



ΕΘΝΙΚΗ  
ΣΧΟΛΗ  
ΔΗΜΟΣΙΑΣ  
ΥΓΕΙΑΣ  
ΥΓΕΙΟΝΟΜΙΚΗ ΣΧΟΛΗ  
ΑΘΗΝΩΝ 1929-1994



## ΠΡΟΣΑΡΜΟΓΗ ΤΩΝ ΠΑΡΟΧΩΝ ΥΓΕΙΑΣ ΣΤΙΣ ΣΥΝΘΗΚΕΣ ΤΗΣ ΠΑΡΑΤΕΤΑΜΕΝΗΣ ΟΙΚΟΝΟΜΙΚΗΣ ΚΡΙΣΗΣ

**Νίκος Μανιαδάκης**

BSc (Athens), MSc (York), PhD (Warwick), Fellow (ESC)

**Καθηγητής & Διευθυντής**

**Τομέας Οργάνωσης και Διοίκησης Υπηρεσιών Υγείας  
Εθνική Σχολή Δημόσιας Υγείας**

# Σύγκρουση συμφερόντων

## Κανένα για αυτήν την παρουσίαση

Εκπαιδευτικές-ερευνητικές-συμβουλευτικές επιχορηγήσεις την τελευταία διετία: Amgen, Pfizer, Abbott, Genesis, Vifor, Merck-Serono, Aventis, AstraZeneca, UCB, Bayer, Celgene, Novo Nordisk, Servier, Boehringer Ingelheim, Alexion

# ΔΟΜΗ ΠΑΡΟΥΣΙΑΣΗΣ

1

- ΜΑΚΡΟΠΡΟΘΕΣΜΕΣ ΤΑΣΕΙΣ

2

- ΠΟΛΙΤΙΚΕΣ ΑΠΟΔΟΤΙΚΟΤΗΤΑΣ

3

- ΠΟΛΙΤΙΚΕΣ ΤΗΝ ΠΕΡΙΟΔΟ ΚΡΙΣΗΣ

4

- ΕΣΥ ΠΡΙΝ ΤΟ ΜΝΗΜΟΝΙΟ

5

- ΕΣΥ ΣΤΟ ΜΝΗΜΟΝΙΟ

6

- ΛΥΣΗ? Η ΠΕΡΙΠΤΩΣΗ ΤΗΣ ΡΑ

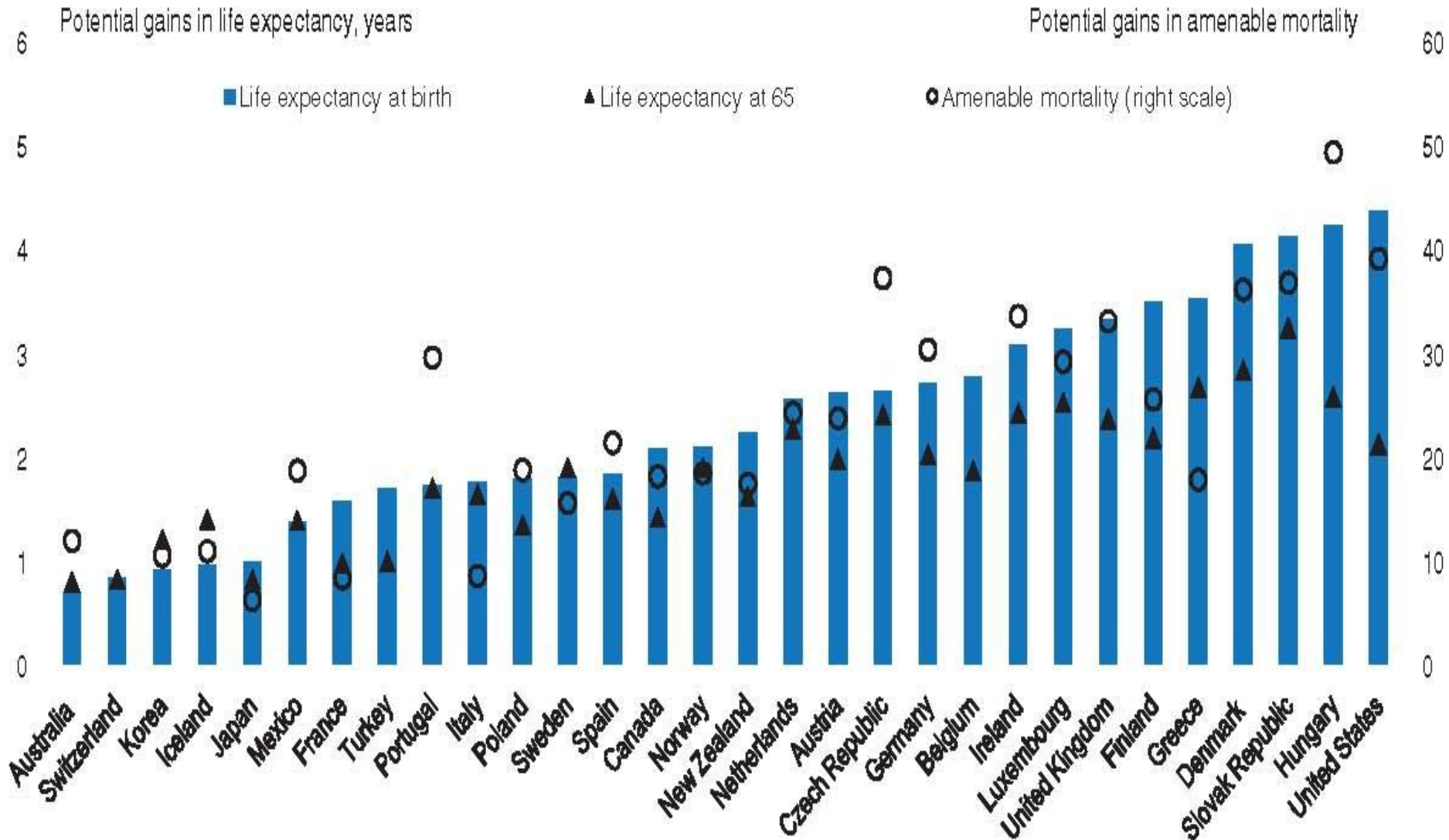
# ΜΑΚΡΟΠΡΟΘΕΣΜΕΣ ΤΑΣΕΙΣ ΚΑΙ ΠΡΟΒΛΗΜΑΤΙΣΜΟΙ

ΠΡΩΤΟ ΜΕΡΟΣ

# Κόστος Παροχών και Στόχοι Συστημάτων Παροχής Υπηρεσιών Υγείας



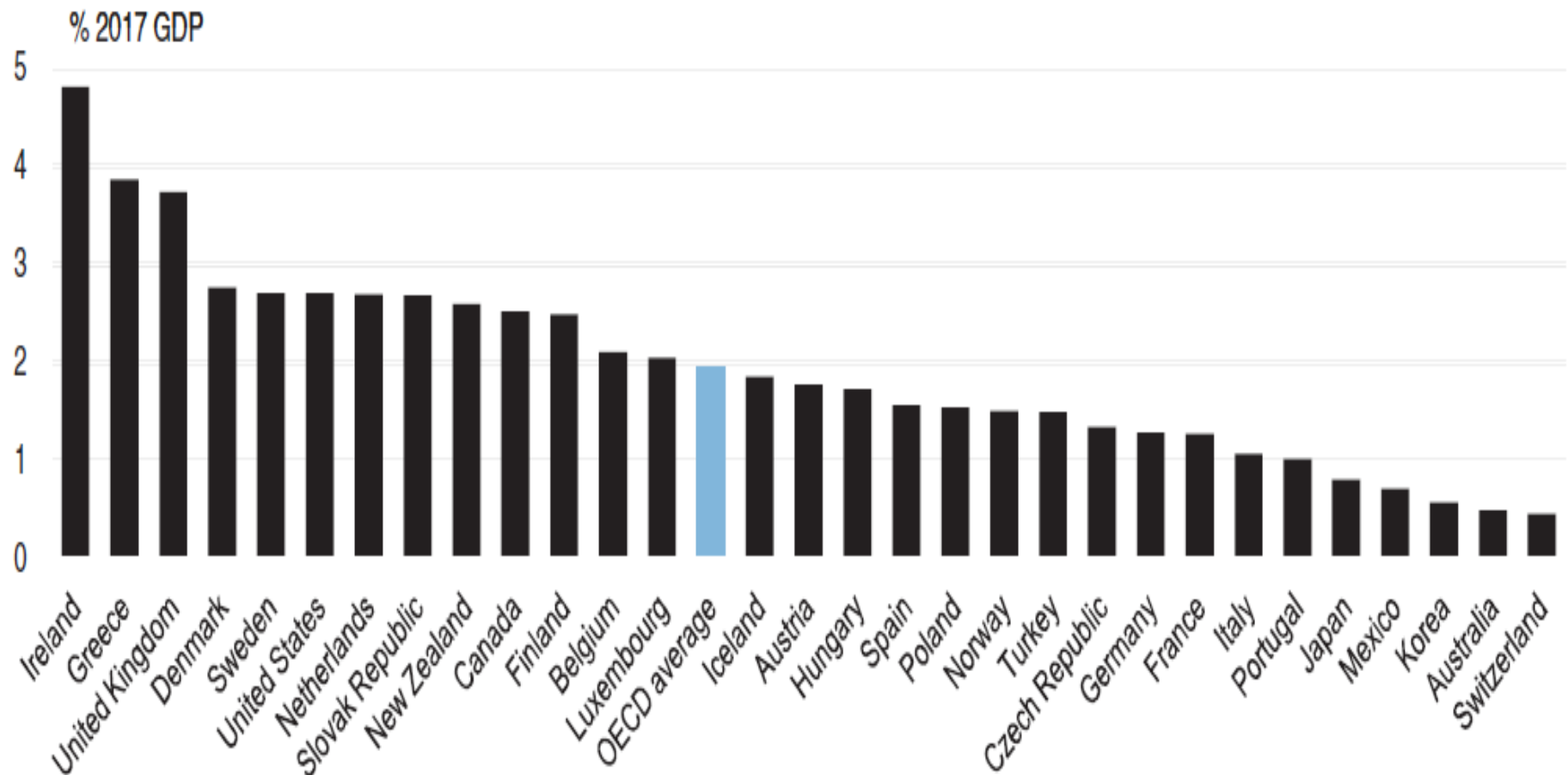
# Οργανωτική Αναποτελεσματικότητα Υγειονομική Διάσταση



Source: OECD Health Data 2009; OECD calculations.

# Οργανωτική Αναποτελεσματικότητα Οικονομική Διάσταση

C. Potential savings in public spending<sup>3</sup>

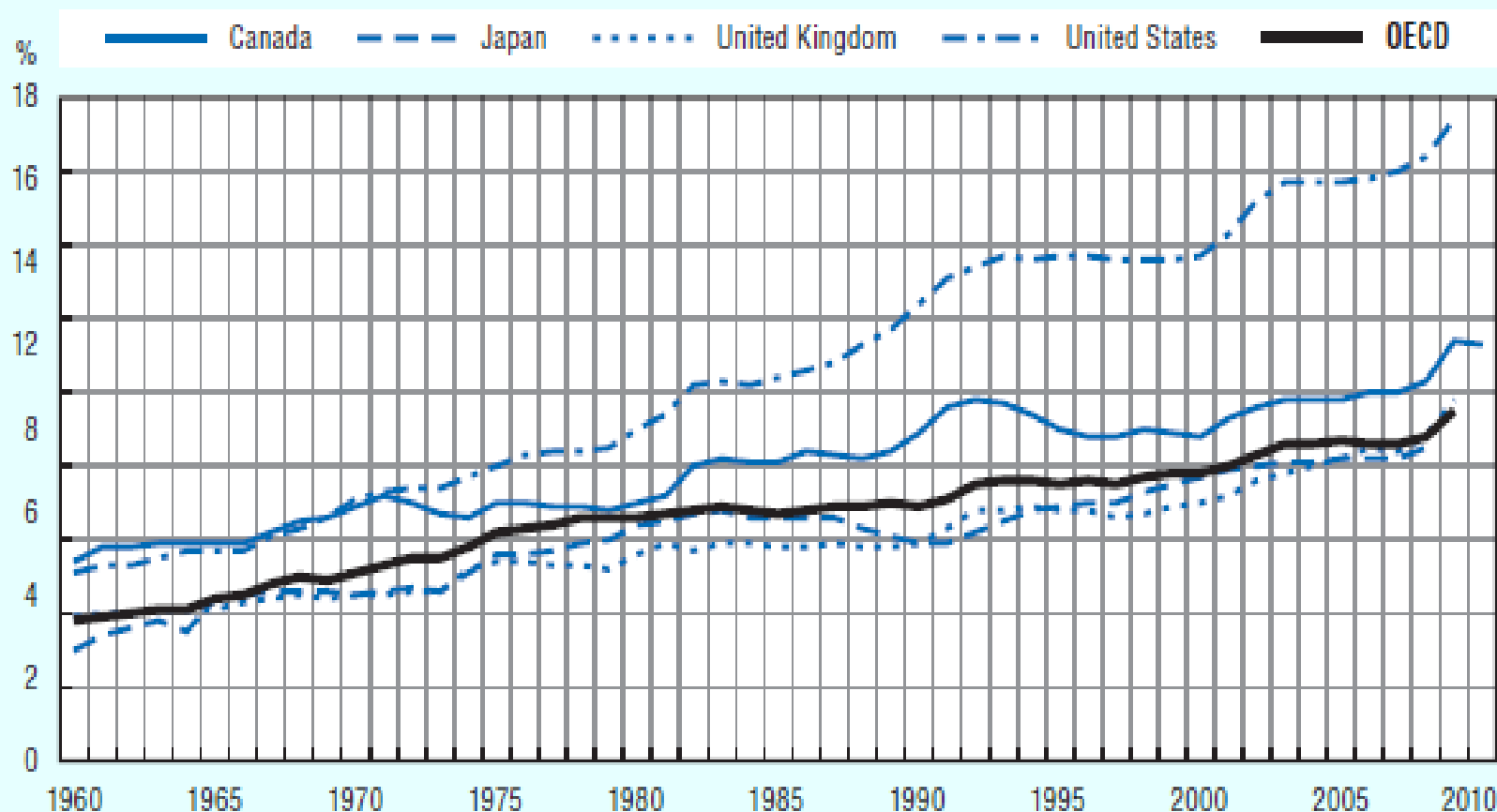


3. Potential savings represent the difference between a no-reform scenario and a scenario where countries would become as efficient as the best performing countries.

Source: OECD Health Data 2009; OECD calculations.

# Η Ραγδαία Αύξηση των Δαπανών Υγείας

Health expenditure as a share of GDP, 1960-2009, selected OECD countries

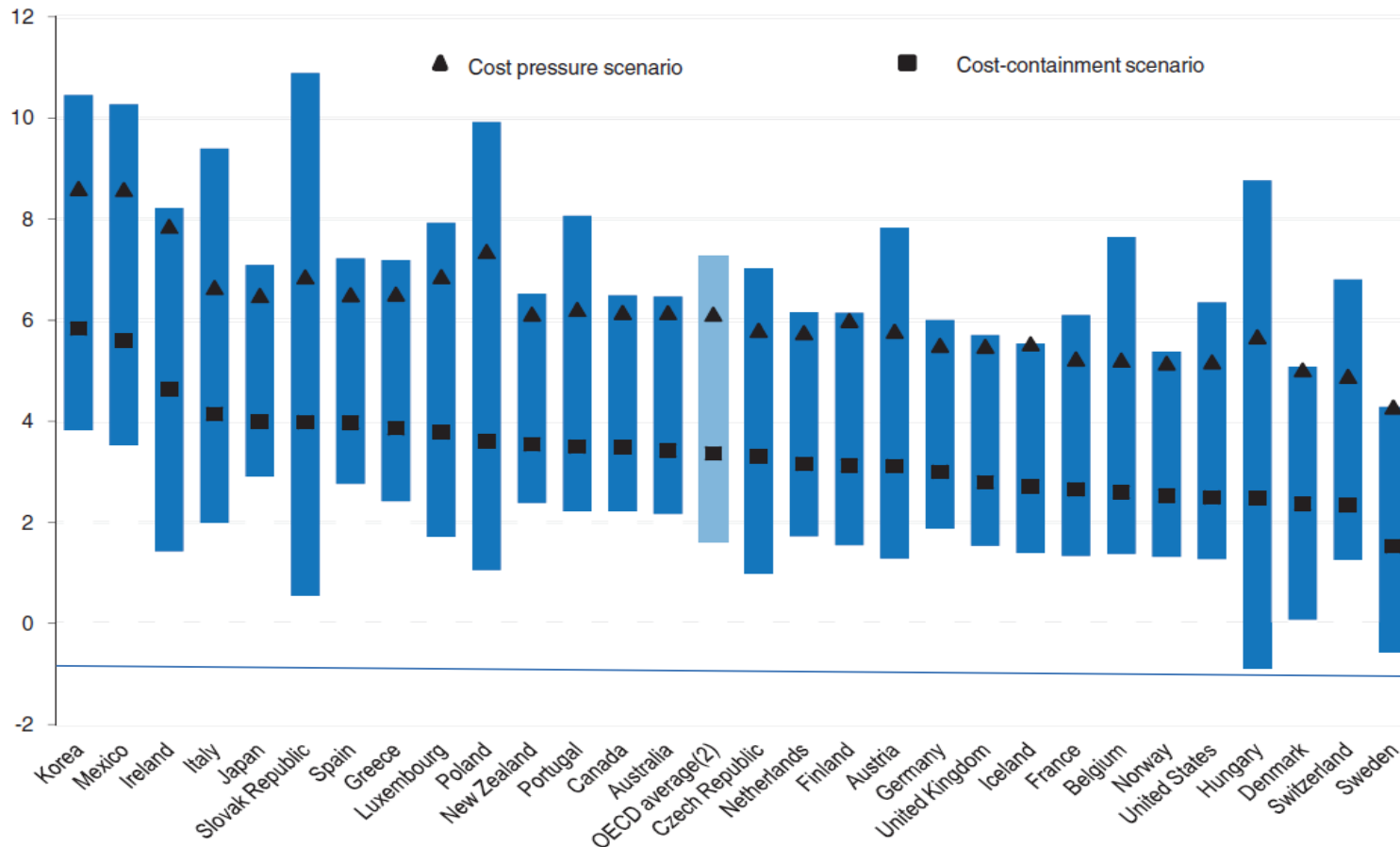


Source: OECD Health Data 2011.



# Μελλοντικές Τάσεις Δαπανών Υγείας

Figure 1.10. Increase in public health and long-term care spending by country  
2005-50<sup>1</sup>, in percentage points of GDP



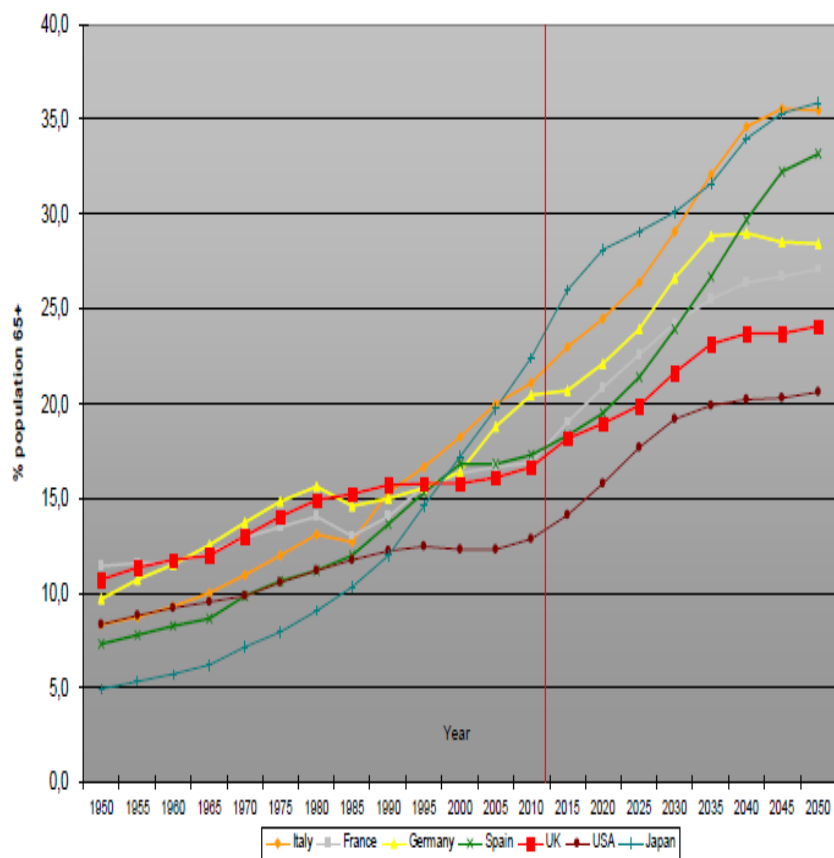
1. The vertical bars correspond to the range of the alternative scenarios, including sensitivity analysis. Countries are ranked by the increase of expenditure between 2005 and 2050 in the cost-containment scenario. Turkey was not included because data limitations made it impossible to calculate one of the scenarios.
2. OECD average excluding Turkey.

Source: Oliveira Martins and de la Maisonnette (2006).

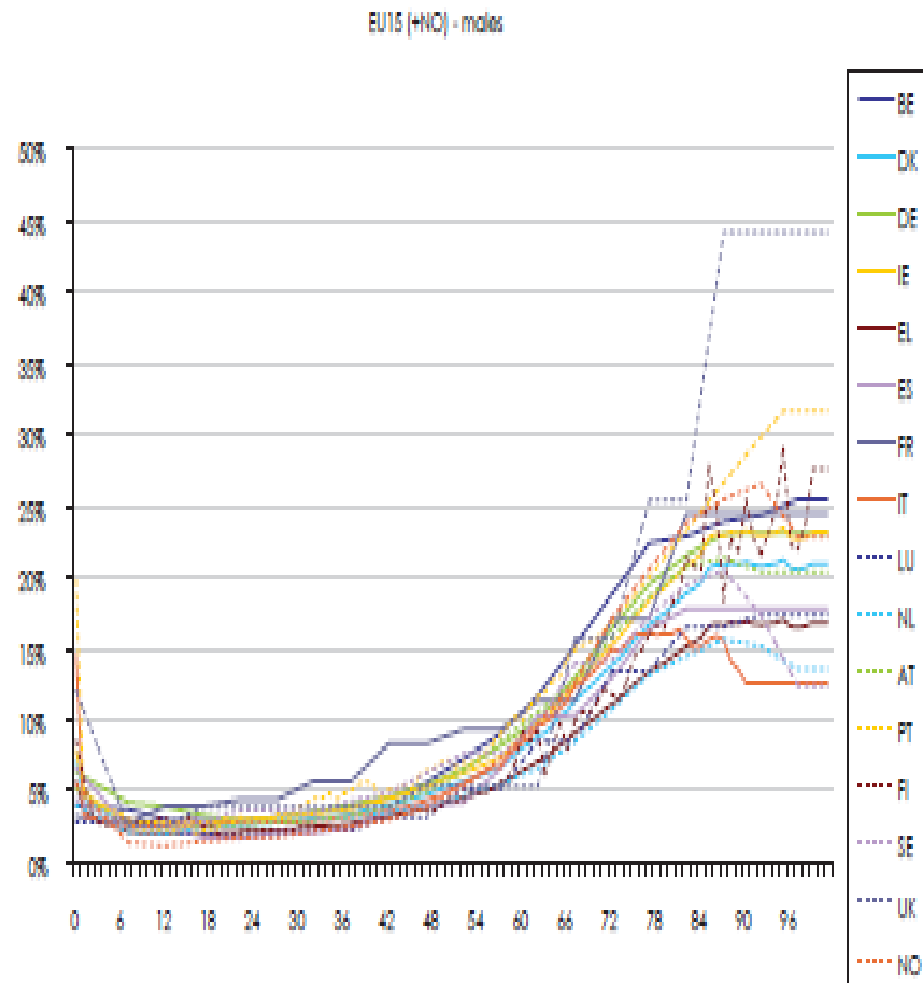
# Δημογραφική Γήρανση και Υγειονομική Δαπάνη

World population evolution (% of +65)

Health spending/capita as % of GDP/Capita

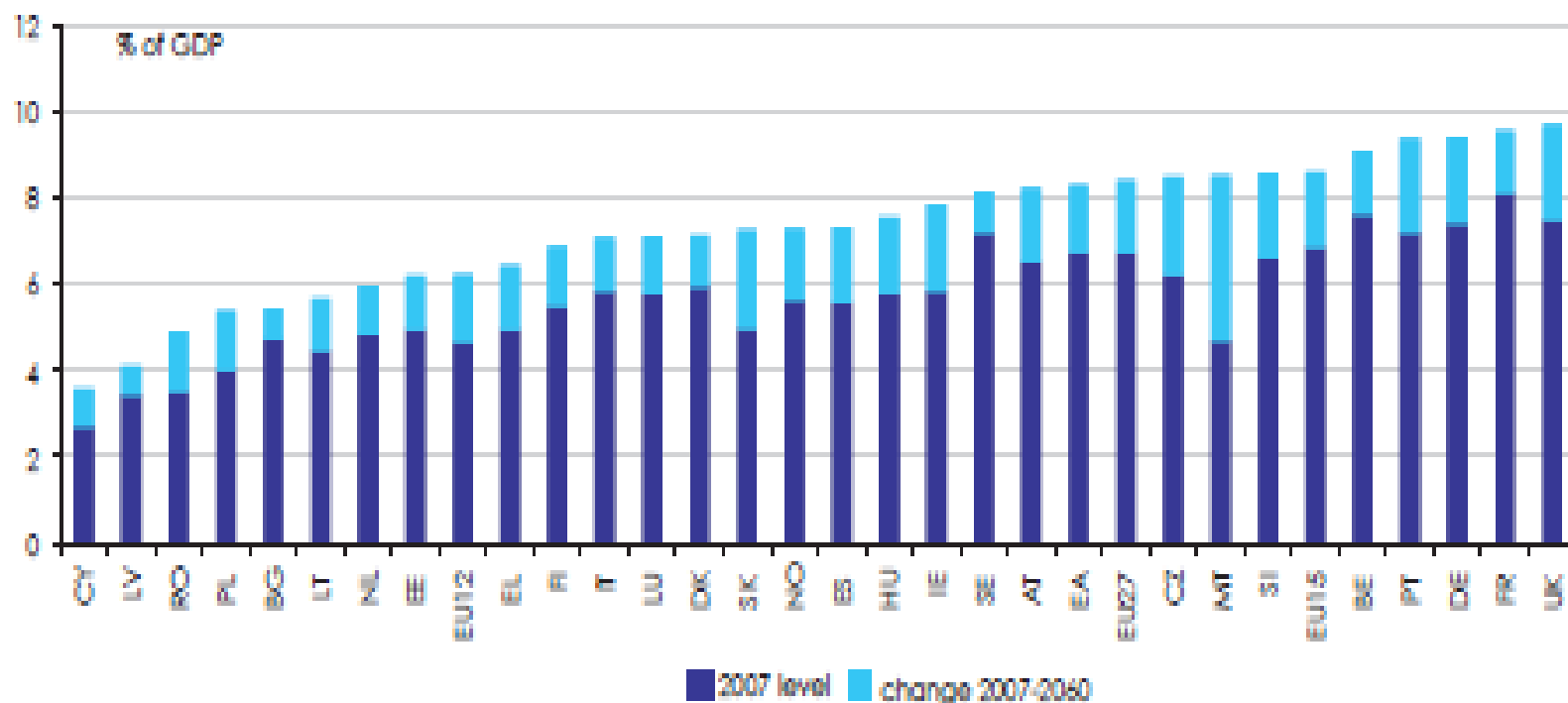


Source: United Nations' Dept Economic & Social Affairs, 2006



# Δημογραφικό και Δαπάνες Υγείας στην ΕΕ

Graph 68 – Impact of demographic change on public expenditure on health care (% of GDP, 2007-2060)



