



**WEBINAR TRANSCRIPTION:  
THE CAUSES OF THE INTERNATIONAL  
VARIATION IN DRUG USAGE: AN EXPLORATION  
OF THE EVIDENCE**

*Presentation by Ellen Nolte, February 2017*

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# THE CAUSES OF THE INTERNATIONAL VARIATION IN DRUG USAGE: AN EXPLORATION OF THE EVIDENCE

**February 8, 2017**

This transcription is based on a webinar presented by **Ellen Nolte**, coordinator of the two offices of the European Observatory on Health Systems and Policies at the LSE and the LSHTM. Nolte presents the findings of a study that sought to explore the causes of international variation in medicines usage in five selected areas: dementia, osteoporosis, cancer, diabetes and hepatitis C. The presentation was focused on understanding the determinants of this variation as an important input to design policies meant to promote rational medicines usage.

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**WEBINAR**  
**THE CAUSES OF THE INTERNATIONAL VARIATION IN DRUG USAGE: AN EXPLORATION OF THE EVIDENCE**

Presented by:  
Ellen Nolte, coordinator of two offices of the European Observatory on Health Systems and Policies at the LSE and the LSHTM

08 - FEB - 2017 / 11:00AM WASHINGTON, DC

# INTRODUCTION

**(Min. 00:15:56)**

The work I will present today is mainly based on projects I have been involved with while I was at RAND Europe. The work was funded by the UK Department of Health. It is a bit old but by no means outdated because it is still of great importance for policy makers to really understand why countries vary in terms of drug usage.

## The causes of international variation in drug usage: an exploration of the evidence

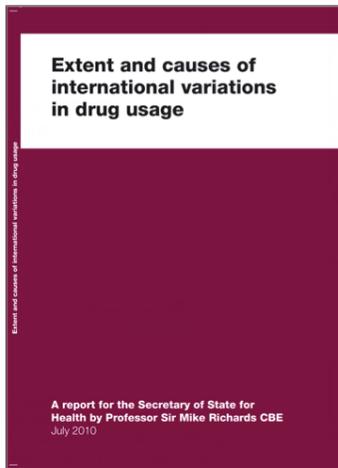
8 February 2017

Ellen Nolte  
European Observatory on Health Systems and Policies

*(based on work undertaken at RAND Europe & funded by the UK Department of Health)*



## Background



- Perception among stakeholders that the usage of new medicines was low in the UK compared to other high income countries
- Comparative analysis of levels of uptake of selected medicines in 14 high-income countries
  - No uniform pattern across disease areas and categories of drugs
  - US ranked first for all therapy areas combined, followed by Spain and France
  - General lower than average levels of usage in Norway, Sweden and New Zealand
  - UK ranked 8<sup>th</sup> out of 14 countries but usage pattern were not consistent across disease areas

Osteoporosis, certain childhood conditions, rheumatoid arthritis, and a few others. The idea was really to use available data on usage to understand whether there were any patterns across these countries. Perhaps not surprisingly that report found that there was no uniform pattern. There were a number of countries, which had consistently higher usage, like the United States, Spain and France, and countries at the other end, that had lower than other levels of usage, such as Norway, Sweden and New Zealand. But when you break it up for disease areas, it was not actually that consistent. When you look at the UK, which is of particular importance to the country of course, it ranked average. But again, usage patterns were not consistent across disease areas.

# BACKGROUND

**(Min. 00:16:28)**

First, let us look at the background of this work. The origins go back to the early 2000s when there was concern in the UK around low survival rates from cancer and the suspicion that perhaps one reason for that, compared to other high-income countries, was insufficient access to new cancer drugs. At that time, Mike Richards was commissioned, by the department of Health, to lead on a comparative analysis of the levels of uptake of selected medicines in fourteen high-income countries. The types of medicines were related to a number of key disease areas like cancer, but also certain others like stroke, dementia, mental health, Hepatitis C,

## Background



- 2014 update of quantitative analysis of Richards report
  - Same method, analysis of same class of medicines (with some additions) and same countries (except Denmark)
  - UK ranked 9<sup>th</sup> (out of 13) for all studied medicines
    - Higher than international average for 5 of 16 categories of medicines: selected cancer medicines, and medicines for the treatment of osteoporosis, respiratory distress syndrome, wet age-related macular degeneration, statins
    - Below international average for remaining 11 categories
    - Compared to average of 5 large European markets (France, Germany, Italy, Spain, UK), per person usage in UK was below the EU5 average for 9 of the 16 medicine categories

## Comparing per person medicines usage in the UK 2008/9 and 2012/13

- Increased relative to the international average in 11 out of 16 classes of medicines
- Remained below the international average for 7 of these 11 medicines/therapeutic areas
  - cancer medicines < 5 years old, alteplase for stroke, second-generation anti-psychotics, dementia, multiple sclerosis, pegylated interferons for hepatitis C, respiratory syncytial virus
- Exceeded the international average for 4 medicines/therapeutic areas
  - cancer medicines > 10 years old, osteoporosis, respiratory distress syndrome and wet age-related macular degeneration
- Fell relative to the international average for 5 medicines/therapeutic areas
  - cancer medicines 6–10 years old, hormonal cancer medicines, thrombolytics for acute myocardial infarction, TNF medicines for rheumatoid arthritis, statins

Source: O'Neill & Sussex, 2014

# BACKGROUND

**(Min. 00:18:24)**

As part of the government's commitment, four years later, the Department of Health commissioned an update of the earlier analysis from 2008/2009 to use the same method and analysis of the same class of medicines, plus some newer medicines, and the same countries, except for Denmark where the data was not available. This was done to understand if there had been any change in any of these countries in terms of the aggregate usage. It found that the pattern was still quite inconsistent, and for the UK in particular there was a small improvement regarding some medicines but at the same time a reduction for some other medicines.

