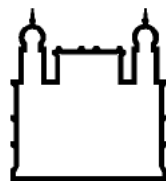


Introduction to influencing physician prescribing behaviour and cross national comparative studies

Prepared by Brian Godman



Ministério da Saúde

FIOCRUZ
Fundação Oswaldo Cruz

1. Introduction

2. Initiatives and measures

3. Statins

4. Renin-angiotensin inhibitors

5. Antibiotics

6. Summary

Growing pressures on pharmaceutical expenditure will continue with ongoing reforms

- Pharmaceutical expenditure grew by 50% in real terms during past decade - 60% of total expenditure in some countries
- This is set to continue unless addressed due to:
 - ❑ ageing populations and rising levels of NCDs
 - ❑ continued inappropriate prescribing
 - ❑ stricter clinical targets
 - ❑ continued launch of new premium priced products
- This is resulting in ongoing initiatives across countries to improve the rational use of medicines. These include:
 - ❑ Models to optimise the use of new medicines including new expensive oncology medicines
 - ❑ Initiatives to enhance the use of low cost generics
 - ❑ Initiatives to improve the utilisation of anti-infectives

Key learning points

- Demonstrate why it is important to analyse policy and other initiatives before planning new initiatives – especially with scarce personnel and resources
- How to collate multiple demand-side measures into meaningful categories for comparisons within/ across countries where this occurs
- Confirm the utility of using DDDs and DIDs (DDD/ one thousand inhabitants/ day) for undertaking cross national comparisons in ambulatory care
- Confirm that multiple demand-side measures typically needed to influence physician behaviour

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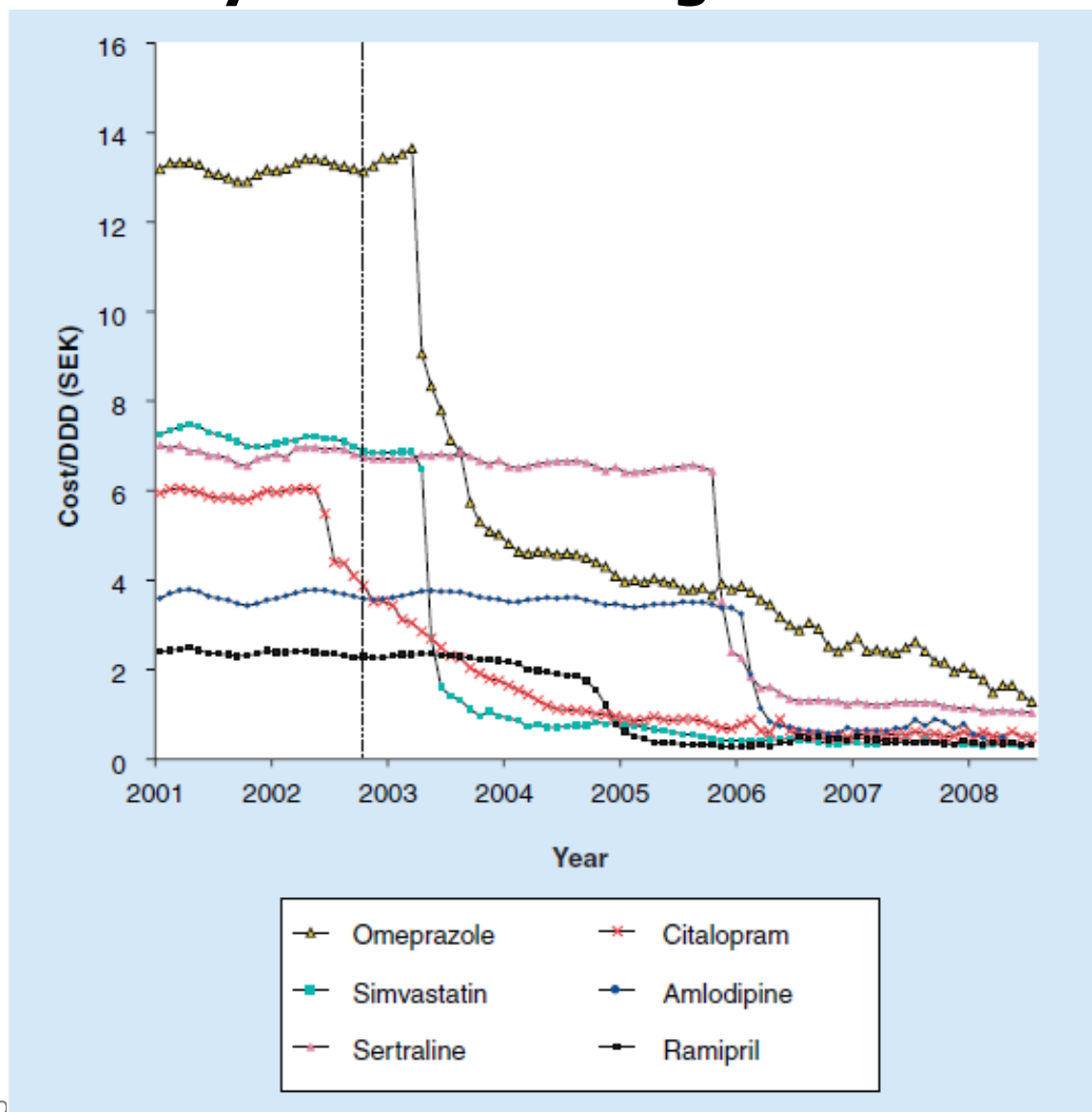
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Pharmaceutical policy and initiatives incorporate a number of areas

