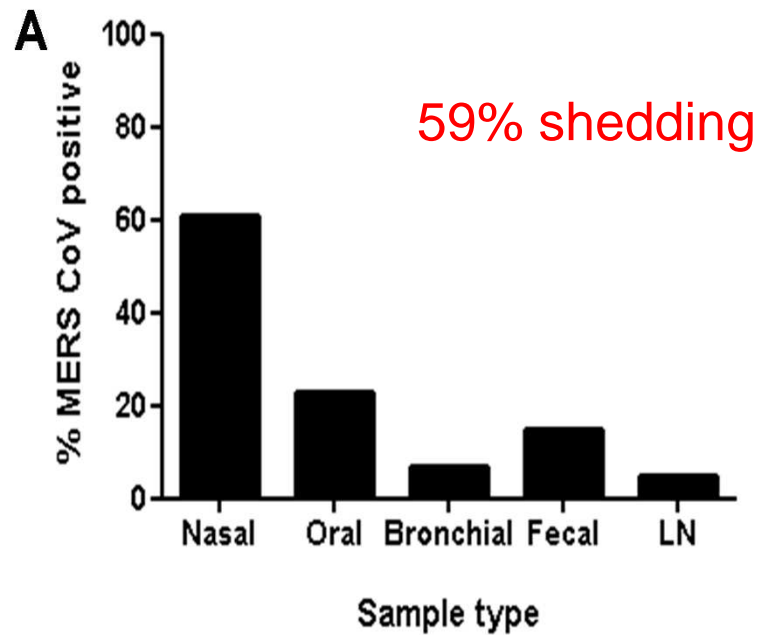
6.8% camel workers seropositive
all healthy!

Camel slaughterers 4/5
Sheep slaughterers 3/104

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High shedding rates slaughterhouse camels Qatar, n=105



