HPR253

Drug Development And Launch Timeline Analysis Across High-income Countries: From Clinical Trial To HTA

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Objectives

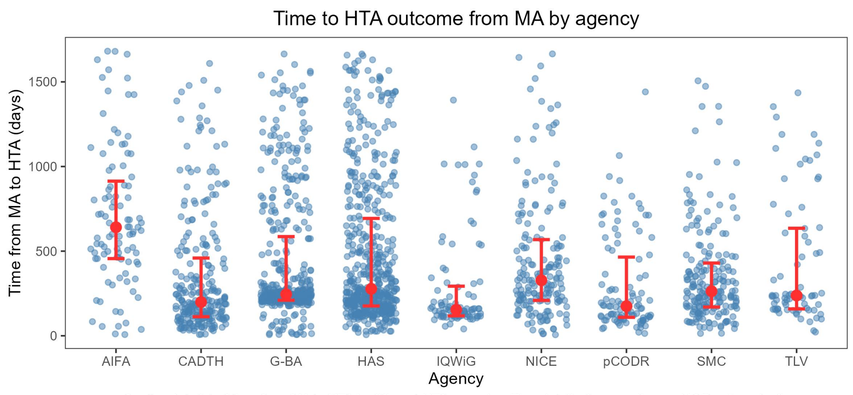
- This study aims to examine the time intervals between key steps in drug development and launch, specifically focusing on pivotal clinical trials, regulatory approval, and HTA decisions.
- Additionally, it seeks to explore how drug characteristics, clinical trial design, regulatory pathways, and firm characteristics influence these timelines.

Methods

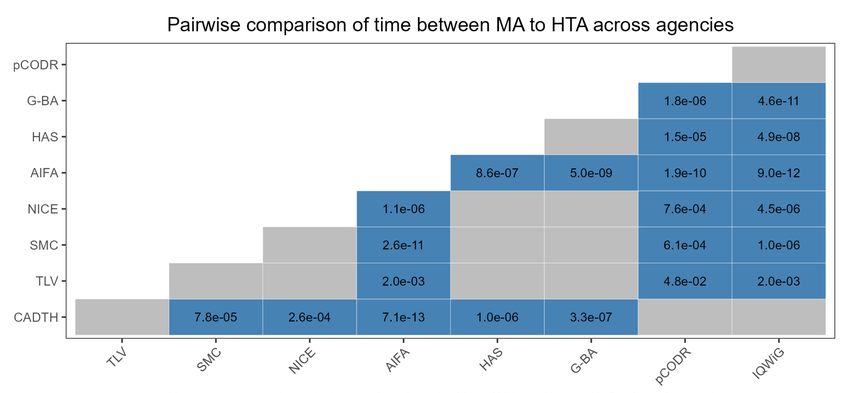
- HTA agency websites in England (NICE), Scotland (SMC), Germany (G-BA and IQWiG), France (HAS), Italy (AIFA), Sweden (TLV), and Canada (CADTH, pCODR) were automatically screened to compile a comprehensive list of HTA outcomes spanning 2011 to 2024. ClinicalTrials.gov and regulatory agency websites (FDA, EMA, and Health Canada) were similarly screened to gather clinical trial (CT) and marketing authorisation (MA) data. Due to the unavailability of MHRA data, NICE and SMC outcomes after January 1, 2021, were excluded. Only FDA-approved brands were included, and vaccines were excluded from the analysis.
- HTA data was matched to MA data (EMA and Health Canada), and MA data to FDA data, based on indication text and decision date similarity, using the PyTorch deep learning framework.
- Hypothesis testing, Kaplan-Meier analysis, and Cox proportional hazards (PH) survival analysis were conducted to assess the impact of various attributes on timelines, using R. Due to the fully retrospective nature of this study, no censoring was applied.

Results

- The dataset included 2,152 HTA outcomes across all included agencies for 328 distinct medicine brands, with HTA decisions dates ranging from June 2011 to July 2024. The pooled median time from MA to HTA decision across all agencies was 292 days, with a median of 199 days for Canada and 315 days for the pooled EU and UK agencies.
- In Canada, the median time to reimbursement was 210 days for CADTH, while among European agencies, Germany (G-BA) had the shortest median time to HTA at 259 days, and Italy had the longest at 643 days. Figure 1 displays time to HTA for both initial and re-evaluation outcomes across agencies. Pairwise comparisons of all agencies revealed statistically significant differences, even after applying the Bonferroni correction.



