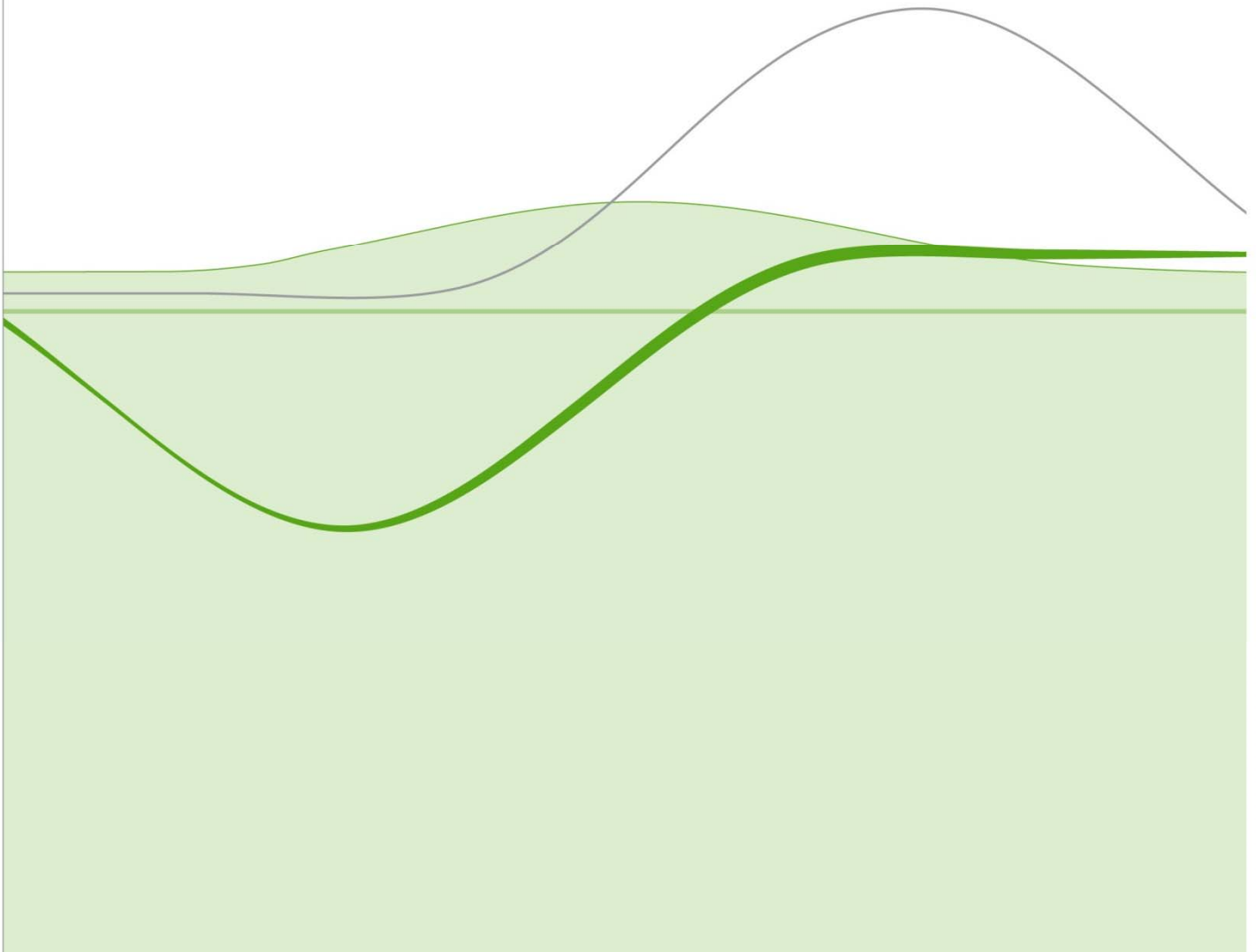


# Projecting Expenditure on Medicines in the NHS

Second Edition

January 2014

Phill O'Neill, Jorge Mestre-Ferrandiz,  
Ruth Puig-Peiro and Jon Sussex



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## **ABSTRACT**

Expenditure on medicines is a readily identifiable element of health service costs. As such, it is the focus of much attention by payers, not least in the UK despite the fact that the ex-manufacturer cost of medicines represents less than 10% of total UK National Health Service (NHS) expenditure. Projecting future spending on medicines enables the likely cost pressure to be allowed for in planning the scale and allocation of NHS resources. Simple extrapolations of past trends in medicines expenditure fail to account for changes in the rate and mix of new medicines becoming available and in the scope for windfall savings when some medicines lose their patent protection. The original research paper (as well as the subsequent article published in *Pharmacoeconomics* (O'Neill et al., 2013)) describes the methodology we have used to project medicines expenditure in the UK to 2015 at list prices. This second edition adds an Appendix extending the results to 2018, as well as distinguishing between gross sales (at list prices) and net sales (following discounts). Note that our original projections to 2015 have not changed.

Unlike any of the other forecasting approaches mentioned in the literature, we have adopted a product-by-product, pack-by-pack, expert-driven, bottom-up approach. Also, unlike other studies, our projections of the impact of loss of market exclusivity by existing medicines and the rate of uptake of newly launched medicines have been obtained from regression analysis of UK data, i.e. they are drawn directly from experience to date in the relevant market.

For any projections, it is also important to address uncertainty by modelling a number of scenarios. In addition to a baseline scenario, we have created two other illustrative scenarios; many others also would be conceivable. We believe that our methodology provides a robust and comprehensive framework for projecting UK NHS medicines expenditure over the medium term.

## **INTRODUCTION**

Expenditure on medicines is a readily identifiable element of health service costs. As such, it is the focus of much attention by payers, not least in the UK despite the fact that the ex-manufacturer cost of medicines represents less than 10% of total UK National Health Service (NHS) expenditure (Hawe, et al., 2011). Projecting future spending on medicines enables costs to be included in planning the scale and allocation of NHS resources.

