Serological surveillance of FMDV transmission events over time in an isolated buffalo herd in the Kruger National Park

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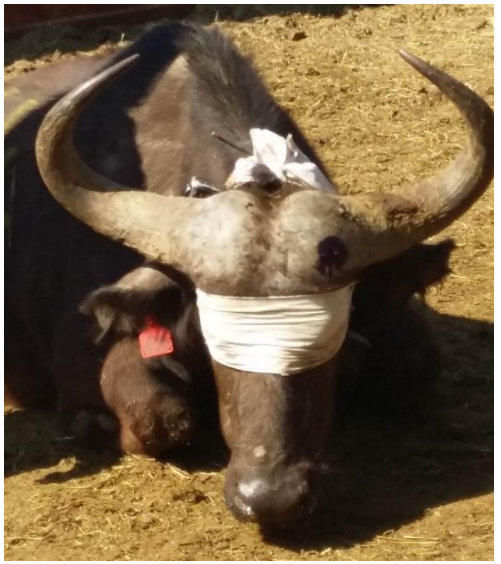


- Buffalo ecology, behaviour and physiology strongly mediated by seasonal cycles: body condition drops (nutritional restriction, dry season (KNP: June-Sept), re-gained with rains & new grass growth.

- Immunity in African buffalo varies seasonally in KNP (Beechler et al. 2009).
- Innate immune responses stronger in dry season (adaptive responses down-regulated)
- Trade-offs between immunity to intra- vs extra-cellular pathogens are detectable in dry season, but not in wet season.

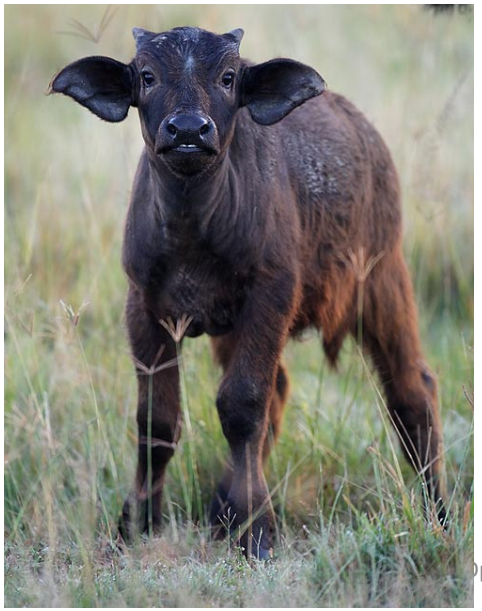
- Buffalo primary maintenance host of FMD but clinical FMD is mild, no obvious signs of FMD.

- Consequently, we expect strong seasonal variation, driven by resource availability, in co-infection patterns and immunity in free-ranging buffalo; which may mediate FMDV transmission dynamics.

- Buffalo virus recovery (field studies)
  - from individuals for 5yrs
  - isolated buffalo population (30-100) for 24 years

* FMDV can perpetuate long-term without re-introduction from neighbouring populations.

- However, the frequency & titre of virus recovered decreases over time and can clear virus over 15 months.
- significant number of animals fail to maintain persistent infection for prolonged periods as proportion of persistently infected animals falls after reaching a peak in 1-3 year age-group.
- Serological surveys - 98% exposed to SAT 1, 2 and 3 serotypes by 2 years old.
- FMDV must maintain a high force of infection in buffalo population continually.


•Given prolonged annual birth pulse, the virus might be maintained as typical "childhood" infection (circulating through new susceptible calves following loss of protective maternal immunity after 3-8 months of age) with the latest born calves of one year sparking the new epidemic.

•preliminary models of FMDV dynamics in free-ranging African buffalo suggest that calf-to-calf transmission alone is unlikely to result in long-term persistence of FMDV.

•Or annual epidemics among susceptible calves may be initiated by persistent carriers, or novel antigenic variants

FMDV specific	Mat. Protected	Susceptible	Infected	Recovered	Carrier	Recrudescent
Esophageal-pharyngeal viral titer	-	-	++	-	+	++
Mucosal antibody	-	-	++	-	+	++
Circulating antibody	+	-	-	+	+	+
Neutralizing antibody titres	+	-	-	+	+	+
Viremia	-	-	+	-	-	-

South Africa's FMD zones

Legend

- FMD Infected Zone
- FMD Protection Zone
- FMD High Surveillance Area
- Provinces

Limpopo
KNP
North West
Gauteng
Mpumalanga
Free State
KwaZulu-Natal
Northern Cape
Eastern Cape
Western Cape

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0 50 100 200 300 400 500 Kilometers

