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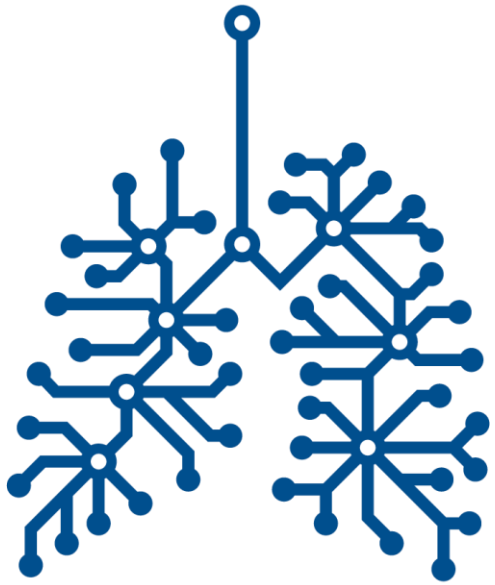

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Experimental Respiratory Syncytial Virus Infection in Adults 60-75 years

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Conflict of interest disclosure

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❑ **I have the following real or perceived conflicts of interest that relate to this presentation:**

Affiliation / Financial interest	Commercial company
Grants/research support:	n/a
Honoraria or consultation fees:	n/a
Participation in a company sponsored bureau:	n/a
Stock shareholder:	Alex Mann is an employee of and has shares in hVIVO
Spouse / partner:	n/a
Other support / potential conflict of interest:	n/a

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Rationale/Aims

Human vaccine challenge studies in 60-75 year-old subjects enables exploration of…

- RSV vaccine-induced immune response and efficacy in the context of potential immune senescence
- Identify the correlates of protection from RSV infection and disease in one of the vaccine's target populations

- This was a pilot study to establish the safety and pathogenicity in 60-75 year-old subjects

Study Design: RSV 60-75 yrs

Age – 60-75 yrs (8%≥70yrs), initially 60-69yrs, then 70-75yrs

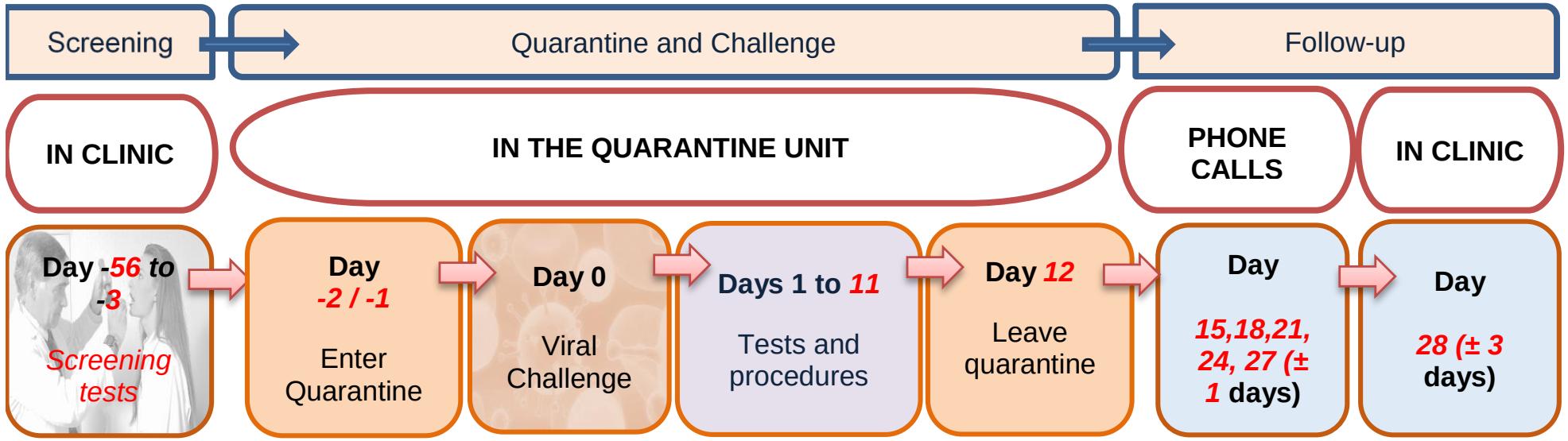
Gender – 6 Female/18 Male

Smoking history – non-smokers / social / low level smokers

Acceptable comorbidities – e.g. stable age related conditions (investigator discretion)

