

Strategic Response to External Reference Pricing

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- *“The practice of using the price(s) of a new medicine in other countries to derive a benchmark price. This benchmark is used in setting or negotiating the price of the product.”*
WHO (2013)
- Choice of the basket based on GDP, proximity, ad hoc considerations
Espin et al. (2014)
- Relatively simple to apply: extensive reliance in the EU with the exception of Sweden and UK
Rémuzat et al. (2015), Espin et al. (2014), Kanavos et al. (2020)
- Drawback: **explicit interplay** across pharmaceutical regulations
Stargardt & Schreyögg (2006), Toumi et al. (2014)

Introduction: Example 1

Legend

- Adopter
- Reference countries



Introduction: Example 2

Legend

- Adopter
- Reference countries



Manufacturers can potentially suffer from negative externalities as they can no longer price discriminate. This leads to:

- **Price increase** in reference countries (theoretical)
Garcia Mariñoso et al. (2011), Geng & Saggi (2017), Ackermann (2010), Birg (2018), Pecorino (2002) Dubois et al. (2022)
- Strategic **launch delays** (empirical and theoretical)
Maini & Pammolli (2023), Kyle (2007), Houy and Jelovac (2015)
- Concede **secret discounts** on list prices (surveys and simulations)
Vogler et al. (2015), Morgan et al. (2017), Persson & Jönsson (2016), Riccaboni et al. (2022)

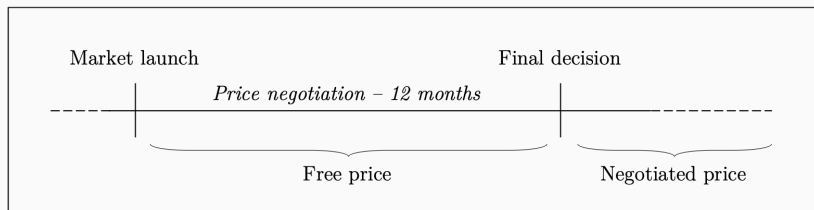
Research Question: what happens to prices when a country is included in the ERP set of another country?

Introduction

- Consider a Manufacturer (M) and two countries, Home (H) and Foreign (F), where **H refers to the price set by F**
- Intuition (coming from the theoretical framework):
 - If F belongs to H 's ERP set, the marginal impact of F 's prices on M 's global profit increases
 - Effect positively depends on how "closely" H refer to F ("stringency" of ERP)
 - Relationship between F 's size and the strategic effect depends on F 's weight in the H 's ERP set
 - If the weight of the foreign price is independent of (decreasing in) K , the strategic effect is larger the smaller K . If the weight of the foreign price is increasing in K , the strategic effect may increase or decrease with its market size.

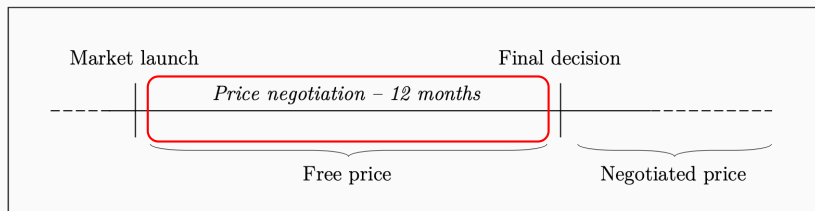
Empirical Analysis

- Source of variation: introduction of AMNOG bill in 2011 in Germany
- Innovative drugs now subject to price negotiation, but free pricing during the negotiation window (12 months)



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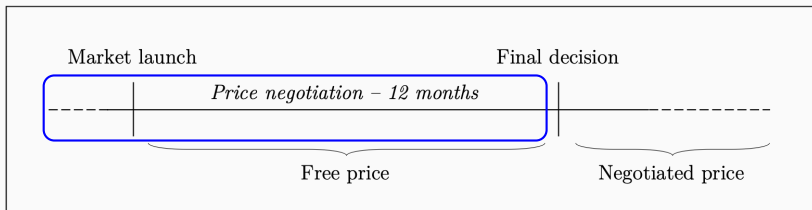
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- EU prices (AUT, BEL, CZE, DNK, FIN, FRA, UK, IRL, ITA, NLD, POR, SWE, SVK and ESP) ⇒ **ERP**

Empirical Analysis

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- EU prices (AUT, BEL, CZE, DNK, FIN, FRA, UK, IRL, ITA, NLD, POR, SWE, SVK and ESP) \Rightarrow **ERP**
- Products launched in those countries are potentially subject to *strategic effect* > 0

