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Potential Public Health Benefits of Recombinant Influenza Vaccines in Older Adults in England and Wales

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Using recombinant influenza vaccine instead of adjuvanted egg-grown inactivated influenza vaccine could deliver substantial public health benefits and economic value, averting over 100,000 influenza cases and 2,500 hospitalisations annually and generating approximately £24.2 million in annual NHS savings

OBJECTIVE

To evaluate the public health benefits and cost-effectiveness of using recombinant influenza vaccine (RIV) versus adjuvanted egg-grown inactivated influenza vaccine (aIIV) in older adults in England and Wales

CONCLUSIONS

RIV could offer public health benefits and economic value compared to aIIV for older adults in England and Wales through reduced influenza cases and sequelae, thereby decreasing the healthcare resource burden

BACKGROUND

- In the United Kingdom (UK), seasonal influenza contributes substantially to National Health Service (NHS) winter pressures[1,2]. Influenza cases in older adults were the main drivers of economic impact, with up to £100 million expended in direct hospitalisation costs across England per influenza season (2016-2020)[3]
- The Joint Committee on Vaccination and Immunisation issues annual influenza vaccine recommendations. For the forthcoming season (2025/26), three enhanced vaccines, RIV, aIIV and high-dose egg-grown inactivated influenza vaccine were most recently recommended for older adults (aged over 65 years)[4]
- Despite the longer market presence and published effectiveness data for both RIV and aIIV in the local context[5,6], comprehensive cost-effectiveness studies comparing RIV and aIIV are limited, and head-to-head data on clinical effectiveness are lacking

METHODS

Model population: older adults (aged over 65 years)

Model, perspective and structure:

- A static two pathway decision-tree model analysing healthcare outcomes and costs from an England/Wales healthcare payer perspective **(Figure 1)**

Model inputs: Key model input parameters are summarized in **Table 1**

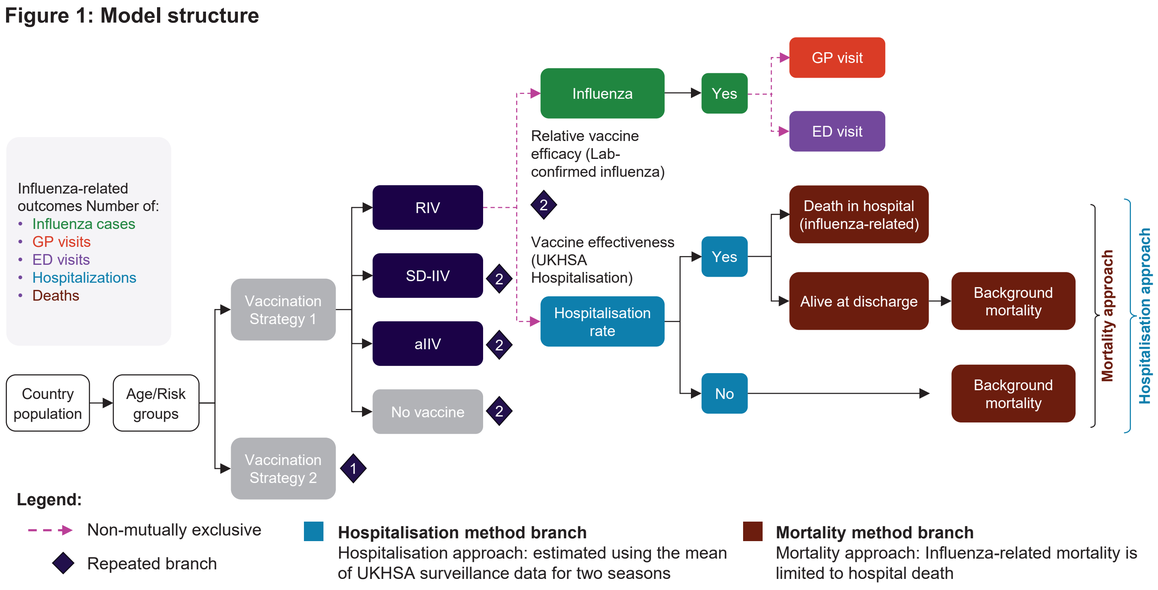
Outcomes:

- Clinical outcomes including influenza cases, general practitioner (GP) visits, emergency department (ED) visits, hospitalizations and deaths and related costs, Life years (Lys), Quality-adjusted life years (QALYs), and Incremental cost-effectiveness ratio (ICERs)
- QALYs and LYs lost because of premature influenza-related mortality are captured over a lifetime horizon and are discounted at a rate of 3.5%
- All costs were reported in 2024 GBP, with vaccination costs for RIV and aIIV both set at £17.55 per dose[7,8]

Scenario analysis: Multiple scenario analyses examined are described in **(Table 2)**

Sensitivity analysis: Probabilistic sensitivity analyses (PSA) and deterministic two-way sensitivity analysis (TWSA) were used to explore various scenarios of RIV and aIIV including potential seasonal variations in vaccine effectiveness on hospitalisation (based on UKHSA data) as well as scenarios exploring vaccine efficacy on influenza cases, GP visits and ED visits (based on cluster RCT in nursing homes)[9,10]

Figure 1: Model structure



RESULTS

- In the base case analysis, using RIV instead of aIIV averted 102,398 influenza cases, 21,508 GP visits, 6,714 ED visits, 2,540 hospitalisations, and 520 deaths annually **(Figure 2)**
- Analysis indicated savings with RIV in terms of influenza-associated prescription medication costs (£ 0.21 million), GP visit costs (£2.91 million), reduced ED presentation costs (£2.78 million), and hospitalisation costs (£24.21 million) **(Figure 2)**
- RIV dominated aIIV with incremental cost savings of £2.69 per person, resulting in an incremental net monetary benefit (NMB) of £10.76 per person **(Table 3)**
- Scenario analyses showed robustness across various assumptions, with RIV consistently dominating aIIV
- TWSA examining realistic variation in VE, and the subsequent impact on hospitalisation outcomes demonstrated fewer hospitalisation events for RIV compared to aIIV in 98.5% of the area of the heatmap **(Figure 3a)**
- In addition, TWSA on the absolute vaccine efficacy revealed fewer influenza cases and healthcare utilisation (GP visits and ED presentations) in 96.3% of the heatmap area **(Figures 3b, 3c, and 3d)**

Table 3: Cost-effectiveness analysis – RIV versus aIIV (age ≥65) probabilistic base case, mean (95% CrI), per person

Value per person	RIV	aIIV
Total costs	£35.03 (£34.94 to £35.12)	£37.66 (£37.55 to £37.76)
Total QALYs	7.14 (7.14 to 7.14)	7.14 (7.14 to 7.14)
Incremental costs	-	-£2.69 (-£2.72 to -£2.66)
Incremental QALYs	-	<0.0001
Incremental NMB	-	£10.76 (£10.64 to £10.89)
ICER (£/QALY)	-	Dominant (-£6,561/QALY)

STRENGTH & LIMITATIONS

- Our model incorporated up-to-date, country-specific data, utilised randomized controlled trial (RCT)-driven data for vaccine efficacy against LCI infection and employed a separate influenza hospitalisation pathway to account for VE against hospitalisations using contemporaneous UKHSA data
- The use of a separate pathway for influenza hospitalisations reduced uncertainty surrounding the attack rate and enabled precise modelling of hospitalisation rates aligned with observed data
- As no RCTs directly compared RIV versus aIIV, we estimated relative vaccine benefits using the best available rVE data for both vaccines against the common standard-dose quadrivalent influenza vaccine comparator

