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# Uptake of Innovation in Europe

IMS Health, October 2013

# About IMS Health

- IMS Health is the world's leading information, services and technology company dedicated to making healthcare perform better.
- With a global technology infrastructure and unique combination of real-world evidence, advanced analytics and proprietary software platforms, we connect knowledge across all aspects of healthcare to help clients improve patient outcomes and operate more efficiently.
- Our expert resources draw on data from 100,000 suppliers, and on insights from more than 40 billion healthcare transactions processed annually, to serve more than 5,000 healthcare clients globally.
- Customers include pharmaceutical, medical device and consumer health manufacturers and distributors, providers, payers, government agencies, policymakers, researchers and the financial community
- As a global leader in protecting individual patient privacy, IMS Health uses de-identified healthcare data to deliver critical, real-world disease and treatment insights. These insights help biotech and pharmaceutical companies, medical researchers, government agencies, payers and other healthcare stakeholders to identify unmet treatment needs and understand the effectiveness and value of pharmaceutical products in improving overall health outcomes.

# *Disclaimer*

This analysis is produced by IMS responding to a brief from EFPIA looking at the uptake of innovation in Europe. Work on this topic has been an on-going development in co-operation with a range of stakeholders and is not meant as a policy statement, it is a point of view produced for discussion purposes

The analyses, their interpretation, and related information contained herein are made and provided subject to the assumptions, methodologies, caveats, and variables described in this report and are based on third party sources and data reasonably believed to be reliable. No warranty is made as to the completeness or accuracy of such third party sources or data.

# Introduction

During the 2010 Belgian Presidency, a study reporting on access to innovation in the European Union was completed by IMS Health Belgium in collaboration with the Belgian Health Authorities. The study demonstrated the issue of un-equal access to medicine between countries; with Eastern Europe particularly impacted.

As a continuation of this study, IMS Health has produced an update of the initial analysis to reflect the dynamics three years on. In addition a more focused view has been given to three key therapy areas, with widely-acknowledged innovation versus standard care

Various methods exist to monitor the uptake of innovation, each with strengths and weaknesses. Assessing a basket of products as was done in The Belgian Presidency study provides interesting results, however differences in clinical practice across countries means that within a class, some medicines may be used more frequently than others. To account for this, IMS Health has developed a more accurate approach, focussing on innovative clusters of products within a given therapy area.

This study updates the analysis using the Belgian Presidency approach and presents IMS's new analysis of three specific innovative clusters:

1) Anti-coagulants
2) Anti-diabetics
3) Hepatitis C

# Update of the *2010 Belgian Presidency Study:*

## RIZIV/INAMI & IMS Health, 2010
## Understanding and measuring pharmaceutical innovation across the European Union

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# Selection method for Belgian Presidency Study

- To be consistent with the previous study, the same basket of products was analysed to produce the updated view
- Innovative medicines were identified based on whether they applied for Class 1 or orphan designation when applying for reimbursement in Belgium between 2005-09
- The results were benchmarked vs. France using the purely scientific ASMR rating system of the French Transparency commission. Those submitted for class II in Belgium, but achieved a rating of I or II in France were carried forward (2 products)

| # PROD | DESCRIPTION |
|---|---|
| 69 | Dossiers for the first time submitted in Belgium in the period 2005-2009 as class 1 |
| 44 | Dossiers for the first time submitted in Belgium in the period 2005-2009 as class orphan |
| 2 | Dossiers for the first time submitted in France in the period 2005-2009 receiving ASMR I-II and submitted in Belgium in the period 2005-2009 as class 2 |
| 3 | Reyataz, Erbitux and Protelos were submitted before 2005 but were added upon request |

- Products were then removed which did not:
  - receive desired rating (BE – Class 1 or Orphan, FR I, II)
  - (at the time of study) have sales data of 1 year of sales in at least 12 countries
- Since completion of the first study in 2010, one of the products has been withdrawn following EMA recommendations
- The final sample included 46 "innovative" products as deemed by Belgium/ French payer

*Source: RIZIV/INAMI & IMS Health, 2010, Understanding and measuring pharmaceutical innovation across the European Union*

# Differences in the definition of innovation

**INAMI RIZIV innovation EU – acceptance overlap analysis**

| INNOVATION ACCEPTANCE PER COUNTRY | # | % |
|---|---|---|
| Products considered innovative in Belgium and France | 24 | 29 |
| Products considered innovative in Belgium only | 34 | 42 |
| Products considered innovative in France only | 9 | 11 |
| Products not considered innovative | 15 | 18 |

**This definition of "innovation" is therefore predominantly Belgian focused**

*Source: RIZIV/INAMI & IMS Health, 2010, Understanding and measuring pharmaceutical innovation across the European Union*



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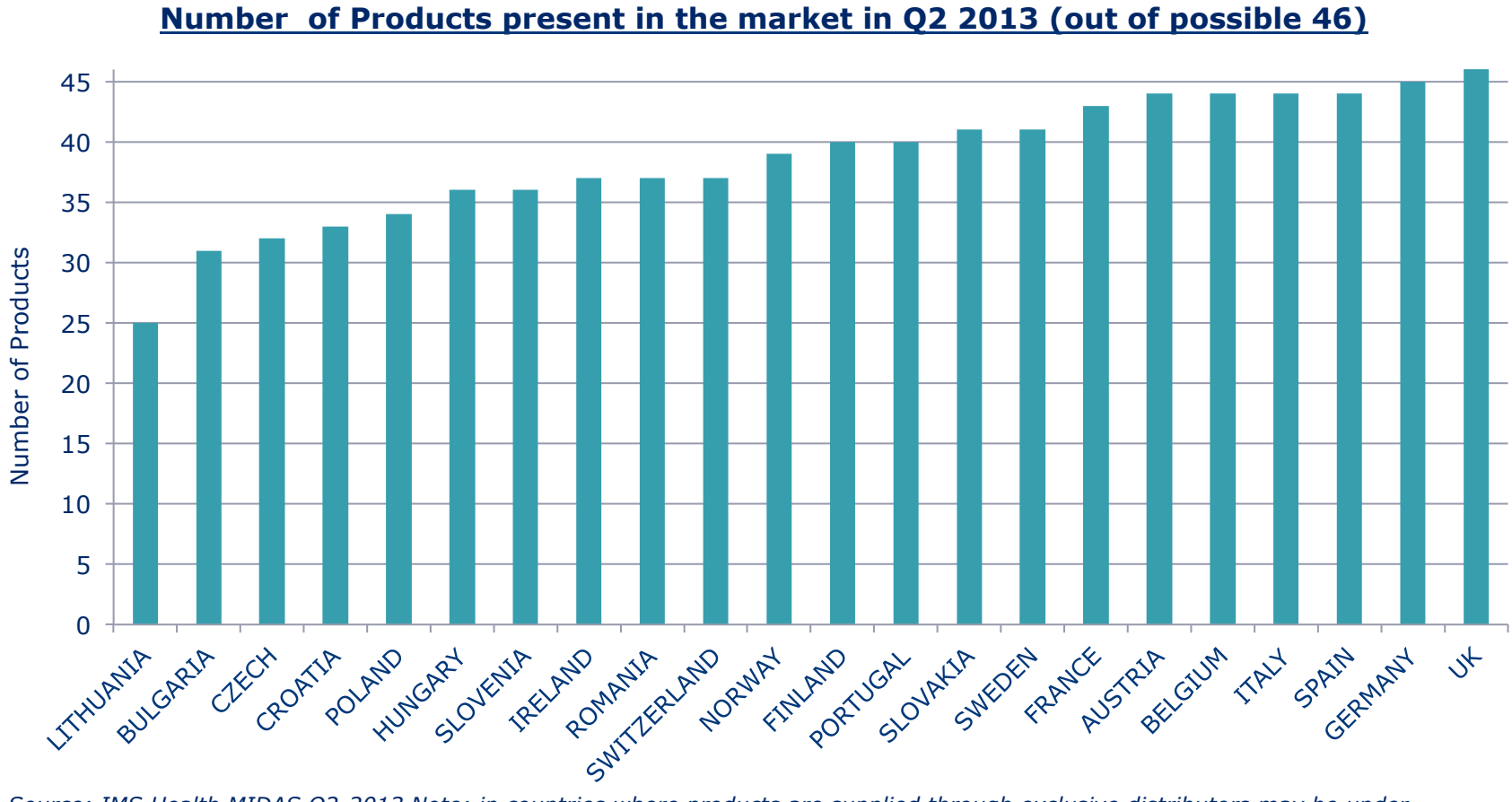
# Number of sample products available in each country




*Source: IMS Health MIDAS Q2-2013 Note: in countries where products are supplied through exclusive distributors may be under-represented in our audits*



