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Clinical and Economic Perspectives on Influenza and COVID-19 Vaccine Combinations

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A recombinant protein influenza and COVID-19 combination vaccine would ensure equal protection and better safety. Granular modelling of reactogenic events is pivotal in accurately estimating the clinical and economic outcomes of mRNA vaccines

OBJECTIVE

- This study evaluates the public health and economic impact of current standalone vaccination versus mRNA and recombinant protein combination vaccines in older adults aged over 65 years In the United States (US)

CONCLUSIONS

The recombinant protein vaccine combination demonstrated notable clinical and economic outcomes, benefiting from its enhanced influenza component and established safety profile

Moreover, by addressing the vaccine coverage rates (VCR) disparity between influenza and COVID-19, combination vaccines offer substantial clinical and economic advantages over standalone vaccinations

BACKGROUND

- Influenza and COVID-19 impose a significant burden for older adults in the US[1,2], yet COVID-19 vaccination rates lag significantly behind those for influenza, and only one-third receive both vaccines simultaneously[3,4]
- Combination influenza-COVID-19 vaccines, currently in phase II/III trials, may reduce administration burden and increase VCR

METHODS

Model input

The model incorporated recent US, age-specific demographics[5,6], disease patterns, VCR, and 2024 healthcare costs[7], excluding vaccine acquisition **(Table 1)**

Perspective

US healthcare payor perspective

Model structure and Time horizon

We modeled health and economic impact following standalone or combination vaccinations in a one-year time horizon **(Figure 1)**

Vaccine Efficacy Assumptions

Among alternatives, vaccine efficacy (VE) against COVID-19 was set equal, and considered a relative VE of 15.3% for recombinant influenza vaccine against standard dose[8]

VCR

Outcomes assume combined vaccines to even out current influenza VCR at 51.1%

Adverse events (AEs)

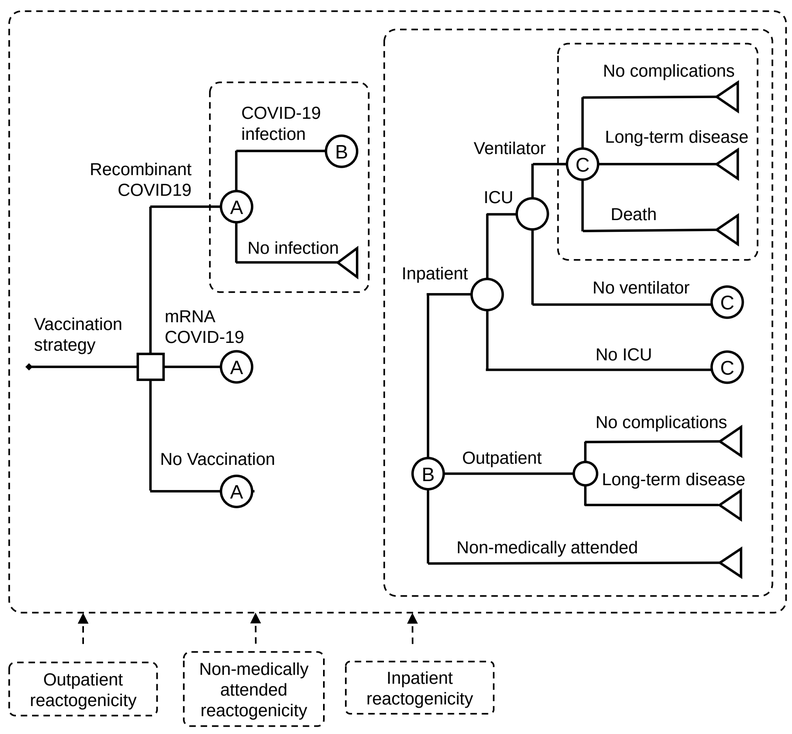
Post-vaccination AEs, grade 1 or 2, and 3 were classified according to their healthcare-seeking behaviour as non-medically attended, or outpatient, respectively

Table 1. Key Model Inputs

Parameter	Value	Source
Epidemiology & Demographics		
Population size (65+ years), millions	58	9,10
Vaccination coverage rate	0.74	11
Influenza attack rate	0.04	11
Inpatient influenza probability	0.04	12
Outpatient influenza probability	0.62	12
Influenza death probability	0.01	12
Vaccine efficacy	0.58	12
Reactogenicity		
mRNA vacccine Grade 1 reactions	43% / 26%	13*
SoC vaccine Grade 1 reactions	26% / 22%	13*
mRNA vacccine Grade 2 reactions	29% / 31%	13*
SoC vaccine Grade 2 reactions	2% / 8%	13*
mRNA vacccine Grade 3 reactions	3% / 8%	13*
SoC vaccine Grade 3 reactions	1% / 1%	13*
Costs		
Inpatient influenza cost	$0.0	7
Outpatient influenza cost	$391.0	7
Outpatient reaction cost	$90.8	7

