

The Impact of Foreign Pharmaceutical Patents on Innovation in Chile

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India's Glivec decision, 1 April 2013

- Novartis's patent application on Glivec (Gleevec) in India rejected by Supreme Court for obviousness
- Crucial issue: are new forms (beta crystalline form) of known substances (imatinib mesylate) patentable?
- Novartis's reaction: "cautious" about introducing new drugs to India, undertaking new investments, and conducting R&D in India...

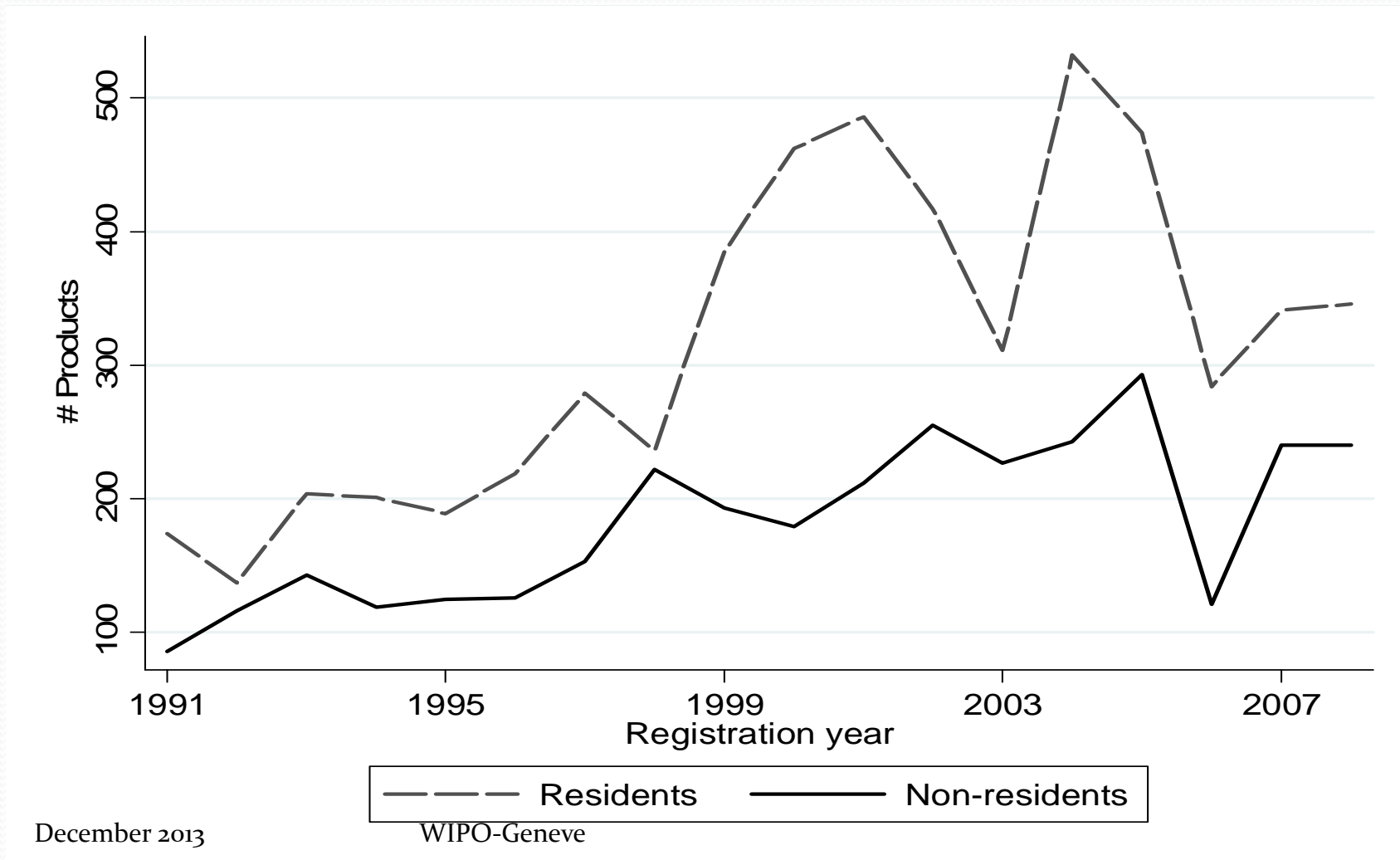
Current policy debate

- Proposals to restrict secondary patents:
 - **Brazil's** Projeto de Lei n° 5.402/2013 (includes provision similar to 3d of India's Patent Act).
 - **South Africa's** proposed National Policy on IP:
“[Legislation] should exclude diagnostic, therapeutic and surgical methods from patentability, including new uses of known products, as is the case under the TRIPS agreement.”
 - **TPP's** draft Article QQ.E.1: critical issue - patentability of new uses or methods of using a known product and “enhanced efficacy of a known product” threshold.