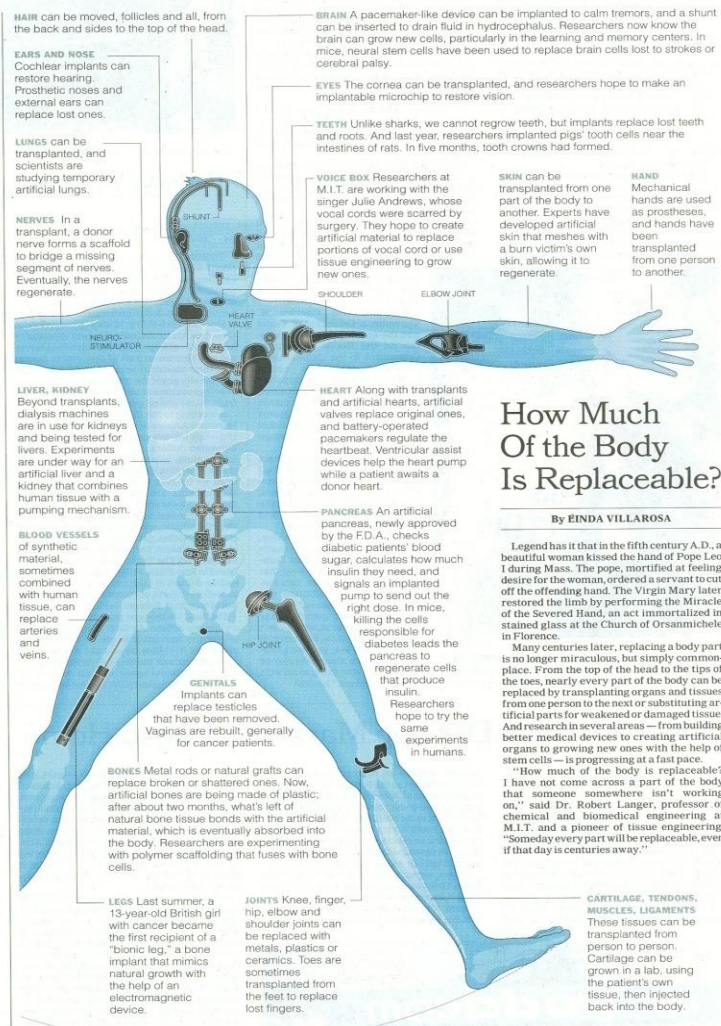
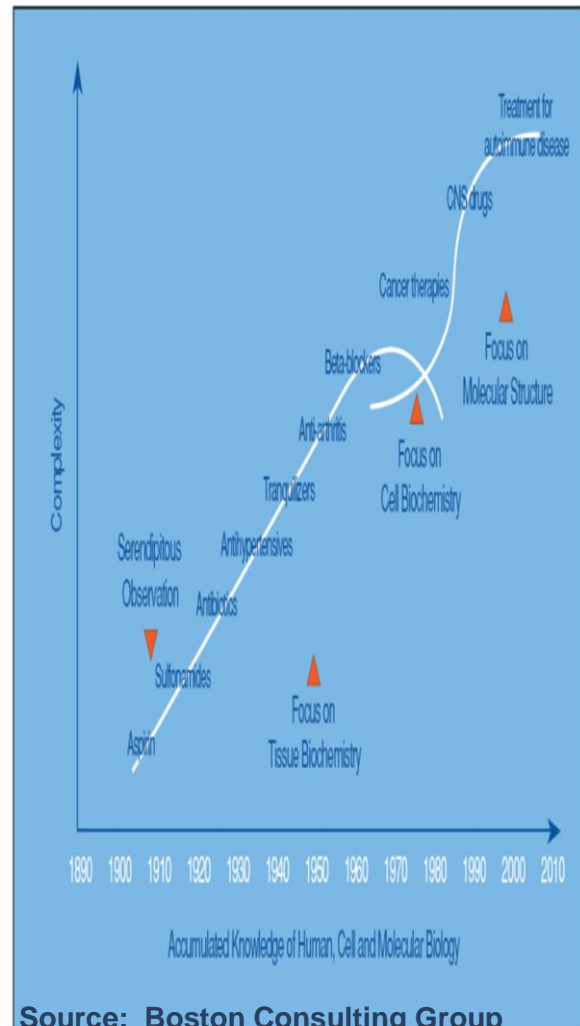
Source: Commission services, EPC.

# Η Τεχνολογική Επανάσταση στην Υγειονομική Περίθαλψη

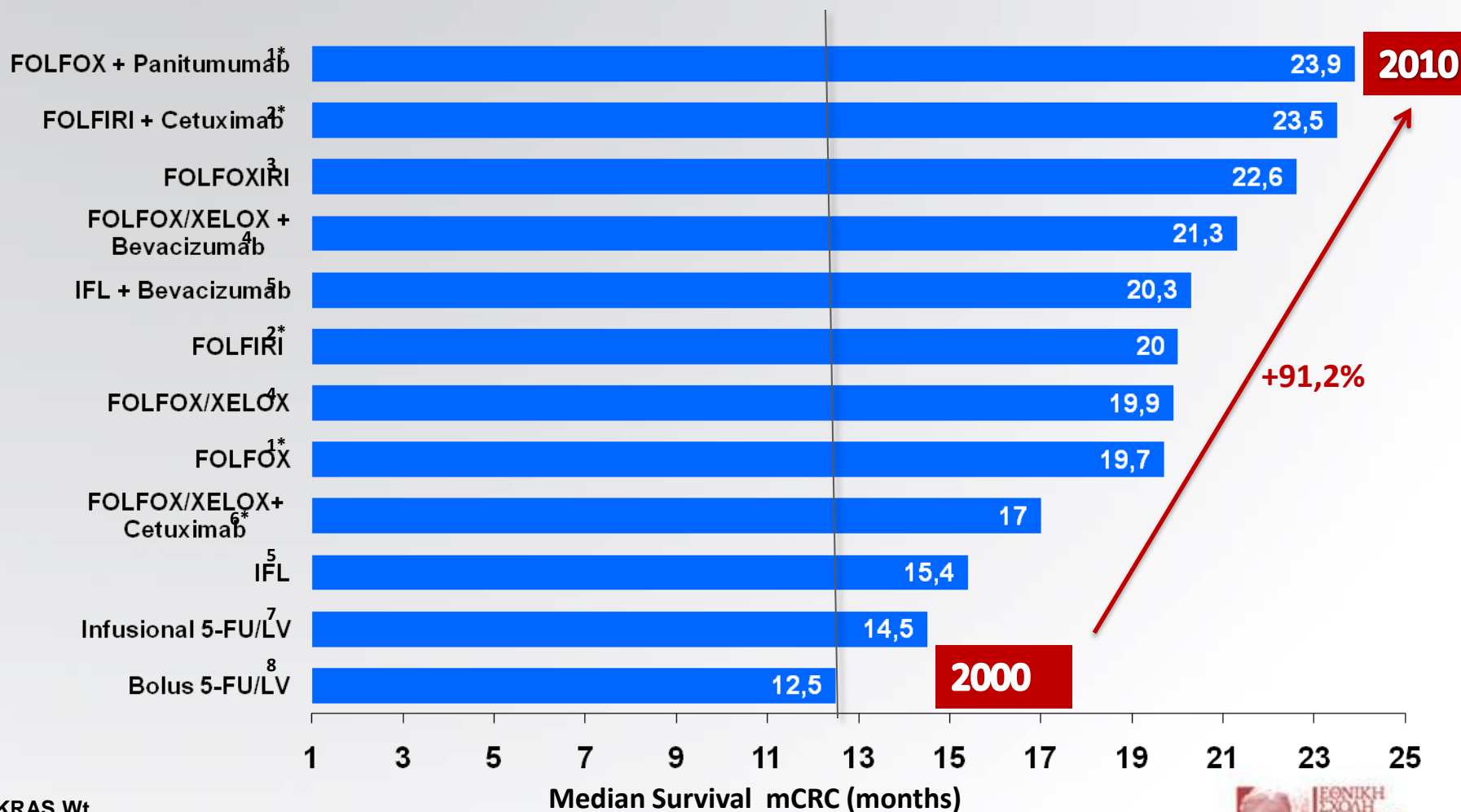
## Φάρμακα

## Συσκευές

## Εξοπλισμός



# Διάμεση Επιβίωση 1<sup>ης</sup> Θεραπείας στο Μεταστατικό Καρκίνο του Παχέος Εντέρου Σχεδόν Διπλασιάστηκε σε 10 Χρόνια



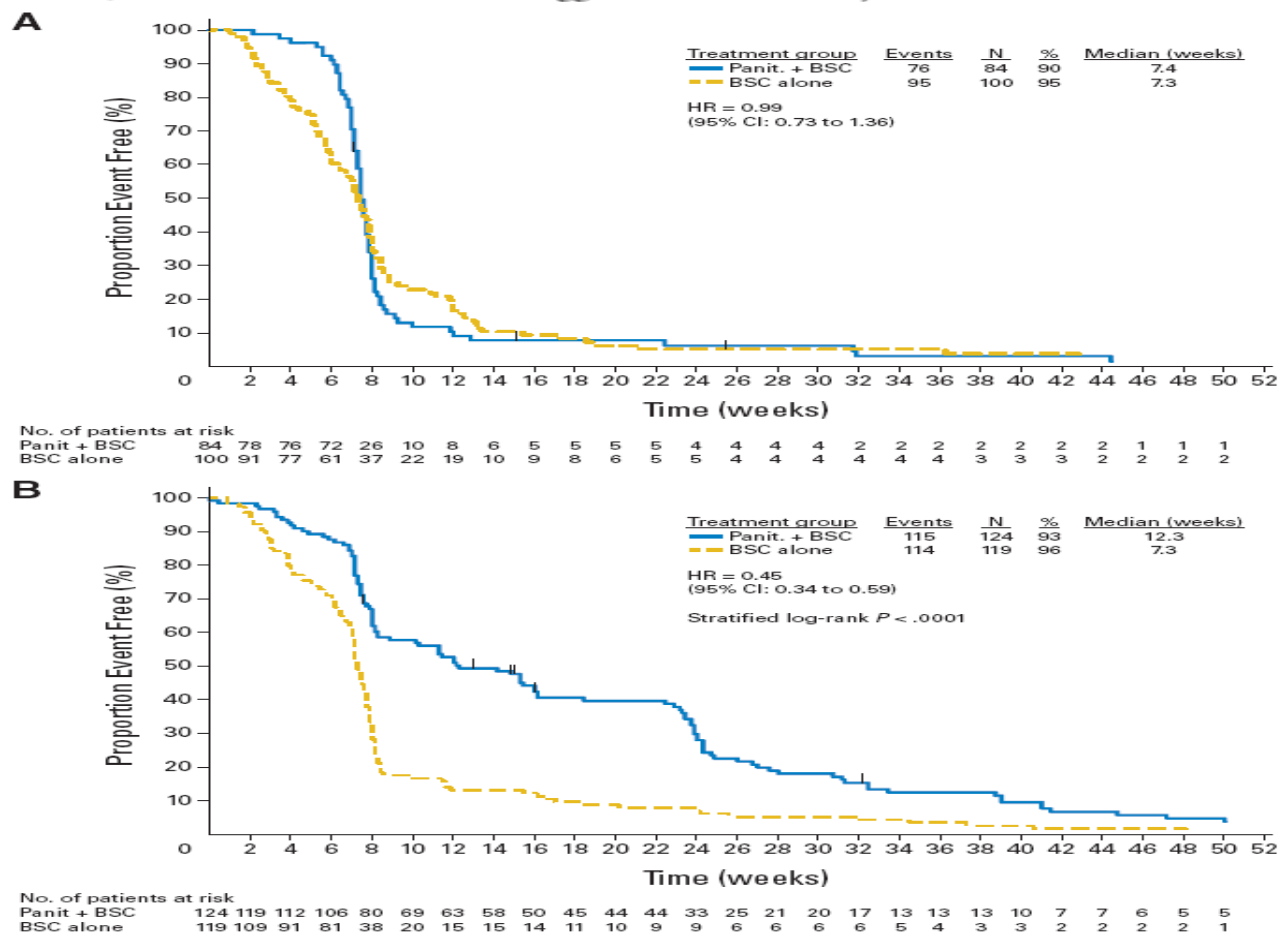
1.Siena S, et al. ASCO-GI 2010. 2.Van Cutsem E, et al. ASCO-GI 2010; 3.Falcone A, et al. JCO 2007; 4.Saltz LB, et al. JCO 2008; 5Hurwitz HI, et al. NEJM 2004; 6. Maughan T. et al. ASCO GI 2010 7.De Gramont A, et al. JCO 2000; 8.Saltz LB, et al. NEJM 2000;



# Στοχεύουμε με Βιολογικούς Παράγοντες

## Wild-Type *KRAS* Is Required for Panitumumab Efficacy in Patients With Metastatic Colorectal Cancer

Rafael G. Amado, Michael Wolf, Marc Peeters, Eric Van Cutsem, Salvatore Siena, Daniel J. Freeman, Todd Juan, Robert Sikorski, Sid Suggs, Robert Radinsky, Scott D. Patterson, and David D. Chang



**Fig 2.** Progression-free survival by treatment within *KRAS* groups. Progression-free survival by randomized treatment in (A) mutant and (B) wild-type *KRAS* groups. Hazard ratios (HR) are shown for panitumumab (panit.) versus best supportive care (BSC) adjusted for randomization factors (Eastern Cooperative Oncology Group score, geographic region).

\*2 στην Επιβίωση =  
\*466 στο Κόστος!!

VOLUME 25 • NUMBER 2 • JANUARY 10 2007

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

## Cost of Cancer Care: Issues and Implications

Neal J. Meropol and Kevin A. Schulman

**Table 4.** Cost of Colorectal Cancer Treatment

Regimen	Cost per 6 Months (\$)
FU/LV daily for 5 days, monthly	96
Infusional FU/LV every 2 weeks	352
Capecitabine for 14 days, every 3 weeks	11,648
Irinotecan every 3 weeks	30,100
Irinotecan weekly for 4 weeks, every 6 weeks	21,500
FOLFIRI every 2 weeks	23,572
FOLFOX every 2 weeks	29,989
Bevacizumab (alone) every 2 weeks	23,897
Cetuximab monotherapy weekly	52,131
Panitumumab	44,720

NOTE. Only drug costs included. Costs based upon average sales price for 70 kg patient with body surface area 1.7 m<sup>2</sup>. Wholesale acquisition costs were used for panitumumab, as average sales price was not available at the time of publication.

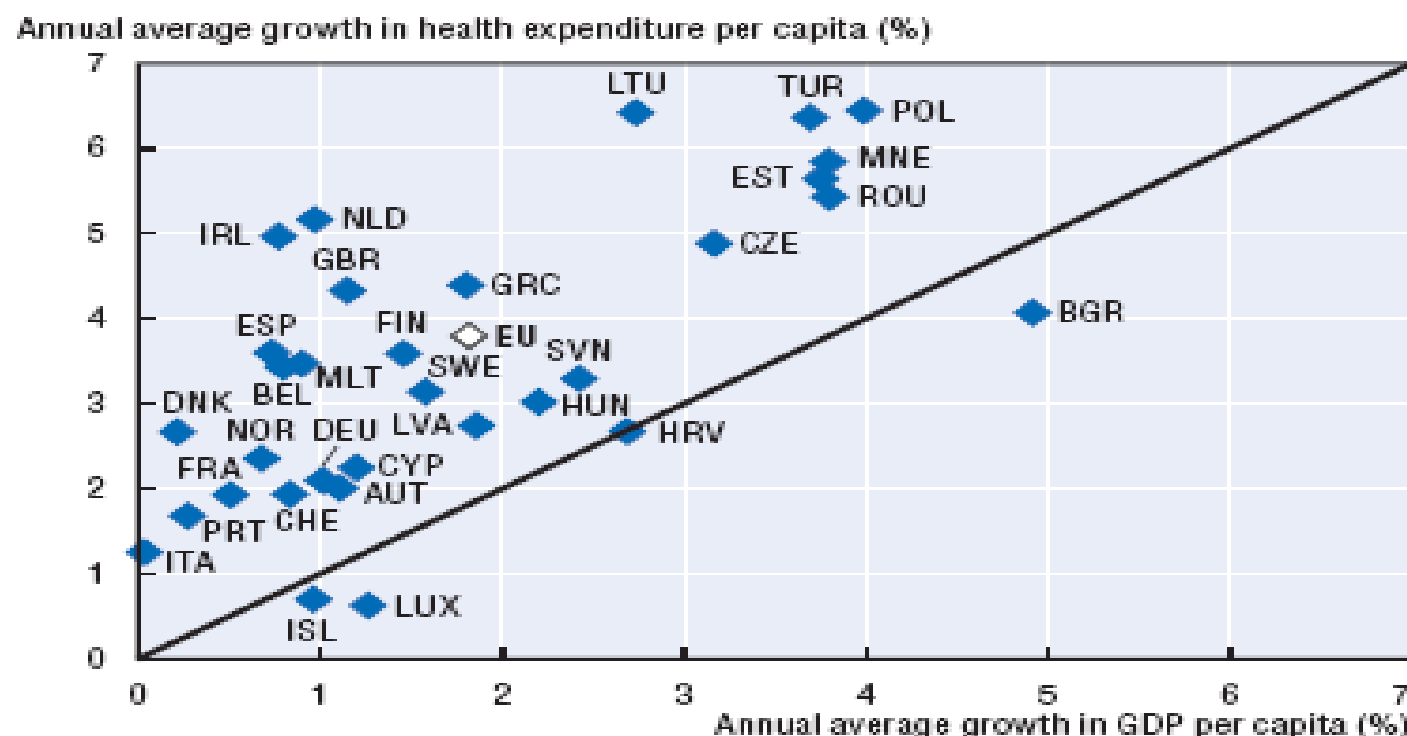
Abbreviations: FU, fluorouracil; LV, leucovorin; FOLFIRI, irinotecan, LV, and infusional fluorouracil for 46 hours; FOLFOX, oxaliplatin, LV, infusional FU for 46 hours.





# Αύξηση Δαπανών Υγείας και ΑΕΠ

## 5.3.2. Annual average growth in health expenditure and GDP per capita, in real terms, 2000-10 (or nearest year)

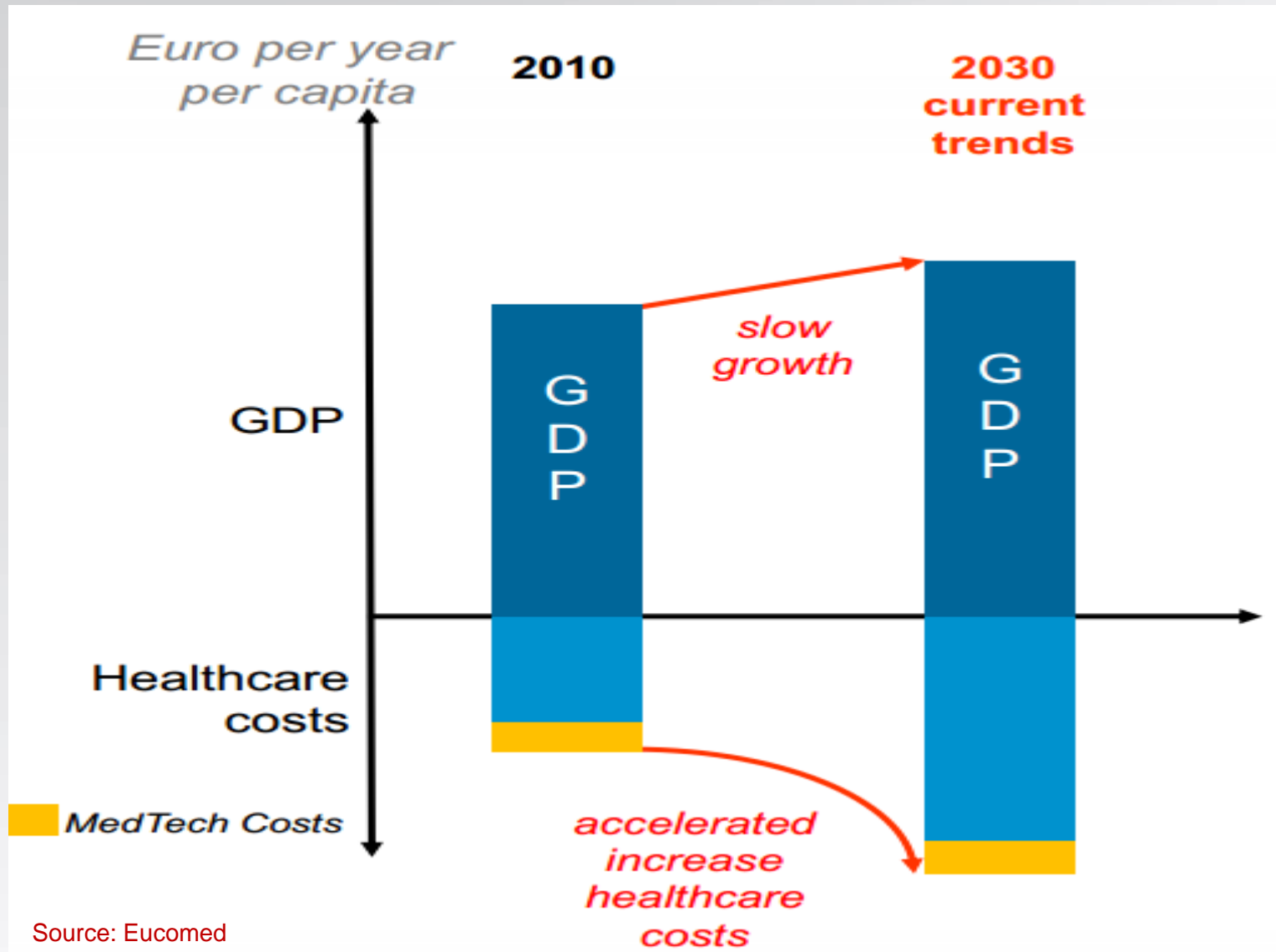


Source: OECD Health Data 2012; Eurostat Statistics Database; WHO Global Health Expenditure Database.

StatLink  <http://dx.doi.org/10.1787/888932705482>

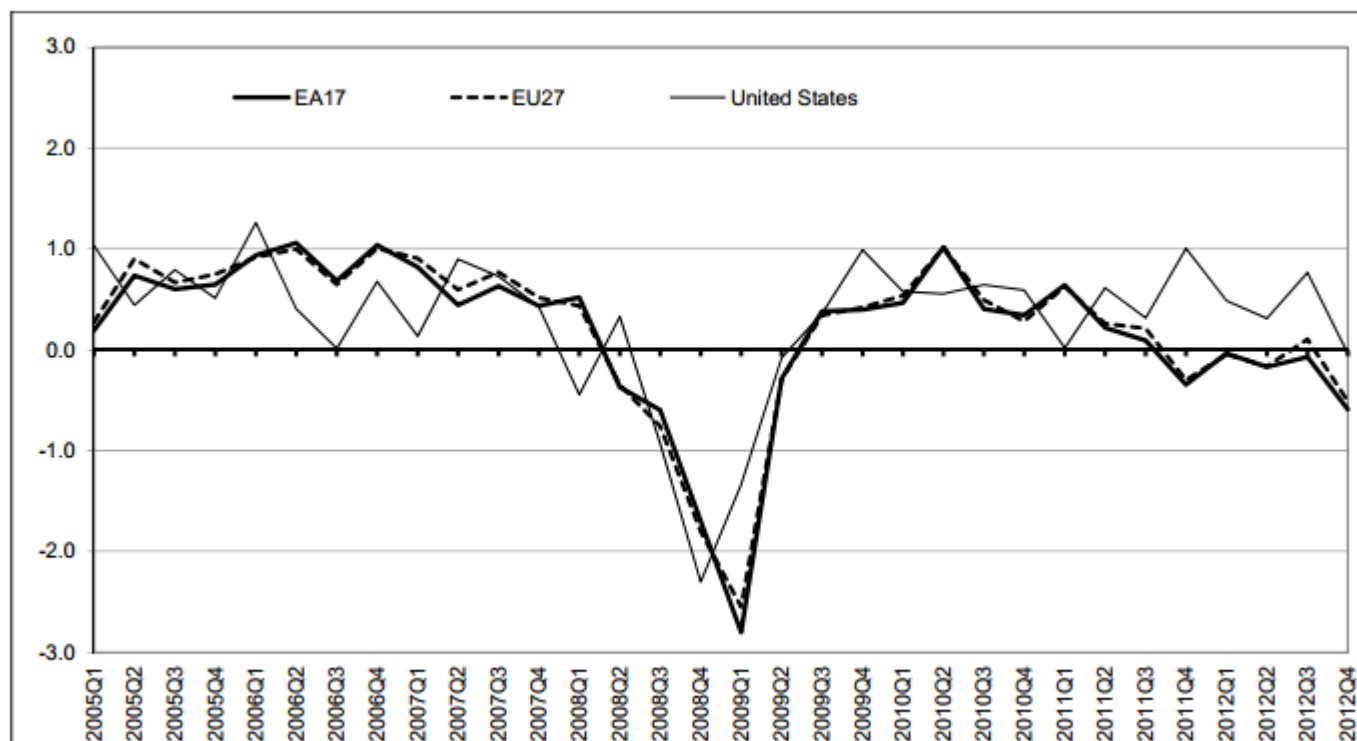


# Η Αύξηση στο ΑΕΠ δεν Δύναται να Χρηματοδοτήσει την Αύξηση των Δαπανών Υγείας



24/2013 - 14 February 2013

**EU27, euro area and United States GDP growth rates**  
% change over the previous quarter




# ΑΕΠ και Δαπάνες Υγείας

**Annual average growth in real per capita expenditure on health and GDP, 2000-09 (or nearest year)**

Annual average growth rate in real health expenditure per capita (%)

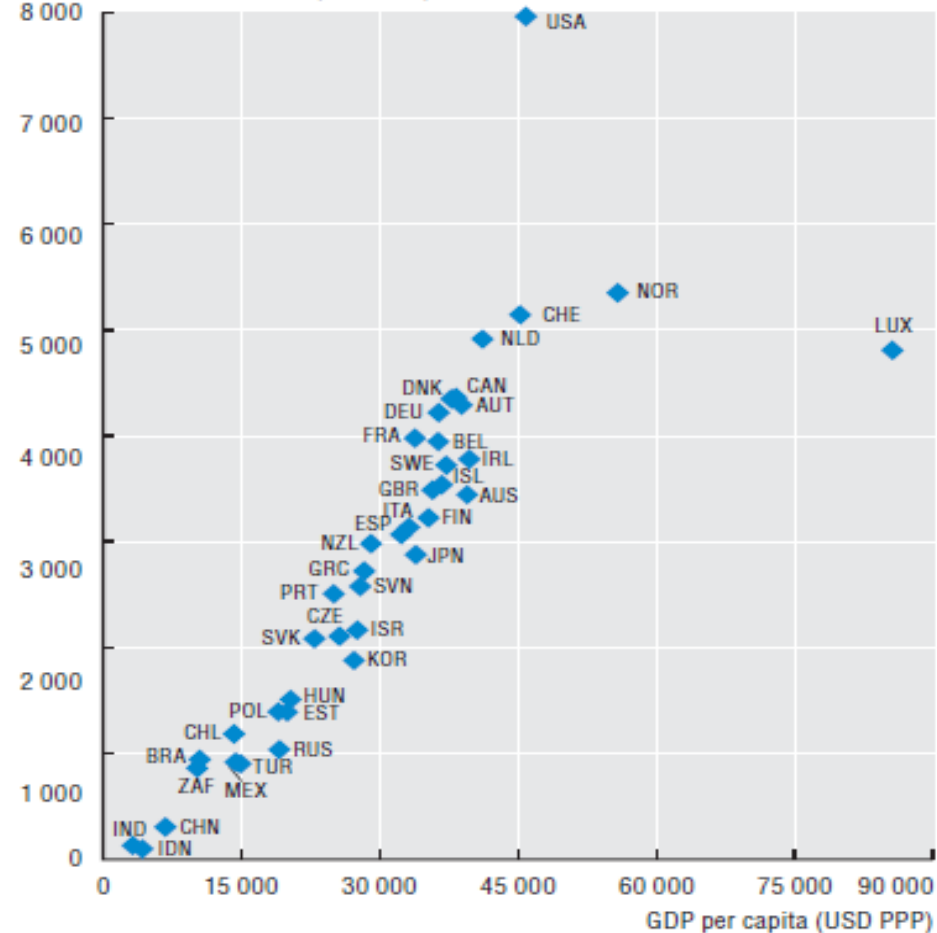


Source: OECD Health Data 2011.