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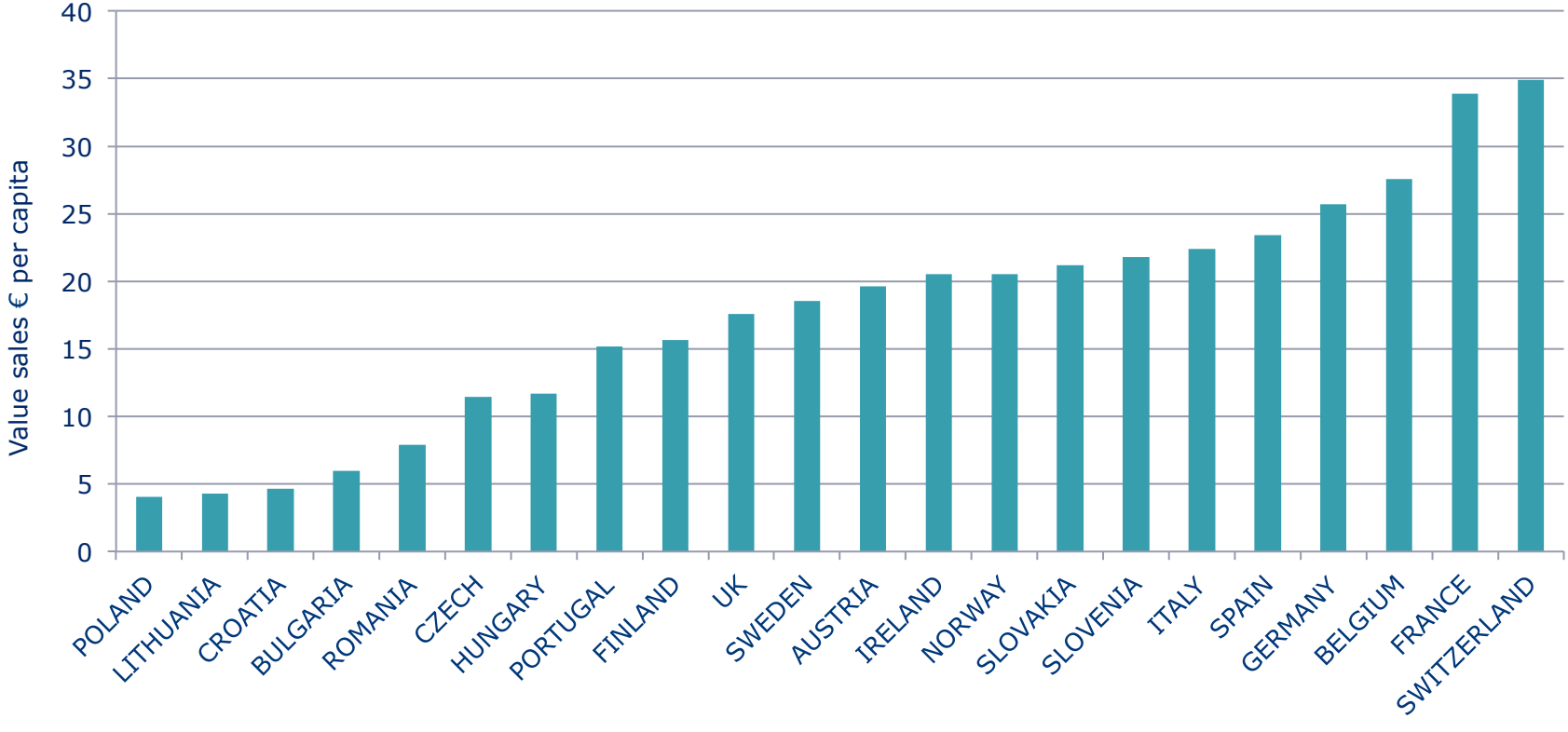
# Pharmaceutical sales valued at average European price before rebates and discounts

**Pharmaceutical value sales (€ per capita) of 46 "innovative" products at European average ex-manufacturer price before rebates and discounts**




*Source: IMS Health MIDAS Q2-2013. Population numbers based on 2012 figures from Eurostat. Countries where IMS does not audit the hospital market have also been excluded from the analaysis (Estonia, Greece, Latvia, Netherlands and Luxembourg) In some countries uptake may be impacted by parallel trade which cannot be adjusted for*



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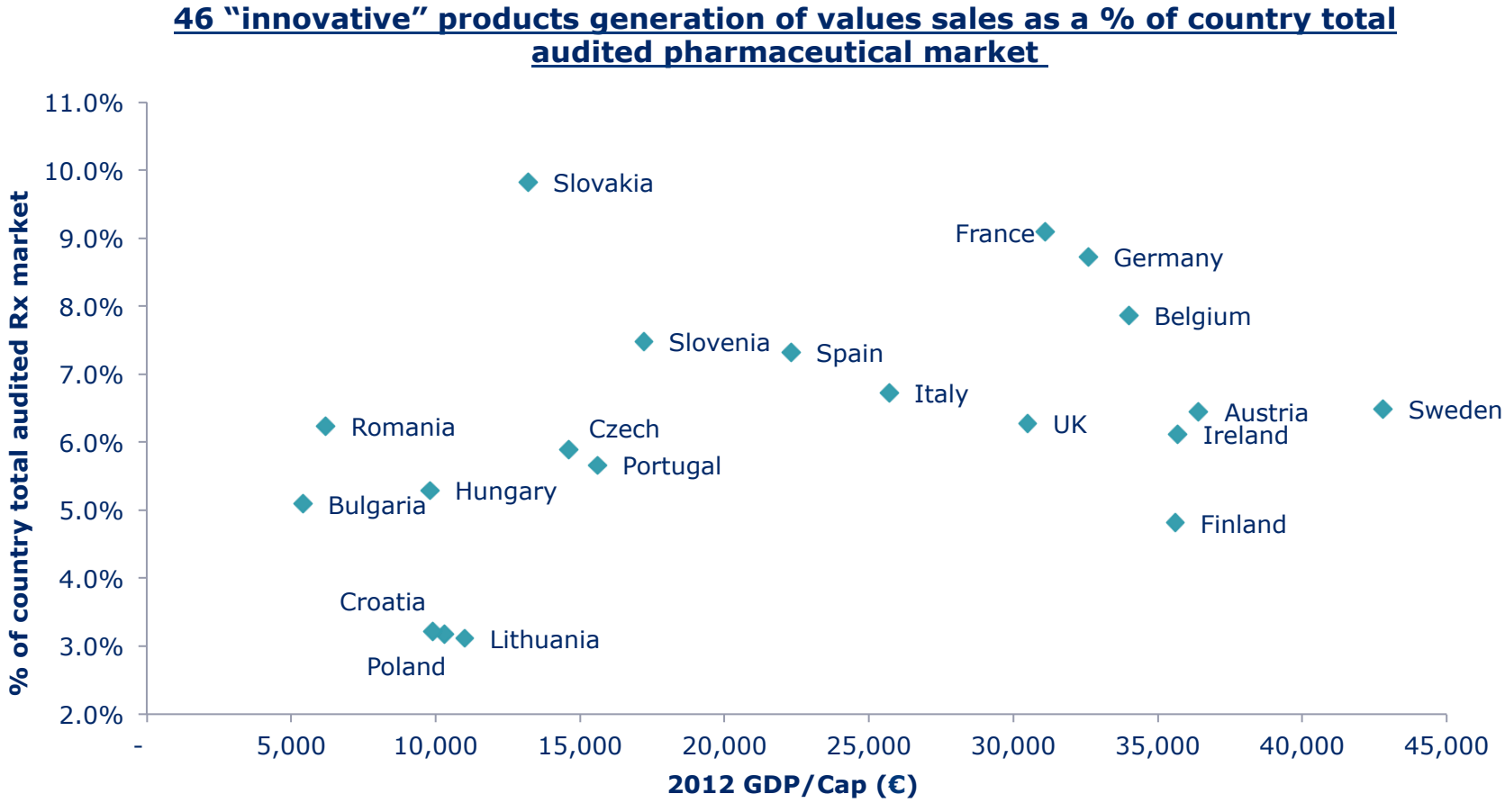
# Uptake of innovation as % total country sales correlated to GDP/Cap




*Source: IMS Health MIDAS Q2-2013. GDP/ Capita Eurostat. Note: outlying countries with high GDP/ cap, have been excluded for display purposes (Norway and Switzerland). Countries where IMS does not audit the hospital market have also been excluded from the analaysis (Estonia, Greece, Latvia, Netherlands and Luxembourg). In some countries uptake may be impacted by parallel trade which cannot be adjusted for*



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# Therapy area focus: uptake of “innovative clusters”

# Defining innovative clusters

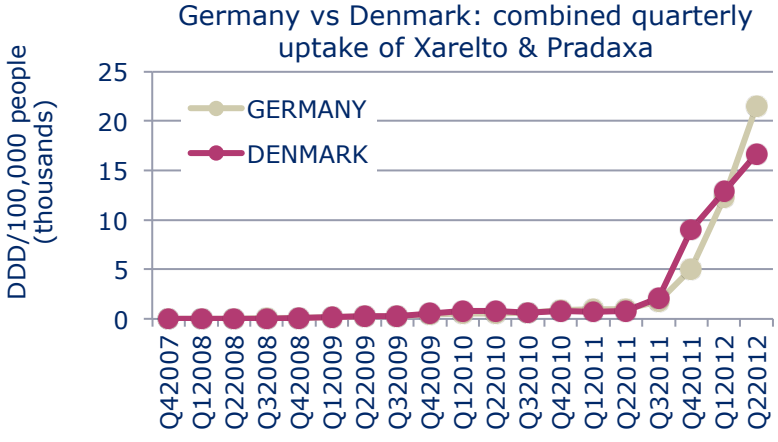
## INNOVATIVE PRODUCTS VS INNOVATIVE CLUSTERS

There is no single definition of "innovation". Although some may define it as the first medicine to market with a novel characteristic, whether this be delivery form, mode of action or improved efficacy (list not exhaustive), the reality is often more complex. Firms often compete, in the R&D phase, to develop the first (and best) in a given class. Rather than one new product coming to market, then, it is not unusual for a cluster of new innovations to arrive in quick succession. Differences in clinical practice – as well as commercial strategies – across countries may lead to different products taking the lead in any given country. It arguably, therefore, makes more sense to base international comparisons on clusters of new medicines rather than individual products.

**Definition of an innovative cluster:** ***products launched within close time proximity, for the same indication with a common, novel characteristic distinguishing them from the standard treatment of care. Products will therefore be competing for market share of the same patient population***

**Example:** Both Pradaxa and Xarelto were launched into the European market in 2008 and the two products have been competing head to head ever since. Launch strategy has had a great impact on the uptake success of one over the other and can confound the measure of innovation. To get around this the two products have been grouped together to form an innovative cluster.