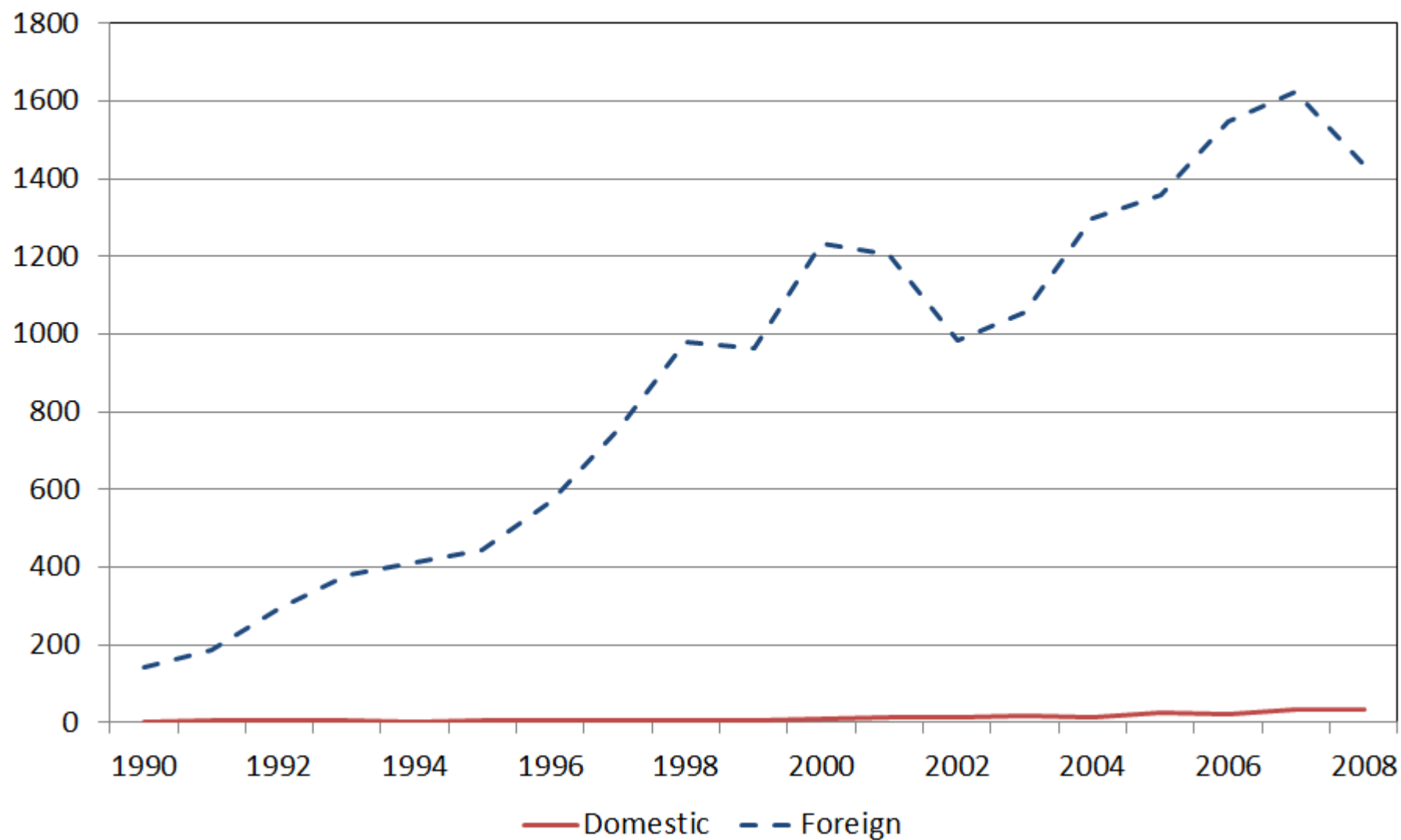
The big questions...

- Pharmaceuticals often important argument for strengthening of Intellectual Property (IP) system in developing countries
- Does stronger patent protection promote:
 - The decision by foreign multinationals to sell drugs in developing countries?
 - Technology transfer to developing countries?
 - Foreign direct investment?
 - The development of a domestic, innovative pharmaceutical industry?

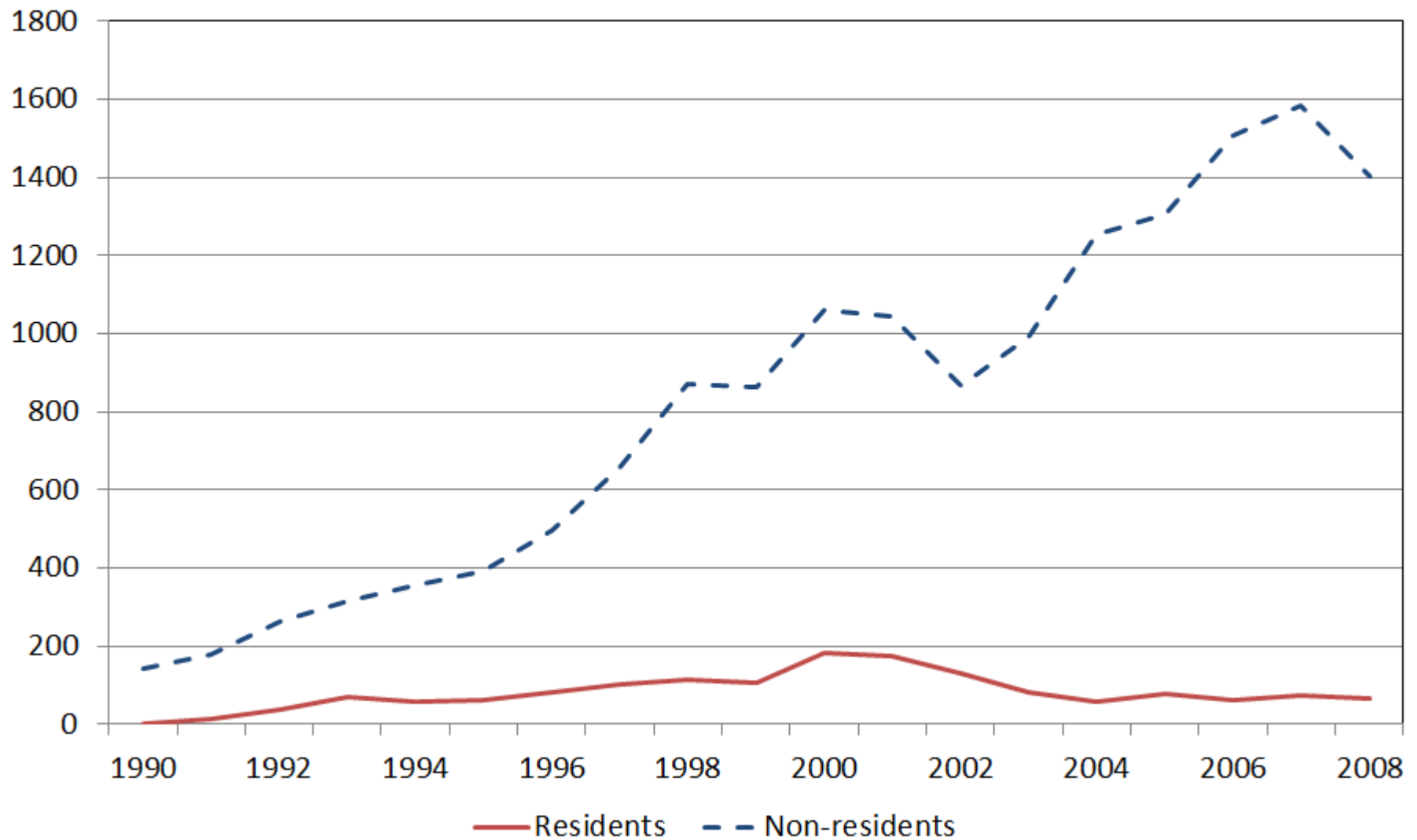
Total pharmaceutical **products registered** with ISP (Chilean Public Health Institute)



