Affordable innovation - Future Directions in Pharmaceutical Policy

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Department of Essential Medicines and Health Products
October 2015

World Health Organization

BUSINESS

How Clinton Hopes to Make American Drug Prices

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Tuberculosis
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Drug-price hikes don't lead to better cures. We must find another way forward

Philipp du Cros

Hillary Clinton speaks at Moulton Elementary School in Des Moines, Iowa on September 22, 2015. (Brian Frank / Reuters)

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Where we started from

Period	Number of approved NCEs	Innovation index	NCEs listed in 1999 WHO EDL	NCEs listed in WHO EDL indicated for a neglected disease
1975–79	248	0·339	2*	0
1980–84	256	0·308	16†	6
1985–89	277	0·278	8‡	4
1990–94	280	0·314	4§	1
1995–99	332	0·324	7¶	5
Total	1393	..	37	16
5-year average	279	0·313	7	3

NCEs=new chemical entities. *Cisplatin, levothyroxine. †Aciclovir, *benznidazole*, captopril, cimetidine, cetriaxone, clavulinic acid, factor VIII concentrate, factor IX complex, iohexol, nifedipine, *nifurtimox*, *oxamniquine*, *pentamidine*, *praziquantel*, *pyrazinamide*, testosterone enantate. ‡*Albendazole*, ceftazidine, ciprofloxacine, fluconazole, *ivermectin*, *halofantrine*, *mefloquine*, zidovudine. §Atenolol, ciclosporin, *eflornithine*, imipenem-cilastatin. ¶*Liposomal amphotericin B*, *artemether*, *atovaquone*, etoposide, nevirapine, *rifabutine*, *rifapentine*. Italics indicate approval for a neglected-disease indication.
Sources: EMEA and FDA data;
IMS statistics; WHO essential drug list (EDL, available at www.who.int/medicines/edl/edl11-alpha.html); reference 5.

Trouiller et al, Lancet 2002:359:2188-2194 .

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The NEW ENGLAND JOURNAL of MEDICINE

Forbes / Pharma & Healthcare

The Little Black Book o

AUG 11, 2013 @ 11:10 AM **185,122** VIEWS

The Cost Of Creating A New Drug Now $5 Billion, Pushing Big Pharma To Change

The $2.6 Billion Pill — Methodologic and Policy Considerations

Jerry Avorn, M.D.

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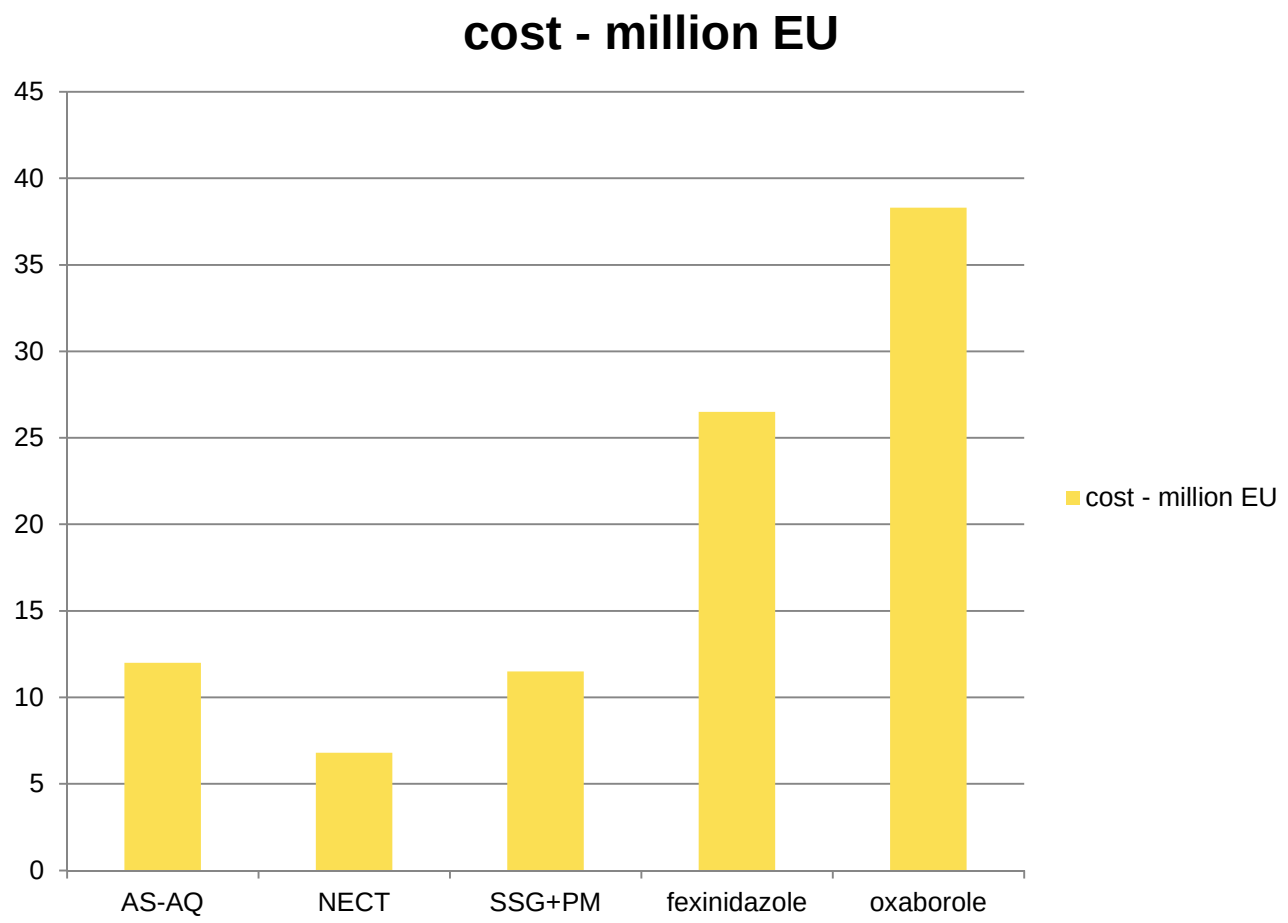
DNDi product development costs



http://www.dndi.org/images/stories/pdf_aboutDNDi/DNDiModel/DNDi_CostOfDev_FactsFigures

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A changing industry

Table 1
Recent history of large pharmaceutical mergers (survivors are ranked by 2010 worldwide sales).

1.	Pfizer 2009: Acquired Wyeth (which resulted from 1994 merger of American Cyanamid and American Home Products). 2003: Acquired Pharmacia (which acquired Upjohn in 1995). 2000: Acquired Warner-Lambert.
2.	Johnson & Johnson (no major mergers).
3.	Novartis 2011: Acquired Alcon. 1996: Resulted from merger of Ciba Geigy and Sandoz.
4.	Roche 2009: Consolidated 1990 acquisition of Genentech. 1995: Acquired Syntex.
5.	Bayer (no major mergers).
6.	Merck 2009: Acquired Schering-Plough.
7.	Sanofi-Aventis 2011: Acquired Genzyme. 1999: Name changed after merger of Rhone-Poulenc and Hoechst. 1995: Hoechst acquired Marion Merrell Dow. 1995: Rhone-Poulenc acquired Fisons. 1990: Rhone-Poulenc acquired Rorer.
8.	Glaxo SmithKline 2000: SmithKline Beecham merged with Glaxo. 1995: Wellcome merged with Glaxo. 1989: Beecham merged with SmithKline.
9.	Abbott (no major mergers).
10.	Astra Zeneca 1999: Zeneca Group merged with Astra AB.
11.	Eli Lilly (no major mergers).
12.	Bristol-Myers Squibb 2001: Acquired duPont Pharmaceuticals. 1989: Bristol-Myers and Squibb merged; name change.

Comanor & Schering J Health Econ 2013:32;106-113.

