Cost-effectiveness Analysis of Pharmacogenetic Testing to Guide Treatment for Children with Asthma

EE216

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Introduction

- Children with copies of the **Arg16 allele** for the ADRB2 gene encoding the β2-adrenergic receptor have an **increased risk of asthma exacerbations** with long-acting β2 agonist (LABA) use (OR = 1.52, 95%CI: 1.17, 1.99)[1].
- This exacerbation risk could **decrease** if prescribed a leukotriene receptor antagonist (LTRA) instead.
- **Pharmacogenetic testing** has the potential to mitigate this exacerbation risk by identifying the relevant children with two copies of the Arg 16 allele before prescribing[2].
- A recent **meta-analysis** demonstrated that the addition of asthma controller treatment according to the Arg16Gly genotype reduced exacerbation rates (-0.08, 95%CI: -0.16, -0.00)[3].

Objective

The study aims to evaluate whether genotype-guided treatment for asthma is clinically effective and is good value for money when compared with the usual approach to prescribing.

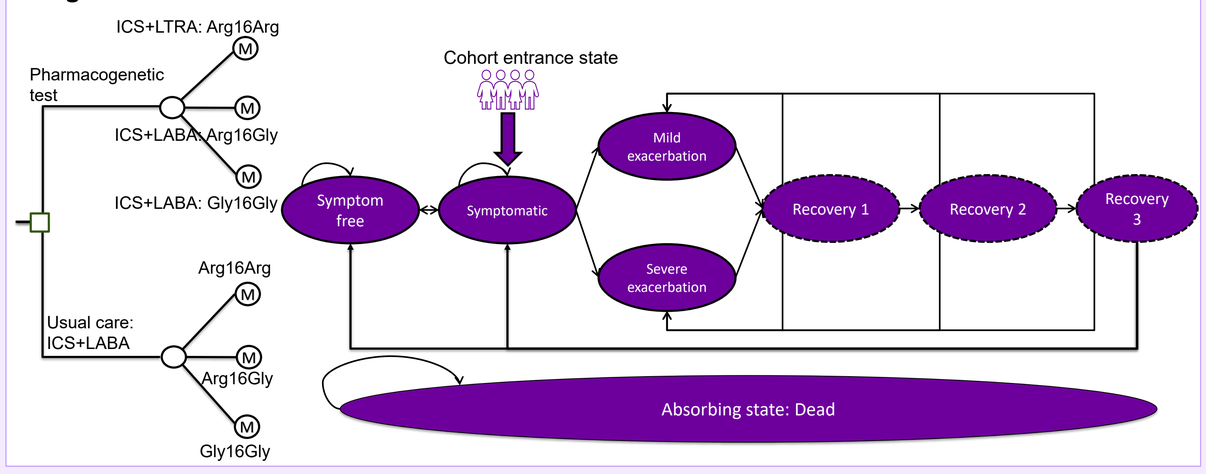
Methods

- A model-based economic evaluation simulated the cost-effectiveness of genotype testing for a hypothetical cohort of children with persistent asthma. The decision problem is summarized in the PICO table.

Population	Intervention	Comparator
Children aged 6-years, with persistent asthma uncontrolled at step 2 (inhaled corticosteroids monotherapy (ICS)) and requiring the initial add-on therapy at step 3	Following genotyping, Arg16Arg subgroup are prescribed with montelukast (LTRA) added to ICS, but Arg16Gly and Gly16Gly subgroup are prescribed with salmeterol (LABA) with ICS	Usual care, prescribing all children salmeterol (LABA) with ICS
Outcomes	**Time horizon**	**Perspective**
NHS costs (£, price year: 2024), Quality-adjusted life years (QALYs), Asthma exacerbation counts	Six years, from the start of age 6 to the end of age 11-years	Healthcare system, England

- The ***Decision tree*** stratified the patients by ADRB2 genotypes.
- The ***Markov model*** showed mutually exclusive health states that a patient with asthma can experience.
- ***Probabilities of exacerbation*** given different treatments were estimated from a meta-analyses[1].
- ***Costs*** included costs of medication, consultation, hospitalization and pharmacogenetic testing.
- ***Model parameters*** were sourced from published journals including clinical trial analyses[2] and meta-analyses[1,3].
- ***QALYs*** were calculated by multiplying the time in each health state by the according quality-of-life score. The quality-of-life scores were estimated by the EQ-5D-3L (UK valuation tariff)[4].
- ***Analysis*** The outcomes were calculated on a per-patient basis and then **scaled-up** into the population level over 10 years.