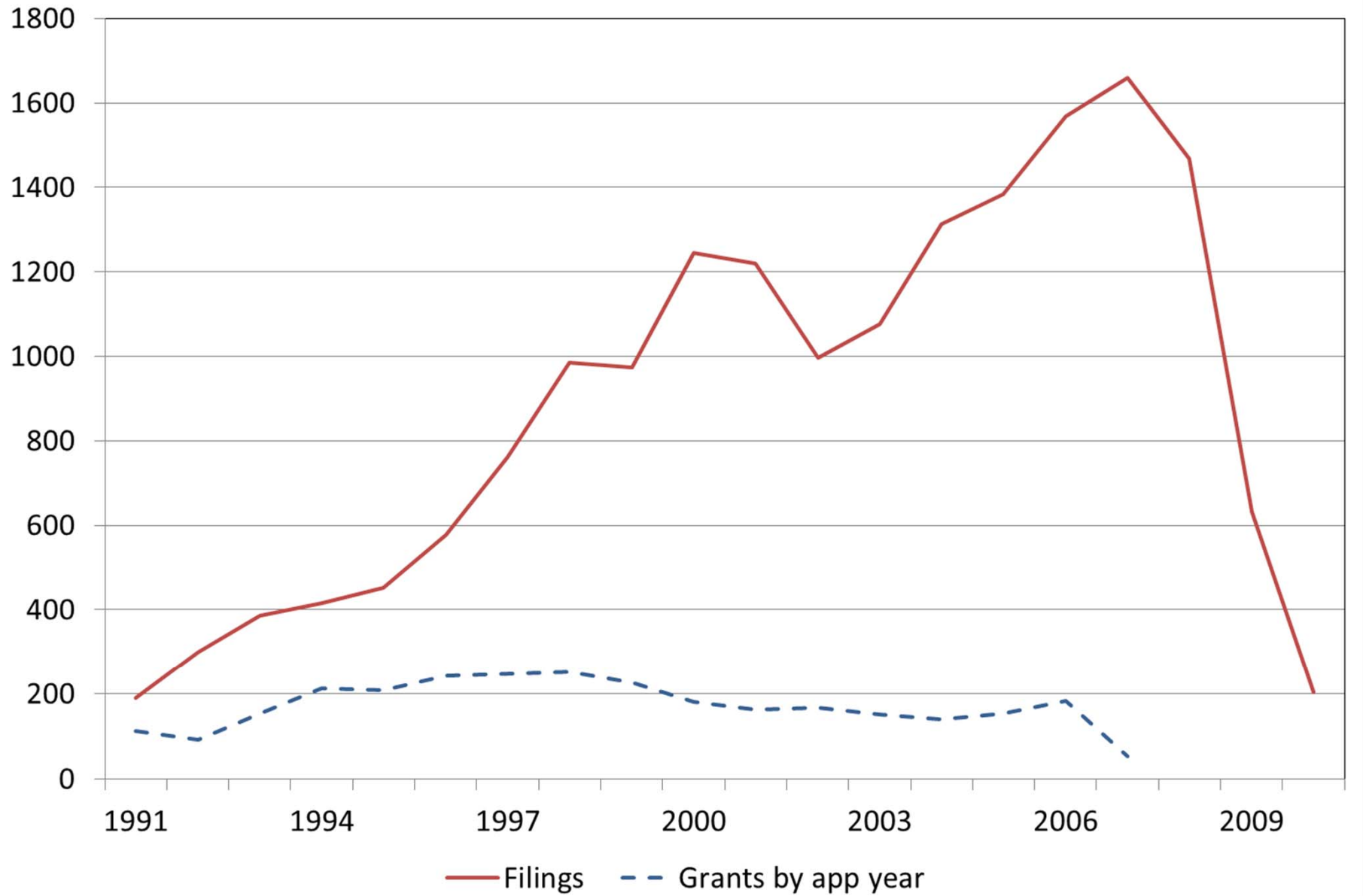
Total pharmaceutical patent filings by domestic and foreign entities in Chile



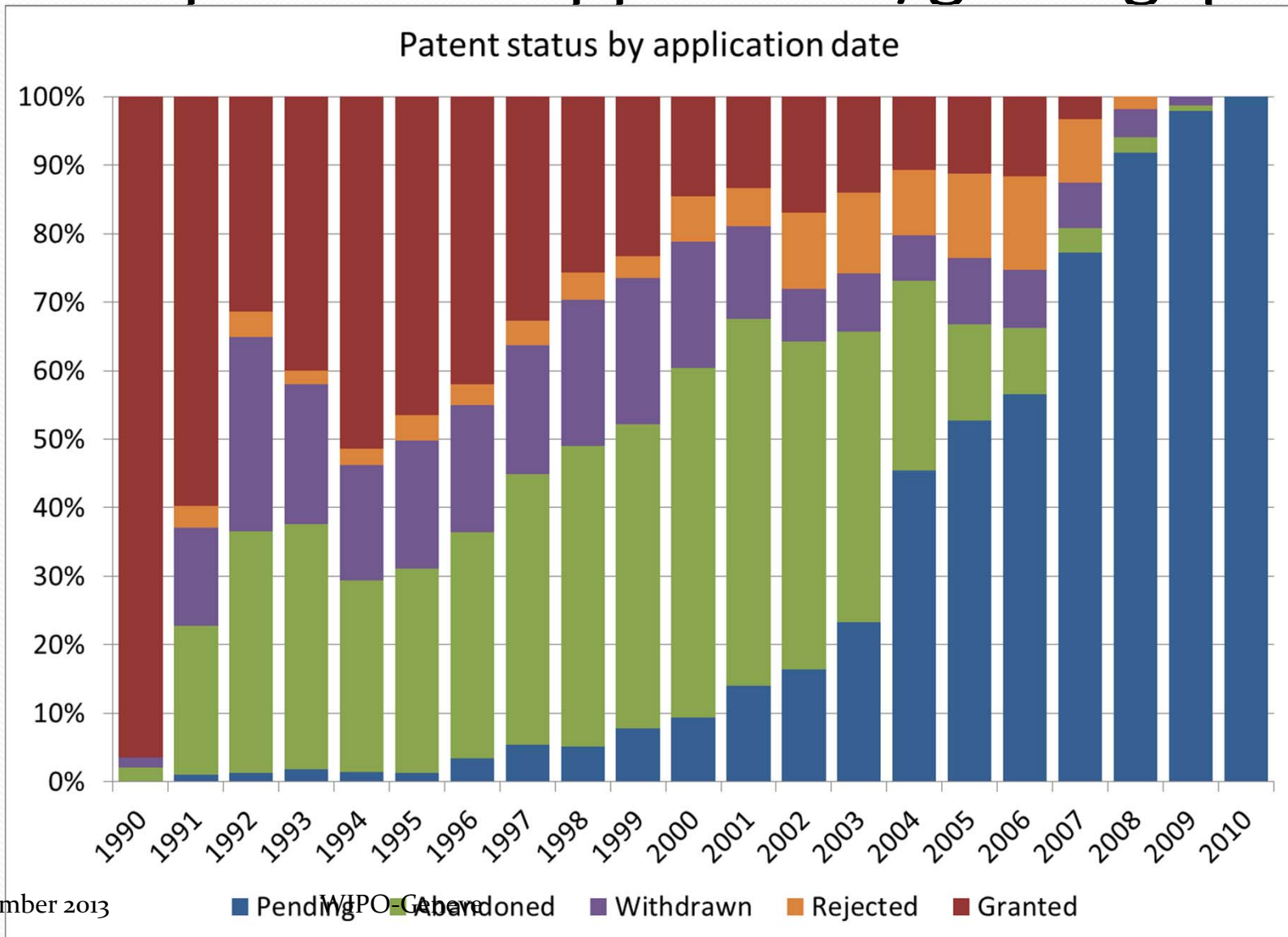
Total pharmaceutical patent filings by residents and non-residents in Chile