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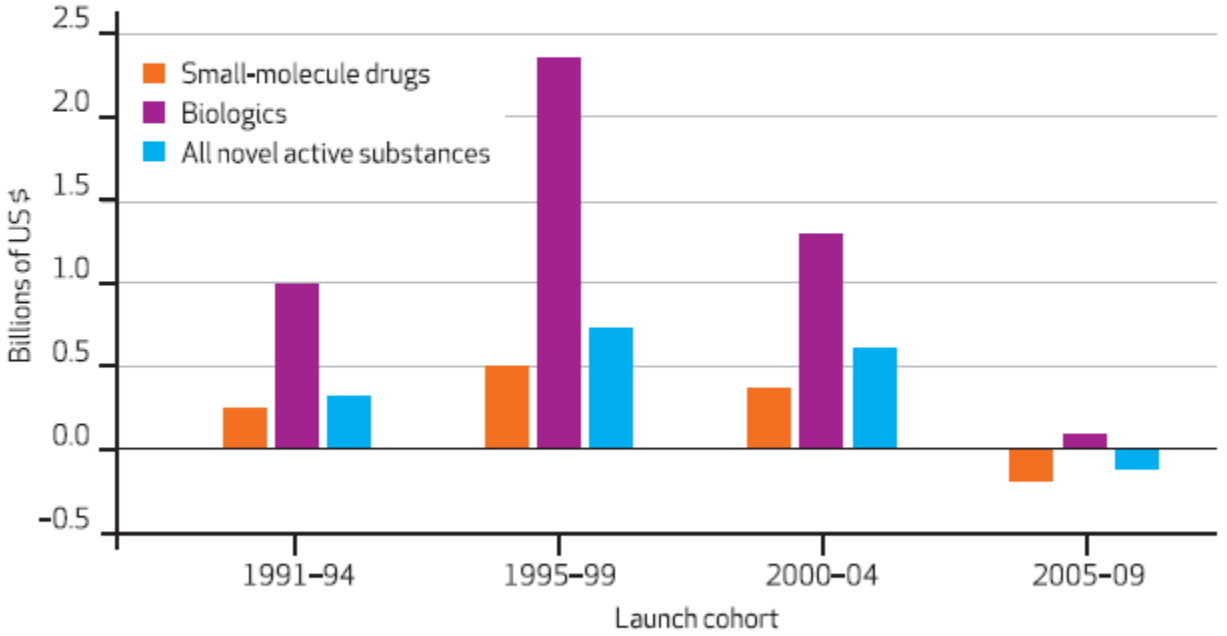
EXHIBIT 4

Average Lifetime After-Tax Net Returns Of Novel Active Substances, By Launch Cohort, 1991–2009



SOURCE Authors' analysis of 1991–2012 data from IMS Health Inc.'s MIDAS database.

Berndt et al, Health Affairs 2015:34;245-252.

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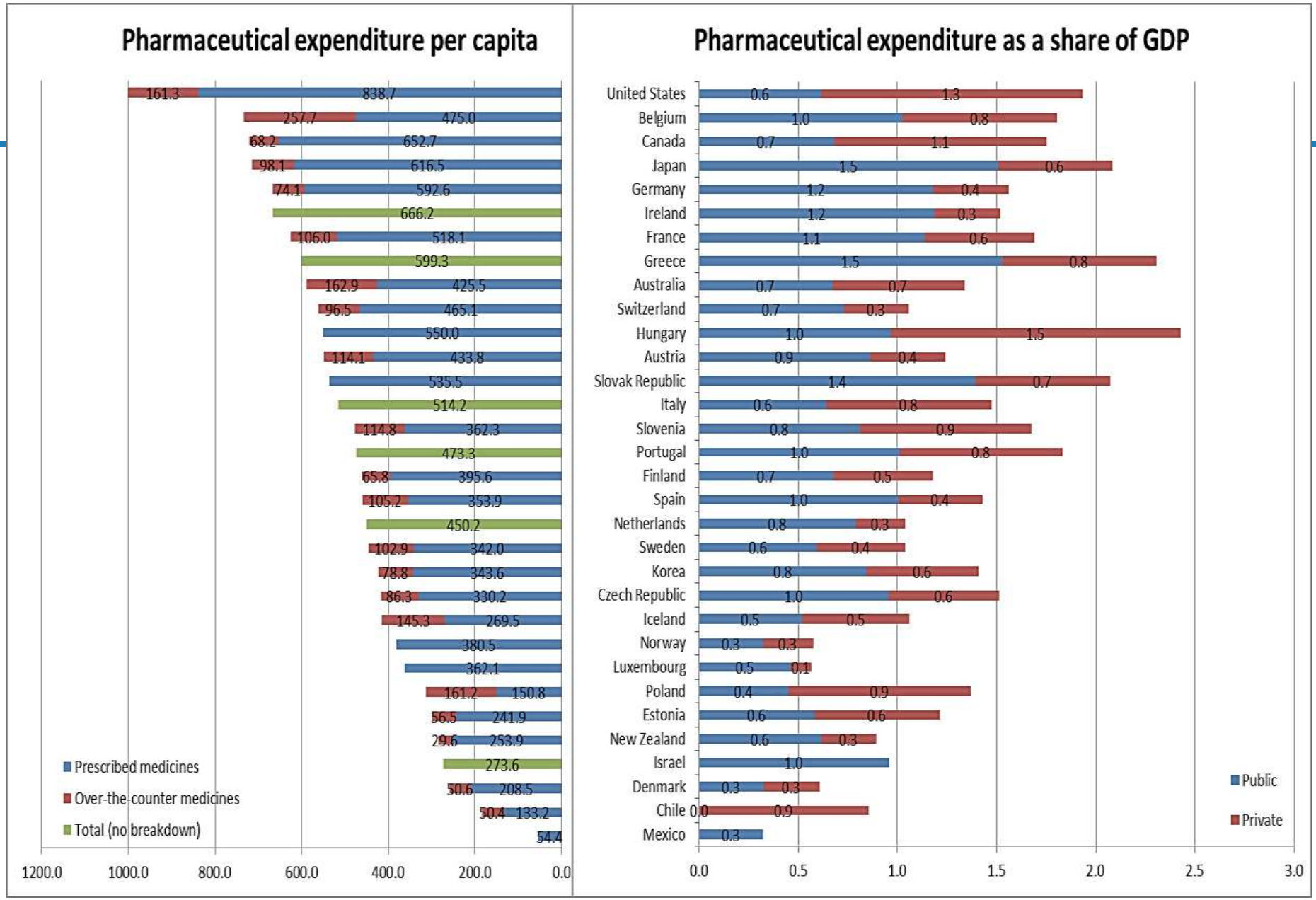
What are we spending?



OECD, 2014

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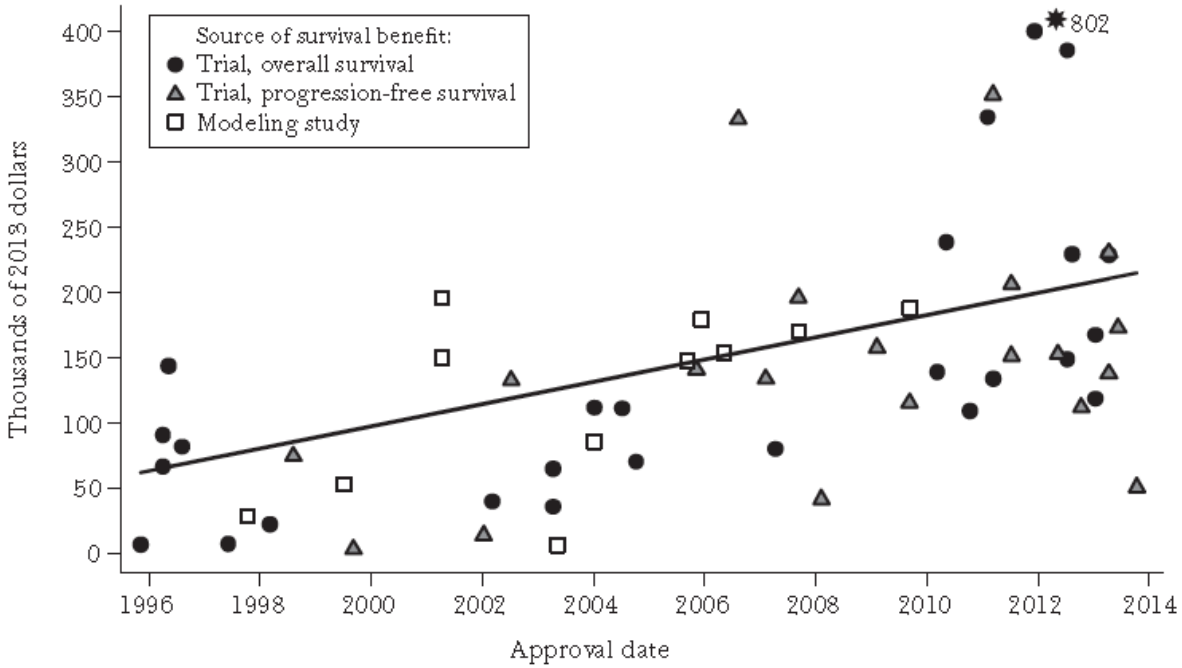
What is happening with market entry prices?

Figure 2

Drug Price per Life Year Gained versus Drug Approval Date



Source: Authors.

Notes: The best fit line is: Price per life year gained = $54,100 + $8,500 × Approval Year. Approval Year = 0 for 1995, 1 for 1996, . . . 19 for 2014. For purposes of display, we recoded one value from $802,000 to $400,000.

Howard DH, Bach PB, Berndt ER, Conti RM. Pricing in the market for anticancer drugs. J Econ Persp 2015;29: 139–162.