Empirical Model: Treated Countries

Legend

- Adopter
- Reference countries



- **Pricing Insights IMS database (IQVIA)**
 - Entry list prices, launch date
 - 65 non-generic **anti-cancer drugs** authorized by EMA in 2007-2017
 - 16 OECD countries (no US, Greece)
 - Price per mg → Product comparable across sizes, strengths and countries
 - Total of 570 country-product pairs [▶ List](#)
- **Global Burden of Diseases (GBD):** prevalence
- **World Bank Indicators:** GDP per capita

Empirical Model

- Test the presence of strategic effect on **entry prices** of products launched in countries **included in German ERP set**
- Diff-in-diff approach (TWFE)

$$\ln Price_{ict} = \beta_0 + \theta Strategic_{ict} + X_{ict} + \zeta_i + \eta_t + \mu_c + \epsilon_{ict}$$

- $Strategic_{ict}$: =1 if country c belongs to the reference set of Germany and product i in country c is launched after 2011
- ζ_i : product fixed effect capturing unobserved drug's quality.
- η_t : time fixed effect, capturing product-invariant shocks to prices.
- μ_c : country fixed effect capturing differences in prices among countries.
- X_{ict} : $TIMESINCE_{it}$, GDP_{ct} and $EXRATE_{ct}$

Results

<i>Dep. Var.: ln Price</i>	<i>Main</i> (1)	<i>No 2011</i> (2)	<i>No BE, DK</i> (3)
Strategic	0.066** (0.028)	0.068** (0.028)	0.078*** (0.028)
ln GDP pc	-0.164 (0.150)	-0.172 (0.154)	-0.139 (0.156)
Time since first launch (in years)	-0.066* (0.036)	-0.116*** (0.031)	-0.063 (0.043)
Exchange rate	0.382*** (0.131)	0.340** (0.135)	0.377*** (0.130)
Constant	2.825* (1.616)	2.922* (1.677)	2.543 (1.691)
Product, Country, Year FE	Yes	Yes	Yes
Observations	570	536	475
R^2 adjusted	0.998	0.998	0.998

Standard errors (in parentheses) are clustered at the product level. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$

Results

- The difference between the price of products included in the German ERP set and those that were not is 6.6% greater after the reform
- Product obsolescence has a significant negative impact: an additional year from the first launch across all markets is associated with a 6.6% reduction in entry price
- GDP per capita is statistically not significant: one possible reason is that the effects are already captured by country fixed effect
- Exchange rate has significant coefficient of 0.382. The value of prices in local currency matters, irrespective of the corresponding value expressed in Euro

Corollary

If the weight of the foreign price (α) is independent of (decreasing in) K , the strategic effect is larger the smaller K . ***If the weight of the foreign price is increasing in K , the strategic effect may increase or decrease with its market size.***

- If $\partial\alpha/\partial K > 0$, two opposing forces:
 - The greater K , the greater the difference between a successful and unsuccessful negotiation in $F \rightarrow$ firm accepts a lower price
 - The greater K , the greater the impact of F 's price on global profit through $\alpha \rightarrow$ firm push for higher price
- Divide the sample of product-country pairs between those **above and below the median value of prevalence** (as proxy of mkt size)

Results: Market size heterogeneity /2

<i>Dep. Var.: Ln Price</i>	
Strategic=1 × Above=1	0.053** (0.023)
Strategic=1	0.043 (0.029)
Above=1	-0.023 (0.022)
Constant	2.317 (1.632)
Expl. Vars.	Yes
Product, Country, Year FEs	Yes
Observations	570
R^2 adj.	0.998

Standard errors in parentheses. * $p < 0.10$,
** $p < 0.05$, *** $p < 0.01$

Key assumptions for the identification





Parallel trend assumption: difference between prices of products in countries included in German ERP set and prices of those in countries that are excluded, remained the same had AMNOG not been introduced

Possible threats to PTA:

- The way prices are negotiated (including national ERP regulation) changed after 2011 in some countries. [▶ Leave-one-out](#)
- Germany changed how it sets prices in the first 12 months since each product's market authorization (ruled out by companion paper...)
- Entry order of products across countries changed after 2011. Firms anticipated/postponed launches across countries based on the ability to affect German prices through AMNOG's ERP. [▶ Launch schedule](#)
[▶ Entry order](#)

Additional Robustness Checks

Additional robustness checks

- Two-way clustering as in Cameron & Miller (2015) 
- In-time placebo 
- Placebo randomization 
- Measurement error in the dependent variable 

Conclusions

- Empirical evidence of spillover effects due to ERP
- AMNOG legislation in Germany led to 6.6% price increase in referenced countries
 - Not due to high-priced (low-priced) products being launched before (after) than in Germany because of the reform
 - The effect is likely to be greater for relatively larger markets as compared to that of the ERP adopter
- Use of list prices
 - List prices increase may be compensated by confidential discounts, reducing the size of the (net) spillover effect...
 - If that is the case, the strategic response we document prevents H from achieving (part of) the reduction in domestic prices

Thanks for your attention!

