COMPARE Trial: Comparing Outcomes of mRNA and Protein-based COVID-19 Vaccines and Impact on Reactogenicity

P0468

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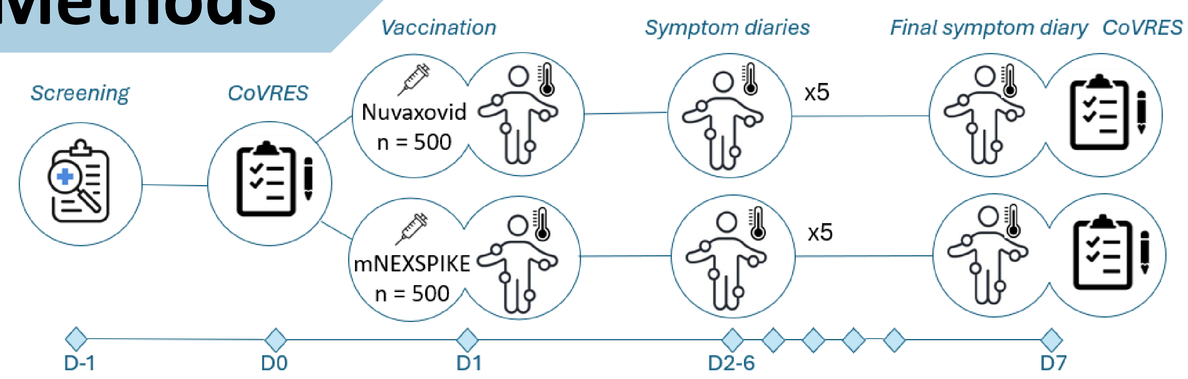
Introduction

COVID-19 vaccine uptake is low with concerns of side effects cited by over half of adults as a reason for declination[1,2]. While existing evidence suggests favorable reactogenicity of the recombinant protein COVID-19 vaccine compared to mRNA-based vaccines[3], there has not been an appropriately powered, randomized, and blinded trial to address this question.

Objectives

- **Compare risk of ≥1 systemic reaction within 7 days: recombinant protein (Nuvaxovid®) vs mRNA (mNEXSPIKE®)**
- Compare number, severity, duration of systemic/local reactions
- Compare risk of experiencing ≥3 systemic symptoms
- Assess disruption to work/social activities using the COVID-19 Vaccine Reaction Experience Survey (CoVRES)
- Evaluate future vaccine intent and platform preference

Methods



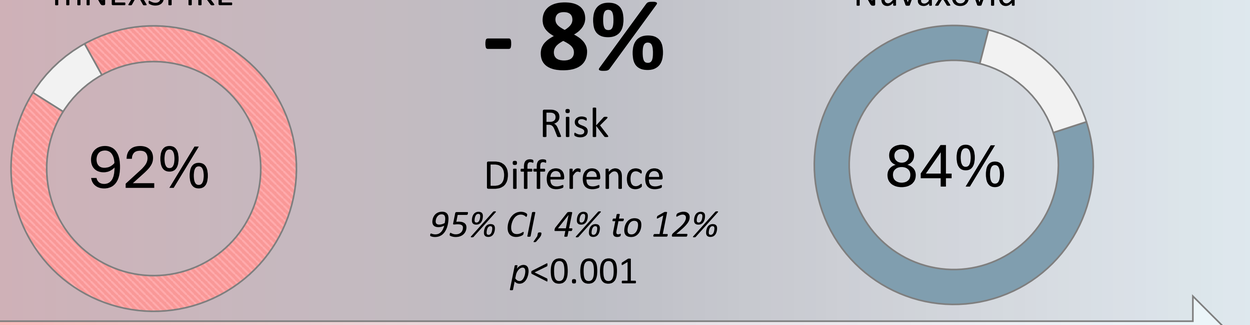
1,000 adults were randomized 1:1 in a double-blinded trial to receive either the **Nuvaxovid recombinant protein vaccine (Sanofi)** or the **mNEXSPIKE mRNA vaccine (Moderna)**. Patient-reported outcomes (PRO) and CoVRES responses were recorded on days 1 and 7.