Over time, the quantity of medicines demanded by patients, the number and therapeutic range of medicines available to be prescribed and their prices all change. The size and age mix of the population and the prevalence of illness, combined with the size of the national income from which health care must be resourced, are each important, long-term influences on total NHS expenditure and on medicines' part of that total. But spending on medicines is also strongly influenced by the lifecycle of medicines themselves: the stream of new medicines being launched as outputs from industry research and development (R&D) pipelines, the regulation of those medicines prices by the government (in the UK, as in many other markets) and the loss of market exclusivity by medicines as patents expire and prices fall in the face of generic competition.

This means that there are two broad options for projecting future medicines expenditures: top down, based on assumptions about future trends in macroeconomic variables such as GDP and demography, or bottom up, based on medicine-by-medicine analysis of likely future developments in quantities prescribed and prices. In the long run, a top down approach may provide a reasonable approximation. But a more accurate, year-by-year picture over the medium term requires a bottom-up analysis, owing to the uneven, but partly predictable, impact year by year of new launches and losses of exclusivity. Knowing the current R&D pipeline of potential new medicines and the loss-of-exclusivity (LOE) dates of existing medicines provides much information about how medicines expenditure may change. We report the development of a bottom-up model to project UK NHS medicines expenditure over a seven-year period from 2012 to 2018 inclusive.

The stream of new therapies being launched onto the market every year may improve on, and hence substitute for, existing medicines, but in many cases permits treatment of illnesses or patient groups not previously treated (Marchant, 1997). Empirical literature, reviewed in Mestre-Ferrandiz, et al. (2012), shows the rate at which medicines eventually achieve market launch, based on reaching various milestones in the R&D process. This information, combined with public domain lists of medicines known to be in companies' R&D pipelines, enables estimates to be made of the likely rate at which new medicines will be launched onto the market in the next few years.

