The Illusion of the Average Patient: Standard HTA Frameworks May Systematically Underestimate Health Gains in Heterogeneous Populations

HTA77

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> **With identical average response rates, a new targeted therapy can still uniquely help a distinct subgroup of patients in highly heterogeneous populations, which is value that average-effect HTA comparisons would miss.**

1 BACKGROUND

- **Health technology assessment (HTA)** informs reimbursement and access by comparing a new therapy with existing options, usually on the expected outcomes of an **average patient** or subgroup.[1,2]
- This suits treatments that improve average outcomes but may incompletely capture value when **response varies substantially** between patients.[2]
- Targeted therapies acting on **distinct biological pathways** can reach the same response rate while helping **different patients**.
- This is the **responder-overlap problem**: a new drug adds little if it helps patients who already respond but adds responders if it reaches patients who do not.

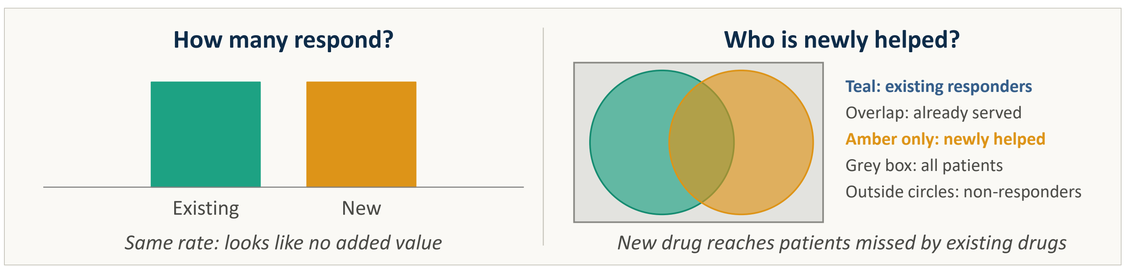
Where this could matter – Heterogeneous diseases with several targeted therapies

Asthma | Atopic dermatitis | Psoriasis | Rheumatoid arthritis

Figure 1. Possible disease areas for responder-overlap value (illustrative).

2 OBJECTIVES

- Develop a **disease-agnostic patient-level simulation** that quantifies the incremental benefit of adding a new treatment to a market of existing options, when **all treatments have equal response rates**.
- Examine how the share of patients **uniquely helped** varies with **population heterogeneity** and the **number of existing treatments**.
- Show when average-efficacy comparisons miss value that comes from **who responds**, not **how many** respond.



3 METHODS

Simulation framework: from patient heterogeneity to incremental responders

Synthetic patients
Virtual patients with **five biomarkers** (set averages, spread and correlation)

→ **Treatment scores**
Each treatment is linked to certain biomarkers. A patient's **score** shows how well they match.

→ **Response**
A patient **responds** if their score is above the 60th percentile for that treatment.

→ **Incremental responders**
Patients who respond to the new treatment but **to none of the existing ones**.

Biomarker fingerprints (illustrative)

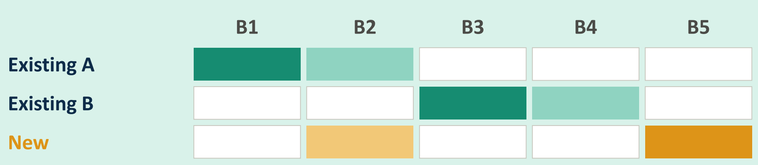


Figure 2. Treatments with equal response rates target different biomarkers (B1–B5); darker = stronger match. Schematic, not model inputs.

- Response was based on **several biomarker-driven disease processes**. A higher score meant a closer match between the patient and the treatment.
- Heterogeneity was changed by varying the **spread of the biomarkers** in three scenarios: low, moderate and high.
- All treatments were set to have **similar response rates**; the setup gave about 43–44%.
- We tested **1 to 4 existing treatments** plus one new treatment. The main outcome was the **% of patients helped only by the new treatment**.

THE VALUE GAP: The difference between the value seen from average treatment effects and the extra health gain from matching patients to the right treatment. This gap is likely to grow as populations become more varied and treatments more different.

4 RESULTS

- A new treatment helped extra patients **even though all treatments had the same response rate**. With 2 existing treatments, it helped **3%, 15% and 17%** of patients (low, moderate, high heterogeneity).