StatLink  <http://dx.doi.org/10.1787/888932526141>

**Total health expenditure per capita and GDP per capita, 2009 (or nearest year)**

Health spending per capita (USD PPP)



Source: OECD Health Data 2011; WHO Global Health Expenditure Database.

StatLink  <http://dx.doi.org/10.1787/888932526084>

# ΠΟΛΙΤΙΚΕΣ ΑΥΞΗΣΗΣ ΤΗΣ ΑΠΟΔΟΤΙΚΟΤΗΤΑΣ ΚΑΙ ΑΠΟΤΕΛΕΣΜΑΤΙΚΟΤΗΤΑΣ

ΔΕΥΤΕΡΟ ΜΕΡΟΣ

# Πολιτικές Ελέγχου Ζήτησης

	AT	BE	CY	DE	DK	EE	EL	ES	FI	FR	HU	IE	IT	LT	LV	MT	NL	NO	PL	PT	RO	SE	SK	SI	UJ
<b>ΙΑΤΡΟΙ</b>																									
Κατευθυντήριες Οδηγίες																									
Έλεγχος συνταγογράφησης																									
<b>ΑΣΘΕΝΕΙΣ</b>																									
Συμμετοχή στο κόστος																									
<b>ΦΑΡΜΑΚΟΠΟΙΟΙ</b>																									
Υποκατάσταση με γενόσημα																									

# Πολιτικές Ελέγχου Προσφοράς

	AT	BE	CY	DE	DK	EE	EL	ES	FI	FR	HU	IE	IT	LT	LV	MT	NL	NO	PL	PT	RO	SE	SK	SI	UJ
<b>ΤΙΜΟΛΟΓΗΣΗ</b>																									
Με βάση οικονομική αξιολόγηση																									
Με βάση τιμές σε άλλες χώρες																									
<b>ΕΛΕΓΧΟΣ ΔΑΠΑΝΗΣ</b>																									
Rebates , εκπτώσεις, επιστροφές																									
<b>ΑΠΟΖΗΜΙΩΣΗ</b>																									
Με τιμές αναφοράς /HTA																									



# Έμφαση στην Οικονομική Αξιολόγηση των Υπηρεσιών-Παροχών Υγείας

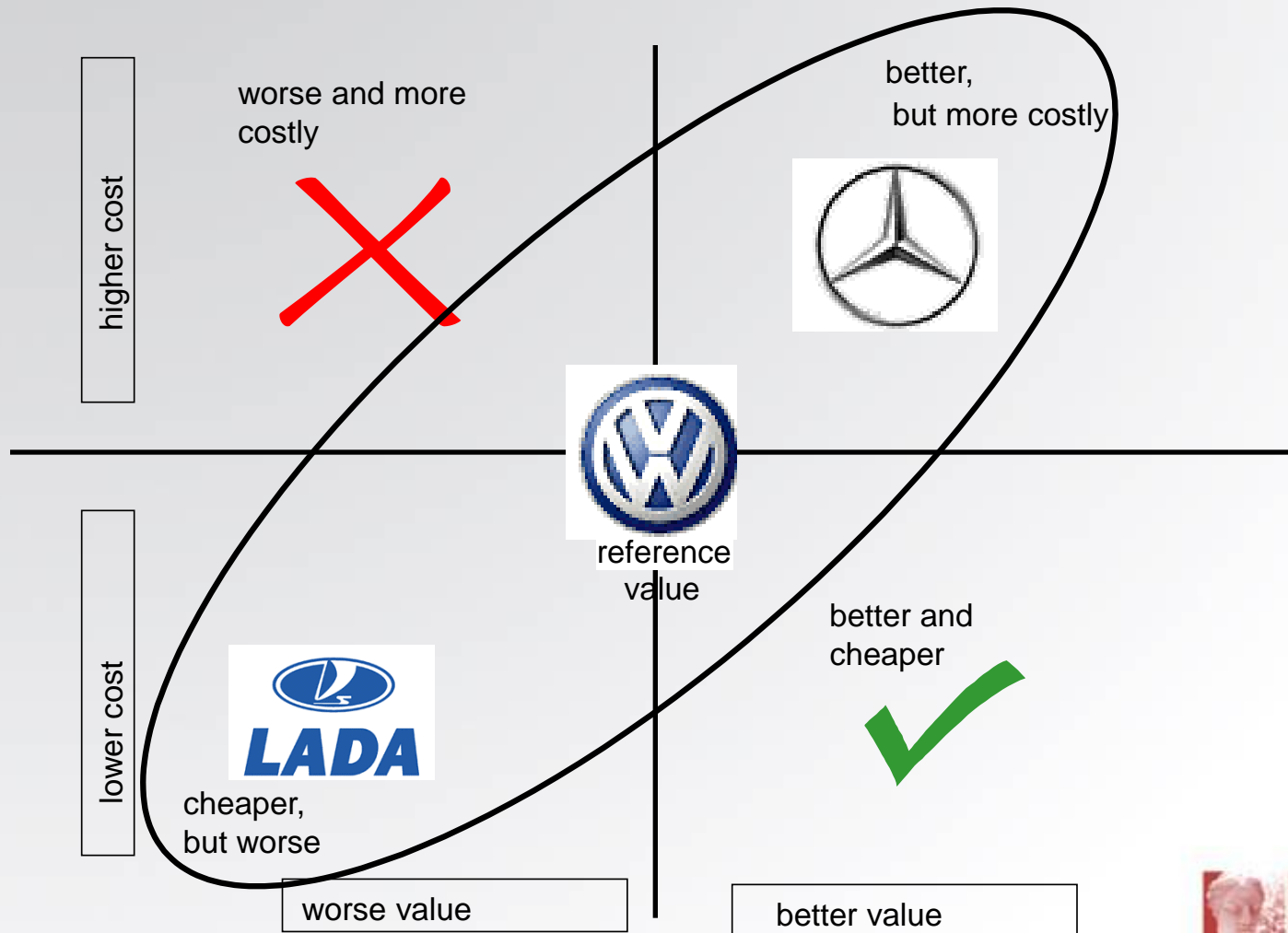
## Αποτελεσματικότητα, Ασφάλεια, Ποιότητα

- Αποφασίζουμε με καθαρά κλινικούς όρους που να επενδύσουμε τα χρήματα που διαθέτουμε για την υγεία
- Μεγιστοποιούμε το όφελος ανά άτομο εάν επιλέγουμε την αποτελεσματικότερη θεραπεία και υπάρχουν απεριόριστοι οικονομικοί πόροι
- Εάν οι πόροι είναι περιορισμένοι και δεν φτάνουν να καλύψουν όλες τις ανάγκες κάποιοι θα χάσουν

## Σχέση Κόστους - Αποτελεσματικότητας

- Αποφασίζουμε στην βάση της σχέσης κόστους και οφέλους από την παροχή μια υπηρεσίας ή μιας τεχνολογίας
- Απαιτείται διότι η πόροι είναι περιορισμένοι και δεν επαρκούν για να καλύψουν τις ανάγκες οι οποίες είναι απεριόριστες
- Ενδεχόμενα σε ατομικό επίπεδο κάποιοι να μην λάβουν την αποτελεσματικότερη θεραπεία, αλλά το κοινωνικό σύνολο είναι κερδισμένο

# We are paying more for better technology-outcome



# Η σχέση κόστους-οφέλους



Source: adapted from Prof. Matthias Graf von der Schulenburg



# Κριτήρια Αξιολόγησης

<b>0 ή λιγότερο</b>	<b>Εξοικονόμηση – Κυρίαρχη</b>
<b>1 - 20,000</b>	<b>Εξαιρετικά ελκυστική</b>
<b>20,001 - 40,000</b>	<b>Ελκυστική</b>
<b>40,001 - 60,000</b>	<b>Οριακά</b>
<b>60,001 - 100,000</b>	<b>Ακριβή</b>
<b>&gt; 100,000</b>	<b>Απαγορευτική</b>

# Η Σχέση C/E Διαφέρει και η Επιλογή Εξαρτάται από το Πόσο Διατιθέμεθα/Μπορούμε να Πληρώσουμε

VOLUME 25 • NUMBER 2 • JANUARY 10 2007

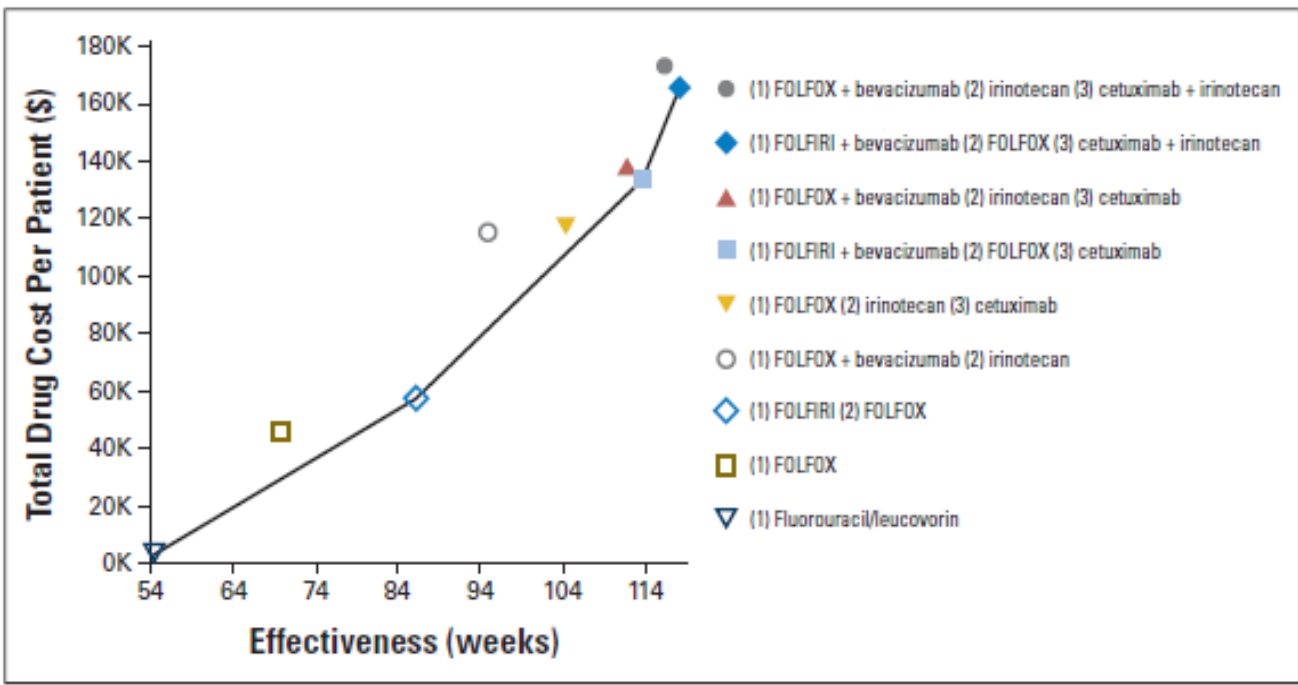
JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

## Cost of Cancer Care: Issues and Implications

Neal J. Meropol and Kevin A. Schulman

Cost of Cancer Care



**Fig 3.** Cost effectiveness of colon cancer treatment. Reprinted with permission.<sup>21</sup> FOLFOX, oxaliplatin, leucovorin (LV) infusional fluorouracil (FU); FOLFIRI, LV, infusional FU, and irinotecan.

## Consultations

- ▶ MoorLDI2 Burns Imager - a laser Doppler blood flow imager for the assessment of burn wounds: medical technologies consultation
- ▶ Follicular non-Hodgkin's lymphoma - rituximab: appraisal consultation
- ▶ Thrombocytopenic purpura - romiplostim: second appraisal consultation
- ▶ CG47 Feverish illness in children: review proposal consultation
- > [See all consultations](#)
- > [Read how NICE involves patients and the public](#)

[Join a committee](#)[Attend a meeting](#)[Any questions?](#)[Consultancy services](#)

# Welcome to the National Institute for Health and Clinical Excellence

NICE is an independent organisation responsible for providing national guidance on promoting good health and preventing and treating ill health.

**NHS  
Evidence**

NHS Evidence helps you find, access, and use high quality clinical information.

> [Search NHS Evidence](#)

## Guidance latest

## Guidance implementation

## Quality initiatives



- ▶ SeQuent Please balloon catheter for in-stent coronary restenosis
- ▶ Preventing unintentional injuries among under-15s in the home
- ▶ Preventing unintentional road injuries among under-15s: road design
- > [See all latest guidance](#)

## NICE cost-saving support



NICE has identified 23 sets of recommendations that, if fully implemented, could help the NHS to save millions of pounds, whilst maintaining or improving the quality of care.

- ▶ [Find out more about NICE and cost saving](#)  
2 Nov 2010

## Latest news



- ▶ NHS Evidence: Helping students identify high-quality information  
9 Dec 2010
- ▶ NICE gives green light to balloon catheter, in first medical technology guidance  
6 Dec 2010
- > [See all latest news](#)

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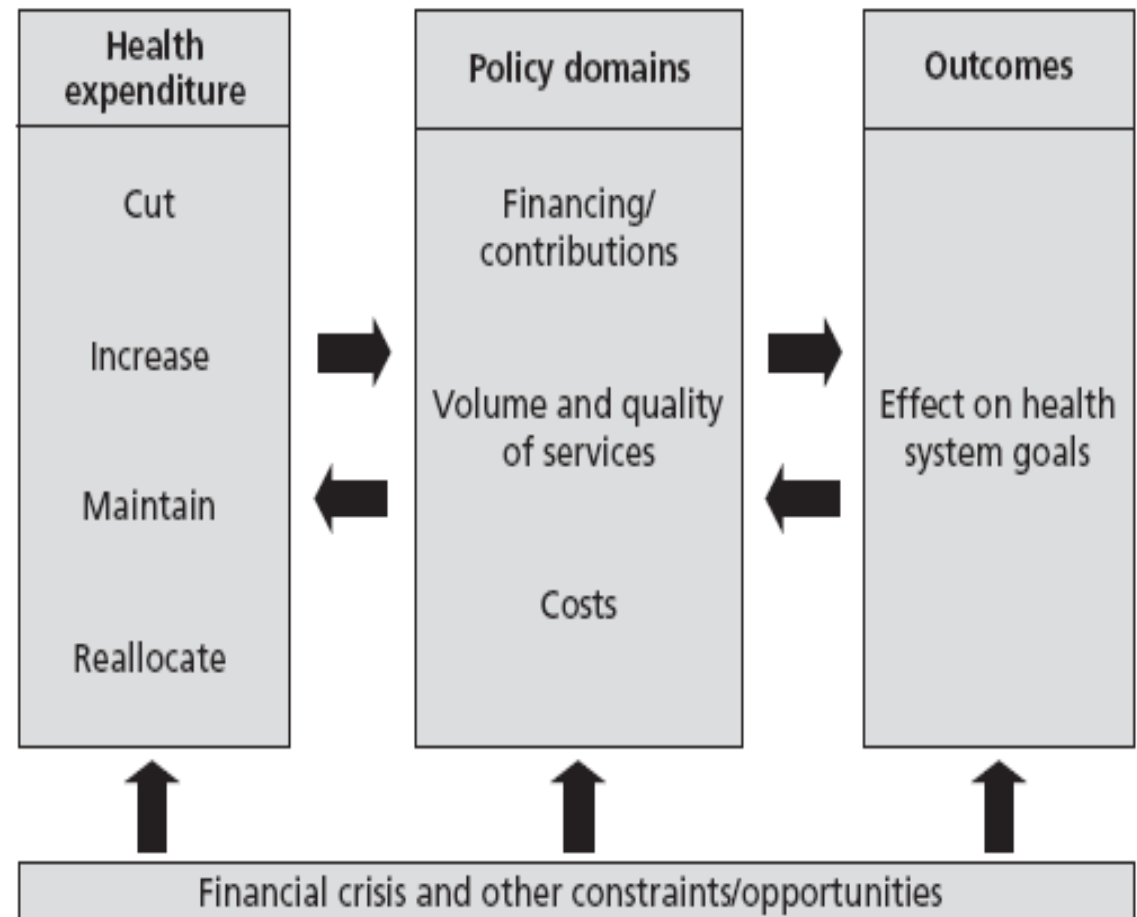
# ΕΞΟΡΘΟΛΟΓΙΣΜΟΣ ΤΗΝ ΠΕΡΙΟΔΟ ΤΗΣ ΚΡΙΣΗΣ

ΤΡΙΤΟ ΜΕΡΟΣ

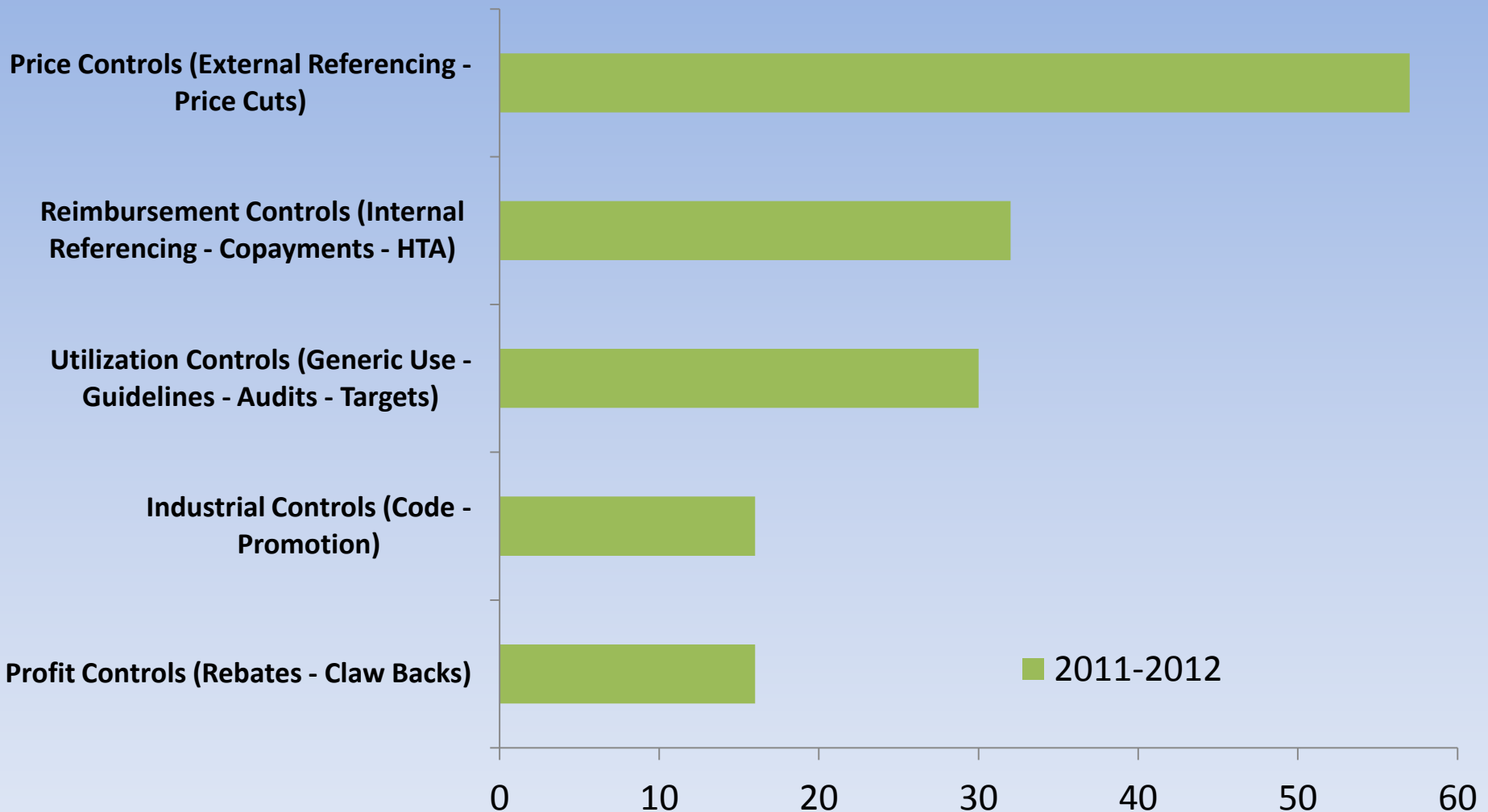
# Health policy responses to the financial crisis in Europe

Philipa Mladovsky, Divya Srivastava,  
Jonathan Cylus, Marina Karanikolos,  
Tamás Evetovits, Sarah Thomson,  
Martin McKee

Fig. 1. Health policy responses to the financial crisis and other economic shocks



# Survey of Most Common Mechanisms to Sustain Pharmaceutical Expenditure in 2011-12 (53 countries – 300 policies)

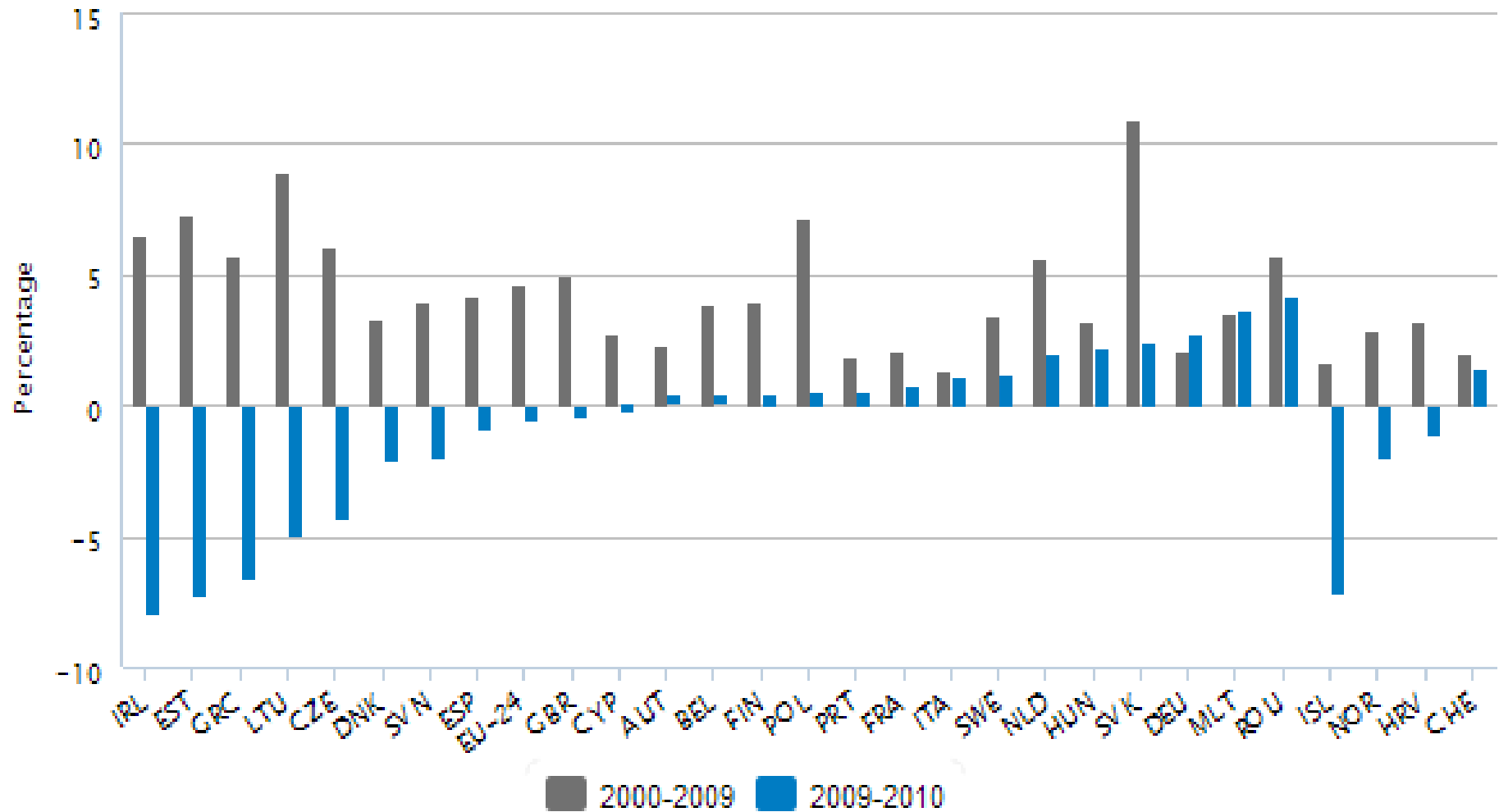


# Health spending in Europe falls for the first time in decades

## Health spending in the EU falls in 2010

Annual growth rate in health expenditure per capita

**Active  
CHART**



# ΣΥΣΤΗΜΑ ΥΓΕΙΑΣ ΚΑΙ ΠΑΡΟΧΕΣ ΠΡΙΝ ΤΗΝ ΚΡΙΣΗ

ΤΕΤΑΡΤΟ ΜΕΡΟΣ



Chart 7.1.2. Annual average growth rate in real health expenditure per capita, 1997-2007