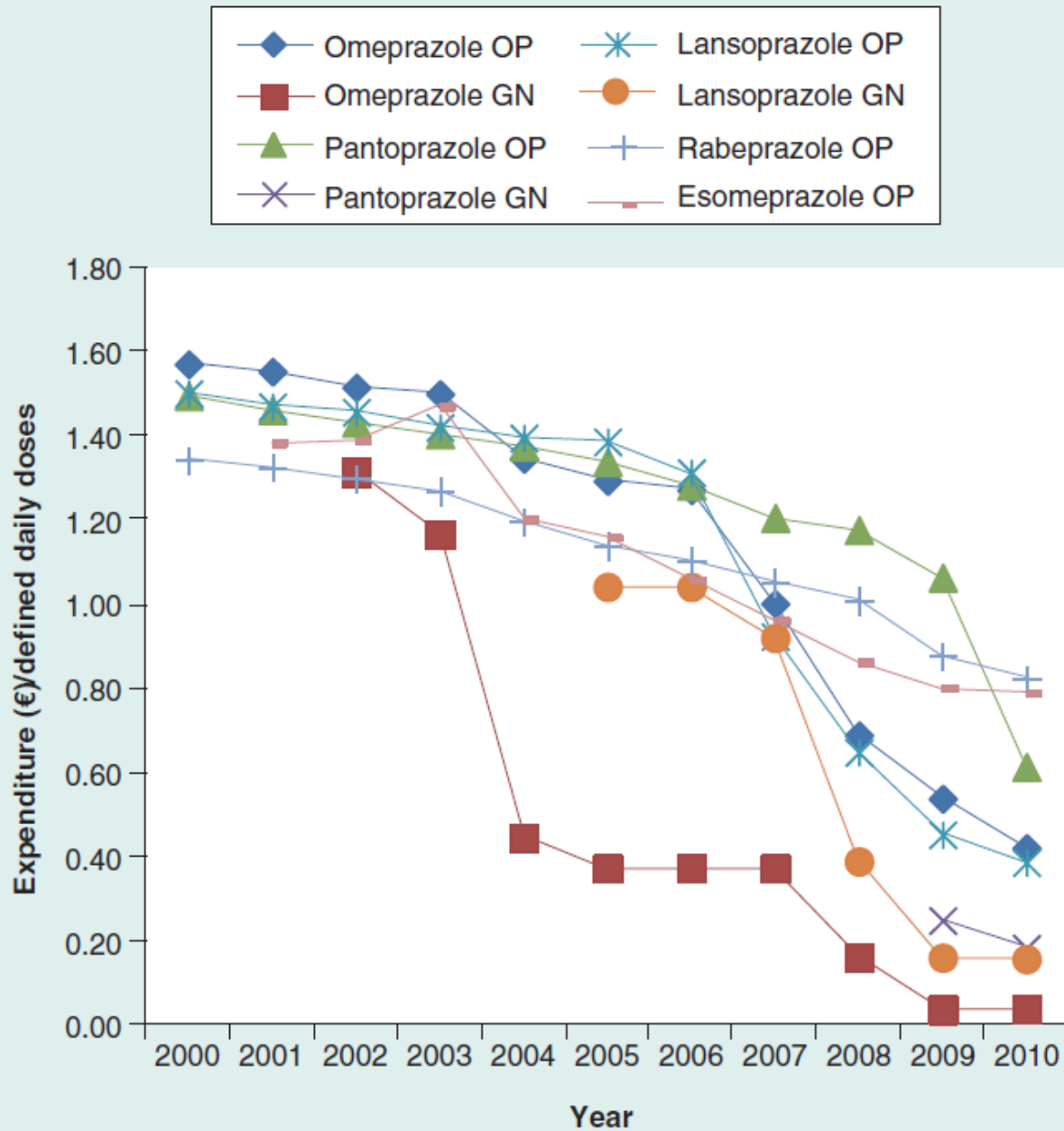
- Pharmaceutical policy is designed to improve the safe and effective use of medicines. This incorporates a number of areas including:
 - ❑ issues of unmet need and access to medicines
 - ❑ pricing of medicines and cost containment
 - ❑ improving the rational use of medicines (RUM)
 - ❑ issues of innovation and service provision
- Issues regarding pharmaceutical expenditure can be divided into:
 - ❑ **supply-side measures** - principally concerned with the pricing of medicines and associated regulations
 - ❑ **demand-side measures** - principally concerned with interventions/activities designed to influence the subsequent utilization of medicines

Compulsory generic substitution has lowered generic prices in Sweden - prices are falling further with the instigation of monthly auctions for generics

**Cost/DDD
for 6
products in
top 25
prescribed
ambulatory
care
products in
Sweden on a
DDD basis.
Generics 4%
to 13% of
pre-patent
loss prices in
2008**



Preference pricing policies in the Netherlands led to low prices for generic omeprazole (similarly for generic simvastatin)



Demand side measures

What demand-side measures/ initiatives can be introduced within countries to improve the rational use of medicines?

Demand-side measures can be collated under the 4 Es to compare their influence across countries

- Demand side initiatives can be collated under 4 'E's – well accepted by payers and endorsed in publications:
 - **Education** – e.g. Academic detailing, benchmarking, guidelines and formularies
 - **Economics** – e.g. financial incentives for physicians, pharmacists or patients
 - **Engineering** – e.g. prescribing targets - % of PPIs as generics, % of statins as generics, % of patients achieving agreed BP and lipid goals
 - **Enforcement** – e.g. prescribing restrictions, compulsory generic substitution

The definition of the 4Es and examples include:

Measure	Explanation and initiatives
Education	<ul style="list-style-type: none"> • Activities range from simple distribution of printed material to more intensive strategies including academic detailing and monitoring of prescribing habits • Examples include: <ul style="list-style-type: none"> ○ Education of trainee doctors in medical schools to prescribe by INN (International Non-Proprietary Name), e.g. UK ○ Information and other campaigns among patients to address any fears about the effectiveness and/ or safety of generics including speaking with patients to address any fears, e.g. France ○ Physicians and pharmacists developing a list of potentially non-substitutable products where there are concerns with bioequivalence as well as the therapeutic equivalence of generics, e.g. Sweden and UK
Engineering	<ul style="list-style-type: none"> • This refers to organisational or managerial interventions • Examples include substitution targets for certain drugs in community pharmacies if physicians are still prescribing the originator, e.g. France
Economics	<p>This includes financial incentives for physicians, patients and pharmacists, e.g.:</p> <ul style="list-style-type: none"> • Higher co-payments for patients if they wish to receive a more expensive product than the current referenced price molecule, e.g. Finland, Sweden • Devolution of drug budgets to physicians with sanctions for over budget situations (e.g. Germany, Sweden and UK)
Enforcement	<p>This includes regulations by law such as mandatory INN prescribing or mandatory generic substitution at pharmacies apart from a limited number of agrees situations, e.g. Lithuania and Sweden</p>

Ref: Wettermark, Godman et al 2009; Godman, Wettermark, Bishop et al 2012; Godman, Bennie et al 2012

Typically European countries have introduced a range of different demand side measures to enhance prescribing of generic vs. patented PPIs and statins. However, their intensity varies leading to differences in efficiency

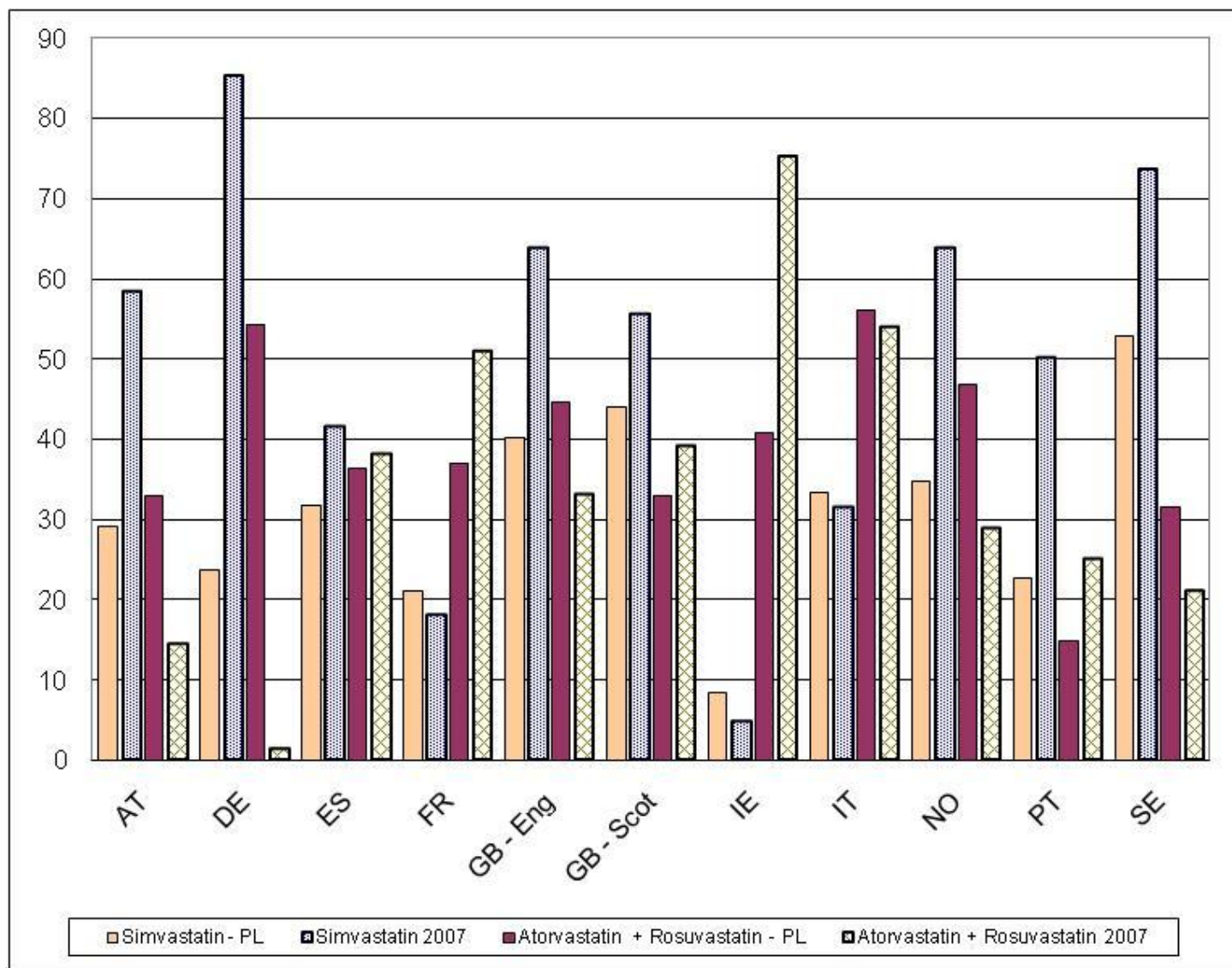
Country	Education	Engineering	Economics	Enforcement
AT	√		√	√
DE/ States	√	√	√	√
EE	√	√	√	√
ES/ regions	√	√	√	√
FR*	√	√	√	√
GB – En	√	√	√	
GB - Scot*	√	√	√	
IE	√			
IT/ Regions	√	√	√	√
LT	√	√	√	√
HR	√	√	√	√
NO	√			√
PO	√		√	√
PT	√	√	√	√
RS			√	Selected drugs
SE	√	√	√	√
SI	√		√	Selected drugs
TR	√			