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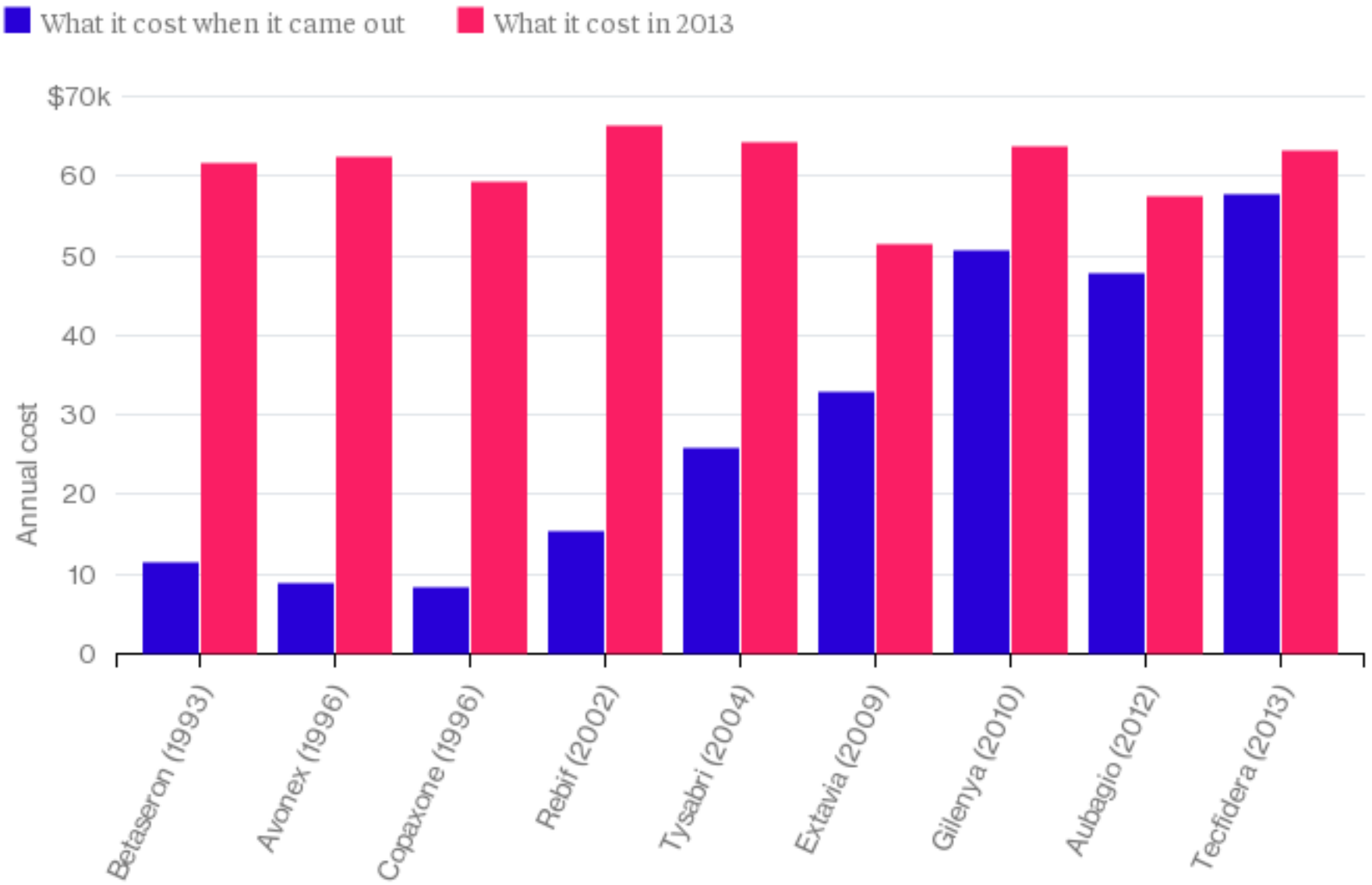
Multiple Sclerosis Drug Prices Only Go Up

Medications introduced years ago now cost as much as newer, high priced therapies

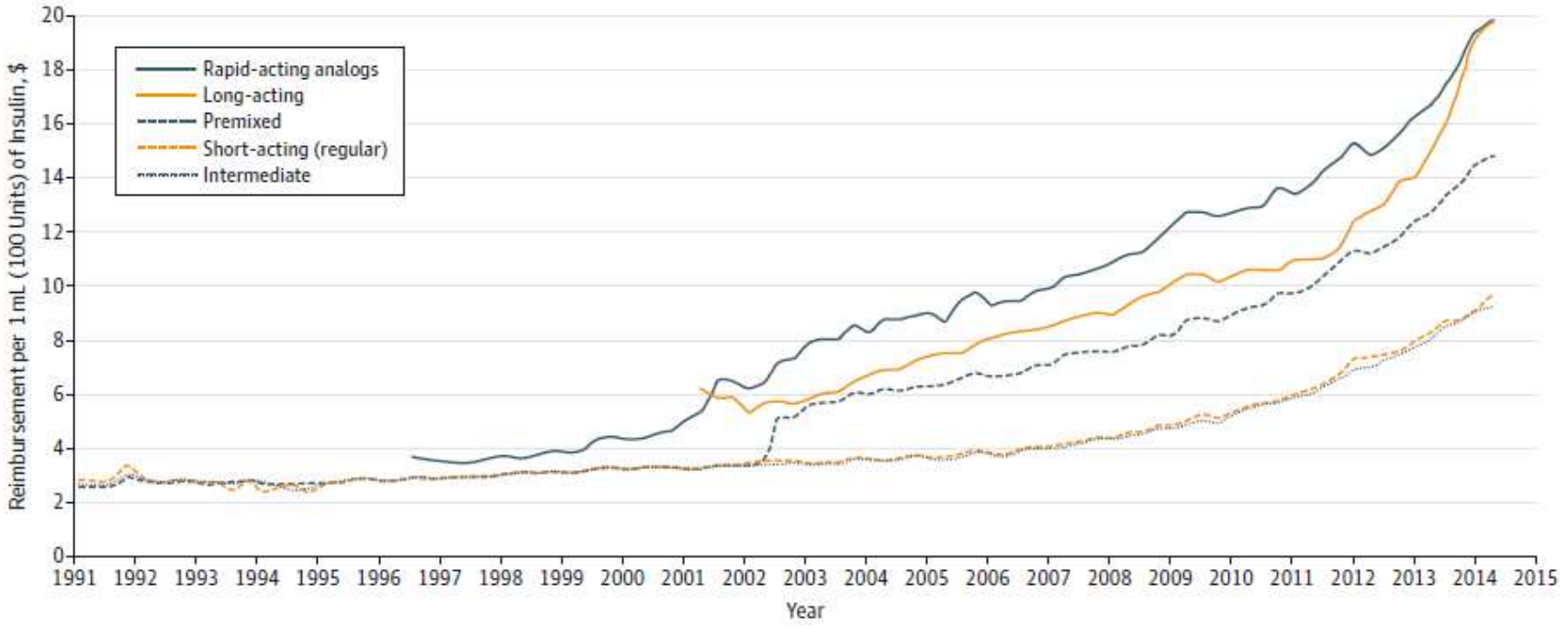


Source: Neurology

Bloomberg

From the payers perspective

Figure 1. Medicaid Reimbursement Trends for Covered Insulin Products From 1991 Through 2014



Reimbursements were adjusted by the Bureau of Labor Statistics' annual Consumer Price Index for All Urban Consumers.

Luo, Avorn & Kesselheim. JAMA Intern Med 2015:175:1681-1686.

