

## BACKGROUND

OM-85 (Broncho-Vaxom®) is a bacterial lysate used to prevent recurrent respiratory tract infections (RTIs) in children [1]. To support OM-85 development in children in the challenging landscape for respiratory clinical trials during the COVID-19 pandemic, we developed a computational mechanistic model of RTIs and OM-85 mechanism of action, overlaid with an epidemiological model of common respiratory viruses [2]. This model reproduces the placebo-controlled and interventional arms of multiple OM-85 studies in children. OM-85 has also shown potential to protect elderly adults and patients with chronic obstructive pulmonary disease (COPD) from recurrent RTIs [3, 4]. Therefore, we aimed to expand the model's context of use to these populations, to generate in silico data that would further support the benefits of OM-85 for adult populations.

By implementing physiological differences between healthy adults, elders and COPD patients, our mechanistic model can capture viral dynamics in each subpopulation at the individual and populational level

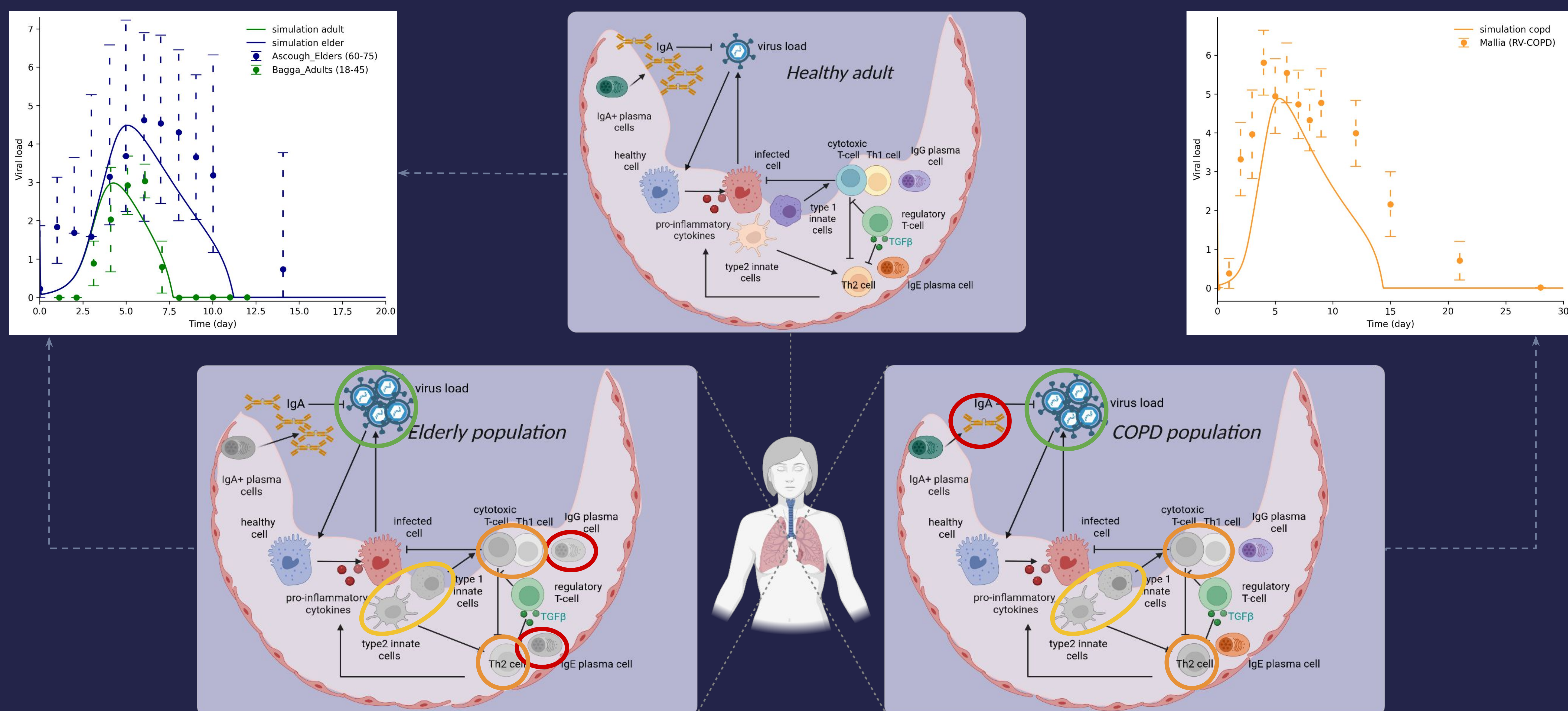


Figure created with BioRender.com

## METHODS

For the elderly and COPD populations, we calibrated the model on data from viral challenges and epidemiological data in the corresponding groups. For this, we introduced changes to the immunological reactions to viral infections based on the evidence present in the literature for these populations [5, 6].

For the **elderly population**, we:

- Increased viral load needed to activate the immune response, reflecting **lower reactivity of dendritic cells**.
- Decreased T cell activation due to **lower cell receptor diversity and increased natural decay**.
- Decreased IgG and IgA efficacy, due to **weakened B cell activity**.

For the **COPD population**, we:

- Reduced T cell efficacy due to **T-cell exhaustion and increased natural decay**.
- Increased viral load required to activate the immune response due to **weakened immune system**.
- **Reduced efficacy of IgA**, reflecting concentration of IgA in the airway epithelium surface.
- Reduced clearance of the virus due to **weakened mucociliary functions**.