No known "at-risk" factors – e.g. cardiovascular, respiratory disease

Antibody screening – Subjects only excluded if no pre-existing MNA titre to RSV Memphis 37b



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PCR viral load time course in infected 18-55 & 60-75 year old subjects

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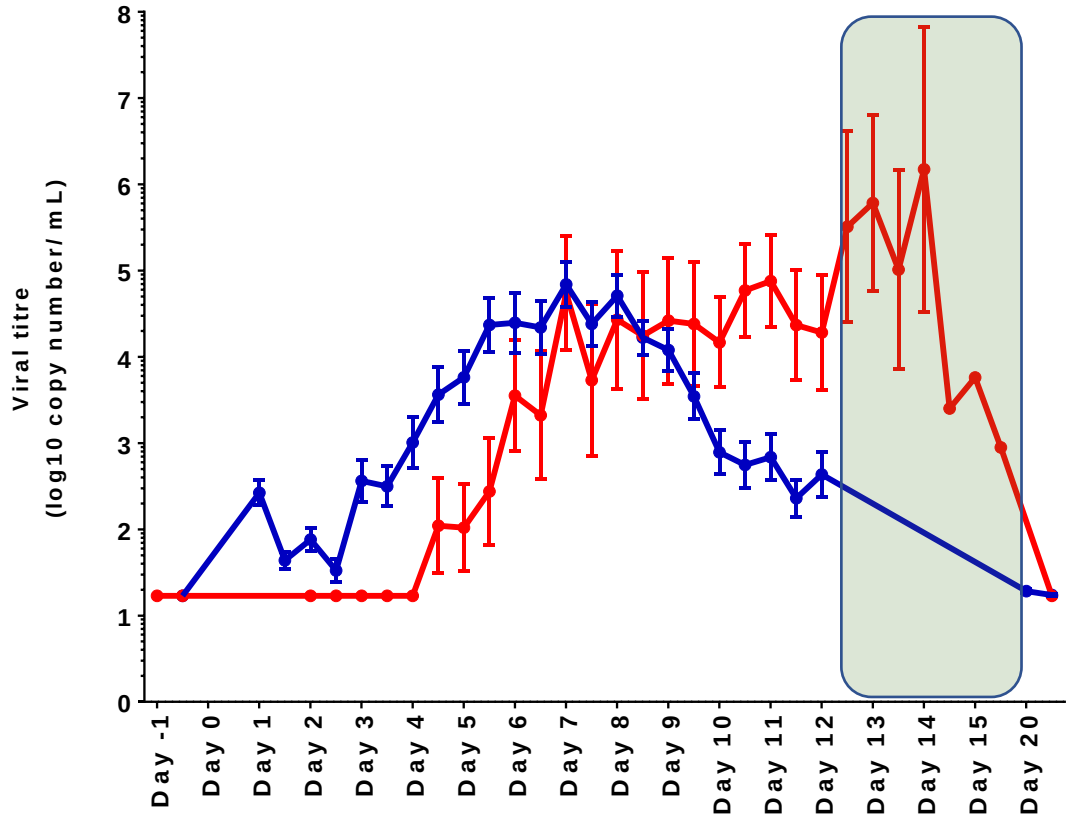