Cross sectional studie KSA

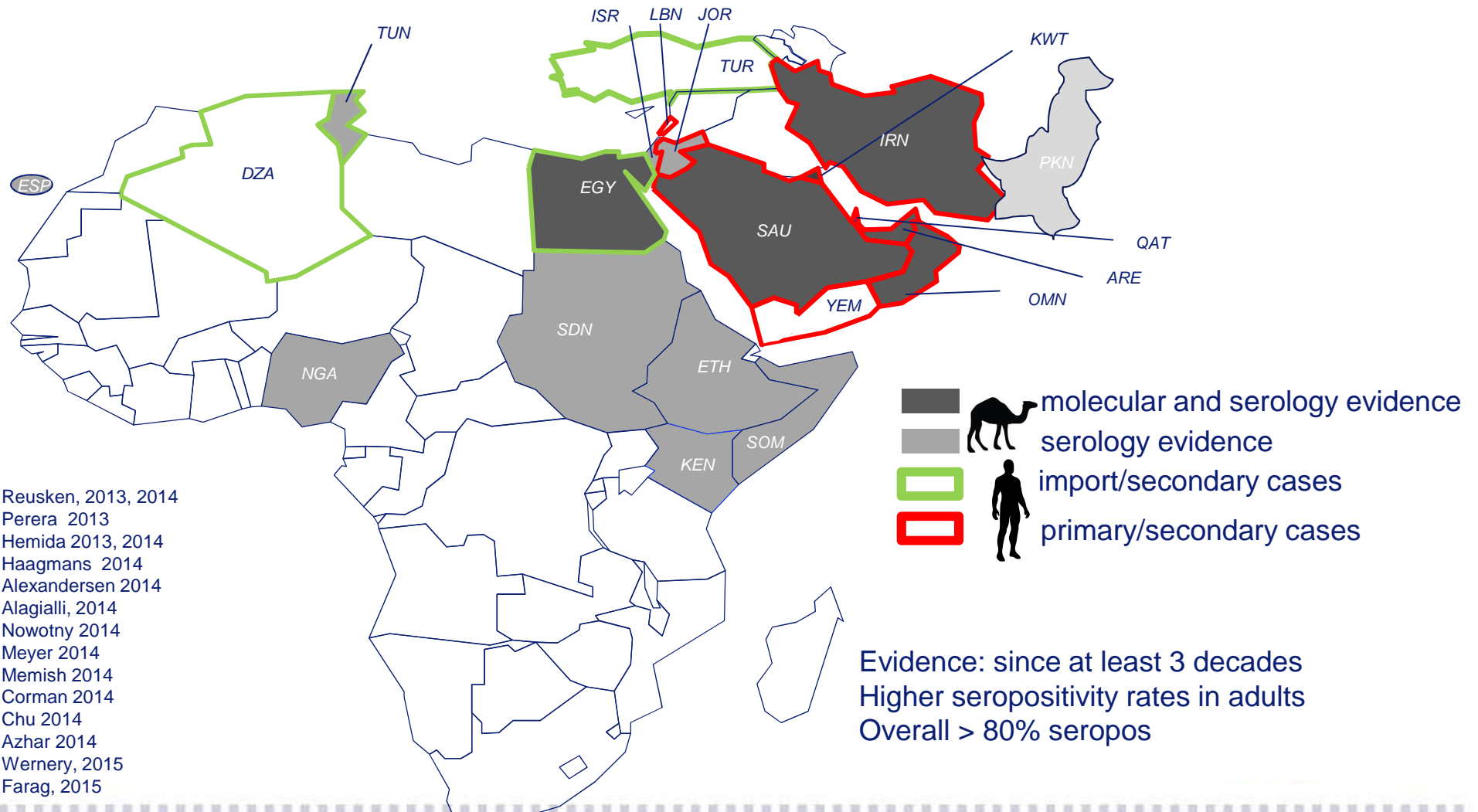


	Year of sampling	Total number	rELISA positive		Stage 1 seropositive		Stage 2 seropositive	
			n (%; 95% CI)	p value	n (%; 95% CI)	p value	n (%; 95% CI)	p value
General population	2012-13	10 009	152 (1.5%; 1.3-1.8)	NA	17 (0.2%; 0.1-0.3)	NA	15 (0.2%; 0.1-0.2)	NA
Camel shepherds	2014	87	6 (6.9%; 2.8-13.8)	p=0.0003	2 (2.3%; 0.3-7.4)	p=0.0009	2 (2.3%; 0.3-7.4)	p=0.0004
Slaughterhouse workers	2013	140	6 (4.3%; 1.8-8.7)	p=0.0224	5 (3.6%; 1.3-7.7)	p<0.0001	5 (3.6%; 1.3-7.7)	p<0.0001

Data are n (%; 95% CI) from a serosurvey, unless otherwise specified. p values refer to comparison with the general population cohort (χ^2 test with Yates correction two-tail test; OpenEpi). rELISA=recombinant ELISA. NA=not applicable.

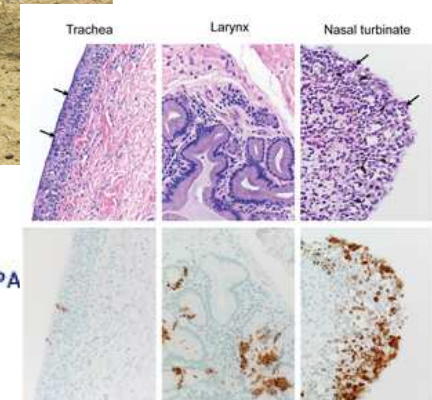
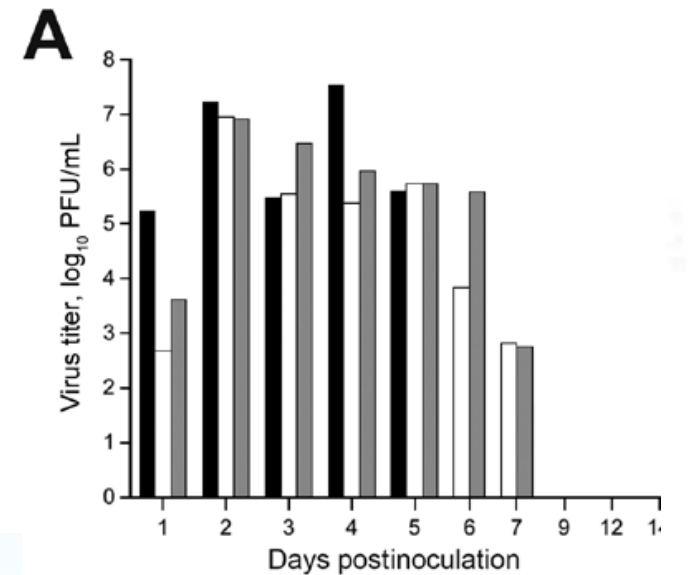
Table 1: Middle East respiratory syndrome coronavirus antibodies in the general and subpopulations of Saudi Arabia

