Erasmus MC
University Medical Center Rotterdam

PPRI
Pharmaceutical Pricing and Reimbursement Information

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Biosimilars: same quality, lower price, improved patient access

Arnold G. Vulto FCP PharmD PhD

Professor of Hospital Pharmacy & Practical Therapeutics

Erasmus University Medical Center Rotterdam

The Netherlands

a.vulto@erasmusmc.nl

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Agenda

Erasmus MC

- Introduction and Perspective
- Learnings from generic medicines
- Is the same true for biosimilars?
  - Variability by region and molecule
- Why Norway is succesful
- A safe future? Potential threats
- Take home message

Conflict of Interest

Generics and Biosimilars Initiative
Building trust in cost-effective treatments
www.gabionline.net

- I declare no personal financial interest in any pharmaceutical bussiness
- I entertain friendly relationships with all innovative and generic / biosimilar companies
- As a co-founder I have a societal – but not financial - interest in the advocacy of cost-effective treatments via the Generics & Biosimilar Initiative (GaBI)
- My employer – Erasmus University Hospital - receives any honoraria (advisory boards, speakers honoraria) if they let me speak at scientific or commercial meetings.

Generic medicines succesfully drive the market

- The expectations of the biosimilars-market are driven by the success of the generics market

Marketeffects of the introduction of generic medicines

- 3 categories
  - 1. No of users increase, total cost decrease
  - 2. No of users stabilises, total cost decrease
  - 3. No of users decrease, total cost decrease faster

Ref: Dylst, Vulto & Simoens (2015) Exp Rev Pharmacoecon Outcomes Res

Based on GIP Prescription Database, The Netherlands

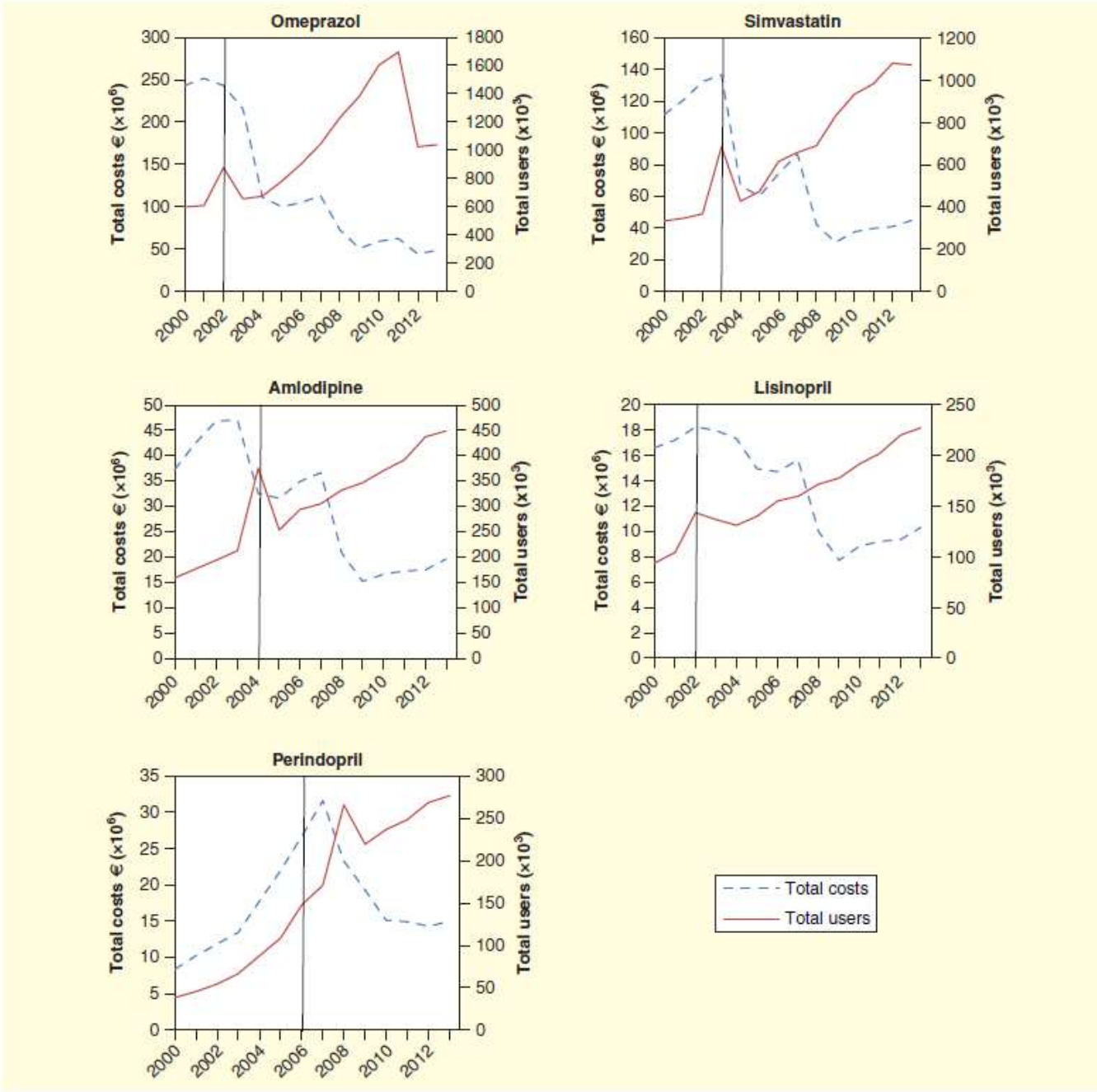

Figure 1. Evolution of total costs and total number of users for five active substances of which the total number of users increased after generic entry whereas the total costs decreased. The vertical line indicates the time of generic entry.