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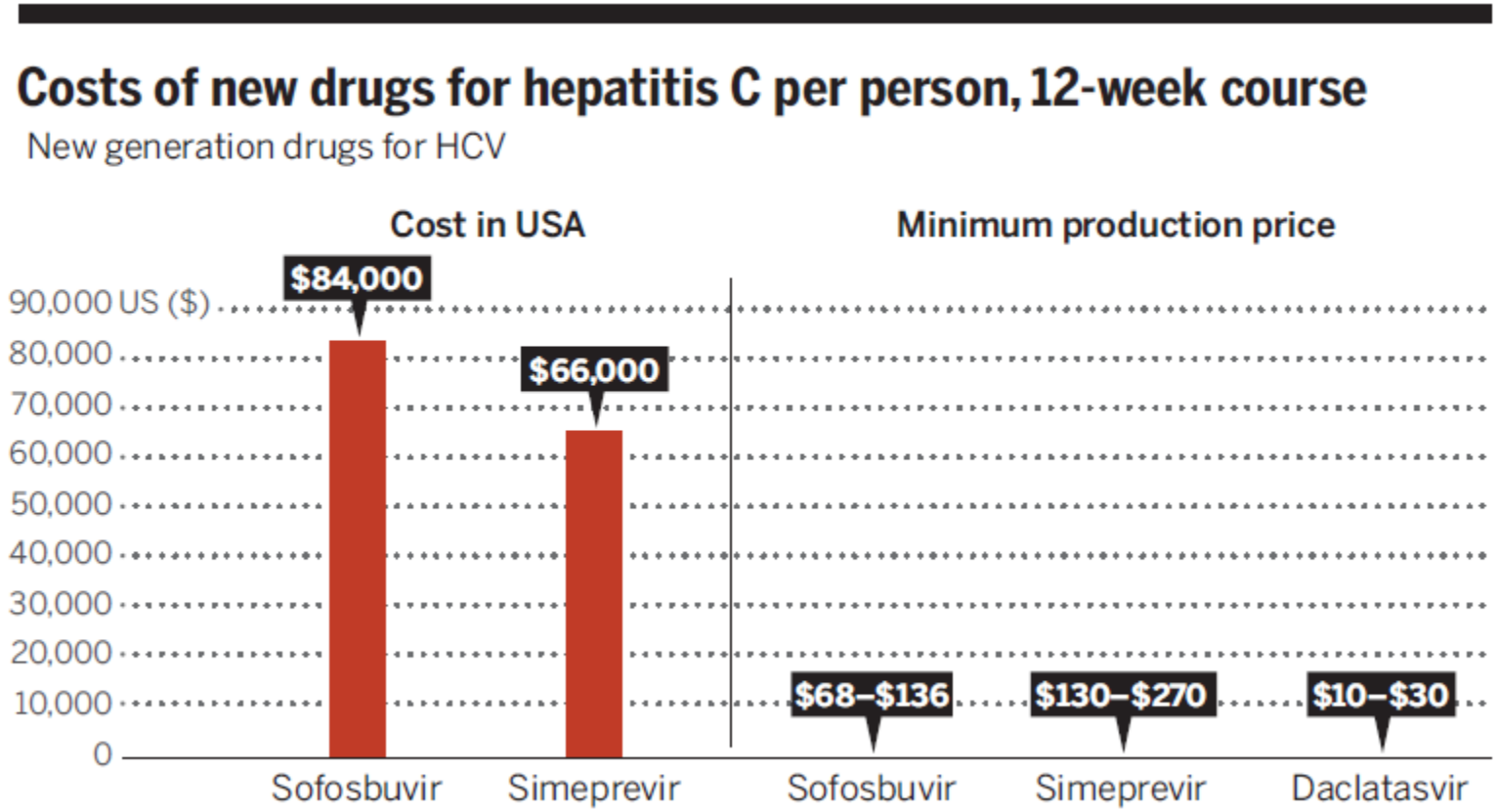
Cost of hepatitis C treatments?



Hill A, Cooke G. Science 2014; 345(6193):141-142

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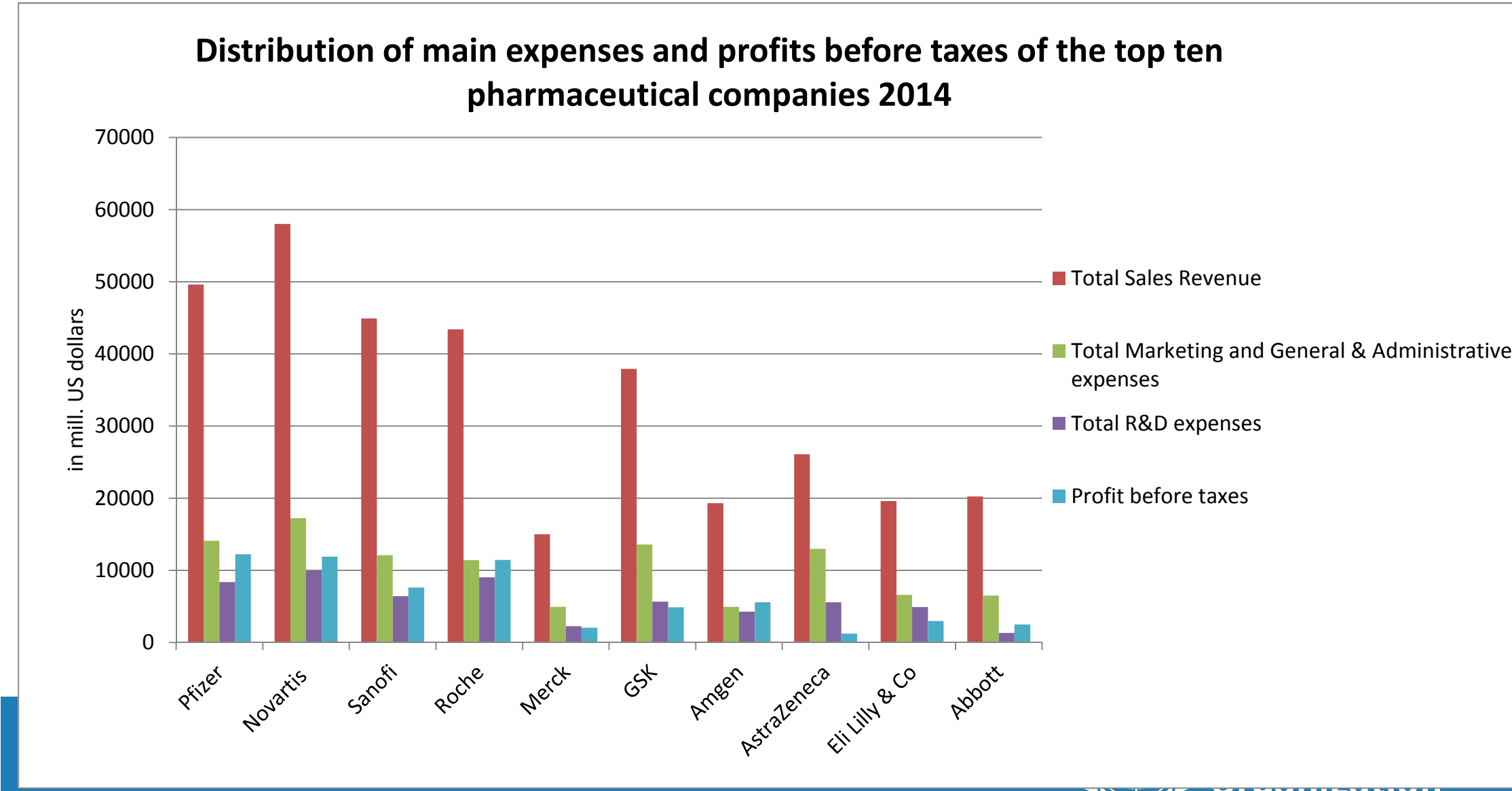
Is R&D the main cost driver?



THE OTHER SIDE OF THE PROBLEM

Shortages

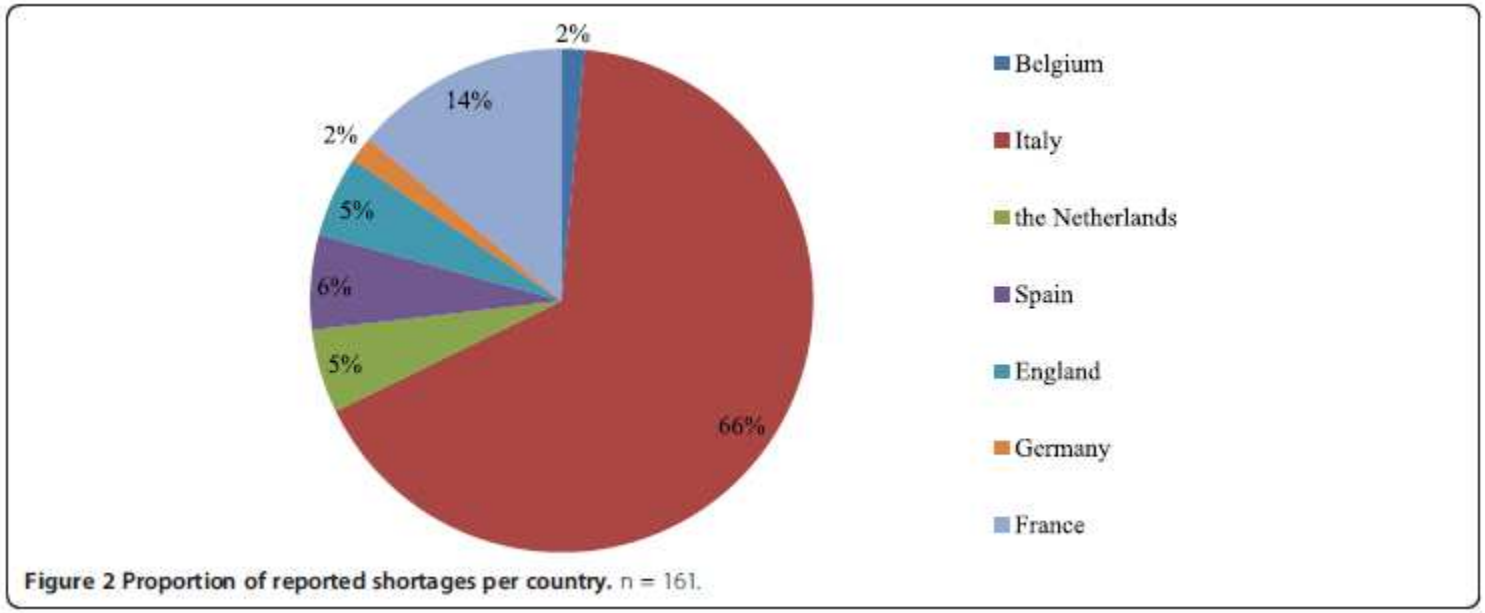


Figure 2 Proportion of reported shortages per country. n = 161.