Total pharmaceutical patent filings and grants by filing year



What explains the application/grant gap?





Our Research Questions

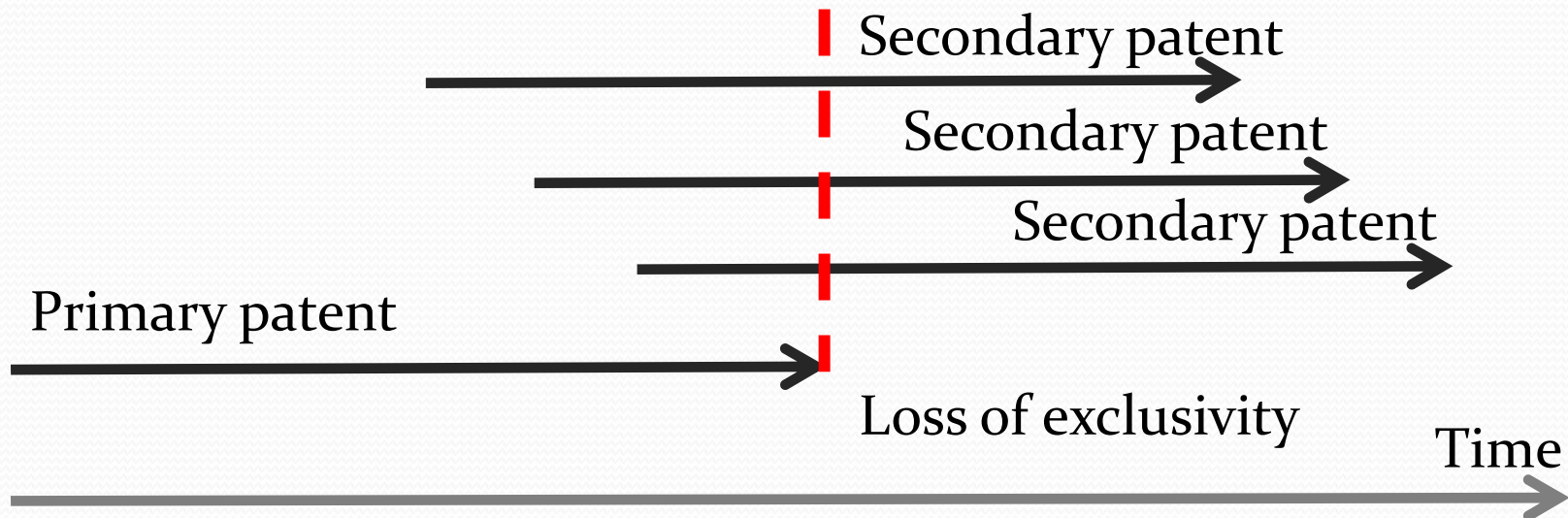
- What is the share of patents held by foreign pharma companies associated with drugs commercialized on the domestic market?
 - This measures “working” of patents
- Do foreign pharma firms use strategic patenting behavior to keep domestic generic producers off the market?
 - This measures impact on (broadly defined) “innovation”

Patenting strategies

- Multiple functions of patents: ensure freedom to operate, bargaining etc
- Are patents also used to block/delay entry of generics and avoid loss of (broad) exclusivity?
- Primary vs secondary patents
 - Extend patent life
 - Increase patent breadth
 - Facilitate follow-on inventions (“evergreening”)