Category 1:

Number of users increase, total cost decrease

(mind X-axis: Millions of Euros)

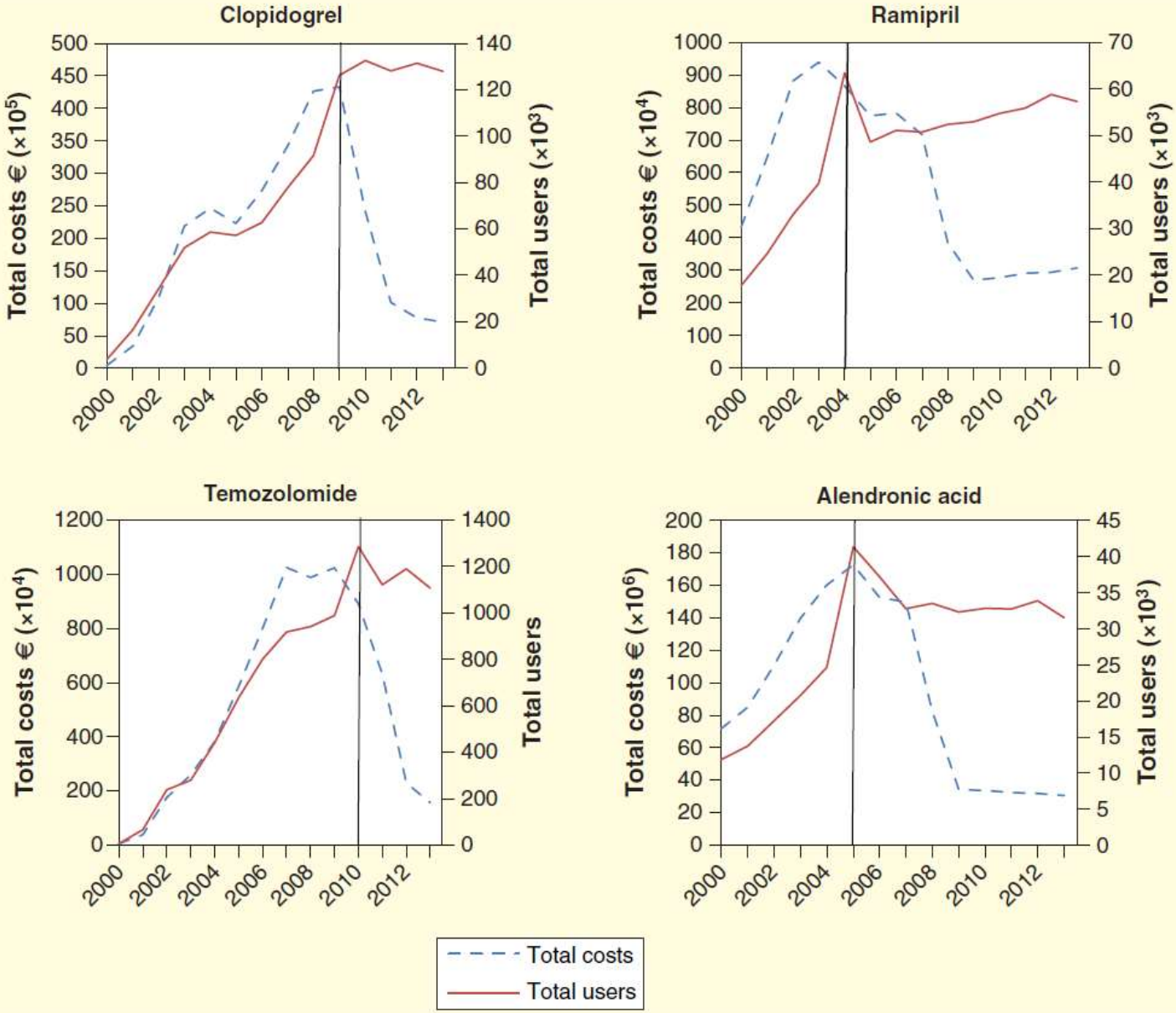

Figure 2. Evolution of total costs and total number of users for five active substances of which the total number of users remained constant after generic entry, whereas the total costs decreased. The vertical line indicates the time of generic entry.

- Category 2:
- Number of users stabilises, total cost decreases (dramatically)

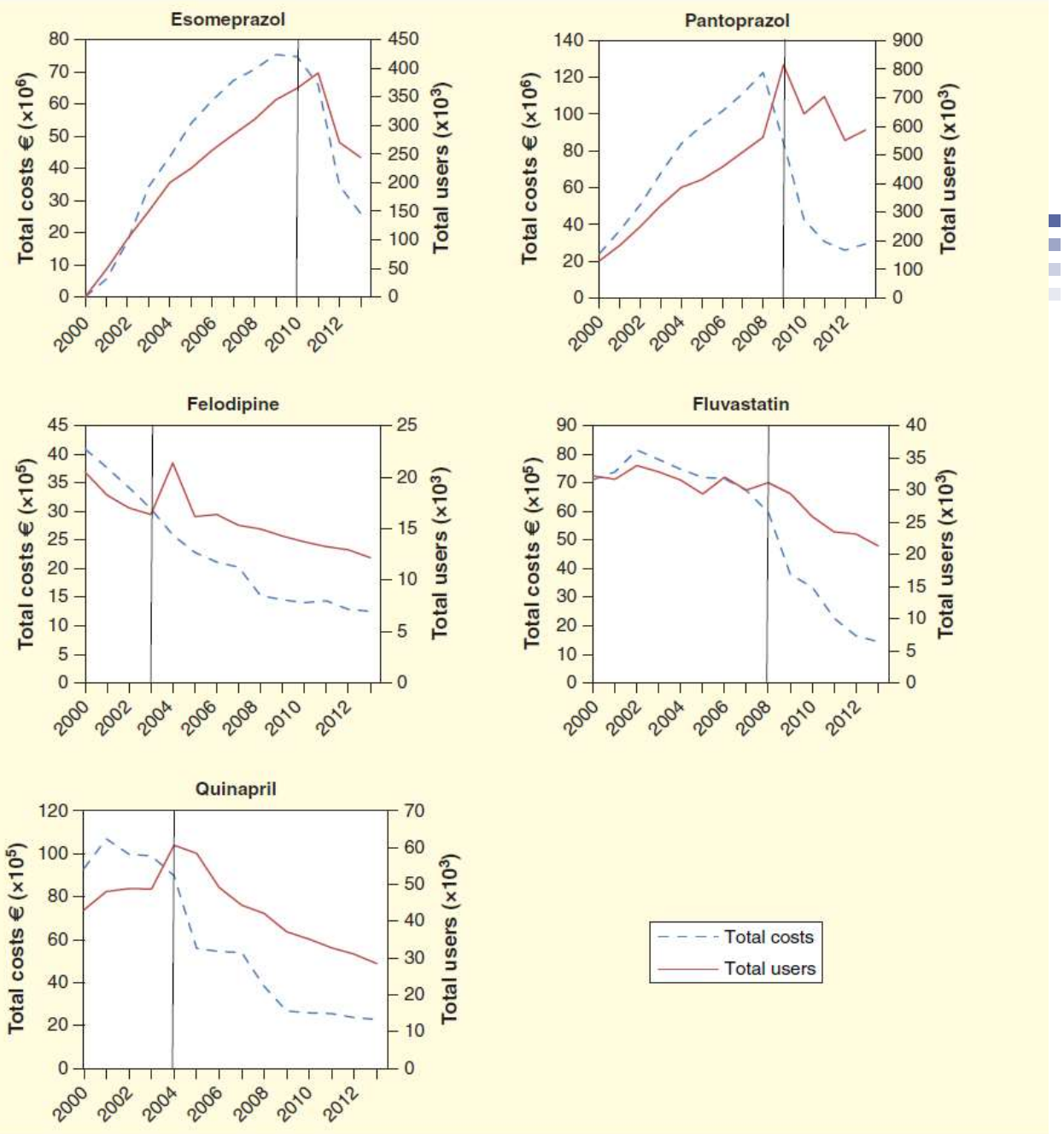

Figure 3. Evolution of total costs and total number of users for five active substances of which the total number of users decreased after generic entry, whereas the total costs decreased. The vertical line indicates the time of generic entry.