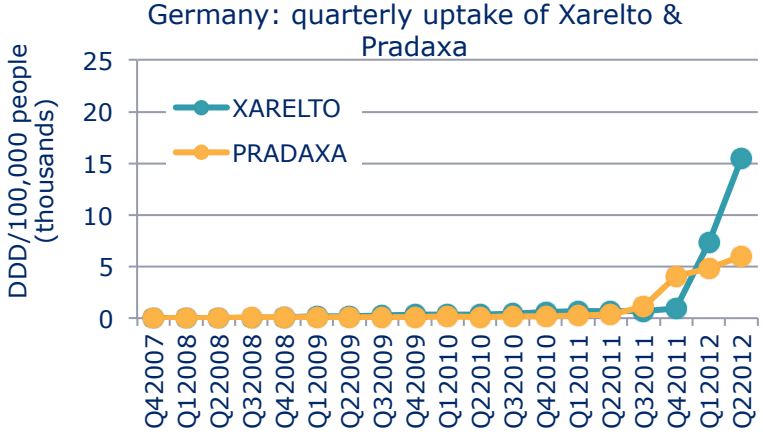
# Example of cluster effects

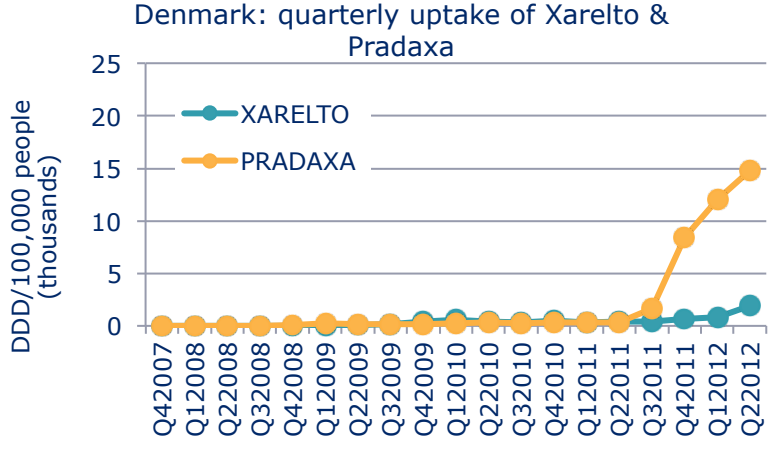



At the individual product level, Xarelto out-performed in the German market

In contrast, in Denmark the uptake of Pradaxa was superior to Xarelto

Combing the uptake of both products and comparing Denmark and Germany, relatively similar levels and rates of uptake are seen. This illustrates the importance of using innovative clusters as opposed to individual products, which may not paint the right picture




*Source: IMS Health MIDAS Q2-2012. EuroSTAT population statistics.*



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# Rationale for "innovative" designation of three product clusters

1) Anti-coagulants: recent therapeutic advances have provided treatment options which are not only more efficacious, but have a better safety profile than the standard care warfarin
2) Anti-diabetics: between the two groups (DPP 4's and GLP 1's) there are a number of innovative characteristics. Firstly, both employ a unique mechanism of action, whilst in addition the GLP 1's also help promote weight loss, while the oral delivery mechanism of DPP4's makes taking this medication much more patient-friendly versus injectable insulin. Both of these latter properties are likely to influence patient adherence, particularly important as diabetes is a disease which is heavily reliant on the patient for treatment success
3) Hepatitis C: standard care is not efficacious in certain patient populations, however when used in combination with innovative hepatitis C products there is an improvement in sustained virologic response (SVR), the best indication of successful hepatitis C therapy

# Anti-coagulants: treatment overview & options

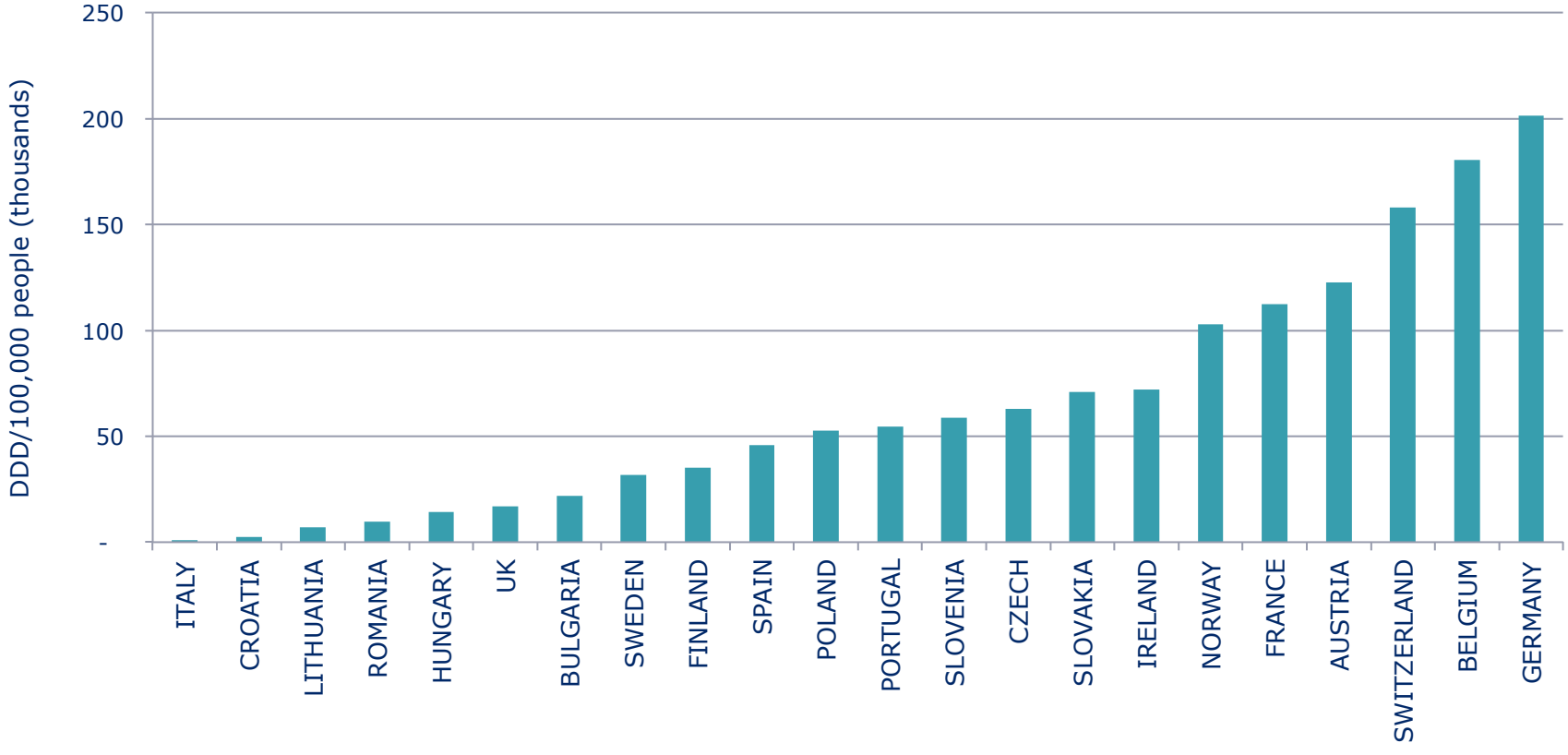
- Patients who suffer from atrial fibrillation (a type of irregular heart beat) have an increased risk of blood clots, the root cause of serious diseases/events such as; acute coronary syndromes, ischemic stroke and deep vein thrombosis. Anti-coagulants act to thin the blood to prevent strokes and cardiac issues
- The standard of care, warfarin requires routine blood monitoring checks and dose adjustments, to avoid excess bleeding and other risks. Pradaxa and Xarelto are both novel oral agents which not only improve stroke prevention, but also generate less bleeding and remove the need for ongoing monitoring.

| PRODUCT | MOLECULE | EMA APPROVAL |
|---|---|---|
| PRADAXA | Dabigtran Etexilate | 2008 |
| XARELTO | Rivaroxban | 2008 |

Note: to ensure adequate sales history newer anti-coagulants have been excluded from this analysis

# Uptake of innovative anti-coagulants

**Europe: Uptake of Innovative Anti-coagulants (DDD/100,000 people)**
**MAT Q2 2013**

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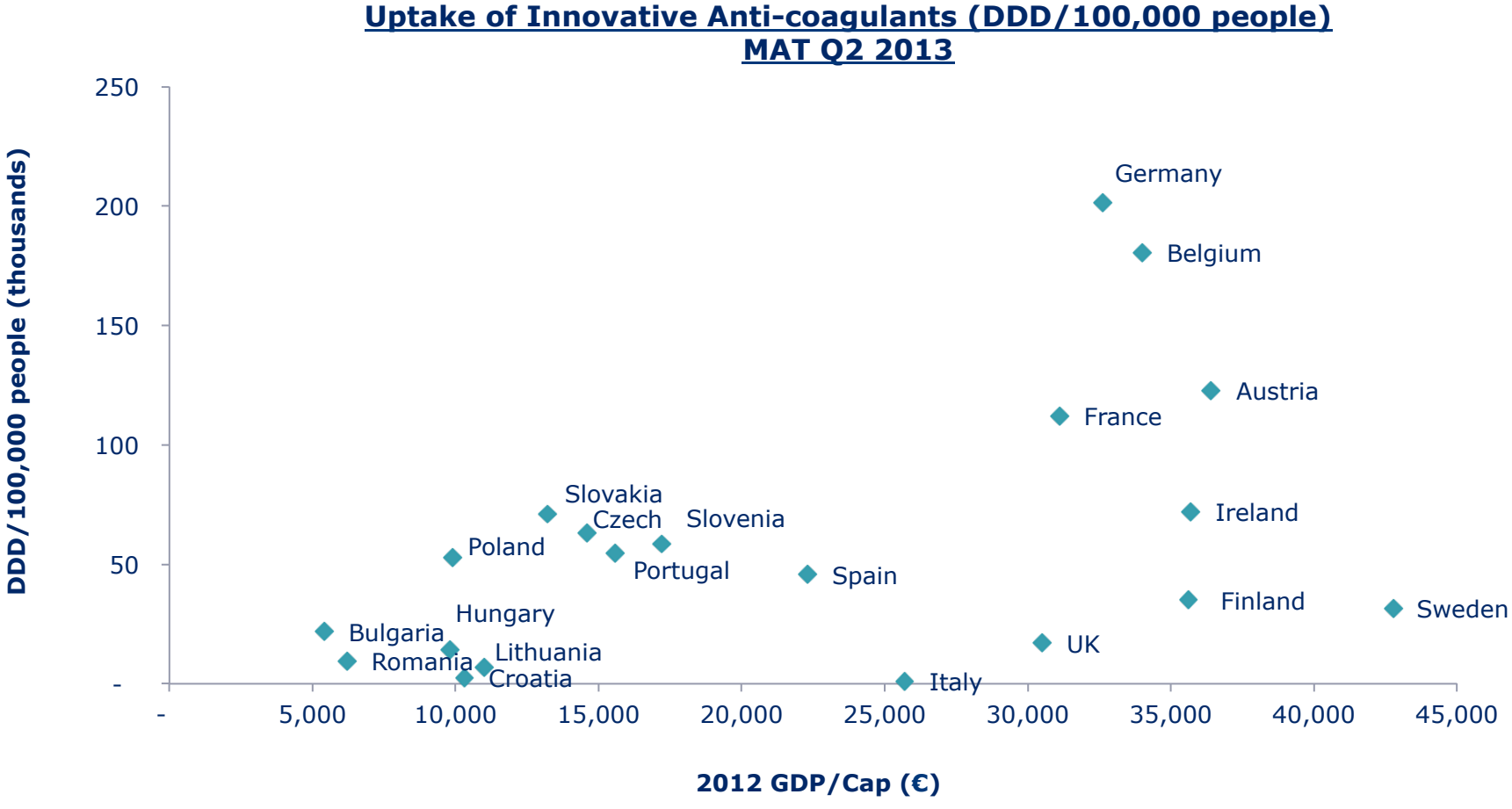
# Uptake/GDP Correlation