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Health authorities should enhance the utilisation of low cost statins to save costs

- All statins typically considered similar at therapeutically equivalent doses - demonstrated by:
 - ❑ Germany introducing referencing pricing for the statins in 2004 based on generic simvastatin as the authorities believed no differences between the statins
 - ❑ Published meta-analyses demonstrating no differences
 - ❑ SIGN in Scotland advocating 40mg simvastatin for patients with diabetes/ secondary prevention
- Consequently, health authorities should enhance the use of low cost generic simvastatin to save costs with generic simvastatin priced as low as 2% of patented product prices
- Some health authorities were more active than others with instigating multiple measures to enhance the prescribing of generic simvastatin leading to appreciable differences

The intensity and nature of the reforms impacts on utilisation, e.g. statins in Ireland and France vs. UK (y axis is % utilisation vs. all statins DDD basis)

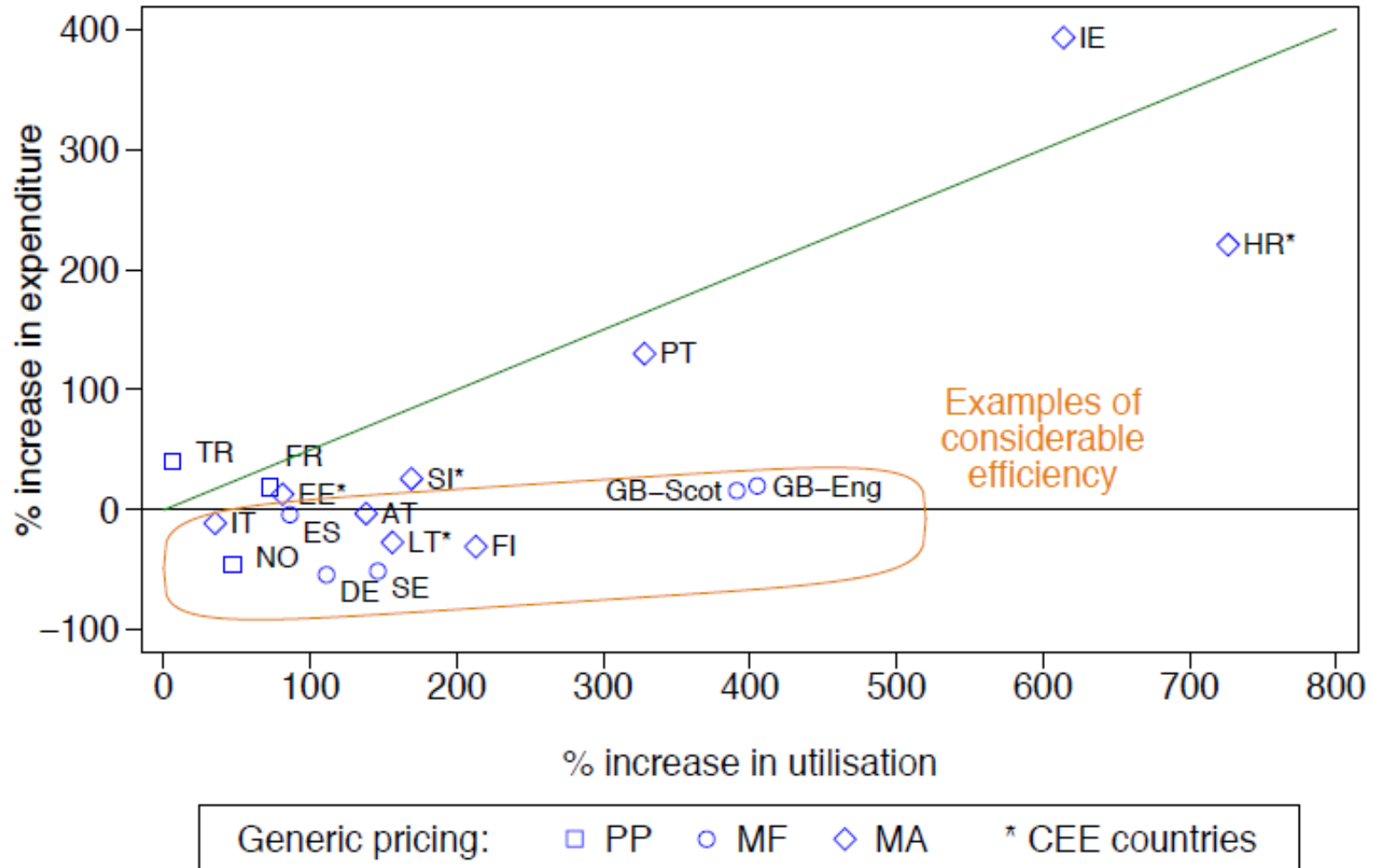


Appreciable differences in generic utilisation (PPIs and statins) leading to considerable differences in efficiency

Country	Class	Utilisation 2007 vs. 2001	Expenditure 2007 vs. 2001	€/1000 inhabitants/year in 2007
AT	PPI	↑ 3.6 fold	↑ 2.1 fold	€19299
	Statins	↑ 2.4 fold	↓ 3%	€9555
DE	PPIs	↑ 3.2 fold	↑ 1.4 fold	€13864
	Statins	↑ 2.1 fold	↓ 54%	€6833
FR*	PPI	↑ 2.1 fold	↑ 38%	€15194
	Statin	↑ 72%	↑ 19%	€14896
GB – Eng	PPI	↑ 2.3 fold	↓ 38%	€6186
	Statin	↑ 5.1 fold	↑ 20%	€13439
IE	PPI	↑ 2.4 fold	↑ 2.6 fold	Over €60,000
	Statin	↑ 7.1 fold	↑ 4.9 fold	Over €60,000
SE	PPI	↑ 42%	↓ 48%	€5832
	Statins	↑ 2.5 fold	↓ 51%	€5192