Dromedaries as source for MERS-CoV



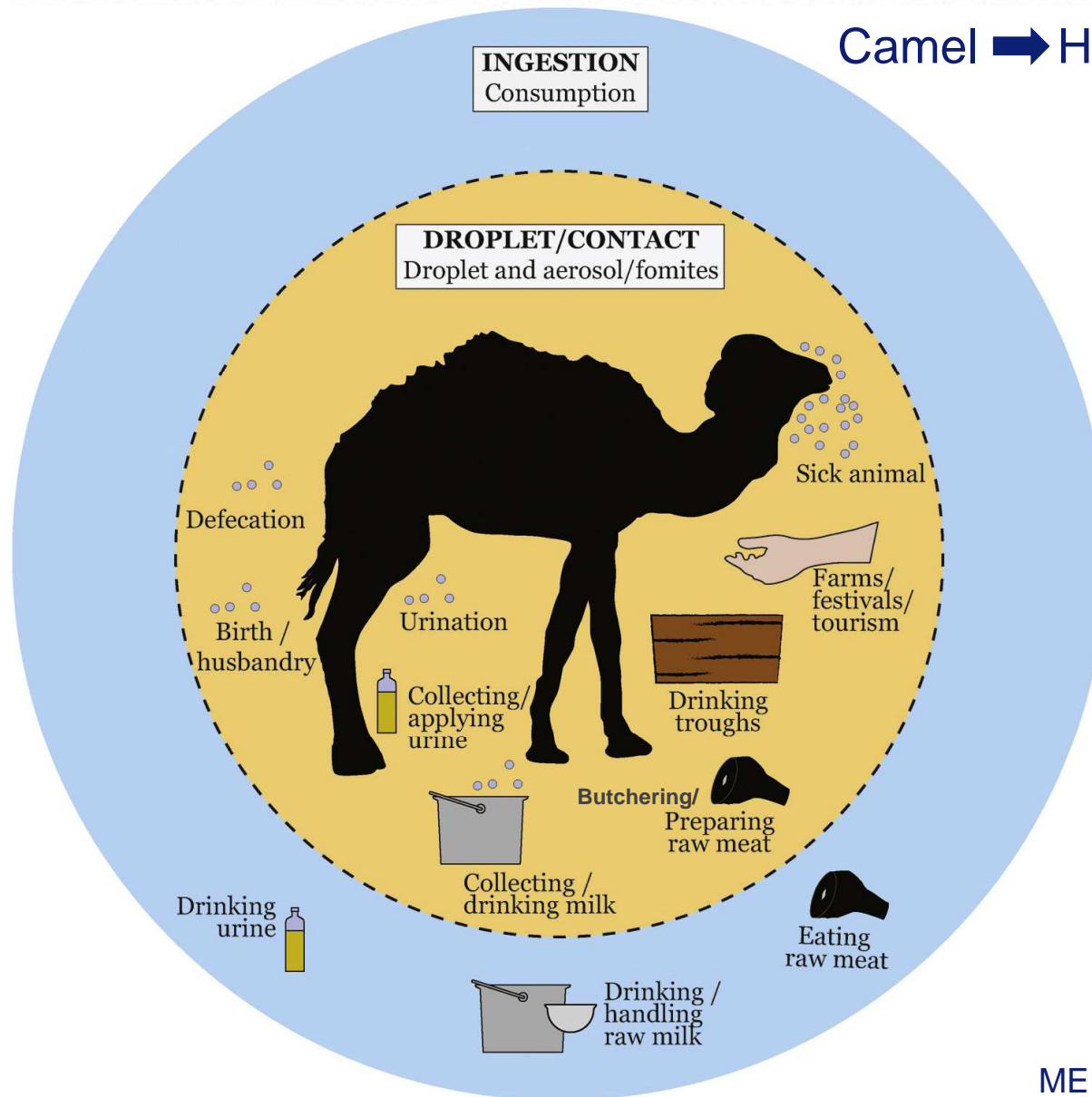
Dromedaries and MERS-CoV

- mild respiratory disease
- replication in URT
- shedding mainly from URT
- higher frequency shedding in camels < 2 yrs
- time-limited infection
- re-infection



Adney et al., EID 2014
Wernery et al., EID 2015
Hemida et al., EID 2014
Farag et al., IEE 2015
Haagmans et al., 2015 in press

Camel ➡ Human ?