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Appendix

<i>Included</i>	<i>First obs</i>	<i>Pre</i>	<i>Post</i>	<i>Excluded</i>	<i>First obs</i>	<i>Pre</i>	<i>Post</i>
Austria	Q1 2007	14	50	Hungary	Q3 2008	2	3
Belgium	Q1 2007	12	22	Norway	Q1 2007	13	42
Denmark	Q3 2007	14	47	Poland	Q4 2010	1	4
Finland	Q1 2007	11	25	Switzerland	Q2 2007	8	30
France	Q1 2007	12	32	Turkey	Q3 2010	1	1
Ireland	Q3 2007	12	25				
Italy	Q1 2007	9	21				
Netherlands	Q3 2008	3	22				
Spain	Q1 2007	13	15				
Sweden	Q1 2007	10	33				
UK	Q1 2007	16	48				
		126	340			25	80

Table 3.6: Leave-one-out analysis/1

<i>DV: lnPrice</i>	AUT	BEL	DNK	FIN	FRA	HUN	IRL	ITA
STRAT	0.0756** (0.0289)	0.0796*** (0.0285)	0.0748*** (0.0265)	0.0745*** (0.0274)	0.0646** (0.0257)	0.0737** (0.0288)	0.0679** (0.0282)	0.0690** (0.0290)
Expl. Var.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Obs.	504	533	506	531	523	563	530	537

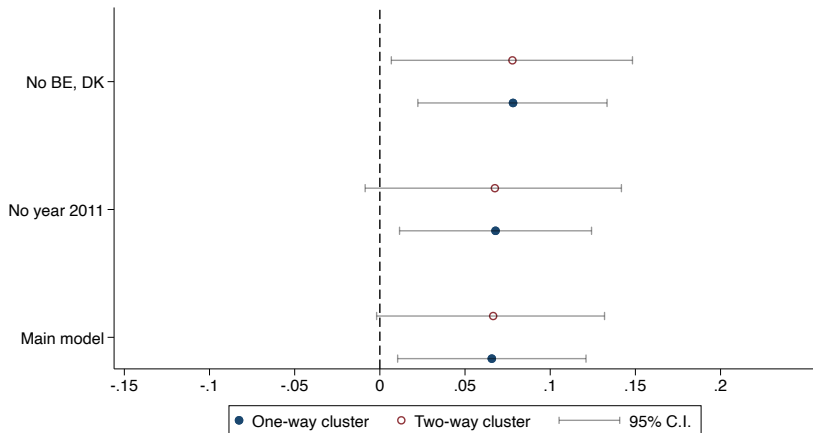
Table 3.7: Leave-one-out analysis/2

<i>DV: lnPrice</i>	NLD	NOR	POL	ESP	SWE	CHE	TUR	UK
STRAT	0.0706** (0.0278)	0.0680 (0.0490)	0.0778*** (0.0277)	0.0663** (0.0278)	0.0812*** (0.0286)	0.0689** (0.0286)	0.0668** (0.0277)	0.0594* (0.0299)
Expl. Var.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Obs.	542	512	562	539	524	531	565	503

Robustness Checks: Two-way clustering

◀ Back

- Each cluster is nonnested: errors might be correlated within product and within country independently (Cameron & Miller, 2015).
- We do so for STRAT across the main specifications with command `boottest` (Roodman et al., 2019).

