Poster EE760

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Is there a Place for First-Generation mRNA Seasonal Influenza Vaccines? Unraveling the Clinical and Economic Consequences of Increased Reactogenicity in U.S. Older Adults

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BACKGROUND

- Clinical trials (CT) of first-generation influenza messenger ribonucleic acid (mRNA) vaccines have demonstrated comparable immune response to standard inactivated (egg-based or recombinant) influenza vaccines, accompanied by substantially higher rates of post-vaccination reactions[1,2].
- There is uncertainty about whether these vaccine profiles are fit for broad seasonal use or if they could influence vaccine acceptance, trust, and overall coverage.

OBJECTIVE

We modeled the potential clinical and economic consequences of reactogenicity and vaccination hesitancy among older adults aged 65+ years in the United States (US).

METHODS

- One-year disease-transition model mirroring the course of immunized individuals, considering reactogenicity and the consequences of influenza in those infected, from a payor perspective (figure 1) .
- Model inputs were informed by US-specific demographics[3,4], epidemiology[5,6,7], and direct costs[8] expressed in constant 2023 US$ (table 1).
- Equal vaccine acquisition cost and efficacy across technologies was assumed.
- Healthcare-seeking behavior was classified as non-medically or outpatient attended, for grades 1-2 and 3 reactions, respectively.
- Model outputs present deterministic scenarios of post-vaccination reactions based on a range of early phase mRNA CT results (+/-10%), market penetration (10%-30%), and vaccination hesitancy (10-30%) affecting vaccination coverage rates (VCR).

Table 1. Key disease-transition model inputs

	Concept	Value	Source
Epidemiology & Demongraphics	Population size (65+ years)	58m	*1,2*
	Vaccination coverage rate	0,74	5
	Influenza attack rate	0,04	5
	Inpatient influenza probability	0,04	6
	Outpatient influenza probability	0,62	6
	Influenza death probability	0,01	6
	Vaccine efficacy	0,58	7
	RNA vacccine Grade 1 reactions	43% / 26%	1*
	SoC vaccine Grade 1 reactions	26% / 22%	1*
	RNA vacccine Grade 2 reactions	29% / 31%	1*
	SoC vaccine Grade 2 reactions	2% / 8%	1*
	RNA vacccine Grade 3 reactions	3% / 8%	1*
	SoC vaccine Grade 3 reactions	1% / 1%	1*
Costs	Inpatient influenza cost	$20 648,0	8
	Outpatient influenza cost	$391,0	8
	Outpatient reaction cost	$90,8	8

** Local / Systemic reactions*

RESULTS

- The introduction of mRNA vaccines up to 30% market share would increase, on average, 164% (range 145-184) the number of post-vaccination Grade 3 reactions, leading to additional 0.6million (0.5-0.7) medical events. (table 2). This scenario equates to $13.5m (10.8-16.4) in added outpatient costs (figure 2).
- The supplementary number of patients experiencing Grade 1-2 reactions would range from 3.0m (2.5-3.6m [+12%]) to 9.0m (7.4-10.7m [+37%]) for market share scenarios of 10% and 30%, respectively.