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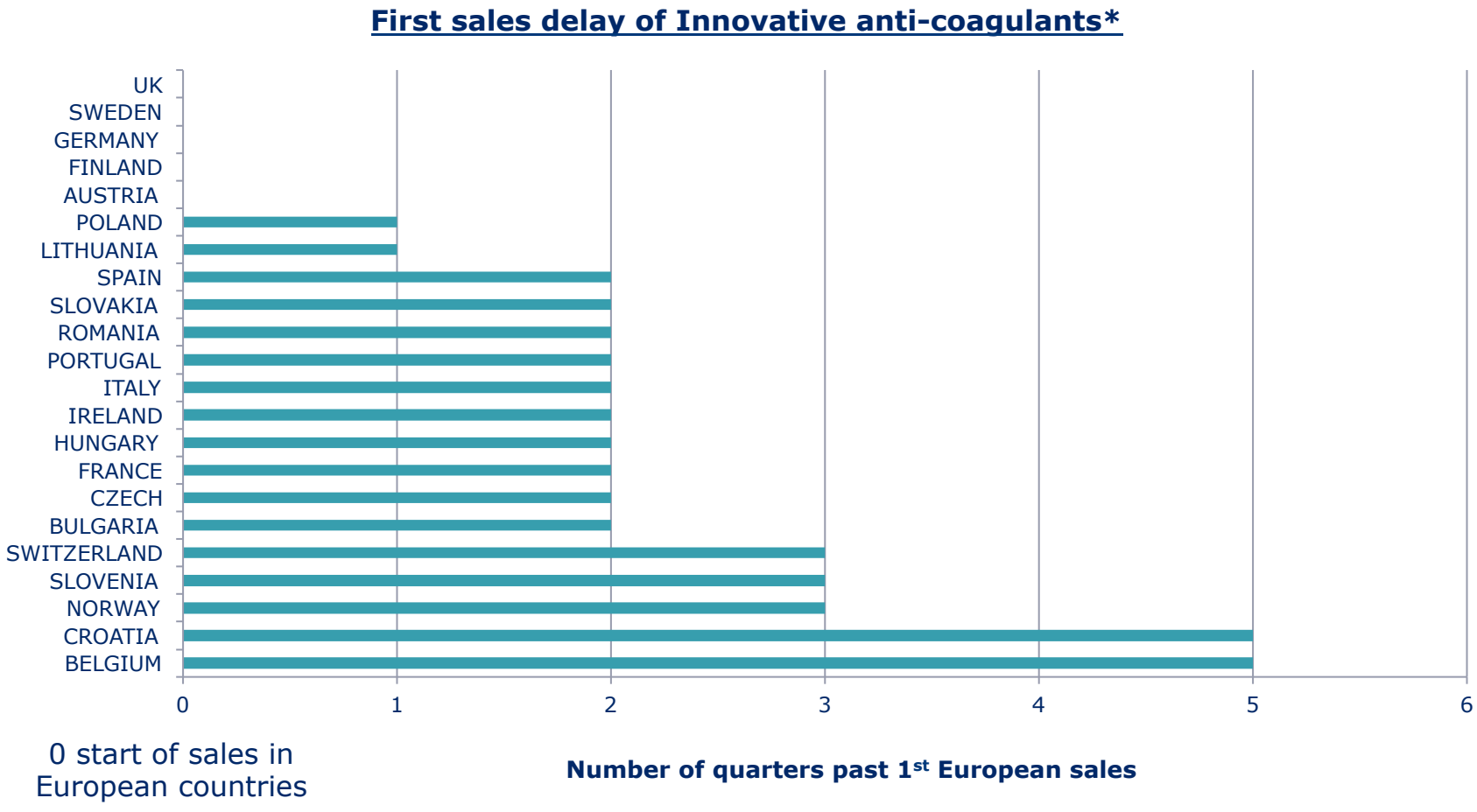
# First sales delay of Innovative Anti-coagulants




*Source: IMS Health MIDAS Q2-2013.. Countries where IMS does not audit the hospital market have also been excluded from the analaysis (Estonia, Greece, Latvia, Netherlands and Luxembourg) * Launch measured by start of sales of the 1st to market anti-coagulant in each country*



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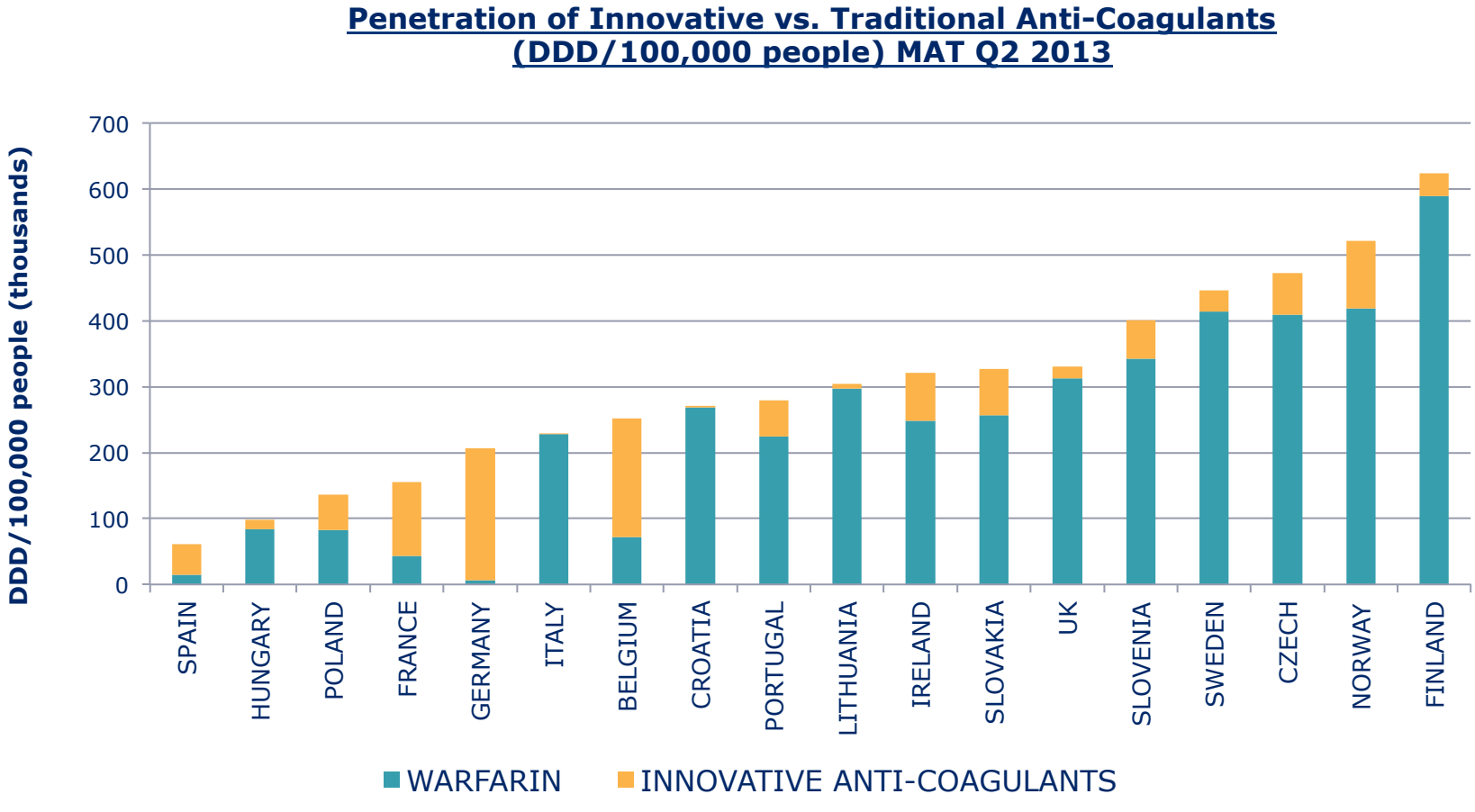
# Innovative anti-coagulants vs. warfarin




*Source: IMS Health MIDAS Q2-2013.. Countries where IMS does not audit the hospital market have also been excluded from the analaysis (Estonia, Greece, Latvia, Netherlands and Luxembourg) . Note alternative Vitamin Kantagonists are available e.g. Phenprocoumon and Acenocoumarol, but for the purpose of this study focus is on Wafarin. In some countries uptake may be impacted by parallel trade which cannot be adjusted for*