Total vs. incremental responders (% of patients)

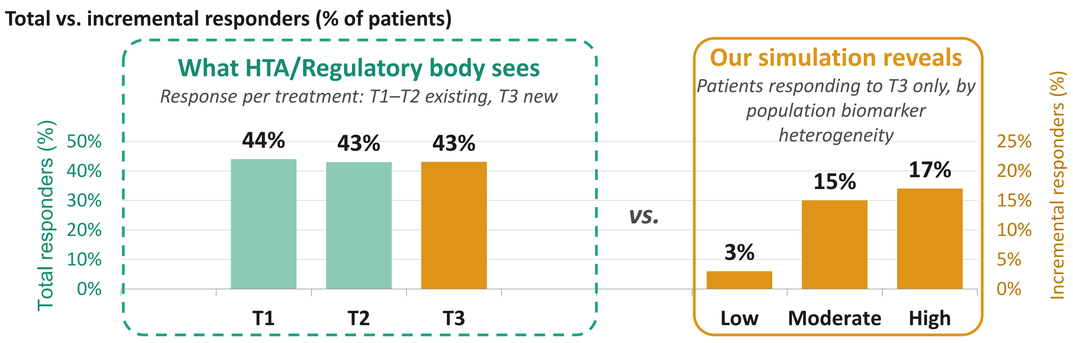


Figure 3. HTA sees similar response rates (43–44%). With 2 existing treatments (T1, T2), our simulation shows the new treatment (T3) helps an additional 3–17% of patients who respond to neither.

- Gains were **larger in more heterogeneous populations** and fell as more treatments were available, but did **not disappear**: with 4 existing treatments, incremental responders remained at 2% (moderate) and 5% (high).

Incremental responders from adding one new treatment, by number of existing treatments (% of patients)

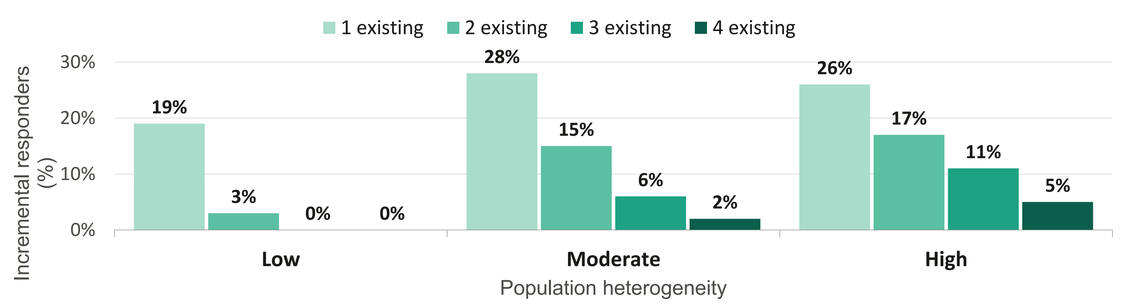


Figure 4. Adding one new treatment: incremental responders rose with heterogeneity and fell as the number of existing treatments increased.

5 DISCUSSION

- The value of an extra therapy depends not only on its average response rate, but also on how far its responders **overlap** with those of existing treatments.
- For NICE, **pairwise comparisons of average effects** may miss this value; weighing responder overlap could measure gains to patients poorly served today.
- Subgroup analysis is the main way HTA addresses heterogeneity,[2,3] but it does not explicitly quantify responder overlap.
- The model assumes a **perfect link** between treatments and biomarkers, and that any patient can have **any combination of biomarkers**.
- Results are illustrative and not yet calibrated to real-world data; future work could use real-world response data and test other treatment numbers, heterogeneity levels and biomarker–treatment specificity.

6 CONCLUSION

- Value depends on **heterogeneity, targeting and number of existing treatments**.
- Treatments with similar average efficacy can **benefit different patients**; extra targeted therapies add responders through better matching.
- Heterogeneity raised this benefit from **3% to 17%** of patients; it **shrinks but persists** as options grow.

HTA focused on average treatment effects could overlook population-level health gains.

REFERENCES

1. Jiao B, Carlson JJ, Garrison LP Jr, Basu A. Evaluating policies of expanding versus restricting first-line treatment choices: a cost-effectiveness analysis framework. *Value Health*. 2024;27(4)
2. Saing S, Hannink G, Geuzinge HA, Koffijberg H. Addressing subgroup-specific treatment effects to avoid inefficient care: the conflict between statistical and health economic analyses. *Value Health*. 2025;28(8)
3. Espinoza MA, Manca A, Claxton K, Sculpher MJ. The value of heterogeneity for cost-effectiveness subgroup analysis: conceptual framework and application. *Med Decis Making*. 2014;34(8):951-964

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