- Category 3:
- Number of users is decreasing (shift in therapy), but cost is decreasing stronger

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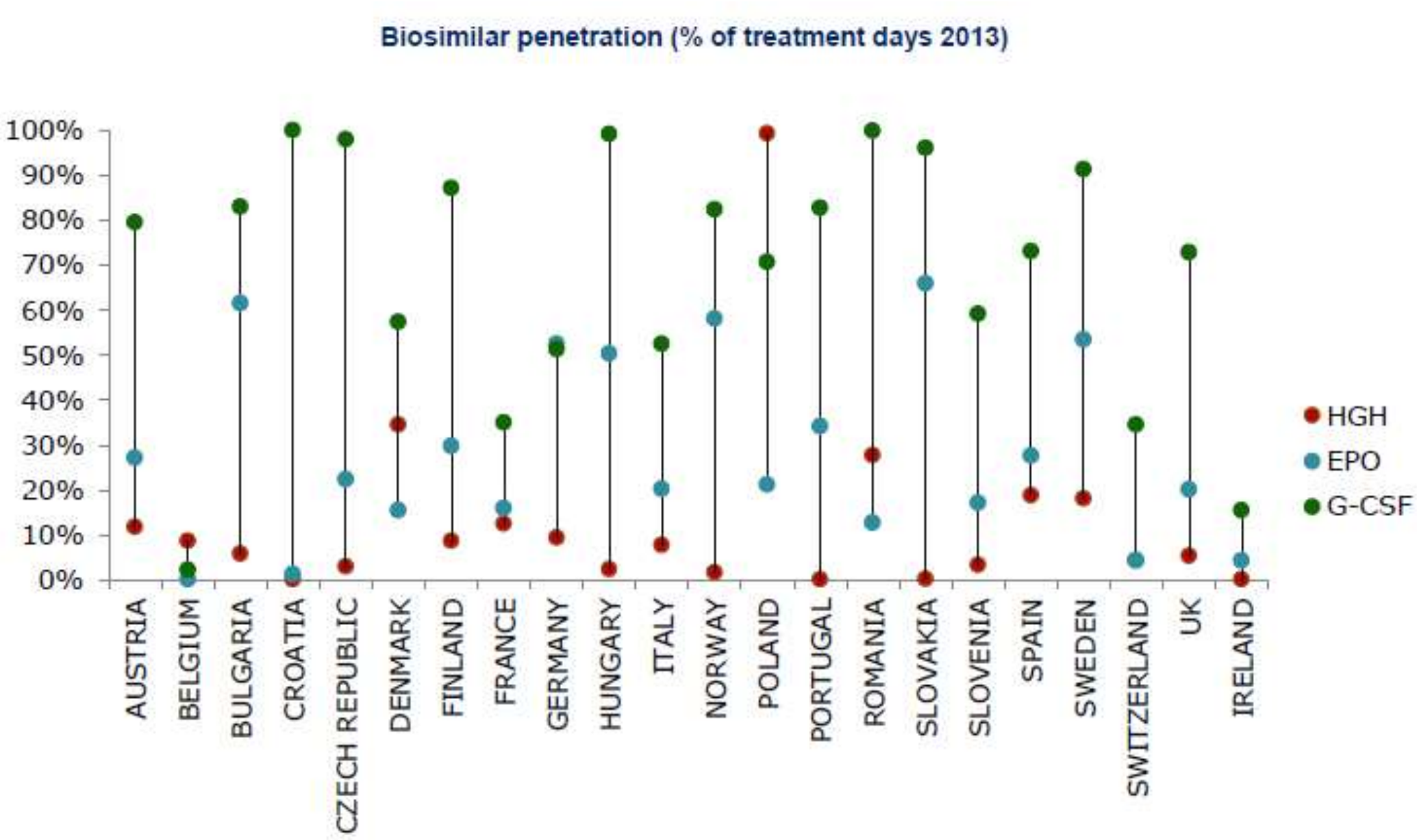
Three generations of therapeutic proteins

- **Generation 1**: substitution products
  - Hormones like growth factors or insulin
  - Effect visible / measurable in hours or days
- **Generation 2**: proteins with a specific pharmacological effect
  - Like TNF-alfa inhibitors
  - Effect only visible after some time, but not in all patients
- **Generation 3**: proteins with a less concrete clinical effect
  - “Targeted therapies” in oncology
  - The effect is a statistical chance some time in the future (survival)