Patenting strategies: length

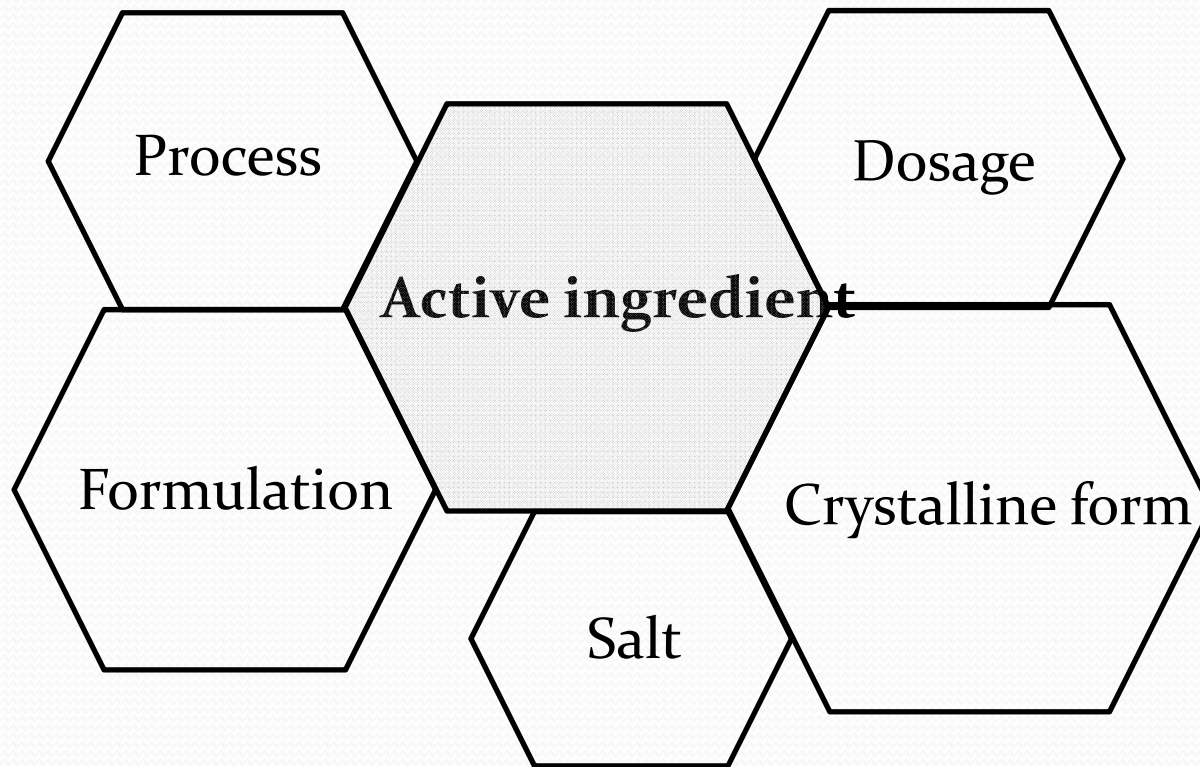
- Patent cluster to extend lifetime



- Incremental innovation or fencing strategy?

Patenting strategies: breadth

- Patent cluster to extend breadth:



- Incremental innovation or fencing strategy?



Patenting strategies: anecdotal evidence

"We were recently successful in asserting the crystalline form patent in [name of country], where we obtained an injunction against several generic companies based on these patents by 'trapping' the generics: they either infringe our crystalline form patent, or they infringe our amorphous form process patent when they convert the crystalline form to the amorphous form."

Anonymous pharmaceutical company quoted in EU Commission (2009)



Patenting strategies: anecdotal evidence

“The entire point of the patenting strategy adopted by many originators is to remove legal certainty. The strategy is to file as many patents as possible on all areas of the drug and create a 'minefield' for the generic to navigate. All generics know that very few patents in that larger group will be valid and infringed by the product they propose to make, but it is impossible to be certain prior to launch that your product will not infringe and you will not be the subject of an interim injunction.”

Anonymous generic producer quoted in EU Commission (2009)

Patenting strategies: empirical evidence

- EU Commission (2009):
 - primary to secondary patent ratio **1:7**
 - pending patents **1:13**
 - granted patents **1:5**
 - Disproportionately more secondary patents after product launch
- Kapczynski et al. (2012):
 - Of new drugs with FDA in 1991-2005: 56% formulation, 24% salts, crystalline forms etc., 63% methods of use (secondary patents)
 - Secondary patents filed after FDA approval and extend exclusivity lifetime by 4-5 years
 - More secondary patents the higher is the branded drug's sales

Data Construction

- Objective: **link products with patents & trademarks**
- **Chilean patent office (INAPI):** Universe of patents and trademarks filed with INAPI between 1991 and 2010 by domestic and foreign entities.
- **National public health institute (ISP):** All drugs registered in Chile. The information includes active ingredients of all registered products, the owner of the drug, whether the drug is produced domestically or abroad, etc. (*but not patent numbers*)
- **Merck Index (MI) and US FDA Orange Book (OB):** MI provides first filing of patent protecting active ingredients. OB provides US patents of active ingredients.

Data Construction

Example of Drug-AI-Patent-TM Mapping

ISP

Drug Name: "ECALTA POLVO LIOFILIZADO PARA SOLUCION INYECTABLE 100 MG"

Owner: LABORATORIO PFIZER CHILE S.A.

Distributors: PFIZER CHILE S.A, NOVOFARMA S.A

Quality Controls: CONDECAL LTDA.

Active Ingredient: ANIDULAFUNGINA

INAPI

AI Patent: 199300289

Title: "COMPUESTOS ANTIFUNGICOS Y ANTIPARASITARIOS, DERIVADOS DE PEPTIDOS CICLICOS, PROCEDIMIENTO PARA SU OBTENCION, COMPOSICIONES FARMACEUTICAS QUE LO CONTIENEN UTILES COMO INHIBIDORES DEL CRECIMIENTO DE HONGOS Y PARASITOS"

