Reducing the transmission and annual burden of influenza in the UK with baloxavir marboxil: A cost-effectiveness analysis using evidence from the CENTERSTONE trial

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Background

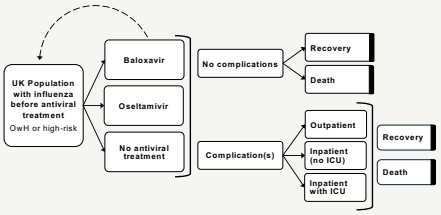
- Influenza causes millions of symptomatic cases and thousands of deaths annually in the UK, driving high health care resource utilization and productivity losses.[1-5]
- The risk of infection among close contacts is highest in the home due to the proximity and duration of exposure to an infected household member.[6,7]
- Baloxavir marboxil (baloxavir)▼ is a single-dose oral antiviral treatment that reduces the duration of influenza symptoms, rapidly stops viral shedding, and is approved for uncomplicated influenza in more than 80 countries worldwide.[8,9]
- Baloxavir significantly reduced influenza virus transmission among household contacts within 5 days of treatment vs placebo (29% adjusted relative risk reduction) in the phase 3 CENTERSTONE trial (NCT03969212).[10]

This study estimated the cost-effectiveness of reducing influenza virus transmission with baloxavir in the UK using data from the CENTERSTONE trial.

Methods

- A cost-effectiveness model was developed to compare baloxavir, oseltamivir, and no antiviral treatment in the UK (**Figure 1**).
- The model estimated annual influenza cases, general practitioner (GP) visits, hospitalizations, deaths, costs, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICERs).
- Outcomes were assessed for the total population as well as high-risk and otherwise healthy (OwH) subgroups; analyses were conducted over a lifetime horizon with 3.5% annual discounting of costs and QALYs. All costs were adjusted to 2024 GBP.

Figure 1. Cost-effectiveness model design



Bolded sides indicate terminal nodes; dotted line indicates change in size of the infected population attributable to antiviral treatment. ICU, intensive care unit; OwH, otherwise healthy; UK, United Kingdom.

Influenza infections and transmission

- The model assumed 8.4 million annual influenza infections based on global estimates scaled to the UK population.[11,12]
- The overall antiviral treatment rate was 17%, composed of 30% and 12% treatment rates among high-risk and OwH subgroups, respectively.[13,14]
- Baloxavir was assumed to reduce transmission by 5.0% (4.97%), derived from the 29% adjusted relative risk reduction observed in the CENTERSTONE trial applied to the 17% treatment rate.[10]
- Oseltamivir was assumed to have no impact on virus transmission based on mixed evidence regarding the potential for oseltamivir to meaningfully reduce virus transmission.[15-20]

Antiviral treatment costs and side effects

- Unit costs per treatment course were £100 for baloxavir and £14.64 for oseltamivir.[21]
- Side effect rates were derived from CAPSTONE trials, most commonly diarrhea and nausea;[6,7] adverse events were assumed to last 7 days, requiring £10 in over-the-counter patient costs per episode.[22]

Influenza-related complications and mortality

- The model captured a range of influenza-related complications with rates ranging from 2.8–5.1% among treated individuals and 7.6–12.2% among untreated individuals.[14,23]
- Background mortality rates were applied to individuals without complications; those with complications could require GP visits, hospital admission, or intensive care unit (ICU) stays.[23]

Health state utilities

Utility values were 0.96 for the general population, 0.81 for uncomplicated influenza, and 0.90 for recovery after ICU stay; utility decrements were applied for complications and antiviral side effects.[23,24]

Societal impact of influenza and antiviral treatment

The societal impact of baloxavir treatment was estimated by linking QALY gains to economic productivity, expressed as gross value added per economically active person; age-stratified contributions were applied to reflect different roles in the workforce and household.

Note: Prior work employing similar methods has used the term "social impact," however, this analysis focused on direct and indirect costs as the "societal impact" and the terms are used interchangeably.