A retrospective drug utilisation study was undertaken documenting changes in utilisation patterns and costs before and after generic simvastatin as multiple measures introduced in most countries over time preventing time series analyses

Another way of showing this was to document changes in utilisation (DIDs) and expenditure 2001 to 2007 for the statins. Typically patented statins not reimbursed in Central and Eastern European (CEE) countries

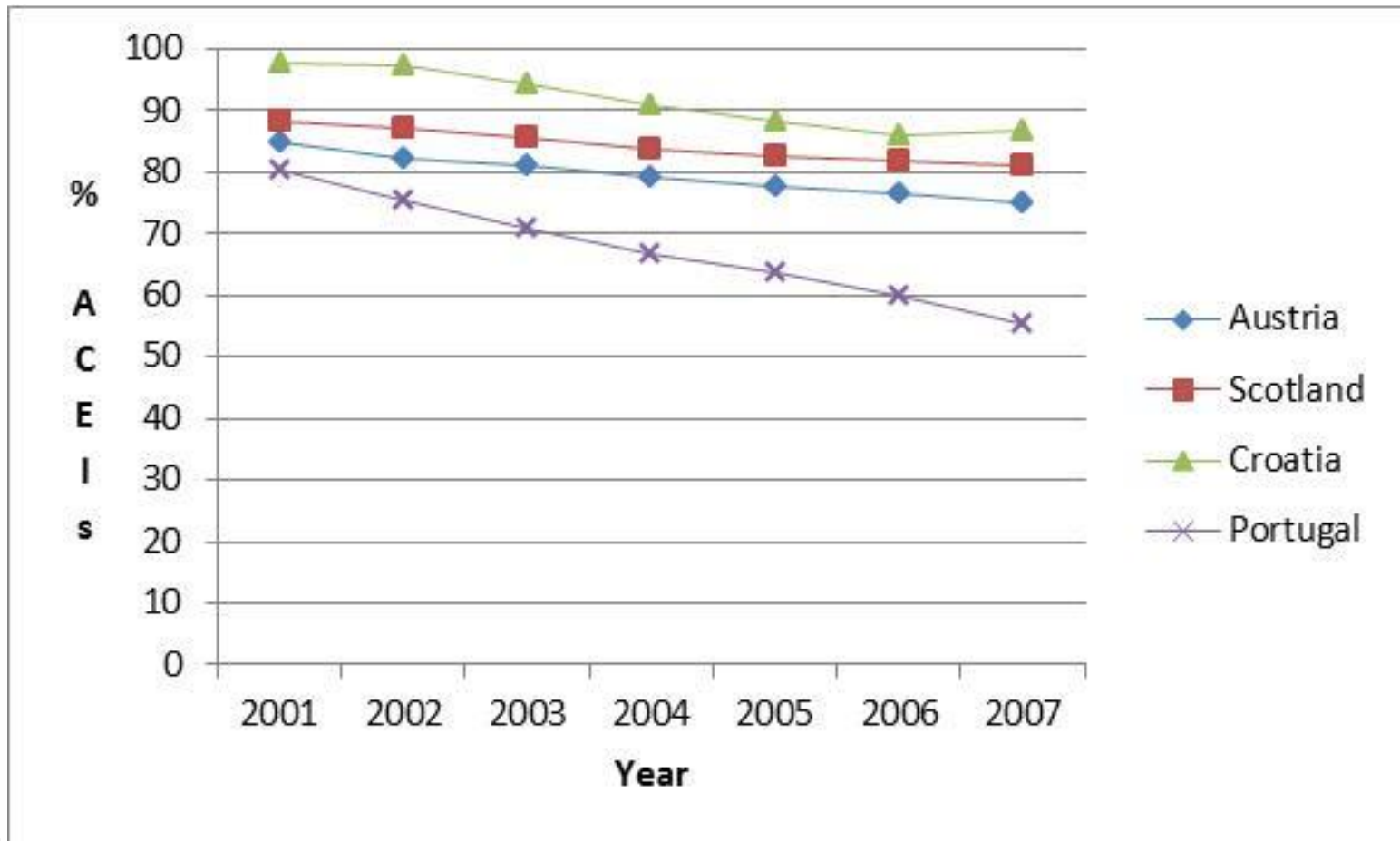


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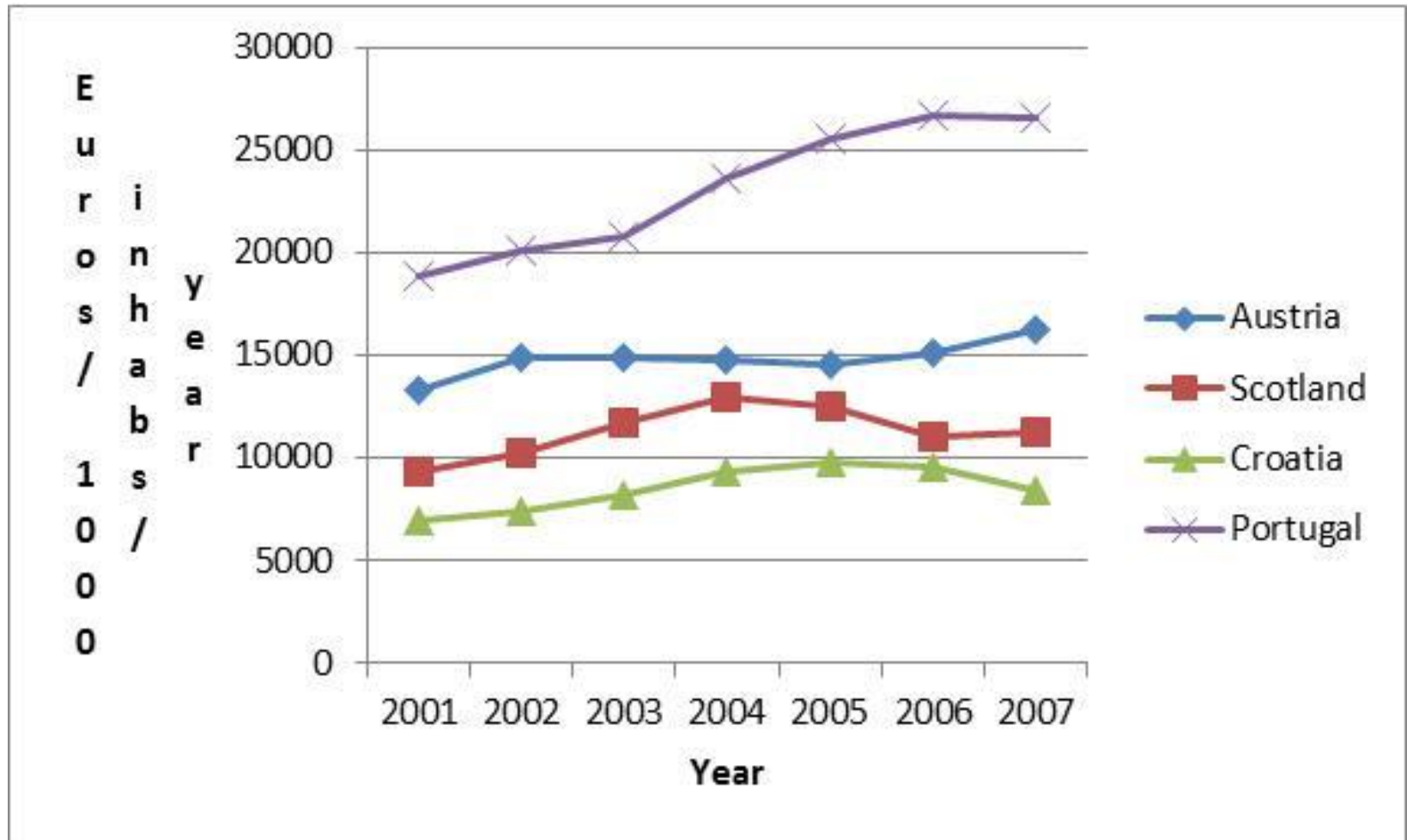
Health authorities should enhance the use of low cost renin-angiotensin inhibitors to save costs