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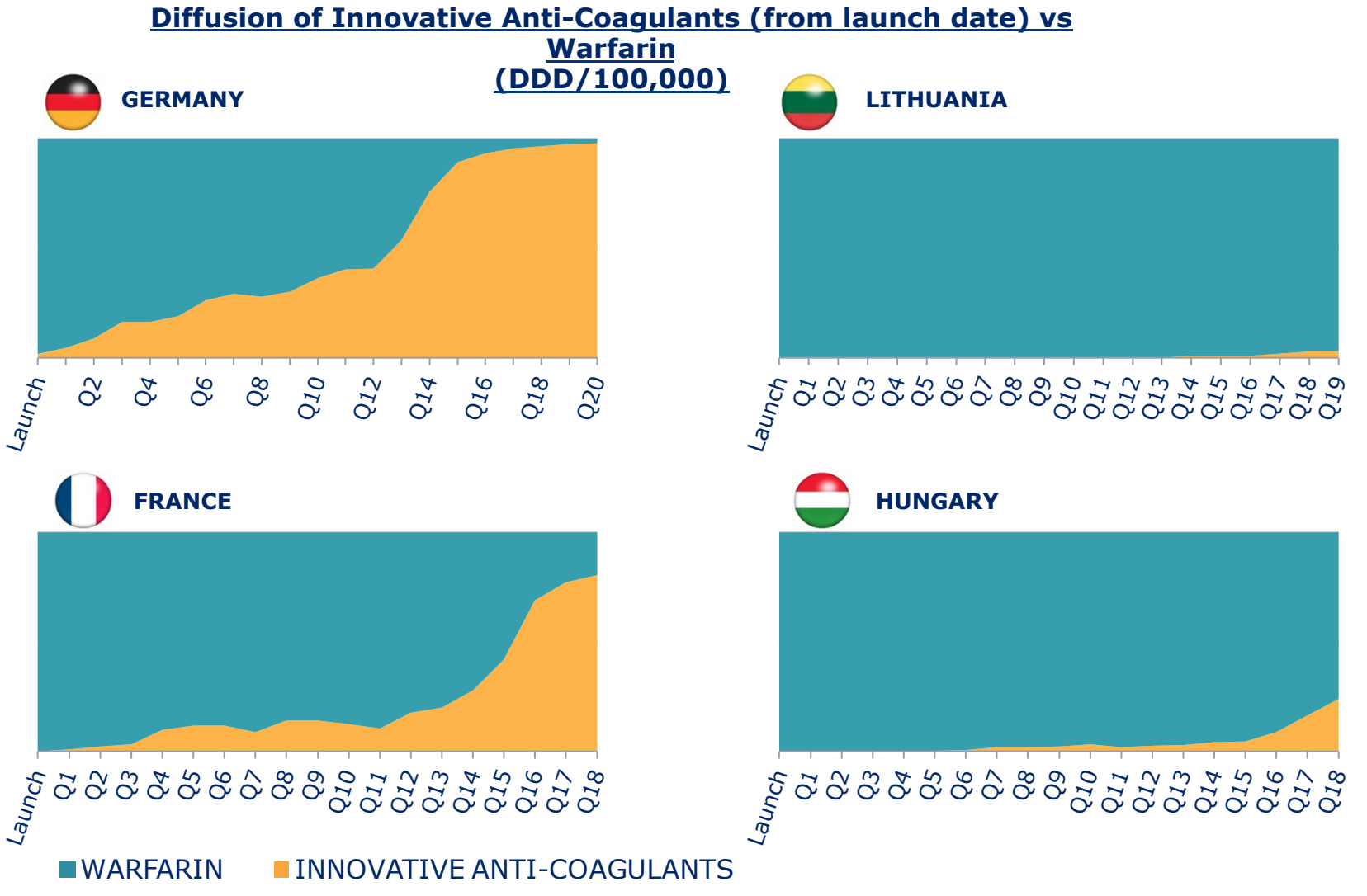
# Innovative anti-coagulants diffusion curve

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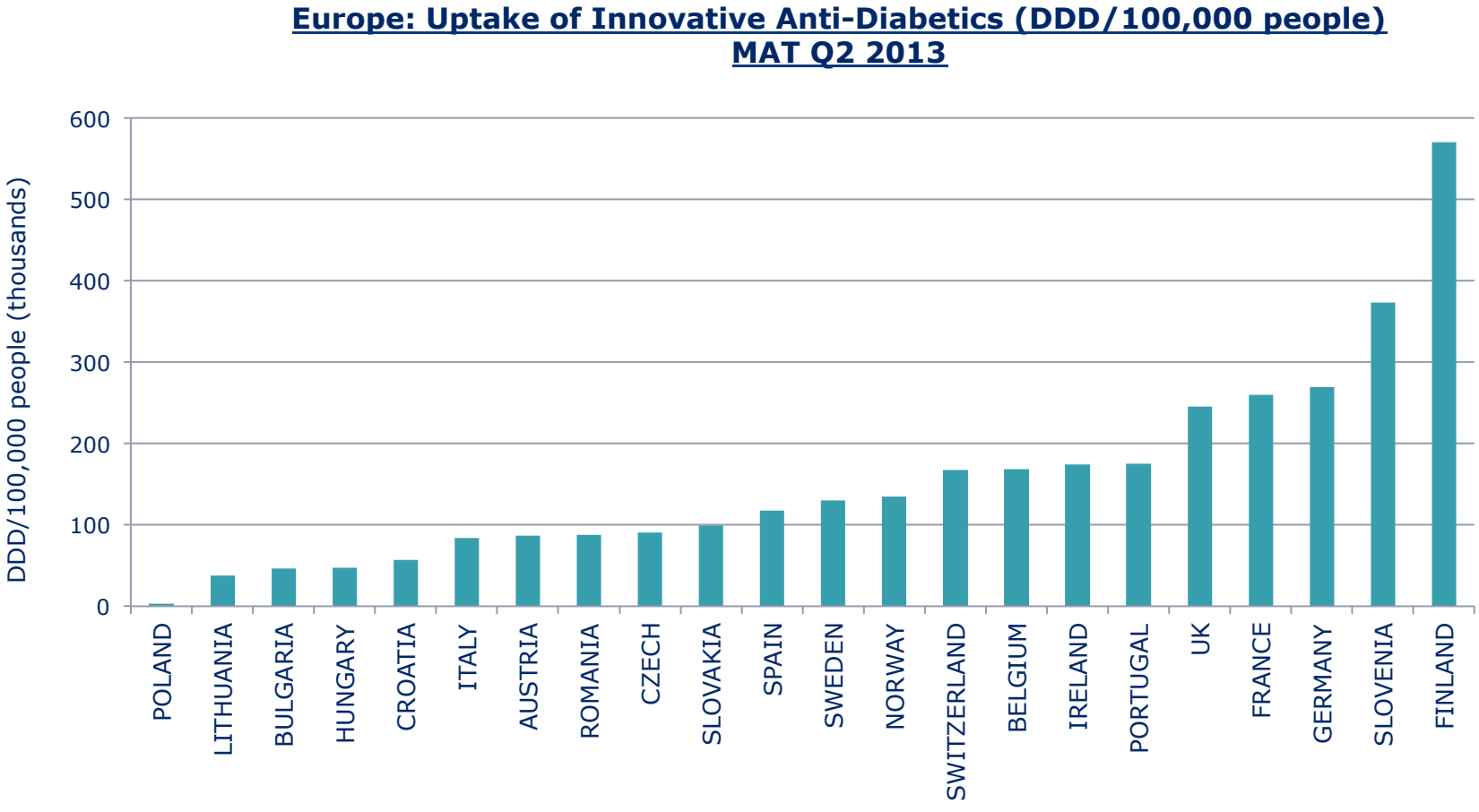
# Anti-diabetics: treatment overview & options

- Diabetic patients suffer from a life-long inability to regulate their blood sugar levels, due to either the inability to produce insulin (Type 1 diabetes) or developing insulin resistance (Type 2 diabetes). Innovative anti-diabetics are used to treat Type 2 diabetes in situations where patients are unable to remain stabilised on first line treatments metformin and/or sulfonylurea.
- These innovative medicines are classified as so for two reasons;
  - Firstly they were scientific breakthroughs in terms of providing novel mechanisms of action for controlling insulin versus the use injectable insulin
  - Secondly, diabetes is characterised by a number of factors which can implicate patient adherence to treatment; chronic disease with no cure, complex treatment regime, greatly impacted by lifestyle choices and treatment success largely driven by the patient. The DPP4's provided the first oral anti-diabetics, making treatment easier for patients, otherwise expected to use injections.

| PRODUCT (CLASS) | MOLECULE | EMA APPROVAL |
|---|---|---|
| JANUVIA (DPP4) | Sitagliptin | 2007 |
| GALVUS (DPP4) | Vildaiptin | 2007 |
| ONLGYZA(DPP4) | Saxagliptin | 2009 |
| BYETTA (GLP-1) | Exenatide | 2006 |
| VICTOZA (GLP-1) | Liraglutide | 2009 |

Note: to ensure adequate sales history newer anti-diabetics have been excluded from this analysis

# Uptake of innovative anti-diabetics

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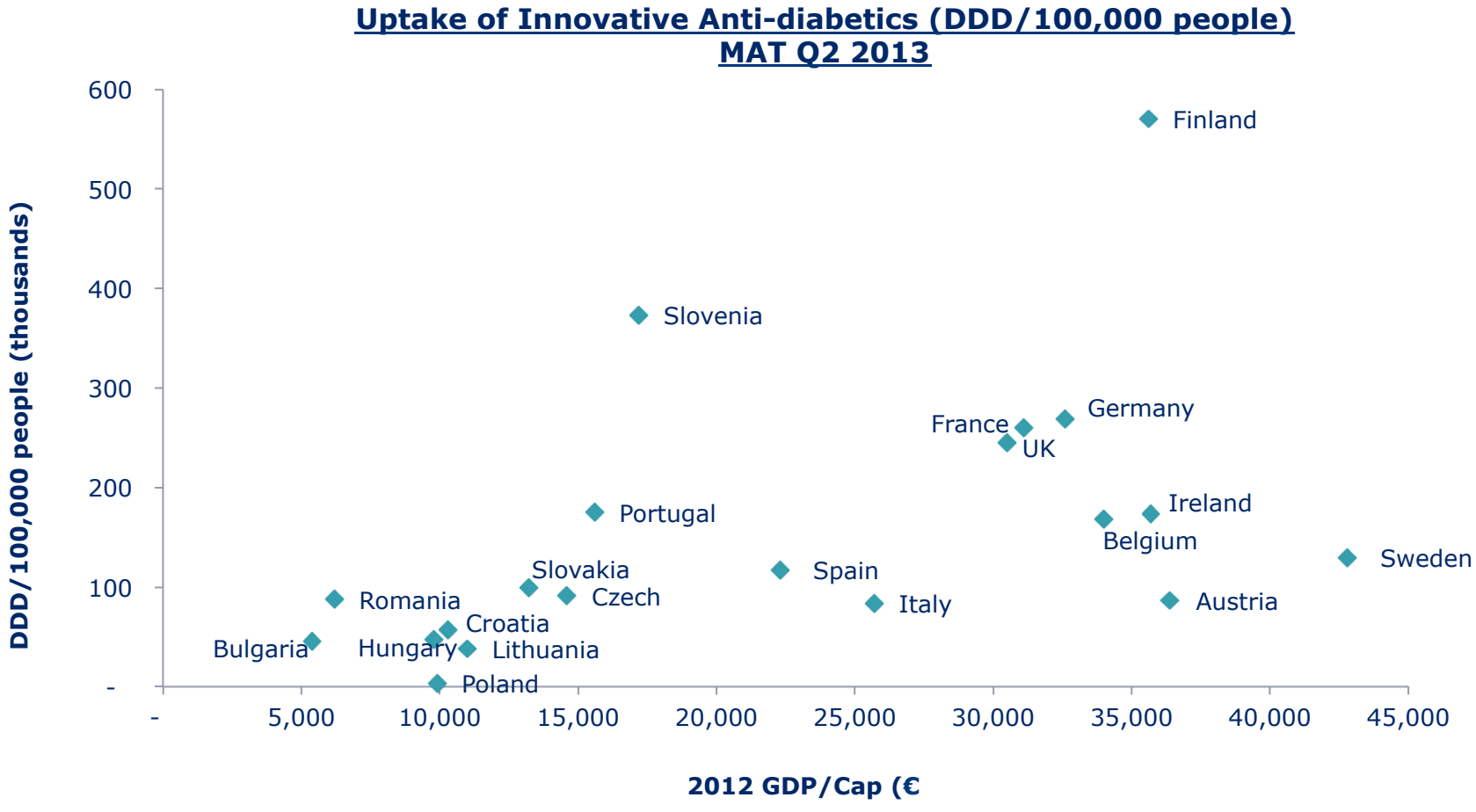
# Uptake /GDP Correlation