# COMPARING PER PERSON MEDICINES USAGE IN THE UK 2008/9 AND 2012/13

**(Min. 00:19:19)**

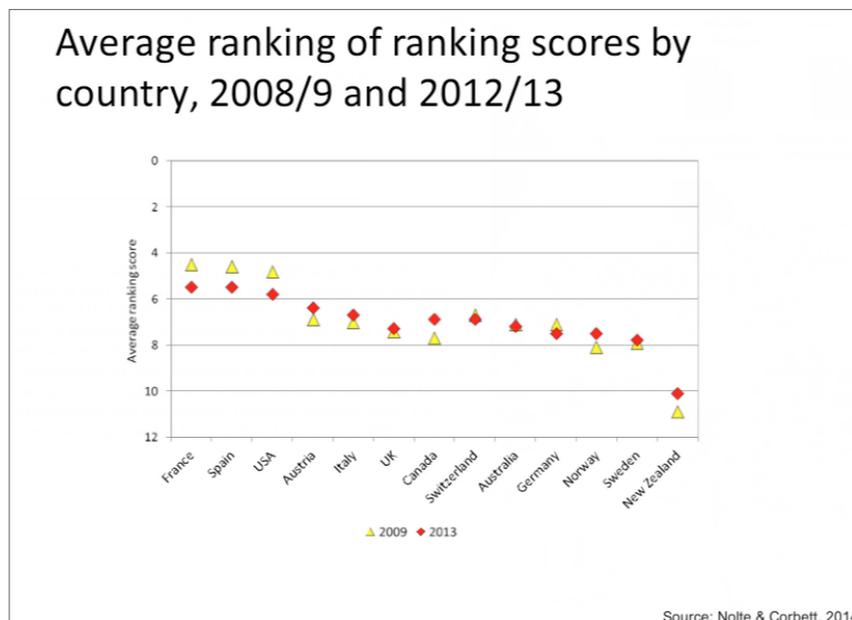
If we look in greater detail at what happened between 2008/9 and 2012/13, which was the latest data available at that time, O'Neill and Sussex found that the per-person medicines usage in the UK had increased relative to the international average in 11 out of these 16 classes but it

continued to lag behind in a number of areas, especially newer cancer medicines, certain treatments for strokes, second-generation anti-psychotics, for the treatment of mental health issues such as dementia or multiple sclerosis. It was higher for older cancer medicines, for osteoporosis, childhood conditions and age related macular degeneration. For others, there was a slight worsening. Overall however the data is quite difficult to interpret.

## AVERAGE RANKING OF RANKING SCORES BY COUNTRY, 2008/9 AND 2012/13

**(Min. 00:20:25)**

If you just look at the overall ranking of these thirteen countries over time, you see that overall the scores have actually shifted only slightly for all areas of diseases combined. France, Spain and the U.S. tended to be higher on average for all the disease areas that were looked at. New Zealand, Sweden and Norway were below the average. But overall, if you specifically focus on the red dots, which indicate the latest data, there seems to be some converging of countries ranking going on over the last four years or so. The key question is: What does this mean and what does this tell us about medicine usage in these countries?



## What explains international variation in drug usage?

- What is the optimum level of drug usage in different disease areas?
- To what extent does high or low usage indicate appropriate or indeed inappropriate use?
- The appropriate level of usage may vary because of different factors at work in different system contexts
  - high drug usage in some areas might reflect overuse because of weaknesses in disease prevention whereas low usage would point to effective and timely treatment
  - low usage in other areas might point to failure to meet patients' needs while high usage could indicate optimal treatment

Source: Nolte & Corbett, 2014

by the factors, which act at different levels within different systems. For example, high drug use in some areas might reflect overuse because there are maybe weaknesses in the disease prevention. In these particular areas, low usage would actually be preferably and an indication of effective and timely treatment, or in contrast, low usage in other areas, particular when you think about mental health, might point to failure to meet patients' needs while higher usage could indicate optimal treatment.

The quantitative data we have does not tell us it just tells us whether the high use was appropriate or the low use was appropriate or inappropriate, it just tells us that there is variation.

# WHAT EXPLAINS INTERNATIONAL VARIATION IN DRUG USAGE?

**(Min. 00:21:18)**

I think one of the key messages is that it is good to know these levels of usage but it does not really tell us whether usage is appropriate or inappropriate. For example, the appropriate levels of usage are pretty much determined

## Richards review 2010

### Explaining differences in usage

2.24 Importantly, this study set out not only to quantify the extent of any variation, but also to comment on its possible causes. At the beginning of the project, a series of hypotheses were developed by the steering group, which might explain variations in usage. The hypotheses are summarised in Box 3.

#### Box 3: Summary of hypotheses used in seeking to explain the causes of international variations

A variety of hypotheses were tested with experts:

*System factors will explain levels of drug usage, including:*

- levels of expenditure on health;
- the proportion of overall health budget spent on medicines;
- the extent of restrictions on prescribing;
- the nature of pharmaceutical marketing activity within a sector; and
- the impact of investment in primary and secondary prevention.

*Reimbursement factors will explain levels of drug usage, including:*

- the relative price of a drug in a particular country;
- the existence of health technology assessment processes; and
- health technology assessment outcomes which have a strong effect on prescribing behaviour.

*Service organisation and capacity factors will explain levels of drug usage, including:*

- the extent of national prioritisation for a disease area;
- the impact of direct access to specialists;
- the existence of initiatives to influence prescribing practice;
- capacity limitations at different stages of the patient pathway; and
- funding mechanisms for different modes of drug administration.

#### Box 3 (continued)

*Cultural factors will explain levels of drug usage, including:*

- clinical attitudes towards risk;
- the extent of research activity;
- clinical attitudes towards national guidance and direction;
- the influence of different professions, for example pharmacists;
- patient attitudes towards treatment; and
- the existence of well-developed charities and patient support organisations.

*Epidemiological factors will explain levels of drug usage, including:*

- differences in incidence and/or prevalence; and
- stage of diagnosis impacting upon how many patients are suitable for a particular drug.