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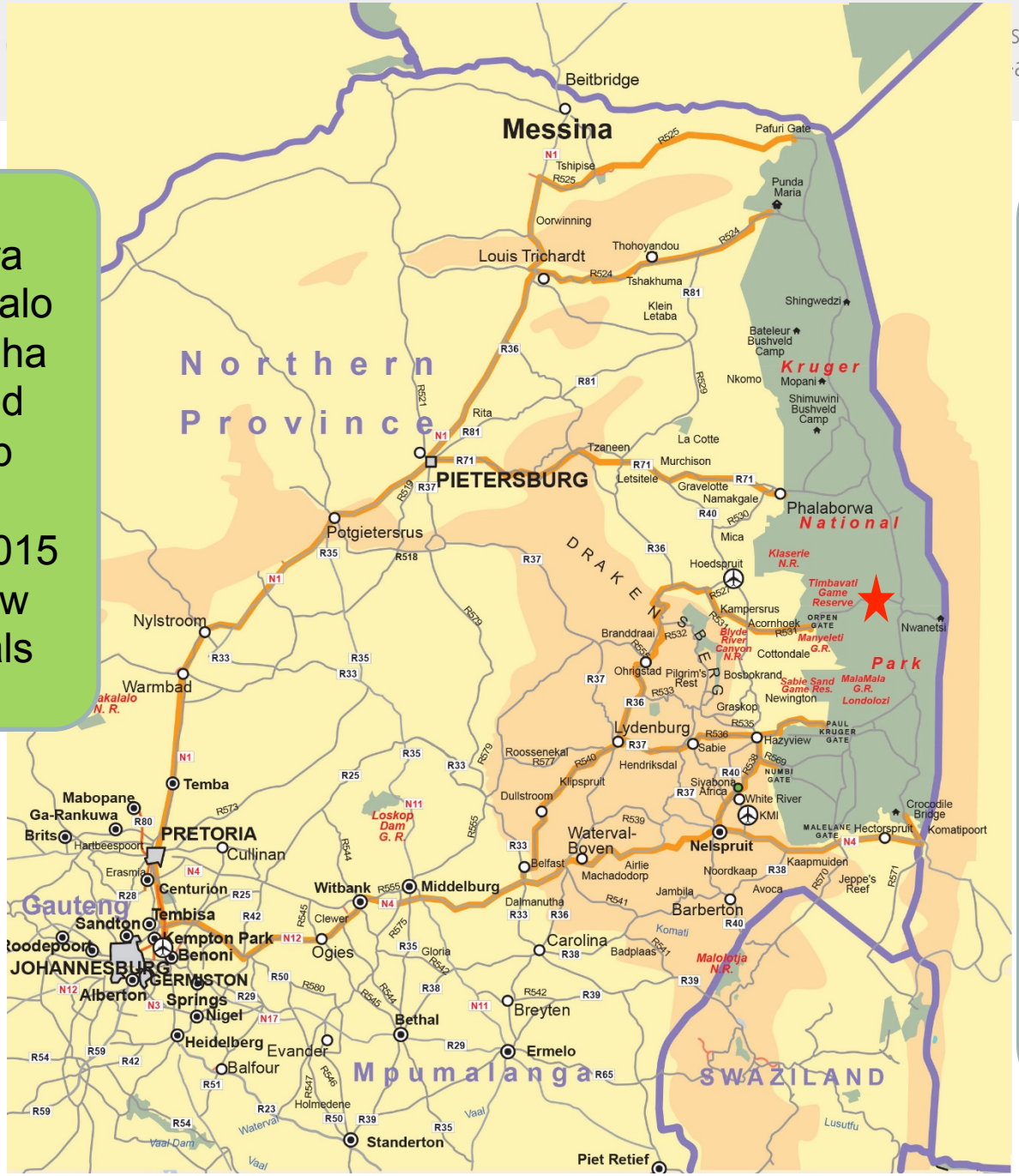
Agriculture, Forestry and Fisheries
REPUBLIC OF SOUTH AFRICA

Map created by:
Sub-directorate Epidemiology
Directorate Animal Health
Date: 24/07/2014

Satara
64 buffalo
in 900 ha
fenced
camp

June 2015
30 new
animals



FMD
Transmission
study:

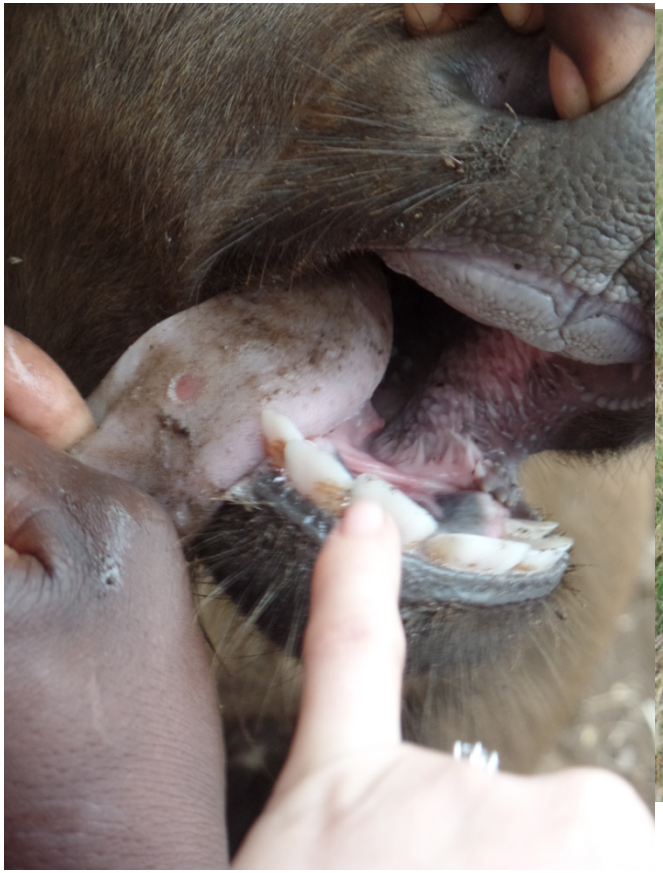
Sample every
2 months
for 3 years

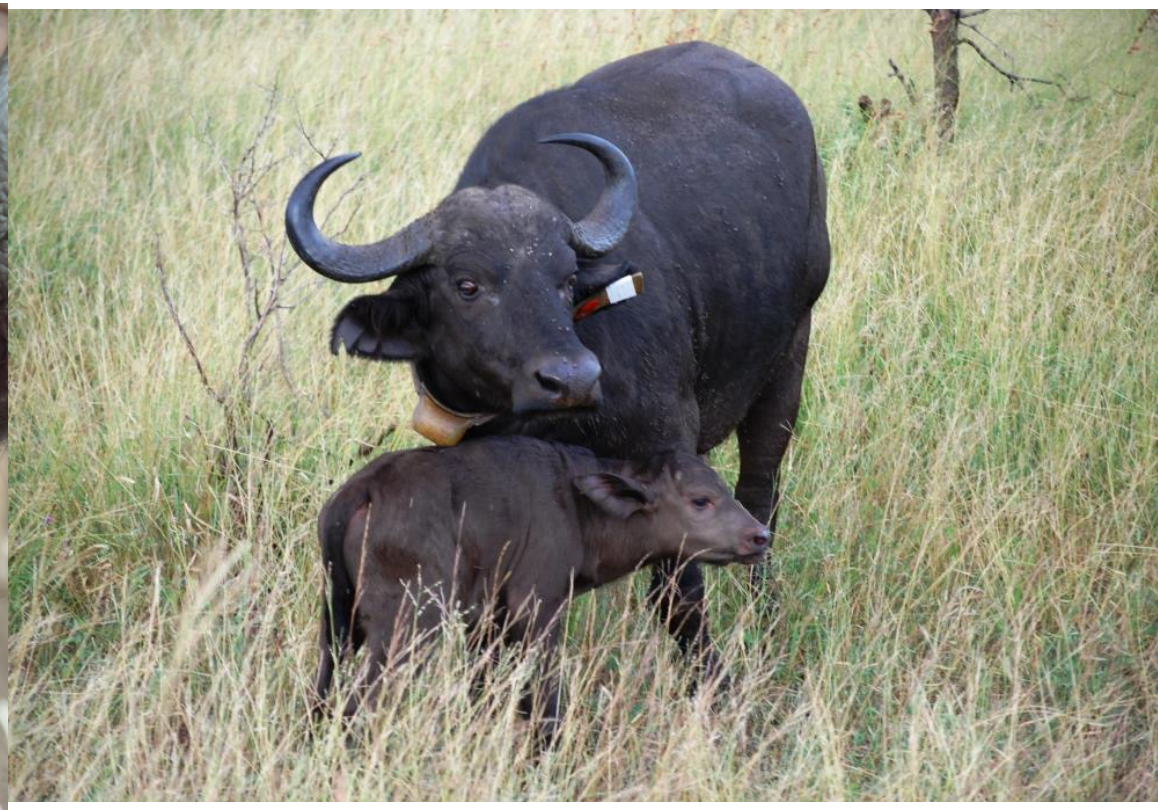
FMD:
Probangs
Tonsil swabs
Serum

Monitor FMD in
herd via
serology &
molecularly

Aims:

1. What is the seroprevalence of FMDV in herd (ages, sex) over time?
2. How variable are maternal FMDV antibodies and their drop-off over time?
3. What predicts antibody levels in mother - condition, antibody levels ?