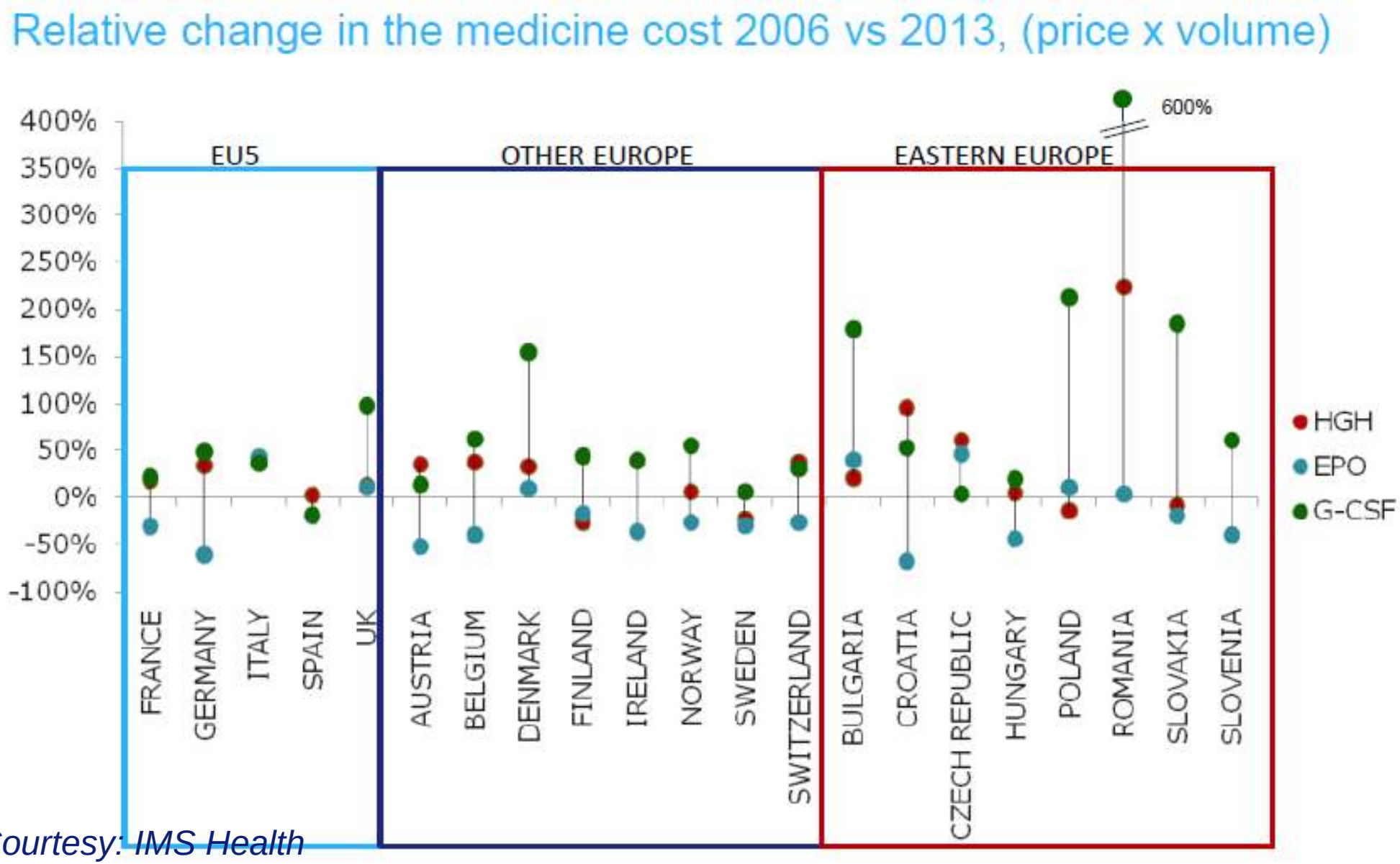
Uptake of first generation biosimilars

- It varies by therapeutic area and by region



Courtesy: IMS Health

But total cost may have increased

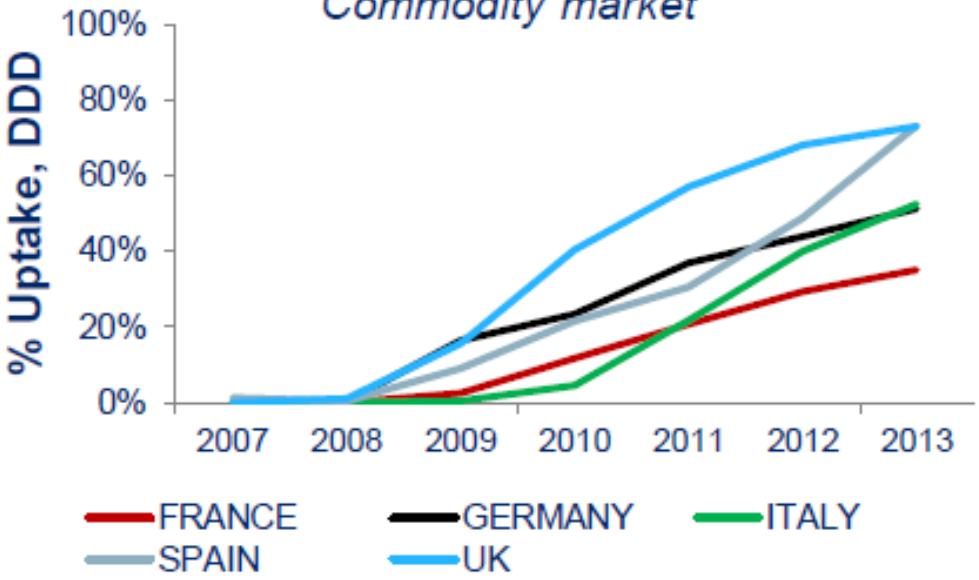


Courtesy: IMS Health

Reasons for variation (source: IMS Health)

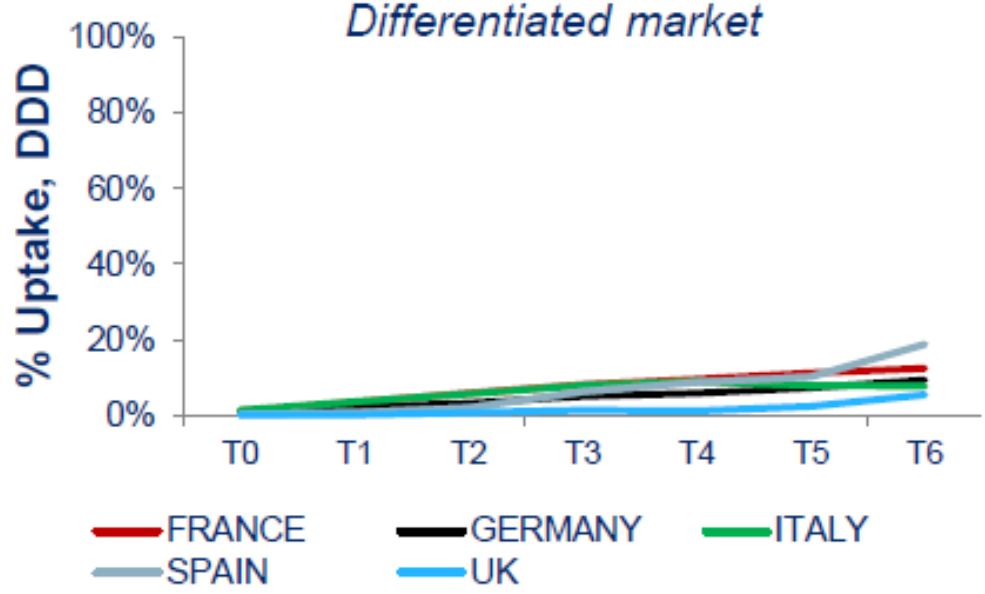
Stakeholder landscape and treatment cycle are the key determinants

Filgrastim uptake 2007-2013, yearly
Commodity market



- ✓ Payer-driven market access (e.g. Tender, step-wise algorithms)
- ✓ Price-driven competition
- ✓ Acute treatment and/or frequent cycling among therapies