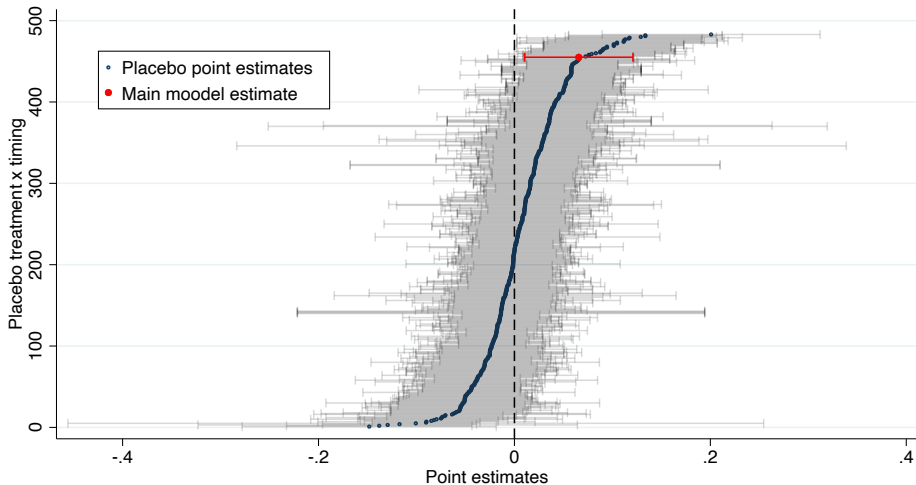


- *STRAT1* compares 2009-11 (*Post1=1*) with 2007-09 (*Post1=0*)
- *STRAT2* compares 2011-13 (*Post2=1*) with 2009-11 (*Post2=0*)
- ...

Table 3.8: In-time placebo test

<i>DV: ln Price</i>	(1)	(2)	(3)	(4)
STRAT1	-0.003 (0.111)			
STRAT2		0.113*** (0.032)		
STRAT3			0.020 (0.023)	
STRAT4				0.044 (0.032)
Expl. Vars.	Yes	Yes	Yes	Yes
Product FE	Yes	Yes	Yes	Yes
Country FE	Yes	Yes	Yes	Yes
Year FE	Yes	Yes	Yes	Yes
Observations	102	162	242	329
R^2 adjusted	1.000	0.999	0.997	0.998

- Placebo reforms in 32 quarters between 2008 and 2016
- 16 countries adopting placebo reforms (*with their own ERP set*)
- 16×32 random combinations of pre- and post-treatment periods and “adopting country”
- Placebo reform is the same as the AMNOG bill in Germany
- The coefficient of interest of the main model corresponds to the combination "Germany \times Q1 2011"
- Our preferred estimate at the right end of the distribution of all possible estimates



- Firms might try to set high list prices and concede a substantial (confidential) discount to restore the ability to price discriminate
- If so, the increase in list prices that we document could be compensated by such discounts, so that the effect is overestimated:

$$\ln Price_{ict}^* = \ln Price_{ict} - u_{ict},$$

where:

- $\ln Price_{ict}^*$: true (net) price
 - $\ln Price_{ict}$: observed (list) price
 - u_{ict} : (strictly) one-sided measurement error capturing confidential discount, with conditional mean different than zero but > 1
- So that the main specification has **omitted variable problem**:

$$\ln Price_{ict} = \alpha + \beta STRAT + \sum_j^k \delta_j x_j + \zeta_i + \eta_t + \theta_c + \varepsilon_{ict} + u_{ict}$$

- We follow Millimet & Parmeter (2021): analogy between measurement error of the dependent variable with inefficiency term in the **stochastic frontier analysis (SFA)**
- In our case: SFA cost function with a composite error term
 - idiosyncratic disturbance $\varepsilon_{ict} \sim N(0, \sigma_\varepsilon^2)$
 - inefficiency term $u_{ict} \sim N^+(0, \sigma_u^2)$
 - heteroskedastic measurement error

$$\sigma_{u_{ict}}^2 = \exp(\gamma_0 + \gamma_1 \ln \text{REFERENCING}_{ict} + \gamma_2 \ln \text{PREV}_{ict})$$

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- In our case: SFA cost function with a composite error term
 - idiosyncratic disturbance $\varepsilon_{ict} \sim N(0, \sigma_\varepsilon^2)$
 - inefficiency term $u_{ict} \sim N^+(0, \sigma_u^2)$
- Heteroskedastic measurement error, whose variance depends on:
 - *PREV*: prevalence in market c
 - *REFERENCING*: size of all markets ($-c$) that the observed list price might potentially be affecting through the ERP channel

$$\sigma_{u_{ict}}^2 = \exp(\gamma_0 + \gamma_1 \text{REFERENCING}_{ict} + \gamma_2 \text{PREV}_{ict})$$

<i>Dep. Var: Ln price</i>	(1)	(2)
Strategic	0.058** (0.026)	0.058** (0.026)
ln GDP pc	-0.208 (0.170)	-0.209 (0.169)
Time since first launch (years)	-0.075* (0.040)	-0.072* (0.041)
Exchange rate	0.309** (0.141)	0.325** (0.141)
Constant	3.228* (1.865)	3.236* (1.862)
Product, Country, Year FE	Yes	Yes
<i>Variables driving $\sigma_{u_{ict}}^2$</i>		
Mkt size in referencing countries (Millions)	0.301 (0.259)	0.454 (0.410)
Prevalence (Millions)		-2.484 (5.852)
Constant	-4.956*** (0.524)	-5.172*** (1.022)
Observations	571	571

