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Introduction

Time to drug availability (TTA) in European countries varies significantly across drugs and years of reimbursement.¹

Other studies have investigated average TTA or time to market (TTM) of drugs in Italy and the determinants of AIFA decisions,²⁻⁵ with one study focusing on the impact of Covid-19 on TTM.⁶ This analysis, which found an increase in TTM of 108 days between drugs negotiated during the pandemic and drugs negotiated prior to the pandemic, was conducted on data from 2015-2021 and would benefit from a longer timeframe of analysis.

The aim of this study is to update the previous research and evaluate the pandemic's impact on drugs' TTM[§] in an expanded timeframe (2015-2022), to provide a more comprehensive assessment of the work of the Italian Medicines Agency (AIFA) committees ahead of the foreseen reform.

Methods

The previous analysis⁶ was updated to include all the new active substances, excluding vaccines, that received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) between January 2015 and December 2022 and completed the Italian negotiation pathway. Data were retrieved from an IQVIA proprietary database on Italian negotiation dynamics.

The analysis was carried out in four steps:

- Observations were classified into the Pre-COVID, Fully COVID, or Partially COVID groups, according to the timing of their negotiation process (before, after, or across March 2020). The Partially COVID and Fully COVID groups were expanded to include the new observations, while the Pre-COVID group remained unchanged.
- Differences in TTM among the three periods were inspected descriptively, and two-sample tests were performed to re-evaluate the potential role of co-variables influencing TTM.
- A nearest-neighbor matching estimator analysis was implemented with the new identified relevant co-variables.
- Sensitivity analyses on matching estimation options were conducted, to test robustness of the selected model.

Results

In 2022, 24 new drugs met the inclusion criteria for the analysis, bringing our sample to 387 unique combinations of molecule and indication.

Descriptive analyses showed a difference in TTM only for the Partially COVID period (average TTM: 435.7 days), while no difference was observed between the Fully COVID vs Pre-COVID periods (average TTM: 283.7 and 283.2 days) (Table 1).

With respect to the previous study, three additional variables had a mean time-difference statistically different from zero and were thus included in the matching estimation equation: accelerated assessment, orphan medicine status, and reimbursement in class A, A-PHT, or H (Table 1).

Inferential analysis confirmed the results from the previous study: the average treatment effect of the Partially COVID period was +124.6 days (p=0.00) (vs. +108.0 days [p=0.00] in the 2015-2021 timeframe),⁶ while the difference in average TTM between the Fully COVID and Pre-COVID periods was not statistically significant (Table 2).

Sensitivity analyses confirmed solidity of the model, showing an average increase in TTM for the Partially COVID period varying between 101 days (-18.9%) and 139 days (+11.3%) in all considered scenarios (Figure 1).

Conclusions

This study confirmed previous evidence on the impact of Covid-19 on drugs TTM in Italy: while TTM increased significantly during the pandemic, it decreased back to its pre-pandemic averages in the Fully COVID period, highlighting the temporary nature of the shock.

Table 1. Univariate analysis of the association between the time to market of negotiated drugs in Italy and relevant covariates

	Mean time to market (days)		Significant in 2021 analysis [§]
	NO	YES	
Fully COVID ^a	283.24	283.74	✓
Partially COVID^a	283.24	435.70	✓
EMA conditional approval	308.52	328.48	x
EMA approval under exceptional circumstances	305.53	515.38	✓
EMA approval with accelerated assessment	314.23	364.00	x
Advanced therapy	308.61	359.30	x
First indication	290.22	319.38	x
Orphan medicine status	297.66	343.97	x
Early access ^b	300.70	333.52	x
Innovativeness status	314.93	278.90	x
AIFA monitoring registry	294.24	330.97	✓
Presence of a MEA	299.76	354.38	✓
Negotiated confidential discount	274.35	323.91	✓
Reimbursed medicines	255.04	317.69	n.a.
Therapeutic Area^c	-	-	✓