- It is generally recognised that only a limited number of patients experience a cough with ACEIs (only a few patients discontinued treatment in the clinical trials due to coughing)
- Consequently, the goal of health authorities should be to limit the utilisation of patented ARBs versus generic ACEIs (as seen as equally effective)
- More recently, limit the utilisation of patented ARBs vs. generic losartan with all ARBs again seen as essentially similar at therapeutically equivalent doses
- Mixture of retrospective studies and time series analyses undertaken to examine the impact of health authority activity. Health authorities are learning from each other – allowing for time series analyses with generic losartan

Multiple demand-side measures limited ARB utilisation vs. generic ACEIs in Scotland versus Portugal, matching the influence of prescribing restrictions for ARBs in Austria and Croatia (ARBs second line – greater intensity of follow-up in Croatia vs. Austria) - y axis = % ACEIs vs. total renin-angiotensin inhibitors on a DDD basis



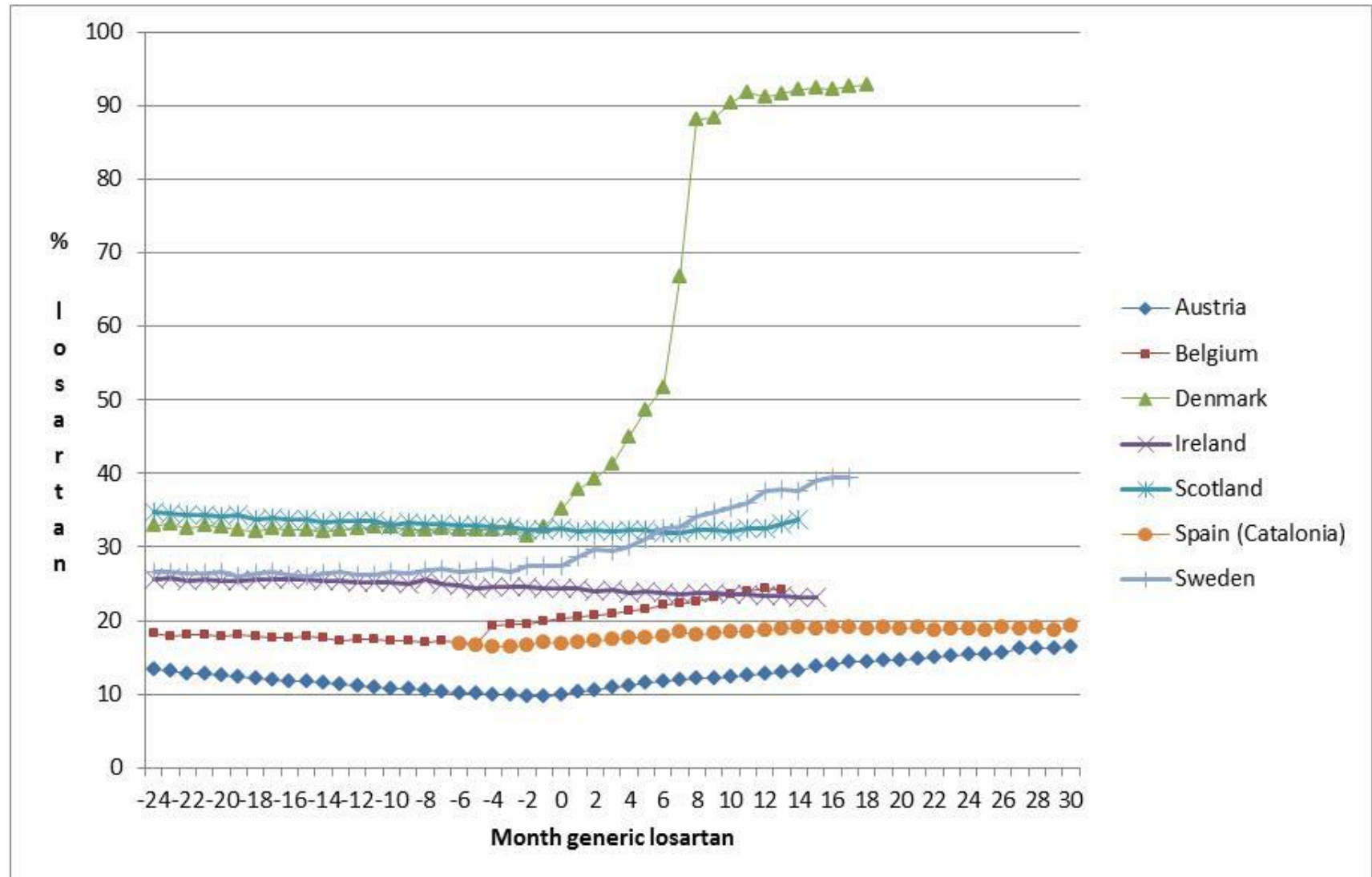
As a result, limited the increase in expenditure on renin-angiotensin inhibitors in Scotland in recent years when adjusted for populations versus Portugal despite increased utilisation (159% Scotland, 72% Portugal)



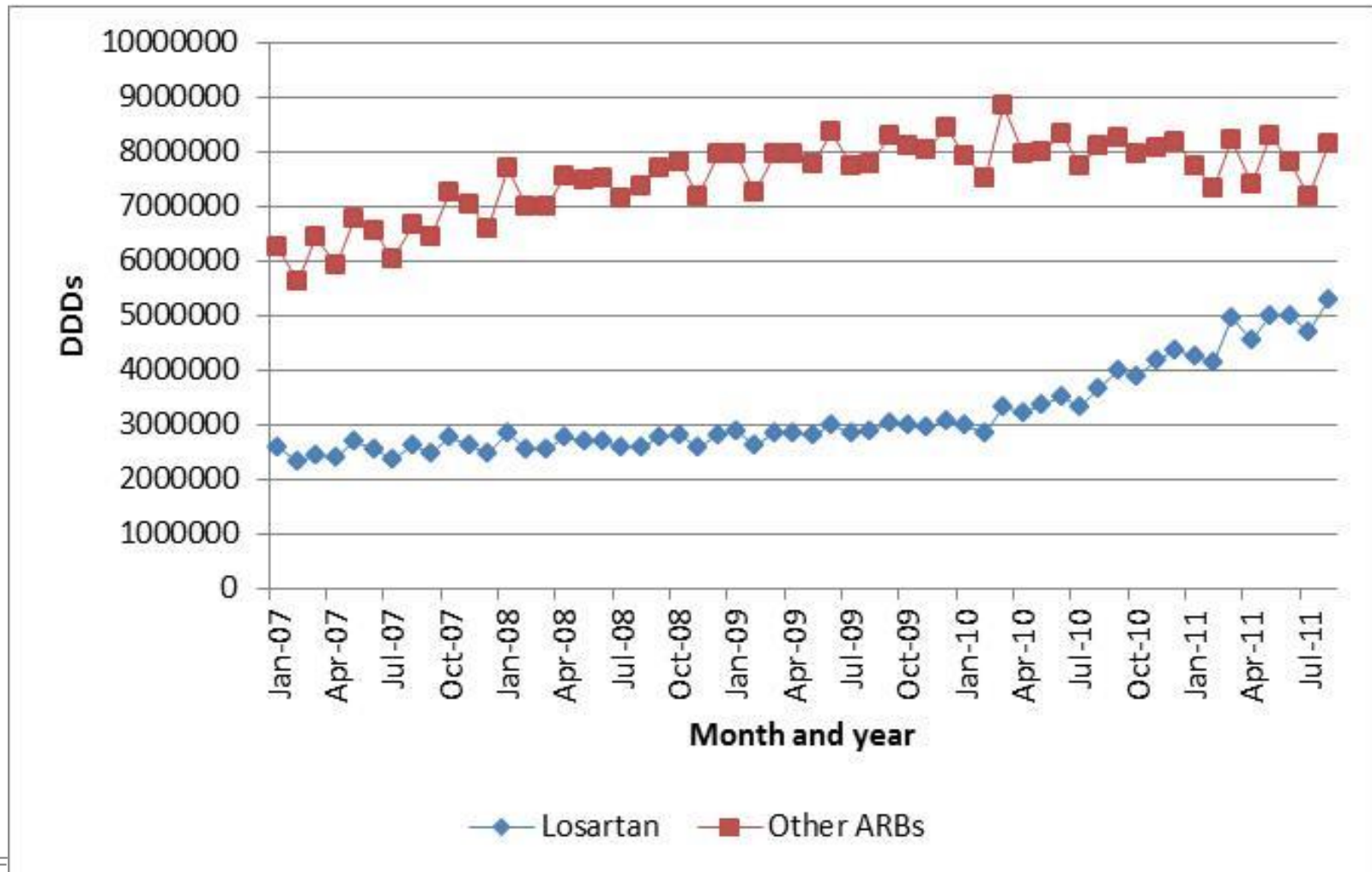
Different activities were undertaken by health authorities in Western European countries in response to generic losartan (first generic ARB)