Patents protect new medicines from generic copies usually for 20 years from the date the patent was filed. However, the long duration of the R&D process means that medicines typically have around 10 years or less of patent protection remaining at the time they appear on the market (Mestre-Ferrandiz, et al., 2012). Supplementary Protection Certificates (SPCs) can extend that protection for limited periods for some medicines, e.g. when a six-month extension is given as reward for a company agreeing

to a Paediatric Investigation Plan (PIP) for a different medicine. When medicines lose market exclusivity, other organisations are free to manufacture and sell generic copies of the original medicine without incurring the large sunk costs of R&D, which average around £900 million per new molecular entity reaching the market (Mestre-Ferrandiz, et al., 2012). As a result, in the face of generic competition the price of the medicine typically falls rapidly and the originator loses market share; the degree of competition will depend on a number of factors, including size of the market pre-patent expiry, demand-side policies (including incentives for prescribers) and supply-side policies (such as complexity of manufacturing and price regulation in the off-patent market) (DH and ABPI, 2002; Puig-Junoy, 2010)). The date of patent expiry of all medicines on the market is public information, as is where SPCs have been awarded and the duration of the additional exclusivity they afford to a named medicine. Thus, the date at which a medicine may become subject to generic competition can be predicted accurately.

The scarce and international literature on projecting medicines expenditure records a range of timescales and approaches. Thiébaud and colleagues (Thiébaud, et al., 2013) simulate a range of scenarios and predict that over a 25-year timescale, to 2029, the impact of population growth and ageing will lead to increasing numbers of people living with chronic illnesses and will add between 1.1% and 1.8% per annum to reimbursable outpatient medicines expenditure on the population aged 25+ in France. Theirs is a top-down and partial model focusing solely on demographic change and the impact of chronic illness.

The US Centers for Medicare and Medicaid Services (CMS) for many years have published ten-year projections of US total national health care spending. In August 2011, it published a projection to 2020 (Keehan, et al., 2011). Prescription drugs are one element of the total projection. The details of the CMS method are unstated, but it appears to be essentially a top-down model, driven by econometric analysis of past spending trends, actuarial estimates of future population changes and assumptions about growth in GDP. An overall adjustment then is made to the projected prescription drug trends to allow for major brand-name medicines losing patent protection, and also to allow for major health care reform (e.g. Patient Protection and Affordable Care Act, 2010).

In an apparently conceptually similar way to the CMS, IMS Health produces five-year forecasts of pharmaceutical market growth at national level for many countries (Connor, et al., 2003). These forecasts are essentially top-down, driven by assumptions about GDP growth, combined with econometric analyses of past trends. The outputs from this process are then adjusted in discussion with 'experts, opinion leaders and management' (Connor, et al., 2003) for critical factors that are expected to cause deviations from trends, such as expected legislation and regulatory changes, changes in demographic trends, major patent expiries and expected changes in trends of new launches.

Hoffman and colleagues have published a series of short term—one-year—projections of total prescription medicines spending in the US, taking a more bottom-up approach. Their latest projection at time of writing is for 2012 (Hoffman, et al., 2012). They identified the main factors influencing the projection of medicines expenditure as being: medicines coming out of the R&D pipeline leading to new launches and the rate at which they diffuse post-launch; the growing number of medicines for which generic versions are available; drug shortages; and the growing number of biosimilars (i.e. copies of

biological medicines). Hoffman, et al. (2012) do not report how they make their projection, but refer to projections of parts of the US medicines market by Express Scripts and Medco Health, and to the total national projection by the CMS. They also discuss particular new medicines they anticipate will launch in 2012 and particular medicines for which they expect generic versions to become available for the first time in 2012. They then offer an estimate of the expected range of growth in spending on total prescription medicines in the coming year.

Wettermark and colleagues (Wettermark, et al., 2010) forecast medicines expenditure in the Stockholm metropolitan region of Sweden two years ahead: for 2010 and 2011 based on extrapolation of a time series regression of total annual medicines spending there from 2006 to 2009. The extrapolations are adjusted for patent expiries and the new medicine launches expected. Additional factors explicitly considered are the expected impact of new clinical guidelines from national bodies or the regional Drugs and Therapeutics Committee (DTC) and the impact of health service reforms that are expected to increase patient access to medicines. The information collected was discussed by the authors with a range of clinical experts from the Stockholm DTC system.