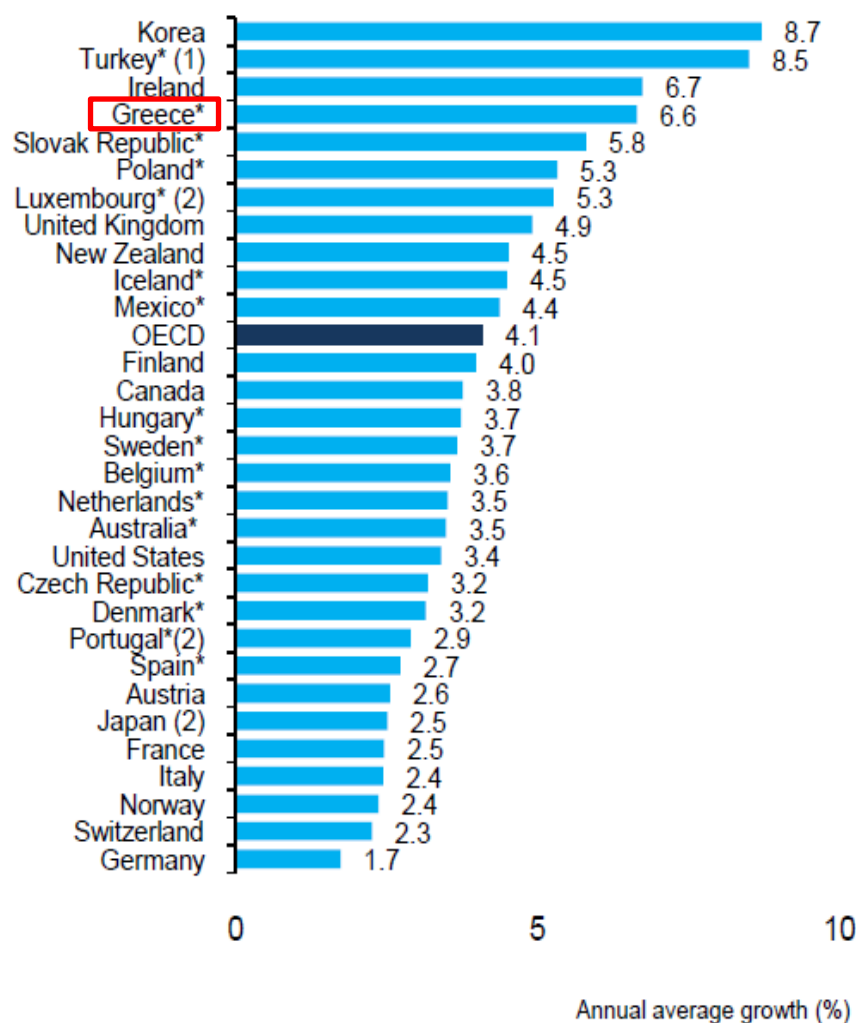
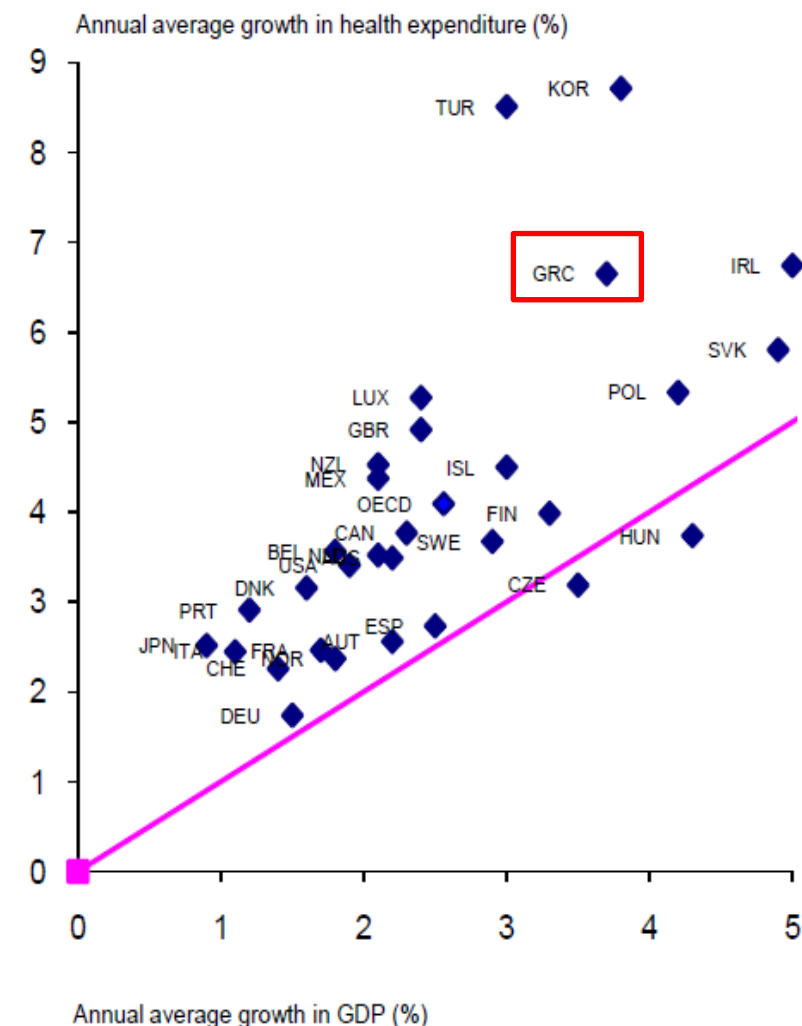


Chart 7.1.3. Annual average growth in real per capita expenditure on health and GDP, 1997 to 2007



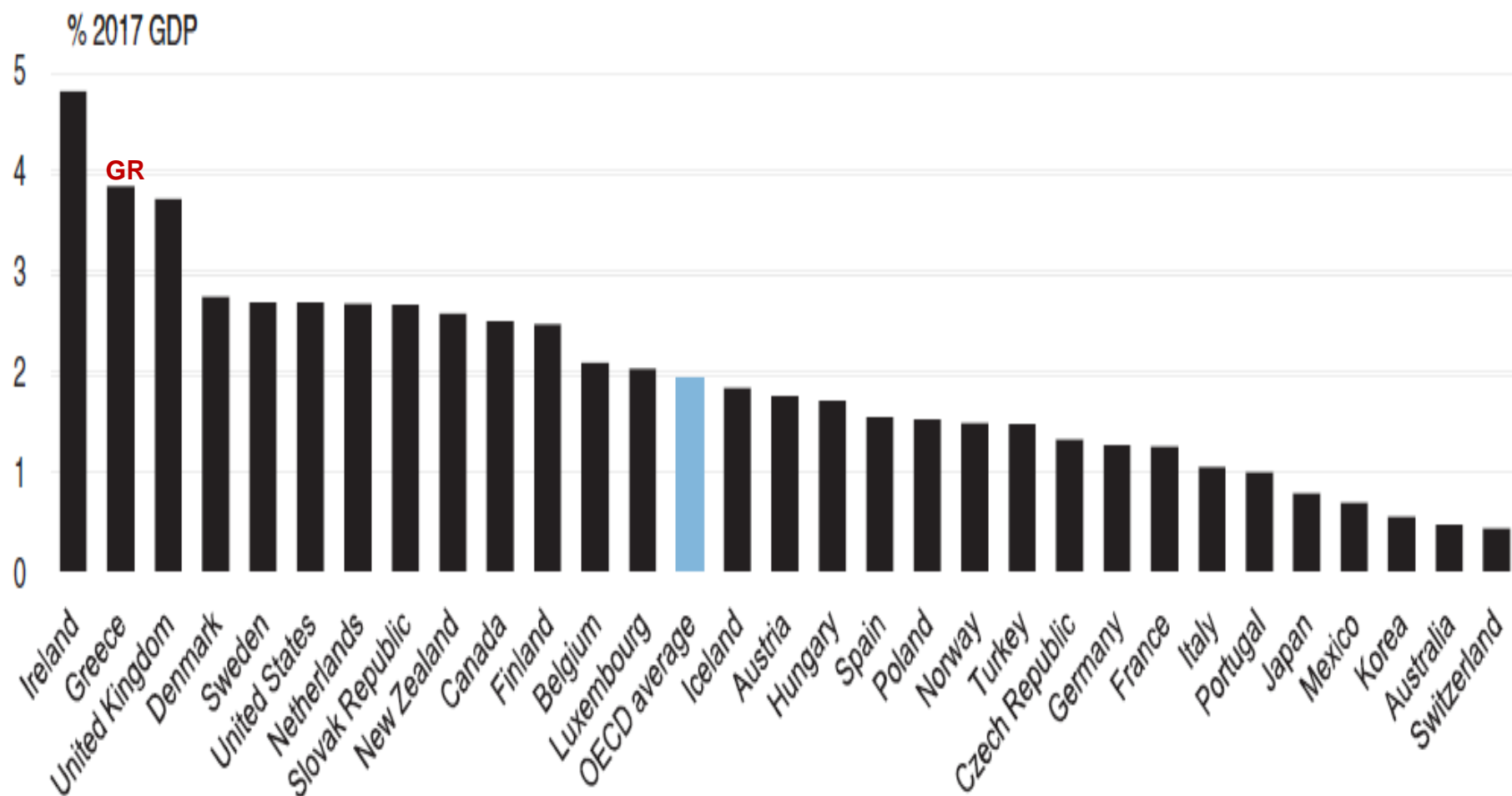
1. 1997-2005. 2. 1997-2006.

\* Growth rates adjusted. See box "Definition and deviations".

Source: OECD Health Data 2009.

# Αναποτελεσματικό Οικονομικά

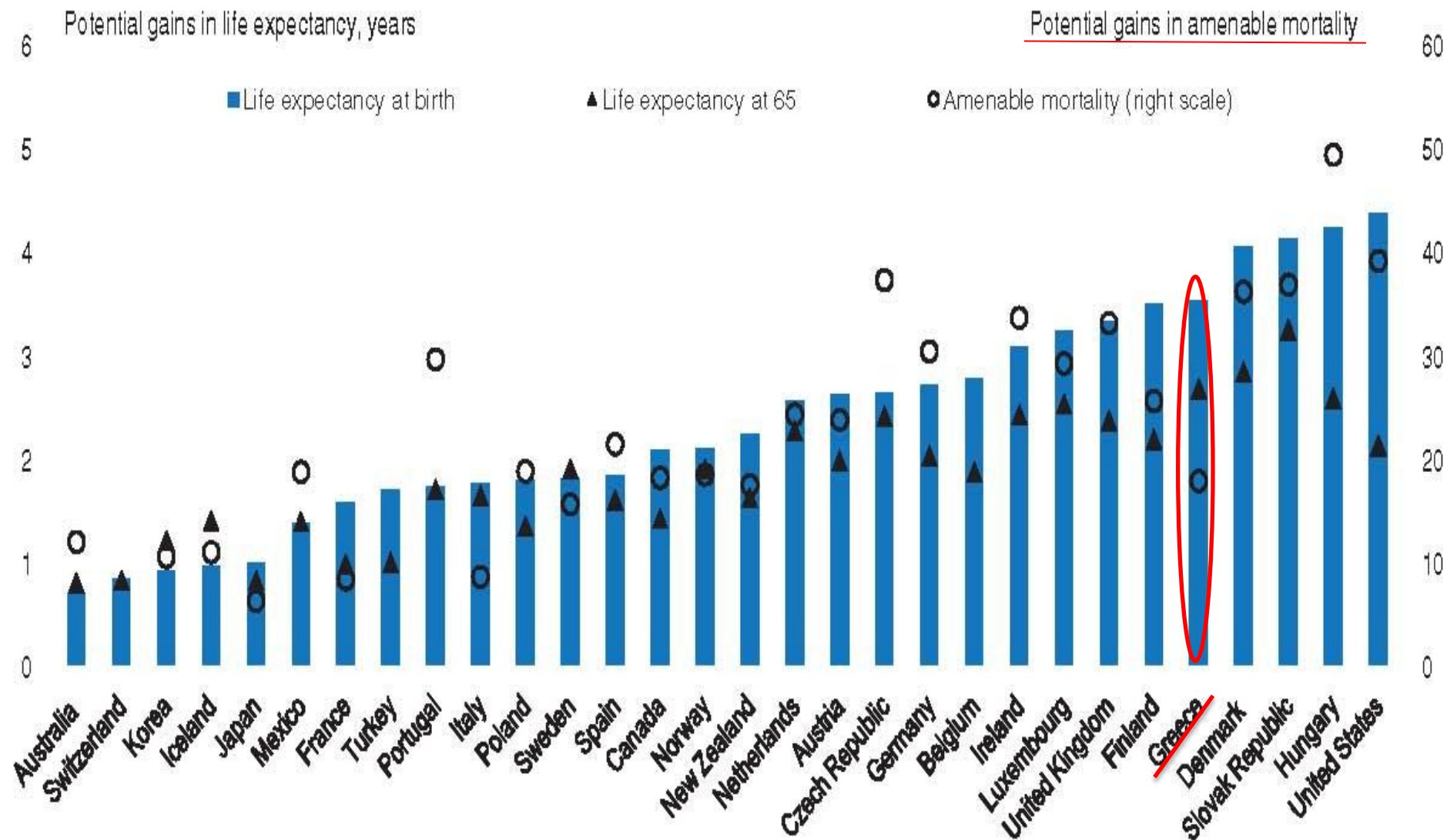
## C. Potential savings in public spending<sup>3</sup>



3. Potential savings represent the difference between a no-reform scenario and a scenario where countries would become as efficient as the best performing countries.

Source: OECD Health Data 2009; OECD calculations.

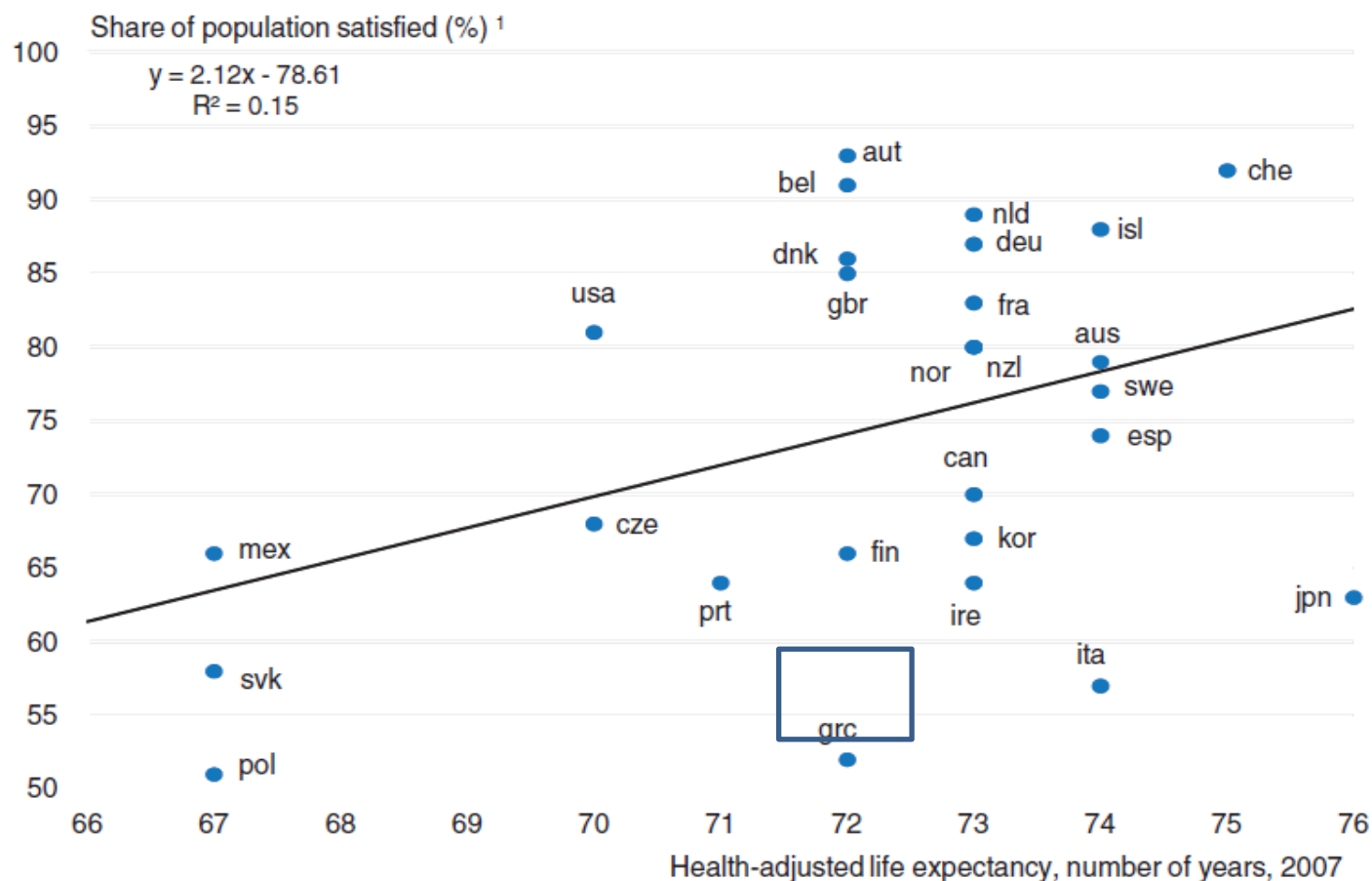
# Αναποτελεσματικό Υγειονομικά



In this panel, all DEAs were performed with two inputs: health care spending *per capita* and a variable referred to in Panel B as ENV. ENV is a composite indicator of the socio-economic environment (GDP *per capita*, educational attainment) and lifestyle factors (nitrogen oxide emissions, consumption of fruit and vegetables, lagged consumption of alcohol and tobacco – 1990 data). All DEAs refer to 2007 except in the case where amenable mortality rates were taken as the outcome since these are only available until 2003 and for 27 countries.

# Χαμηλή Ικανοποίηση Χρηστών

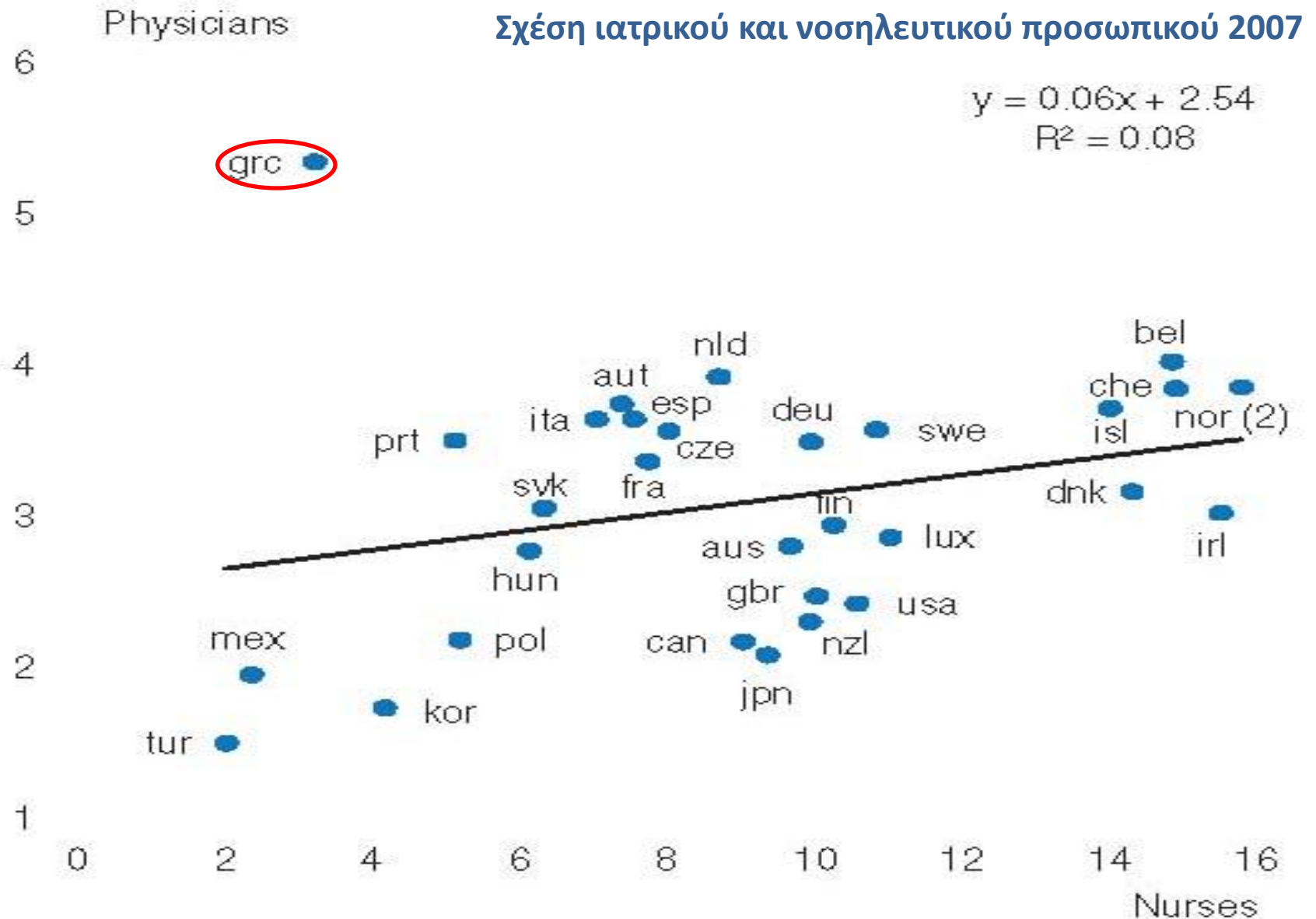
Figure 1.6. Public satisfaction and health-adjusted life expectancy



1. Share of population satisfied with availability of quality health care, 2008.

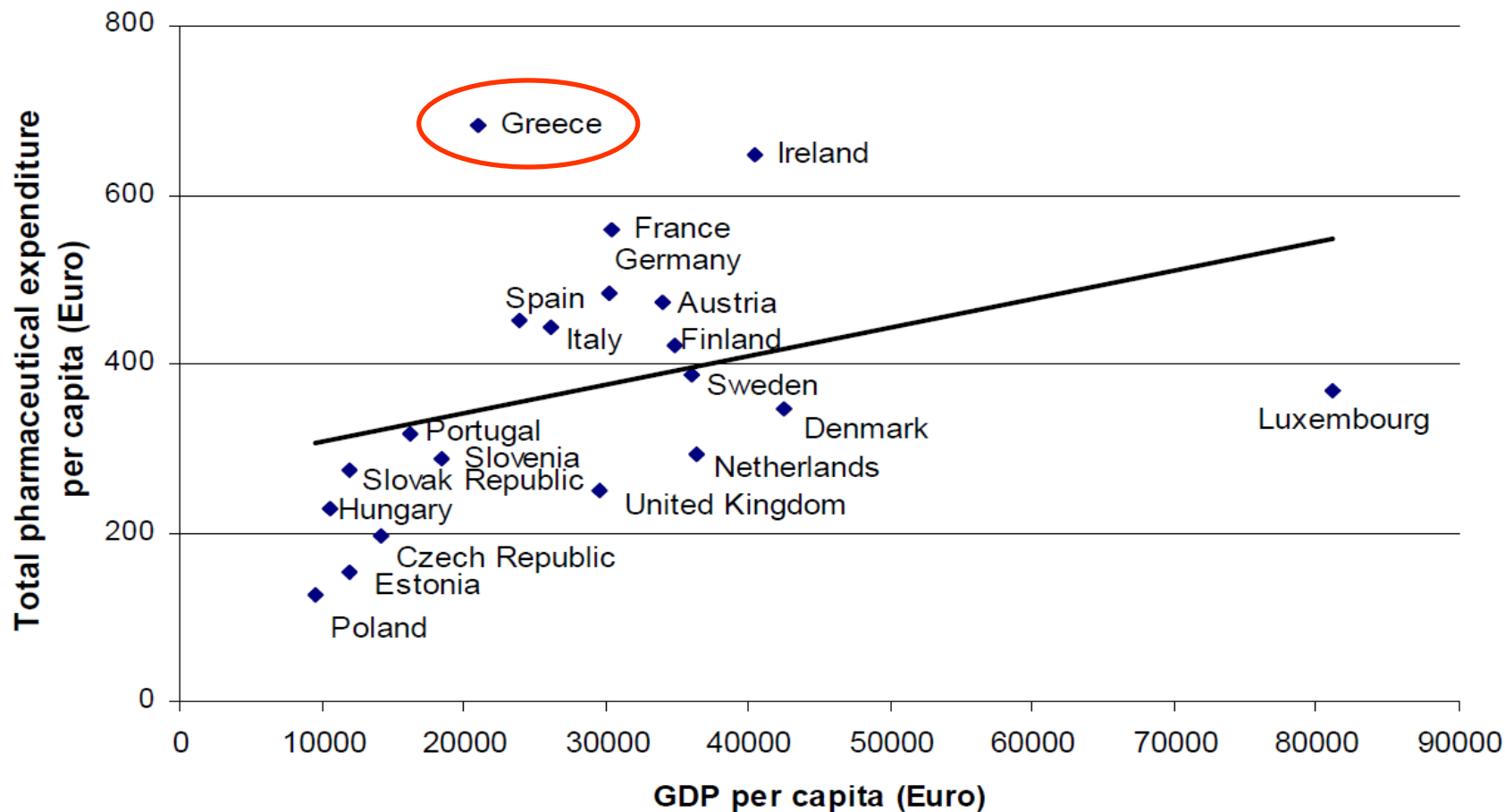
Source: WHO, *World Health Statistics 2010*; OECD Health Data 2009.

# Αναποτελεσματικό στην Κατανομή Ανθρωπίνων Πόρων



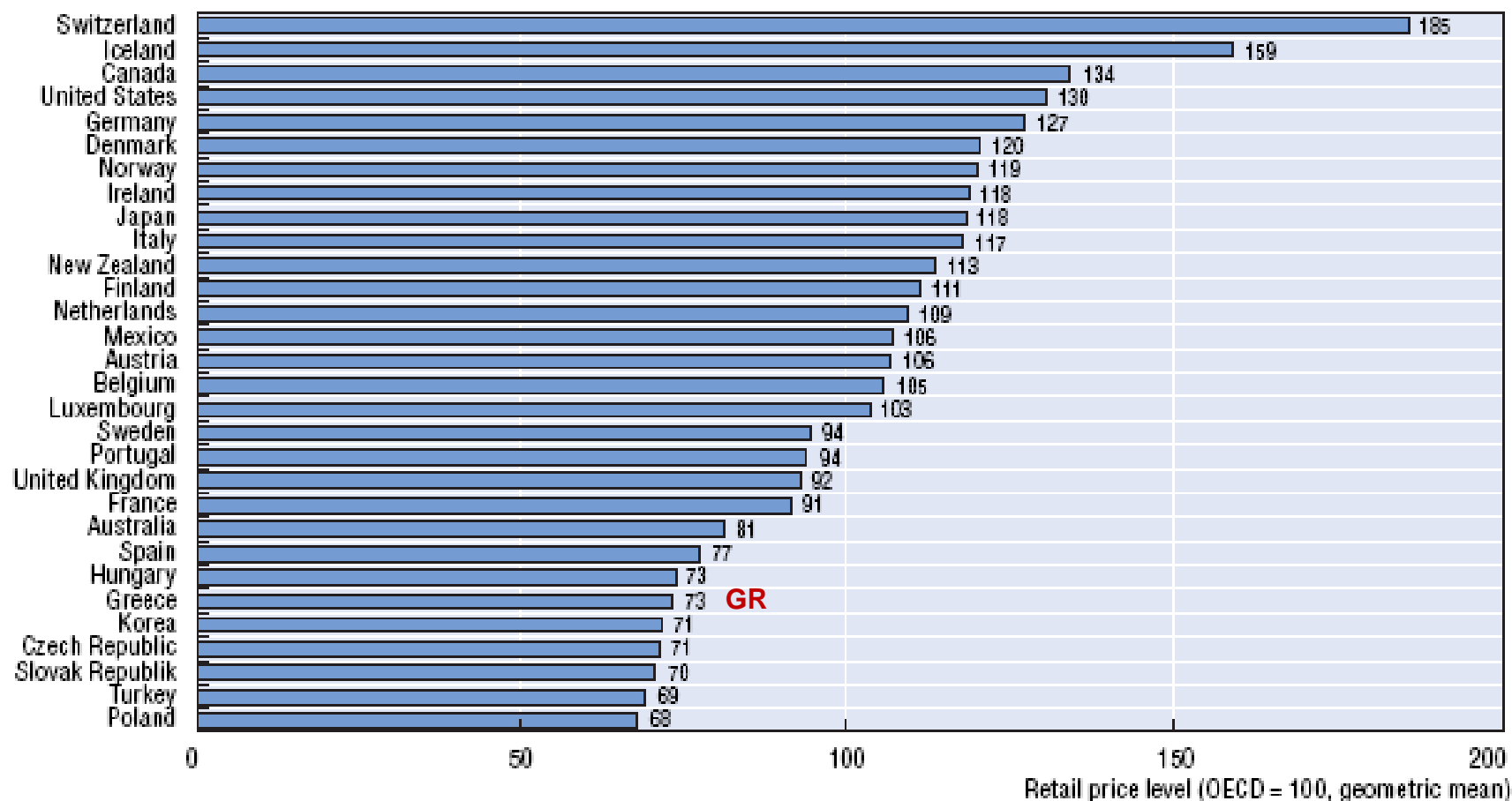
# Υψηλή Φαρμακευτική Δαπάνη

Figure 5: Pharmaceutical expenditure per capita (Euro) and GDP per capita, 2008



# Παρότι οι Τιμές Ήταν Σχετικά Χαμηλές

Figure 1.8. **Relative retail pharmaceutical price levels in OECD countries, 2005**

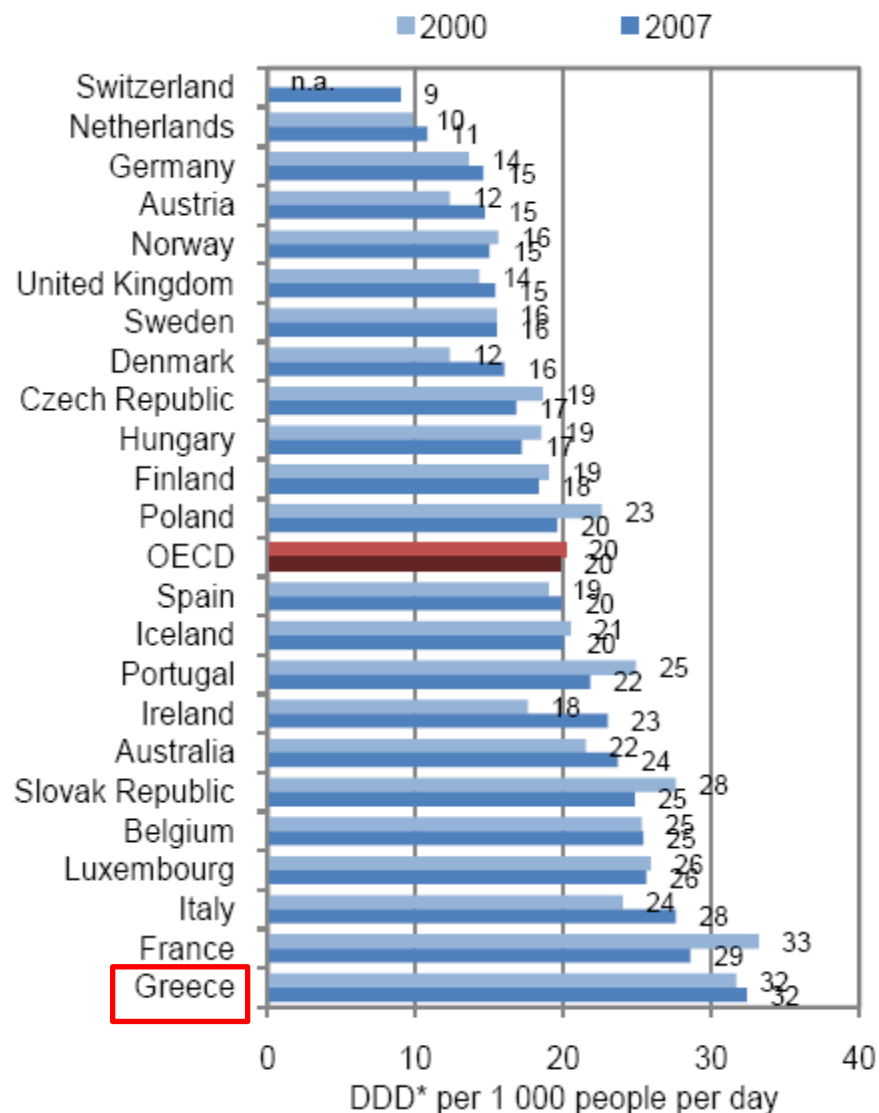


Note: Prices were converted to a common currency (USD) using the 2005 average exchange rate.