Somatropin uptake 2007-2013, yearly
Differentiated market



- ✓ Complex stakeholder landscape with higher physician influence
- ✓ Competition based on multiple marketing levers
- ✓ Chronic treatment and/or long therapeutic cycles

IMS INSTITUTE FOR HEALTHCARE INFORMATICS

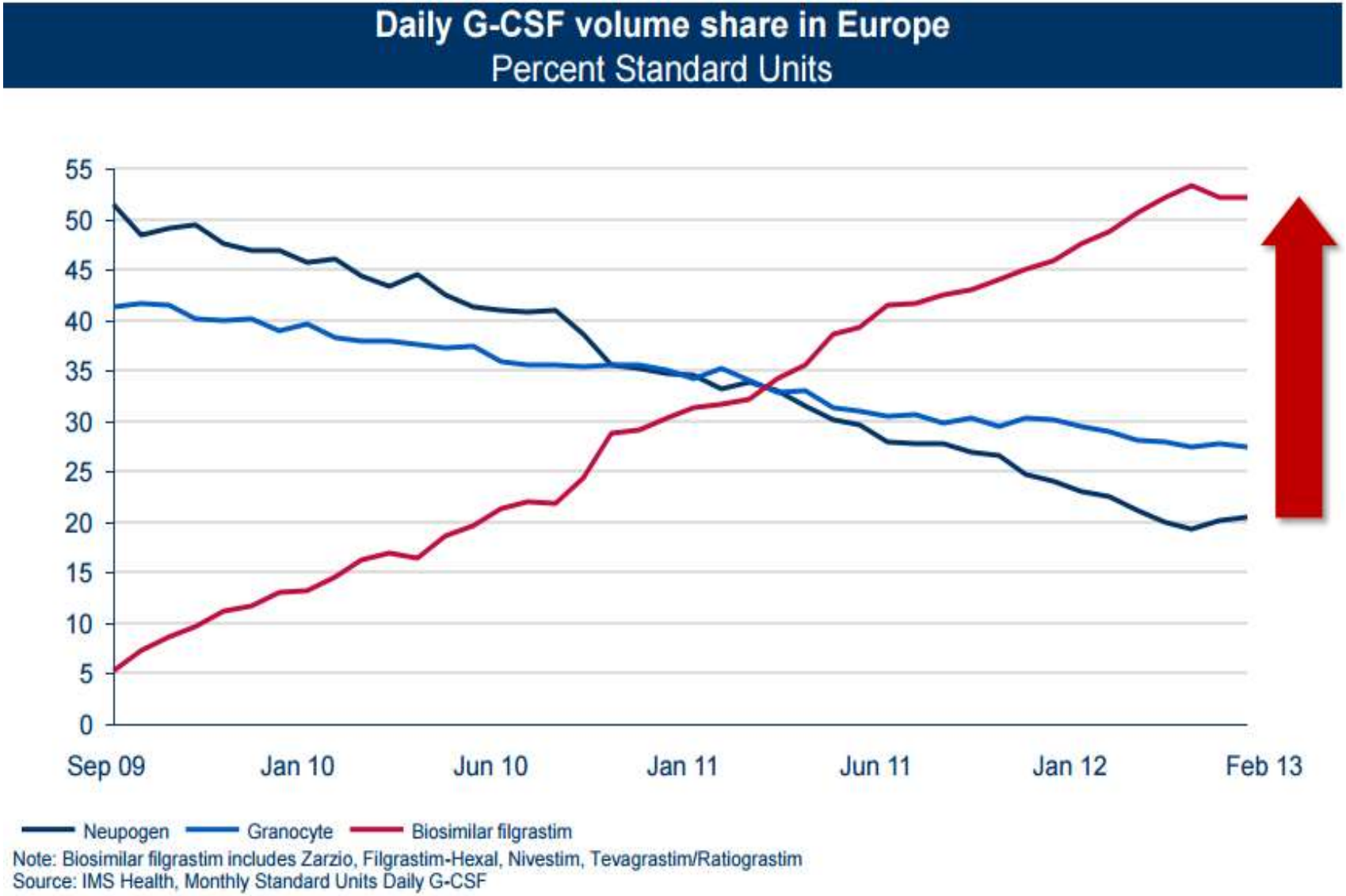
October 2014

Assessing biosimilar uptake and competition in European markets

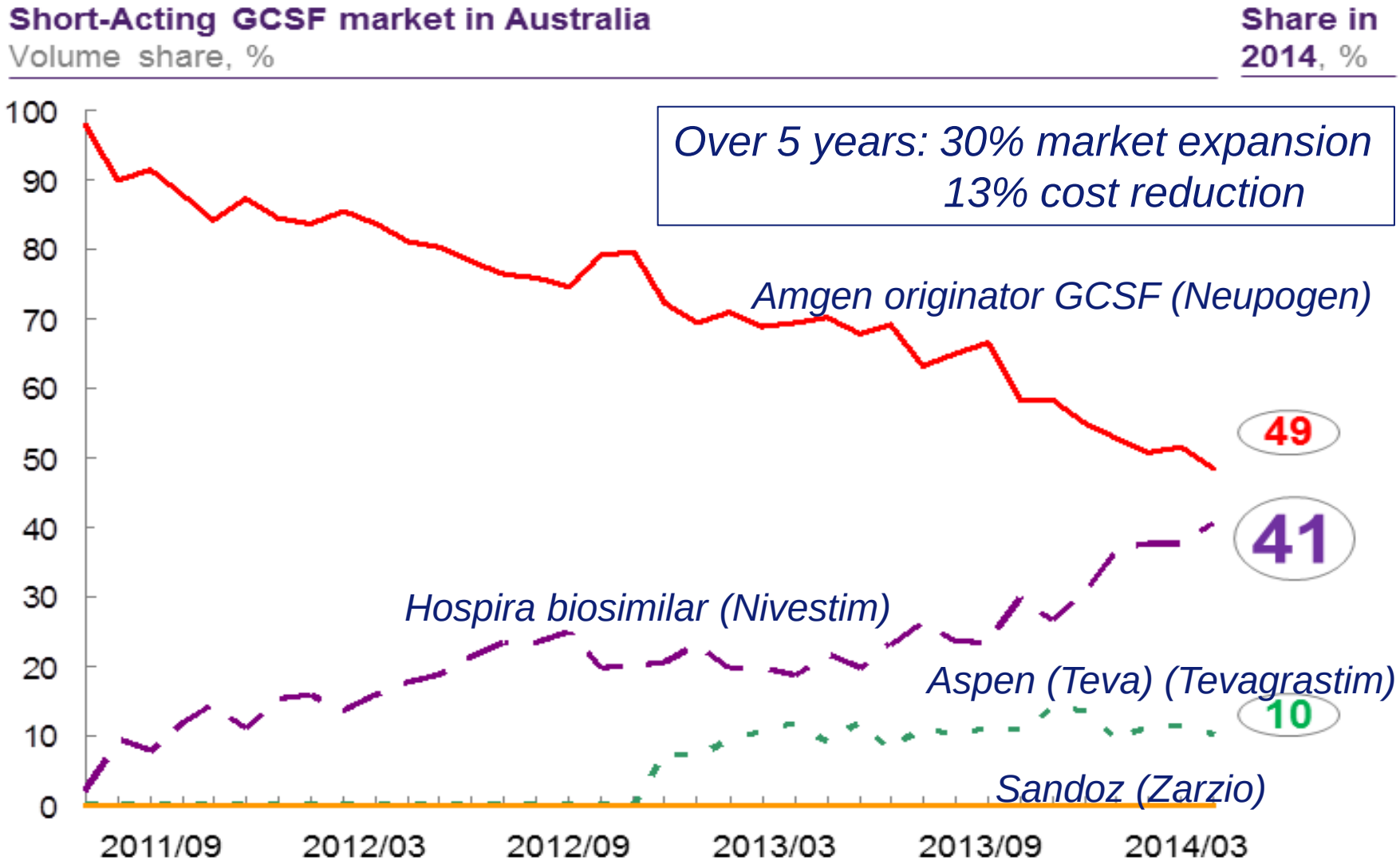
- Differences in the use of biosimilars are not just explained by epidemiology and disease factors, but reflect local adoption of treatment practices and guidelines influenced by funding decisions and payer actions.