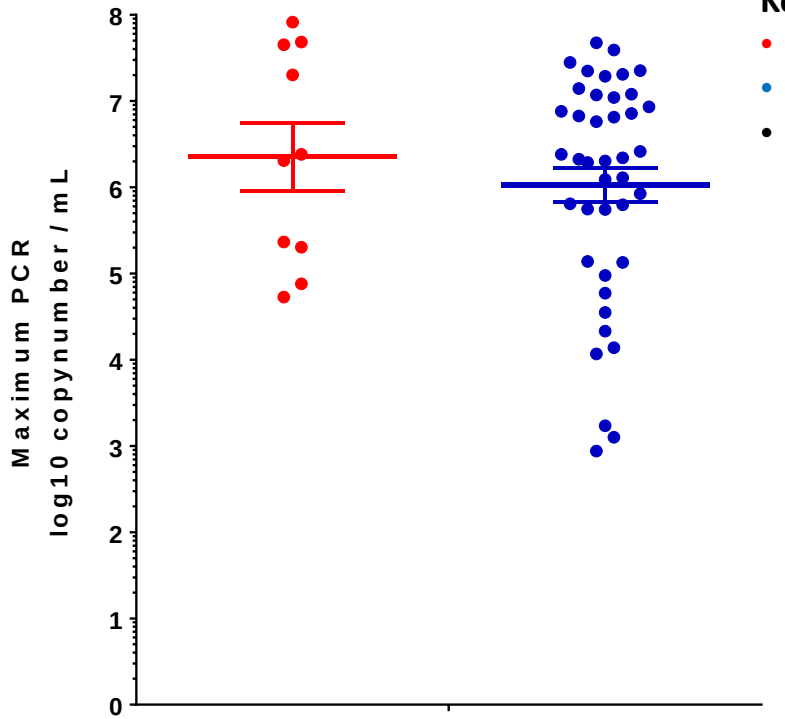

Key:

- Red = 60-75 year olds
- Blue = 18-55 year olds
- **Infected:** 2 quantifiable PCR within 2 days

- A proportion of infected 60-75 year old subjects have a delayed onset of virology compared to the younger subject model (all 18-55 year old subjects discharged on day 12)
- No statistical differences between 18-55 and 60-75 year old model maximum viral titres

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Total symptom time course in infected 18-55 & 60-75 year old subjects

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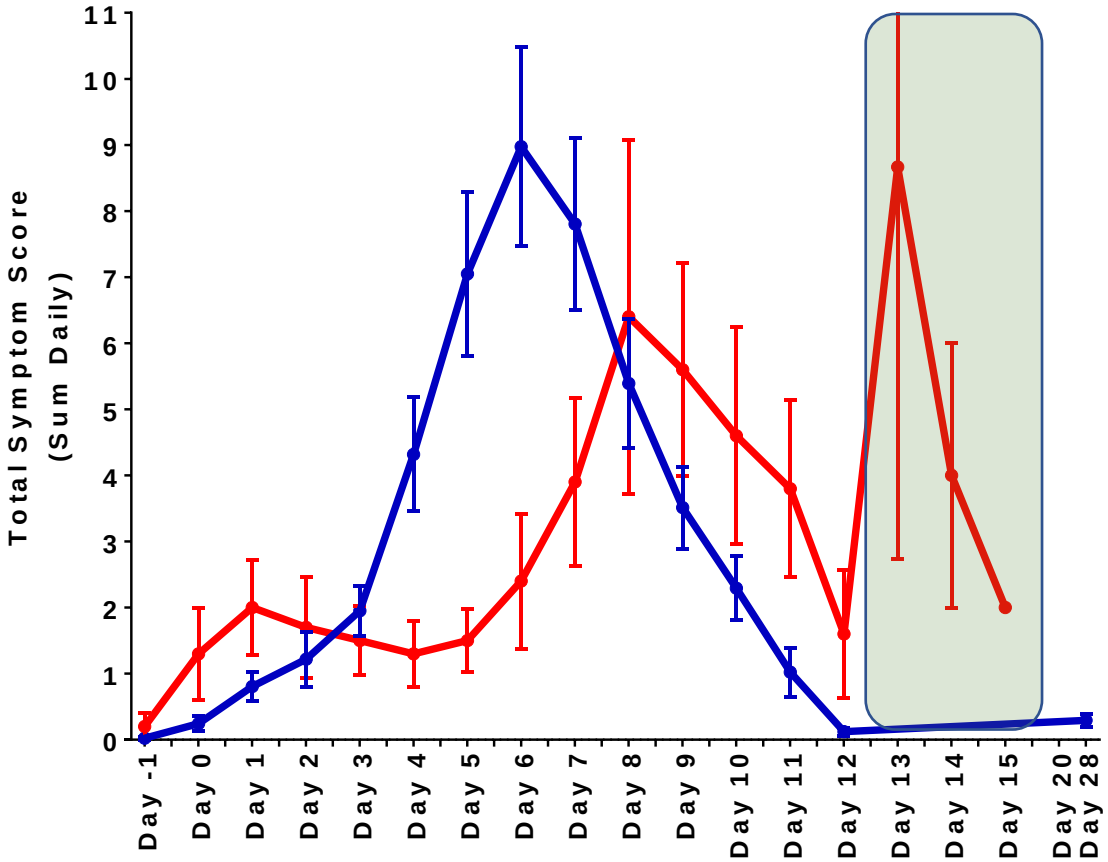