Abbreviations: Soc, Standard of care
* Local / Systemic reactions

Figure 1. Model structure

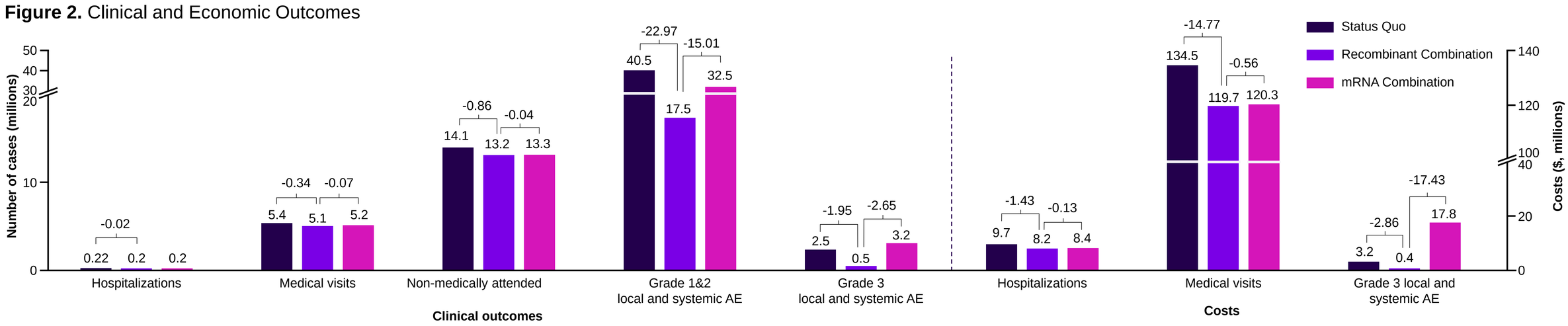


Abbreviations: ICU, Intensive care unit

RESULTS

- At a 51.1% VCR, 30.31 million out of 59.31 million US older adults were assumed to receive an influenza and COVID-19 vaccination combination
- Compared to combination vaccines, standalone vaccinations increased hospitalizations by 8.9% and medical visits by 6.2%, which translated into $16.2 million in additional costs
- The recombinant protein combination vaccine yielded 17.66 million fewer AEs (15.01 million grade 1 & 2; 2.65 million grade 3 AEs) compared to the mRNA combination vaccine, which equated to $17.43 million grade 3 mRNA-related reactogenicity costs

Figure 2. Clinical and Economic Outcomes



STRENGTH AND LIMITATIONS

- This is the first economic model of an influenza and COVID-19 combination vaccine that comprehensively accounts for the reactogenicity profile, categorized according to standardized grading systems
- The reactogenicity profile of the standard-of-care vaccines was assumed to be comparable to that of the recombinant protein combination vaccine
- All grade 3 AEs were assumed to incur outpatient treatment costs, regardless of whether they were local or systemic reactions
- There's scarce level of evidence concerning the patient loss of utility related to each grade of AEs. As such, those grade 1&2 and grade 3 were assumed from a vaccine study out of the influenza or covid-19 scope

REFERENCES: 1. CDC. COVID-19 Surveillance Data in the United States. CDC; 2024; **2.** CDC. 2023–2024 U.S. Flu Season: preliminary In-season burden estimates. CDC 2024; **3.** CDC. Influenza Vaccination Coverage, Adults 65 Years and Older, United States. CDC; 2025; **4.** CDC. COVID-19 Vaccination Coverage, Adults 65 Years and Older, United States. CDC;2025; **5.** US Population 2023, World Bank; **6.** 2023 Census.gov; **7.** Prosser L et al 2023 (CDC-ACIP series); **8.** Hsiao, A et al. N Engl J Med. 2013:389(25);2245–2255; **9.** Moderna Investor Event - R&D Day and Business Updates 2023. Available at investors moderna events; **10.** Sanofi Vaccines Investor Event 2023. Available at sanofi-investors/financial-results; **11.** Centers for Disease Control and Prevention 2023; **12.** Molinari NA et al 2007;25(27):5086-96; **13.** Demicheli et al 2018;2(2):CD001269

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DISCLOSURES: JBH and MT are employees of Sanofi and may hold stock or stock options

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