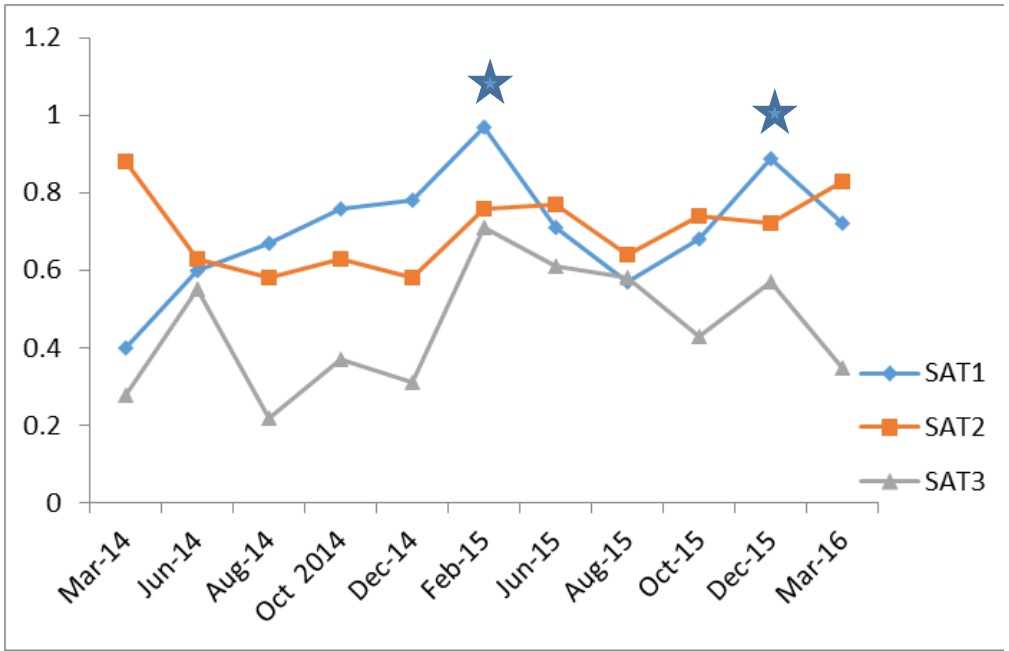


SEROPREVALENCE SAT1 >1.7

Season / Ages+Sex	total	Calf <6m	Calf 6-24m	Females 2-5y	Females 5-12 yr	Males 2-5y	Male 5-12 yr	M >12	F>12	prevalence
Mar-14	50	1(3)	1(13)	3(8)	4(9)	1(6)	2(3)	1(1)	7(7)	0.4
Jun-14	71	2(8)	11(14)	8(10)	7(11)	6(6)	2(3)	1(1)	6(9)	0.6
Aug-14	64	2(7)	8(15)	9(10)	7(10)	6(6)	4(6)	1(1)	6(9)	0.67
Oct 2014	62	0(0)	10(17)	9(9)	9(13)	8(8)	4(6)	0(0)	7(9)	0.76
Dec-14	55	0(0)	8(15)	6(8)	10(12)	6(6)	5(6)	0(0)	8(8)	0.78
Feb-15	46	2(2)	8(9)	6(6)	12(12)	7(7)	3(3)	0(0)	7(7)	0.97
Jun-15	77	6(19)	4(5)	11(11)	15(19)	6(6)	7(8)	0(0)	6(9)	0.71
Aug-15	69	0(11)	3(7)	6(11)	14(18)	5(6)	6(8)	0(0)	5(8)	0.57
Oct-15	65	0(0)	2(13)	11(11)	13(19)	4(4)	7(9)	1(1)	6(8)	0.68
Dec-15	47	0(0)	1(6)	9(9)	16(16)	3(3)	5(5)	2(2)	6(6)	0.89
Mar-16	60	0(0)	0(8)	8(8)	17(18)	7(7)	8(8)	2(2)	9(9)	0.72

-High prevalence spike Feb '15
-Upward increase from Mar'14-Feb'15
-Decline June-Aug'15