MERS-CoV RNA in traditional milk Qatar

MERS-CoV stable in camel milk 72 h at 4 C
48 h at 22 C

Reusken *et al.*, Eurosurveillance 2014
vDoremalen *et al.*, Eurosurveillance 2013

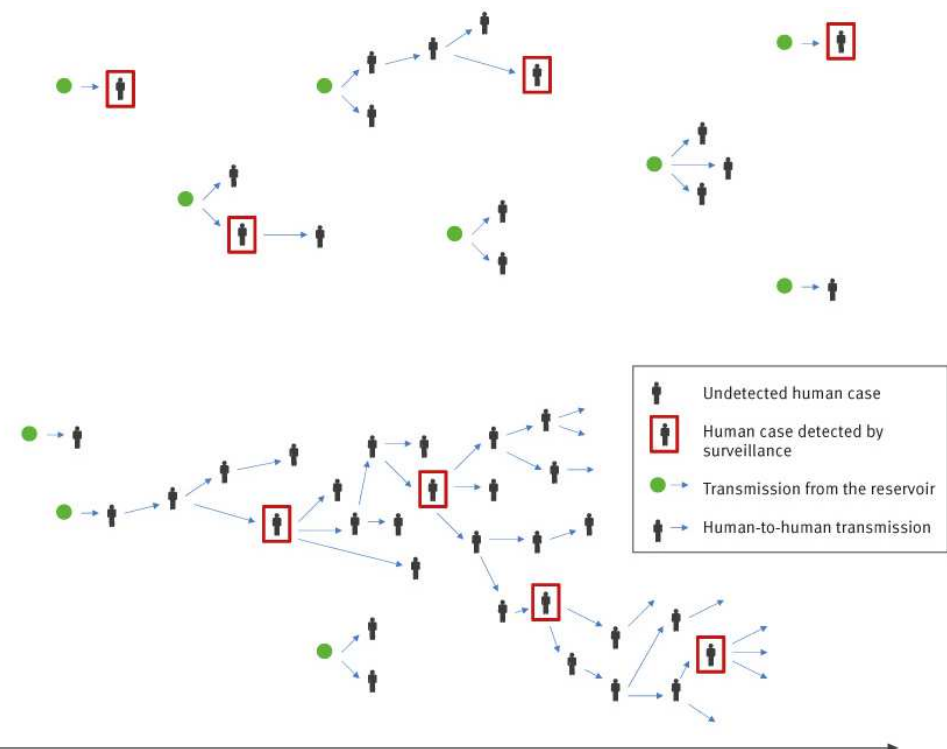


- Wide circulation in dromedary camels
- Multiple zoonotic events since 2012
- sporadic primary transmission camel -> human
- Seasonality, camel weaning period ?-> obscured by sec. transmission
- Occasional amplification through human-2-human transmission
 - nosocomial transmission, household setting (5%)
 - inefficient, low transmission rate in humans seems not self-sustaining ($R < 1$)