2.25 These hypotheses were tested against the findings with a range of UK experts:

- Patient representatives were asked for their observations, including views on the impact of patient preference on levels of drug usage.
- Clinicians were asked for their observations, including whether they were aware of different clinical practices in different countries.
- Pharmacists and public health doctors were asked for feedback from their professional networks.
- Academics were asked to provide any examples of studies looking at differences in clinical practice and to provide a review of health system factors.
- Manufacturers were asked to provide observations on the reasons for variations in sales.

2.26 These experts were asked to provide feedback in a variety of formats, including:

- workshops for clinicians, pharmacists and public health specialists;
- structured interviews with patients and patient representative groups; and
- written submissions to the project.

of pharmaceutical, service at the retail level, which might explain timely access to treatment; cultural factors such as clinical attitudes towards prescribing; and of course, very important, epidemiological factors because if there is a higher prevalence rate then in theory usage should be higher in order to indicate an appropriate treatment. These hypotheses were then tested in 2010 against a number of UK experts at that time to understand what could be specific to the UK.

# RICHARDS REVIEW 2010

(Min. 00:22:23)

To better understand what this variation is about, Mike Richards in his 2010 report, already looked at some of the potential causes that might explain some of this variation. They formulated a number of hypothesis around system factors, for example levels of expenditure, particularly pharmaceutical expenditure, the way the system is organized and governed, issues around reimbursement and health technology assessment, which might influence the uptake

## What explains differences in international variation in drug usage?

- There is uncertainty about the optimum level of drug usage in different disease areas and the extent to which high or low usage point to appropriate or indeed inappropriate use
- The appropriate level of usage may vary because of different factors at work in different system contexts

### *Richards Review 2010*

- Causes of international variation in drug usage are complex
- Three core areas of importance for drug usage levels in the UK
  - Health technology assessment processes and outcomes
  - Service planning, organisation and direction setting enabling or restricting usage
  - Clinical culture and attitudes towards treatment determining levels of uptake

Source: Nolte & Corbett, 2014

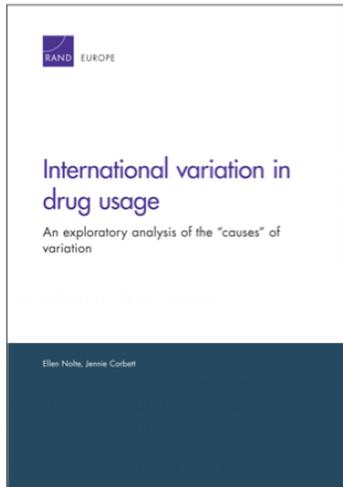
in many other systems. One is around the impact of Health Technology Assessment processes and outcomes. Another one is around service planning, organization, and direction setting to enable or restrict the uptake of pharmaceuticals. The third one is around clinical culture and attitudes towards treatment, which also determines levels of uptake. Based on that, and vis-à-vis the quantitative data that was available in 2014, we were asked to undertake some more qualitative work, to understand better what it is that we can take from the available evidence that would help us to disentangle some of these factors.

# WHAT EXPLAINS DIFFERENCES IN INTERNATIONAL VARIATION IN DRUG USAGE?

**(Min. 00:23:51)**

The conclusion at that time was, not surprisingly, that the causes are quite complex. They identified three core areas to be of importance for levels seen in the UK, but probably also

## An exploratory analysis of the 'causes' of international variation in drug usage



- Builds on 2010 Richards Review
- Provides
  - a summary overview of key features of 13 health systems included in the 2014 quantitative update of the report
  - a summary overview of the principles of drug assessment or approval processes in these 13 countries
  - an exploratory analysis of the “causes” of international variation in medicines usage in five selected areas
    - Dementia
    - Osteoporosis
    - Cancer
    - Diabetes
    - Hepatitis C

### (Min. 00:24:57)

What we did is to provide a summary of the key features of the health systems that the quantitative review has been looking at. We also looked at some of the principles of drug assessment or approval processes in these thirteen countries. Yet, the main focus is on a number of disease areas to trying to understand if there is something specific regarding a disease area, what are the commonalities and differences, and what kind of lessons can we learn. We looked at dementia, osteoporosis, cancer, diabetes and Hepatitis C. These disease areas were chosen for several reasons. One was that, particularly regarding osteoporosis, the UK was consistently shown to be a high user of medicines and for cancer, especially the newer innovative rather on the lower side. Diabetes and Hepatitis C were included because in 2014 innovative patents had come on the market and there was a suspicion by certain stakeholders that those were not properly used or taken up in the same amount in the UK compared to other countries.

# AN EXPLORATORY ANALYSIS OF THE “CAUSES” OF INTERNATIONAL VARIATION IN DRUG USAGE

## What we did

- For each of the five disease areas we reviewed the published evidence on:
  - epidemiological factors such as the disease burden (incidence or prevalence) and stage of diagnosis of the disease to understand 'population need'
  - international variation in drug usage to enable the placing of the quantitative findings into the wider context
  - aspects of health system and service organisation that were shown to have a direct or indirect impact on drug usage, e.g.
    - reimbursement mechanisms
    - access to diagnosis and treatment more broadly
    - other factors identified in the literature
  - Iterative search of the published and grey literature using PubMed & Google Scholar; searches of websites of governmental and non-governmental agencies or organisations for documents on general health-related policies in each country

Source: Nolte & Corbett, 2014

have a direct or indirect impact on drug usage, for example reimbursement mechanisms, access to diagnosis, and any other factors.

Unfortunately, for this particular piece of work we had a very restricted time frame of only eight weeks, so we were not really able to involve stakeholders like professionals, patients and other groups, in trying to understand these various perspectives to understand what was going on the ground. But certainly, our work did manage to identify a number of further lines of inquiry.

I will now run you through some high-level observation. Some of it you will be very familiar with and other information you might have not seen in this type of presentation before. I would like you to get some sense on how much we do know and can learn from the published evidence that helped us to explain variation of drug usage.