Applicant: ELI LILLY AND COMPANY

Trademark: 794721

Denomination: ECALTA

Applicant: VICURON PHARMACEUTICALS INC

Related ISP-TM owner

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Trademark: 712240

Denomination: ECALTA

Applicant: VICURON PHARMACEUTICALS INC

Related ISP-TM owner

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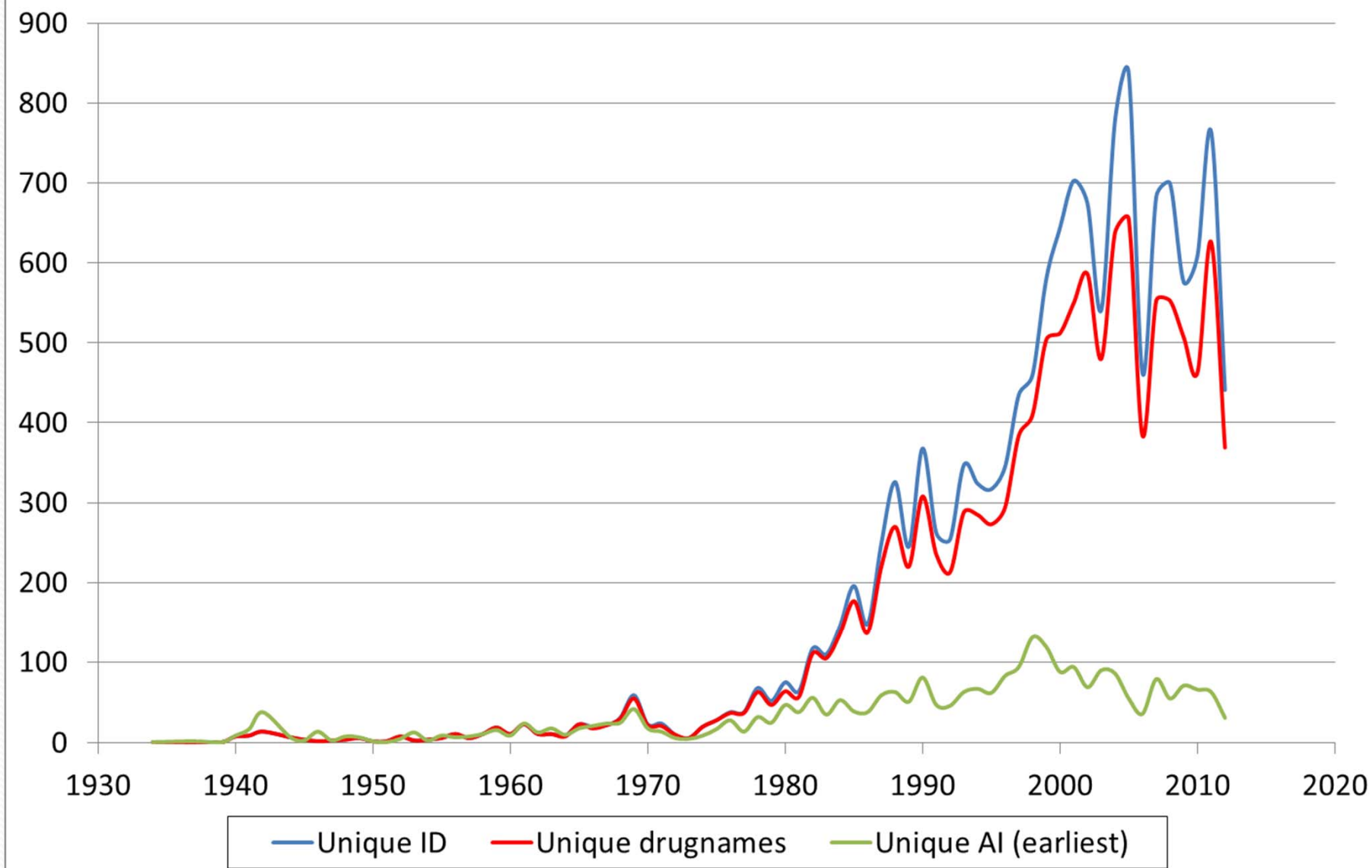
Data challenges

- Active ingredients, patents, trademarks use different classification systems
- A single patent can protect multiple active ingredients (and vice versa)
- A product can be associated with several patents and trademarks
- Active ingredients appear in multiple products
- Spelling of the owner name varies considerably within and across the various data sources

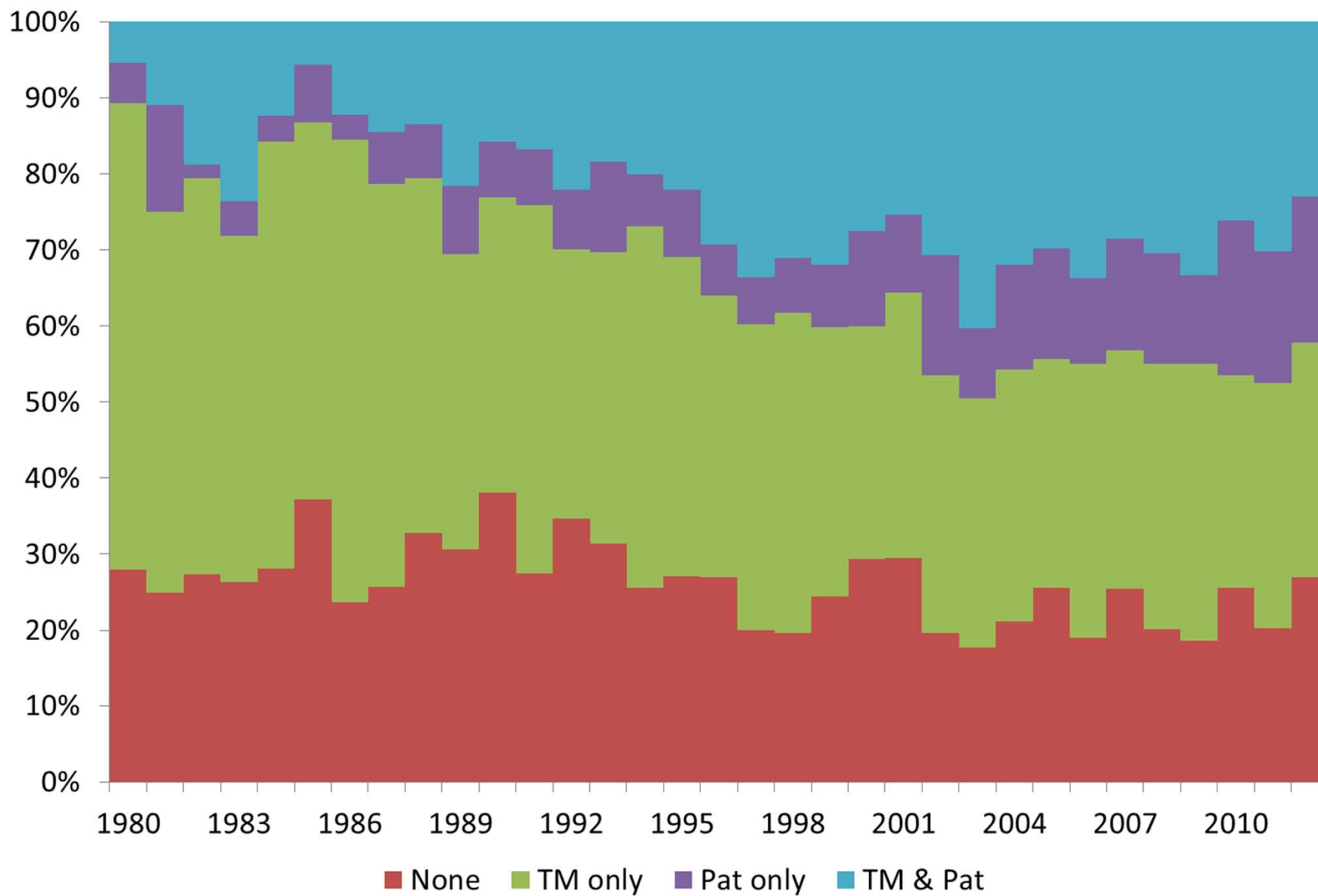
Data construction

- We have an active ingredient-product match from ISP (non-unique in some cases)
- Matching CL patents to active ingredients:
 - 2005-2010: we have a match done by patent examiners specializing in pharma
 - Pre-2005: translate AI description to English; search in Merck Index of first filings and the US Orangebook for US patents associated with the AI; find CL equivalent patents; also do our own search in CL patents and validate by examiners (not finished)
- Matching CL trademarks to products
 - Search by product (drug name) and owner in the trademark database