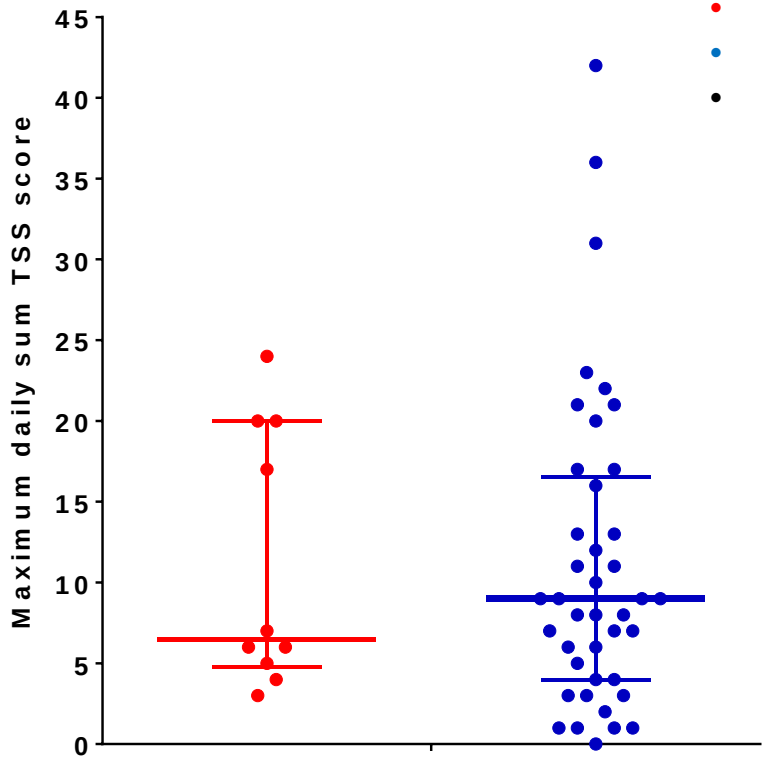

Key:

- Red = 60-75 year olds
- Blue = 18-55 year olds
- **Infected:** 2 quantifiable PCR within 2 days

- 60-75 year old infected subjects had a delayed onset and peak TSS (peak Day 8,9) compared to the 18-55 years old subjects (peak Day 6). Potential that there is greater variation in time to onset with 60-75 yr old age group
- Magnitude of daily sum Total Symptom Score (TSS) similar between the two age groups

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Comparison of nasal discharge weight in infected 18-55 & 60-75 year old subjects

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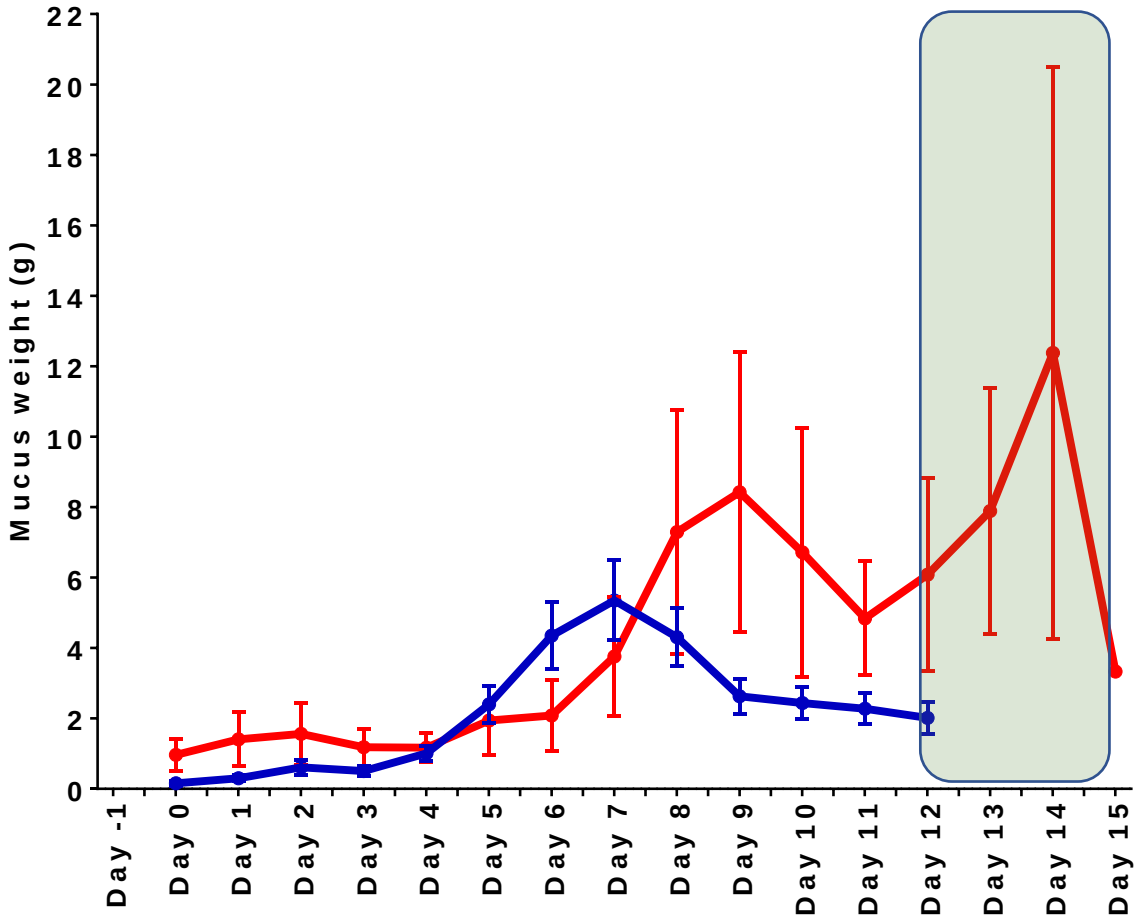