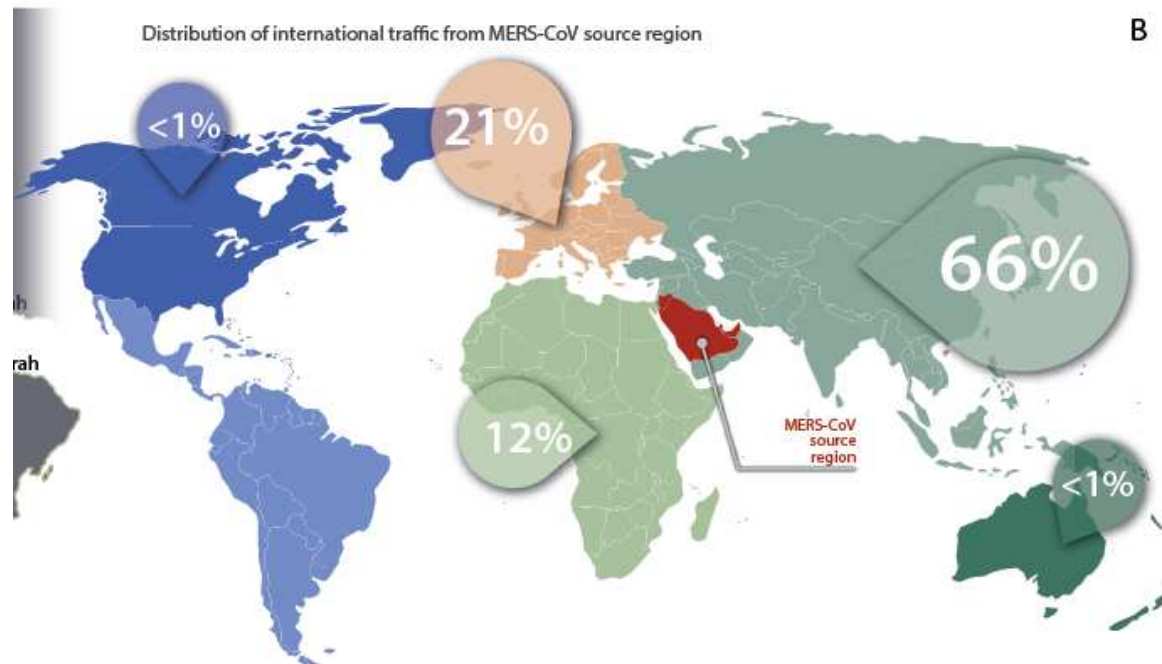
A. Spill-over events from the reservoir

B. Sustained transmission in humans



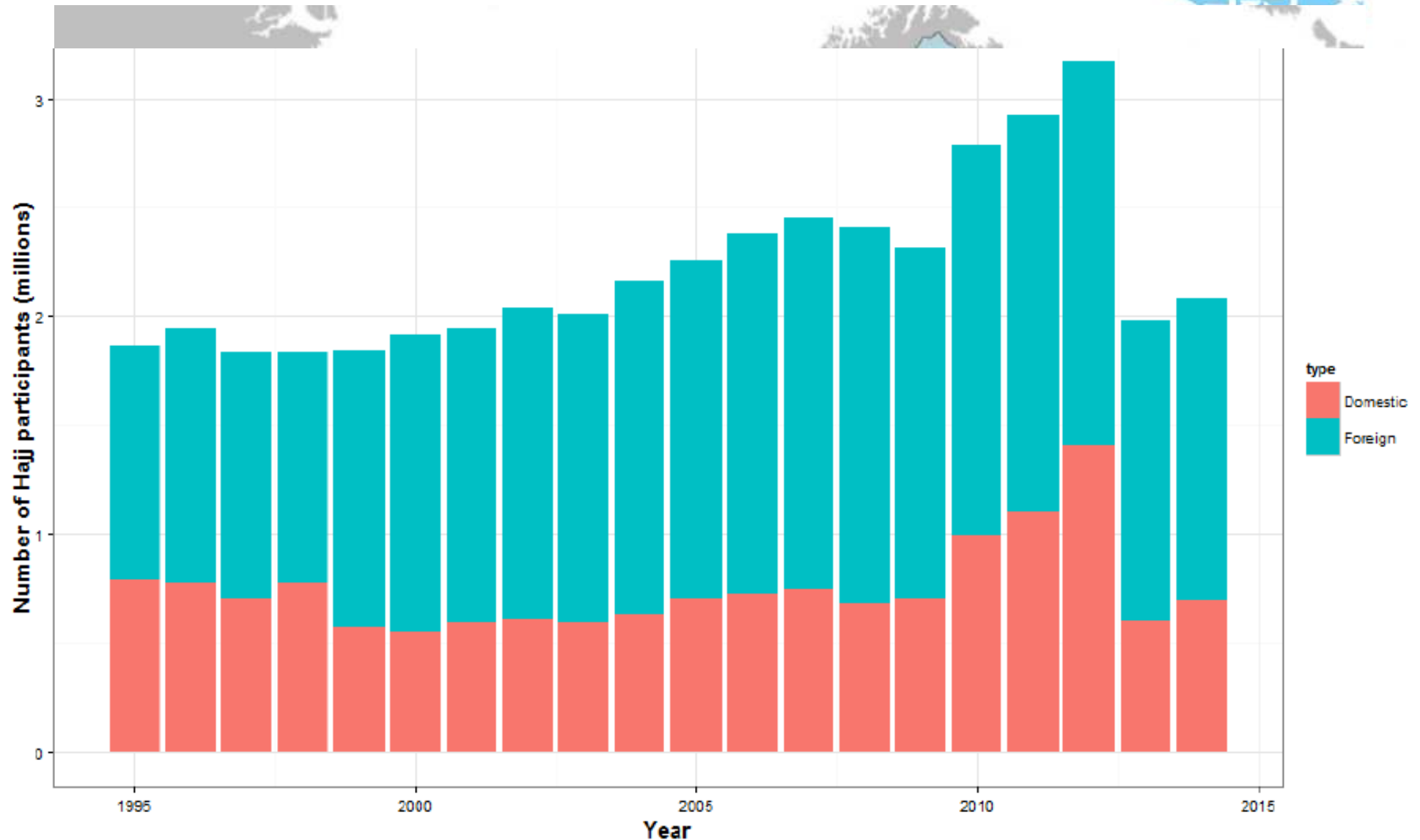


Large potential for international dissimination



Haji: 21-26 sept 2015

1,000 Haji permits per 1,000,000 muslims per country



Source: ECDC

Travel period Haji 2014