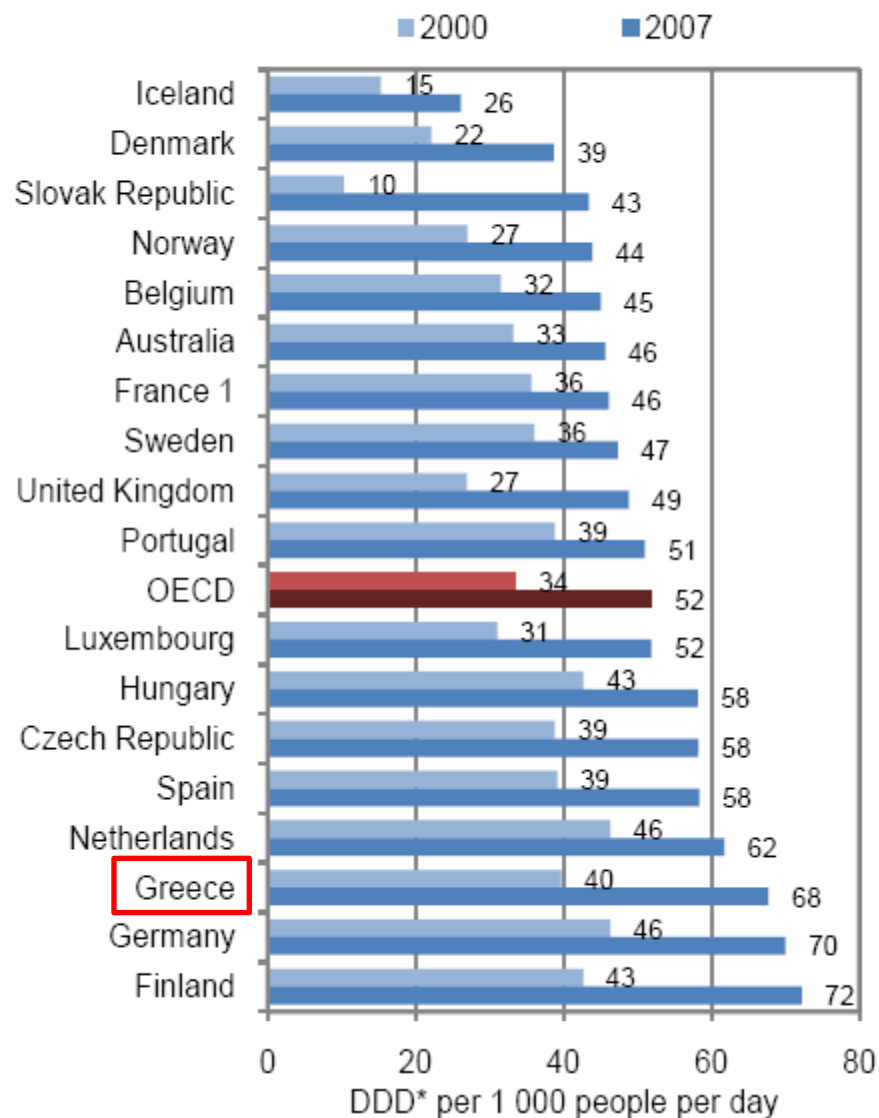
Source: Eurostat-OECD Purchasing Power Parity Programme, 2007.

# Η Ποσότητες Ήταν Μάλλον Μεγάλες !

4.10.4. Antibiotics consumption, DDD\* per 1 000 people per day, 2000 and 2007 (or nearest year)



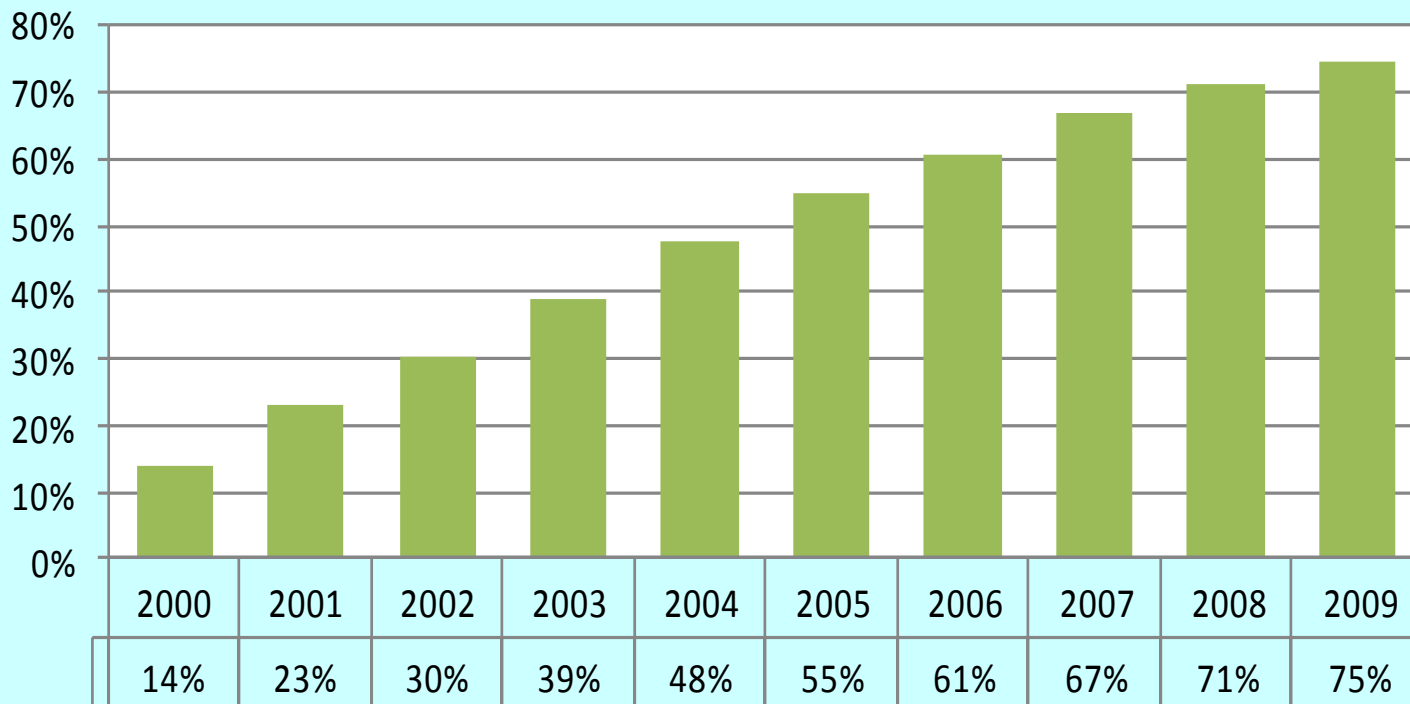
4.10.1. Antidiabetics consumption, DDD\* per 1 000 people per day, 2000 and 2007 (or nearest year)





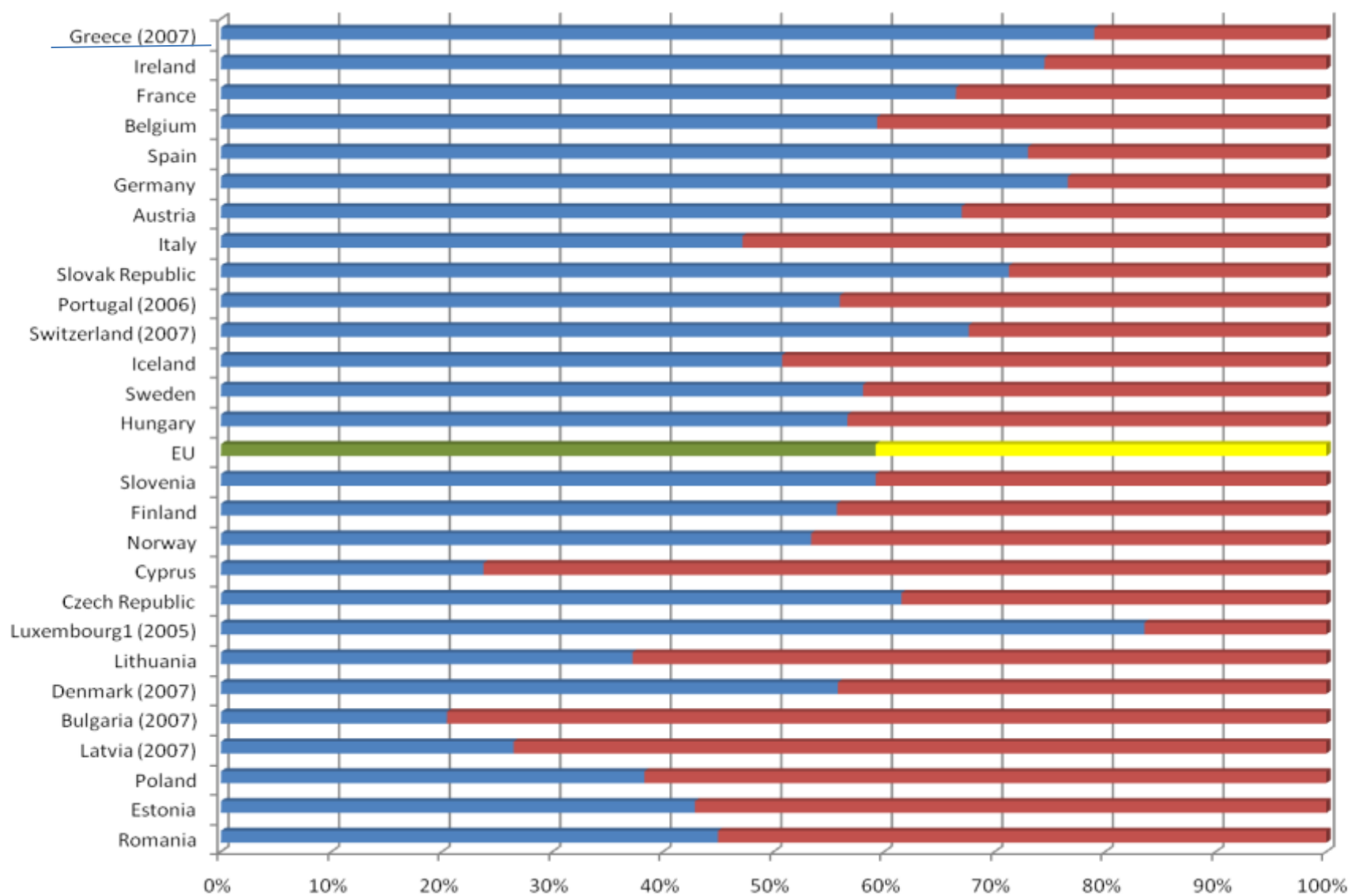
# Υποκατάσταση και Αυξημένη Χρήση Νεότερων/Ακριβότερων Φαρμάκων

Cumulative percent of contribution of new drugs (launch after 1999) in total community drug use



Source: ΙΦΕΤ/IMS 2010

# Χαμηλή Συμμετοχή Ασθενών

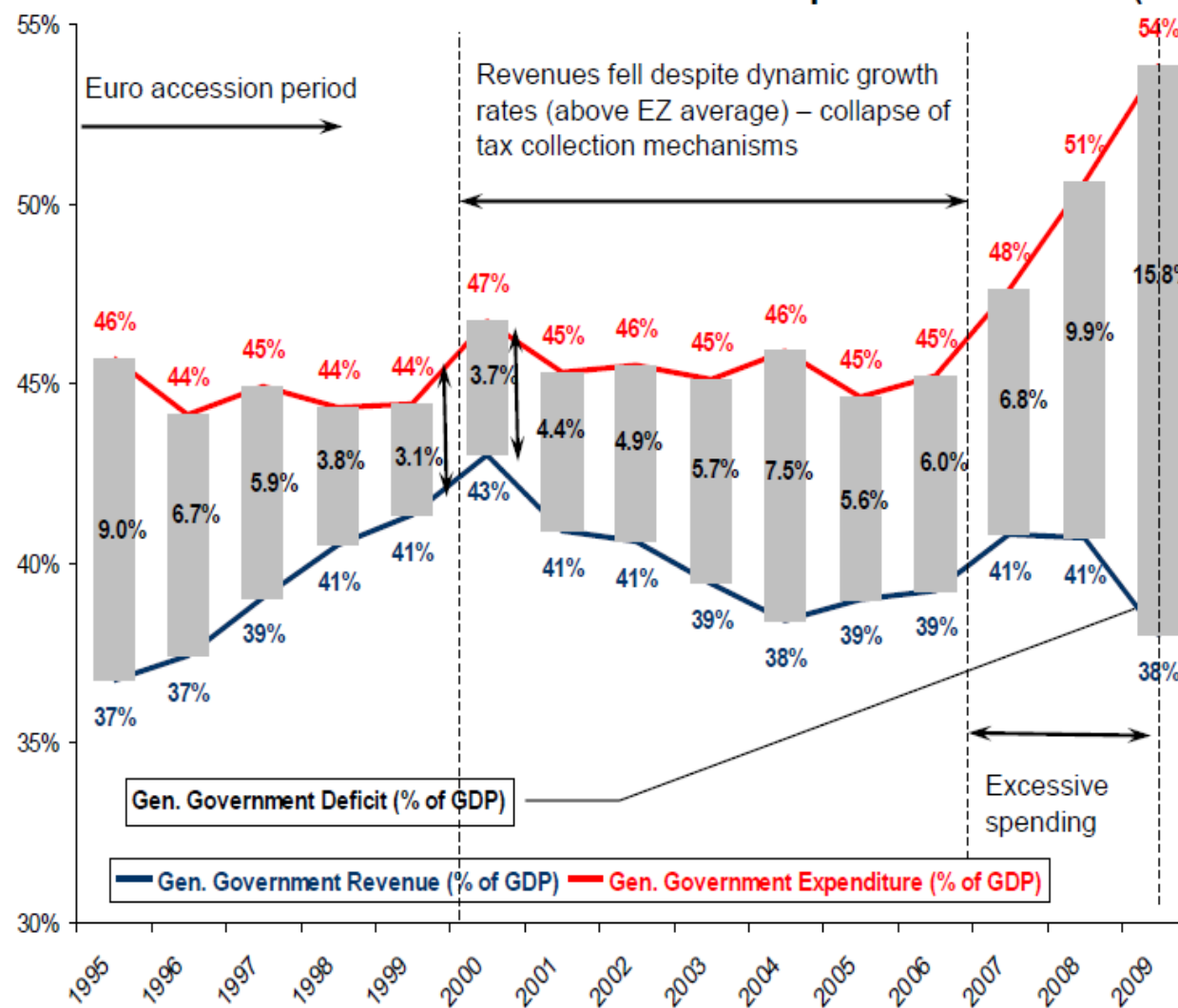


# ΣΥΣΤΗΜΑ ΥΓΕΙΑΣ ΚΑΙ ΠΑΡΟΧΕΣ ΤΗΝ ΕΠΟΧΗ ΤΟΥ ΜΝΗΜΟΝΙΟΥ

ΠΕΜΠΤΟ ΜΕΡΟΣ

# Fiscal Derailment: The lost decade

## Gen. Government Revenue / Expenditure / Deficit (% of GDP)



03/13/2009

Print | E-Mail | Feedback

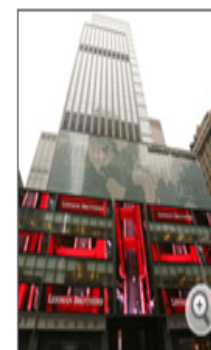
Interview With Lehman Brothers CEO Bryan Marsal

### 'The Global Banking Community Had a Heart Attack'

Bryan Marsal, head of restructuring firm Alvarez & Marsal, has been liquidating assets for Lehman Brothers, the investment bank that collapsed last fall. He talked to SPIEGEL ONLINE about the reasons for the collapse, mistakes made by US leaders and the lessons of the financial crisis.

**SPIEGEL ONLINE:** Lehman filed for bankruptcy on September 15th, 2008. How did you take over?

**Marsal:** I was watching a football game when I received a call from the board of directors of Lehman Brothers. This was at 10:30 at night on September 14th, and they asked me: Would I take on responsibility for the wind-down of Lehman?



Lehman Brothers headquarters, New York, in better times.

**SPIEGEL ONLINE:** How did you react?

**Marsal:** I said yes. And my question to them was: How much planning has gone into this bankruptcy? Their response was: This phone call is the first planning we have done.

**SPIEGEL ONLINE:** This must have been quite a shock.

**Marsal:** Well, when you figure the assets of this entity were \$651 billion (€509 billion), you would have expected there would be a lot of planning going into it.

**SPIEGEL ONLINE:** They were apparently

# EUROPEAN ECONOMY

Occasional Papers 72 | December 2010



## The Economic Adjustment Programme for Greece Second review – autumn 2010

Directorate-General for Economic and Financial Affairs

# Health care spending is a #1 target

## Annex 7: Statement by the European Commission, the ECB and IMF on the Second Review Mission to Greece

November 23, 2010

Our overall assessment is that the program remains broadly on track. The end-September quantitative criteria have all been met. While challenges remain, significant progress has been made, particularly in reducing the fiscal deficit.

Regarding the outlook, the economy is expected to begin turning around in 2011. Wage and price inflation is beginning to moderate, setting the stage for improvements in competitiveness.

In the fiscal area, the deficit reduction by 6 percent of GDP in 2010 is larger than the initially targeted change. At the same time, weaker-than-projected revenue collection and data revisions for 2009 mean that an extra effort will be needed to meet the deficit target of 7.5 percent of GDP in 2011, which the government has reaffirmed. New measures have been agreed to broaden tax bases and eliminate wasteful spending, particularly in the areas of:

- Health spending—which is inefficient relative to other euro zone countries;
- State enterprises—which are a heavy burden on the economy with perennial losses for Greek taxpayers; and
- Tax administration—which has instruments now coming into place to strengthen compliance.

# Παρεμβάσεις Συνοπτικά

## Στόχος Δαπάνη < 6% ΑΕΠ, Φάρμακο: 1% ΑΕΠ

### Νοσοκομεία

- Χάρτης υγείας, συγχωνεύσεις, μηχανοργάνωση, ολοήμερη λειτουργία, έλεγχος αναλωσίμων, διπλογραφικό & αναλυτική λογιστική, προμήθειες, κωδικοποιήσεις, e-prescription, γενόσημα 50% ποσοτήτων, συνταγογράφηση με δραστική, μετακίνηση αρμοδιοτήτων φαρμάκου στο ΥΓΚΑ,, mobility προσωπικού, ανακοστολόγηση και ανατιμολόγηση ιατρικών πράξεων και υπηρεσιών, διαγωνισμοί φαρμάκων, συνταγολόγια, κατευθυντήριες οδηγίες, λίστες και σύστημα τιμών αναφοράς φαρμάκων, rebates, περιθώρια συστήματος διανομής

### Ασφαλιστικό Σύστημα

- Ηλεκτρονική συνταγογράφηση, ενοποίηση παροχών, e-prescription φαρμάκων & εξετάσεων, ΣΥΠΣΥ, ΕΟΠΥΥ, αξιολογήσεις δαπανών, μείωση τιμών φαρμάκων, γενόσημα, μείωση περιθωρίων φαρμακοποιών, χονδρεμπόρων, άρση πλαφόν, ανακοστολόγηση πράξεων



Νέα Μοντέλα Εξοικονόμησης Πόρων: “Αγαπητέ ασθενή για οικονομία, οι μάνατζερ μας ζητούν να κάνουμε επεμβάσεις χωρίς αναισθησία”





# Νέα μοντέλα κατανομής προσωπικού



# Greece: Unmet Need

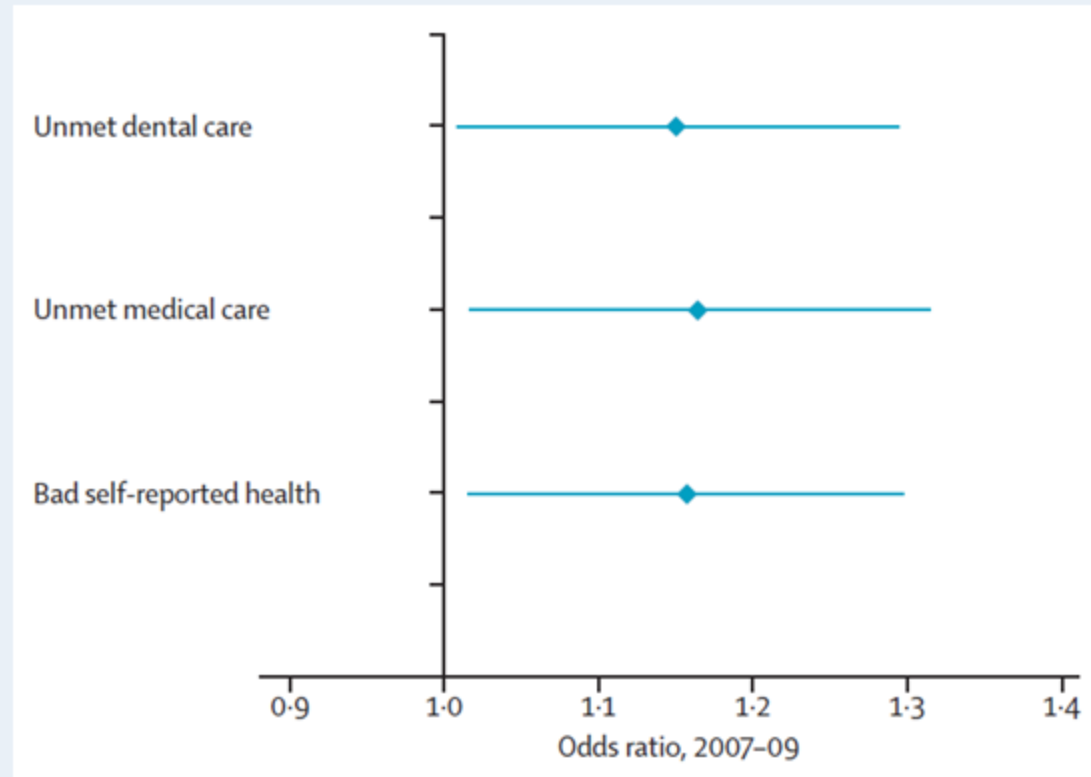
*(people who need care but do not get it)*

-15% rise in people not going to the doctor despite feeling it was necessary

-39% less likely to access to sickness benefits

-24% rise in public hospital admissions between 2009 and 2010

-25% reported decline in private hospital admissions



Source: Kentikelenis A, Karanikolos M, Papanicolas I, Basu S, McKee M, Stuckler D. Health effects of financial crisis: omens of a Greek tragedy. Lancet 2011

# **ΠΏΣ ΝΑ ΕΞΑΣΦΑΛΙΣΟΥΜΕ ΠΑΡΟΧΕΣ ΣΕ ΚΑΘΕΣΤΩΣ ΚΡΙΣΗΣ? Η ΠΕΡΙΠΤΩΣΗ ΤΗΣ ΡΕΥΜΑΤΟΕΙΔΟΥΣ ΑΡΘΡΙΤΙΔΑΣ**

**ΕΚΤΟ ΜΕΡΟΣ**

# Υψηλό Κόστος Ανά Ασθενή

Table 2-6 Mean estimated annual cost per patient (€ 2008)

Country	Total cost per patient	Direct cost (excl. biol)	Biologics	Indirect cost	Informal Care
	Mean, €	Mean, €	Mean, €	Mean, €	Mean, €
Austria	13,776	5,515	444	2,528	5,289
Belgium	15,770	3,959	2,222	4,606	4,983
Bulgaria	2,063	1,552	13	160	338
Cyprus	8,185	2,532	818	1,355	3,480
Czech Republic	6,047	3,144	616	670	1,618
Denmark	16,869	4,648	2,213	2,969	7,039
Estonia	3,929	1,742	254	556	1,377
Finland	13,965	4,243	1,645	2,448	5,631
France	20,522	10,252	1,475	1,284	7,512
Germany	18,791	7,261	1,284	2,576	7,670
Greece	11,460	5,551	1,952	1,466	2,492
Hungary	5,248	1,763	411	837	2,237
Iceland	21,135	5,885	2,005	3,299	9,946
Ireland	16,844	5,645	2,716	2,616	5,867
Italy	11,546	4,552	731	3,290	2,972
Latvia	3,159	1,728	254	352	825
Lithuania	3,371	1,688	254	426	1,003
Luxembourg	20,949	9,314	2,361	3,026	6,248
Malta	6,842	3,753	818	939	1,332
Netherlands	18,047	7,847	1,543	2,214	6,442
Norway	20,700	6,960	2,740	3,149	7,851
Poland	3,720	1,922	88	579	1,132
Portugal	7,492	4,453	818	1,070	1,151
Romania	2,170	1,187	170	272	542
Slovakia	4,263	2,052	549	502	1,160
Slovenia	7,888	3,797	648	1,099	2,344
Spain	9,944	5,383	1,443	1,456	1,662
Sweden	13,063	3,543	2,158	496	6,866
Switzerland	19,547	7,450	1,793	2,835	7,470
United Kingdom	11,997	5,265	888	2,837	3,008
Turkey	2,327	1,126	170	387	645
Average Europe	12,902	5,512	1,028	2,012	4,289
Western Europe	14,997	6,345	1,285	2,355	5,012
Eastern Europe	3,752	1,878	232	513	1,128