We have explicitly modelled, starting from UK data, all of the factors listed by Hoffman, et al. (2012) and Wettermark, et al. (2010), with the exception of drug shortages (mentioned in the US, but not the Swedish, study) because these hitherto have not had a significant impact on the total medicines bill of the UK NHS. We initially extended the approach to look four years ahead, to 2015, based on data to the end of 2011, and subsequently looked a further three years out, to 2018. As in the Stockholm study, we obtained clinical expert input to validate and occasionally to modify our initial projections at the level of individual therapeutic areas. We considered that the impacts of NHS reforms that might affect access to medicines are captured in our baseline data and trends. For our baseline projection, we assumed no NHS policy reforms that were not already known by mid-2012.

Unlike any of the other forecasting approaches mentioned in the literature, we have adopted a product-by-product, pack-by-pack, bottom-up approach, described below. Also unlike the other studies, our projections of the impact of loss of exclusivity and the rate of uptake of newly launched medicines have been obtained from regression analysis of UK data, i.e. are drawn directly from experience to date in the relevant market. Finally, we have modelled projected sales both gross (at list prices) and net (following discounts), as discussed in the appendix.

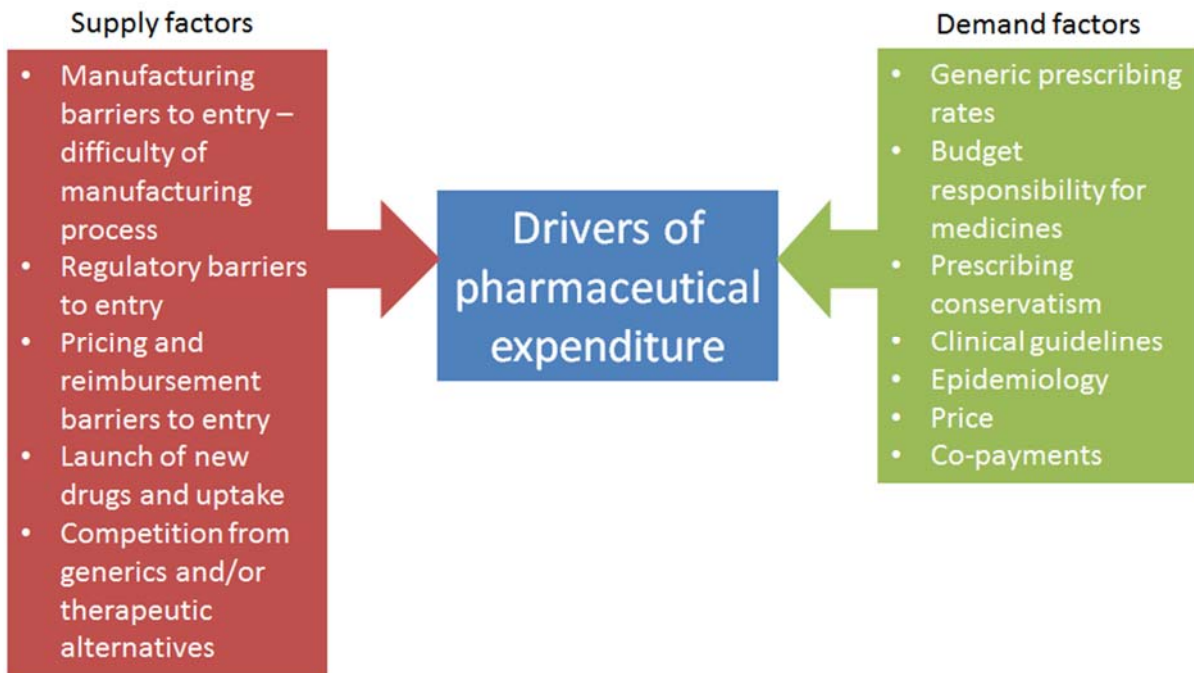


## METHOD: DATA AND BACKGROUND ANALYSIS

### Factors Affecting Prices and Use of Medicines

A number of identifiable supply and demand factors affect usage and degree of price competition between medicines across their lifecycles. Figure 1 shows the underlying structure we have used to think about these factors.