Country	Generic losartan reimbursed	Activities
Austria	October 2008	Prescribing restrictions removed for losartan but not the other ARBs. Potential sanctions for abuse
Belgium	July 2010	Prescribing restrictions removed for losartan; prior authorisation for other ARBs (otherwise 100% co-payment). General co-payment 25%
Bury PCT	July 2010	No immediate measures. This changed in March 2011 with multiple measures including educational activities, switching programmes, prescribing targets and financial incentives
Denmark	April 2010	Delisting of all other ARBs from the reimbursed list apart from losartan
Ireland	March 2010	No specific activities were undertaken to enhance losartan utilisation
Scotland	July 2010	No specific activities as high INN prescribing rates, other priorities and the imminent launch of generics of other ARBs
Spain (Catalonia)	July 2006	No specific activities regarding losartan - apart from general activities enhancing the prescribing of generics
Sweden	March 2010	Multiple activities among the counties including educational programmes, switching programmes and financial incentives

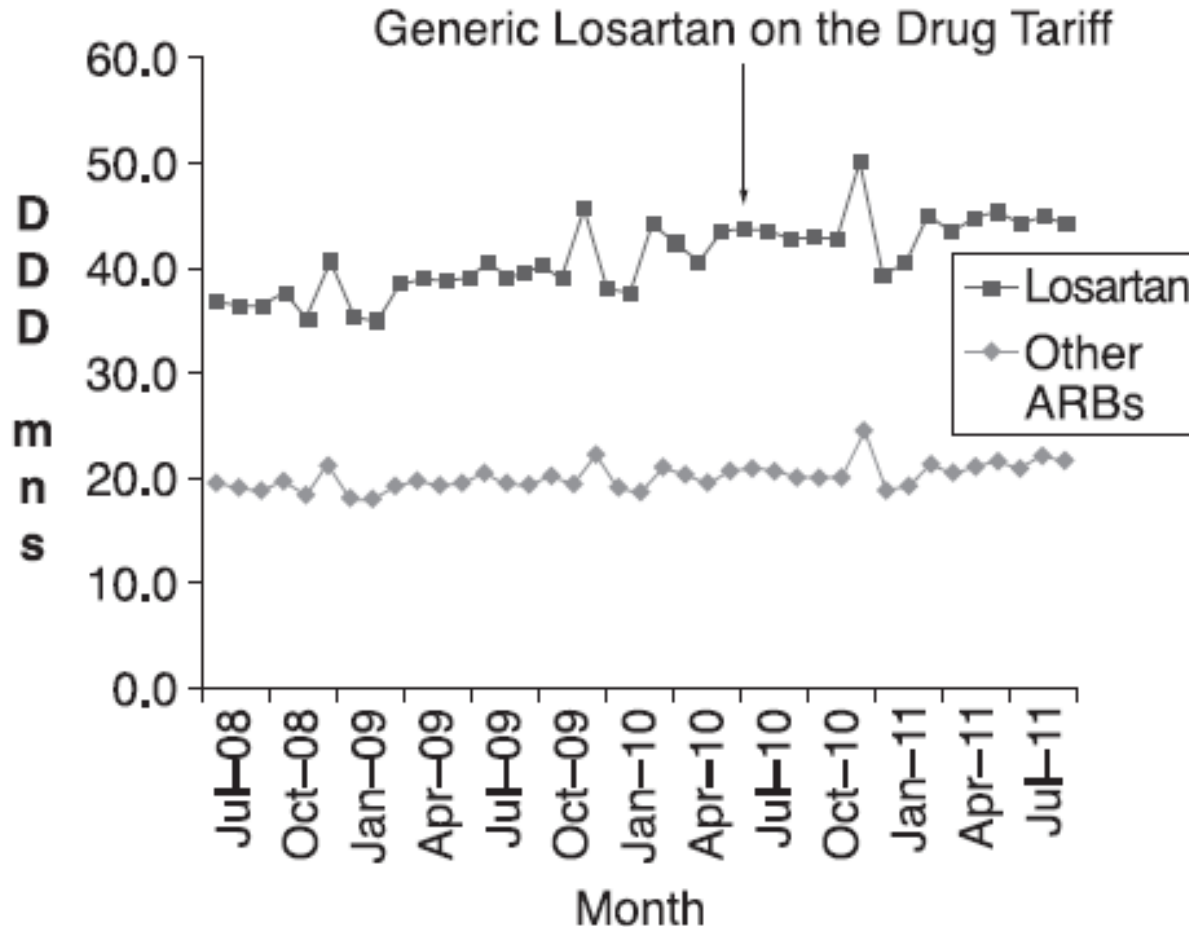
Multiple demand-side activities in Austria, Belgium, Denmark and Sweden increased losartan use once available as generics vs. Ireland, Scotland and Spain



Multiple demand side measures among the Counties in Sweden including guidelines, prescribing targets, financial incentives and therapeutic switching significantly increased losartan utilisation post generics (March 2010) reducing costs (costs ↓ by 26%; utilisation ↑16%)