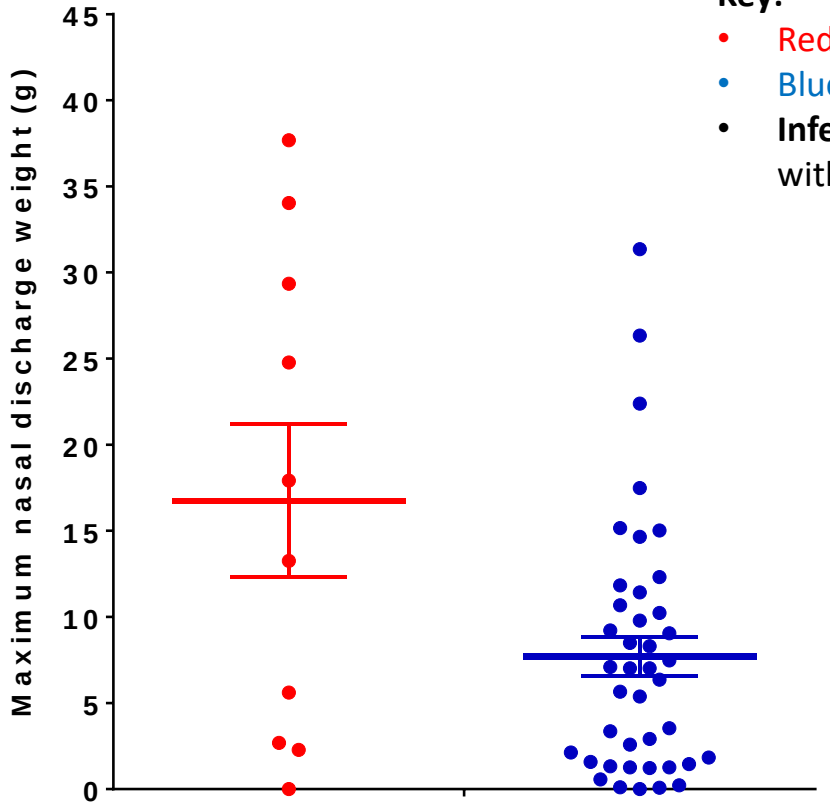

Key:

- Red = 60-75 year olds
- Blue = 18-55 year olds
- **Infected:** 2 quantifiable PCR within 2 days

- A proportion of infected 60-75 yr olds had a delayed onset of nasal discharge weight compared to 18-55 yr old s
- 60-75 yr old subjects had a trend towards greater maximal nasal discharge weight compared to 18-55 yr old sub

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Time to onset & peak PCR viral load in RSV infected 18-55 & 60-75 yr old subjects