Pauwels et al. BMC Health Services Research 2014;14:438.

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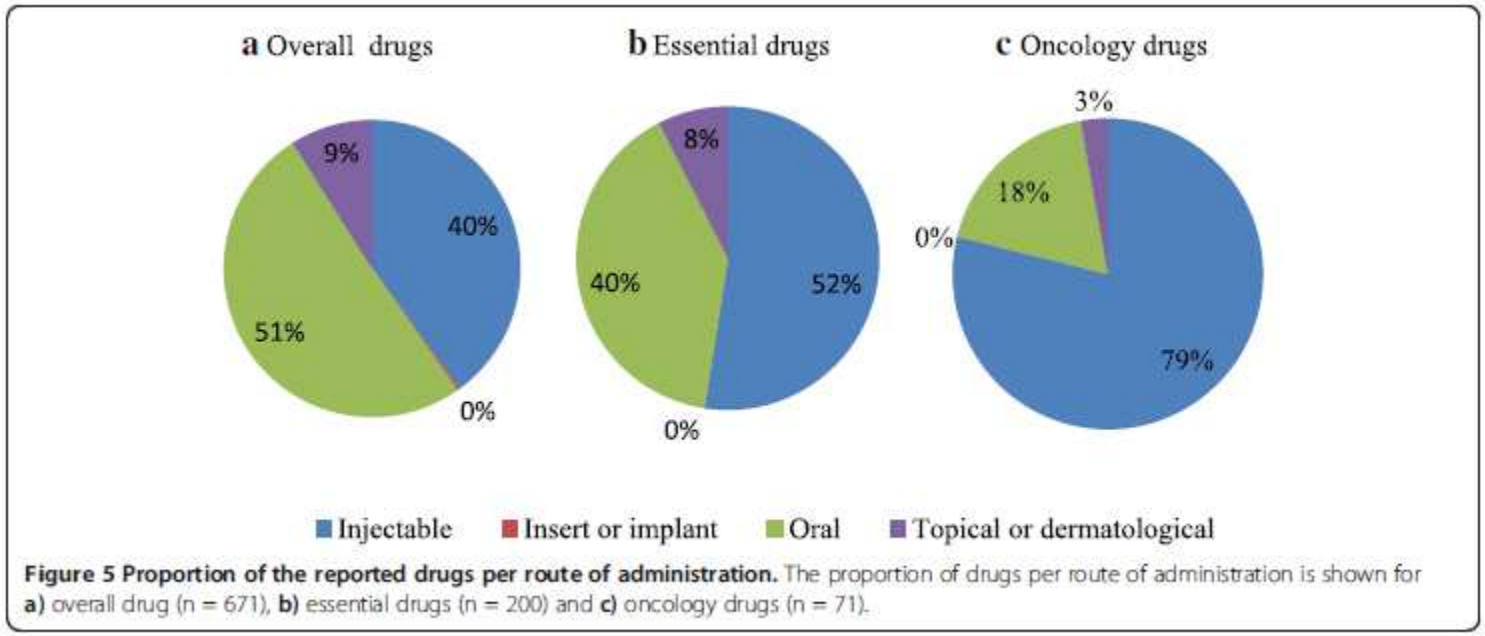

Figure 5 Proportion of the reported drugs per route of administration. The proportion of drugs per route of administration is shown for **a)** overall drug (n = 671), **b)** essential drugs (n = 200) and **c)** oncology drugs (n = 71).

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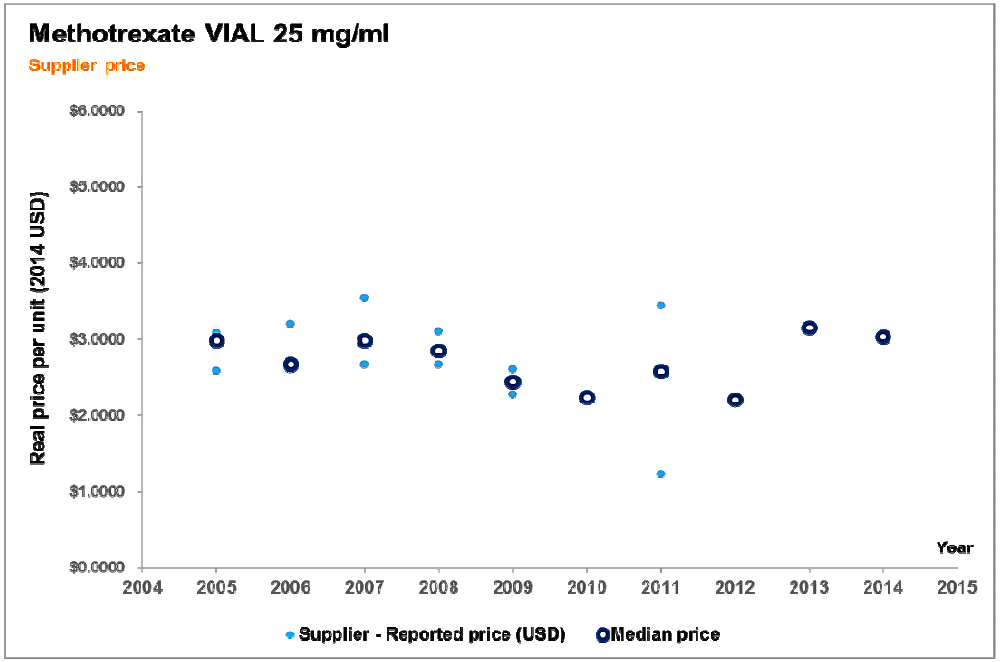
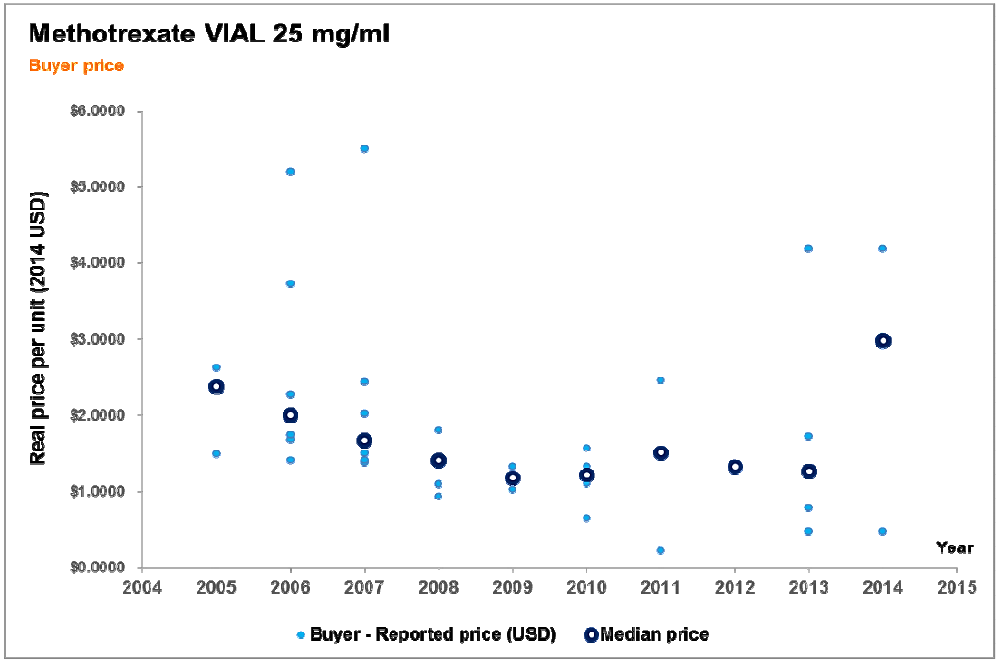
Price to buyer and supplier?