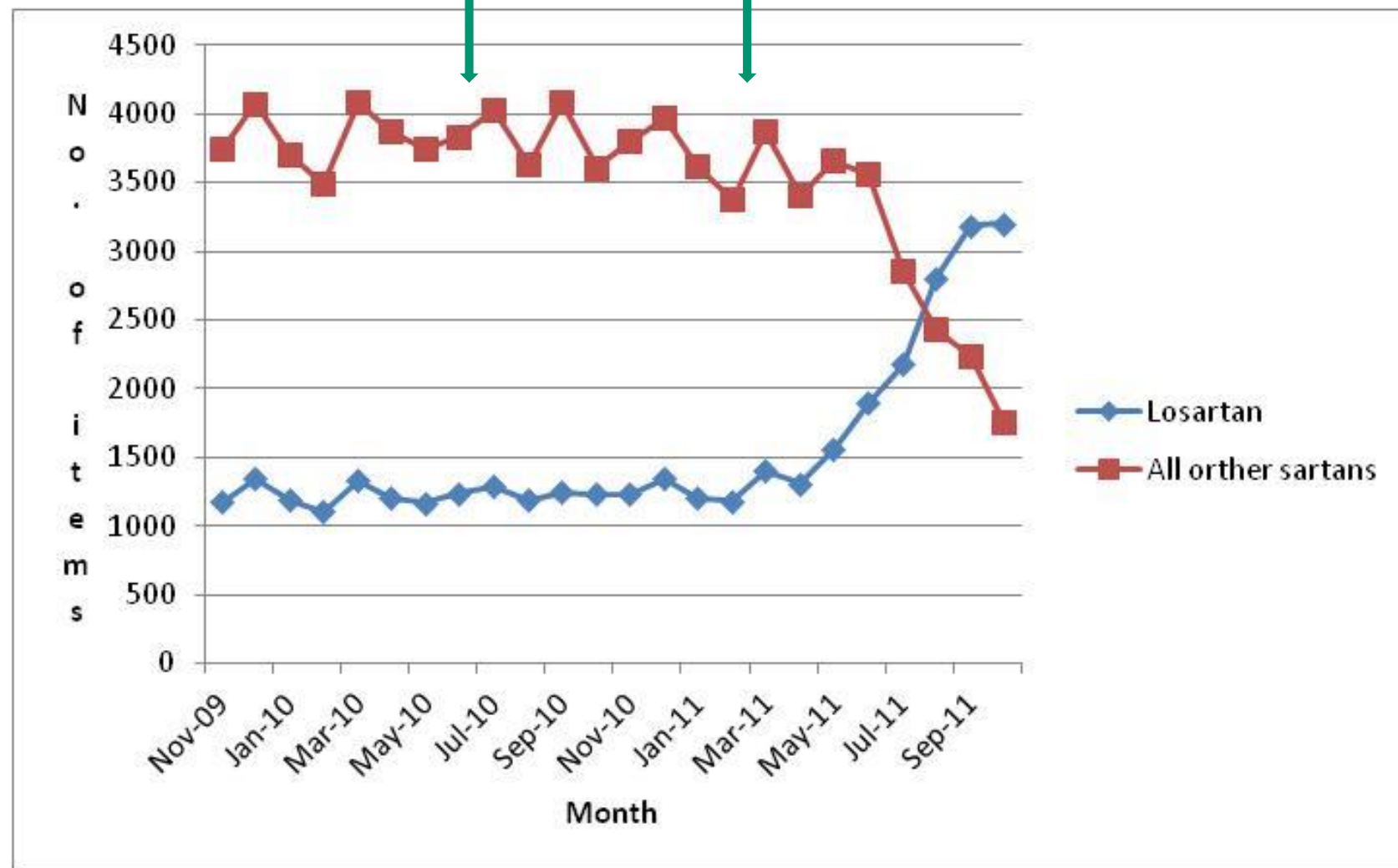
No change in the utilisation of losartan following generics in Scotland even with measures encouraging generic ACEIs (exacerbated by a more complex message). This suggests no 'spill over' effect between classes



These findings of no 'spill over' further endorsed by study in Bury PCT where initially no change in losartan utilisation post generics. This changed with multiple measures (similar to Sweden)

Generic losartan available

Multiple measures for losartan



Demand side measures

What have you learnt so far about the influence of different demand-side measures/ initiatives to improve the rational use of medicines?

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Multiple initiatives have helped reduce inappropriate utilisation of antibiotics in Europe. This will continue

- The inappropriate use of antibiotics is not helped by currently limited adherence to guidelines among physicians in LMIC countries - greater though among physicians in public than private-for-profit sector facilities
- Physicians in private clinics can feel under pressure from patients or parents of children to prescribe antibiotics for viral infections, e.g. URTIs, which could be alleviated through improved physician and patient education
- Multifaceted approaches in Europe (France and Slovenia) helped to appreciably reduce antibiotic utilisation - providing guidance to others

Multiple initiatives have been successful with improving antibiotic utilisation across Europe

- A multifaceted national programme 'Keep Antibiotics Working' was launched in France in 2001 targeting all key stakeholders
- Alongside this, a public service campaign 'Les antibiotiques c'est pas automatique' ('Antibiotics are not automatic') undertaken each winter since 2002 (education)
- Compared to the pre-intervention period (2000–2002), the total number of antibiotic prescriptions per 100 inhabitants, adjusted for the frequency of flu-like symptoms during the winter season, decreased by 26.5% from 2003 to 2007
- The greatest reduction in antibiotic use (-36%) was seen among young children aged 6–15 years

Multiple initiatives have been successful with improving antibiotic utilisation across Europe (cont.)

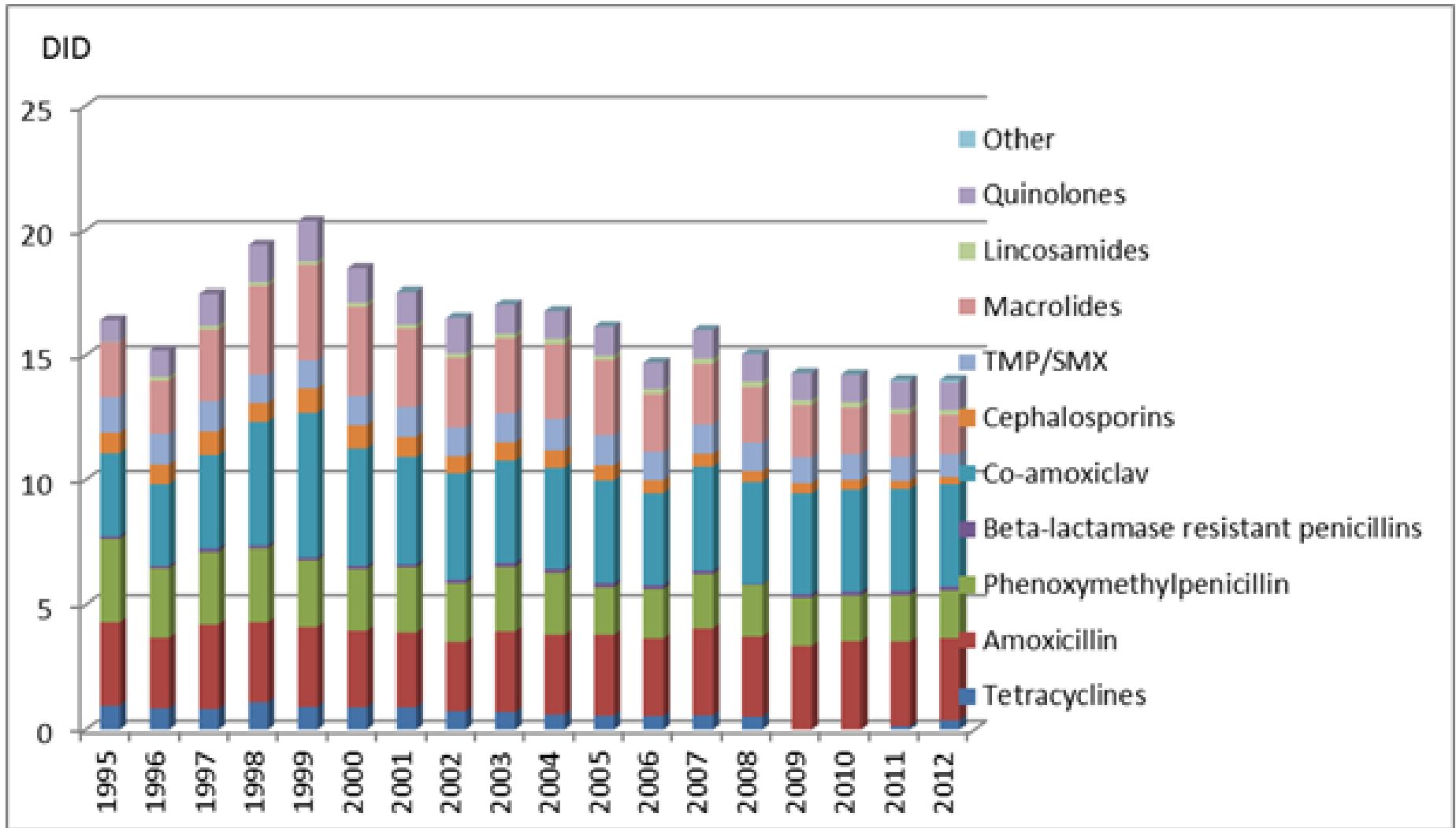
- Multifaceted interventions - including education, engineering, economics and enforcement - were instigated in Slovenia at the end of the 90s to reduce utilisation following a 24% increase in antibiotic consumption
- These were undertaken by all key stakeholder groups including the Ministry of Health, the national health insurance agency and physician groups
- From 1999 to 2012, antibiotic consumption decreased by 2-9% per year, with an overall decrease of 31% ($p = 0.035$), greater for restricted (< 0.0001) than non-restricted antibiotics (0.00018)
- Expenditures on antibiotics also decreased by 53% during the study period