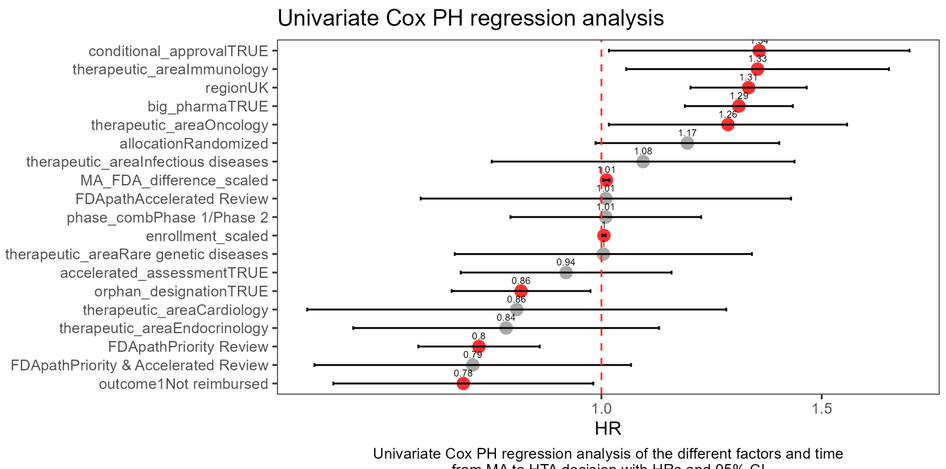
Scatter dot plot of time from MA to HTA in different HTA agencies. The plot displays median and IQR values (red). Extreme outliers, defined by values beyond 1.5 times the IQR, have been excluded to improve clarity.



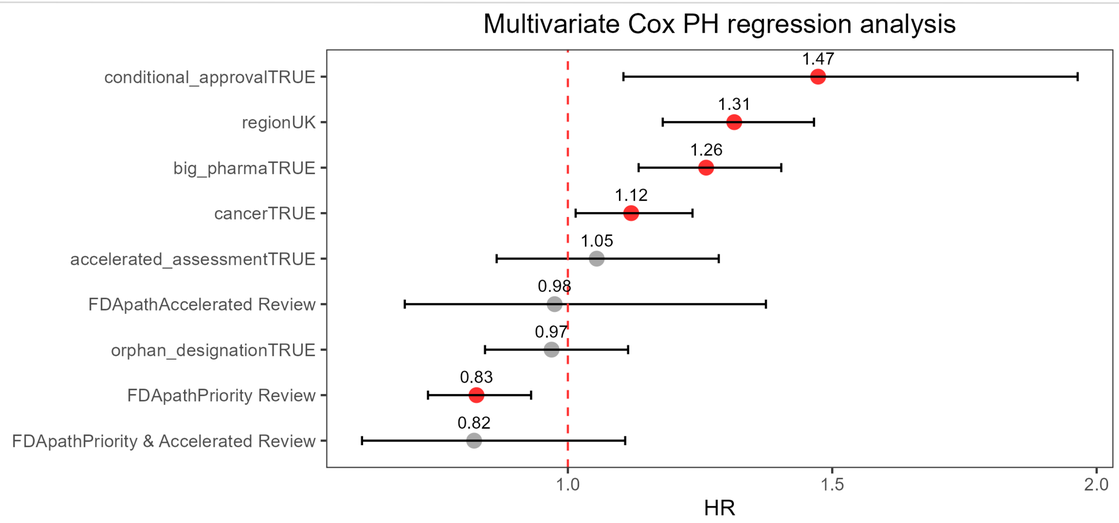
Heatmap representing pairwise p-values from the Mann-Whitney U test with Bonferroni correction, assessing time to HTA decision differences between agencies. Only significant p-values (threshold < 0.05) are labelled in blue.

Univariate Model Cox PH regression

- Therapeutic area, regulatory pathway, region, and company size were significantly associated with variations in time to HTA outcome.
- CT enrollment and duration, as well as the intervals from CT to FDA approval and from FDA to MA in other countries, did not yield meaningful results, potentially due to issues with scaling.



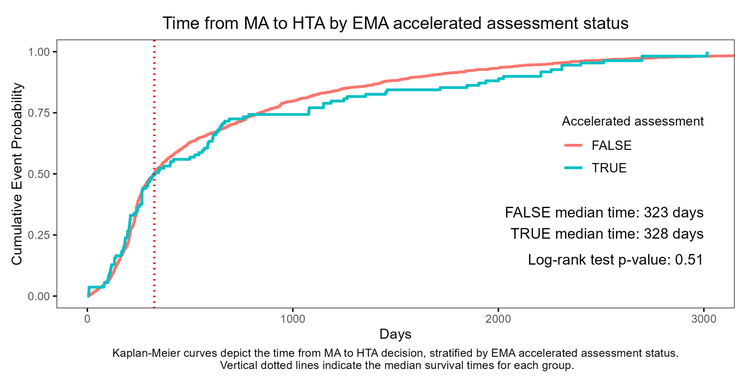
Univariate Cox PH regression analysis of the different factors and time from MA to HTA decision with HRs and 95% CI.