Methotrexate





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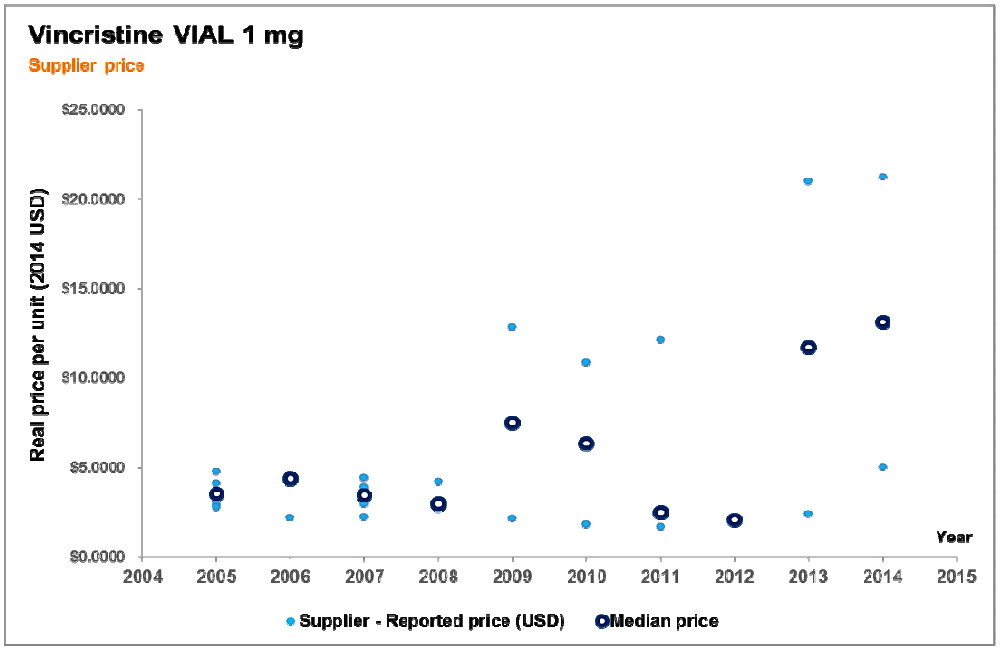
Vincristine 1mg



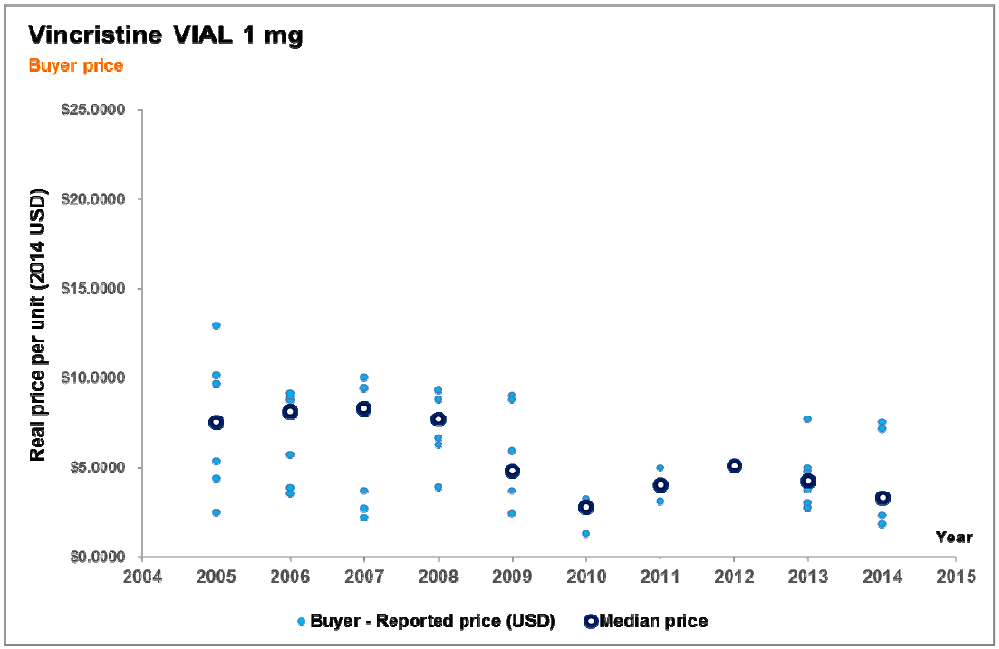


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Table 2. Oncologists' Experiences With Shortages of Specific Drugs

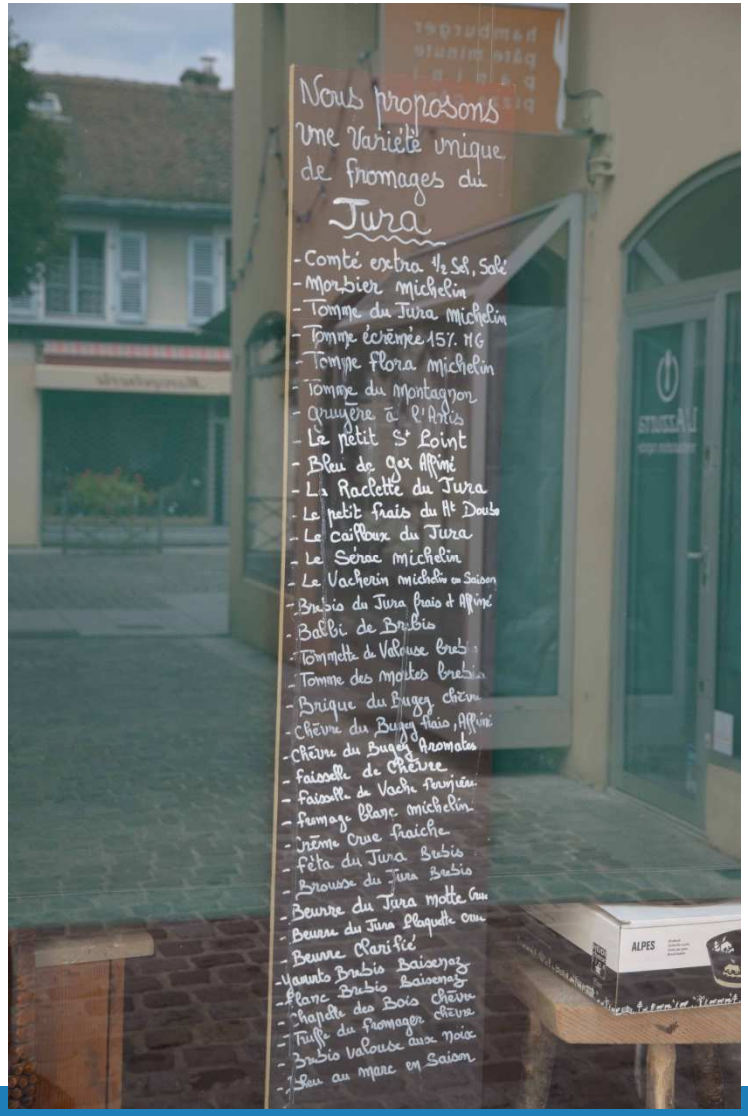
Drug	Any Experience With Shortage				Needed to Use Equally Effective Alternative				Needed to Use Less Effective Alternative				Not Affected by Shortage	
	No.	%	Mean No. of Patients Affected*	SD	No.	%	Mean No. of Patients Affected*	SD	No.	%	Mean No. of Patients Affected*	SD	No.	%
Any drug	245	74	15.6	28.1	201	61	14.9	26.7	92	28	8.8	19.8	85	26
Leucovorin	216	66	13.1	14.3	167	51	13.2	12.5	49	15	11.6	17.6	101	31
Fluorouracil	68	21	9.2	12.6	57	17	8.1	9.1	11	3	13.0	14.7	252	76
Dexamethasone†	51	16	25.6	46.5	35	11	29.8	52.4	16	5	11.9	10.2	272	82
Cyanocobalamin†	42	13	7.0	12.1	20	6	8.1	12.2	22	7	5.9	12.3	277	84
Paclitaxel	35	11	5.0	3.7	26	8	5.2	3.6	9	3	4.7	4.2	285	86
Cisplatin	27	8	4.8	5.5	13	4	3.9	2.0	14	4	5.6	7.6	293	89
Etoposide	27	8	3.6	2.7	12	4	2.3	0.8	15	5	4.5	3.2	295	89

Abbreviation: SD, standard deviation.
* Among patients of the physician reporting any experience with the shortage or needing to use an alternative.
† Supportive medication.

Kehl et al. J Onc Practice 2014:11;e154-e162

WHAT TO DO?