# WHAT WE DID

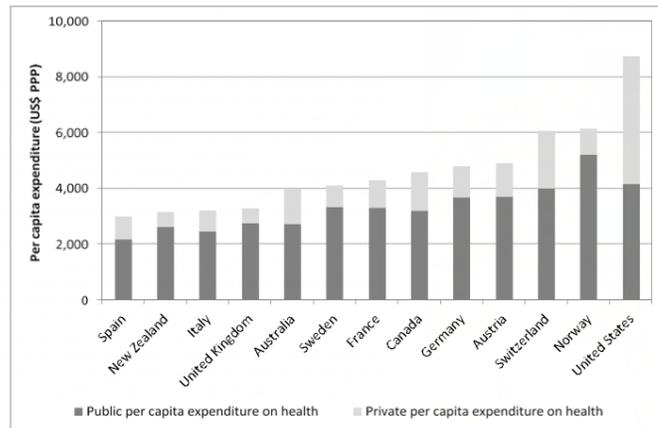
**(Min. 00:26:26)**

What we then did was desk research looking at the published evidence around the burden of disease, to understand if there was a high burden that can lead to higher usage.

We looked at the documented evidence to see what other studies had done in trying to understand international variation in drug usage. Actually, there is very little good research in this area.

We were also looking at literature that has investigated aspects of health system and service organization that may

## High-income countries vary in the way they fund and organise their health systems



Per capita expenditure on health (US\$ purchasing power parity) in 13 OECD countries, 2012 (data source: OECD 2014)

Source: Nolte & Corbett, 2014

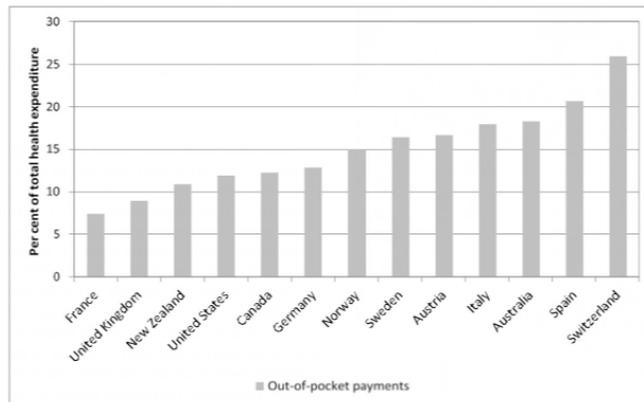
vary in the way they fund and organize their health systems. The countries we have been looking at are diverse, but they do share several very common features. The outlier might be the United States. For example, twelve of these thirteen countries are overwhelmingly publicly funded, partly through taxes and partly through social health insurance. In the U.S., on the other hand, a little over 50% of the system is funded through private sources. We also find that twelve out of these thirteen countries have more or less universal coverage, and even though there are pockets of under-insurance, coverage is pretty much universal. These countries also have fairly generous baskets of services that are funded under the public system. Again, in the United States this depends on the particular system you are covered under. These countries also offer a fairly broad protection regarding out-of-pocket payments.

# HIGH-INCOME COUNTRIES VARY IN THE WAY THEY FUND AND ORGANIZE THEIR HEALTH SYSTEMS

**(Min. 00:28:20)**

One of the key areas to look at is spending. As you know, countries, whether they are high-income countries or not, do

Out-of-pocket payments play a role in all reviewed countries



Household out-of-pocket payments as percentage of total health expenditure in 13 OECD countries, 2012 (data source: OECD 2014)

Source: Nolte & Corbett, 2014

to payments into private insurance. Therefore, these are not direct out-of-pocket payments in terms of cost sharing.

Prescription drugs usually require patient co-payment (2014)

	User charge required	Exemptions			Maximum out-of-pocket limit
		Chronically ill or disabled	Low income	Age	
Australia	Yes	Yes	Yes	Seniors, children	Fixed, dependent on type of patient
Austria	Yes		Yes	Seniors	2% of annual net income
Canada	Yes		Yes		Varies by plan
France	Yes	Yes	Yes		
Germany	Yes	Yes		Children	2% of annual net household income (1% of income for chronically ill)
Italy	Yes	Yes	Yes	Seniors, children	
New Zealand	Yes		Yes	Children	
Norway	Yes	Yes		Seniors, children	Set annually; Nkr €520 for "blue list" drugs
Spain	Yes	Yes			
Sweden	Yes	Yes		Children	
Switzerland	Yes			Children	Set at CHF 700 for adults and CHF 350 for children (treatment costs, incl. drugs)
UK/England	Yes	Yes	Yes	Seniors, children	
US	Varies	Varies	Varies	Varies	Varies

Source: Nolte & Corbett, 2014

# OUT-OF-POCKET PAYMENTS PLAY A ROLE IN ALL REVIEWED COUNTRIES

(Min. 00:29:46)

Looking at out-of-pocket payments in particular you will see that there is a variation between countries. There are particularly high levels indicated for Spain and Switzerland, but these don't refer to cost sharing arrangements but rather

# PRESCRIPTION DRUGS USUALLY REQUIRE PATIENT CO-PAYMENT

(Min. 00:30:16)

What we do find is that these countries, given that we are talking about medicines, issue some form of co-payment.

All of them do. Yet, all of them also have exemptions for particular vulnerable groups like the elderly, children, people with a low income or people with long-term conditions or certain disabilities, to really protect them from catastrophic expenditure related to illness. The data is a bit old but it still applies for these countries.

These are the basics regarding health care system funding, but there are of course other issues such as gatekeeping, which is in place in most these countries. This may also be hypothesized as a potential impediment, or not, to getting access to specialized treatment and by implication to drugs. We were not able to find direct evidence about that.

