Poster EE427

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Spotlight on mRNA Post-Vaccination Reactions: Should First-Generation, Influenza mRNA Candidates Have a Place in U.S. Adult Seasonal Immunization?

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BACKGROUND

- Comparable immune responses and considerably higher post-vaccination reactions have been displayed in trials studying first-generation seasonal influenza messenger ribonucleic acid (mRNA) compared to standard inactivated (egg-based or recombinant) vaccines[1,2].
- It is not clear whether these vaccine profiles would be appropriate for seasonal, population-wide use, or could impact vaccine uptake, confidence and coverage

OBJECTIVE

In United States (US) adults aged 18 to 64, we aimed to estimate the impact of reactogenicity and vaccine hesitancy from a payor's perspective.

METHODS

- Disease-transition model, capturing natural influenza health states in those infected and post-vaccination reactogenicity, in a one-year horizon (figure 1) .
- 2023 US demographics[3,4], epidemiology[5,6,7], and direct costs (expressed in 2023 US$)[8] informed the model inputs (table 1) .
- Equal acquisition cost and efficacy among vaccines was assumed.
- Grade 1&2, and Grade 3 reactions were classified as non-medically and outpatient attended, respectively.
- Results present scenarios of possible mRNA vaccine market shares (10%-30%), vaccination hesitancy (10%-30%) and observed mRNA reactions (baseline, +/-10%).

Figure 1: Influenza vaccination, disease transition model

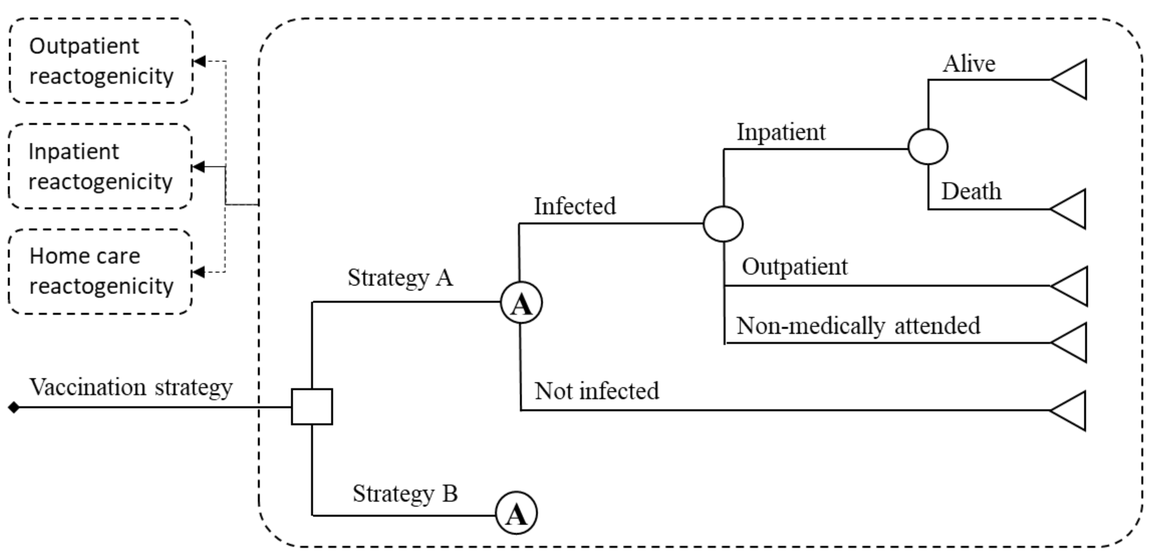


Table 1. Key disease-transition model inputs

	Concept	Value	Source
Epidemiology & Demographics	Population size (18-64 years)	203m	*1,2*
	Vaccination coverage rate 18-49	0,37	5
	Vaccination coverage rate 18-50	0,52	5
	Influenza attack rate	0,09	5
	Inpatient influenza probability	0,03	6
	Outpatient influenza probability	0,31	6
	Influenza death probability	<0,00	6
	Vaccine efficacy	59%	7
	RNA vacccine Grade 1 reactions	34% / 20%	1*
	SoC vaccine Grade 1 reactions	37% / 22%	1*
	RNA vacccine Grade 2 reactions	42% / 43%	1*
	SoC vaccine Grade 2 reactions	9% / 17%	1*
	RNA vacccine Grade 3 reactions	5% / 15%	1*
	SoC vaccine Grade 3 reactions	<0% / 2%	1*
Costs	Inpatient influenza cost	$32 684,0	8
	Outpatient influenza cost	$376,0	8
	Outpatient reaction cost	$90,8	8

