

## Introduction

- Norovirus (NoV) is a contagious virus that causes gastrointestinal illness in humans. It's main symptoms are diarrhea and vomiting.
- Infections can often be asymptomatic but individuals, regardless of their symptoms, shed large amounts of NoV in their stool.
- With a scarcity of available animal models, many aspects of NoV infections are poorly understood.
- The dynamics of viral load within human hosts can explain the course and severity of infection and help researchers develop novel norovirus treatments.

## Materials and Methods

- We used the data collected by two norovirus challenge studies – Leon<sup>1</sup> et. al (2011) and Newman<sup>2</sup> et. al (2016) – to understand the dynamics of viral load in NoV infected subjects.
- Infection was defined as having at least one sample of either stool or emesis test positive by RT-qPCR for NoV RNA
- Out of the 55 subjects, 15 got infected with the virus and their stool viral load was measured over a period of days.
- From their data, we extracted the variables related to shedding and tidied up the data sheets in Rstudio.
- Viral shedding, or total shedding, for each subject each day was measured by:
  - the weight of sample stool X the titer of the sample
- To estimate more accurate shedding and to understand the total amount of virus a patient shed over the course of their infection, we found the Area Under the Curve of their total shedding curve.
- We calculated the means for key variables including peak viral titer, time to peak, and duration of shedding.

## Results

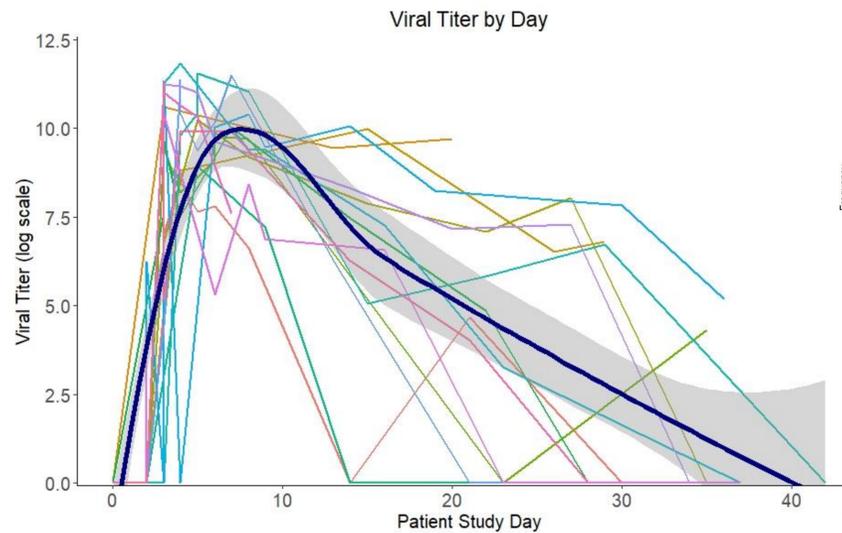


Figure (above): The individual lines represent the viral load shed of different days for each individual subject. The blue loess (locally weighted smoothing) line suggests that most subjects followed a similar trend of rapid viral shedding within the first few days after inoculation and then decreased shedding slowly over time. The peak of the line is at  $y = 9.981$ ,  $x = 7^{\text{th}}$  day.

Name of graph	Mean	Standard Deviation
Distribution of Peak Viral Titer	10.551	0.9809949
Distribution of Viral Shedding Duration	22.33	8.574603
Distribution of Time to Peak Viral Titer	5.067	3.104528
Distribution of Area Under the Curve	3.792e+11	5.47926e+11

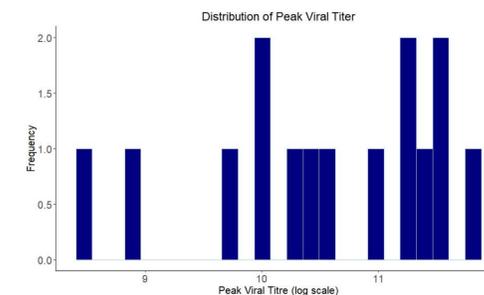


Figure (above): Peak daily shedding titer distribution. Measures are in log<sub>10</sub> scale.

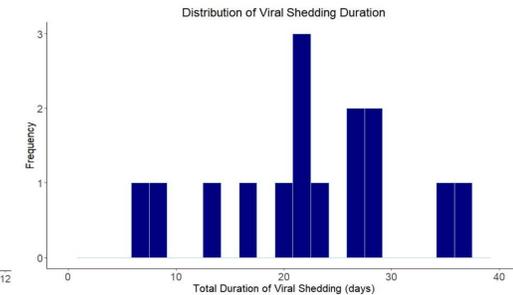


Figure (above): The last day a subject's stool tested positive for norovirus. The minimum number of days was 7 and the maximum was 36.

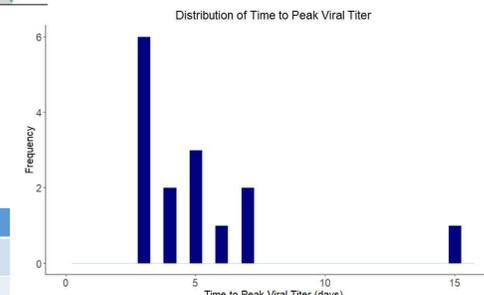


Figure (above): The day patients shed their peak viral titer post inoculation. The minimum number of days was 3 and the maximum was 15.

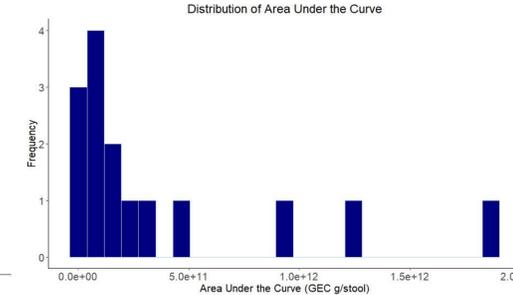


Figure (above): The total amount of virus shed by an individual subject over the course of their infection. Measures are in genomic equivalence copies per gram of stool.

## Discussion

- The limitations of this project were that the 15 infected patients were considered a low power for the research, and some subjects were not followed long enough to get total shedding information.
- For future challenge studies, larger sample sizes should be used to examine the effect of norovirus dosage on humans.
- More comparisons also need to be made between asymptomatic and symptomatic patients.
- Further research is needed to find the correlation between different humans symptoms and viral load in norovirus infected subjects.

## References

- <sup>1</sup>Leon, Juan S et al. "Randomized, double-blinded clinical trial for human norovirus inactivation in oysters by high hydrostatic pressure processing." *Applied and environmental microbiology* vol. 77,15 (2011): 5476-82. doi:10.1128/AEM.02801-10
- <sup>2</sup>Newman, K L et al. "Norovirus in symptomatic and asymptomatic individuals: cytokines and viral shedding." *Clinical and experimental immunology* vol. 184,3 (2016): 347-57. doi:10.1111/cei.12772
- Vegvari, Carolin et al. "How Can Viral Dynamics Models Inform Endpoint Measures in Clinical Trials of Therapies for Acute Viral Infections?" *PLoS onevol.* 11,7 e0158237. 1 Jul. 2016, doi:10.1371/journal.pone.0158237

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