Table 1: Model input parameters

Parameter	Adults(aged ≥65)	Source
Populational parameters		
Population size (England and Wales)	11,465,323	ONS, 2023[11]
Vaccination coverage rate	76.3%	UKHSA 2021/22 season[12]
Background all-cause mortality	2.60%	ONS 2017 to 2019 (weighted average)[13]
Influenza-related hospitalisation rate per 100,000	175.3	14
Vaccine efficacy against LCI		
Influenza attack rate	7.2%	WHO, 2012[15]
Absolute efficacy RIV[a]	65%	16, 17
Absolute efficacy aIIV[b]	50%	17
Probability of GP visit after infection	21%	18
Probability of ED visit after infection	6.60%	calculated[c]
Vaccine effectiveness against influenza-related hospitalisations		
Absolute effectiveness RIV	36.5%	5, 6
Absolute effectiveness aIIV	20.0%	5, 6
Vaccine administration cost	£9.58	NHS BSA 2024[19]
Outpatient costs		
Prescription influenza medications*	£9.90	NHS 2023
Influenza-related GP visit	£135	Pitman et al. 2013[20]
Influenza-related ED visit	£415	NHS Reference Cost 2021/22
Inpatient costs		
Hospitalisation	£9,531	NHS reference costs 2021/22 (£564/day)
Utilities		
Utility - general population	0.73	EQ-5D index value (TTO value set)[21]
Absolute QALYs lost per hospital admission	0.018	Baguelin M et al.,2015[22]
Absolute QALYs lost per case of influenza	0.010	HTA report[23]

[a]Calculated using 50% absolute efficacy of SD-IIV[17] and 30% relative efficacy RIV vs. SD-IIV[16]; [b]Calculated using 50% absolute efficacy of SD-IIV[17] and assumed 0% relative efficacy aQIV vs. SD- IIV; [c]Calculated from HES 2022 data (280,770 ED visits, ICD codes J09-J18) and ONS 2022 population estimates, applying a 7.5% influenza attack rate; [d]Simple mean of the relative effectiveness of RIV versus no vaccine 2022/23 (39% as per JCVI minutes)[5] and 2023/24 (34% as per JCVI minutes)[6]; *Prescription charge as of 1 May 2024

Table2: Scenario analysis

Scenario	Type	Description
1	Influenza-related Hospitalisation Effectiveness	For the 2022-2023 season: RIV, 39% and aIIV, 18% For the 2023-2024 season: RIV, 34% and aIIV, 22
2	Relative Vaccine Efficacy (rVE)	aIIV/SD-IIV: 17% and 22%
3	Attack Rates	2.6%, 7.2%, and 12%
4	Vaccine Coverage	Lowest: 72%, highest: 82.3%
5	Vaccination Strategy	High-risk only: 57.4% RIV, Low-risk only: 42.6% RIV

Figure 2: Base case analysis: influenza-related disaggregated population level and incremental clinical outcomes and costs (RIV-aIIV)