** Local / Systemic reactions*

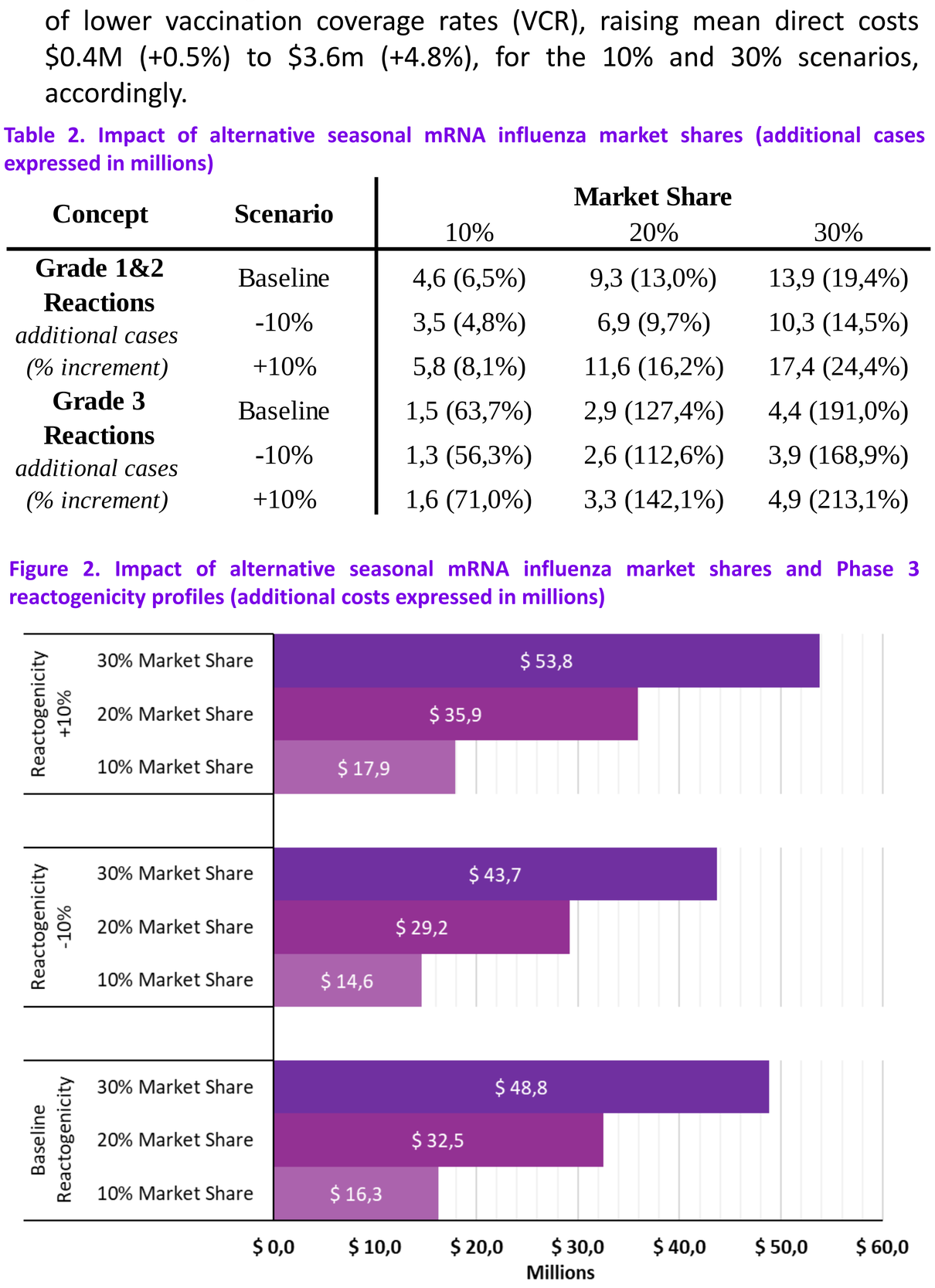
RESULTS

- Augmenting 30% the market share of mRNA vaccines would lead to mean 4.4m (range 3.9-4.9) additional Grade 3 reactions (+191% [169-213] increase), equating in $48.8m (43.7-53.8) outpatient costs (table 2, figure 2) .
- 10% to 30% mRNA market shares result in 4.6m (3.5-5.8 [+6.5%]) to 13.9m (10.3-17.4m [+19%]) excess Grade 1&2 reactogenicity cases, respectively .
- Simultaneous variations in mRNA vaccination hesitancy and market shares would augment inpatient, outpatient and death cases as a result of lower vaccination coverage rates (VCR), raising mean direct costs $0.4M (+0.5%) to $3.6m (+4.8%), for the 10% and 30% scenarios, accordingly.

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 *additional cases (% increment)*	Baseline	4,6 (6,5%)	9,3 (13,0%)	13,9 (19,4%)
	-10%	3,5 (4,8%)	6,9 (9,7%)	10,3 (14,5%)
	+10%	5,8 (8,1%)	11,6 (16,2%)	17,4 (24,4%)
Grade 3 Reactions *additional cases (% increment)*	Baseline	1,5 (63,7%)	2,9 (127,4%)	4,4 (191,0%)
	-10%	1,3 (56,3%)	2,6 (112,6%)	3,9 (168,9%)
	+10%	1,6 (71,0%)	3,3 (142,1%)	4,9 (213,1%)

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



CONCLUSIONS

- **US adult seasonal influenza immunization with first-generation mRNA vaccine, as modeled with recent trial results, depicts substantial increases in post-vaccination reactions and direct costs when compared to licensed vaccines.**
- **Moreover, public hesitancy to vaccination may lead to excess use of healthcare resources as result of lower VCR.**
- **In the development of next generation seasonal influenza vaccines, the importance of the tolerability profile should not be undermined.**

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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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