Distributional Cost-Effectiveness Analysis of Lung Cancer Treatments from an English NHS Perspective

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Background and Objective

- Distributional cost-effectiveness analysis (DCEA) facilitates a quantitative assessment of how health effects and costs of interventions are distributed between population subgroups, and of any ensuing trade-offs between health maximization and equity.
- Implementation of DCEA is currently being explored by the National Institute of Health and Care Excellence (NICE) in England (1).
- Previous research has established a link between lung cancer and socio-economic status. We aimed to conduct an DCEA from the perspective of England's National Health Service (NHS) of two non-small cell lung cancer (NSCLC) treatments recommended by NICE and identify key drivers of the analysis.

Methods

- Population subgroups were defined based on a relative measure of deprivation at the area level, the 2019 index of multiple deprivation (IMD)(4).
- We considered two NICE single technology appraisals (TA) in NSCLC that differ in the populations treated and cost-effectiveness to illustrate the impact of these differences on the analyses:
  - one for a general NSCLC population, atezolizumab vs. docetaxel in relapsed NSCLC after chemotherapy (TA520; 2018), which met the NICE end-of-life criteria (5)
  - one for a rarer driver mutation NSCLC, alectinib vs. crizotinib for first-line anaplastic lymphoma kinase positive advanced NSCLC (TA536; 2018) (6)

Table 1. Population EDEH impact at an opportunity cost threshold of £30,000/QALY

	TA520 atezolizumab	TA536 alectinib
Baseline population QALE (QALE$_b$*N) (1)	3,942,667,355 QALYs	3,942,667,355 QALYs
Post-decision population QALE (QALE$_p$*N) (2)	3,942,665,467 QALYs	3,942,667,446 QALYs
Incremental population QALE (ΔQALE*N) (3)=(2)-(1)	-1,888 QALYs	91 QALYs
Baseline population EDEH (equity weighted QALE) (EDEH$_b$*N) (4)	3,863,434,366 QALYs	3,863,434,366 QALYs
Post-decision population EDEH (EDEH$_p$*N) (5)	3,863,432,534 QALYs	3,863,434,528 QALYs
Incremental population EDEH (ΔEDEH*N) (6)	-1,833 QALYs	162 QALYs
Population equity impact (incremental equity-weighted QALE – incremental QALE) (6-3)	56 QALYs	71 QALYs
A(ε)	0.020	0.020
-ΔA(ε) (equity impact per person)	<0.0001% change, positive	<0.0001% change, positive

Abbreviation: EDEH, equally distributed equivalent health
Notes: QALE$_b$, baseline quality-adjusted life-expectancy at birth per-person; QALE$_p$, post-decision quality-adjusted life-expectancy at birth per-person; ΔQALE, difference in QALE between post-decision and baseline; EDEH$_b$, baseline equally distributed equivalent health per person; EDEH$_p$, post-decision equally distributed equivalent health per person; ΔEDEH, difference in EDEH between post-decision and baseline; N, England population, A(ε), Atkinson index of inequality; -ΔA(ε), relative difference in the Atkinson index of inequality between post-decision and baseline

Figure 1. Equity-efficiency impact plane

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Results

Base-case

- We estimated that 4142 patients would be eligible for atezolizumab, and 477 for alectinib, with 33% of the eligible patients being in the most deprived quintile compared to 12% in the least deprived.
- The equity-efficiency impact plane is presented in Figure 2, and the analysis results in Table 1. The population social welfare impact (EDEH) was small, driven by the size of the patient population and the per-person net health benefit.
- At an OC threshold of £30,000/QALY, alectinib both improves population health (91 QALYs) and decreases health inequities (northeast quadrant), equivalent to 71 QALYs, improving social welfare (162 QALYs).
- Atezolizumab involves a trade-off between reducing health inequities, equivalent to 56 QALYs, and reducing population health (-1,888 QALYs) (southeast quadrant), decreasing social welfare (-1,833 QALYs). This is driven by atezolizumab not being cost-effective at £30,000/QALY.