Figure 1: Decision tree-Markov Model



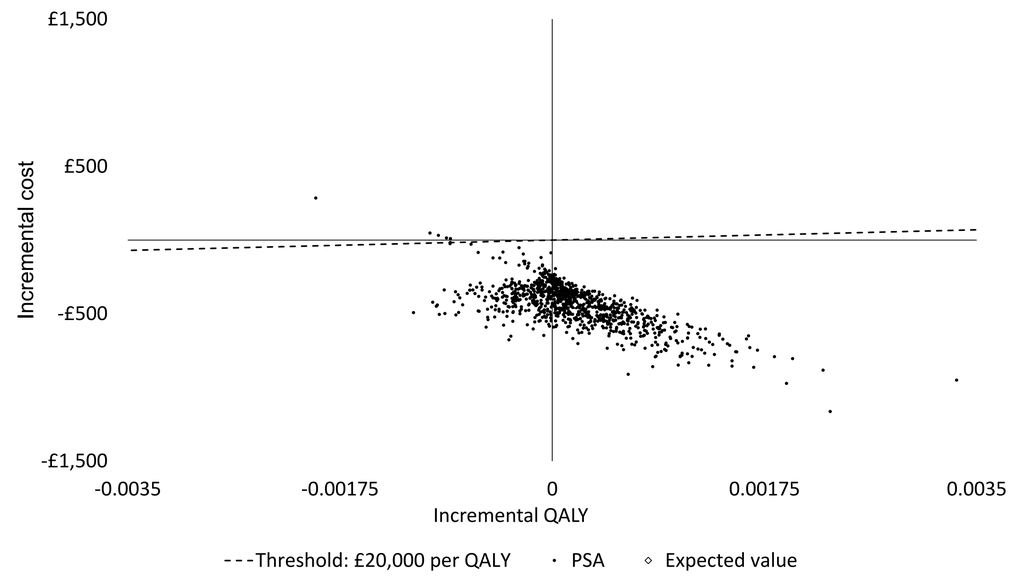
Results

Table 1 Genotype-guided treatment could save £470 and avoid nearly 1 exacerbation per child with asthma.

Strategies	Total cost	Total QALY	Number of exacerbations	Severe exacerbations	Diff in cost	Diff in QALY	Avoided exacerbations	Avoided severe exacerbations
Usual care	£5,070	4.83035	9.599	3.615				
Genotype-guided treatment	£4,601	4.83060	8.863	3.335	-£469	0.00025	-0.736	-0.280

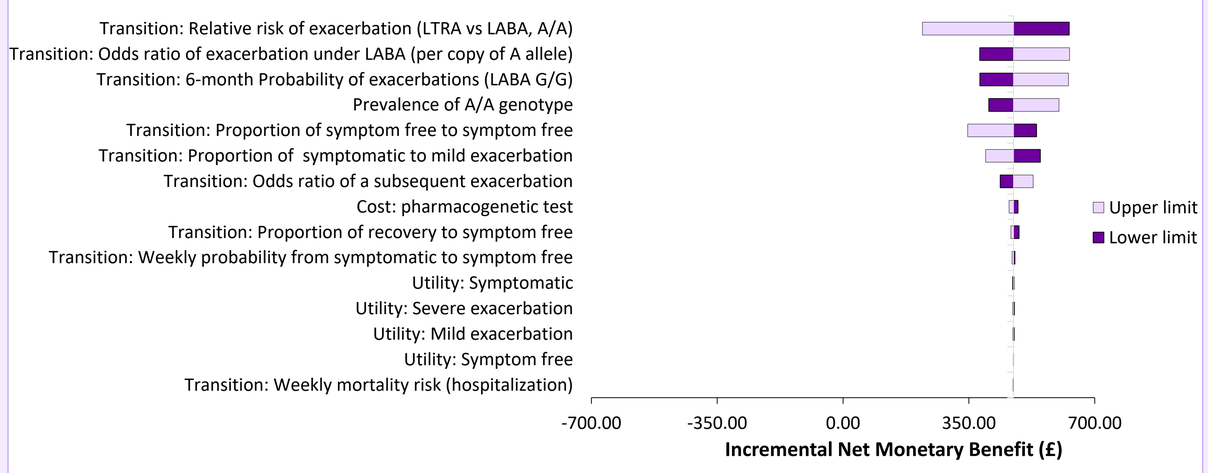
Diff: difference; QALYs: Quality-adjusted life years.