### Most countries have national bodies advising on inclusion of new drugs under public funding

- Decisions are typically informed by formal health technology assessments, which may be carried out by the relevant institutions or commissioned externally
- Public bodies with a *largely* advisory or guidance producing role have been established in Australia, Canada, France and the UK
- In all other reviewed countries, relevant organisations or agencies have a regulatory function (Pharmac in New Zealand; Federal Joint Committee in Germany)
- Some countries have established regulatory bodies separate from the ministry of health, although the ministry has remained the final decisionmaker
- In the US, public payers have established their own systems for appraising new drugs for public funding
  - Patient-centred Outcomes Research Institute (PCORI) tasked with undertaking comparative effectiveness assessments of medical treatments, including drugs, to ‘assist’ decision-making but not mandate

Source: Nolte & Corbett, 2014

# MOST COUNTRIES HAVE NATIONAL BODIES ADVISING ON INCLUSION OF NEW DRUGS UNDER PUBLIC FUNDING

**(Min. 00:31:34)**

What we did find is some very convincing issues around the role of policy regarding the process of including new drugs in the benefit basket. What we know, is that many countries have national bodies advising them on the inclusion of public funding. These are typically informed by formal health technology assessments. Often these technology assessments do draw on cost-effectiveness of drugs, but in all cases cost-effectiveness is only one of the many aspects of new drugs that are being looked at.

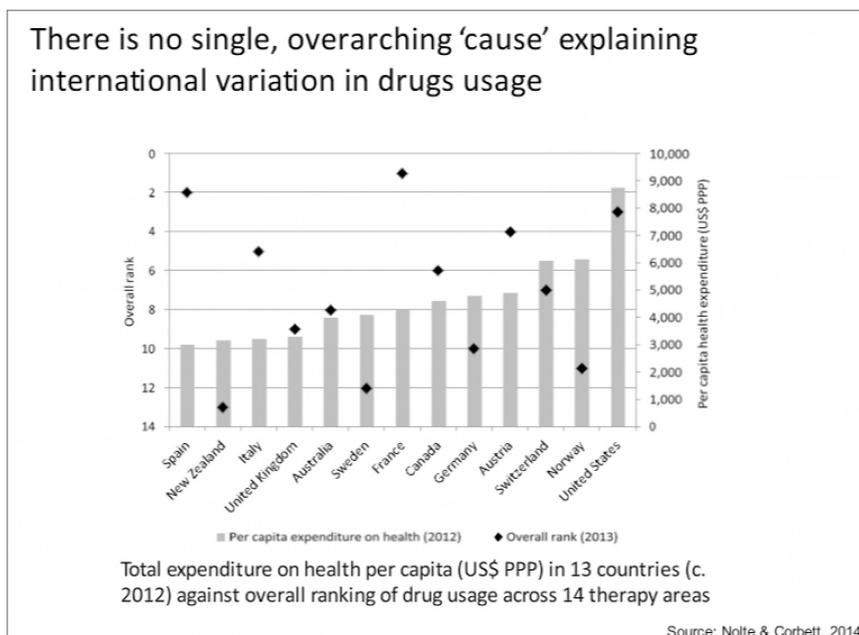
We do know that these bodies have largely an advisory or guidance role in Australia, Canada France and the UK. In a number of countries, they also have regulatory roles, such as Pharmac in New Zealand, or the Federal Joint Committee in

Germany. In some countries, even though they have separate bodies, the Ministry has remained the final decision maker. In the United States, there is no single body responsible for appraising new drugs for public funding. Here the public payers have established their own system. Under the Affordable Care Act the patient-centered Outcomes Research Institute has been tasked with undertaking comparative effectiveness assessments of medical treatments but their function is only to assist decision-making. They have no role in mandating for example reimbursement levels. It is pretty much an advisory body.

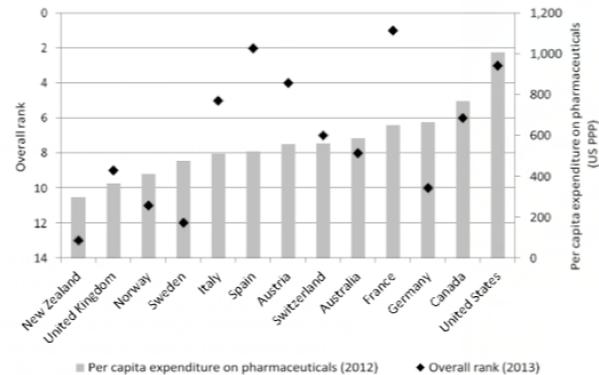
## THERE IS NO SINGLE, OVERARCHING “CAUSE” EXPLAINING INTERNATIONAL VARIATION IN DRUGS USAGE

(Min. 00:33:24)

We also looked at international variation in drug usage, and some of the system factors, and did some very simple correlation analysis between total health care expenditure, which we see on this slide. We plotted the rank, which you remember from an earlier slide on average international drug usage and per-capita expenditure. We find that there is literally no pattern and the correlation coefficient is next to zero. So, there is no obvious correlation.



There is no single, overarching 'cause' explaining international variation in drugs usage



Total expenditure on pharmaceuticals per capita (US\$ PPP) in 13 countries (c. 2012) against overall ranking of drug usage across 14 therapy areas

Source: Nolte & Corbett, 2014

# THERE IS NO SINGLE, OVERARCHING “CAUSE” EXPLAINING INTERNATIONAL VARIATION IN DRUGS USAGE

**(Min. 00:34:04)**

However, if we do narrow down expenditure to pharmaceutical expenditure, there is actually a positive correlation, meaning that countries that have higher expenditure on pharmaceuticals also tend to have a higher level of medicines usage. Perhaps this is not surprising. Yet the question remains whether higher levels of usage are actually appropriate.

## What is the role of policies on the inclusion of new medicines in publicly funded systems?

- Overall processes are multi-faced and complex, and their contribution to international variation in the uptake of drugs remains challenging to disentangle
- Policies determine whether patients have routine access to a given new medicine, in particular where access is made conditional
  - *Osteoporosis*: patients in some European countries may face challenges in accessing osteoporosis medicines where only 50% of the costs are reimbursed

Source: Nolte & Corbett, 2014

# WHAT IS THE ROLE OF POLICIES ON THE INCLUSION OF NEW MEDICINES IN PUBLICLY FUNDED SYSTEMS?

**(Min. 00:34:38)**

Let me go back to what I was saying earlier regarding policies on the inclusion of new medicines. There is some tentative evidence that they can influence uptake, in particular where access is made conditional. For example, in osteoporosis the evidence shows at the time that patients in some European countries, in particular in Spain, were facing challenges in accessing osteoporosis medicine because only 50% of the costs were reimbursed at that time.