-High prevalence adults Dec '15-Mar'16
-Calves 6-24m - low prev Oct'15-Mar '16



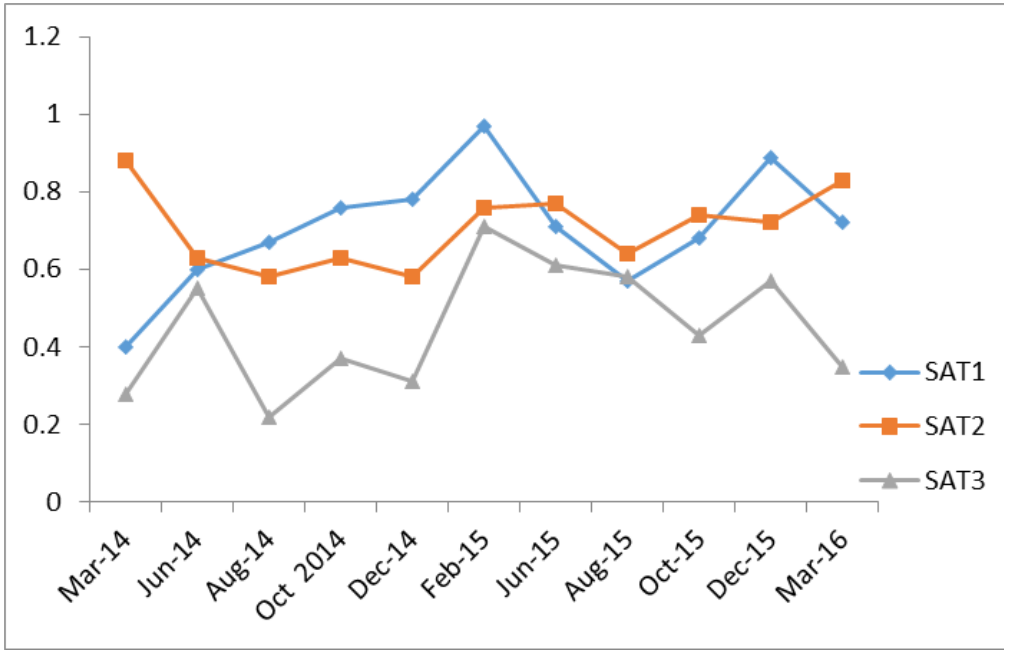
SEROPREVALENCE SAT2 >1.7

Season / Ages+Sex	total	Calf <6m	Calf 6-24m	Females 2-5y	Females 5-12 yr	Males 2-5y	Male 5-12 yr	M >12	F>12	
Mar-14	50	3(3)	7(13)	8(8)	9(9)	6(6)	3(3)	1(1)	7(7)	0.88
Jun-14	71	7(8)	5(14)	7(10)	9(11)	6(6)	3(3)	1(1)	7(9)	0.63
Aug-14	64	0(7)	0(15)	8(10)	8(10)	6(6)	5(6)	1(1)	9(9)	0.58
Oct 2014	62	0(0)	0(17)	6(9)	12(13)	6(8)	6(6)	0(0)	9(9)	0.63
Dec-14	55	0(0)	1(15)	5(8)	10(12)	3(6)	5(6)	0(0)	8(8)	0.58
Feb-15	46	2(2)	4(9)	4(6)	10(12)	6(7)	3(3)	0(0)	6(7)	0.76
Jun-15	77	13(19)	1(5)	6(11)	19(19)	4(6)	7(8)	0(0)	9(9)	0.77
Aug-15	69	2(11)	1(7)	6(11)	16(18)	4(6)	7(8)	0(0)	8(8)	0.64
Oct-15	65	0(0)	3(13)	6(11)	18(19)	3(4)	9(9)	1(1)	8(8)	0.74
Dec-15	47	0(0)	0(6)	5(9)	16(16)	2(3)	5(5)	2(2)	4(6)	0.72
Mar-16	60	0(0)	6(8)	5(7)	18(18)	3(7)	7(8)	2(2)	9(9)	0.83

- Prevalence remains 0.6-0.88
- Slight prevalence spike Mar'14, '15 & '16

low prevalence:

- June-Dec'15 – calves 0-24m & 2-5y females
- Calves 6-24m

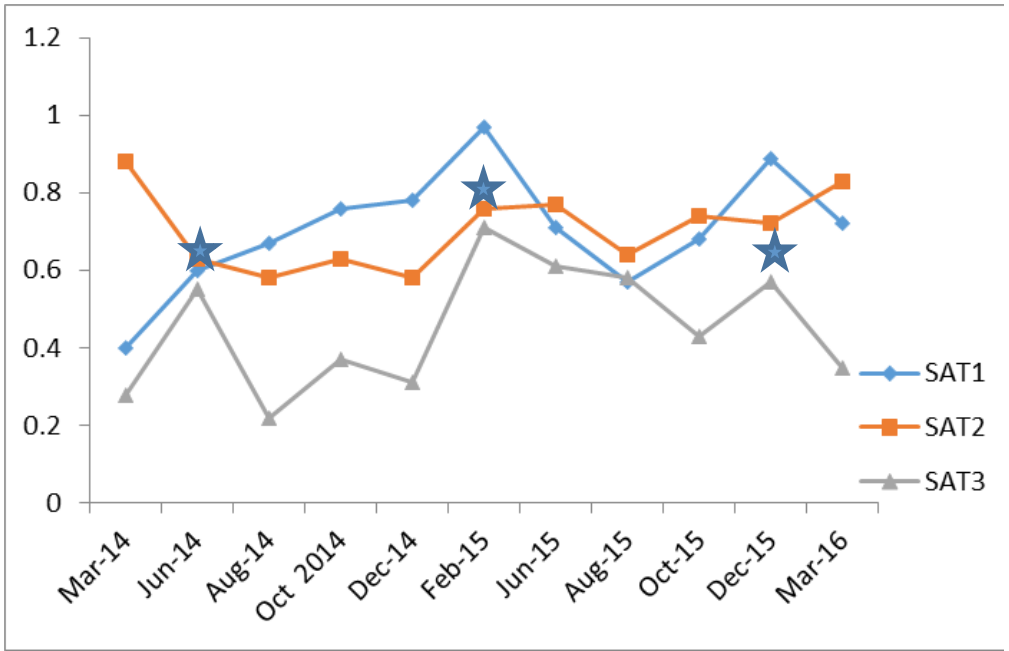


SEROPREVALENCE SAT3 >1.7

Season / Ages+Sex	total	Calf <6m	Calf 6-24m	Females 2-5y	Females 5-12 yr	Males 2-5y	Male 5-12 yr	M >12	F>12	
Mar-14	50	1(3)	1(13)	3(8)	1(9)	1(6)	0(3)	1(1)	6(7)	0.28
Jun-14	71	4(8)	6(14)	7(10)	6(11)	4(6)	1(3)	1(1)	6(9)	0.55
Aug-14	64	0(7)	0(15)	4(10)	2(10)	1(6)	1(6)	0(1)	6(9)	0.22
Oct 2014	62	0(0)	3(17)	4(9)	5(13)	4(8)	1(6)	0(0)	6(9)	0.37
Dec-14	55	0(0)	1(15)	1(8)	6(12)	3(6)	1(6)	0(0)	5(8)	0.31
Feb-15	46	1(2)	2(9)	6(6)	8(12)	6(7)	3(3)	0(0)	7(7)	0.71
Jun-15	77	8(19)	1(5)	7(11)	15(19)	5(6)	4(8)	0(0)	7(9)	0.61
Aug-15	69	0(11)	2(7)	7(11)	14(18)	6(6)	6(8)	0(0)	5(8)	0.58
Oct-15	65	0(0)	0(13)	6(11)	8(19)	2(4)	4(9)	0(1)	8(8)	0.43
Dec-15	47	0(0)	0(6)	5(9)	12(16)	2(3)	3(5)	1(2)	4(6)	0.57
Mar-16	60	0(0)	0(8)	2(7)	13(18)	2(7)	4(8)	0(2)	0(2)	0.35