## RESULTS

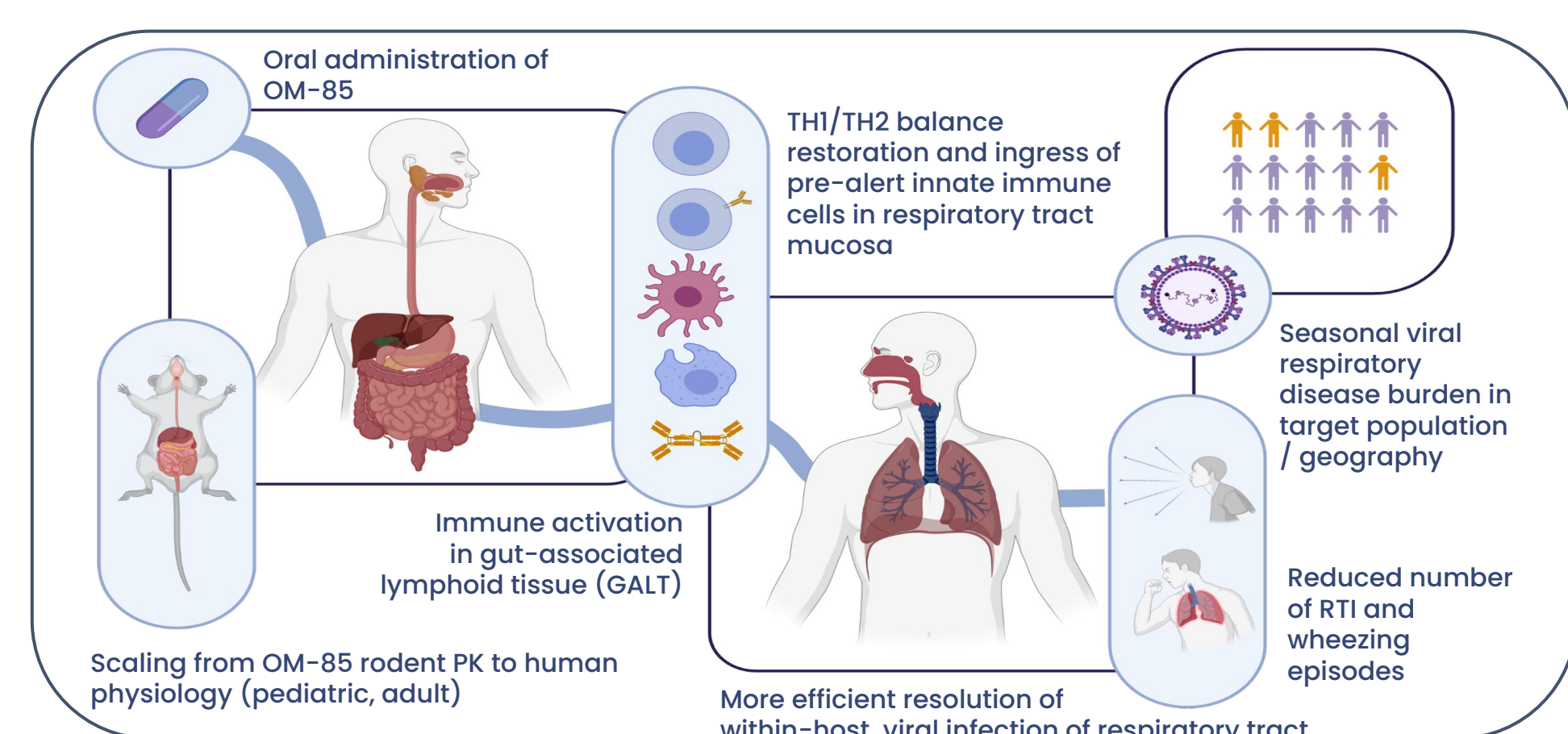


**Fig. 1:** Overall presentation of the model and the interactions with OM-85.

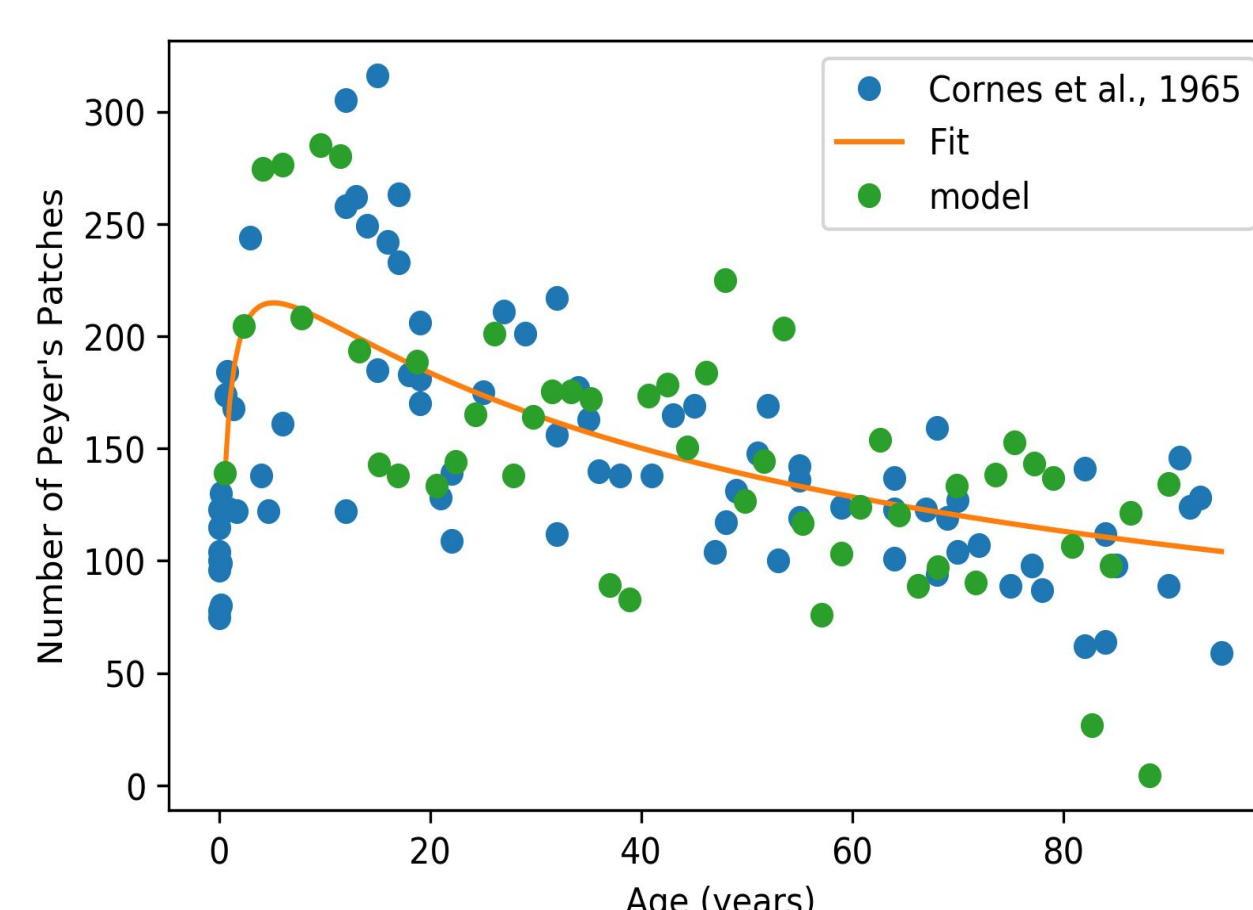


