HTA18

First to launch, first to falter? An investigation into the clinical benefits and HTA outcomes for first-in-class drugs

Civitelli, D[1].; Mills, M.[1,2]; Kanavos, P.G[1]

1. *Medical Technology Research Group, LSE Health, London School of Economics and Political Science, UK*
2. *Hive Health Optimum Ltd. (HTA-Hive), London, United Kingdom*

Background and Objectives

- Existing literature on measuring pharmaceutical innovation **categorises drugs into three groups**: first-in-class (FIC), advance-in-class (AIC) and addition-in-class (AdIC)[1]. The U.S. Food and Drug Administration defines **FIC drugs** as those drugs that **"have mechanisms of action different from those of existing therapies"**[2]
- This classification, however, ignores that **new mechanisms of action do not always translate into improved patient outcomes**.
- Drawing on Health Technology Assessment (HTA) reports across four countries (**England**, **Scotland**, **Australia** and **Canada**), we studied:
    1. Whether FIC drugs delivered, on average, more Quality Adjusted Life Years (QALYs) than AIC and AdIC drugs.
    2. The factors associated with QALY gains.

Methodology

- FDA approvals were screened between **01/01/2014 and 31/12/2019** to identify **FIC and AIC drugs**.
- **AdIC drugs** were identified from an LSE Health Medical Technology Research Group dataset developed as part of the Horizon 2020 funded IMPACT-HTA research project.
- For all included drug-indication pairs, data was extracted from **publicly available HTA reports**. Variables of interest included **regulatory, disease-specific, clinical, economic, evidence uncertainty** and **contextual factors**. **QALY** gains as **reported by the manufacturer** were also collected.
- Where **multiple subpopulations** within the same indication were present, we **averaged the QALY gains**.
- An Ordinary Least Square (OLS) regression model was specified.

Results

Descriptive statistics

- Out of a total sample of **223 observations**, 77 (35%), 49 (22%) and 97 (44%) were FIC, AIC and AdIC drugs, respectively.
- 182 **(82%)** drug-indication pairs **received a positive HTA recommendation** (List or List with Conditions). The remaining observations obtained a negative HTA outcome. **Disease severity** was recognised in 65 **(29%)** reports, whilst **unmet need** was acknowledged in 141 **(63%).**

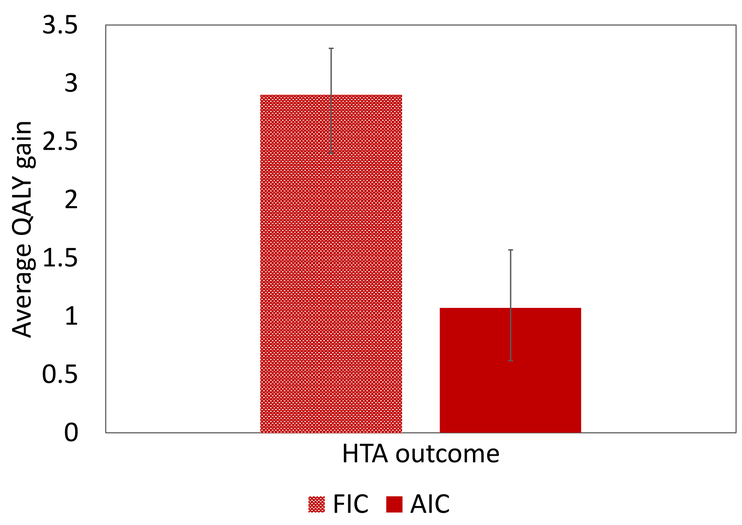
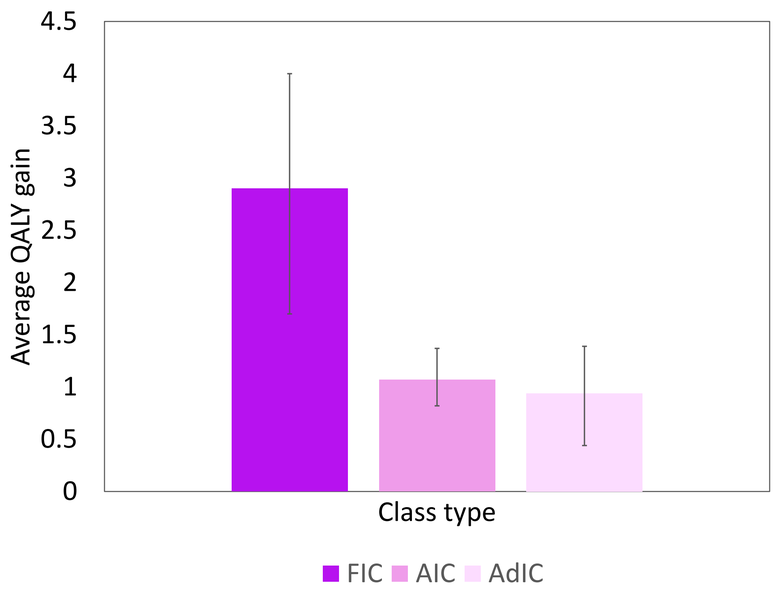


Figure 1 shows that drugs that achieved a **positive HTA outcome were associated with larger QALY gains** than drugs that were rejected at HTA. However, a t-test showed the difference is **not statistically significant**.