OSCIENCE LAB
ECT

Number of passengers

to Saudi Arabia

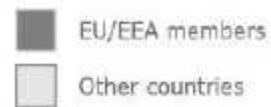
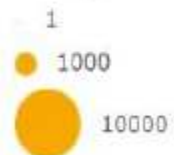
Aug - Oct 2014



Number of passengers

from Saudi Arabia

Aug - Oct 2014



Data source: IATA 2014

Source: ECDC

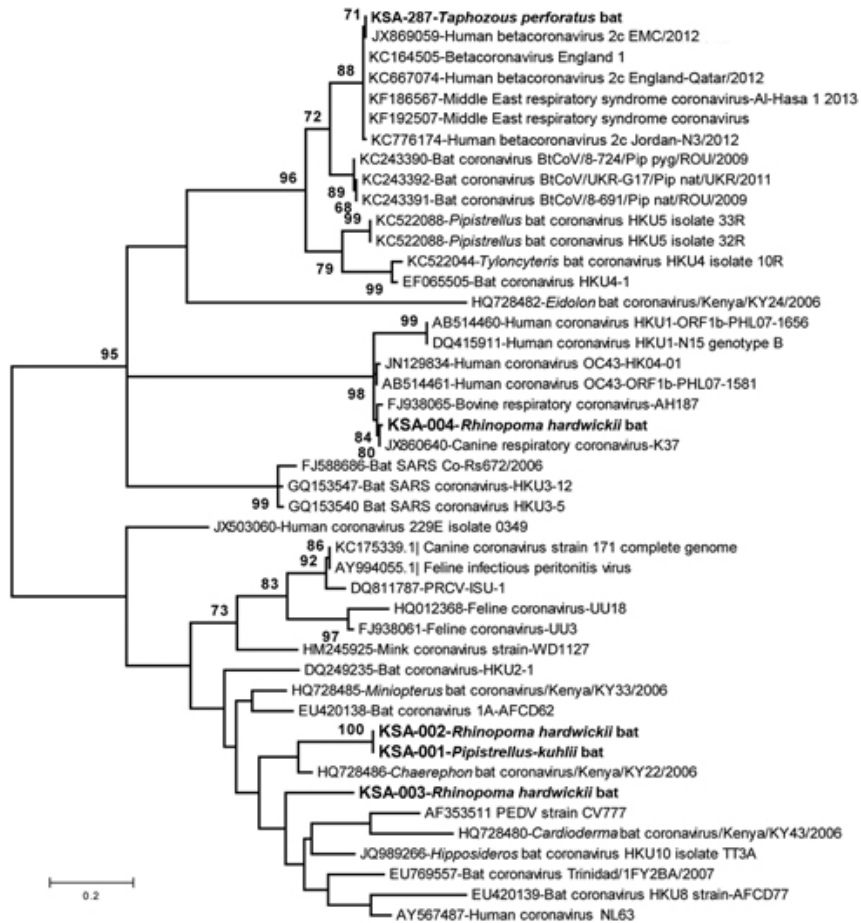
Be alert!!!