# Υψηλό Κόστος στα Συστήματα Υγείας

**Table 2-5 estimated annual cost of RA by country, total**

<i>Country</i>	<i>Total cost of RA (€ 2008)</i>	<i>Total prevalent cases of RA</i>
<i>Austria</i>	420,666,022	30,536
<i>Belgium</i>	618,317,047	39,209
<i>Bulgaria</i>	61,295,241	29,711
<i>Cyprus</i>	19,822,623	2,422
<i>Czech Republic</i>	223,950,063	37,037
<i>Denmark</i>	399,385,899	23,676
<i>Estonia</i>	20,133,404	5,124
<i>Finland</i>	339,073,147	24,279
<i>France</i>	4,653,453,492	226,750
<i>Germany</i>	6,179,460,256	328,844
<i>Greece</i>	487,911,658	42,574
<i>Hungary</i>	198,934,391	37,907
<i>Iceland</i>	22,929,557	1,085
<i>Ireland</i>	253,251,076	15,035
<i>Italy</i>	2,723,687,485	235,898
<i>Latvia</i>	27,707,292	8,771
<i>Lithuania</i>	41,166,056	12,213
<i>Luxembourg</i>	33,288,628	1,589
<i>Malta</i>	9,707,362	1,419
<i>Netherlands</i>	1,027,487,886	56,934
<i>Norway</i>	402,987,901	19,468
<i>Poland</i>	489,374,432	131,546
<i>Portugal</i>	295,031,406	39,379
<i>Romania</i>	162,387,179	74,832
<i>Slovakia</i>	74,879,157	17,567
<i>Slovenia</i>	58,854,828	7,461
<i>Spain</i>	1,586,356,683	159,535
<i>Sweden</i>	543,107,075	41,576
<i>Switzerland</i>	536,933,367	27,469
<i>United Kingdom</i>	3,163,265,560	263,672
<i>Turkey</i>	320,917,123	137,905
<i>Total EU27</i>	24,072,620,328	1,895,497
<i>Total Europe</i>	25,074,806,172	1,943,519
<i>Total Western Europe</i>	23,716,124,129	1,581,350
<i>Total Eastern Europe</i>	1,358,682,043	362,169

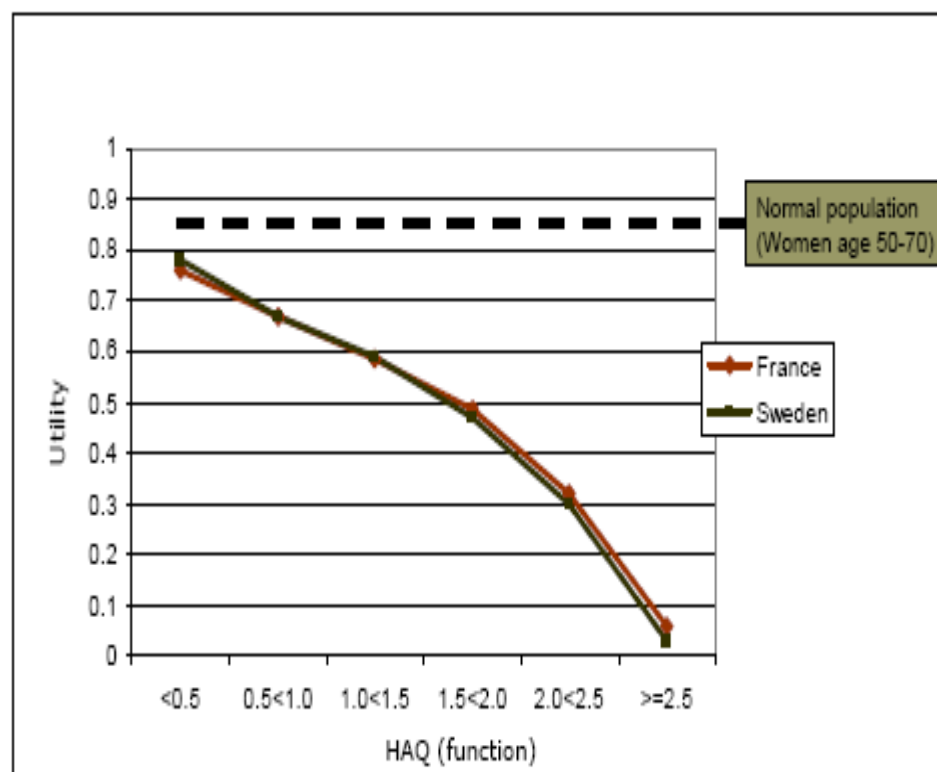


# Ποιότητα Ζωής Χαμηλότερη Από Καρκινοπαθείς

Table 1-6 - Utilities in different chronic diseases.

Disease	Mean utility	Sample size
<i>Other rheumatoid arthritis</i>	0.43	120
<i>Rheumatoid arthritis</i>	0.50	1487
<i>Multiple sclerosis</i>	0.56	13186
<i>Angina pectoris</i>	0.57	284
<i>Acute myocardial infarction</i>	0.61	251
<i>Atrial fibrillation and flutter</i>	0.61	189
<i>Chronic ischaemic heart disease</i>	0.64	789
<i>Gastro-oesophageal reflux disease</i>	0.67	216
<i>Crohn's disease (regional enteritis)</i>	0.69	73
<i>Essential (primary) hypertension</i>	0.69	82
<i>Malignant neoplasm of prostate</i>	0.72	83
<i>Non-insulin-dependent diabetes</i>	0.76	159
<i>Ulcerative colitis</i>	0.79	61

Source: adapted from Curry et al, Value in Health 2005



Source: Adapted from <sup>31, 37, 38</sup>  
Utility was measured in both studies using the EQ-5D.

Kobelt and Kasteng, Access to innovative treatments in rheumatoid arthritis in Europe, EFPIA, 2009

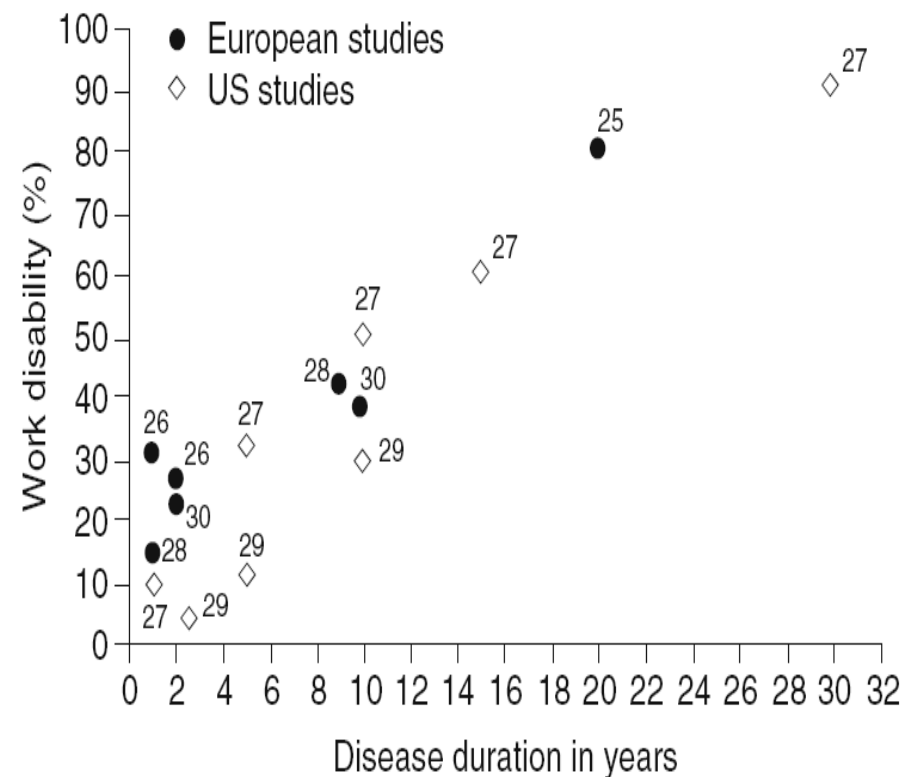
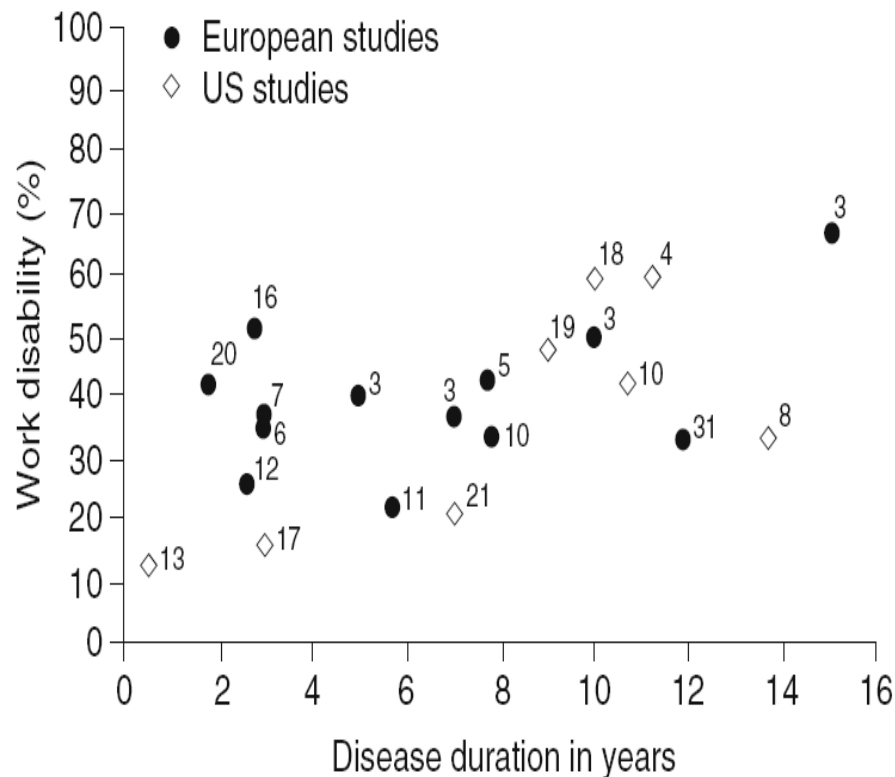
# Σοβαρή Επιβάρυνση στην Παραγωγική Ικανότητα

## The burden of illness of rheumatoid arthritis

Annelies Boonen • Johan L. Severens

S6

Clin Rheumatol (2011) 30 (Supl 1):S3–S8



**Fig. 3** Percentage of work disability with increasing mean disease duration in cross-sectional (*left*) and longitudinal (*right*) studies of RA patients with paid job before disease onset [9]. Reproduced with permission

# Thoughts on health economics in rheumatoid arthritis

Gisela Kobelt

*Ann Rheum Dis* 2007;**66**(Suppl III):iii35–iii39. doi: 10.1136/ard.2007.078964

Thoughts on health economics in rheumatoid arthritis

iii37

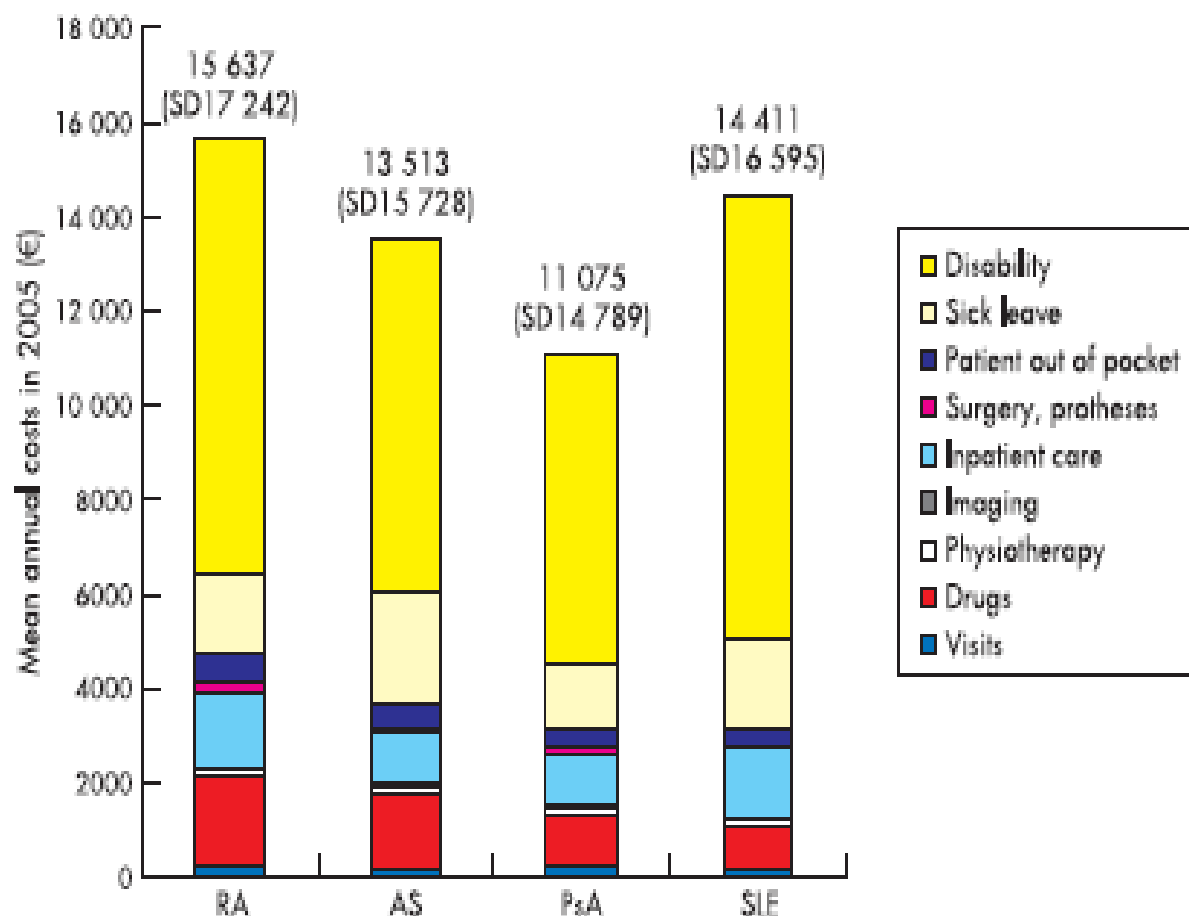


Figure 1 Cost structure in rheumatic diseases for patients <65 years in Germany (adapted from Huscher et al.<sup>2</sup>). AS, ankylosing spondylitis; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.



# ‘Ανεξάρτητα από την Χώρα το Έμμεσο Κόστος Κυριαρχεί

Economic implications of RA / G. Furneri et al.

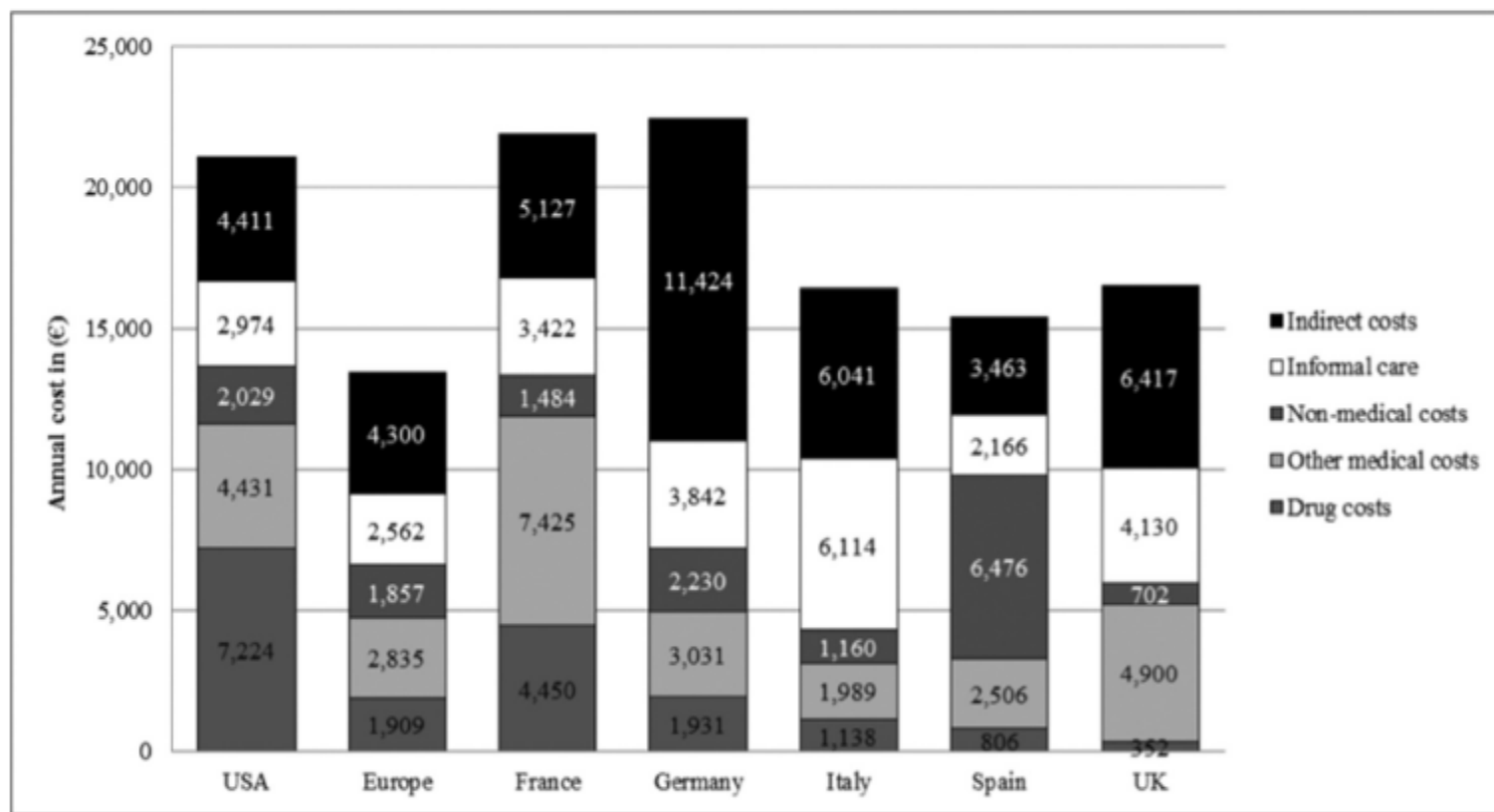
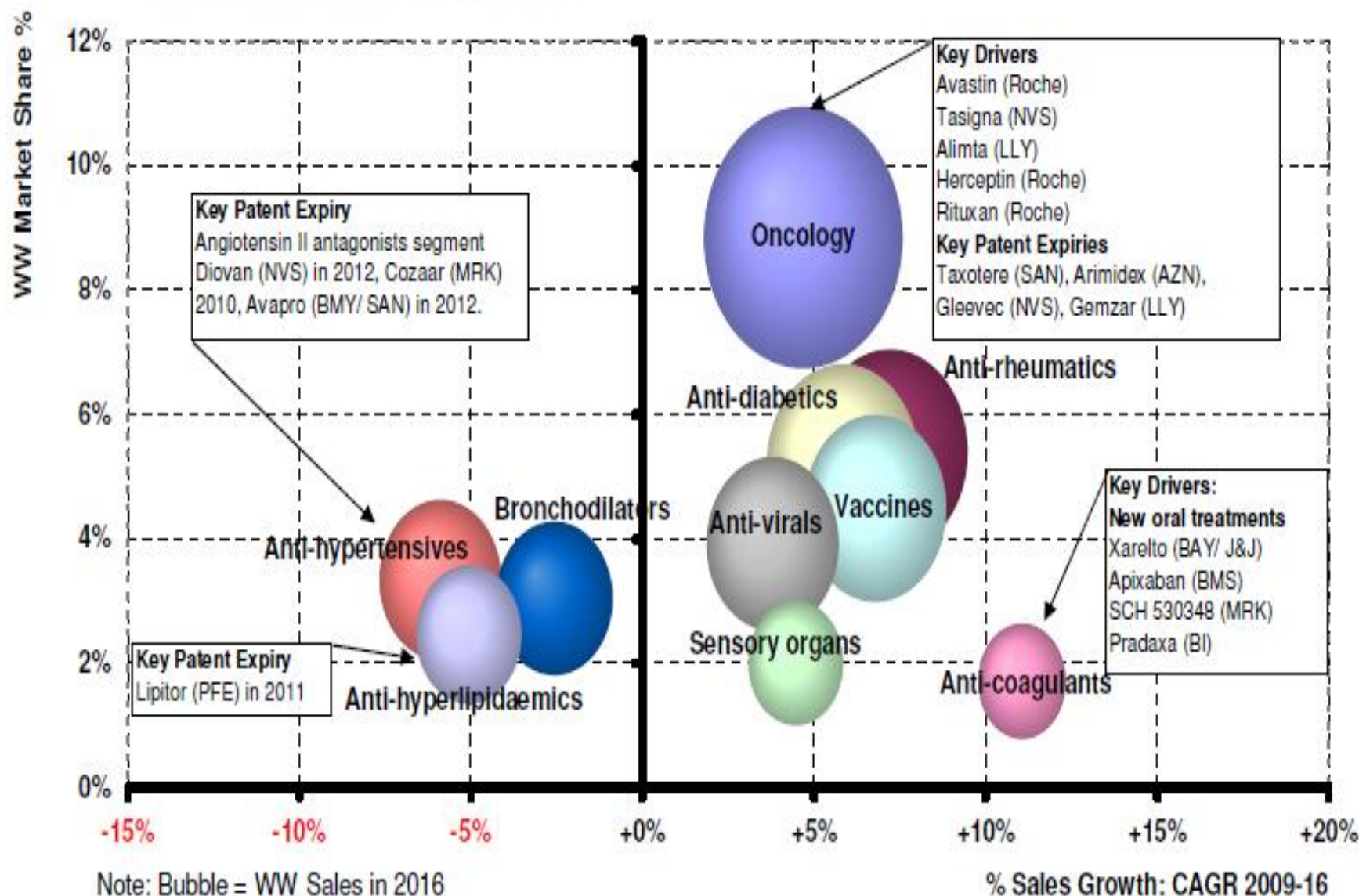


Fig. 2. Distribution of costs from a recent cost-of-illness review (adapted from 2).

# Analysis on Top 10 Therapy Areas in 2016, Market Share & Sales Growth (2009-16)

Source: EvaluatePharma® (30 APR 2010)



# RHEUMATOID ARTHRITIS

National clinical guideline for management  
and treatment in adults

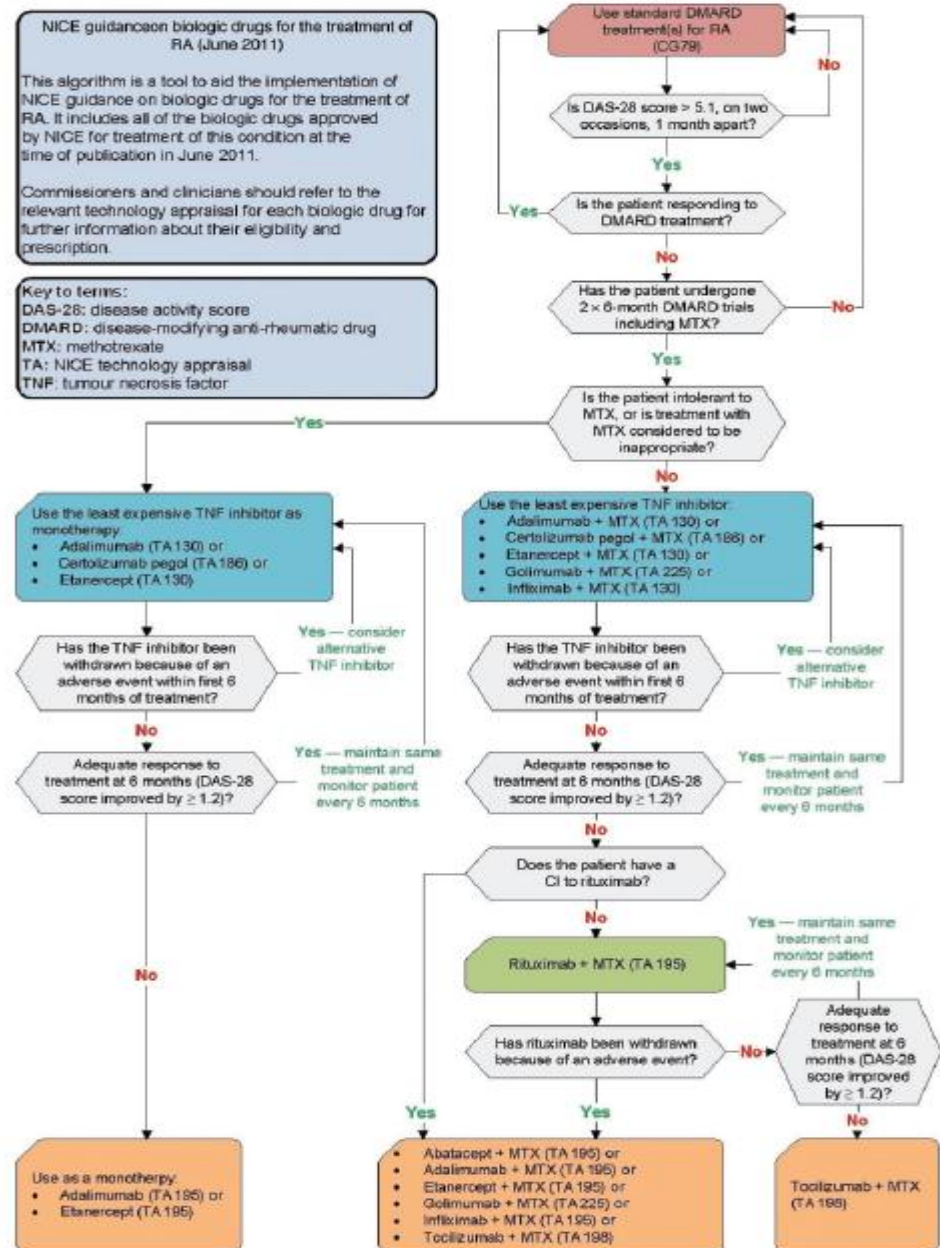
Published by



Royal College  
of Physicians

Setting higher medical standards

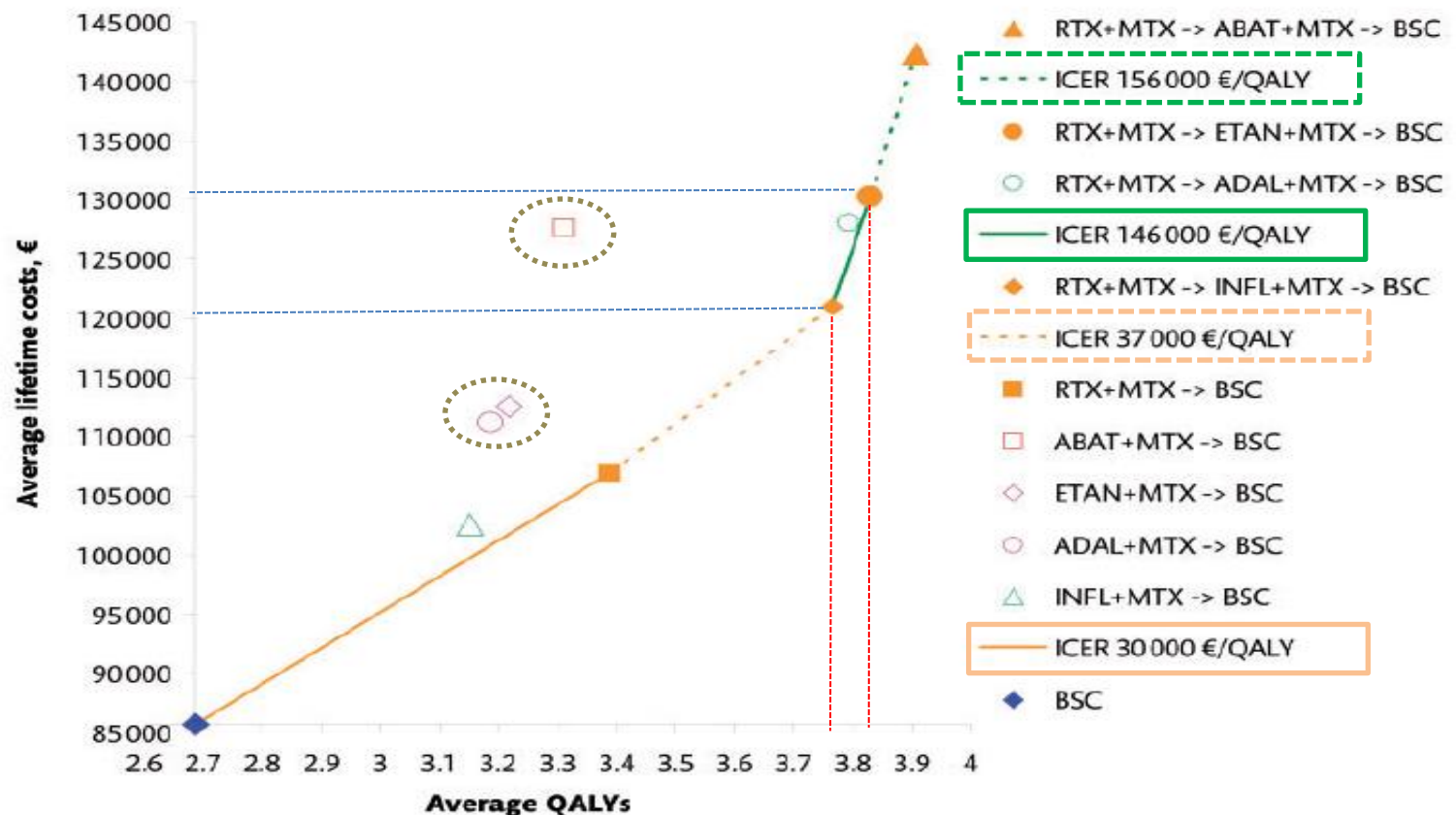
Fig. 1 Algorithm illustrating NICE guidance on biologic drugs for the treatment of RA. NICE (2011) algorithm: 'rheumatoid arthritis'. www.nice.org.uk. Reproduced with permission from NICE. Algorithm was accurate at the time of publication. CI: contraindication.