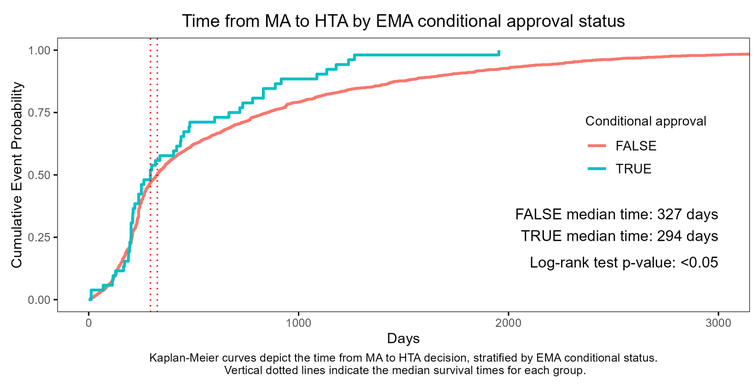
Multivariate Cox PH regression analysis of the selected from univariate analysis factors and time from MA to HTA decision with HRs and 95% CI.

Multivariate Model Cox PH regression

- The multivariate analysis showed that drugs from “Big Pharma” companies (defined as companies with market capitalisation exceeds £50 billion) had a 26% faster rate of reaching an HTA decision compared to smaller companies.
- Cancer treatments had a 12% higher rate of HTA outcome than non-cancer treatments, and drugs reviewed in the UK (NICE and SMC) reached an HTA decision 31% faster than those reviewed by other European agencies, though this result should be interpreted cautiously due to significant inter-agency variation.
- Drugs with conditional approval by the EMA had a 47% faster rate of reaching an HTA decision, while drugs with priority review by FDA had 17% slower rate of reaching an HTA decision after an EMA approval.
- Although orphan designation was significant in the univariate analysis, it was not significant in the multivariate model, indicating it does not independently impact the rate of HTA decision when other factors are considered.

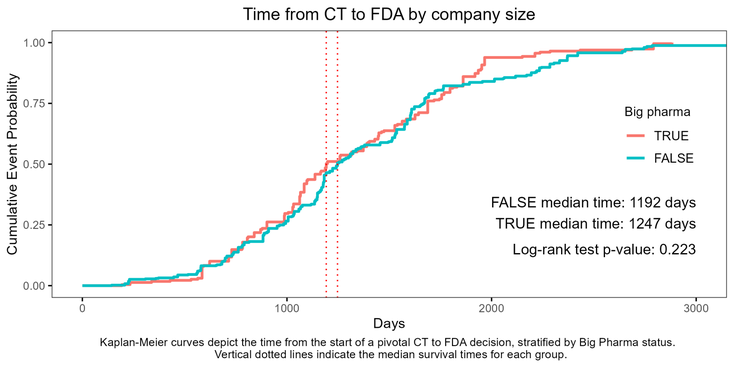


Kaplan-Meier curves depict the time from MA to HTA decision, stratified by EMA accelerated assessment status. Vertical dotted lines indicate the median survival times for each group.

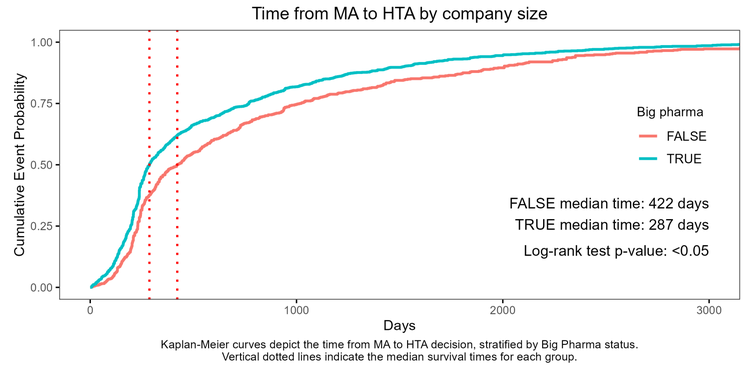


Kaplan-Meier curves depict the time from MA to HTA decision, stratified by EMA conditional status. Vertical dotted lines indicate the median survival times for each group.

- While company size might accelerate time from regulatory approval to reimbursement decision, there are no differences in clinical development timelines.



Kaplan-Meier curves depict the time from the start of a pivotal CT to FDA decision, stratified by Big Pharma status. Vertical dotted lines indicate the median survival times for each group.



Kaplan-Meier curves depict the time from MA to HTA decision, stratified by Big Pharma status. Vertical dotted lines indicate the median survival times for each group.

Conclusions

- Significant variability exists in HTA timelines across regions and therapeutic areas.
- Oncology drugs and products from large pharmaceutical companies are associated with faster time to reimbursement, while drugs from smaller companies face delays, potentially due to limited market access resources.
- Drugs granted conditional approval by the EMA, which is a “fast-track approval of a medicine that fulfils an unmet medical need”, get an HTA decision (positive or negative) faster as well.

Acknowledgements and Contact Information

This research was supported by funding from HTA-Hive, whose commitment has been essential to our progress.

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