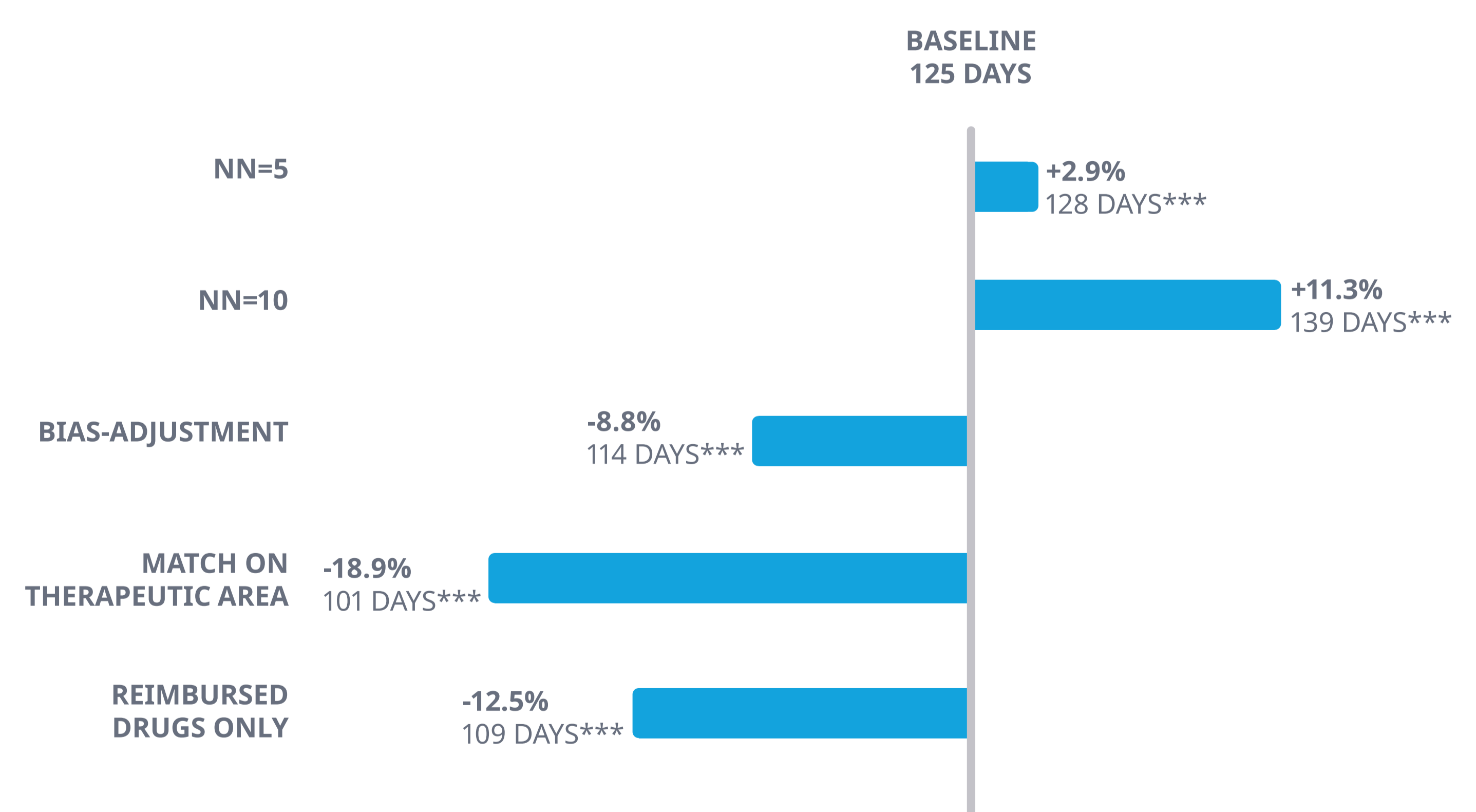
a) Tested against Pre-COVID;
 b) Early access equals "YES" when law 648, 5% fund or compassionate use program were put in place;
 c) T-test for Therapeutic area is not reported because it's a categorical variable with 3+ levels.
 Statistically significant variables (p < 0.1) in the current analysis in bold.
 EMA = European Medicines Agency; AIFA = Italian Medicine Agency; MEA = Managed Entry Agreement

Table 2. Matching estimation results

	ATE	SE	P-Value	95% CI
Partially COVID vs Pre-COVID	124.62	35.68	0.000	54.68, 194.57
Fully COVID vs Pre-COVID	6.13	19.90	0.758	-32.87, 45.13

ATE = Average Treatment Effect; SE = Standard Error; CI = Confidence Interval

Figure 1. Discrete sensitivity analyses results on Partially COVID vs Pre-COVID



NN = number of matches; *** p-value < 0.01

NOTES
 § Time to market is defined in both studies as the number of days between the start of pricing and reimbursement (P&R) dossier evaluation and publication of the P&R resolution in the Italian Official Journal

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