**Figure 1. Factors affecting prices and use of medicines: Structure**



On the left-hand side, under 'supply factors', we mention barriers to entry, which affect the launch of new products, in terms of numbers and uptake, as well as loss of patents and number and type of competitors (therapeutic alternatives and/or generics). Under 'demand factors', key ones identified include factors affecting prescribing decisions (generic prescribing rate, budgets and guidelines), co-payments by patients and prices. Throughout the paper we explicitly state, where relevant, our assumptions for these drivers. Some of these demand and supply factors are more relevant for some therapeutic areas than others—especially in terms of new launches and generic competition.

At a general level, major demand side aspects are assumed constant, as we do not directly model price demand elasticity and income demand elasticity (i.e. what happens to demand when the price of a medicine, or a competitor, changes and what happens to demand when income changes, respectively). Again, on the supply side, and in particular with respect to how pharmaceutical companies interact, the importance of having more or fewer competitors and marketing and detailing efforts, are not modelled directly. However, and as mentioned below, all these interactions are incorporated indirectly when trying to project sales at individual product level.

## **Outline of the Model**

The model used for our projections was built from the product level to the total market. Historical sales, as far back as 2002 when required, were based on IMS's British Pharmaceutical Index (BPI) and Hospital Pharmacy Audit (HPAI) and used list prices. As explained in detail below, we have used different historical data for the different elements of our projections. To facilitate application of expert input and other evidence, the total medicines market was disaggregated into four discrete components or blocks:

1. Products losing exclusivity between 2012 and 2018
2. New products launched between 2012 and 2018
3. Recent products launched in the previous five years, i.e. between 2007 and 2011
4. Non-recent products (i.e. launched before 2007) not expected to lose exclusivity until after 2018.

Each medicine was allocated to one of these four discrete components. Projections for each product in each component were based on a combination of the following factors: historical trends and adjustments made using past experience with other specific medicines or group of medicines (which we term as 'analogues'). In addition, we sought input from a number of experts, primarily from pharmaceutical companies, throughout the entire process—our 'industry experts'. This input focused on specific therapeutic areas and the objective was to ascertain the experts' views about the issues that might drive the evolution during 2012–2018 of the therapeutic areas with which they are familiar. Ultimately, it was up to the researchers to decide whether to include these views in the model. How and when we used this expert input is discussed in greater detail in different parts of the paper, where relevant.

We followed a step-wise approach with our industry experts. We first shared with them some basic information for their specific therapeutic area: historical sales and growth rates for the period 2007 to 2011 (based on IMS data), recent launches, average and therapeutic-specific uptake curves (explained below), estimated future launches (see below) and expected dates when branded medicines will lose patent protection between 2012 and 2018. Our experts then gave us their views on whether past volume and expenditure trends were a good predictor of the future for their therapeutic area, as well as whether standard erosion curves after generic entry or new product uptake curves provided a valid template to use for our projections. Examples of feedback given in this first round included 'impact of new launches small', 'overall trends look reasonable' and 'amend uptake curves for recent products to take account of substitution'. After we completed the first round of interviews with all our experts, we then ran the model and provided a high-level overview of our baseline results, again focusing only on specific therapeutic areas. We asked them if the results looked plausible and whether further refinement was needed. In most cases, no further refinements were needed; for a few, we revised some assumptions around the potential impact of future launches and/or generic competition.