**Fig. 2:** Number of Peyer's patches observed (blue) and predicted by the model (green)

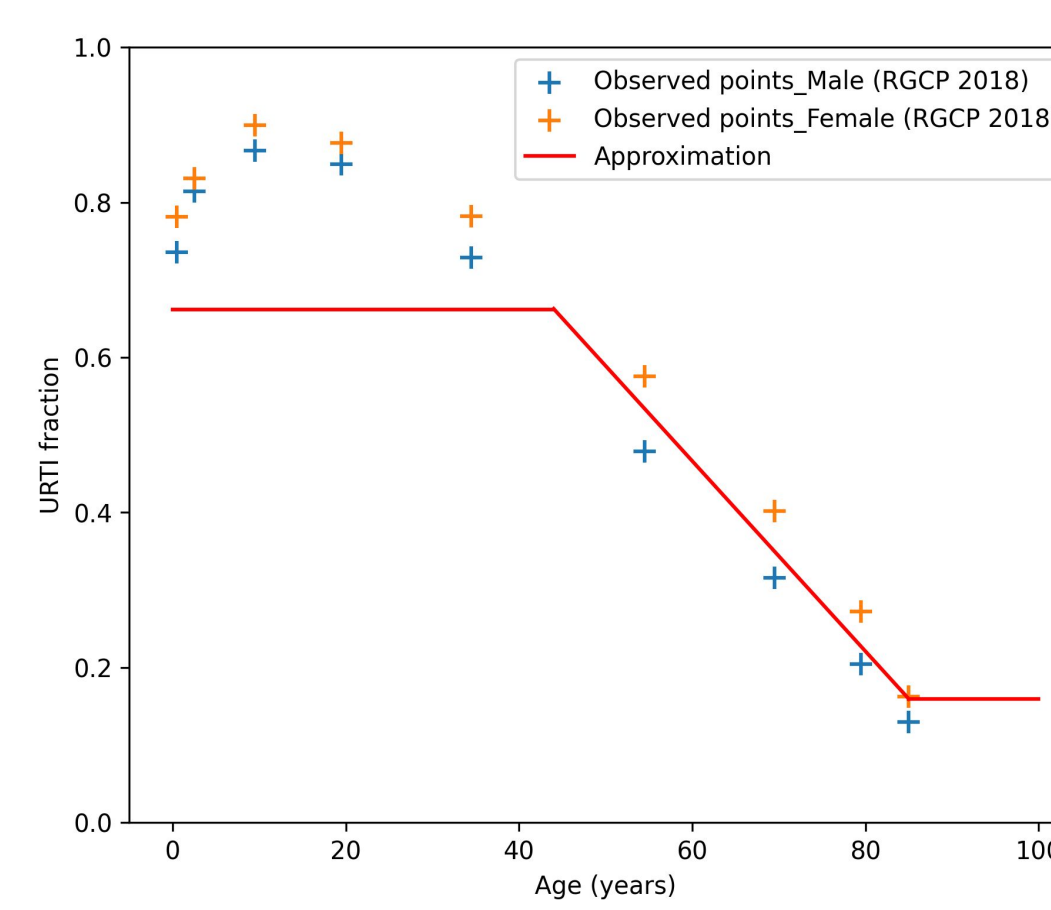


**Fig. 3:** Fraction of URTI in british population (cross) and approximation made in our model (line).  
Dataset from Oxford Royal College of General Practitioners (RCGP) 2018-2019 annual report.