## Original article

**Cost–utility of different treatment strategies after the failure of tumour necrosis factor inhibitor in rheumatoid arthritis in the Finnish setting**Taru A. Hallinen<sup>1</sup>, Erkki J. O. Soini<sup>1</sup>, Kari Eklund<sup>2</sup> and Kari Puolakka<sup>3</sup>

**Fig. 1** The cost-effectiveness efficiency frontier (CEEF) represents the most efficient choices among the compared treatment strategies. The average costs and QALYs gained with BSC are given in the origin.







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# Best Practice & Research Clinical Rheumatology

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## The issue of comparators in economic evaluations of biologic response modifiers in rheumatoid arthritis

Nicole W. Tsao<sup>a</sup>, Nick J. Bansback<sup>b,c</sup>, Kam Shojania<sup>d</sup>, Carlo A. Marra<sup>a,b,\*</sup><sup>a</sup> Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada<sup>b</sup> Pharmacoeconomics Program, Centre for Health Evaluation and Outcomes Sciences, St. Paul's Hospital, Vancouver, BC, Canada<sup>c</sup> School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada<sup>d</sup> Division of Rheumatology, Department of Medicine, University of British Columbia, Vancouver, BC, Canada

### Keywords:

Rheumatoid arthritis

Economic evaluation

Cost effectiveness

Cost-utility analysis

TNF alpha inhibitors

Disease-modifying anti-rheumatic drugs

**Introduction:** Over the last decade, a number of biologic response modifiers (BRMs) have emerged and transformed rheumatoid arthritis (RA) management. Due to their relatively high costs, economic evaluations have attempted to determine their place in the RA treatment armamentarium. This article reviews three key areas where changes to the treatment paradigm challenges findings of existing economic evaluations.

**Methods:** We performed a literature search of economic evaluations examining BRMs approved for use in North America for RA. Only economic evaluations that examined relevant direct costs and health outcomes were included. Data were extracted and summarised, then stratified by patient population and comparators. Reported incremental cost-effectiveness ratios (ICERs) were compared across studies.

**Results:** It appears that tumour necrosis factor (TNF) alpha inhibitors are less cost effective compared to disease-modifying anti-rheumatic drugs (DMARDs) for first-line treatment. In addition, it appears that treatment with a TNF alpha inhibitor in patients who were refractory to previous DMARD therapies is more cost effective, compared to switching to another DMARD. Finally, after an inadequate response to a TNF alpha inhibitor, it appears that therapy with rituximab is more cost effective than treatment with another TNF alpha inhibitor or abatacept.

**Discussion:** It is important to acknowledge that cost effectiveness depends on which comparators are included in the analyses and the evidence for the comparators.

# Καθόλου Ελκυστικοί οι Βιολογικοί στην Πρώτη Γραμμή

**Table 5**

Incremental cost-effectiveness of first line BRM use in rheumatoid arthritis.

BRMs	Comparators		ICERs (\$/QALY) <sup>a</sup>	References
<i>Payer perspective</i>				
ADA	ADA	Sequential DMARDs	119,400	Chen et al., 2006 [18]
	ADA	MTX	87,927	Spalding et al., 2006 [19]
	ADA + MTX	Sequential DMARDs	382,982	Chen et al., 2006 [18]
	ADA + MTX	MTX	268,318	Spalding et al., 2006 [19]
	ADA + MTX	DMARD	63,281	Davies et al., 2009 [22]
ETA	ETA	Sequential DMARDs	110,389	Chen et al., 2006 [18]
	ETA	MTX	123,780	Spalding et al., 2006 [19]
	ETA + MTX	Sequential DMARDs	175,721	Chen et al., 2006 [18]
INF	INF + MTX	Sequential DMARDs	1,464,344	Chen et al., 2006 [18]
	INF + MTX	MTX	564,663	Spalding et al., 2006 [19]
	INF + MTX	DMARD	71,936	Davies et al., 2009 [22]
TNF alpha inhibitors (as a class)	3 sequential TNF alpha inhibitors (N/R) + MTX	DMARDs (LEF, SSZ, HCQ or MTX) > TNF alpha inhibitors	DMARDs dominant	Finckh et al., 2009 [21]
	TNF alpha inhibitor + MTX	MTX	139,744	Schipper et al., 2011 [23]
<i>Societal perspective</i>				
ETA	ETA + MTX	MTX	14,728	Kobelt et al., 2011 [24]
INF	INF + MTX	DMARD combination	141,827	van den Hout et al., 2009 [20]
TNF alpha inhibitors (as a class)	3 sequential TNF alpha inhibitors (N/R) + MTX	DMARDs (LEF, SSZ, HCQ or MTX) > TNF alpha inhibitors	DMARDs dominant	Finckh et al., 2009 [21]
	TNF alpha inhibitor + MTX	MTX	137,843	Schipper et al., 2011 [23]

BRM = biologic response modifier; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year; ADA = adalimumab; DMARD = disease-modifying anti-rheumatic drug; MTX = methotrexate; ETA = etanercept; INF = infliximab; TNF = tumour necrosis factor; N/R = not reported; LEF = leflunomide; SSZ = sulfasalazine; HCQ = hydroxychloroquine.

<sup>a</sup> All costs reported in Canadian dollars, 2012.

# Οριακά Ελκυστικοί στην Δεύτερη Γραμμή Ωστόσο με Σκιές σε Ορισμένες Περιπτώσεις!

670

N.W. Tsao et al. / Best Practice & Research Clinical Rheumatology 26 (2012) 659–676

**Table 6**

Incremental cost-effectiveness of second line BRM use in rheumatoid arthritis.

BRMs	Comparators		ICERs (\$/QALY) <sup>a</sup>	References
Compared to DMARDs				
Payer perspective				
ABA	ABA + MTX	MTX	58,376	Vera-Llonch et al., 2008 [67]
ADA	ADA + MTX	DMARD	58,778	Bansback et al., 2005 [38]
	ADA	DMARD	69,952	Bansback et al., 2005 [38]
	ADA	Sequential DMARDs	317,650	Chen et al., 2006 [18]
ETA	ADA + MTX	Sequential DMARDs	145,083	Chen et al., 2006 [18]
	ADA + MTX	MTX	33,396	Soini et al., 2012 [46]
	ETA	Sequential DMARDs	154,057	Jobanputra et al., 2002 [31]
	ETA	Sequential DMARDs	109,883	Barton et al., 2004 [33]
	ETA	Sequential DMARDs	38,775	Brennan et al., 2004 [34]
	ETA + MTX	DMARD	60,188	Bansback et al., 2005 [38]
	ETA	DMARD	62,152	Bansback et al., 2005 [38]
	ETA	Sequential DMARDs	164,482	Coyle et al., 2006 [26]
	ETA	Sequential DMARDs	106,784	Chen et al., 2006 [18]
	ETA + MTX	Sequential DMARDs	112,191	Chen et al., 2006 [18]
INF	ETA + MTX	MTX	32,465	Soini et al., 2012 [46]
	ETA + MTX	MTX	ETA dominates	Nguyen et al., 2012 [45]
	INF + MTX	MTX	46,028	Wong et al., 2002 [30]
	INF + MTX	Sequential DMARDs	213,637	Jobanputra et al., 2002 [31]
	INF + MTX	MTX	48,204	Kobelt et al., 2003 (Sweden) [32]
	INF + MTX	MTX	69,946	Kobelt et al., 2003 (UK) [32]
	INF + MTX	Sequential DMARDs	147,746	Barton et al., 2004 [33]
	INF + MTX	DMARD	81,350	Bansback et al., 2005 [38]
	INF + MTX	MTX	79,824	Barbieri et al., 2005 [36]
	INF + MTX	Sequential DMARDs	128,448	Coyle et al., 2006 [26]
TCZ	INF + MTX	Sequential DMARDs	313,144	Chen et al., 2006 [18]
	INF + MTX	MTX	37,225	Lekander et al., 2010 [44]
	TCZ + MTX	MTX	29,654	Soini et al., 2012 [46]
TNF alpha inhibitors (as a class)	TNF alpha inhibitors	Usual treatment (DMARDs)	291,531	Welsing et al., 2004 [35]
	TNF alpha inhibitors	DMARDs	53,802	Brennan et al., 2007 [40]

# Το Ίδιο Ισχύει στην Τρίτη Γραμμή

**Table 7**  
Incremental cost-effectiveness of BRM use in rheumatoid arthritis patients with inadequate response to TNF alpha inhibitors.

BRMs	Comparators		ICERs (\$/QALY) <sup>a</sup>	References
Compared to DMARDs				
ABA	ABA + MTX	MTX	63,326	Yuan et al., 2010 [55]
	ABA + DMARD (N/R)	DMARD (N/R)	51,623	Vera-Llonch et al., 2008 [42]
	ABA + MTX	BSC	111,690	Hallinen et al., 2010 [54]
	ABA + MTX	DMARDs	79,546	Malottki et al., 2011 [56]
ADA	ADA + MTX	BSC	84,916	Hallinen et al., 2010 [54]
	ADA + MTX	DMARDs	71,053	Malottki et al., 2011 [56]
ETA	ETA + MTX	BSC	83,967	Hallinen et al., 2010 [54]
	ETA + MTX	DMARDs	80,582	Malottki et al., 2011 [56]
INF	INF + MTX	BSC	60,211	Hallinen et al., 2010 [54]
	INF + MTX	DMARDs	74,782	Malottki et al., 2011 [56]
RTX	RTX + MTX	MTX	73,659	Yuan et al., 2010 [55]
	RTX + MTX	BSC	50,422	Hallinen et al., 2010 [54]
	RTX + MTX	Sequential DMARDs	33,067	Kielhorn et al., 2008 [52]
	RTX + MTX	DMARDs	43,709	Malottki et al., 2011 [56]
Compared to BRMs				
ABA	ABA + MTX	RTX + MTX	270,539	Malottki et al., 2011 [56]
	ABA + MTX	ADA + MTX	96,118	Malottki et al., 2011 [56]
	ABA + MTX	ETA + MTX	78,303	Malottki et al., 2011 [56]
	ABA + MTX	INF + MTX	86,382	Malottki et al., 2011 [56]
ADA	ADA + MTX	ETA + MTX	ADA dominates	Malottki et al., 2011 [56]
	ADA + MTX	INF + MTX	42,466	Malottki et al., 2011 [56]
ETA	ETA + MTX	INF + MTX	946,059	Malottki et al., 2011 [56]
RTX	RTX	3 sequential TNF alpha inhibitor therapies	RTX dominates <sup>b</sup>	Lindgren et al., 2009 [57]
	RTX + MTX	ADA + MTX > INF + MTX > sequential DMARD therapy	26,314	Kielhorn et al., 2008 [52]
	RTX + MTX	ADA + MTX	40,868	Merkesdal et al., 2009 [53]
	RTX + MTX	ADA + MTX	RTX dominates	Malottki et al., 2011 [56]
	RTX + MTX	ETA + MTX	RTX dominates	Malottki et al., 2011 [56]
	RTX + MTX	INF + MTX	RTX dominates	Malottki et al., 2011 [56]

BRM = biologic response modifier; ICER = incremental cost-effectiveness ratio; QALYs = quality-adjusted life years; ABA = abatacept; MTX = methotrexate; ADA = adalimumab; DMARD = disease-modifying anti-rheumatic drug; N/R = not reported; BSC = best supportive care; ETA = etanercept; INF = infliximab; RTX = rituximab; TNF = tumour necrosis factor.

<sup>a</sup> All costs reported in Canadian dollars, 2012.

<sup>b</sup> Societal perspective.



- Ποιος συνυπογραφεί
- Τι εξετάσεις κάνει
- Σε ποιόν συνταγογραφεί
- Υπό τι προϋποθέσεις
- Τι συνταγογραφεί
- Με τι κριτήρια
- Σε τι περιβάλλον
- Σε τι δόση και συχνότητα
- Πότε ξεκινά η θεραπεία
- Πόσο την αξιολογεί
- Πότε την μειώνει
- Πότε την σταματά
- Σε τι μεταβαίνει
- Με τι κριτήρια
- Μεθοδολογικά ζητήματα

## **Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a tumour necrosis factor inhibitor: a systematic review and economic evaluation**

K Malottki, P Barton, A Tsourapas, AO Uthman, Z Liu, K Routh, M Connock, P Jobanputra, D Moore, A Fry-Smith and Y-F Chen



March 2011  
10.3310/hta15140



## Original article

# Quantifying the economic burden of productivity loss in rheumatoid arthritis

Ivana Filipovic<sup>1</sup>, David Walker<sup>2</sup>, Fiona Forster<sup>1</sup> and Alistair S. Curry<sup>1</sup>

## Abstract

**Objective.** In light of the large number of recent studies and systematic reviews investigating the cost of RA, this article examines the methods used to assess the impact of RA on employment and work productivity, and provides an overview of the issues surrounding work productivity loss in the RA population.

**Methods.** A review of the published literature was conducted in order to identify relevant articles. These articles were then reviewed and their methodologies compared. The various methods used to calculate economic loss were then explained and discussed.

**Results.** We found that although methods of lost productivity and associated costs varied between studies, all suggest that RA is associated with significant burden of illness. Economic analyses that exclude indirect costs will therefore underestimate the full economic impact of RA. However, the methods used to calculate productivity loss have a significant impact on the results of indirect cost analyses, and should be selected carefully when designing such studies. Several factors relating to the disease, the job and socio-demographics have been found to predict work disability.

**Conclusions.** Consideration of these factors is vital when measuring the extent of both absenteeism and presenteeism, and will allow for more accurate estimation of the impact of RA on work productivity. This information may also guide interventions aiming to prevent or postpone work disability and job loss.

**Key words:** Rheumatoid arthritis, Cost, Economic, Productivity, Burden of illness.

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## Concise Report

# Dose escalation of the anti-TNF- $\alpha$ agents in patients with rheumatoid arthritis. A systematic review

R. Ariza-Ariza, F. Navarro-Sarabia, B. Hernández-Cruz, L. Rodríguez-Arboleya, V. Navarro-Compán and J. Toyos

**Objective.** To estimate the proportion of rheumatoid arthritis (RA) patients on anti-tumour necrosis factor (anti-TNF) who require dose escalation.

**Methods.** Systematic review of the scientific literature. Infliximab, etanercept and adalimumab studies in RA were considered. Primary outcome was the proportion of patients requiring dose escalation. American College Rheumatology (ACR) and Disease activity score (DAS) responses post-escalation were assessed when available.

**Results.** From 1801 references, 16 studies with 8510 patients were included. Of all the infliximab patients, 53.7% underwent dose escalation. Forty-four per cent of the infliximab patients experienced dose increase and 8.3%, frequency increase. The ACR20 response to dose escalation ranged from 27 to 36% and DAS28 improved from 5.2 to 4.5 in one study and from 4.1 to 3.7 in another. Of the etanercept patients, 17.5% experienced a dose increase but changes on the mean dose were not statistically significant.

**Conclusions.** Dose escalation is common in patients treated with infliximab, and less frequent with etanercept. In a proportion of patients, the dose escalation seems effective. The design and evidence level of the available studies limit the strength of the conclusions.

KEY WORDS: Rheumatoid arthritis, Anti-TNF agents, Dose escalation.

# Differences in Annual Medication Costs and Rates of Dosage Increase Between Tumor Necrosis Factor–Antagonist Therapies for Rheumatoid Arthritis in a Managed Care Population

Daniel A. Ollendorf, MPH<sup>1</sup>\*; David Klingman, PhD<sup>1</sup>; Elisabeth Hazard, PhD<sup>1</sup>; and Saurabh Ray, PhD<sup>2</sup>

<sup>1</sup>IMS Health, Inc., Norwalk, Connecticut; and <sup>2</sup>Abbott Laboratories, Abbott Park, Illinois

## ABSTRACT

**Background:** Tumor necrosis factor (TNF) antagonists are commonly used to treat rheumatoid arthritis (RA). Differences in the dosage and mode of administration of these agents may result in differential rates of dosage adjustment and costs of care.

**Objective:** This study compared dosing patterns and annual costs associated with the use of the subcutaneous TNF antagonists adalimumab and etanercept, and the intravenous TNF antagonist infliximab.

**Methods:** A large managed care database (PharMetrics) was used to identify patients with RA who newly initiated TNF-antagonist therapy with adalimumab, etanercept, or infliximab on or after January 1, 2003, and had at least 6 months of continuous health plan enrollment before initiation of therapy and 12 months of continuous enrollment after initiation. The patients were followed over 12 months of enrollment. Annual pharmacy, inpatient, and outpatient costs were estimated based on plan reimbursements and were compared between cohorts. The average daily dosage (ADD) between prescription refills was used to compare the percentages of patients with greater-than-expected dosing (GTED), defined as 2 consecutive increases in ADD relative to the patient's established maintenance dosage.

**Results:** A total of 2382 patients (568 adalimumab, 1181 etanercept, 633 infliximab) were included in the analysis. Significantly more patients had GTED with infliximab compared with adalimumab and etanercept (32.1%, 8.5%, and 4.7%, respectively; both comparisons,  $P < 0.05$ ). For patients with a dosage increase, the mean time to the first GTED was significantly shorter for infliximab compared with adalimumab and etanercept (154.5, 173.3, and 167.9 days; both,  $P < 0.05$ ). The mean annual costs of anti-TNF therapy, adjusted for baseline differences, were significantly greater for infliximab compared with adalimumab and etanercept (\$15,617, \$12,200, and \$12,146; both,  $P < 0.05$ ).

There were also significant differences between infliximab relative to adalimumab and etanercept in total RA-related medication costs (\$16,280, \$12,989, and \$12,794;  $P < 0.05$ ) and total pharmacy costs (\$17,854, \$14,805, and \$14,398;  $P < 0.05$ ).

**Conclusion:** Patients initiating TNF-antagonist treatment for RA with infliximab incurred annual medication costs that were nearly 30% greater than costs in those initiating therapy with adalimumab or etanercept, in part because of the significantly greater rate of GTED in infliximab recipients. (*Clin Ther.* 2009;31:825–835) © 2009 Excerpta Medica Inc.

**Key words:** rheumatoid arthritis, dosage increase, adalimumab, infliximab, etanercept, cost impact.

## INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disorder characterized by pain, joint swelling, and, in severe cases, progressive destruction of joint tissue. RA affects ~1% of the US population, and >70% of those affected are women.<sup>1</sup> Medications for RA include NSAIDs, analgesics, corticosteroids, disease-modifying antirheumatic drugs (DMARDs), and biologic therapies. Use of DMARDs, particularly methotrexate (MTX), has been the standard treatment for RA for >20 years and continues to be an option for some patients.<sup>2,3</sup> The most commonly used biologic therapies in patients with moderate to severe RA are the 3 tumor necrosis factor (TNF) antagonists approved by the

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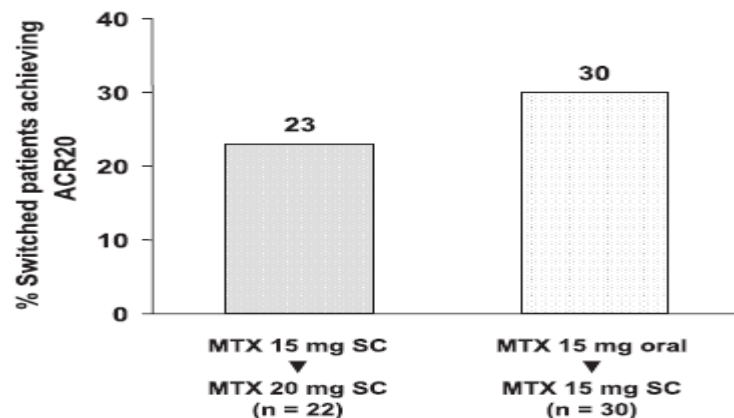
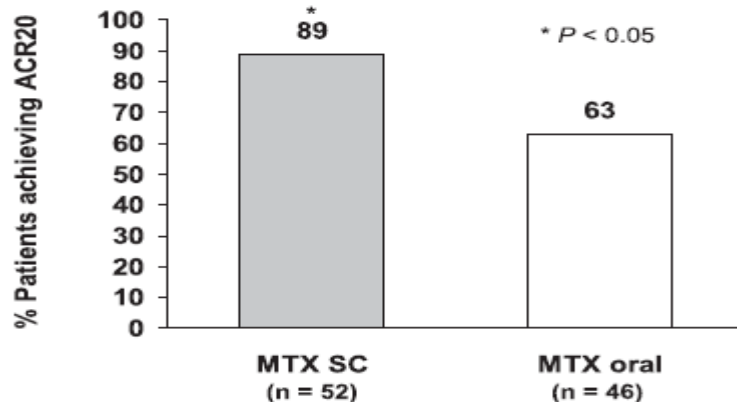
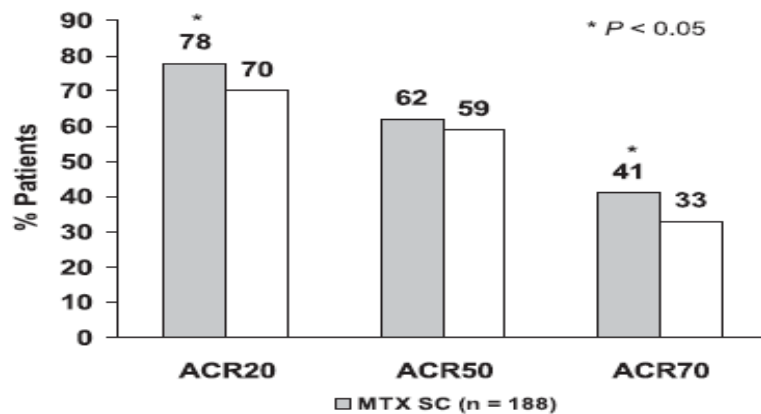




# Comparison of the Clinical Efficacy and Safety of Subcutaneous Versus Oral Administration of Methotrexate in Patients With Active Rheumatoid Arthritis

Results of a Six-Month, Multicenter, Randomized, Double-Blind, Controlled, Phase IV Trial

J. Braun,<sup>1</sup> P. Kästner,<sup>2</sup> P. Flaxenberg,<sup>3</sup> J. Währisch,<sup>3</sup> P. Hanke,<sup>4</sup> W. Demary,<sup>5</sup> U. von Hinüber,<sup>5</sup> K. Rockwitz,<sup>6</sup> W. Heitz,<sup>7</sup> U. Pichlmeier,<sup>8</sup> C. Guimbal-Schmolck,<sup>8</sup> and A. Brandt,<sup>8</sup>  
for the MOC-MTX 6/RH Study Group



**Conclusion.** This 6-month prospective, randomized, controlled trial is the first to examine oral versus SC administration of MTX. We found that SC administration was significantly more effective than oral administration of the same MTX dosage. There was no difference in tolerability.