We also had a Steering Group<sup>1</sup> that providing general oversight of the model and assumptions. The Steering Group provided valuable feedback for different pieces of

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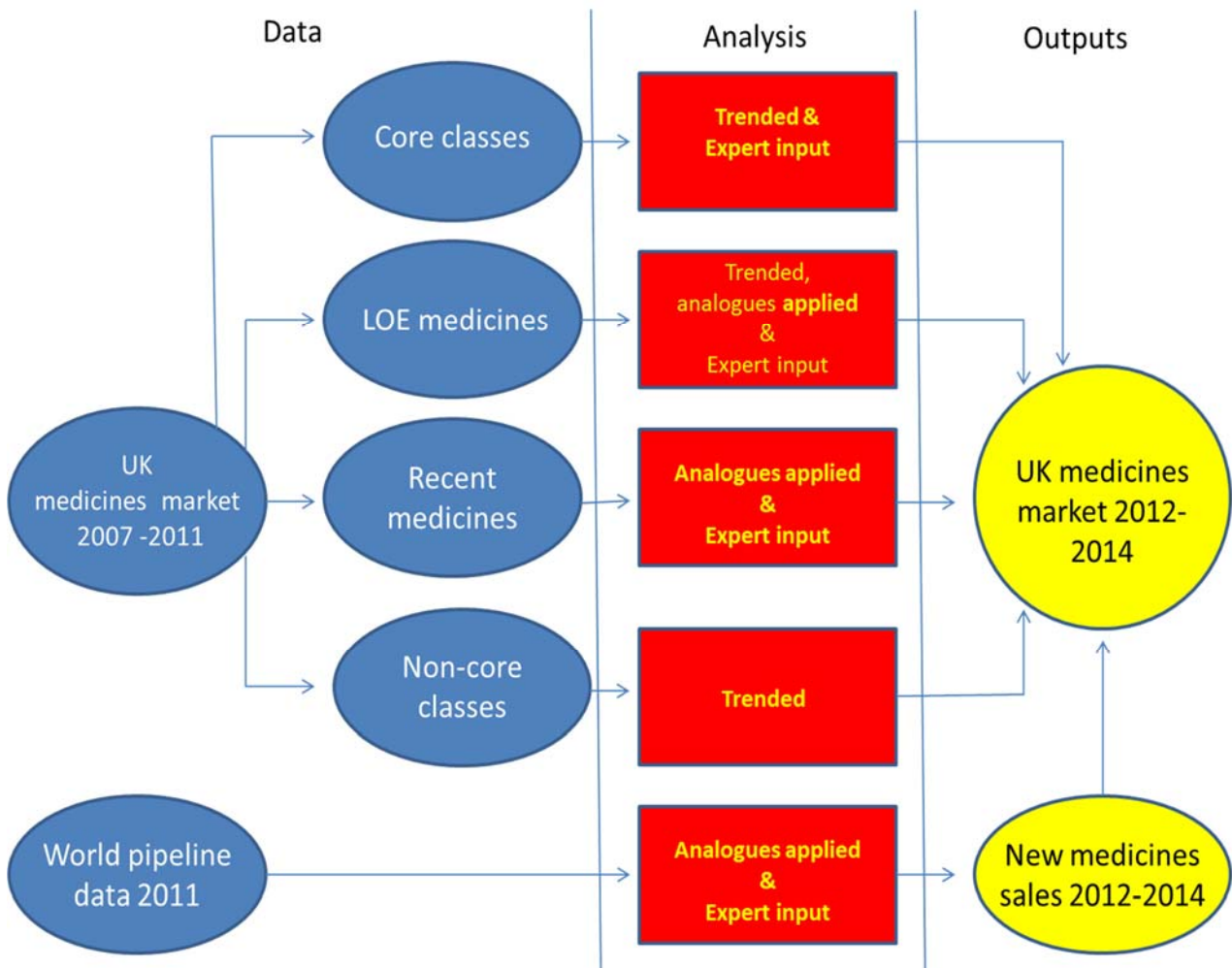
<sup>1</sup> The Steering Group included John Kearney (Amgen), Geoff Bailey (ABPI), Alison Clough (ABPI), Rob Day (Pfizer), Ayesha Kanji (AT Kearney), Sol Magaz (AT Kearney), Tricia Porter (GSK) and Tim Williams (formerly MSD).

analysis that were used in our model, including databases for products currently in the pipeline, scenarios and how to model the substitution effect. Again, we discuss below when we considered this feedback.