Figure 1: Influenza vaccination, disease transition model

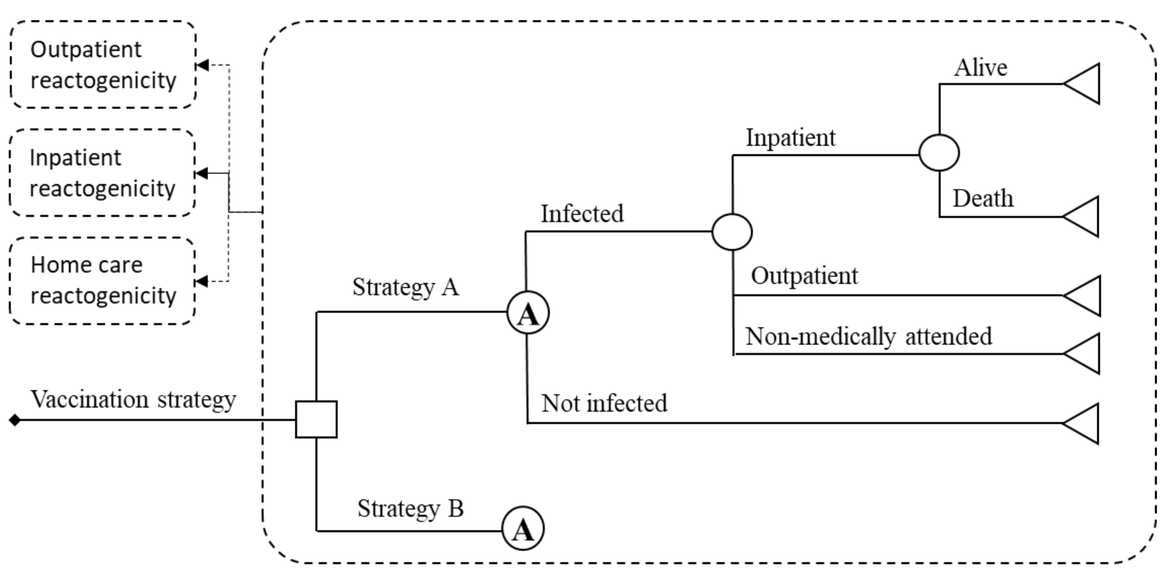


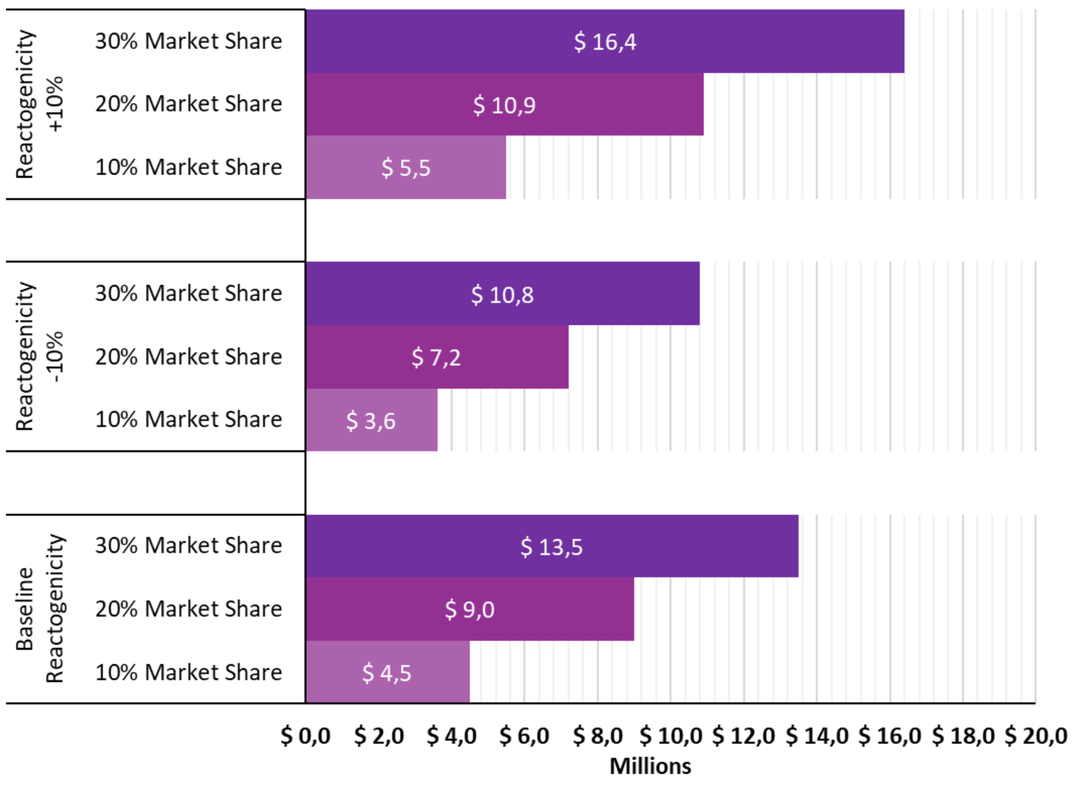
Table 2. Impact of alternative seasonal mRNA influenza market shares (additional cases expressed in millions)

Concept	Scenario	Market Share 10%	20%	30%
Grade 1&2 Reactions	Baseline	3,0 (12,2%)	6,0 (24,4%)	9,0 (36,6%)
additional cases	-10%	2,5 (10,0%)	4,9 (20,0%)	7,4 (30,0%)
(% increment)	+10%	3,6 (14,4%)	7,1 (28,9%)	10,7 (43,3%)
Grade 3 Reactions	Baseline	0,4 (54,8%)	0,8 (109,5%)	1,2 (164,3%)
additional cases	-10%	0,4 (48,3%)	0,7 (96,6%)	1,0 (144,9%)
(% increment)	+10%	0,4 (61,2%)	0,9 (122,5%)	1,3 (183,7%)

RESULTS (CONT.)

- When simultaneously varying mRNA market shares and vaccination hesitancy, an increased frequency in inpatient and outpatient visits, and deaths could be expected, varying from 0.8% to 6.8% for the scenarios raising 10% and 30%, respectively.

Figure 2. Impact of alternative seasonal mRNA influenza market shares and Phase 3 reactogenicity profiles (additional costs expressed in millions)



CONCLUSIONS

- **Modeling early mRNA influenza vaccination CT into cases and costs scaled at US population level in older adults results in scenarios displaying increased healthcare resource utilization, that could compromise VCR.**
- **A better tolerability profile is needed for next generation, seasonal influenza vaccines.**

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CONFLICTS OF INTEREST:
Jose Bartelt-Hofer, Joshua Nealon and Maribel Tribaldos: Sanofi — employee, may hold stock and/or stock options in the company.

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