# Pharmacoeconomics of subcutaneous methotrexate

Figure 2: Continuation rates

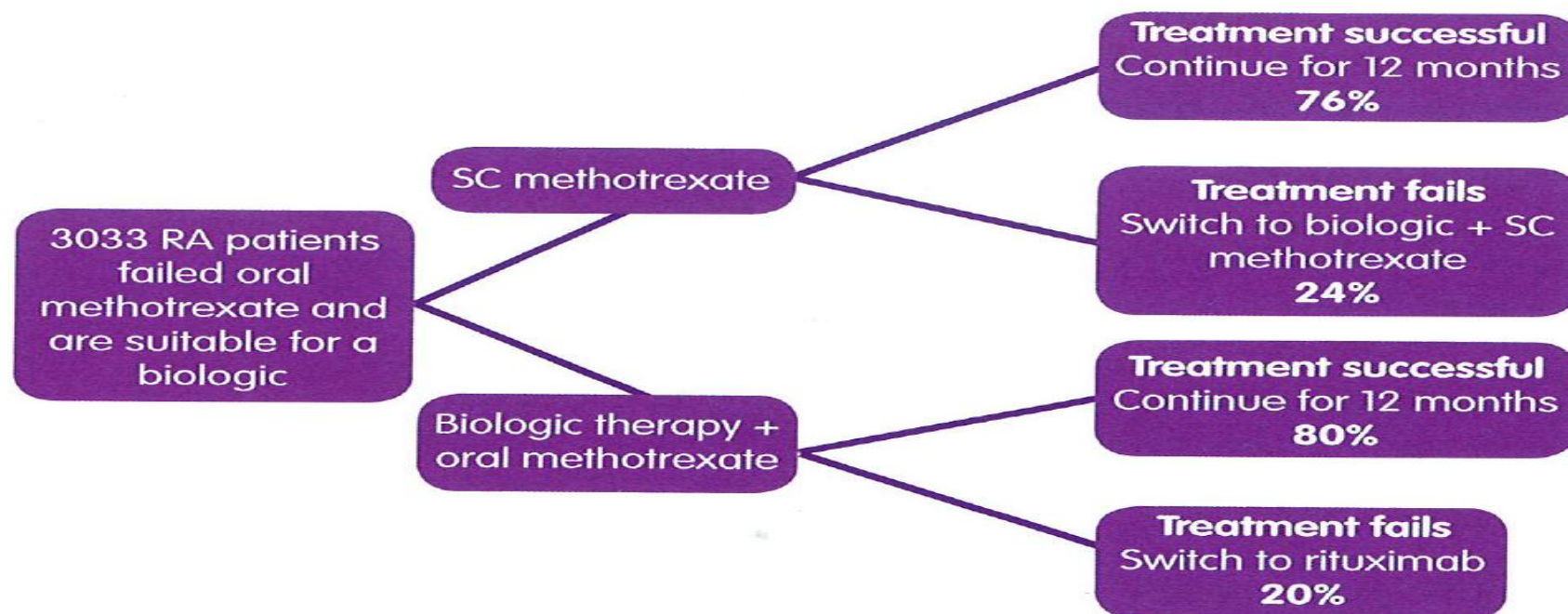


Table 3 Annual cost for each treatment option based on the UK population of RA patients eligible for treatment

SC methotrexate arm	Cost	Biologic arm	Cost
74% continue for 1 year	74% of 3033 pts = 2,244 @ £2,622/pt = £5,883,768	80% continue for 1 year	80% of 3033 pts = 2,426 @ £12,656/pt = £30,703,456
26% Require additional biologic	26% of 3033 pts = 789 @ £8314/pt = £6,559,746	20% require switch to a course of Rituximab	20% of 3033 pts = 607 @ £11,153 = £6,769,871
Total	£12,443,514		£37,473,327

# Economic aspects of treatment options in rheumatoid arthritis: a systematic literature review informing the EULAR recommendations for the management of rheumatoid arthritis

*Ann Rheum Dis* 2010;**69**:996–1004. doi:10.1136/ard.2009.126714

Monika Schoels,<sup>1,2</sup> John Wong,<sup>2</sup> David L Scott,<sup>3</sup> Angela Zink,<sup>4</sup> Pamela Richards,<sup>5</sup> Robert Landewé,<sup>6</sup> Josef S Smolen,<sup>1,7</sup> Daniel Aletaha<sup>7</sup>

**Results** Despite diverse methodological approaches, health economic analyses are concordant: at onset of disease, traditional disease-modifying antirheumatic drugs (DMARDs) are cost effective—that is, treatment merits outweigh treatment costs. If DMARDs fail, therapeutic escalation with tumour necrosis factor  $\alpha$  inhibitors (TNFi) is cost effective when standard dosing schemes are employed. If TNFi fail, rituximab or abatacept is cost effective. Economic evidence for switching TNFi remains sparse.

**Conclusions** The costly sequelae of insufficiently controlled RA justify intensive escalations of treatment in this disease. By maintaining function, patients are kept in the work process, reducing indirect costs. Quality of life is improved at an expense commonly accepted for chronic diseases. Effective control of disease activity seems to be a prudent use of societal resources.



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## Systematic literature review on economic implications and pharmacoeconomic issues of rheumatoid arthritis

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G. Furneri<sup>1</sup>, L.G. Mantovani<sup>2</sup>, A. Belisari<sup>1</sup>, M. Mosca<sup>3</sup>, M. Cristiani<sup>1</sup>, S. Bellelli<sup>4</sup>,  
P.A. Cortesi<sup>1,5</sup>, G. Turchetti<sup>4</sup>

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**Conclusions.** *RA represents a clinical and economic burden for healthcare systems. Although attributable RA costs have been extensively evaluated over the last decades, several issues, especially concerning the use of expensive therapies, must be addressed and frequently updated. Future research should also provide health economic evidence from usual practice settings, and on the economic impact of different therapeutic approaches to pursue specific clinical targets in individual patients.*

*Clin Exp Rheumatol 2012; 30 (Suppl. 73): 572-584.*



Table 4-1 Comparison of prices, health expenditures and ability to afford

Country	TNF price index <sup>1</sup> Germany = 100	Relative health expenditure/capita <sup>4</sup> Germany=100	Affordability index <sup>6</sup>
<i>Austria</i>	82	107	77
<i>Belgium</i>	81	103	79
<i>Bulgaria</i>	78	28 <sup>5</sup>	278
<i>Czech republic</i>	87	45	193
<i>Denmark</i>	90	100	90
<i>Estonia (uncorrected)</i>	52 <sup>2</sup>	31 <sup>5</sup>	169
<i>Finland</i>	81	79	102
<i>France</i>	81	102	79
<i>Germany</i>	100	100	100
<i>Greece (retail)</i>	78	74	105
<i>Hungary</i>	76	45	169
<i>Ireland</i>	82	91	90
<i>Italy</i>	72	78	93
<i>Latvia (uncorrected)</i>	57 <sup>3</sup>	30 <sup>5</sup>	190
<i>Lithuania (uncorrected)</i>	73	25	294
<i>Luxembourg</i>	81	180 <sup>5</sup>	45
<i>Netherlands</i>	72	94	77
<i>Norway</i>	67	134	50
<i>Poland</i>	73	27	271
<i>Portugal (hospital)</i>	84	63	133
<i>Romania</i>	84	19 <sup>5</sup>	440
<i>Slovakia</i>	100	39	257
<i>Slovenia</i>	80	64 <sup>5</sup>	126
<i>Spain</i>	82	73	113
<i>Sweden</i>	83	95	87
<i>Switzerland</i>	80	128	62
<i>United Kingdom</i>	64	82	78

1) Price index based on un-weighted average of the 3 TNF inhibitors Germany = 100

2) Data for only 1 product

3) Data for 2 products only

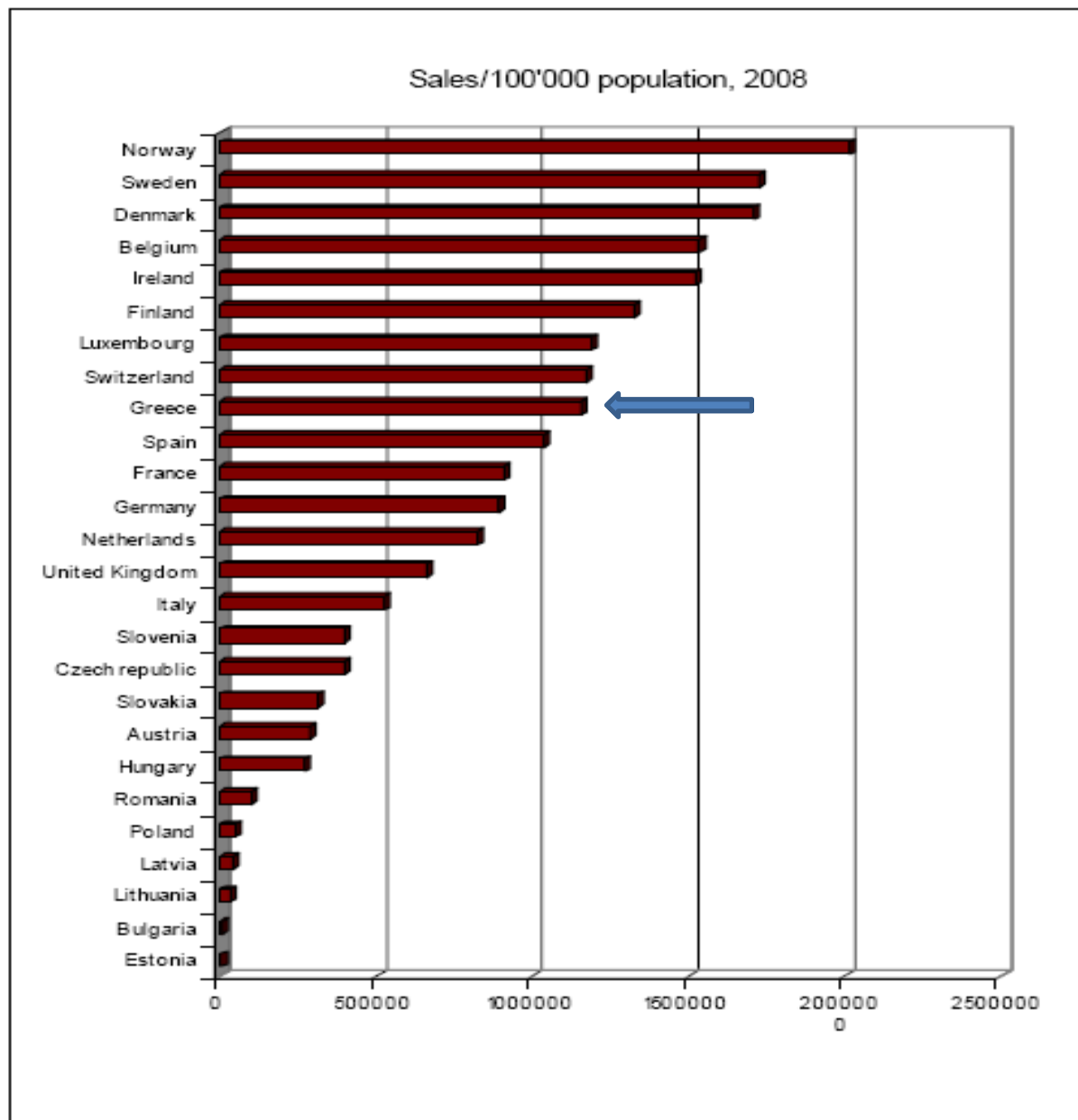
4) Source: OECD Health Data 2008

5) Source: WHO statistical information system, 2006 adjusted

6) Calculated comparing the index of health care expenditures to the price index. Higher indexes indicate lower affordability.

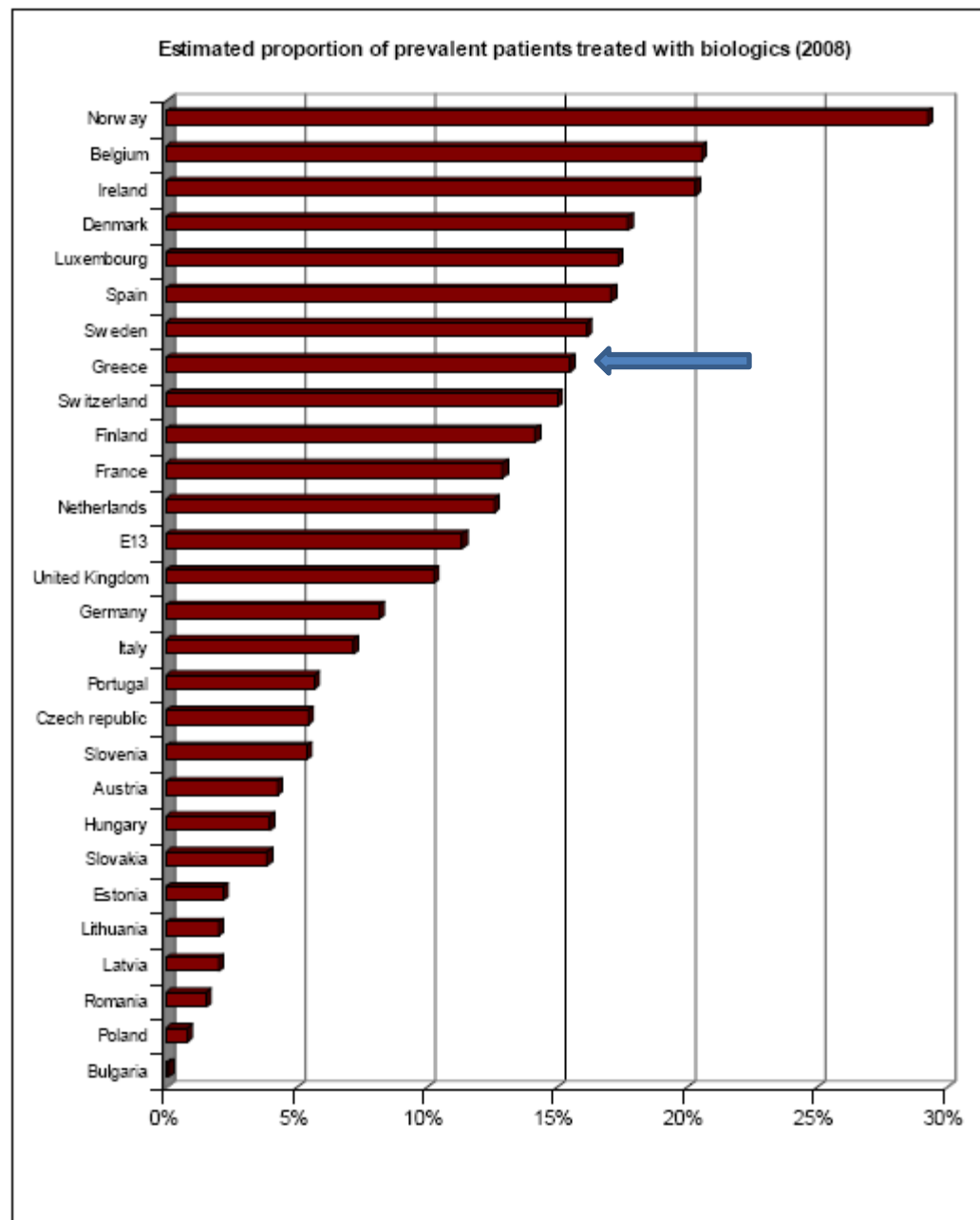


Figure 3-2 Estimated sales per country (per 100,000 population)



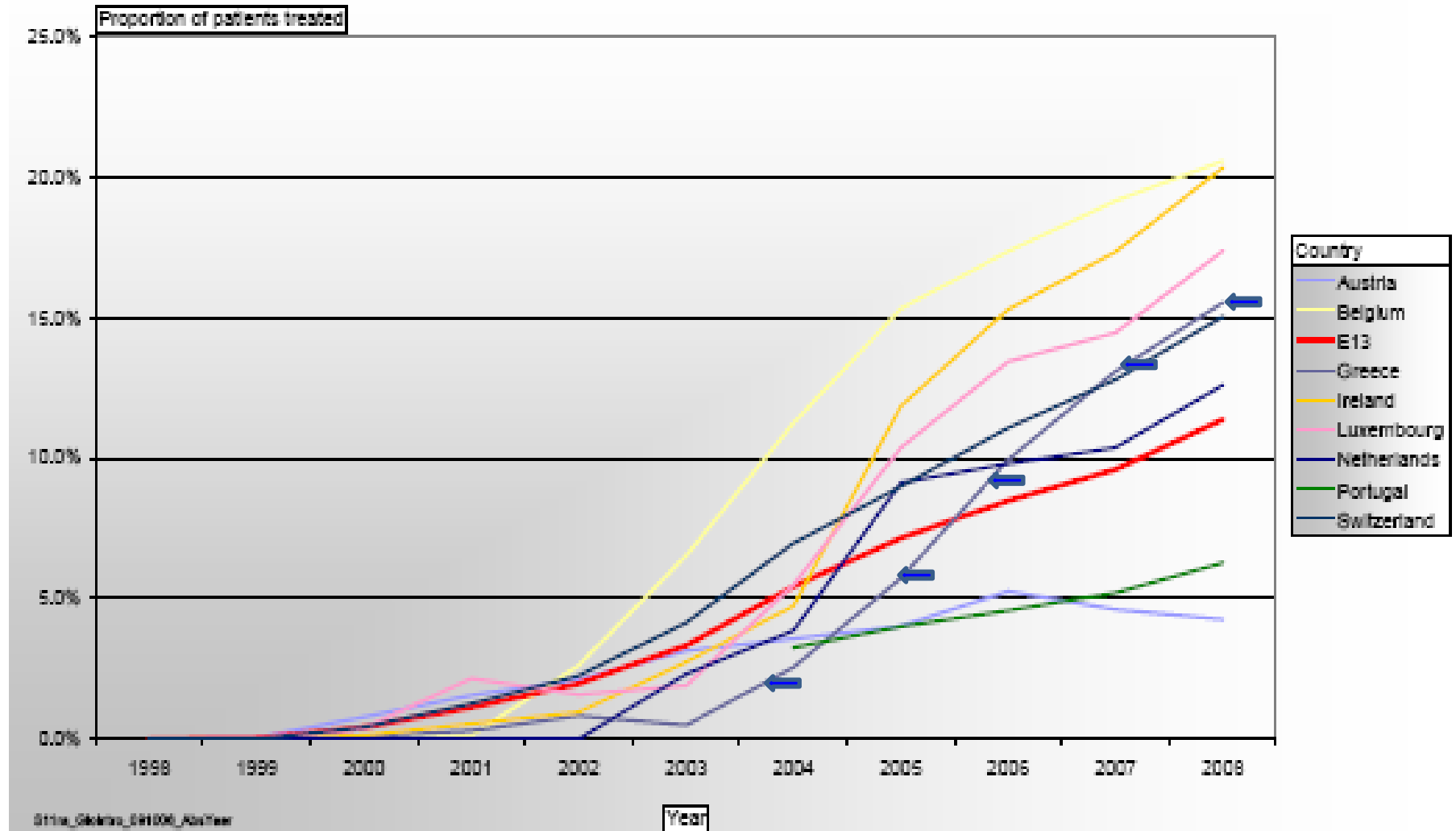
Kobelt and Kasteng, Access to innovative treatments in rheumatoid arthritis in Europe, EFPIA, 2009

Figure 3-19 Proportion on treatment end of 2008



**Figure 3-10 Estimated proportion of patients on treatment (small W.European markets)**

Molecule: (All)



**Table 4-2 Eligibility criteria for access to biologics and related use (from <sup>5</sup>)**

<b>Country</b>	<b>Level DAS28 required</b>	<b>Previous DMARD treatment required</b>	<b>Minimum time on previous DMARDs</b>	<b>Evaluation of effect</b>	<b>Estimated use of biologics</b>
<b>Belgium</b>	-	2, 1 one of them MTX	6 months in total	3-6 months	20.6%
<b>Czech Republic</b>	>5.1	2, 1 one of them MTX	6 months each	3 months	5.4%
<b>Denmark</b>	Persistent synovitis in $\geq 6$ joints	2, 1 one of them MTX	4 months each	4 months	17.7%
<b>France</b>	>5.1 >3.2 despite of corticosteroids	1	3 months	-	12.9%
<b>Germany</b>	-	2, 1 one of them MTX	6 months in total	3 months	8.2%
<b>Italy</b>	>5.1	2, 1 one of them MTX	3 months each	3 months	7.2%
<b>Spain</b>	>3.2	- 1 - 0 in case of aggressive disease	4 months	4 months	17.1%
<b>Sweden</b>	>3.2	- 2, 1 one of them MTX - MTX only in case of aggressive disease	2-3 months total	2-3 months	16.2%
<b>United Kingdom</b>	>5.1	2, 1 one of them MTX	6 months each	3 months	10.3%

DAS28 = Disease activity score, 28 joints; MTX = methotrexate

# ΒΗΜΑ ΠΡΩΤΟ

## Οδηγίες

## Οδηγίες?

*The National Collaborating Centre  
for Chronic Conditions*

*Funded to produce guidelines for the NHS by NICE*

## RHEUMATOID ARTHRITIS

National clinical guideline for management  
and treatment in adults



**Royal College  
of Physicians**  
Setting higher medical standards

*Published by*

## ΡΕΥΜΑΤΟΕΙΔΗΣ ΑΡΘΡΙΤΙΔΑ

### ΦΑΡΜΑΚΕΥΤΙΚΗ ΑΝΤΙΜΕΤΩΠΙΣΗ

#### ΒΑΣΙΚΕΣ ΑΡΧΕΣ ΘΕΡΑΠΕΙΑΣ

- Στόχος της θεραπείας πρέπει να είναι η επίτευξη της ύφεσης ή χαμηλή ενεργότητα νόσου, όσο το δυνατό νωρίτερα (3-6 μήνες). Αν ο στόχος δεν επιτυγχάνεται, η θεραπεία πρέπει να τροποποιείται μετά από συχνή και αυστηρή παρακολούθηση (τροποποίηση τρέχουσας θεραπείας ανά 1-3 μήνες).
- Θεραπεία με συνθετικά τροποποιητικά της νόσου φάρμακα (DMARDs) πρέπει να αρχίζει ταυτόχρονα με την διάγνωση της ρευματοειδούς αρθρίτιδας
- Αν ο θεραπευτικός στόχος δεν επιτευχθεί με την χορήγηση του πρώτου DMARD και αν υπάρχουν δυσμενείς προγνωστικοί παράγοντες\* τότε θα πρέπει να προστίθεται βιολογικός παράγοντας. Αν δεν υπάρχουν δυσμενείς προγνωστικοί παράγοντες μπορεί να γίνει αλλαγή σε άλλο DMARD ή να γίνει συνδυασμός τροποποιητικών της νόσου φαρμάκων (λεφλουνομίδη, κυκλοσπορίνη, σουλφασαλαζίνη, ενέσιμος χρυσός, Δ-πενικιλλαμίνη, υδροξυχλωροκίνη)
- Η καταστολή της ενεργότητας της νόσου απαιτεί δια βίου φαρμακευτική αγωγή και περιοδική ιατρική παρακολούθηση.
- Η παρουσία κλασικών παραγόντων κινδύνου για καρδιαγγειακή νόσο πρέπει να εκτιμάται ανά έτος και να αντιμετωπίζεται αποτελεσματικά.

*\*Σαν δυσμενείς προγνωστικοί παράγοντες θεωρούνται:*

α. Παρουσία RF ή/και αντι-CCP αντισωμάτων (ιδιαίτερα σε υψηλούς τίτλους)

β. Ακτινολογικές διαβρώσεις σε άκρα χέρια ή/και πόδια

γ. Υψηλή ενεργότητα νόσου (με βάση δείκτες ενεργότητας νόσου, του αριθμού των διογκωμένων αρθρώσεων ή την παρουσία πρωτεϊνών οξείας φάσεως)

# ΒΗΜΑ ΔΕΥΤΕΡΟ

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K Malottki, P Barton, A Tsourapas, AO Uthman,  
Z Liu, K Routh, M Connock, P Jobanputra,  
D Moore, A Fry-Smith and Y-F Chen

Health Technology Assessment  
NIHR HTA programme  
[www.hta.ac.uk](http://www.hta.ac.uk)

**NICE guidance on biologic drugs for the treatment of RA (June 2011)**

This algorithm is a tool to aid the implementation of NICE guidance on biologic drugs for the treatment of RA. It includes all of the biologic drugs approved by NICE for treatment of this condition at the time of publication in June 2011.

Commissioners and clinicians should refer to the relevant technology appraisal for each biologic drug for further information about their eligibility and prescription.

**Key to terms:**  
DAS-28: disease activity score  
DMARD: disease-modifying anti-rheumatic drug  
MTX: methotrexate  
TA: NICE technology appraisal  
TNF: tumour necrosis factor

**Flowchart:**

**Path 1 (Left):**

- Start: Use standard DMARD treatment(s) for RA (CG79)
- Decision: Is DAS-28 score  $\geq 5.1$ , on two occasions, 1 month apart?
- If **Yes**: Is the patient responding to DMARD treatment?
- If **No**: Has the patient undergone  $2 \times 6$ -month DMARD trials including MTX?
- If **Yes**: Is the patient intolerant to MTX, or is treatment with MTX considered to be inappropriate?
- If **No**: Use the least expensive TNF inhibitor as monotherapy:
  - Adalimumab (TA130) or
  - Certolizumab pegol (TA186) or
  - Etanercept (TA130)
- Decision: Has the TNF inhibitor been withdrawn because of an adverse event within first 6 months of treatment?
- If **Yes**: consider alternative TNF inhibitor
- If **No**: Adequate response to treatment at 6 months (DAS-28 score improved by  $\geq 1.2$ )?
- If **Yes**: maintain same treatment and monitor patient every 6 months
- If **No**: Use as a monotherapy:
  - Adalimumab (TA195) or
  - Etanercept (TA195)

**Path 2 (Right):**

- Start: Use standard DMARD treatment(s) for RA (CG79)
- Decision: Is DAS-28 score  $\geq 5.1$ , on two occasions, 1 month apart?
- If **Yes**: Is the patient responding to DMARD treatment?
- If **No**: Has the patient undergone  $2 \times 6$ -month DMARD trials including MTX?
- If **Yes**: Is the patient intolerant to MTX, or is treatment with MTX considered to be inappropriate?
- If **No**: Use the least expensive TNF inhibitor + MTX (TA130) or:
  - Adalimumab + MTX (TA130) or
  - Certolizumab pegol + MTX (TA186) or
  - Etanercept + MTX (TA130) or
  - Golimumab + MTX (TA225) or
  - Infliximab + MTX (TA130)
- Decision: Has the TNF inhibitor been withdrawn because of an adverse event within first 6 months of treatment?
- If **Yes**: consider alternative TNF inhibitor
- If **No**: Adequate response to treatment at 6 months (DAS-28 score improved by  $\geq 1.2$ )?
- If **Yes**: maintain same treatment and monitor patient every 6 months
- If **No**: Does the patient have a CI to rituximab?
- If **No**: Rituximab + MTX (TA195)
- Decision: Has rituximab been withdrawn because of an adverse event?
- If **Yes**: Use:
  - Abatacept + MTX (TA195) or
  - Adalimumab + MTX (TA195) or
  - Etanercept + MTX (TA195) or
  - Golimumab + MTX (TA225) or
  - Infliximab + MTX (TA195) or
  - Tocilizumab + MTX (TA198)
- If **No**: Adequate response to treatment at 6 months (DAS-28 score improved by  $\geq 1.2$ )?
- If **Yes**: maintain same treatment and monitor patient every 6 months
- If **No**: Tocilizumab + MTX (TA198)





# ΒΗΜΑ ΤΡΙΤΟ

## Διαπραγματεύσεις - Συμφωνίες

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### Biosimilars in rheumatology: pharmacological and pharmacoeconomic issues

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G. Lapadula<sup>1</sup>, G.F. Ferraccio

*Clin Exp Rheumatol* 2012; 30 (Suppl. 69):  
S102-S106.

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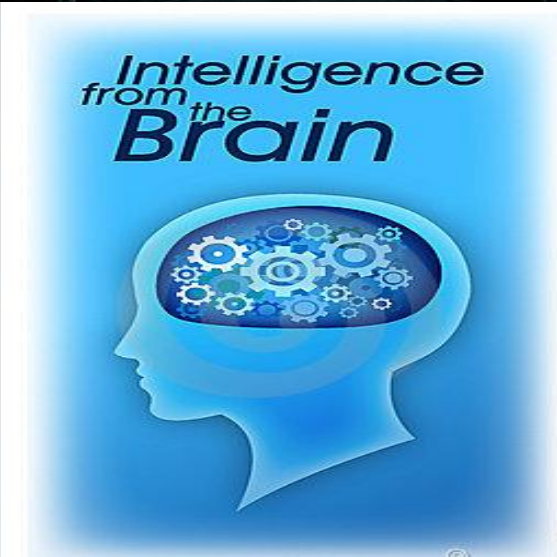
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INNOVATION



B<sup>+</sup>  
BE POSITIVE



~~Reactive~~  
Proactive

BE COOL









ΕΘΝΙΚΗ  
ΣΧΟΛΗ  
ΔΗΜΟΣΙΑΣ  
ΥΓΕΙΑΣ  
ΥΓΕΙΟΝΟΜΙΚΗ ΣΧΟΛΗ  
ΑΘΗΝΩΝ 1929-1994



**Ευχαριστώ θερμά για την προσοχή σας!**