- This highlights the need for physician education and introduction of national policies to increase the use of biosimilars.

Granulocyte Colony Stimulating Factor (GCSF - filgrastim) in EU (source: IMS 2014)



Granulocyte Colony Stimulating Factor (GCSF - filgrastim) in Australia (source: IMS 2014)



First generation biosimilars: increased access in EU?
(unit: treatment days; comparison 2006 and 2014)

- Different molecules show different patterns

- GCSF: + 100% (market share biosimilars: 20%)

- Growth hormone: +44% (market share biosimilar: 9%)

- Erythropoetin: + 16% (market share biosimilars: 15%)

(more data to be released by EU-commission end 2015)

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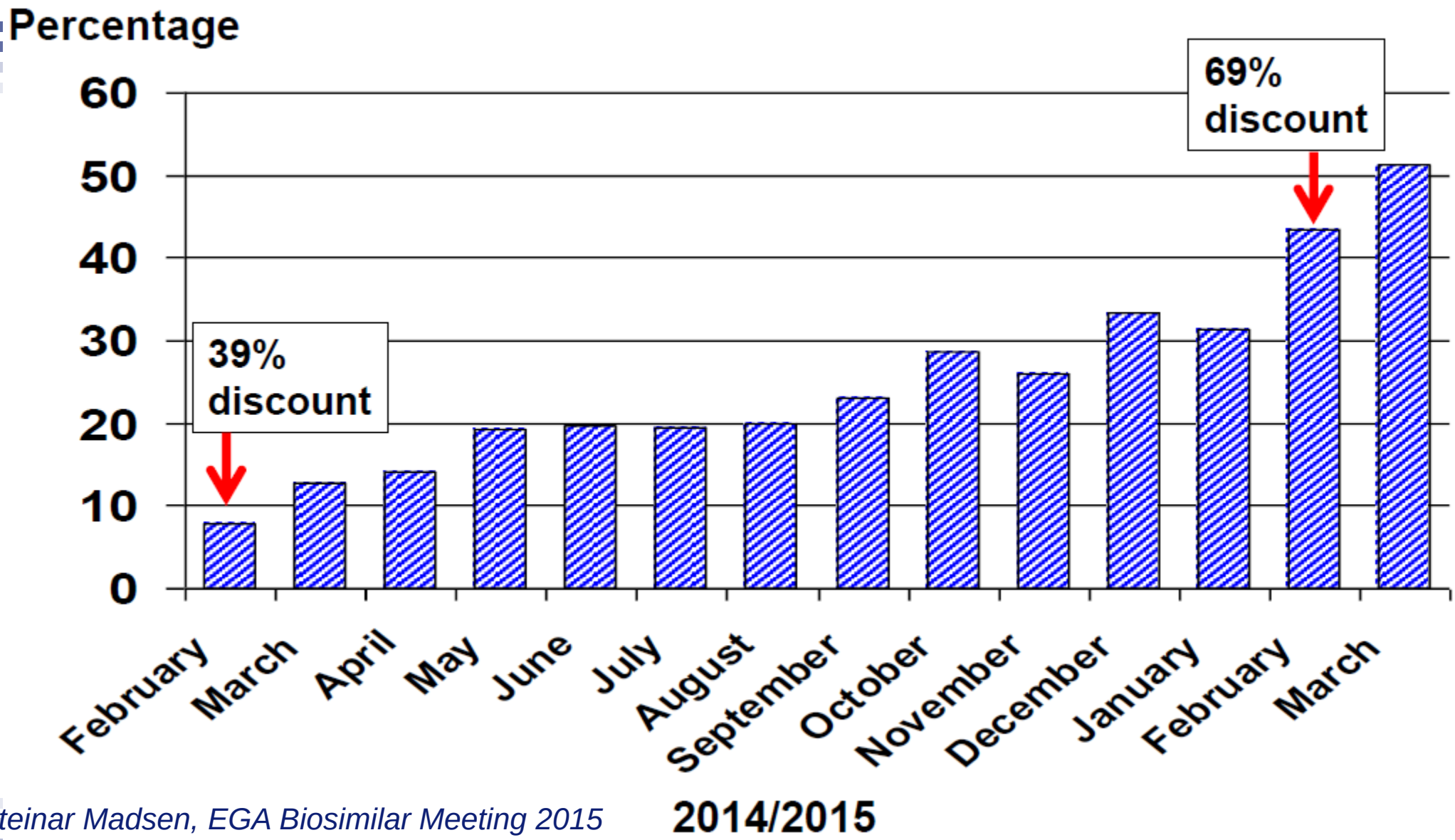
Infliximab biosimilar in Norway

Patient	Tender year	Remicade	Remsima	Savings	Savings (%)
Rheumatoid arthritis, 70 kg, one year treatment	2014	84 000 NOK 10 500 EUR 14 000 USD	51 000 NOK 6 400 EUR 8 500 USD	33 000 NOK 4 100 EUR 5 500 USD	39%
	2015	83 400 NOK 9 700 EUR 11 000 USD	26 000 NOK 3 000 EUR 3 400 USD	57 400 NOK 6 700 EUR 7 600 USD	69%