## Availability of osteoporosis treatments in 7 European countries, 2012

	Bisphosphonates	SERMs	Strontium ranelate	PTH analogues	Denosumab	Reimbursement	Reported impediment to treatment
Austria	Yes	Yes	Yes	Yes	Yes	100%	No
France	Yes	Yes	Yes	Yes	-	65%	Yes (professional)
Germany	Yes	Yes	Yes	Yes	Yes	100%	No
Italy	Yes*	Yes	Yes	Yes	Yes	100%	Yes (professional)
Spain	Yes	Yes	Yes	Yes	Yes	50%; 100% for pensioners	Yes (patient)
Sweden	Yes*	Yes	Yes	Yes	Yes	100%	No
UK	Yes	Yes	Yes	Yes	Yes	100%	No

Notes: Bisphosphonates – alendronate, ibandronate, risedronate, zoledronic acid; PTH – parathyroid hormone derivatives (PTH, teriparatide); SERMs – selective oestrogen receptor modulators; \*not all bisphosphonates available

Adapted from Kanis et al. (2013), Hernlund et al. (2013)

Source: Nolte & Corbett, 2014

a lot in this field. It shows the availability of osteoporosis treatments in seven European countries in 2012. When you look at the right-hand side you see that countries such as France or Spain have imposed certain reimbursement threshold, which in case of France has been reported by professionals to pose an impediment to treatment. In Spain, it has been reported by patients to be an impediment. Interestingly in Italy, even though reimbursement was 100%, the study reported impediments on treatment. I will come back to that.

We can say that policies that are related to considerations of whether or not to include a drug in the public system, and whether or not there are particular conditions linked to that, will have, not surprisingly of course, potential problems for the end user.

# AVAILABILITY OF OSTEOPOROSIS TREATMENTS IN SEVEN EUROPEAN COUNTRIES IN 2012

**(Min. 00:35:24)**

This is illustrated further on this slide, which we have adapted by work form John Kanis and colleagues who have worked

## What is the role of policies on the inclusion of new medicines in publicly funded systems?

- Overall processes are multi-faced and complex, and their contribution to international variation in the uptake of drugs remains challenging to disentangle
- They determine whether patients have routine access to a given new medicine, in particular where access is made conditional
  - *Osteoporosis*: patients in some European countries may face challenges in accessing osteoporosis medicines where only 50% of the costs are reimbursed
  - Evidence for dementia, osteoporosis, hepatitis C and, to certain degree, cancer finds that factors *other* than policies on the inclusion of new medicines in publicly funded systems may be equally or more important in affecting uptake:
    - access to (timely) diagnosis
    - whether or not the disease area is designated a national priority;
    - the clear identification of responsibilities for managing the disease and the existence of designated care pathways

Source: Nolte & Corbett, 2014

# WHAT IS THE ROLE OF POLICIES ON THE INCLUSION OF NEW MEDICINES IN PUBLICLY FUNDED SYSTEMS?

**(Min. 00:36:49)**

However, when we were digging further into these five disease areas, what became obvious is that these policies on the inclusion of new drugs are very important, but potentially more important, are things. These are centered around access to timely diagnosis, whether or not the disease areas a national priority, and whether there are identified responsibilities for managing the disease in question, and whether there are designated care pathways. We found that this was a common issue for dementia, osteoporosis, Hepatitis C and to a certain degree cancer as well.

I will guide you through some of the evidence we have found here.

## Access to timely diagnosis

- Evidence for all four disease areas highlights the key role of ensuring access to timely diagnosis to enable appropriate treatment, including drug treatment

### *Osteoporosis*

- access to bone density measurement technology (such as dual-energy X-ray absorptiometry) is a potentially greater barrier to treatment than the actual reimbursement of drugs
- Bone densitometry may in principle be available, related investigations may not be (fully) reimbursed, or only reimbursed under certain conditions, which could limit access (e.g. Germany and France)
- Some evidence that bone density measurement is associated with anti-osteoporotic drug prescription

Source: Nolte & Corbett, 2014

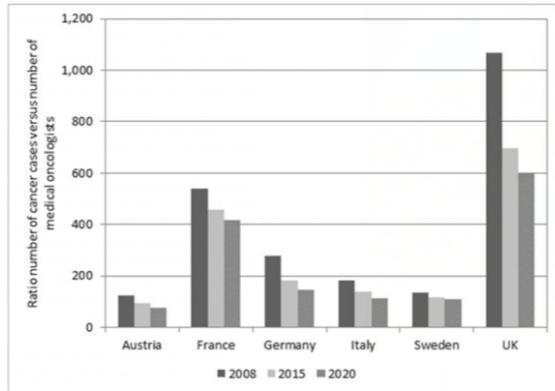
as a potential greater barrier to the treatment. What we found is that the technology to measure bone density may be available in principle. For example, Italy has a very high density of this particular equipment to measure bone density, but the related studies are not fully reimbursed and that is the key impediment, or they are only reimbursed under certain conditions. This was also reported for France and Germany. So, in principle the drugs are available, and they may even be available for free, but because there are restrictions on bone density measurements, people who might need the drugs actually can't get them due to various reasons and because they can't access the diagnosis, which is required to then be prescribed the actual drugs. There is some evidence that bone density measurement is associated with the rate of anti-osteoporosis drug prescription. There is some tentative evidence that there is a direct link between diagnosis and treatment. Again, a lot of that is maybe not surprising, but it is interesting to see actual data around that.