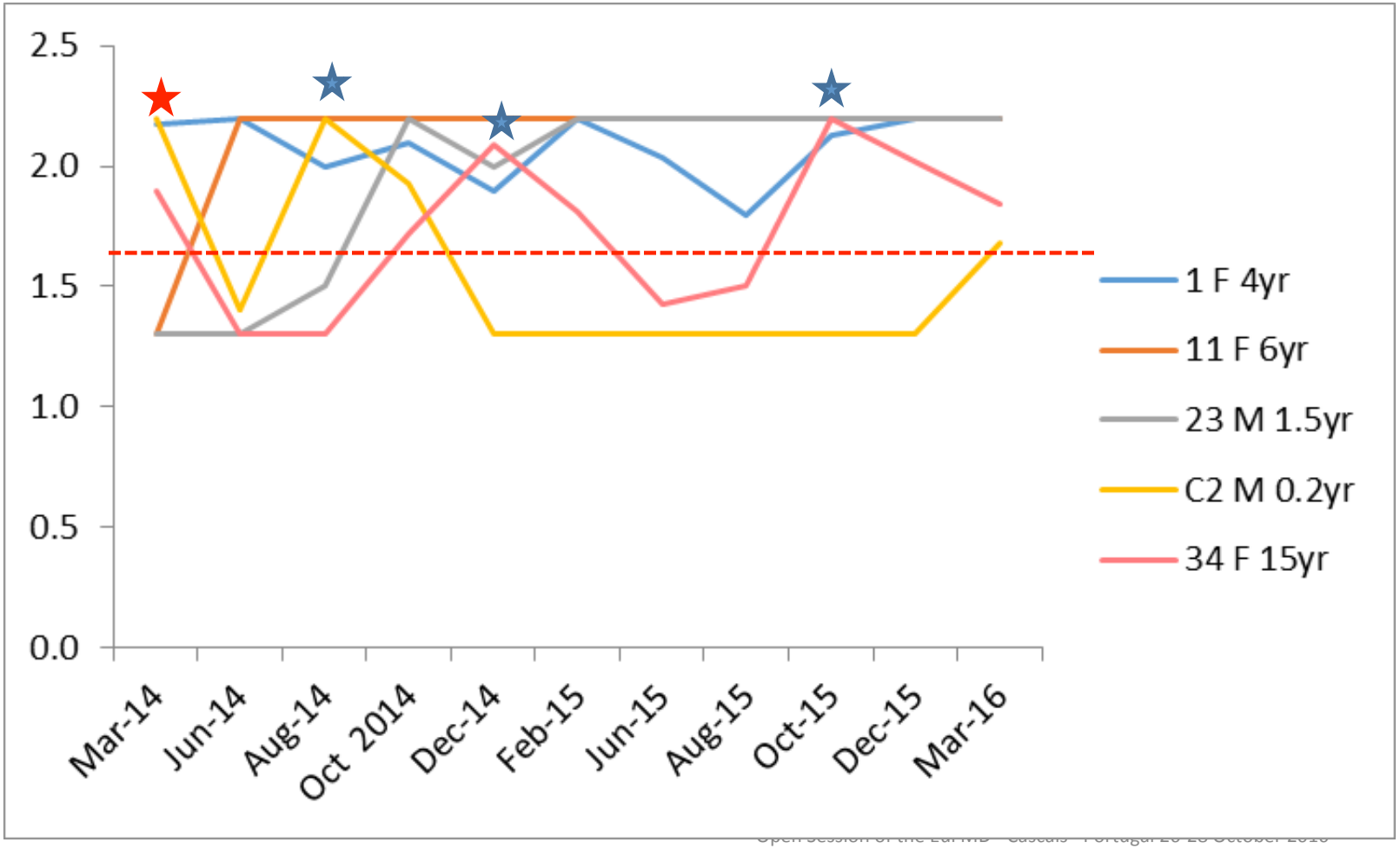
- Peaks in June'14, Feb'15 & Dec'15
- Remains lower compared to SAT1&2.
- Low prevalence in each age group.