Figure 1. Average QALY gain by HTA outcome (95% CI)



In **Figure 2**, a **one-way ANOVA** with Bonferroni correction shows that there are **statistically significant differences between FIC and AIC drugs, and FIC and AdIC drugs**. Specifically, FIC (2.91) drugs provide significantly more QALYs than AIC (1.07) and AdIC (0.94). However, **no differences were observed between AIC and AdIC.**

Figure 2. Average QALY gain by drug class (95% CI)

Econometric model

- Figure 3 shows that **AIC drugs provide significantly less QALYs than FIC products.**
- Having an **oncology indication** is also significantly **associated with less QALYs** compared to non-oncology pharmaceuticals.
- Drugs launching in indications where **disease severity** is recognised are associated with **significantly greater QALY gains** compared to the base case.

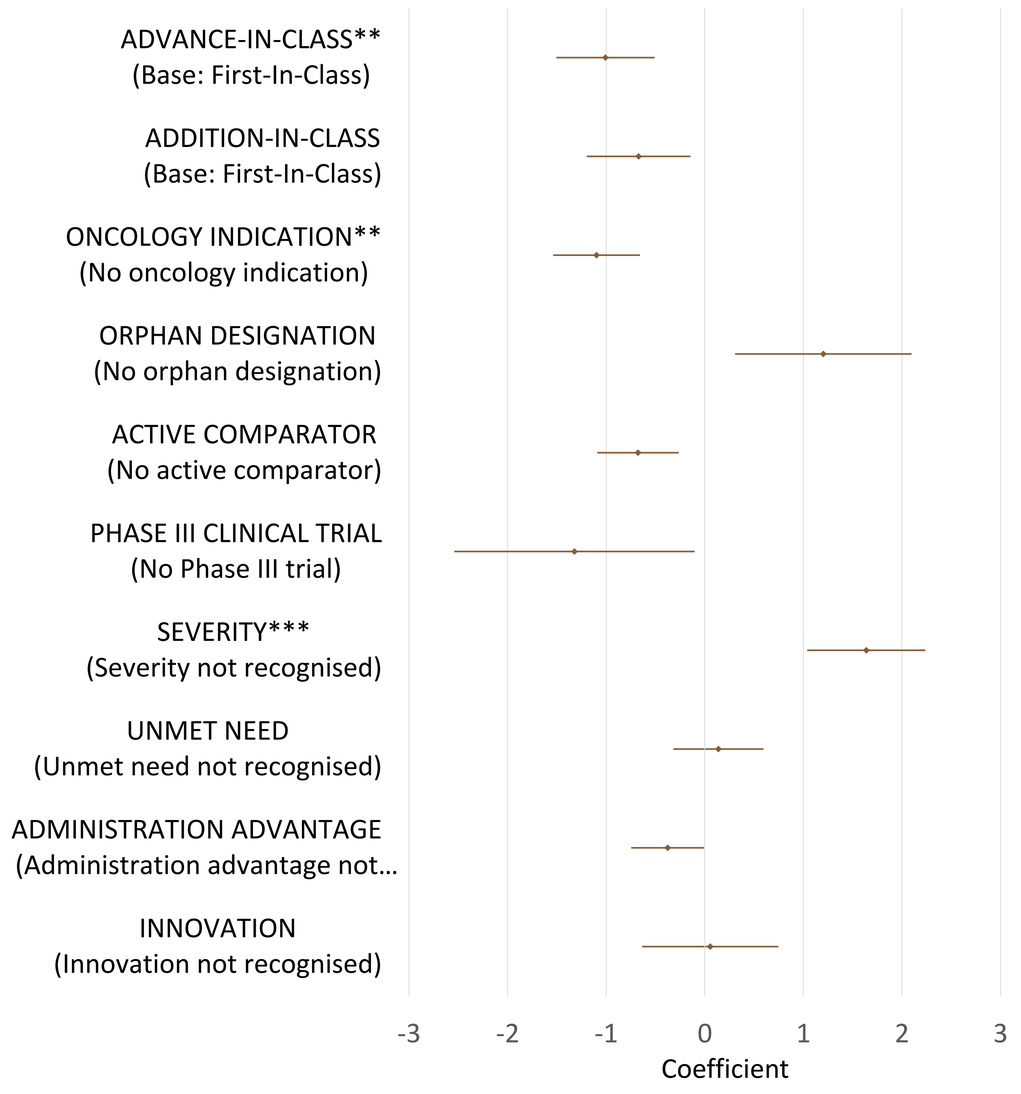


Figure 3. Forest plot of the factors associated with QALY gains

Conclusions

FIC drugs provide significantly more QALY gains compared to AIC and AdIC products. Additionally, disease severity is associated with greater QALY gains, whereas having an oncology indication has the opposite effect. Average QALY gains did not differ by HTA outcome. Our analysis is limited by the scarce availability of QALY estimates in HTA reports.

Contacts

Diego Civitelli: d.Civitelli@lse.ac.uk
Mackenzie Mills: M.J.Mills@lse.ac.uk / m.mills@hiveoptimum.com
Panos Kanavos: P.G. Kanavos@lse.ac.uk

References

1. Lanthier, M., Miller, K. L., Nardinelli, C., & Woodcock, J. (2013). An Improved Approach To Measuring Drug Innovation Finds Steady Rates Of First-In-Class Pharmaceuticals, 1987–2011. *Health Affairs*, *32*(8), 1433–1439. https://doi.org/10.1377/hlthaff.2012.0541;
2. U.S. Food and Drug Administration. (2016, January). *Novel Drugs Summary 2015*. FDA; FDA. https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drugs-summary-2015