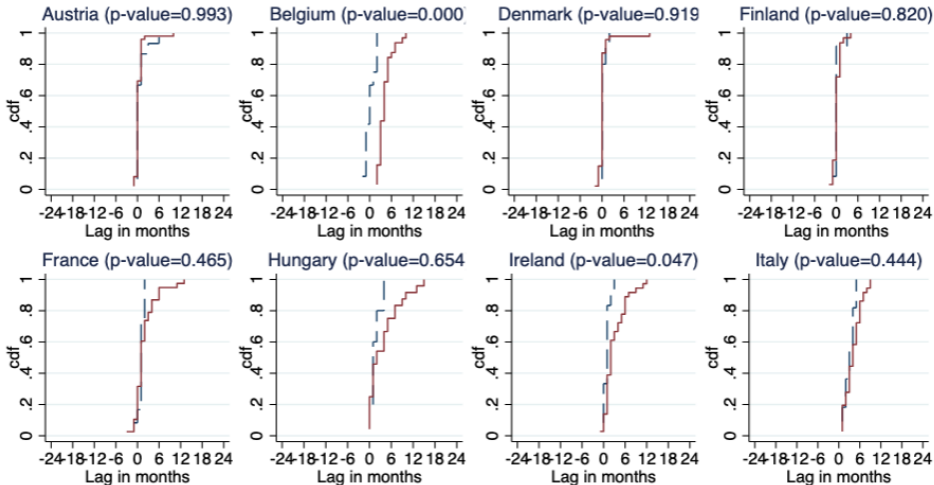
Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$

- There could have been a change in the order in which each product entered each market wrt the German market after 2011
- **Launch schedule of products (rather than price) has changed** in response to German reform
 - Manufacturers might have anticipated (postponed) the launch of expensive (cheap) drugs with respect to Germany
 - Our analysis would include only a selection of treated entry prices after the reform, most likely those with higher prices
- Focus on distribution of lag of the launch of each product in each country with respect to the German launch, pre- and post- reform
- If lag distributions pre and post do not change, Manufacturers have not significantly changed launch schedule
- Performed the **equality of lag distribution test (K-S Test)**

<i>Country</i>	<i>Exact P-value</i>	<i>Country</i>	<i>Exact P-value</i>
Austria	0.993	Netherlands	1.000
Belgium	0.000***	Norway	1.000
Denmark	0.919	Poland	0.725
Finland	0.820	Spain	0.008***
France	0.563	Sweden	0.397
Hungary	0.654	Switzerland	0.644
Ireland	0.047**	Turkey	0.115
Italy	0.444	UK	0.491

* $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$. Exact p -values of the two-sample Kolmogorov-Smirnov test for equality of distribution of launch lags from German launch, pre- and post-2011, by country.

Robustness Checks: Launch schedule /3

[◀ Back](#)

- Test whether the effect is due to high-priced products being launched prior than in Germany because of the reform
- Two sets of countries: $HIGH_c = 1$ if **pre-reform prices** in country c are relatively high
- Dependent variable is $POSTG_{ic} = 1$ if product i in country c is launched within one year since the launch in Germany
- We test the coefficient of the interaction term of the following model

$$POSTG_{ict} = \beta_0 + \beta_1 (HIGH_c \times Post_{ict}) + \beta_2 HIGH_c + \beta_3 Post_{ict} + \epsilon_{ict}$$

<i>DV: POSTG</i>	(1)	(2)	<i>Treated</i>	<i>Controls</i>
Post=1 × HIGH=1	-0.033 (0.063)	-0.065 (0.062)	-0.015 (0.065)	-0.244 (0.444)
Post=1	-2.406*** (0.247)	-0.029 (0.497)	-0.254 (0.632)	0.747 (1.322)
HIGH=1	0.061 (0.062)	-0.018 (0.147)	0.131 (0.154)	3.041 (2.303)
Constant	2.229*** (0.100)	-1.282 (3.022)	1.059 (3.430)	32.068 (22.756)
Expl. Vars.	No	Yes	Yes	Yes
FE	Yes	Yes	Yes	Yes
Observations	747	747	586	161
R^2 adjusted	0.621	0.646	0.648	0.697

Standard errors in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$