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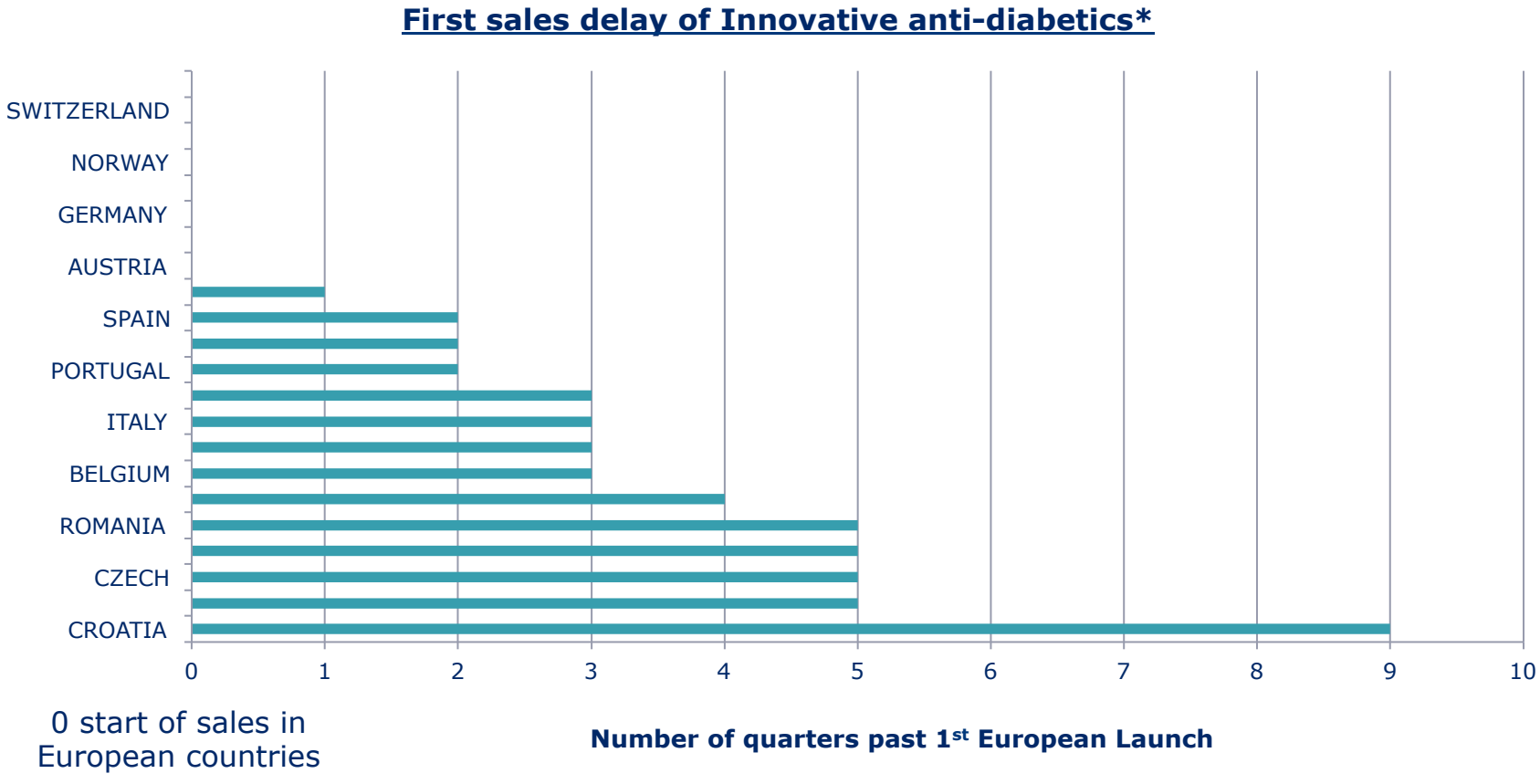
# First sales delay of Innovative Anti-diabetics

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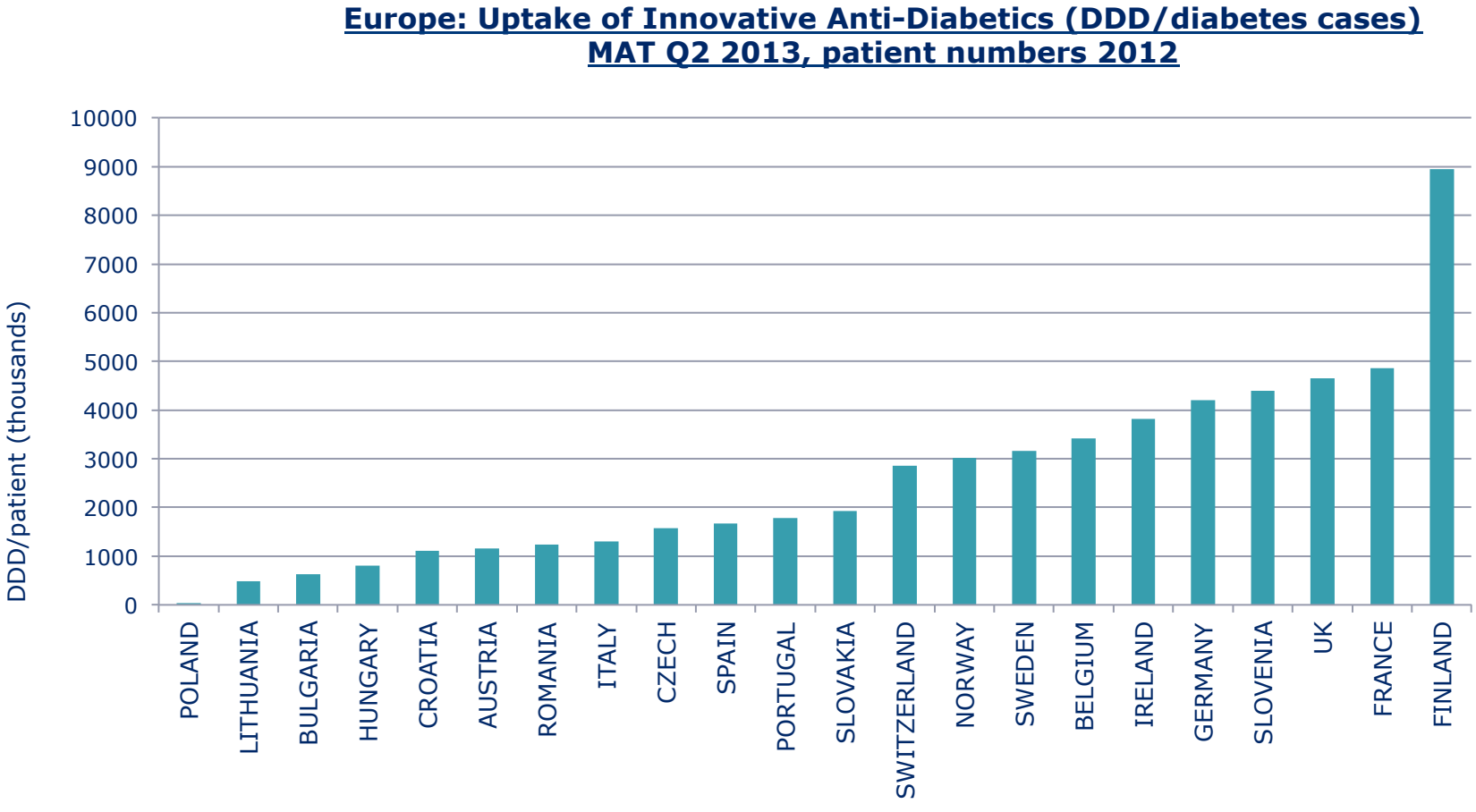
# Uptake of innovation relative to the number of diabetes cases




*Source: IMS Health MIDAS Q2-2013. International diabetes federations – 2012 number of diabetes cases. http://www.idf.org/atlasmap/ atlasmap Countries where IMS does not audit the hospital market have also been excluded from the analaysis (Estonia, Greece, Latvia, Netherlands and Luxembourg) In some countries uptake may be impacted by parallel trade which cannot be adjusted for*