Figure 2: The probability that the genotyping strategy is cost effective* was 98.4%.



*Probability: the proportion of simulated incremental cost and incremental QALY pairs that fall below the cost-effectiveness threshold (dashed line).

Figure 3: The cost-effectiveness results were robust when varying every input parameter.



*Input parameters values were varied between their 95% confidence interval if reported, or ±25% variation otherwise. Incremental net monetary benefit is an estimate of cost-effectiveness, where INMB>0 means the genotype-guided treatment is cost-effective.

Scenario analyses on treatment effectiveness, strategy uptake, turnaround time and ethnic subgroup analysis were performed. The results were consistently in showing that genotype testing was cost-effective.

Table 2: Population clinical and economic benefits by rolling out the genotyping strategy.

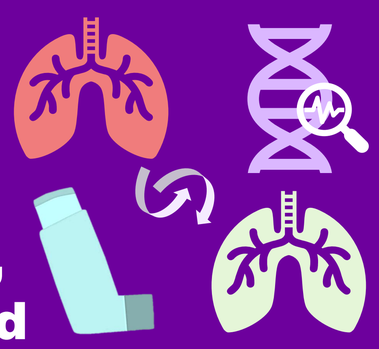
Ten-year incident cohort size*	Incremental costs	Incremental QALYs	Avoided exacerbations	Avoided severe exacerbations
75702	-£35.5 million	18.59	-55729	-21187

Discussion

- **Decision makers** can use this study to inform the economic value of ADRB2 pharmacogenetic testing to support the wider provision of genotype-guided treatment in the UK.
- The economic evaluation can aid **health technology assessment bodies**, such as NICE, to inform the change of national guidelines.
- **Clinicians** can leverage the promising evidence to support pharmacogenetic testing as a standard component of care for relevant children.
- Our study can be used as a framework for decision-makers in **other countries** to help generate relevant economic evidence for their own healthcare settings.

Conclusion

Genotype-guided prescribing in children with moderate asthma was cost-effective, reducing exacerbations and saving healthcare costs.



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References

1. Turner S, Francis B, Vijverberg S, Pino-Yanes M, Maitland-van der Zee AH, Basu K, et al. Childhood asthma exacerbations and the Arg16 β2-receptor polymorphism: A meta-analysis stratified by treatment. J Allergy Clin Immunol. 2016;138(1):107-13.e5.
2. Ruffles T, Jones CJ, Palmer C, Turner S, Grigg J, Tavendale R, et al. Asthma prescribing according to Arg16Gly beta-2 genotype: A randomised trial in adolescents. The European respiratory journal. 2021;58(2):2004107.
3. Slob EMA, Vijverberg SJH, Ruffles T, Noij LCE, Biermann J, Brouwer AFJ, et al. Genotype-Guided Asthma Treatment Reduces Exacerbations in Children: Meta-Analysis of Two Randomized Control Trials. Allergy. 2025;80(4):1006-14.
4. 1.Briggs A, Nasser S, Hammerby E, Buchs S, Virchow JC. The impact of moderate and severe asthma exacerbations on quality of life: a post hoc analysis of randomised controlled trial data. Journal of Patient-Reported Outcomes. 2021;5(1):6.

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