We further divided therapeutic classes into 'core' or 'non-core', described in greater detail below. 'Core' therapeutic areas covered approximately 80% of the UK market by value in 2011 and were explored in greater detail. Primary care and secondary care medicines markets were modelled separately.

The structure of the model is shown in Figure 2, divided into data, analysis and outputs. In the rest of this section, we provide an overview of the characteristics of the model, followed by more detail on key methodological aspects of the model for the data and analysis components in Figure 1. Section 3 reports on the results.

**Figure 2. Structure of the projection model**



Note: LOE = loss of exclusivity', which occurs when branded products lose patent protection and face generic competition.

We decided that the lowest appropriate unit of disaggregation was formulation as this was the minimum level of granularity where changes in volumes or prices were applied.

This level of disaggregation matches the EPhMRA Anatomical Therapeutic Chemical (ATC) classification level 4 (EphMRA, 2014). For each disaggregated unit in the model, changes can be made per year to the volume or price during the projection period. In addition, and as described in greater detail later, different formulations face different degrees of competition from generic versions, which is important to take into account for our modelling purposes. For new products yet to be launched, however, this level of granularity is not meaningful.

Results in this paper are reported at therapeutic level, defined as ATC1 for most classes with the exceptions of class L (antineoplastics and immunomodulators) and class J (systemic anti-infectives). For class L, L1 and L2 are reported separately as they cover most cancer medicines; L3 and L4 include immunomodulating medicines, which are an important and distinct class of medicines. Within Class J, anti-infective medicines and HIV medicines have been assessed and reported separately.

As part of the analysis, we sought expert input for the core therapeutic areas from clinical experts from a number of pharmaceutical companies throughout the process. These semi-structured discussions occurred one-to-one between the authors and the experts and focused on a number of issues for specific therapeutic classes. In particular, the objective was to identify events that could mean that the past would not be a good guide to the future (2012–2018), such as significant new products and/or significant LOE, or any new therapeutic-area-specific initiatives. Throughout this paper, we report where such input led to any adjustment to the model.

Another important dimension is how the model incorporates recent and future policy changes in the UK pharmaceutical market. In our model, the baseline scenario assumes no change in future pricing and reimbursement policy or regulatory changes in the UK. Branded medicine price adjustments agreed as part of the 2009 Pharmaceutical Price Regulation Scheme (PPRS) agreement have been incorporated (ABPI and DH, 2008); the Cancer Drugs Fund as applied to England, but not the rest of the UK, has been assumed to continue (DH, 2012). For the other two scenarios, we do not explicitly model any changes in policy, but some of the sensitivity analysis implicitly assumes changes—for instance, policies to improve uptake of new medicines in the 'High' scenario.

## **Data**

The starting point for our analysis was primary care and secondary care data from IMS's Health British Pharmaceutical Index (BPI) and Hospital Pharmacy Audit (HPAI), which cover the whole UK market. Monitoring usage of medicines in primary care using IMS data is comprehensive as it covers more than 90% of the market. The alternative data source for primary care (but only for England, not all the UK) could be the Prescription Cost Analysis (PCA) statistics generated as a by-product of the reimbursement process for community pharmacists and available through a number of sources. PCA is a more accurate measurement of the primary care medicines bill for England as it is a report of the value of medicines reimbursed rather than purchased by pharmacists. However, PCA data do not cover the secondary market. For this reason, we decided to use IMS for the entire market, for consistency, rather than create two distinct databases, one for primary care and one for secondary care.