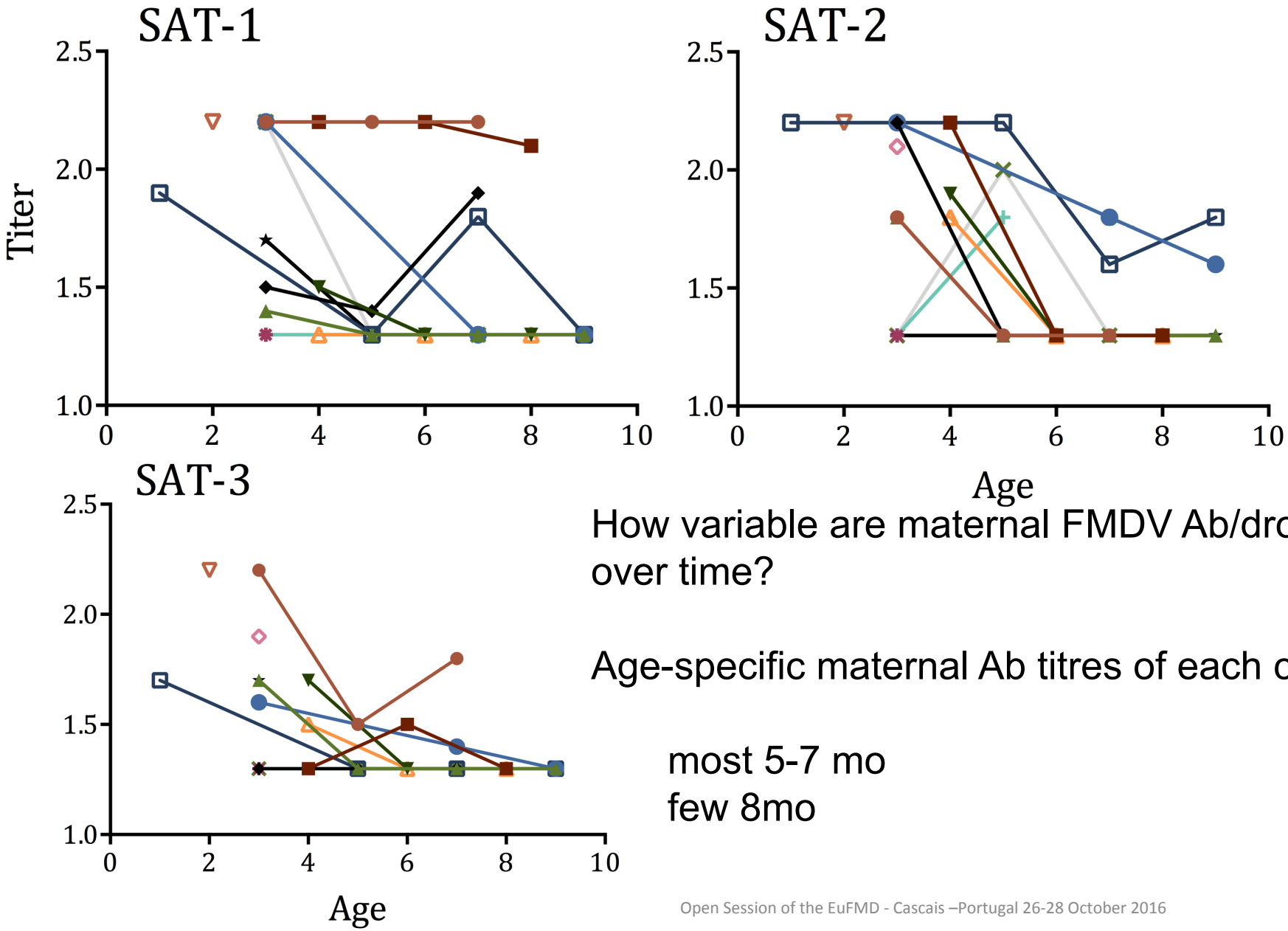
- Possibly sustained through low level transmission
- Competition with SAT1 & 2?



Example of Incidence

Reinfection similar virus after waning Ab?
Superinfection?
Suppression in Ab due to other disease/stress?



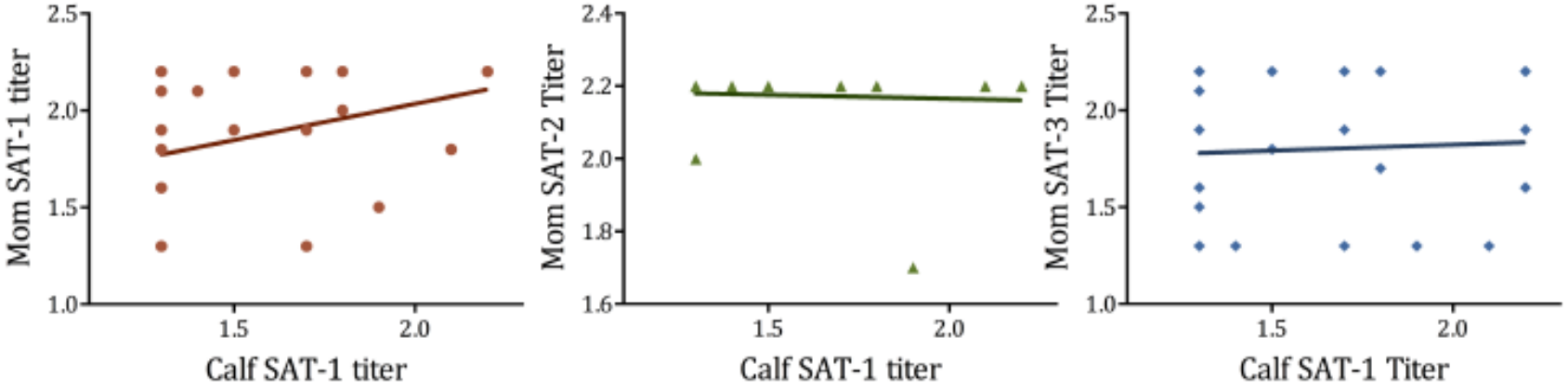


How variable are maternal FMDV Ab/drop off over time?