*Bart Haagmans
Stalin Raj
Saskia Smits
Suzan Pas
Annemiek van der Eijk
Theo Bestebroer
Ron Fouchier
Ab Osterhaus
Marion Koopmans*

Thank you





MERS CoV



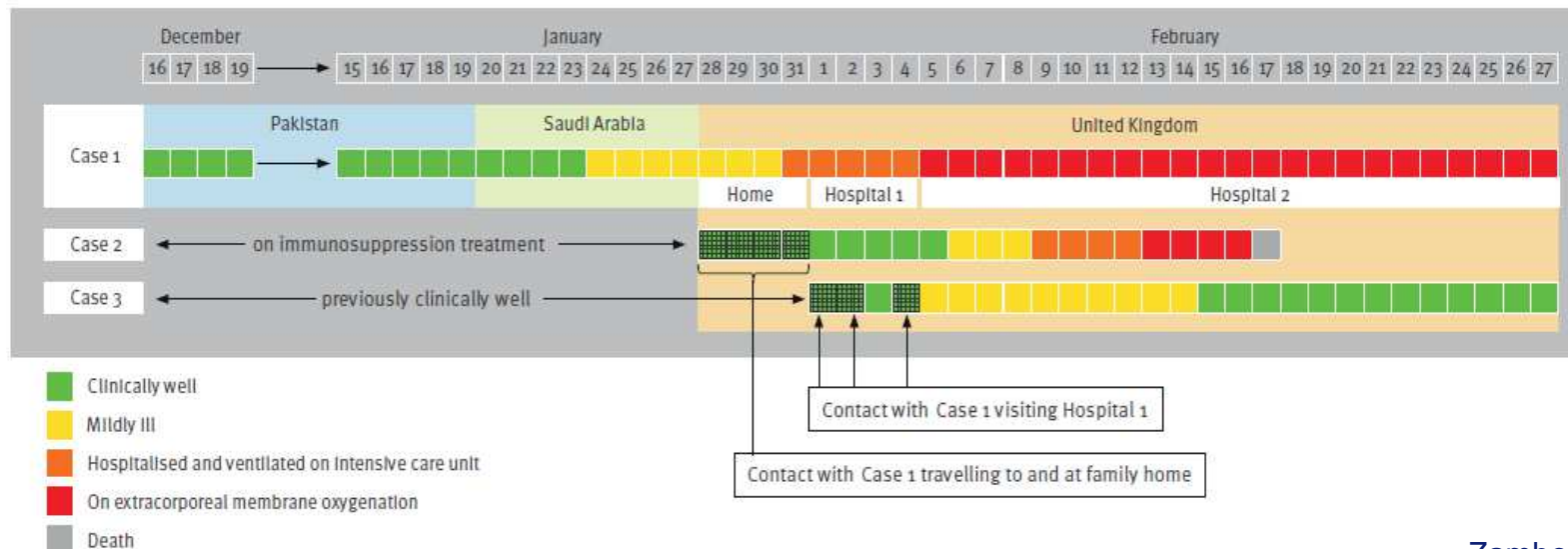
- * 181 nt fragment in conserved RdRp
- * Only 1 bat
- * Sequence identical to strain provided as control.
- No other fragments generated incl with WHO advised tests.