Registrations (ID), products (drugs) and active ingredients (AI) registered at the Chilean ISP



Type of IP protection chosen for each ISP registration



Some details on ISP registrations

Number	Registrations per ingredient	Ingredients per drug
1	995	9,436
2	451	2,013
3	241	548
4	160	218
5	94	109
6	84	49
7	67	23
8	46	13
9	68	27
10+	538	155
Total	2744	12,591

Top 5 registrations	
ASCORBIC ACID	Vitamin C
CHLORPHENAMINE MALEATE	Antihistamine
IBUPROFEN	NSAID
PARACETAMOL	NSAID
PYRIDOXINE HYDROCHLORIDE	Vitamin B6

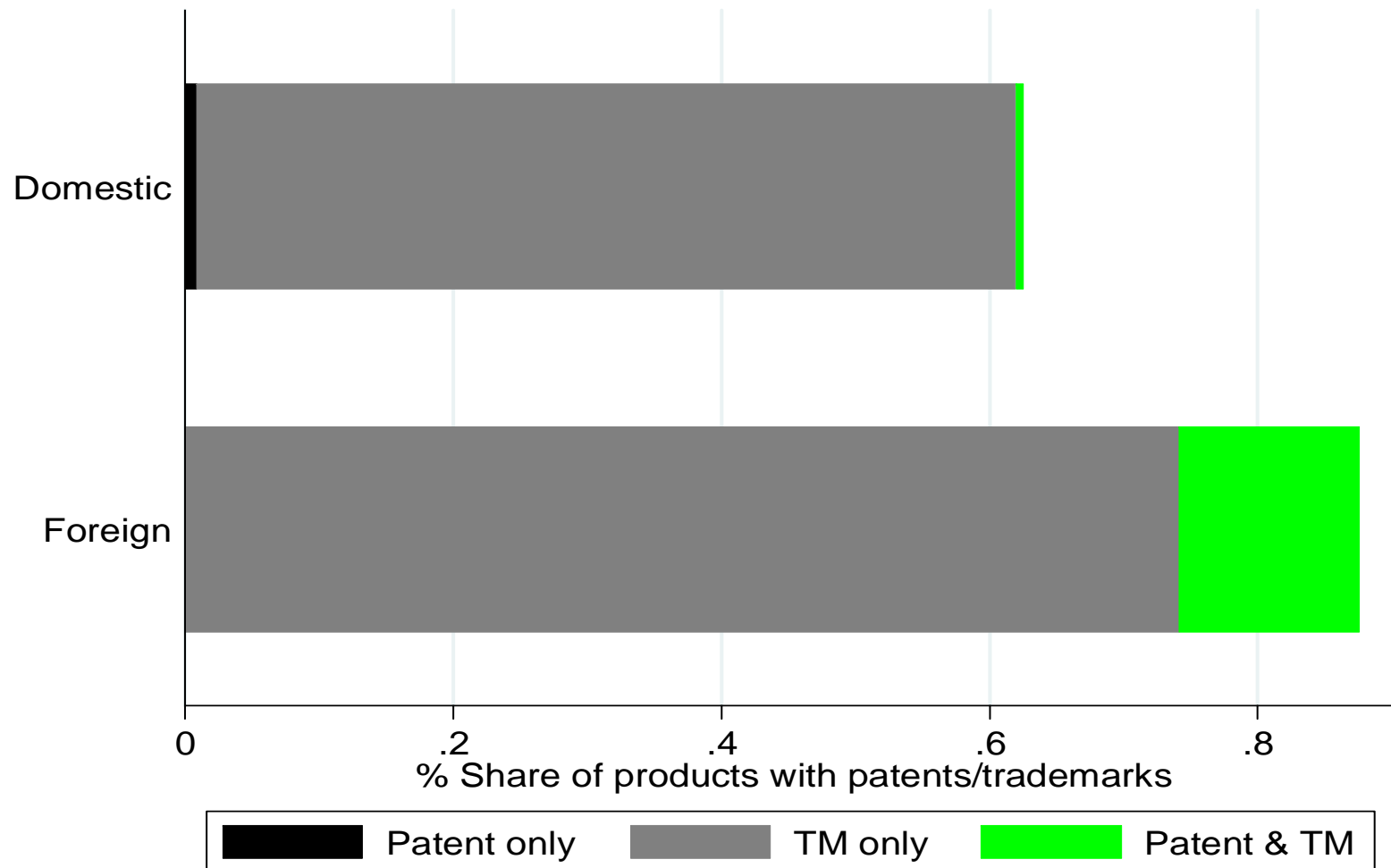
Drugs with the most ingredients are typically multi-vitamins or generics

Top 10 therapeutic classes protected by patents/trademarks

Table 2: Products with TM/patents by therapeutic class

Therapeutic class	% of all products	% TM only	% TM & Patent	% TM or Patent
Antineoplasticos	5.5%	59.5%	21.4%	81.0%
Antibioticos	3.5%	29.6%	0.0%	29.6%
Antianemicos	3.3%	80.0%	0.0%	80.0%
Antidepresivos	1.8%	42.9%	14.3%	57.1%
Vacuna	1.7%	76.9%	0.0%	76.9%
Antipsicoticos	1.7%	69.2%	23.1%	92.3%
Antirretrovirales	1.7%	15.4%	38.5%	53.8%
Antiparkinsonianos	1.6%	75.0%	25.0%	100.0%
Antivirales	1.4%	63.6%	36.4%	100.0%
Antihipertensivos	1.3%	80.0%	0.0%	80.0%
Total/Average	100	69.0%	4.7%	74.0%

Products protected by patents/trademarks by domestic/foreign companies



Products protected by patents/trademarks by nationality (top 10 companies)