Sensitivity analysis

- The results of sensitivity analyses varying the OC threshold and Atkinson inequality aversion parameter (IAP) (the higher the value, the higher the willingness to forego a share of the population health to reduce health inequities) are presented in Figure 2.
- Both treatments improved social welfare if the OC threshold was set at or above the decision threshold.
- At £45,000/QALY, atezolizumab involved a trade-off between maximizing population health and reducing health inequality. Below £25,000/QALY, the EDEH decreases as the Atkinson IAP increases, highlighting that under this assumption, atezolizumab increases health inequities (Figure 2.b).
- Below £25,000/QALY, alectinib reduces total population health but also reduces health inequities, involving a trade-off (Figure 2.a).
- We ran scenario analyses varying the distribution of the patient populations. If the distribution was flat or skewed towards the least deprived, both treatments increased health inequalities.
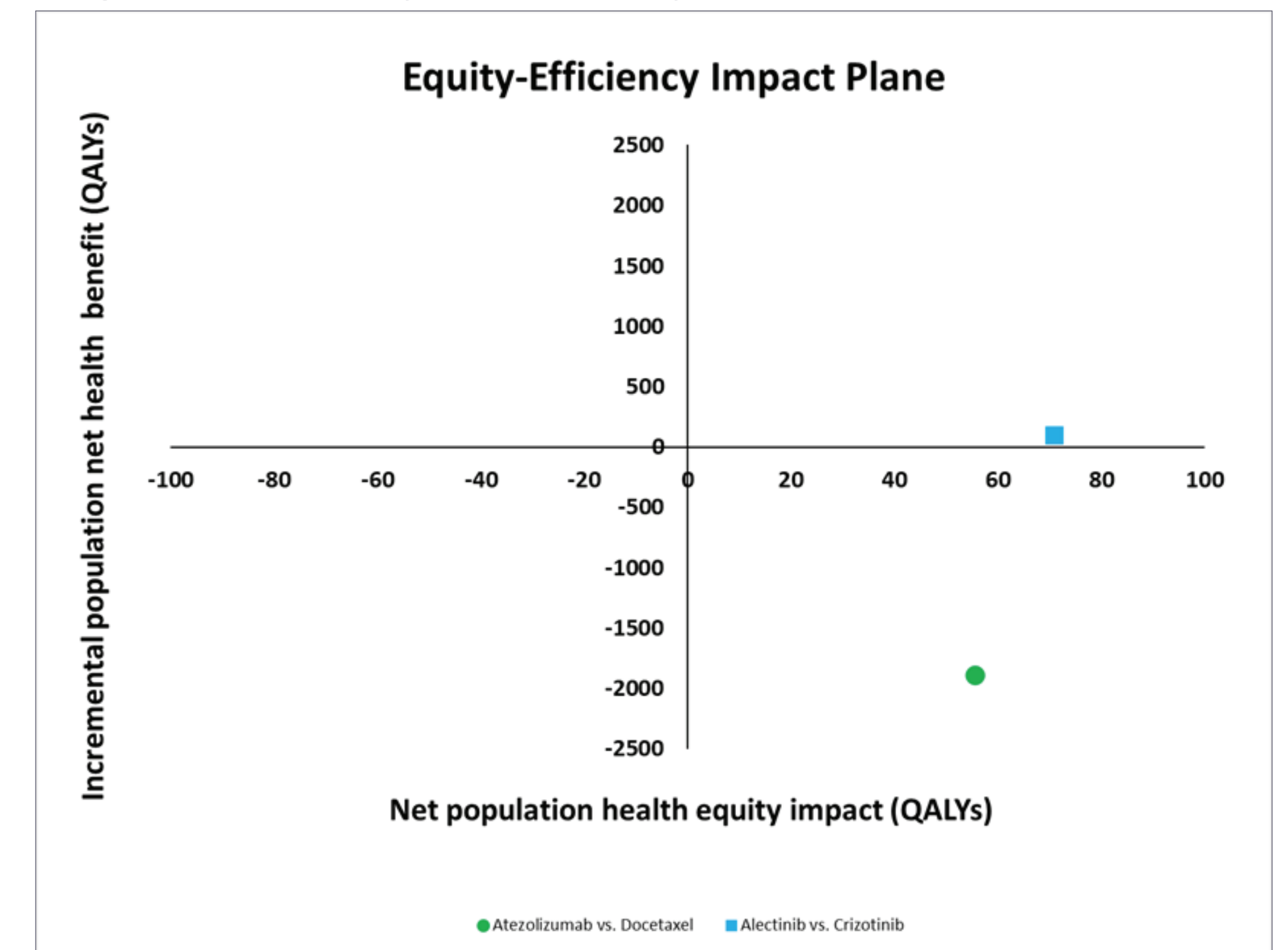
Conclusion

- This study suggests that at an OC threshold of £30,000/QALY, alectinib improves social welfare. Atezolizumab has the potential to improve social welfare under specific assumptions. Incorporating a quantitative assessment of equity impact in decision-making would allow a more comprehensive evaluation of the true value of technologies.
- There is uncertainty around the true cost per QALY at the margin in the NHS, which is a key driver of the analysis, hence its value should be carefully examined. Other key drivers in the analysis were the characteristics of the patient population (size, distribution by deprivation), and level of inequality aversion.
- Guidance for building DCEAs and transparency on how HTA bodies, such as NICE, would interpret the results and incorporate them in the decision-making would be valuable.