Age-specific maternal Ab titres of each calf

most 5-7 mo
few 8mo

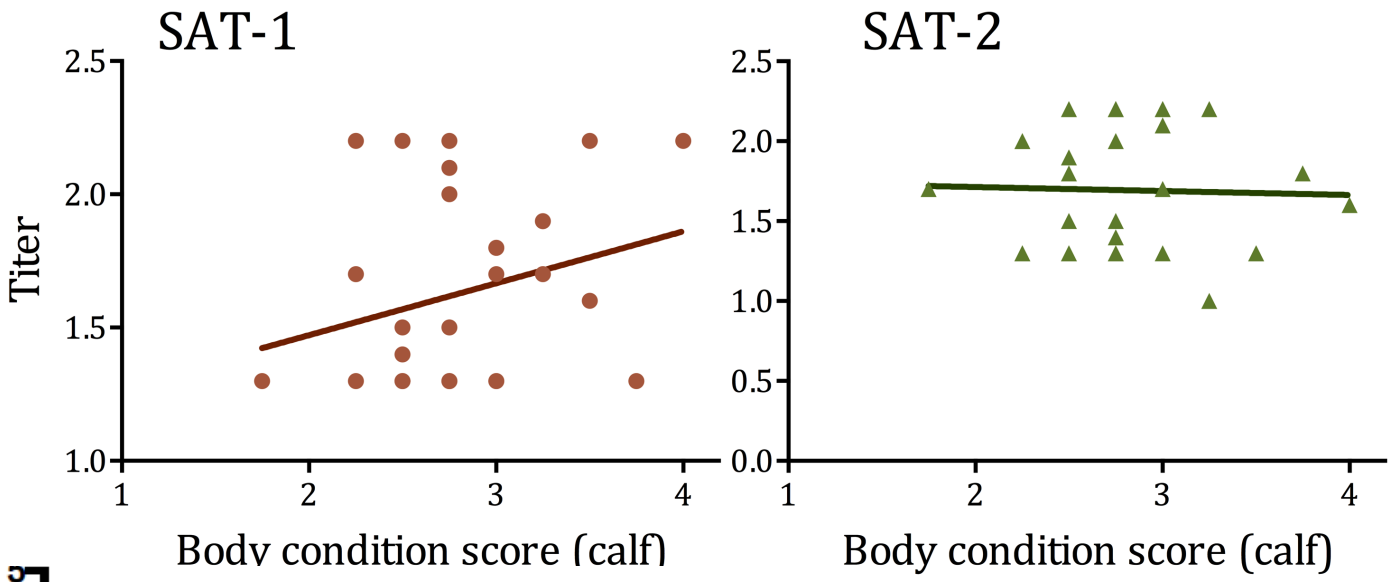
Correlation betw **maternal Ab titres of calf** and **mother titres**

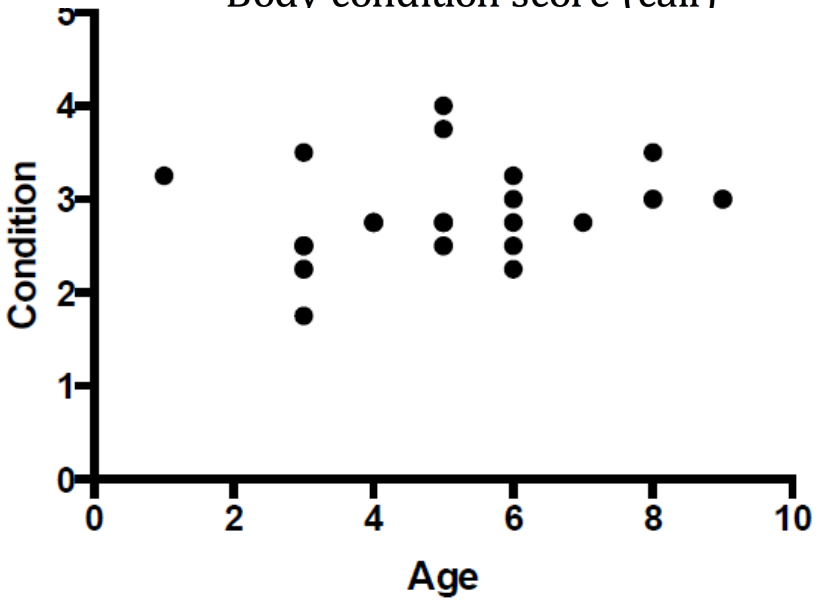


- Reflects March 2014 sampling point (study started) calves <6 mo
- Correlated to other serotype SAT2 & 3 (mom vs calf)
- Significant correlation betw mother SAT1 titre and calf SAT1 titre

- There was no association between SAT2 or SAT3 (not shown).

What predicts antibody levels in mother - condition, antibody levels ?





- A calf's body condition (at first capture) was not significantly associated with FMDV titre for any of the SATs
- More driven by maternal influence

- Condition not correlated with age


F190

Conclusions

- Seroprevalence:

SAT1 fluctuates
SAT2 remains constant
SAT3 remains low but shows peaks

- Maternal Ab titre correlated to calf Ab titre for SAT1
- Body condition not related to Ab titre or age
- Maternal Ab wane 5-7 months

Future work

- Look at Incidence and establish transmission events
- Analyse real-time PCR and virus isolation (probangs/tonsil swabs/sera) data together with serology to differentiate infected vs recovered vs carrier vs recrudescence
- Sequence isolated viruses to determine recrudescence or superinfection
- Other parameters such as co-infections, contacts etc to be modelled.

FMDV specific	Mat. Protected	Susceptible	Infected	Recovered	Carrier	Recrudescent
Esophageal-pharyngeal viral titer	-	-	++	-	+	++
Mucosal antibody	-	-	++	-	+	++
Circulating antibody	+	-	-	+	+	+
Neutralizing antibody titres	+	-	-	+	+	+
Viremia	-	-	+	-	-	-


Thank you!
Questions