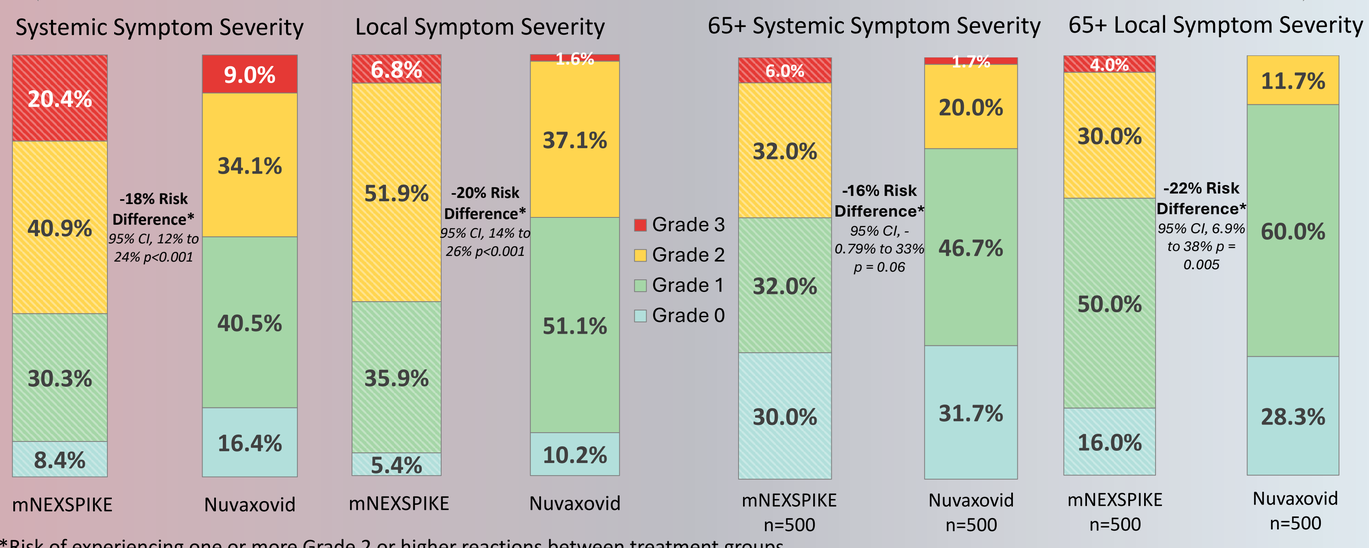
Results

REACTOGENICITY

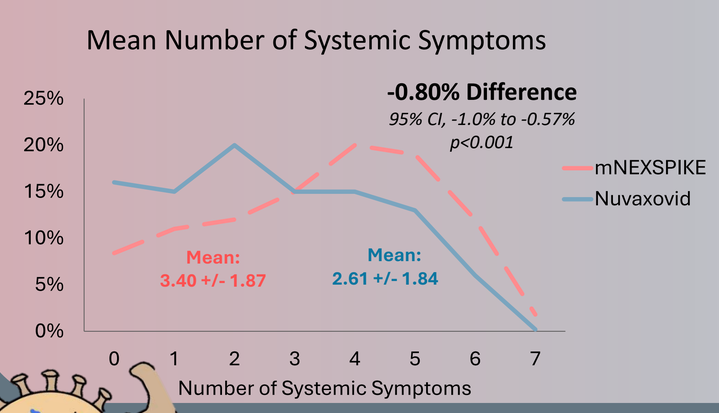
Data completion rate of 99.8% percent: 1000 participants enrolled, 998 retained in study (n = 499 in each vaccine group), 76,846 reactogenicity data points collected