Steinar Madsen, EGA Biosimilar Meeting 2015

Market share biosimilar infliximab in Norway
(based on vials sold)



What were the succes factors in Norway

- An advisory board with most of the (clinical) opinion leaders were involved in deciding on the pre-tender conditions
- To start with, only new patients will receive the biosimilar
- After each year: new tender, again for NEW patients (existing patients will not be changed); further cost reduction
- Savings will be invested in:
  - Treating more patients for less money
  - Trials in support of unresolved areas like extrapolated indications and controlled switching
- This is a win-win for everybody (Torfinn Aanes, National Procurement Board)

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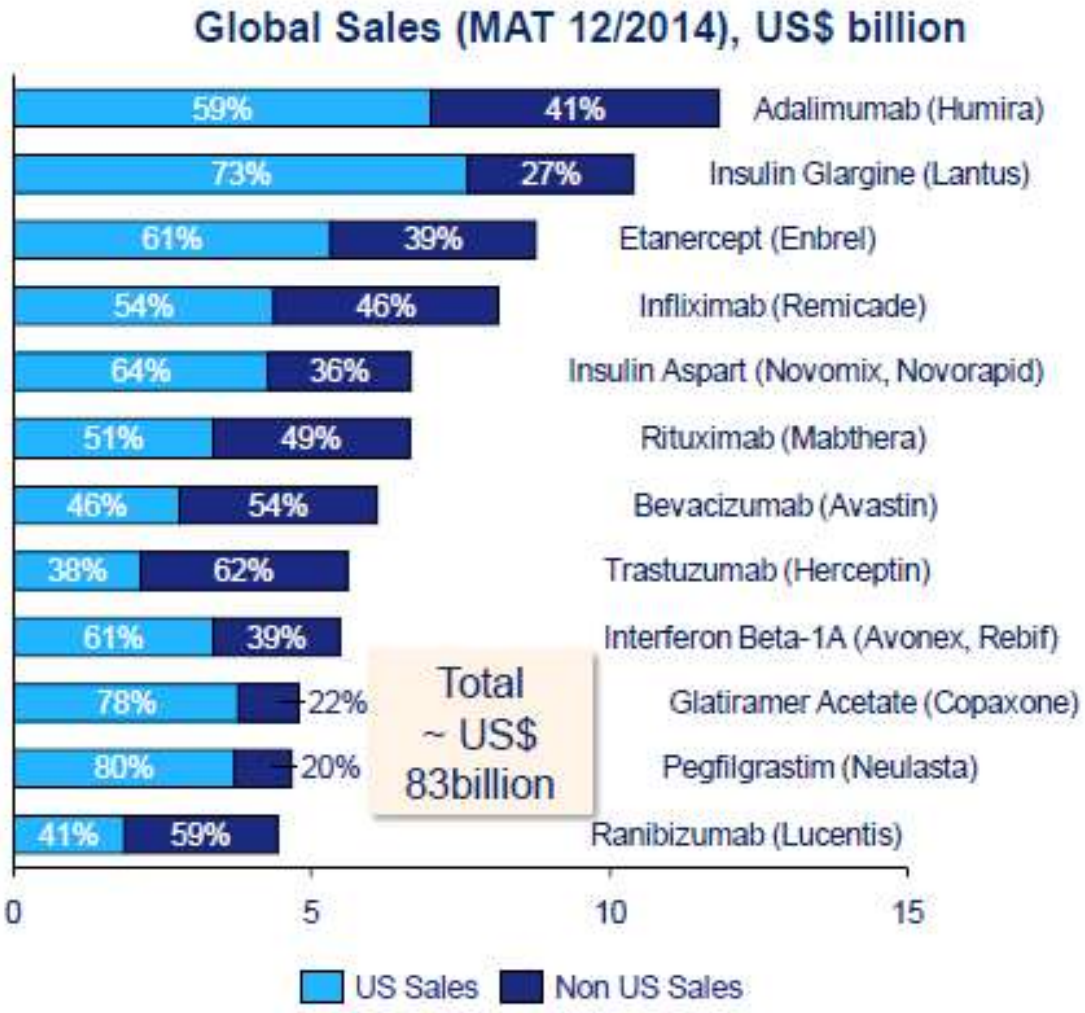
What is there to come?

- August 2015: 3 biosimilars submitted for registration (EMA)
  - Educated guess: etanercept, infliximab, ??

These products will loose market exclusivity by 2020



EU expiry date	US expiry date
2018	2016
2014	2015
2015	2028 (extended)
2015	2018
Expired	Expired
Expired	2018
2019	2019
2014	2019
2015	2016
2017	2014
2015	2015
2016	2016

Not considered existing biosimilars such as Epoetin Alfa expired in EU, but still patent protected in the US

Expectations in the UK

Biosimilars – earliest potential launch date for any indication					
2015	page	2016	page	2017	page
insulin glargine (LY2963016)	68	insulin glargine (MK-1293)	69	insulin glargine (Basalog)	69
follitropin alfa (XM 17)	70	somatropin	69	infliximab (BOW-015)	71
		etanercept (GP2015)	70	etanercept (CHS-0214)	71
		etanercept (SB4)	70	rituximab (MabionCD20)	72
		infliximab (SB2)	71	Infliximab (PF 06438179)	72
		rituximab (BI 695500)	74	trastuzumab (CT-P6)	73
				pegfilgrastim (LA-EP2006)	73
				pegfilgrastim (Neupeg/Pegasta)	73
				trastuzumab (ABP 980)	74
				trastuzumab (PF-05280014)	74
				rituximab (PF-05280586)	75

A safe future?