The policy menu



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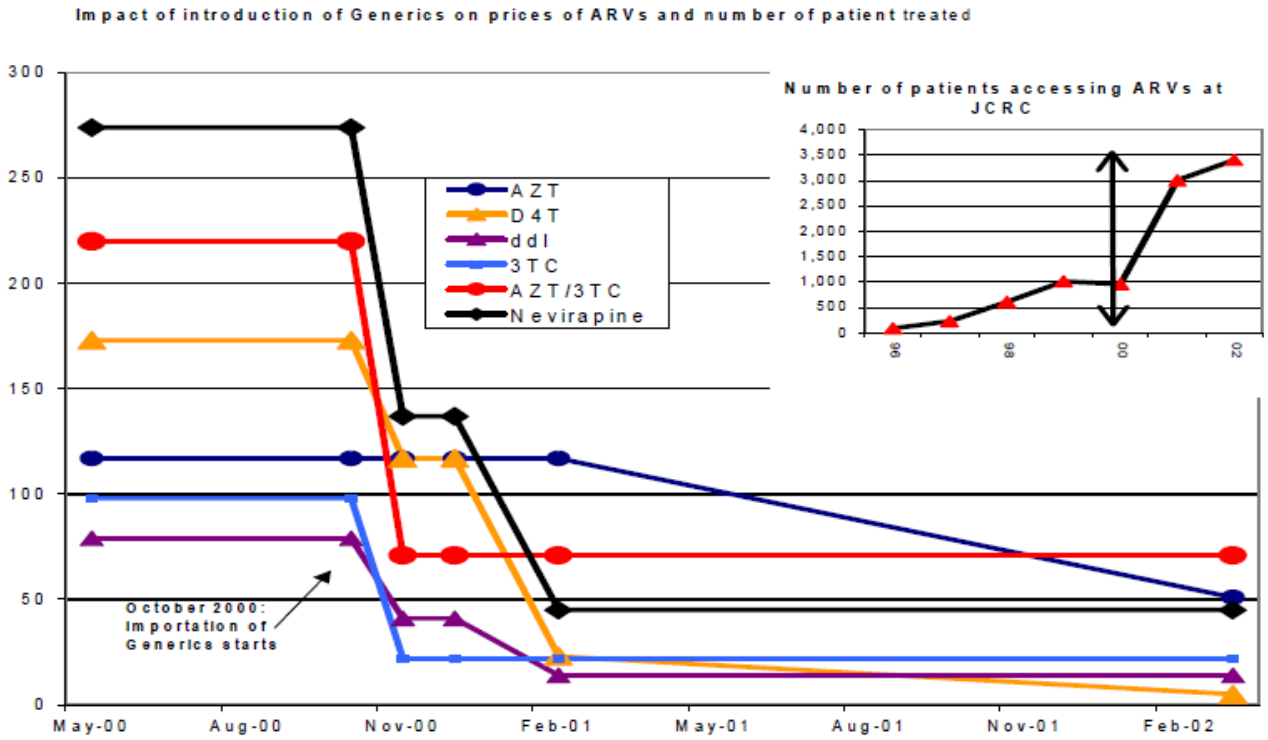
FROM: Policy Options for pharmaceutical pricing and purchasing: issues for low and middle income countries. Nguyen et al Health Policy and Planning 2015.

Policy group	Strategy
Pricing techniques	• External reference pricing • Internal reference pricing • Pharmacoeconomic evaluation efor value based pricing (HTA) • Cost plus pricing • Profit ceilings
Implementing pricing policies	• Fixing prices at retail/pharmacy level, Maximum Retail Prices • Fixing prices at wholesale level – maximum whole sale price • Fixing price ate ex-manufacturer and importer level • Limiting price increases, price freezes • Price cuts • Margin cuts • Fixed mark-ups • Capped mark-ups • Regressive mark-ups • Fixed dispensing fees • Prohibiting discounts
Purchasing policies	• Positive list • Negative list • Price volume agreement • Health outcome agreement • Tender • Pooled procurement
Others	• Co-payments • Brand premiums • Safety nets • Generic substitution

What has worked?

Generic competition



OXFAM Briefing Paper 26 2002.

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Reference pricing

Implications for US Prescription Drug Spending

■ Table 3. Impact of Reference Pricing on Expenditures and Resource Consumption

Policy	Author (Year)	Drugs Class	Time Frame[a]	Percent Change	Absolute Change
Monthly Patient Expenditure					
Canada 1997	Schneeweiss (2003)	Calcium channel blockers		–12%	–$6
Canada 2003	Mabasa (2006)	Proton pump inhibitors		–12%	–$8
Germany 2005	Stargardt (2010)	Statins		–18%	–€49
US 2005	Johnson (2011)	Proton pump inhibitors		–7%	–$2
Changes in Annual Payer Expenditure					
Canada 1995	Grootendorst (2002)	Nitrates		–52%	–$3.8 million[b]
Canada 1997	Grootendorst (2002)	ACE inhibitors			–$84,000
		Calcium channel blockers			–$4.09 million[b]
	Grootendorst (2004)	NSAIDs		–44%	–$4 million[b]
Norway 2003	Brekke (2007)	Multiple classes[c]		–14%	–$75 million NOK
Germany 2005	Stargardt (2010)	Statins			–€94.4 –108.7 million
US 2005	Johnson (2011)	Proton pump inhibitors	at 1 year		–$2.5 million
			at 2 years		–$2 million
			at 3 years		–$1.6 million

Lee et al. Am J Managed Care 2012;18(11):e429-e437

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Current approaches

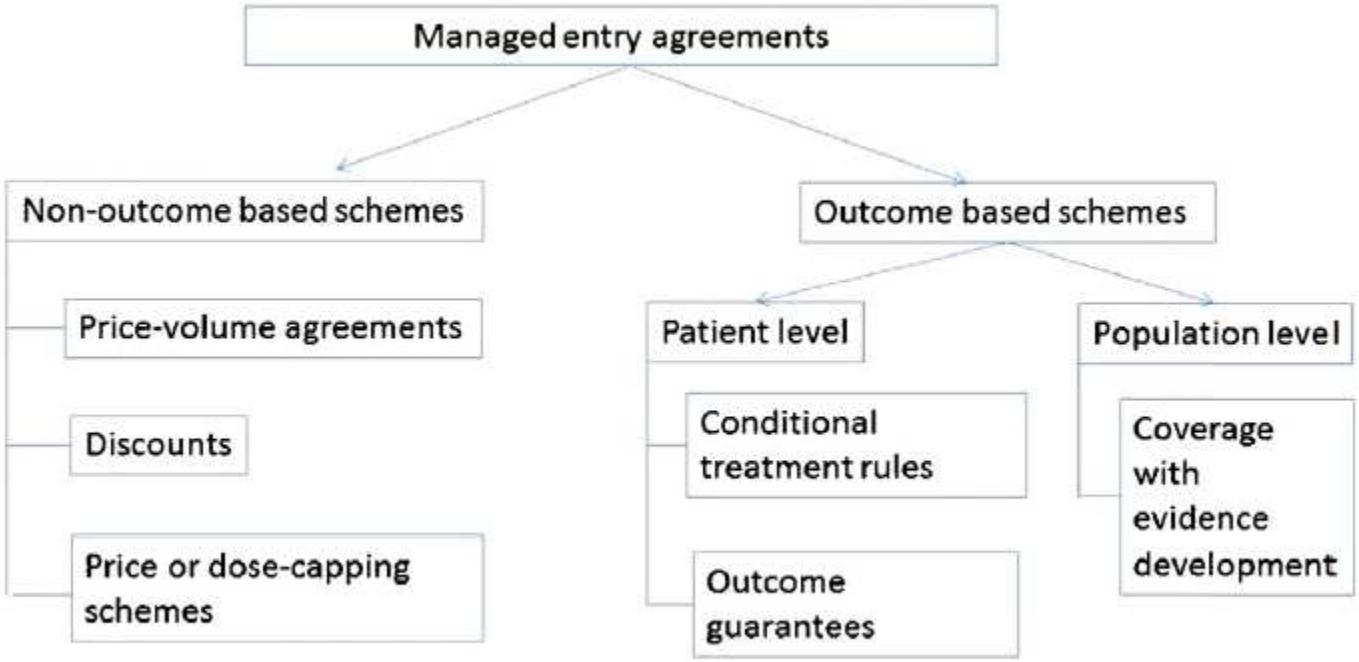

Fig. 1. Taxonomy of managed entry agreements.

Vitry & Roughead Health Policy 2014;117:345-352.