Scenario analyses

The following scenario analyses were conducted to test the robustness of the base case findings:

Virus transmission: Alternative transmission reduction rates for oseltamivir (3%) and baloxavir (3–15%)

Complications: Alternative rates of complications with baloxavir

Treatment rate: Higher antiviral treatment rates (34% overall; 60% high-risk, 24% OwH) to simulate epidemic/pandemic preparedness

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▼This medicinal product is subject to additional monitoring, which will allow quick identification of new safety information. Healthcare professionals are asked to report any potential side effects to the local regulatory authority and to http://www.medinfo.roche.com or directly to the local Roche drug safety team (http://www.roche.com/products/local_safety_reporting.htm).

Results

Base case cost-effectiveness results across the UK population

- Total annual costs of influenza without antiviral treatment were £1.093 billion.
- Baloxavir prevented 412,902 cases and 42,175 influenza-related GP visits per year vs no antiviral treatment or oseltamivir (**Table 1**).
- Baloxavir was dominant vs no antiviral treatment, providing a total of £11.9 million in cost savings and 81,178 additional QALYs.
- Compared with oseltamivir, baloxavir added £65.2 million in total costs with 21,231 additional QALYs (ICER, £3,070/QALY).
- Results were driven by fewer influenza cases and lower risk of complications and hospitalizations with baloxavir (–£146.4 million vs no treatment, –£47.4 million vs oseltamivir).

Table 1. Base case cost-effectiveness results

	Baloxavir	No antiviral treatment	Oseltamivir	Baloxavir vs no antiviral treatment	Baloxavir vs oseltamivir
Influenza cases, n	**7,987,098**	**8,400,000**	**8,400,000**	**-412,902**	**-412,902**
Influenza-related GP visits	815,821	857,996	857,996	-42,175	-42,175
Influenza-related GP visits, direct costs	£28,553,742	£30,029,860	£30,029,860	-£1,476,118	-£1,476,118
Antiviral drug costs	£135,381,311	£0	£20,844,432	£135,381,311	£114,536,879
Patients with antiviral treatment-related side effect	674,750	0	1,161,342	674,750	-486,592
Influenza-related complications, direct costs	£916,919,771	£1,063,367,691	£964,320,968	-£146,447,921	-£47,401,197
Total costs	**£1,081,529,574**	**£1,093,397,551**	**£1,016,356,602**	**-£11,867,978**	**£65,172,972**
Total QALYs lost	410,244	491,422	431,475	-81,178	-21,231
Incremental costs				**-£11,867,977**	**£65,172,972**
Incremental QALYs				**81,178**	**21,231**
ICER				**Dominant***	**£3,070**

*Dominant interventions (baloxavir in this case) provide greater efficacy at a lower cost than comparators (no antiviral treatment). GP, general practitioner; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

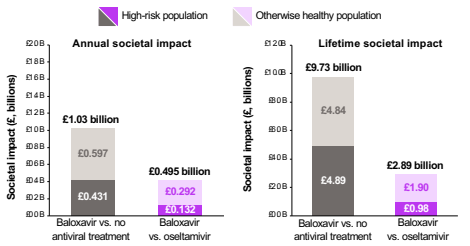
Socioeconomic burden of influenza

- The socioeconomic burden of influenza without antiviral treatment ranged from £4.46 billion in 2016 to £4.95 billion in 2019, reaching £5.73 billion in 2022 during the post-COVID period.

Societal impact of baloxavir treatment

- The annual population-level societal impact of baloxavir vs. no antiviral treatment was +£1.03 billion per year, and +£495 million per year for vs. oseltamivir (**Figure 2**).
- The lifetime population-level societal impact of baloxavir treatment during one influenza season (not accounting for treatment in future seasons) was +£9.73 billion vs. no antiviral treatment, and +£2.89 billion vs. oseltamivir (**Figure 2**).
- When the societal impact of reducing virus transmission with baloxavir was applied to the model in addition to the direct costs in the base case analysis, baloxavir was dominant vs. no antiviral treatment and oseltamivir.