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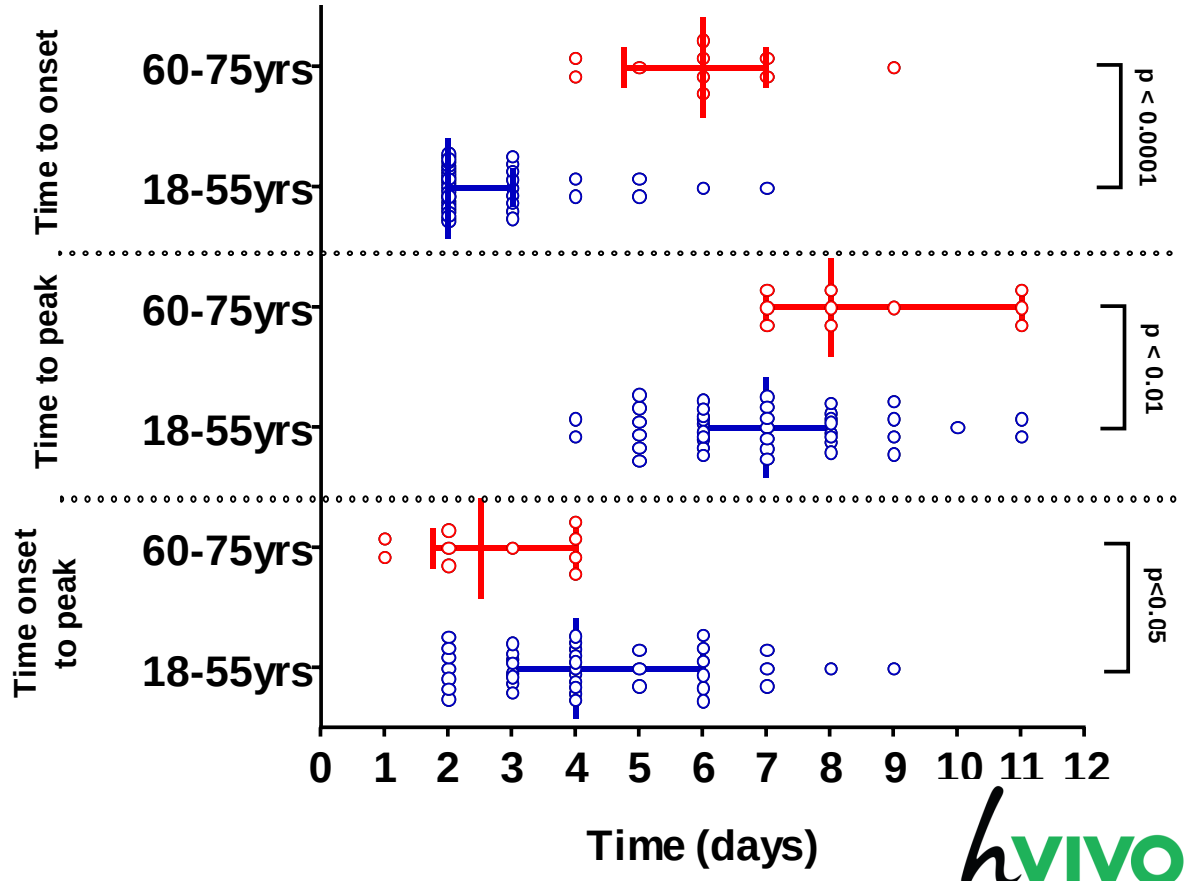
As a group, 60-75 yr old subjects had a significantly longer time to onset and time to peak viral PCR than 18-55 yr old subjects

Key:
- Red = 60-75 year old infected
- Blue = 18-55 year old infected
- **Infected:** 2 quantitative PCR within 2 days

Time to onset PCR:
- 60-75 yr old subjects had a significantly longer time to onset viral PCR than 18-55yr old subjects (median ~ 4 days later , $p<0.0001^{*}$)

Time to peak PCR:
- 60-75 yr old subjects had a significantly longer time to peak viral PCR 60-75 yr old (median ~ 1 day later, $p<0.01^{*}$)

Time from onset to peak PCR:
- 60-75 yr old subjects had a significantly shorter time from onset to peak PCR (median ~2 days earlier, $p<0.05^{*}$)



* Mann-Whitney, two sided, non-parametric test

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Conclusions

- This novel RSV challenge of 60-75-year-old volunteers was considered safe and induced an appropriate level of disease
- Older subjects had a longer incubation period and rapid rise to peak viral load
- No evidence of pre-existing neutralisation antibody levels affecting susceptibility to infection or severity of disease.
- The model is ready to progress with assessment of vaccines and drugs targeted at the 60-75-year-old population.

Acknowledgements

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Your trusted and experienced Human challenge CRO partner!

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