Activity	Institution (organizer)	Targeted public	Introduction / frequency
2-day symposium on antibiotics once a year	Dept. of Infectious Diseases of the UMC Ljubljana	GPs	1995 every year
Prescribing restrictions for antibiotics	ZZZS	All physicians	Starting 2000/ permanent
Workshops in Primary health centres	Primary health centres, ZZZS	GPs	2001/ sporadically
Guidelines on treatment of infectious diseases	Medical professionals	GPs	2002
The drug Bulletin "Recept"	ZZZS	All physicians	2003/ twice a year
Workshop on rational prescribing of antibiotics	Faculty of Medicine University of Ljubljana	Specializing GPs	2004/ every year
Flyer "Safe use of drugs"	ZZZS, medical professionals	Lay public	2006/ always available
Booklet "My child has a fever"	ZZZS, medical professionals	Parents	2007/ always available
Workshop in a region with the highest use of antibiotics	National Committee for the Rational Use of Antimicrobials	GPs	2007/ once a year
Antibiotic Awareness Day	MoH and National Committee for the Rational Use of Antimicrobials	Lay public and GPs	2008/ every year
Workshop on rational prescribing of antibiotics	Slovenian society of chemotherapy	Young physicians	2010/ every year
Flyer "Get well without antibiotics" and "Interactions of drugs"	ZZZS, medical professionals	Lay public	2010/ always available
Quality indicators including antibiotics	ZZZS	GPs	2011

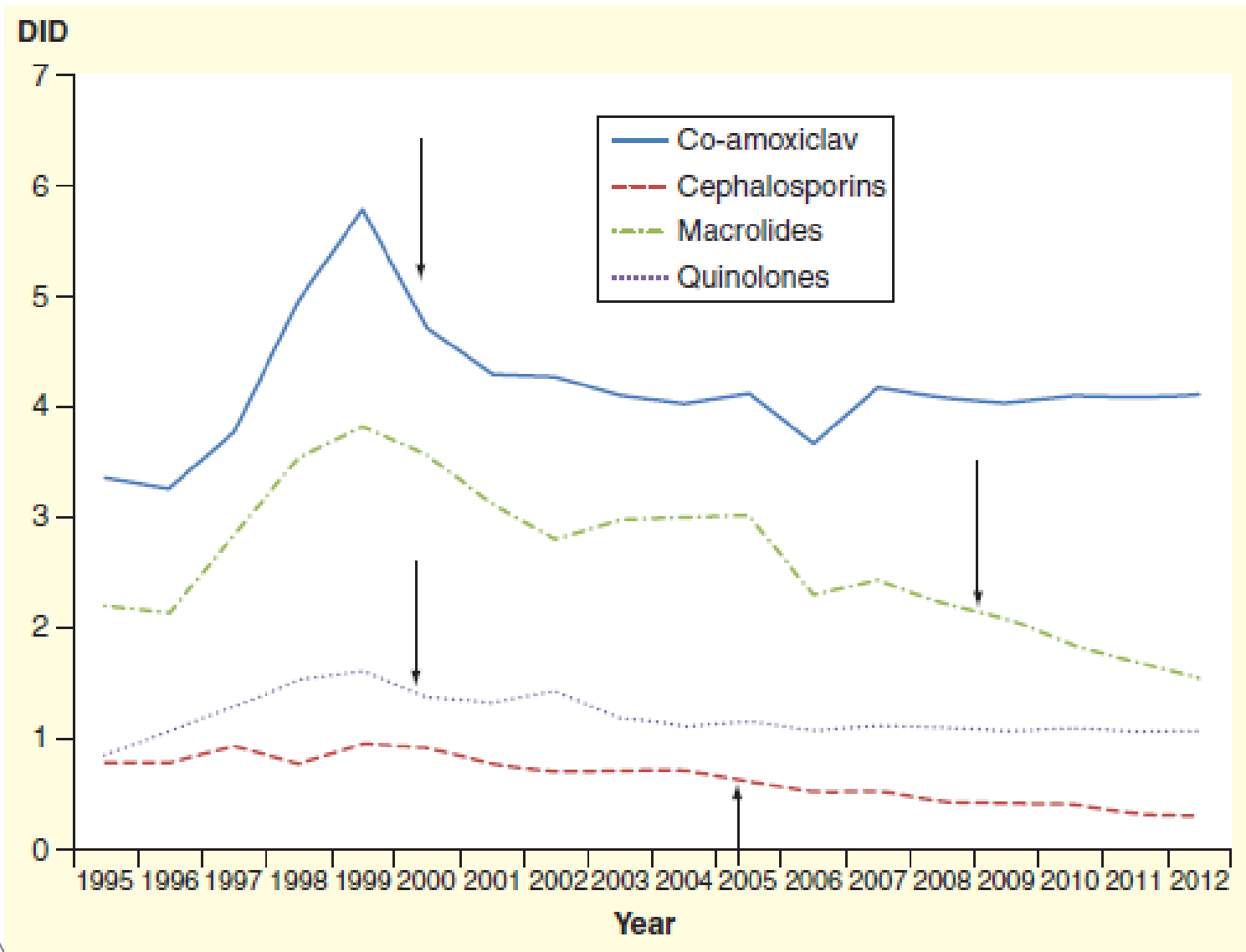
Multiple activities, groups and their frequency in Slovenia from the late 1990s onwards.

ZZZS = national health insurance group

The multiple measures led to a 31% decrease in antibiotic consumption in recent years in Slovenia



Typically greater reduction in utilisation of restricted vs. non restricted antibiotics (arrow = date of restrictions)



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Drug utilisation and policy studies provide a platform for implementing future policies

We have shown that:

- DDDs and DDDs/ one thousand inhabitants/ day help compare medicine utilisation within countries/ classes and across countries/ classes
- 4Es help document demand side measures for comparison purposes within and across countries
- Multiple demand-side measures can favourably influence prescribing patterns across classes and countries with no apparent 'spill over' effect from one class to another
- Patients are important when considering programmes to reduce excessive antibiotic utilisation

Thank You

Any Questions!

Brian.Godman@ki.se; Brian.godman@strath.ac.uk;
mail@briangodman.co.uk