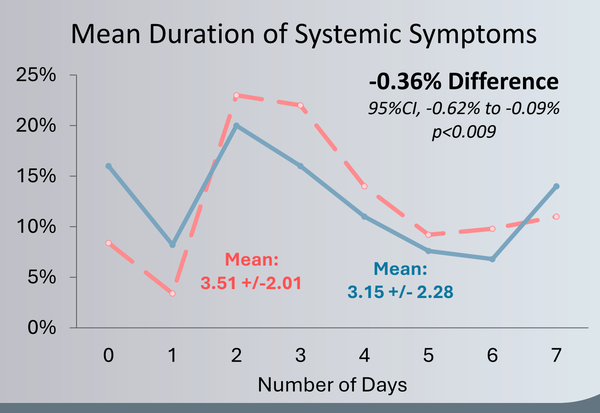
≥1 Systemic reaction within 7 days



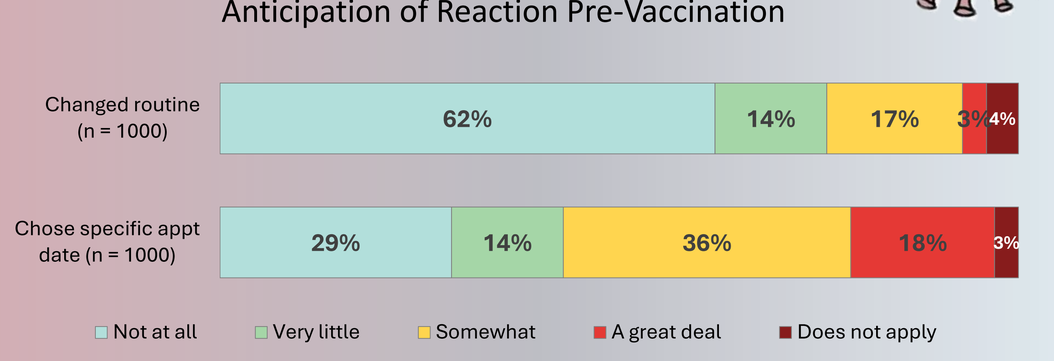


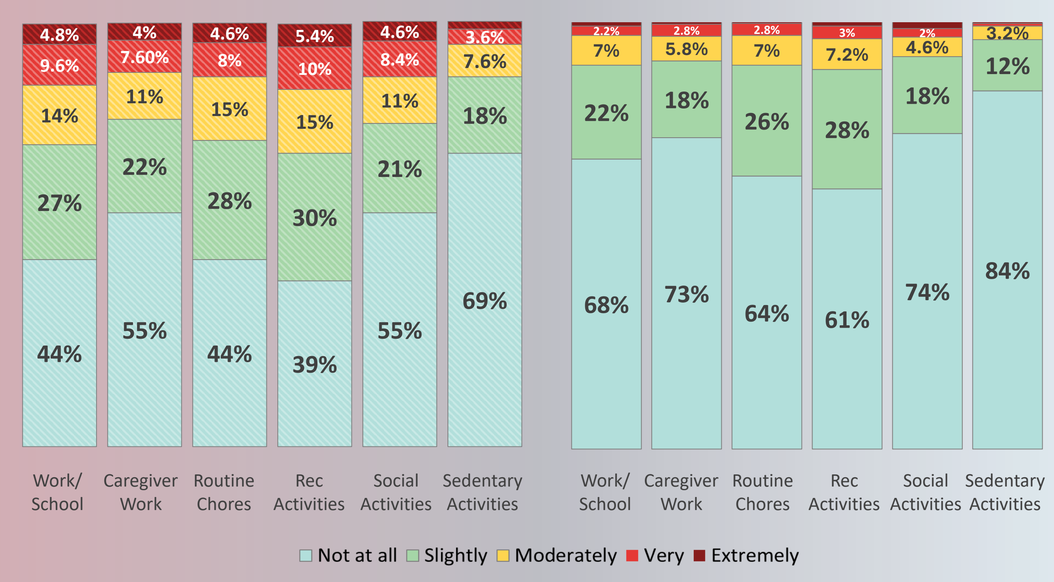
*Risk of experiencing one or more Grade 2 or higher reactions between treatment groups