Figure 2. Societal impact of antiviral treatment with baloxavir



Scenario analyses

- In the **virus transmission scenario**, using a 3% transmission reduction rate with oseltamivir, baloxavir remained cost-effective vs. oseltamivir with an ICER of £11,544 per QALY gained (**Table 2**).
- Baloxavir remained cost-effective from a 3% transmission reduction rate vs. no antiviral treatment (ICER, £221/QALY) and vs. oseltamivir (ICER, £8,571/QALY), and was dominant vs. both no treatment and oseltamivir starting with a 13% transmission reduction rate.
- In the **complications scenario**, baloxavir remained cost-effective vs. no antiviral treatment at any level of influenza-related complications with baloxavir, and with complication rates <7% for baloxavir vs. oseltamivir (**Table 2**).
- In the **treatment rate scenario**, using antiviral treatment rates of 60% for high-risk and 24% for OwH individuals, baloxavir prevented 825,804 influenza cases per year vs. no antiviral treatment or oseltamivir (**Table 3**).
- Baloxavir was dominant vs. no antiviral treatment (140,973 incremental QALYs; lower total costs of £66.7 million) and provided 38,255 incremental QALYs vs. oseltamivir with total incremental costs of £130.2 million (ICER, £3,404/QALY).

Table 2. Virus transmission and complications scenarios

		Base case value	Scenario parameter value	Baloxavir vs no treatment	Baloxavir vs oseltamivir
	Base case	–	–	**Dominant**	**£3,070**
Virus transmission	Oseltamivir transmission reduction	0	3%	Dominant	£11,544
	Baloxavir transmission reduction	5%	3%	£221	£8,571
			5%	Dominant	£3,070
			8%	Dominant	£1,105
			10%	Dominant	£170
			13%	Dominant	Dominant
			15%	Dominant	Dominant
Complications	Rate of influenza-related complications with baloxavir (total population)	2.81%	1%	Dominant	£1,653
			2%	Dominant	£2,331
			3%	Dominant	£3,280
			4%	Dominant	£4,704
			5%	£135	£7,079
			6%	£288	£11,838
			7%	£460	£26,182
			8%	£656	Dominated
			9%	£880	Dominated
			10%	£1,141	Dominated

Table 3. Treatment rate scenario analysis results: impact of higher antiviral treatment rates

	Baloxavir	No antiviral treatment	Oseltamivir	Baloxavir vs no antiviral treatment	Baloxavir vs oseltamivir
Annual influenza cases	**7,574,196**	**8,400,000**	**8,400,000**	**-825,804**	**-825,804**
Received antiviral treatment	2,567,652	0	2,847,600	2,567,652	-279,948
Total costs	**£1,026,740,005**	**£1,093,397,551**	**£896,516,316**	**-£66,657,547**	**£130,223,689**
Total QALYs lost	**350,449**	**491,422**	**388,704**	**-140,973**	**-38,255**
HR population QALYs lost	115,777	189,104	128,423	-73,327	-12,645
OwH population QALYs lost	234,672	302,318	260,281	-67,647	-25,609
Incremental costs				-£66,657,547	£130,223,689
Incremental QALYs				140,973	38,255
ICER				**Dominant**	**£3,404**

GP, general practitioner; HR, high-risk; ICER, incremental cost-effectiveness ratio; OwH, otherwise healthy; QALY, quality-adjusted life-year.

Conclusions

- Influenza imposes a substantial clinical and economic burden in the UK, with direct annual costs exceeding £1 billion in the absence of antiviral treatment.
- Reducing household transmission with baloxavir may prevent ~500,000 cases annually in the UK, leading to overall cost savings, QALY gains, and broader societal benefits driven by fewer cases and complications, and reduced health system burden.
- The impact of baloxavir on influenza transmission may provide substantial population-level economic impacts (gross value added) via direct, indirect, and induced paid effects as well as unpaid effects.
- This model reinforces the cost-effectiveness of baloxavir in the UK, though certain limitations apply:
  - Population characteristics from CENTERSTONE and the literature may not fully align with the UK population
  - Household transmission reductions from CENTERSTONE only accounted for prevention of secondary transmission events
  - Societal impact may be underestimated, as paid productivity benefits were not applied to adults ≥60 years of age
- These findings support the integration of baloxavir into population health strategies, including stockpiling for preparedness, to help mitigate pressures on communities, healthcare systems, and society.

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