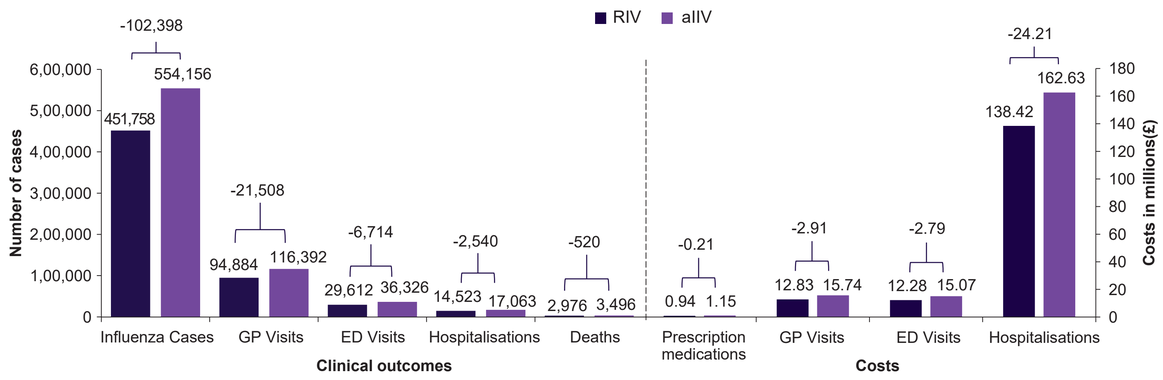
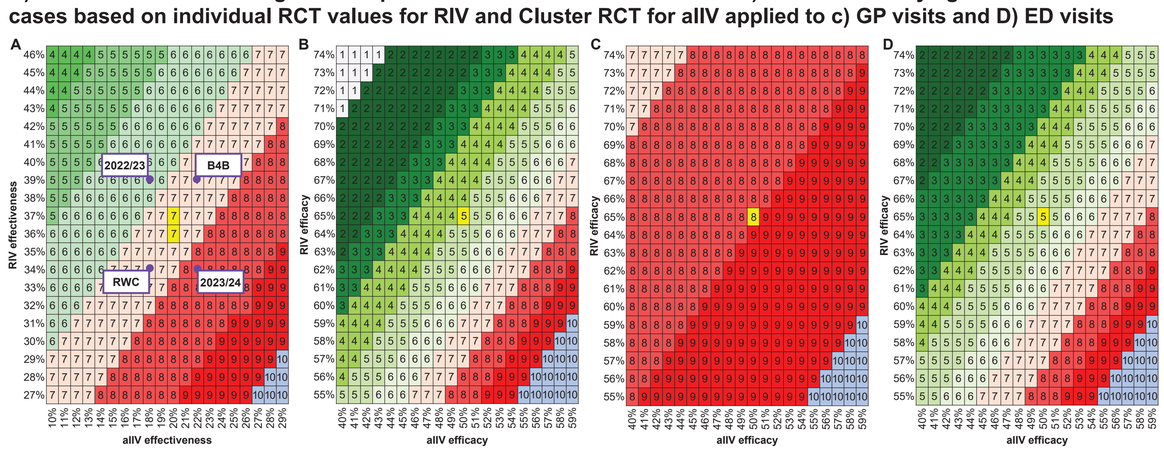


Figure 3: RIV vs aIIV vaccine efficacy and effectiveness against influenza-related outcomes
A) Vaccine effectiveness against hospitalisation based on seasonal rVE B) Vaccine efficacy against influenza cases based on individual RCT values for RIV and Cluster RCT for aIIV applied to c) GP visits and D) ED visits



Note: Purple dots in panel A indicate influenza-related hospitalisation effectiveness values for: Best for both (B4B) (RIV 39% vs aIIV 22%); Reasonable worst case (RWC) (RIV 34% vs aIIV 18%); Influenza-related hospitalisation effectiveness for 2022/23 season (RIV 39% vs aIIV 18%) and 2023/24 season (RIV 34% vs aIIV 22%)

Notes on colour scheme:
Numbers <10 show that RIV is favourable compared with aIIV (i.e. fewer hospitalisations / influenza cases / GP and ED visits with RIV vs aIIV). The number of events avoided was indicated by the size of the numbers. The more events that are avoided, the lower the number (green cells). The fewer events avoided, the higher the number (red cells). Number 10 (blue cells) show that outcomes are favourable to aIIV. Yellow cells highlight the position of the value used in the base case

ABBREVIATIONS: aIIV, adjuvanted inactivated influenza vaccine; B4B, best efficacy data for both vaccines; CrI, Credible interval; ED, emergency department; EQ-5D, EuroQol 5-dimension questionnaire; GP, general practitioner; ICER, Incremental cost-effectiveness ratio; LCI, Laboratory-Confirmed Influenza; Lys, life years; NMB, net monetary benefit; ONS, Office for National Statistics; RCT, randomized controlled trial; RIV, recombinant influenza vaccine; RWC, reasonable worst case for both vaccinations; rVE, relative vaccine efficacy; SD-IIV, standard dose inactivated influenza vaccine; TTO, time trade-off; TWSA, two-way sensitivity analysis; QALYs, Quality-adjusted life years; UKHSA, United Kingdom Health Security Agency; WHO, World Health Organization; - Not applicable

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This poster presents data that has been submitted to the British Journal of General Practice and is currently under consideration and review

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