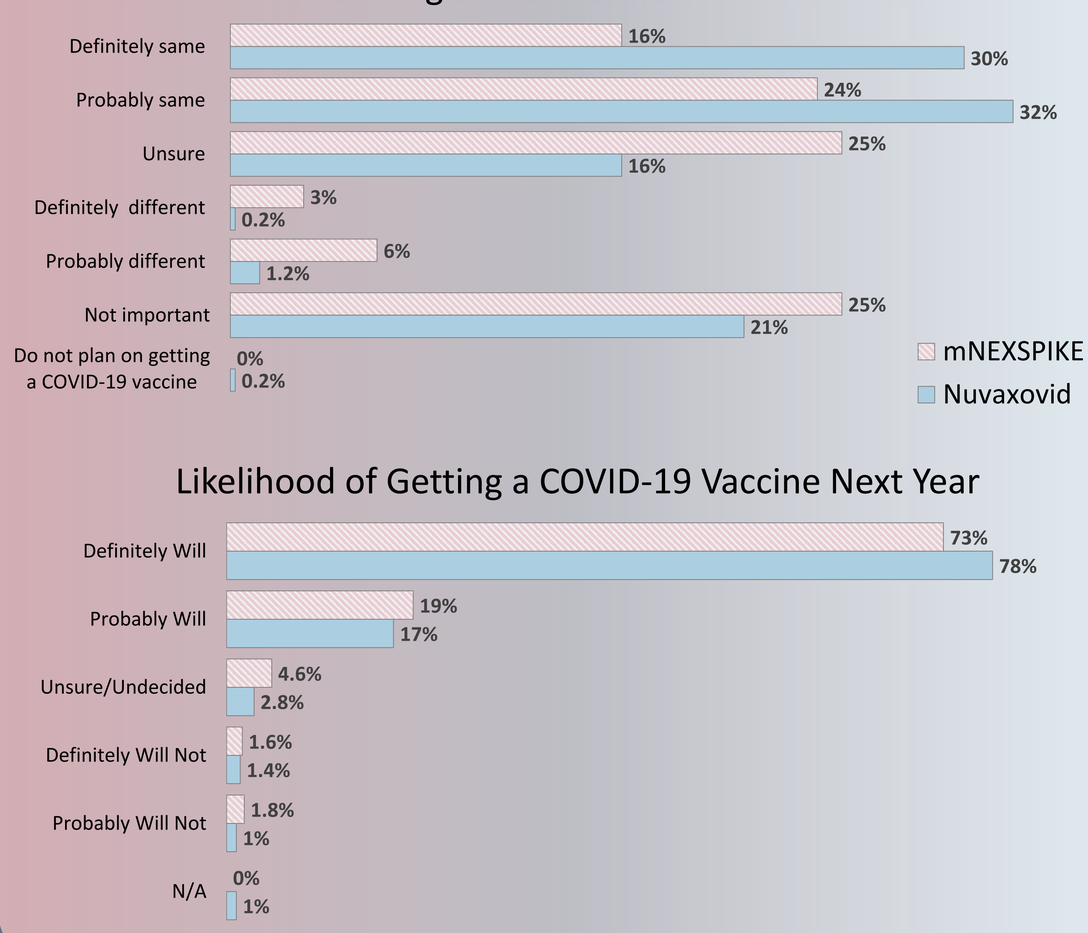




LIFESTYLE IMPACTS (CoVRES)







Conclusion

- Immunization with the protein-based COVID-19 vaccine (Nuvaxovid®, Sanofi) demonstrated a superior tolerability profile, with significantly lower incidences of local and systemic reactions compared to the mRNA-based mNEXSPIKE® vaccine (Moderna)
- PRO and CoVRES analyses indicate less daily life impact for those who received the protein-based vaccine and a greater willingness to receive the same vaccine in the future.

References

1. National Foundation for Infectious Diseases. 2024 National Survey: Attitudes and Behaviors about Influenza, COVID-19, Respiratory Syncytial Virus, and Pneumococcal Disease. Bethesda (MD): NFID. 2024 Sep 25.
2. Vaccination uptake, intent, and confidence. 2025 May 16. RespVaxView. Centers for Disease Control and Prevention.
3. Marchese AM, Rousculp M, Macbeth J, Beyhaghi H, Seet BT, Toback S. The Novavax Heterologous COVID Booster Demonstrates Lower Reactogenicity Than mRNA: A Targeted Review. *J Infect Dis.* 2024 Aug 16;230(2):e496-e502.

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