- More biosimilars to come
- More biosimilars will induce more market pressure
  - Potential risk: price erosion, threat for sustainability
- With insuline glargylin biosimilars enters the family physician market
  - Huge educational effort required
- More countries adapt EU biosimilar framework
  - Without capacity for the rigorous assessment
  - Risk of sub-standard products slipping through, potentially damaging biosimilar reputation

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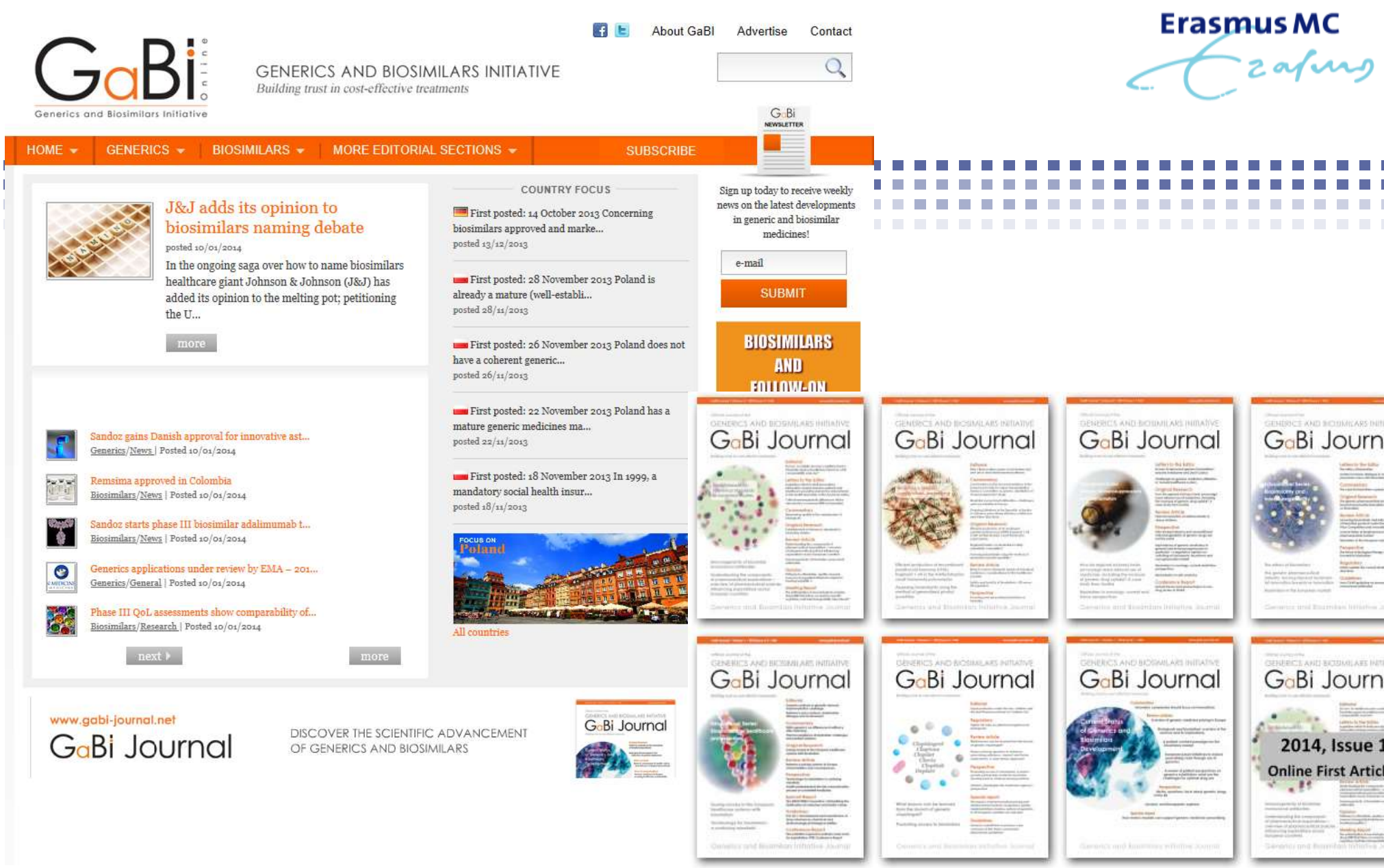
Take home message

- Uptake of biosimilars is much slower than of generic medicines
- Cost per treatment day will go down
- But total cost may grow due to increased access

- Payers can play a crucial role in driving the market
  - For biosimilar insulin massive education required

- Physicians very slow in adopting biosmilars
- Based on experience with 2nd generation & indication extrapolation
  - For 3rd generation huge educational effort required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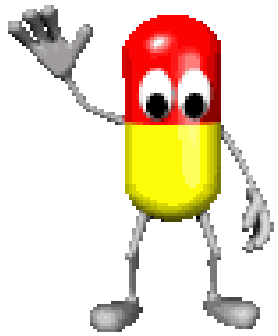

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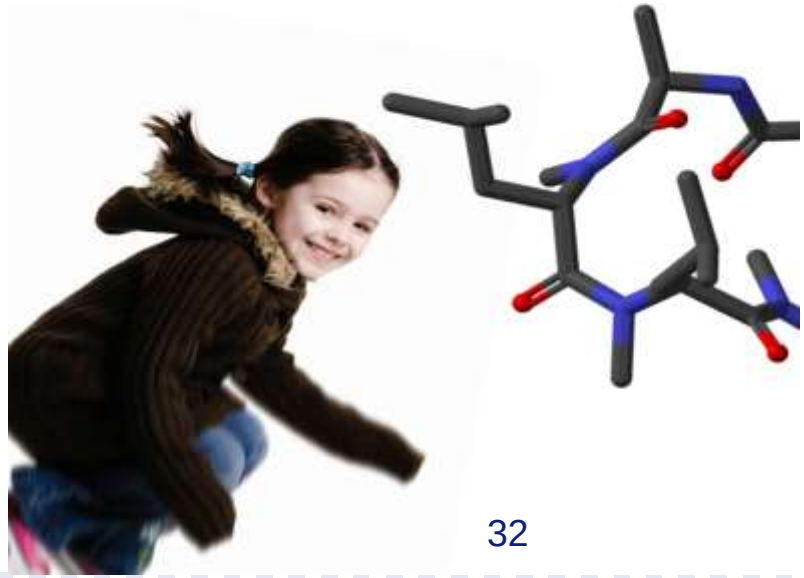

What are we talking about?

- *The only true definition of a biosimilar as of October 2015:*
  - A biosimilar is a pharmaceutical product, that as such has been licensed via the WHO regulatory pathway (=minimum global standard)
- *What does that mean?*
  - It is a copy of an already licensed biotech-drug, for which similarity has been proven in an extensive ***comparability exercise***, encompassing physical, chemical, biological and pharmacological properties, including efficacy and safety
- This excludes all kinds of *bio-questionables* in existence in other regions of the world that have not been endorsed via the WHO pathway as a biosimilar. *Reference to such products as if biosimilars may be inferior is thus WRONG*.

Most large companies are now on the biosimilar bandwagon

- Pfizer / Hospira: “big five” *
- Amgen: “big five” and more
- MSD
- Merck - Serono
- Sandoz: “big five”
- TEVA: “big five”
- Samsung / Biogen: “big five”
- Baxter
- Boehringer Ingelheim “big five”

“Big Five”: adalimumab, etanercept, infliximab, rituximab, trastuzumab