- Data on health benefits and costs were taken from the company base case as the NICE committee's preferred ICERs were not explicitly reported. Hypothetical discounts were applied to the intervention drug costs (as the patient access scheme was not incorporated into the base case results) to generate ICERs falling below the respective decision thresholds [£20,000-£30,000/quality-adjusted life-years (QALY) for alectinib and £50,000/QALY for atezolizumab].
- England population estimates and the distribution by sex-IMD subgroups were taken from the Office for National Statistics (7, 8). Age-standardised lung cancer incidence rates and stage at diagnosis by IMD, reported by the National Cancer Registration and Analysis Service, were combined with the proportion of patients eligible for treatment derived from the resource impact reports for each appraisal available on the NICE website (5,6,9,10).
- Distributions of baseline population health and health opportunity costs (OC) in England were taken from the literature (11,12).
- In the base case, the OC threshold, representing the costs per QALY forgone due to displacing resources in the NHS, was set at £30,000/QALY. Sensitivity analyses were conducted with values from £15,000/QALY, the value used by the English Department for Health and Social Care, based on research by Claxton et al. on the marginal productivity in the NHS (13, 14), to £50,000/QALY, consistent with the former NICE end-of-life threshold.
- We assessed the trade-off between health maximization and equity, measuring social welfare using the equally distributed equivalent health (EDEH) (based on the Atkinson social welfare function), which is the level of health per person that, if equally distributed, would give the same level of social welfare as the current distribution (3). Sensitivity analyses were conducted varying a range of model parameters.

Figure 2. Effect of the opportunity-cost threshold and Atkinson inequality aversion parameter on social welfare, (a) Alectinib, (b) Atezolizumab

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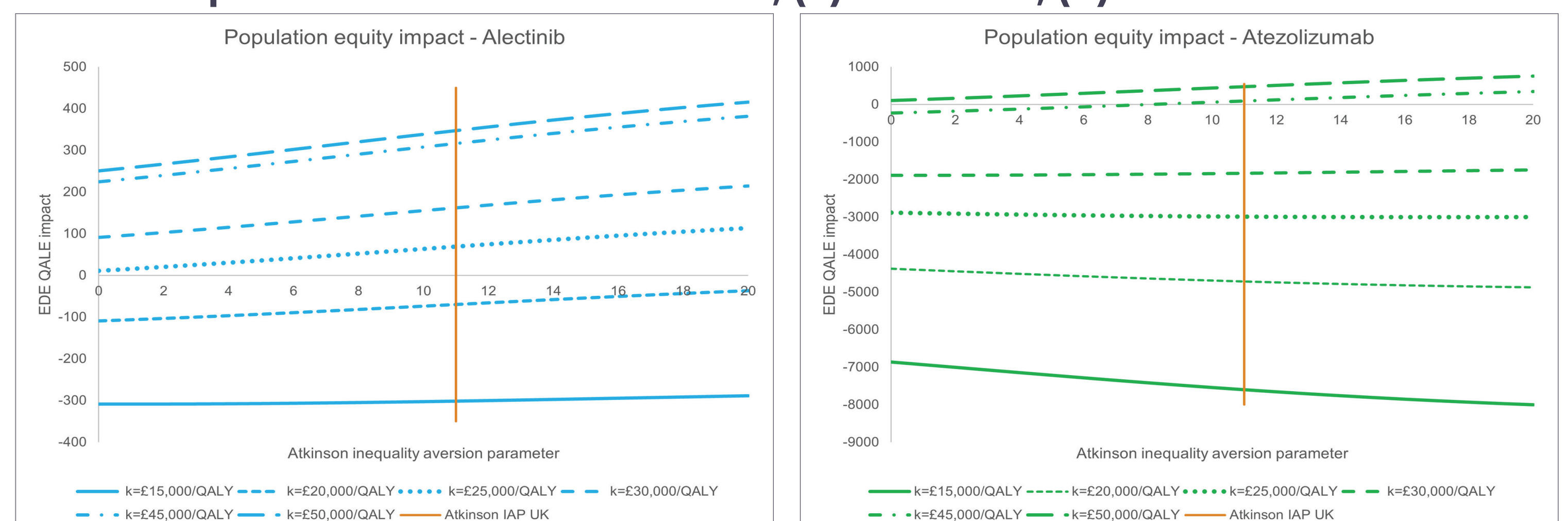
References

1. Dunning et al. NICE CHTE methods review, equalities task and finish group report.2020.
2. Love-Koh et al. Value Health. 2019;22(5):518-26.
3. Cookson et al. Oxford University Press; 2020.
4. Ministry of Housing Communities & Local Government. English indices of deprivation 2012
5. NICE. Atezolizumab for treating locally advanced or metastatic non-small-cell lung cancer after chemotherapy [TA520] 2018
6. NICE. Alectinib for untreated ALK-positive advanced non-small-cell lung cancer [TA536] 2018
7. ONS. Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2020 2021
8. ONS. Population by Index of Multiple Deprivation (IMD), England, 2001 to 2019
9. NCRAS. National Disease Registration Service: staging data in England. 2022
10. NCRAS. Lung cancer cases in England 2019. 2022
11. Love-Koh et al. Value Health. 2015;18(5):655-62.
12. Love-Koh et al. Med Decis Making. 2020;40(2):170-82.
13. Claxton et al. Health Technol Assess. 2015;19(14):1-503.
14. Department of Health and Social Care. Updating the Statutory Scheme controlling the costs of branded health service medicines. 2022

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