The human viral challenge model is well established, safe and ideal to study influenza. It allows researchers to illuminate each step of the infection: baseline, peak and return to healthy. It is possible to stipulate each experimental parameter such as virus strain, environment, sampling methods, schedule of intervention and subjects’ demography (young, older, HLA type, pre-challenge immune response).

The objective of this analysis is to illustrate the complexity of the data at the subject-, study- and cohort levels.

Main endpoints evaluated:
- Symptom score
- Diary card self-reporting
- Physician assessment
- Vital signs
- Spirometry, ECG
- Blood markers and safety
- Haematology, Biochemistry
- Inflammatory pathways
- Virus titration
- RT-qPCR
- Cell-based
- NIAID
- Weight
- Paper tissue count
- Temperature increases are not always observed during influenza infection.

These four graphs present upper respiratory tract, low respiratory tract, systemic and total symptom scores (bars and left axis) and PCR results (right axis) post inoculation. Each graph shows the average results for the following subgroups: not infected, 1st tertile, 2nd tertile and 3rd tertile.

Subjects’ oral temperature were measured 3 times daily from admission to discharge. Each subject serves as their own baseline (defined as day 0 morning). The left graph presents the average and median of delta temperature for each morning reading for the 4 subgroups. The right graph focuses on day 3 sunscreen, point and highlights the fact that temperature increases are not always observed during influenza infection.

The left graph shows daily total symptom scores (average and median) per subgroup post-infection. The score is obtained by combining the total symptom scores from morning, midday and evening symptom diary cards. Day 3 is the peak time point for all subgroups.

The right graph shows daily mucus weight (average and median) per subgroup. The blue line: 1st tertile, 2nd tertile and 3rd tertile.

The below figure shows incidences of single and composite endpoints per subgroup (not infected, 1st tertile, 2nd tertile and 3rd tertile).

This figure shows the frequency of 2 symptoms of once (top graph), grade 2 and 3 symptoms (middle graph) and total symptom score greater or equal to 5 (bottom graph) per time point during the quarantine period.

As most parameters can be standardised, combining data and analysis at subject-, study- and cohort levels will be key to future research. In addition to the most obvious ones, novel and more refined endpoints can be selected and virus-host interaction responses targeted more precisely.

Study design: Typically randomised double-blind placebo-controlled studies that evaluate IAV antiviral activity, safety and efficacy
Study population: 18 to 64 year old healthy subjects with low serum Ab response
Study size: 40 to 140

The human viral challenge model: accelerating the evaluation of respiratory antivirals, vaccines and novel diagnostics. Rob Lambkin-Williams et al. Respiratory Research 2018

REFERENCES