Table 3: Products with TM/patents by owner
% of all

ISP owner	Nationality	products	% Patent only	% TM only	% TM & Patent	% TM or Patent
Laboratorio Recalcine sa	CL	7,2%	5.7%	75,5%	0.0%	81,1%
Novartis Chile sa	CH	5,0%	0,0%	73,0%	24.3%	97,3%
Laboratorio Andromaco sa	CL	4,9%	0,0%	69,4%	0,0%	69,4%
Laboratorio Chile sa	CL	4,3%	0,0%	53,1%	3,1%	56,3%
Roche Chile ltda	CH	3,8%	0,0%	89,3%	10,7%	100,0%
Merck sa	US	3,5%	0,0%	73,1%	26,9%	100,0%
Sanofi Aventis Chile sa	FR	3,2%	0,0%	58,3%	0,0%	58,3%
Laboratorio Biosano sa	CL	3,1%	0,0%	52,2%	0,0%	52,2%
Johnson & Johnson Chile sa	US	3,0%	0,0%	72,7%	27,3%	100,0%
Glaxosmithkline Chile ltda	GB	2,7%	0,0%	75,0%	25,0%	100,0%
Total/Average		100	0,1%	67,4%	4,6%	72,0%

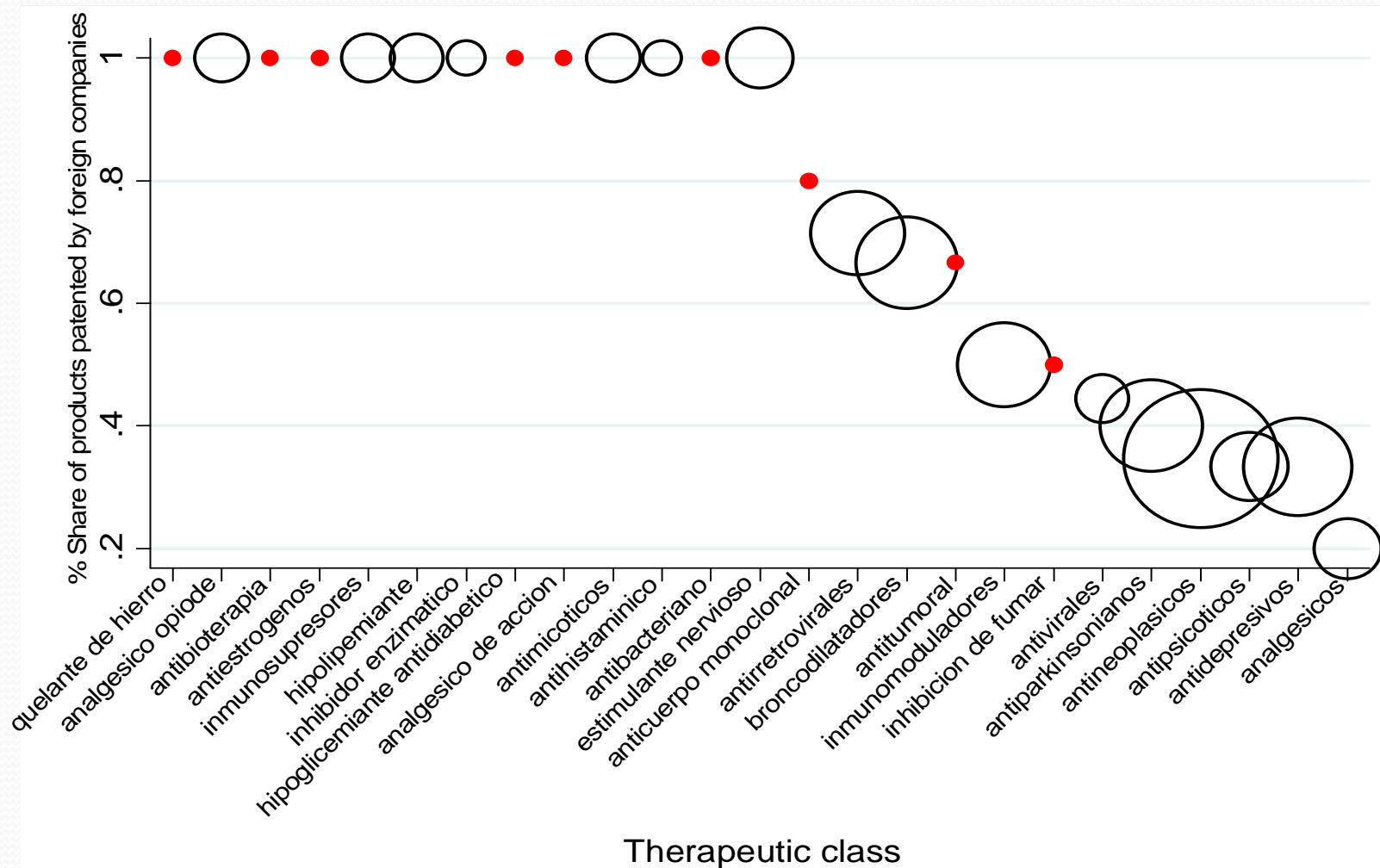
Top 10 therapeutic classes protected by patents by domestic/foreign

Table 4: Products with TM/patents by therepeutic class

Therapeutic class	# Products		% Patented	
	Domestic	Foreign	Domestic	Foreign
Antineoplasticos	16	26	0.0%	34.6%
Antidepresivos	8	6	0.0%	33.3%
Antipsicoticos	4	9	0.0%	33.3%
Antirretrovirales	6	7	0.0%	71.4%
Antiparkinsonianos	7	5	14.3%	40.0%
Antivirales	2	9	0.0%	44.4%
Broncodilatadores	7	3	0.0%	66.7%
Inmunomoduladores	6	2	0.0%	50.0%
Analgesicos	3	5	0.0%	20.0%
Anticuerpo monoclonal	0	5	0.0%	80.0%
Total/Average	72	101	8.6%	67.6%

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Number of domestic company products increases as share of drugs patented by foreigners decreases



Some (regression) correlations

	Dep. Variable: products by domestic producers within therapeutic class				
	Pr(Prod _D)	# Prod _D	Pr(Prod _D)	# Prod _D	# Prod _D
Share of products registered by foreign companies within therapeutic class	-0.919*** (0.013)	-2.871*** (0.404)			
Share of products patented by foreign companies within therapeutic class			-0.239*** (0.041)	-3.691*** (0.281)	
Average # patents for given product within therapeutic class					-1.684 (1.953)
# Obs	1097	1097	561	561	75

Conclusion

- Almost **all pharma patents** in Chile held by **foreign** firms
- Almost **no products** by domestic companies protected by patents
- **Negative** relationship between share of drugs patented by foreign companies and number of drugs by domestic companies
- Tentative evidence for plenty of **strategic patenting** behavior in pharmaceuticals
- Work in progress...