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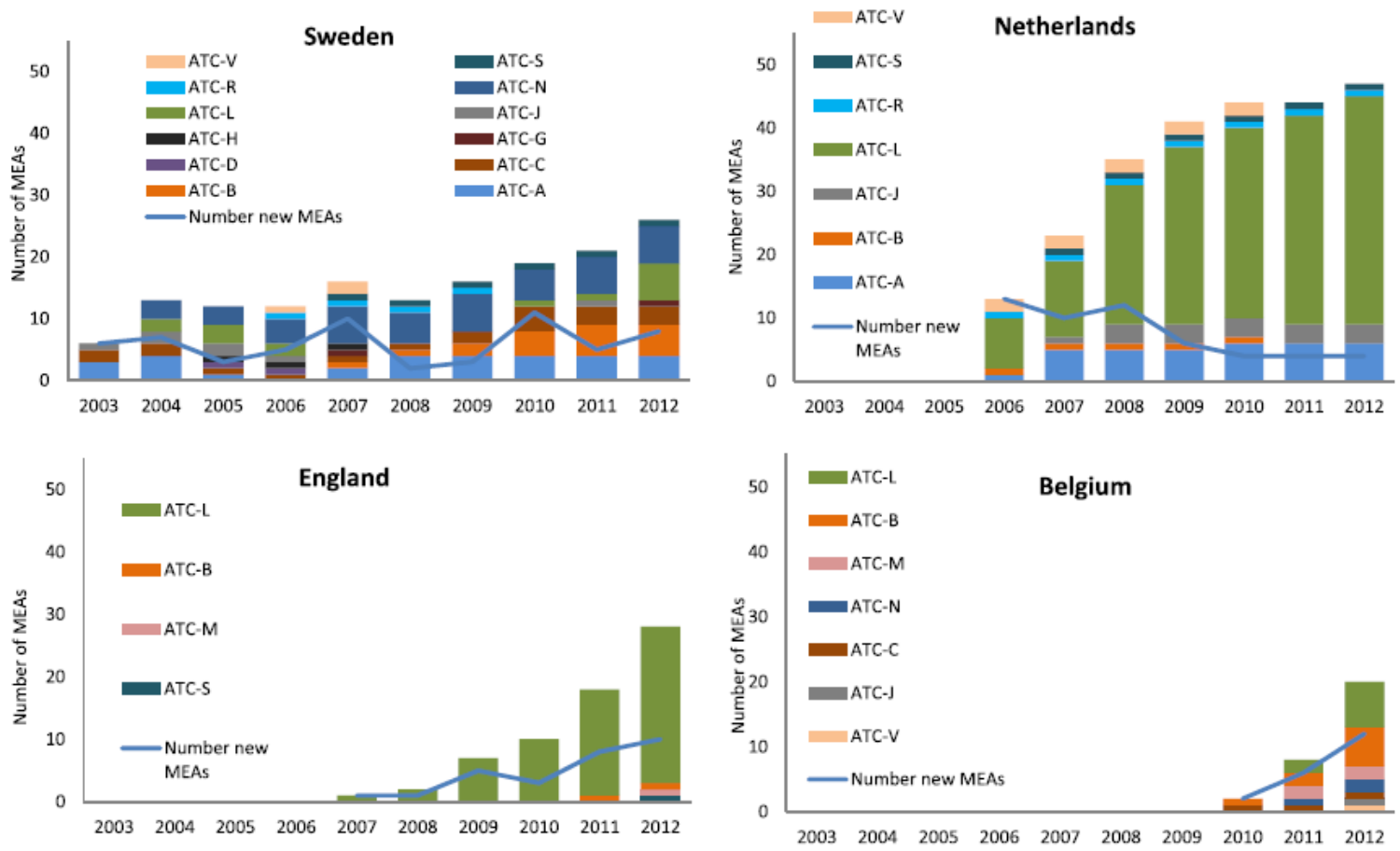

Fig. 1. Trends in MEA implementation since the introduction of the first MEA in the four study countries. Notes: ATC classification: A: Alimentary tract and metabolism; B: Blood and blood forming organs; C: Cardiovascular system; D: Dermatologicals; G: Genito urinary system and sex hormones; H: Systemic hormonal preparations, excl. sex hormones and insulins; J: Anti-infectives for systemic use; L: Antineoplastic and immuno-modulating agents; M: Musculo-skeletal system; N: Nervous system; R: Respiratory system; S: Sensory organs; V: Various. Source: WHOCC ATC-index 2012.

Ferrario & Kanavos. Soc Sci Med 2015; 124:39-47.

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Product development - updated

	NCE (n=336)	Other new product (n=420)*	Vaccine or biological (n=94)†	Total (n=850)
Neglected diseases				
Malaria	3 (1%)	9 (2%)	0	12 (1%)
Tuberculosis	0	7 (2%)	0	7 (1%)
Diarrhoeal diseases	1 (<0·5%)	3 (1%)	3 (3%)	7 (1%)‡
Neglected tropical diseases	0	5 (1%)	0	5 (1%)§
Other	0	1 (<0·5%)	5 (5%)	6 (1%)¶
Subtotal	4 (1%)	25 (6%)	8 (9%)	37 (4%)
Other infectious diseases	35 (10%)	48 (11%)	66 (70%)	149 (18%)
All other diseases	297 (88%)	347 (83%)	20 (21%)	664 (78%)

Data are n (%). NCE=new chemical entity. *New indication, new formulation, or fixed-dose combination. †Includes immunoglobulins and other biological products. ‡For diarrhoea, cholera, cryptosporidiosis, and giardiasis. §For human African trypanosomiasis, Chagas disease, and leishmaniasis. ¶For Japanese encephalitis, haemorrhagic fevers, and snakebite.

Table 1: **New therapeutic products approved or recommended, by disease category (2000–11)**

Pedrique et al. Lancet Global Health 2013

What alternatives are there?

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Essential medicines and health products

Medicine Pricing and Financing

Promoting affordable and fair pricing and effective financing

Equitable access to essential, high-quality and affordable essential medicines and other medical technologies depends on affordable and fair pricing and effective financing schemes. Promoting affordable and fair prices and cost-effective interventions is central to the achievement of universal health coverage.

An 'affordable and fair' price is one that can reasonably be funded by patients and health budgets and simultaneously sustains research and development, production and distribution within a country.

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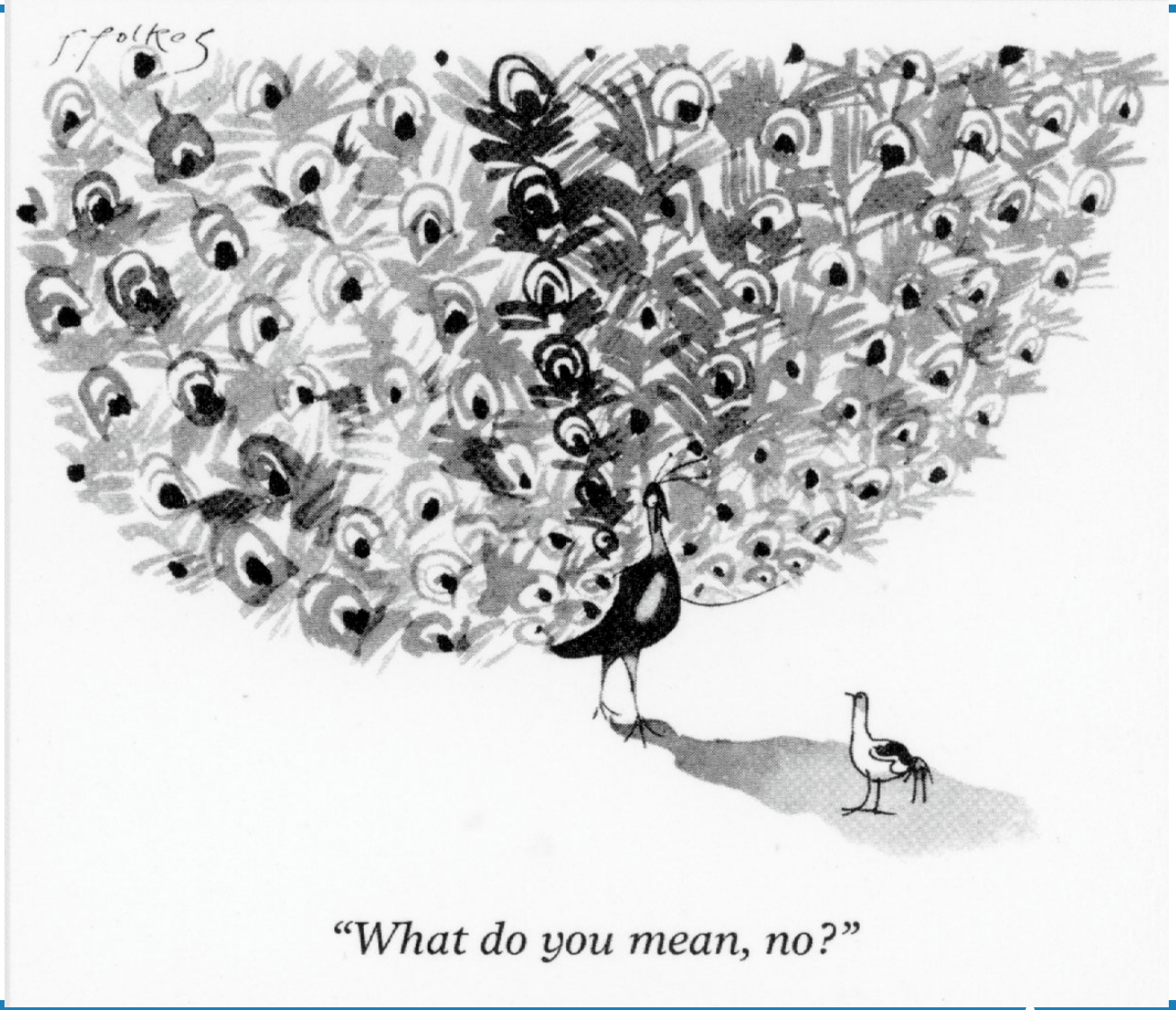
Is it time for a change?



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