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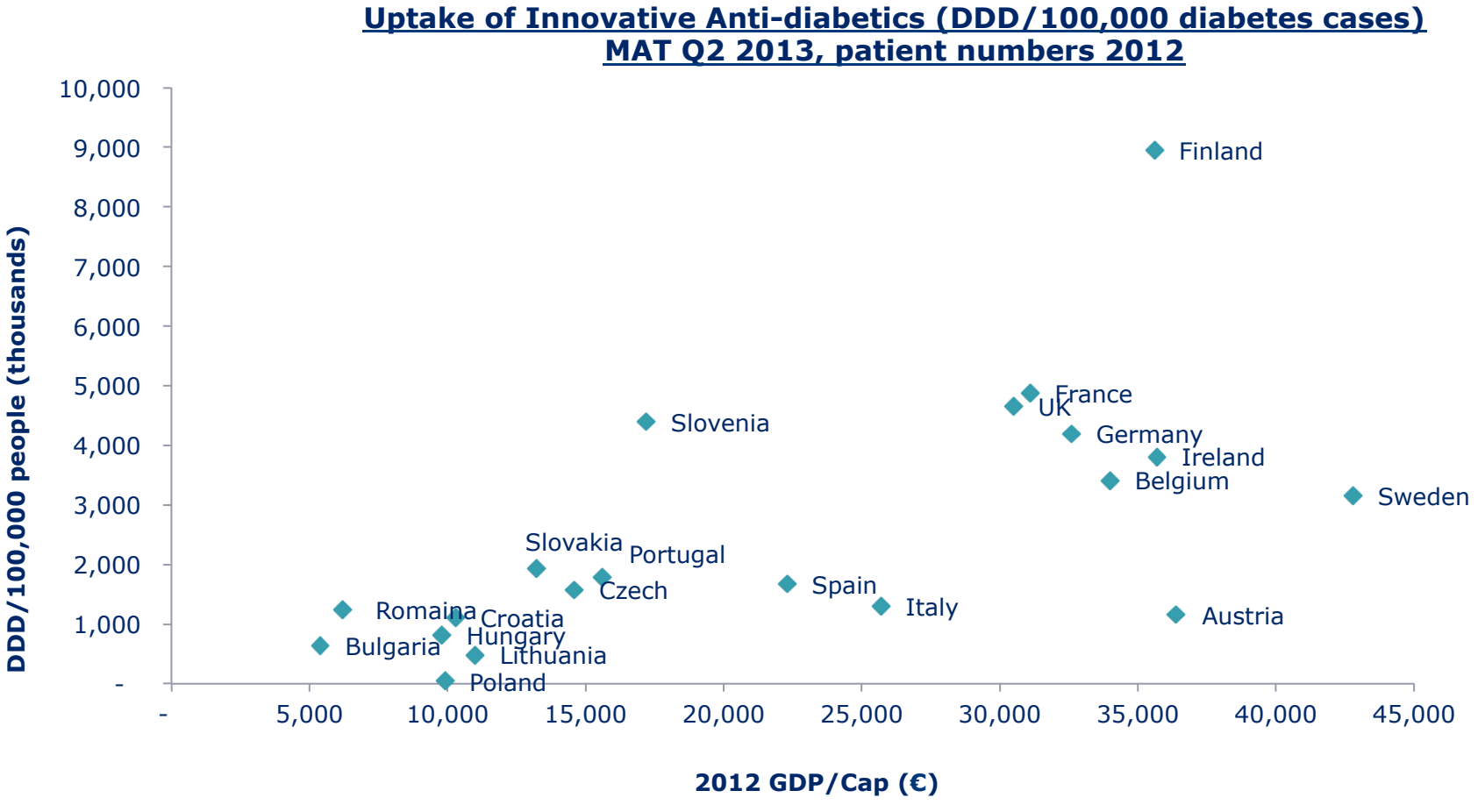
# Uptake per diabetes case/GDP Correlation

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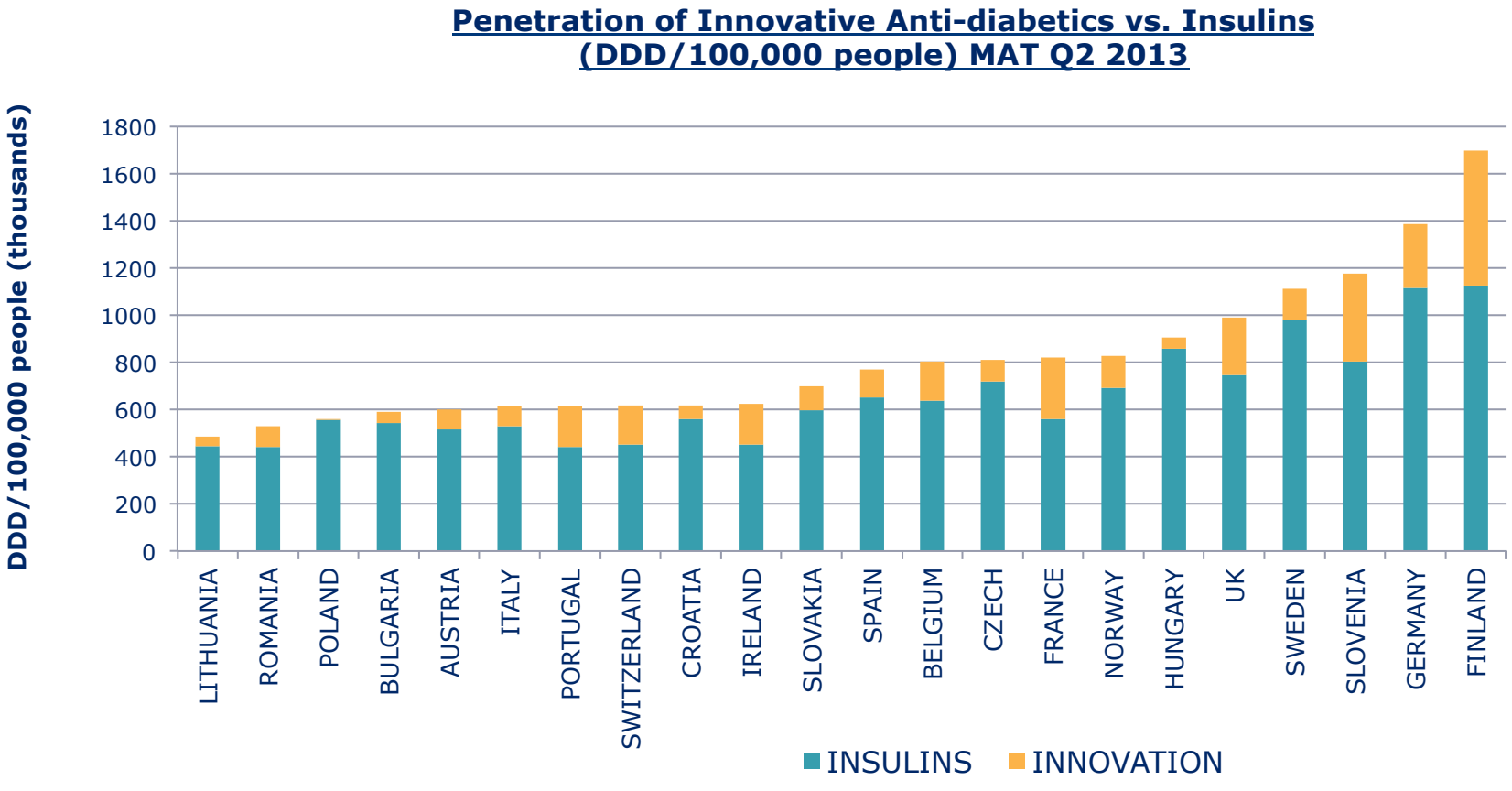
# Innovation vs. Insulins




*Insulins defined as A10C – note analysis does not consider use of alternative anti-diabetic agents (e.g.metformin or* sulfonylurea.) or *combination.*

*Source: IMS Health MIDAS Q2-2013.. Countries where IMS does not audit the hospital market have also been excluded from the analysis (Estonia, Greece, Latvia, Netherlands and Luxembourg) In some countries uptake may be impacted by parallel trade which cannot be adjusted for*



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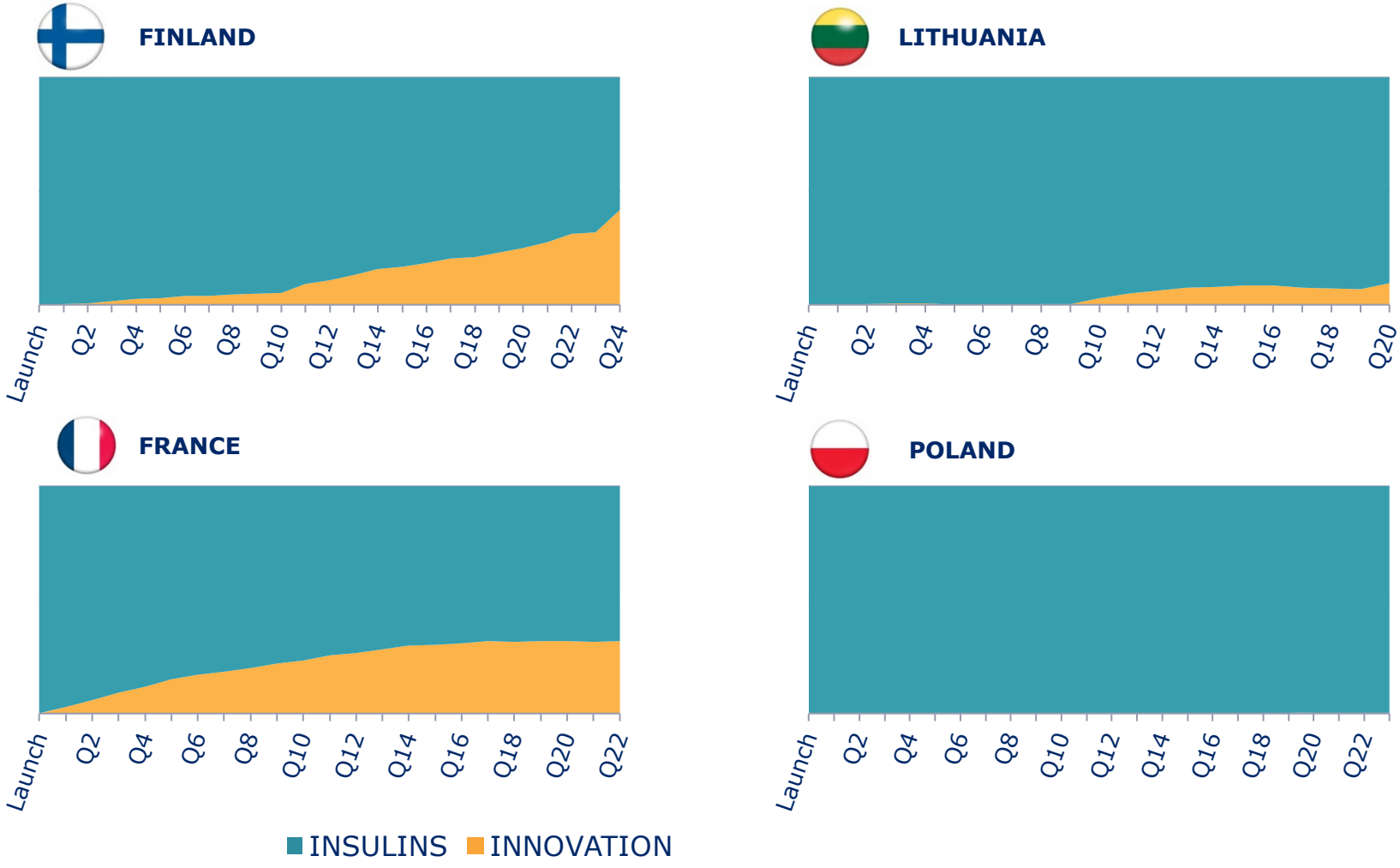
# Innovative anti-diabetics diffusion curve

