Should Cost-Effectiveness Analyses be the Sum of Its Subgroups? Benefits and Risks of Subgroup-Weighted Analyses to Estimate Overall Population Outcomes Guoming Shi¹, Max Clayson²

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INTRODUCTION

- Decisions based on overall population cost-effectiveness analyses (CEA) may lead to inappropriate recommendations for specific subgroups¹. ullet
- To maximize health gains within a constrained budget, a key focus of the National Institute for Care and Health Excellence (NICE), it is essential to understand heterogeneity among subgroups and its influence on cost-effectiveness³.
- CEAs in indications with population heterogeneity may model subgroups individually, rather than an overall population, and weigh the outcomes ulletaccording to subgroup prevalence. However, this approach is uncommon in HTA submissions to NICE, and its implications remain unclear.

OBJECTIVE

To re-evaluate past NICE appraisals that included subgroup analyses ulletto assess the implications of adopting a subgroup-weighted approach.

Figure 1. Appraisal screening and selection process



NICE appraisals with reimbursement recommendations published between June 1st, 2021, and June 20th, 2024;





METHODS

- **Screening:** NICE appraisals with recommendations published between 01-06-2021 and 20-06-2024 which reported incremental costeffectiveness ratios (ICERs) for overall populations and complementary subgroups.
- **Analysis:** Overall ICERs were **recalculated using subgroup ICERs and prevalences**. Recalculations were performed for original and updated base cases and external assessment group (EAG)-preferred analyses when pairwise ICERS were in the north-east quadrant.







Combined weights of at least two subgroups are equivalent to that of an overarching group for the purpose of weighted ICER calculation.

Results

- Nine appraisals were included; six with full positive recommendations, one with a restricted subgroup recommendation, two not recommended.
- ICERs from 26 subgroups ranged from -97.5% to +570% of the base case ICER and 39 weighted ICER recalculations were performed.
- Most (64%) recalculated ICERs were <10% different than the base case, 13 recalculations (33%) increased the ICER by >10%, and one recalculation (3%) reduced the ICER by >10%. Four (10%) recalculations increased the ICER above the £30,000 per quality-adjusted life-year threshold.
- Additionally, the EAG recommended a weighted approach in TA958 to derive the overall ICER (not included in analysis). This approach was also

applied in TA860 and TA710 (not included), considering the strong heterogeneity among subgroup patients.

Table 1. Overview of included NICE appraisals

400%

-200%

0%

400%

Appraisal	م ب ب اndication	Subgroups	Recommendation
TA926	Severe alopecia areata	4	No
TA893	Relapsed or refractory B-cell acute lymphoblastic leukaemia	6	Yes
TA890	Pruritus in people having haemodialysis	2	Yes
TA871	Preventing migraine	2	Yes
TA860	Refractory cytomegalovirus infection after transplant	1	Yes
TA825	Severe active granulomatosis	3	Yes
TA805	Reducing the risk of cardiovascular events	4	Restricted to subgroup
TA789	Advanced non-small-cell lung cancer	1	Yes
ΤΔ777	Excessive daytime sleepiness	3	No

Conclusions

- Subgroup-weighted analyses have been used in some recent NICE **appraisals** to partially address heterogeneity challenges.
- Recalculated **weighted results** generally aligned with overall population results but tended to slightly increase ICERs.
- Among the limited appraisals reviewed, most received **full** population recommendations despite showing highly **variable** subgroup ICERs.

REFERENCES

1. Stevens W, Normand C.



Optimisation versus certainty: understanding the issue of heterogeneity in economic evaluation. Soc Sci Med.

2. Espinoza MA, Manca A, Claxton K, Sculpher MJ. The Value of Heterogeneity for Cost-Effectiveness Subgroup Analysis: Conceptual Framework and Application. Medical Decision Making.

3. NICE health technology evaluations: the manual.

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+5%

+10%

Increased

Increased

above 20K above 30K

-10%

-5%