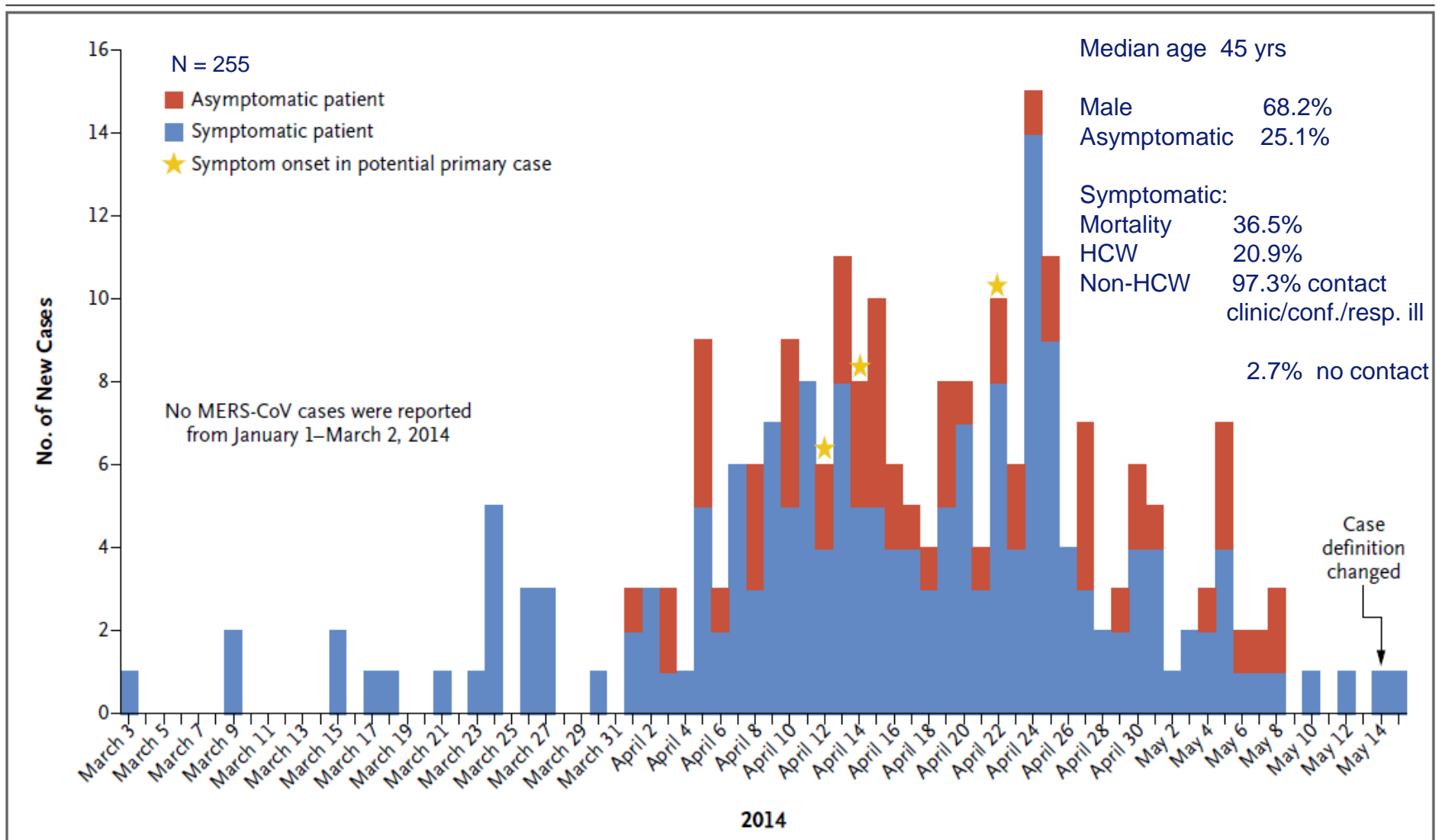
Cluster in the UK – Jan/Feb 2013 -> H2H transmission



- 3 confirmed cases
 - Primary case: 60Y male, travelling from Pakistan/Saudi Arabia
 - Onset on 24 January, 5 days after arriving in KSA (Makah/Medina)
 - Traveled to UK 4 days later, died 19 March
 - Secondary cases: household and hospital contacts (West Midlands area, UK)
 - 38y.o. son, immunosuppressed, onset 6 Feb, died on 17 Feb
 - 30y.o. niece, onset 5 Feb
- Lessons learned:
 - Human-to-human transmission confirmed.
 - co-infections happen (flu).

Drosten et al., NEJM 2014: H2H transmission in household contacts 5%





Oboho *et al.*, NEJM 2015

⇒ H2H transmission, amplification in health care facilities

⇒ No evidence for sudden increase in primary cases; exposure to animals was not assessed in this study!