**Diffusion of Innovative Anti-Diabetic (from launch date) vs Insulin (DDD/100,000)**

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# Hepatitis C: treatment overview & options

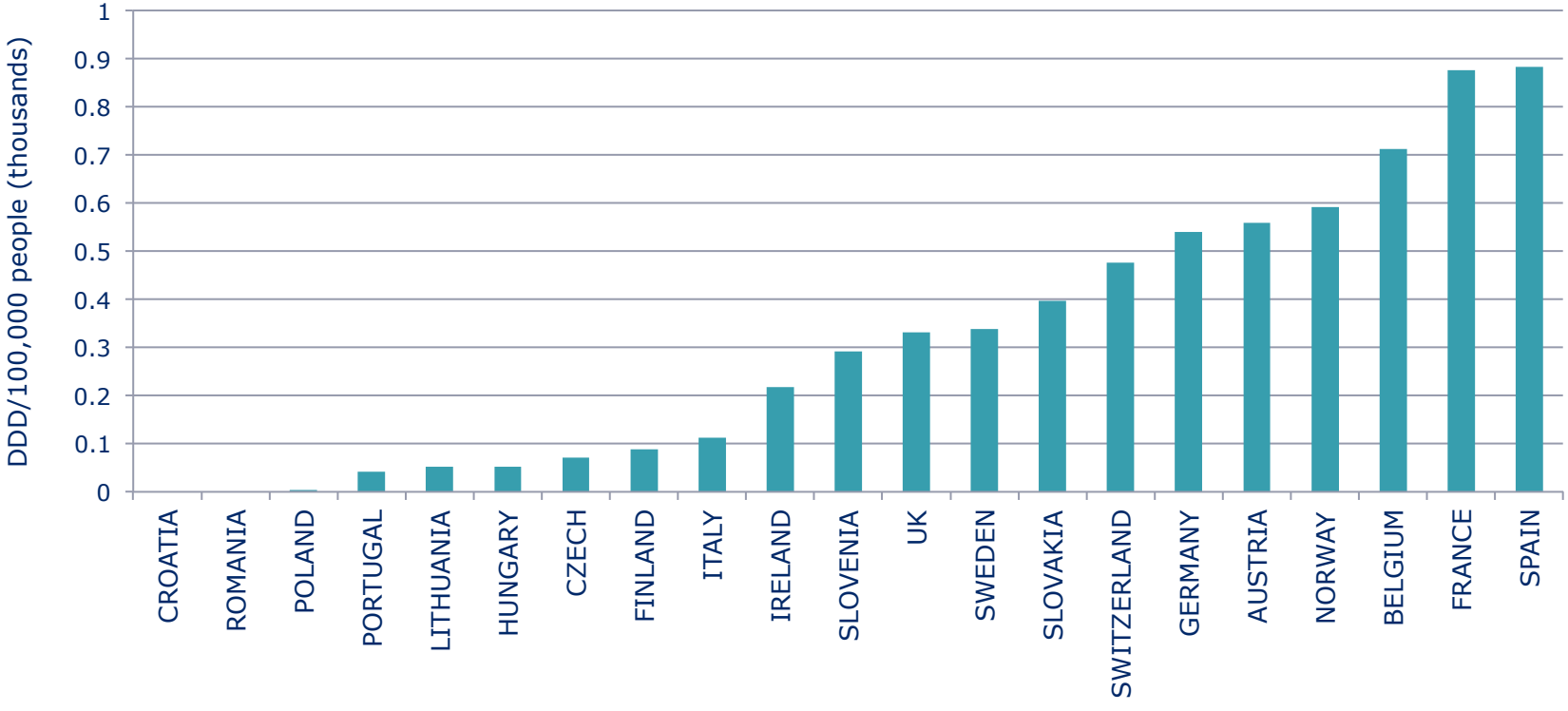
- Hepatitis C (HCV) is an infectious disease, which if left untreated, chronic infection can lead to cirrhoses of the liver or liver cancer
- Traditional treatment consists of pegylated interferon alpha and ribavirin. However, not only are there a number of negative side effects [flu-like symptoms (e.g. Fever, malaise etc.), anaemia and depression (not exhaustive)], the cure rates are extremely low, particularly in certain patient populations (Genotype 1, metabolically-impaired, African-American and co-infected (HCV &HIV) patients)
- 1st generation HCV protease inhibitors (innovative HCV drugs) have been approved for use in combination with pegylated interferon alpha and ribavirin.

| PRODUCT | MOLECULE | EMA APPROVAL |
|---|---|---|
| INCIVO | Telaprevir | 2011 |
| VICTRELIS | Bocerprevir | 2011 |

- These innovative medicines are classified as so for two reasons;
  - Firstly, they reduce the length of therapy for early respondent patients
  - Secondly, they have a higher success rate in Genotype 1 and African-American patients

# Uptake of innovative Hepatitis C products

**Europe: Uptake of Innovative Hepatitis C Products (DDD/100,000 people)**
**MAT Q2 2013**

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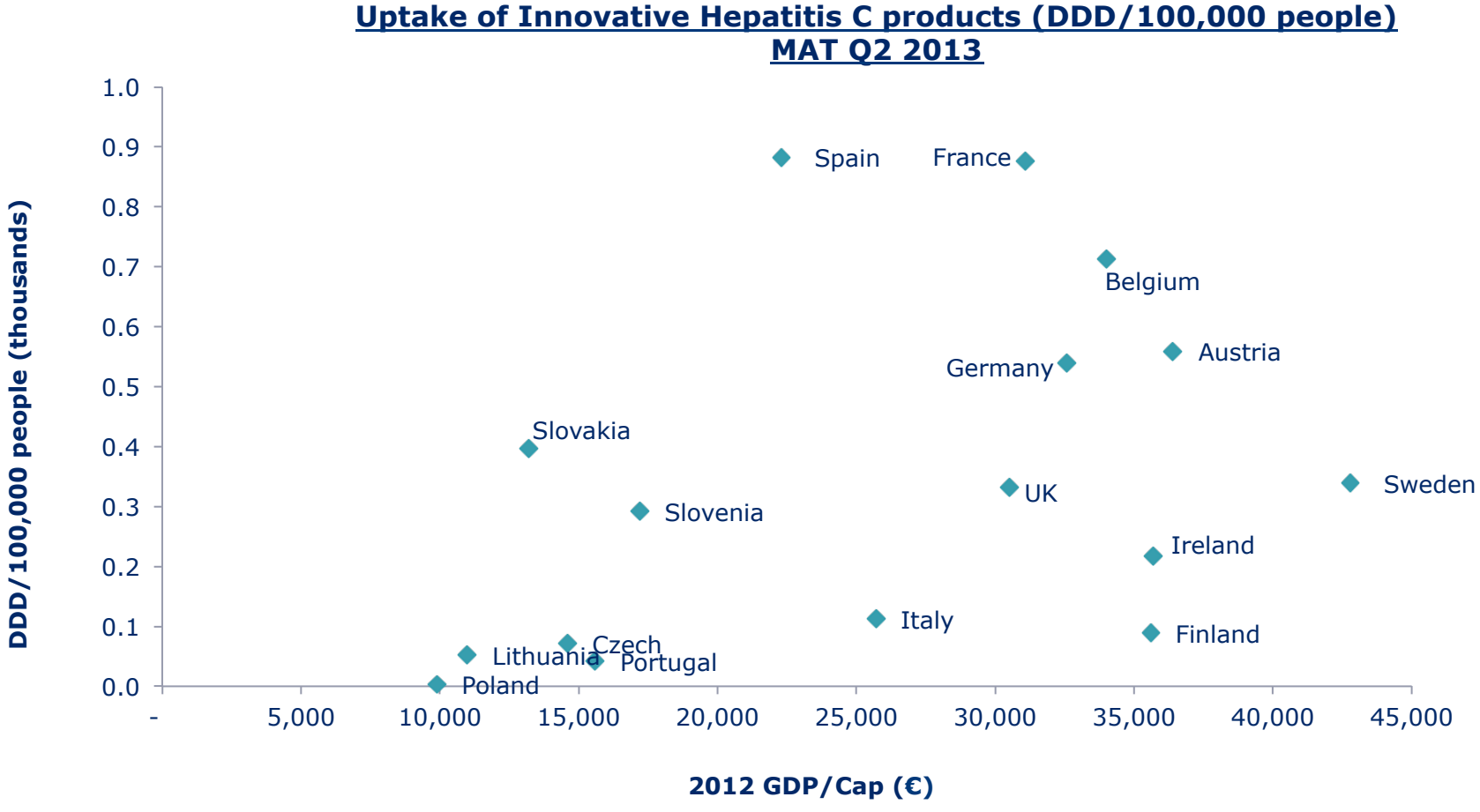
# Uptake /GDP Correlation

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# Conclusions

- Persistent differences exist in the uptake and diffusion of innovative medicines in Europe
- Differences in the uptake and diffusion of medicines are broadly associated with GDP per capita
- Differences in clinical practice and commercial strategy mean that product level comparisons of uptake are sometimes less meaningful than an analysis of innovative 'clusters' within given therapy areas
- A therapy area-based analysis of innovative clusters could be used to monitor the effect of policy change on the equality of access to new medicines across Europe

# UPTAKE OF INNOVATION IN EUROPE

## Thank You

- For further information please contact:
  - Claire Machin, Senior Consultant, IMS Health cmachin@uk.imshealth.com
  - Per Troein, VP Supplier Relations, IMS Health ptroein@uk.imshealth.com

Further details: www.imshealth.com