# ACCESS TO TIMELY DIAGNOSIS

**(Min. 00:37:46)**

If we start with the access to timely diagnosis, as I said, in these four disease areas we found that ensuring access will enable access to a proper treatment and by implication to drugs. Osteoporosis is an interesting example and it has also been studied quite well, which helps to identify some of these factors. What we found is that, in fact, it is not the access to the drug as such, it is actually access to bone density measurement technology, which has been seen

Ratio of the number of new cancer cases and of the number of medical oncologists in 6 countries



Adapted from Azambuja et al. (2014)

Source: Nolte & Corbett, 2014

**(Min. 00:39:49)**

Another interesting example regarding cancer, which is not based on direct empirical evidence, but something worth investigating is shown on the next slide, related to access to specialists on cancer. This was an interesting study published by Azambuja et.al. They looked at the projected new cases of cancer in several European countries, and plotted that against the expected number of medical oncologists in those six countries, between 2008 and 2020, as you can see from the differently shaded bars. What you can see quite clearly is that especially in the UK, to a latter degree in France, the number of cases per oncologist is considerably higher in the UK compared to Austria, Sweden and Italy. This implies that access to a specialist may be more difficult in the UK compared to other countries. Of course, the number of medical oncologists does not tell us anything about whether the care they provide is of higher quality and appropriate. Yet, it does give you some indication that access to specialist treatment may be restricted, and therefore access to newer drugs might be equally restricted.

# RATIO OF THE NUMBER OF NEW CANCER CASES AND OF THE NUMBER OF MEDICAL ONCOLOGISTS IN 6 COUNTRIES

## National prioritisation

- Designating a given condition a national priority is likely to lead to increases in medicines access and usage

### *Dementia*

- Where comprehensive plans for the detection and treatment of dementia have been put in place, these were likely to increase the number of people diagnosed with the disease and of those receiving treatment
- 2009 National Dementia Plan in England was shown to be associated with an increase in dementia diagnosis rate
  - dementia diagnosis rates were highly correlated with prescription rates, the rate of prescriptions for dementia drugs increased by 11 per cent in 2010 and 24 per cent in 2011 compared with 2009

### *Osteoporosis*

- UK also identified osteoporosis as a priority, which was likely associated with an observed rapid increase in uptake in osteoporosis medicines

Source: Nolte & Corbett, 2014

There was a review of dementia plans in a number of European countries, which found that where these plans were in place these were likely to increase the number of people diagnosed with the disease and those receiving treatment. In particular, an evaluation of the 2009 National Dementia Plan in England was associated with an increase in dementia diagnosis, and subsequently with prescription rates. For dementia, there is also a huge under-detection so this correlation is perhaps not surprising. The same was observed for osteoporosis in the UK, where it was identified as a priority and this was slightly associated with a rapid increase in uptake in these medicines. In these cases, it is just a correlation and we don't know about the quality of the treatment. We just know it has led to an increased uptake.

# NATIONAL PRIORITIZATION

**(Min. 00:41:21)**

The second area I mentioned, and which was also identified by Mike Richards in his earlier work, is the issue of national prioritization. Here we find a couple of examples for dementia, for osteoporosis and cancer. Probably it is not surprising to many of us that if you assign funding to a certain area it will be addressed and in particular that if you funding for access it will be taken up.

## Osteoporosis or musculoskeletal disease as a national priority in 7 EU countries

	National health priority (date)	Government support	Scope	Action plan
Austria	No			
France	Yes (2004)	Yes	Nutrition, exercise, falls prevention	No
Germany	No			
Italy	Yes (2005)	Yes	Nutrition, falls prevention	Uncertain
Spain	No			
Sweden	Yes (2012)	Yes	Not yet defined	No
UK	Yes (2009)	Yes	Nutrition, exercise, fracture liaison services	Indirect

Adapted from Kanis et al. (2013)

Source: Nolte & Corbett, 2014

As you can see in this table, a few countries have prioritized it but not many. There is some indirect evidence that has been linked to increasing uptake.

# OSTEOPOROSIS OR MUSCULOSKELETAL DISEASE AS A NATIONAL PRIORITY IN 7 EU COUNTRIES

(Min. 00:43:00)

I think an interesting example in this context is the cancer drugs fund. Sorry, I will step back to look at this slide. In this slide, I highlighted findings from Kanis again on osteoporosis.

## Cancer Drugs Fund in England

**Does uptake analysis?**

**Background:** The C...  
**Methods:** The cost...  
**Results:** The cost...  
**Interpretation:** The...  
**Conclusion:** The...  
**Keywords:** NICE, cancer drugs fund, chemotherapy, cost-effectiveness

**House of Commons**

**“In the last five years about 80,000 people received drugs through the Fund... (but there is no data) to assess the impact of the Fund on patient outcomes, such as extending patients’ lives, or to demonstrate whether this is a good use of taxpayers’ money.”**

**“The cost of the Fund grew from £175 million in 2012/13 to £416 million in 2014/15, an increase of 138% in two years.”**

**“There is agreement that the Fund is not sustainable in its current form and NHS England and the National Institute for Health and Care Excellence (NICE) are currently consulting on proposals to reform the Fund from April 2016.”**

Source: Nolte & Corbett, 2014

# CANCER DRUGS FUND IN ENGLAND

(Min. 00:43:30)

But what I wanted to focus on is the cancer drugs fund in England, which was set up in 2010 as a means to improve access to cancer drugs that would otherwise not have been

the case under NHS rules. Essentially, it was established to speed up access to newly introduced drugs that were not yet approved by NICE. A number of studies have come out since then; most recently a review by the House of Commons, via the Parliament looking specifically at the bylaw of the cancer drug fund. What has been shown is that there has been increased access to drugs that perhaps had have negative appraisals by NICE for not being cost-effective. Yet, the key issue is that there is no data whether this also has led to improved patient outcomes, such as extending their lives or the good use of public money. Also, there has been a lot of money put into that, to the extent that the cancer drug fund is now being viewed as financially unsustainable. There is currently work going on to see how it could be managed better in the future. The key issue is that it has increased access to drugs, which were not actually deemed cost-effective by NICE. Yet, it has not increased the access to drugs, which were already approved as beneficial by NICE. This is quite a complicated area and it highlights that just pumping in money might not necessarily guarantee appropriate prescribing.