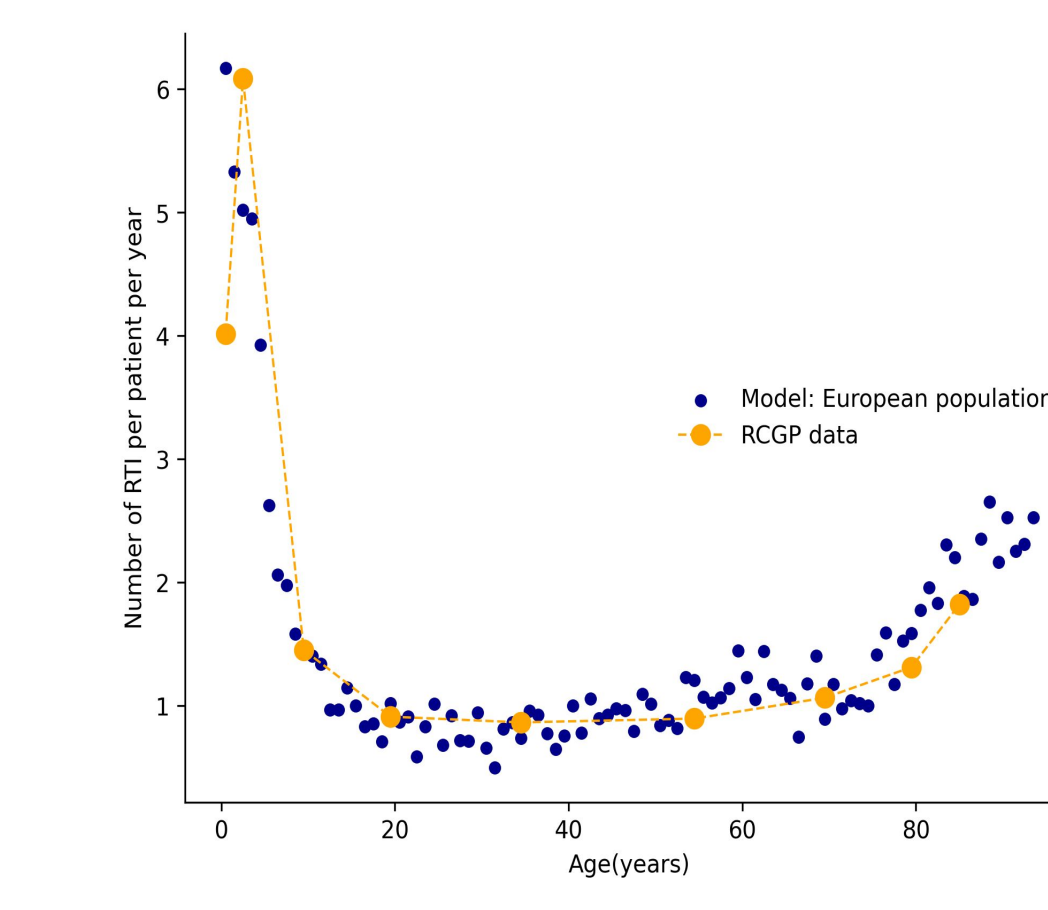


**Fig. 4:** Epidemiological data for RTIs in british population (yellow) and in our virtual population (blue).

## CONCLUSION

- We developed a **computational mechanistic model** able to account for changes in the immune response to viral infections due to **age-related immunosenescence** and **chronic inflammation in COPD patients**.
- This comprehensive modeling approach can be used to **explore the efficacy of OM-85 on the prevention of RTI in various populations** and **generate in silico data** to further support the benefits of OM-85 in adult populations.

## REFERENCES

- [1] Yin et al. (2018). DOI: 10.1016/j.jintimp.2017.10.032; [2] Arsène et al. (2022). DOI: 10.1038/s41467-022-29534-8; [3] Gareri et al. (2023). DOI: 10.2174/1574887118666230518112806; [4] Troiano et al. (2021). DOI: 10.15167/2421-4248/jpmh2021.62.3.1734; [5] Hou et al. (2024). DOI: 10.1038/s41541-024-00874-4; [6] de Fays C et al. (2022). DOI: 10.3390/cells11081324