## Disease management and care pathways

- Studies in the fields of dementia and osteoporosis highlighted the importance of identifying clear pathways with assigned responsibilities for managing a given disease or condition

### *Osteoporosis*

- Suggestion that patients should principally be managed at the primary health care level by general practitioners, with specialist referral reserved for difficult cases
- Core role for fracture liaison services, providing a system for the routine assessment and management of postmenopausal women and older men who have sustained a low trauma fracture
- Evidence finds that uncertainty about responsibilities among care providers was linked with patients falling “through the cracks”, hindering access to appropriate and timely treatment, in particular among those at increased risk for fragility fractures

Source: Nolte & Corbett, 2014

# DISEASE MANAGEMENT AND CARE PATHWAYS

## **(Min. 00:45:37)**

The final area is disease management and care pathways. It is really about the importance of knowing who is responsible along the care pathway for a particular patient to ensure that they don't fall through the cracks. Osteoporosis is again a nice example to show that. There is international work by John Kanis suggesting that most patients with osteoporosis should be managed by the primary health care level, by general practitioners. The option to be referred to a

specialist should be reserved for difficult cases. There is also increasing evidence that access to fracture liaison services will actually help improve outcomes. What has been shown again and again, and this is not only for osteoporosis but also for rheumatoid arthritis, dementia or even diabetes, is that if there is uncertainty about the responsibility, therefore who is responsible for the patient, the risk is that patients fall through the cracks. This means that they then don't have access to an appropriate and timely treatment and consequently also access to the drugs, which may help to improve outcomes.

This was just a quick run-through of what was a rather complicated review process.

### Summary and conclusion

- There is considerable variation in the usage of medicines for different therapeutic areas across high-income countries
- France, Spain and the US tend to have higher than average levels of usage for all therapy areas combined while usage levels tend to be lower in Norway, Sweden and in particular New Zealand
- The 'causes' of this variation are multi-faceted and complex, and high or low levels of uptake may not mean that usage is (in)appropriate
- Policies that determine the inclusion of new medicines in the publicly funded basket of services affect medicines uptake in different settings
- Equally or more important factors include: access to (timely) diagnosis, whether the disease area is a designated national priority, and identified care pathways and responsibilities
- It is likely that any given level of use of a given medicine in one country is determined by a set of factors the combination and the relative weight of which will be different in another country

Source: Nolte & Corbett, 2014

# SUMMARY AND CONCLUSIONS

**(Min. 00:47:10)**

I would like to summarize some of the key issues I have been speaking about. There is considerable variation in the usage of medicines. We find that France, Spain and the U.S. tend to have higher than average levels of usage for all therapy areas combined, while usage levels tend to be lower in Norway, Sweden and particularly in New Zealand.

The causes of this variation are multi-faceted and complex, and high levels of usage don't mean that this usage is appropriate or inappropriate. We know that policies that determine the inclusion of new medicines in the publicly funded basket of services affect medicine uptake in different settings but that other factors may be equally or even more important such as access to timely diagnosis. It is likely that we still have not quite understood that any given level of use of a given medicine in a country is determined by a set of factors. The combination and relative weight of these will be different in another country. We all must interpret the data in the context in which it arises.

# QUESTIONS AND ANSWERS

**(Min. 00:53:34)**

**Question from Giancarlo Romano: What are the best studies on the determinants of medicines consumption and use?**

**Answer Ellen Nolte:** There are not that many unfortunately. It was hard to find any good evidence on that. I don't know whether you have seen reports my presentation is based upon. It does give you some references for some areas. It is difficult to find studies that considered the direct relationship between medicines consumption and disease areas. The OECD does some general assessment of consumption levels for selected areas like antimicrobial or certain diabetes drugs etc. What I think is still missing is to study whether observed levels are appropriate. That would help us to understand better whether medicines are used in an effective way. This is an area where we need to have more systematic research. I think the osteoporosis work is quite interesting since John Kanis et. all. have looked at it more strategically. Some of the challenges with some of this research is that it tends to be funded by the pharmaceutical industry and it is sometimes quite hard to interpret. Also, some of the data is not easily available. For example, the quantitative

analysis was based on IMS data, which is propriety to the pharmaceutical industry and it is very expensive to get your hands on. What is problematic with that as well, is that ideally you would want to relate it to the number of people with that particular condition, to adjust them to prevalence to have a better comparison. The quantitative study did not do that. It has been done for some areas, like diabetes but a lot of it is based on different data sources so it is often quite exploratory than confirmatory.

**(Min. 00:57:13)**

**Question from Ana María Diaz: From your view, which is the most direct relation between prescription/use and the health system organization?**

**Answer Ellen Nolte:** I think it is very similar. It pretty much depends on incentives that are being put in place. Again, I think that osteoporosis is an interesting example. You may remember the issue regarding access to bone density measurement in different countries. There were countries such as Italy, which is a tax-funded system, where there is fairly strict gatekeeping in place. In France, they have a voluntary gatekeeping system in place as well, as in Germany, although there it is not really enforced. Yet, these countries have reported that access to drugs is not the problem as such; the problem is to get the indication to

be then able to prescribe the drugs. Certainly, in Germany people will only be entitled to access prescription drugs for osteoporosis following bone density measurement, which you can only get if you meet certain thresholds. Some of these thresholds may not be appropriate. There is some concern in the osteoporosis community, for example that everybody from the age of 70, especially women, should be given bone density measurement. There may not be a problem with prescribing osteoporosis drugs as such, but the condition upon which this can be done depends on the diagnosis. I don't think that that has to do particularly with the organization of the health system as such. It is more about the way conditions are being placed upon by policies about inclusion or exclusion of treatments and drugs. Here you have a good example of the impact of the inclusion of certain treatments in the overall benefits package.