From IMS, only products defined as 'ethical', 'generic', 'NHS prescription bound' and 'NHS reimbursable' were included in the sample. Classes not considered as medicines, notably medical tests and gases, were excluded. The unit of quantity chosen was 'counting units'. Hospital and primary care data were extracted separately and each product was attributed to one of the four components of the model, described earlier. Details of the rationale for apportionment are set out below in the discussion of the analysis undertaken for each component.

Some secondary care medicines with potentially significant impact on growth in expenditure are in part supplied through the home care channel. We understand that IMS does not cover the entirety of the home care channel. We therefore surveyed key companies in this segment. The companies were identified using information supplied by the Department of Health Commercial Medicines Unit on medicines supplied through home care. We then identified and surveyed companies commercialising at least five medicines supplied through the home care route. Companies with significant market share in specific markets where home care is distributed were also targeted. The companies were invited to validate IMS annual secondary care volume data for 2007 to 2011 using their own data generated through distribution of their medicines. This additional volume data was added to each product in the baseline prior to any forecasting or trending was undertaken.

## **Analysis**

All medicines were apportioned to one of the four discrete components of the model as previously described. To project sales for each component of the model, the historical data were either trended, had 'analogues' applied to adapt growth based on historical evidence, or adjusted based on experts' specific advice. Most components of the model had more than one type of analysis applied, in which case the hierarchy was to trend baseline data, then apply analogues and then adjust in the light of expert input, as explained above. For trending purposes, out of 341 ATC4 categories modelled in total, we adjusted the trends for 31 of them in primary care and two in secondary care.

The next sections take in turn our approach for the key components, in this order: new products, LOE products, recent products and non-recent/non-LOE products. Before we do this, however, we set out the distinction between core and non-core therapeutic areas.

## **Identification of Core Therapeutic Areas**

Therapeutic areas that are a large component of the medicines bill by value or have had a disproportionate impact on recent growth warrant close scrutiny and thus were classified as 'core' therapeutic areas. Areas that are relatively small in terms of share of the total bill and have a relatively slower rate of evolution in growth can be anticipated to have a small impact on overall growth in the bill over the forecast period; these were labelled 'non-core' therapeutic areas.

To identify core therapeutic areas, we extracted primary and secondary care sales for 2010 and 2011 by ATC4 class from IMS data. ATC1 classes that experienced growth or shrinkage greater than +/- 10% in 2011 compared to 2010, or that had greater than a 10% market share by value in 2011, were nominated as core classes. These threshold percentages were chosen so that the core areas cover around 80% of the market to

make the analysis reliable while still being manageable. In 2011, core classes comprised more than 80% of the UK NHS medicines bill by value. Table 1 shows the core (with a 'y' in the second column) and non-core therapeutic areas (with an 'n' in the second column).

**Table 1. Core and non-core ATC1 therapeutic classes**

<b>ATC1 Class</b>	<b>Core therapeutic area</b>
A Alimentary tract and metabolism	y
B Blood and blood forming organs	y
C Cardiovascular system	y
D Dermatological	n
G Genito-urinary system and sex hormones	y
H Systemic hormones	n
J Systemic anti-infectives	y
L Antineoplastics and immunomodulators	y
M Musculo-skeletal system	y
N Nervous System	y
P Parasitology	n
R Respiratory system	y
S Sensory organs	y
V Various	n

Source: Authors' analysis based on IMS BPI and HPAI 2010 and 2011 data

## **New Products**

To project expenditure of new launches during the forecast period, two key elements are essential:

1. Identify which drugs should be expected to be launched in the UK between 2012 and 2018
2. Place them in uptake curves, i.e. how fast use of them will grow.

For the second step, we carried out a historical analysis looking at uptake of products launched in the UK for the period 2003–2010. This timeframe was believed to be long enough to capture sufficient information on historical uptake. We stopped at 2010 so that we could have at least year one of sales for products launched in 2010. We did not include launches in 2011, as the available sales data for these products would be minimal. Moreover, we worked on a yearly basis and products launched in 2011 would have less than one year of sales.

Rather than attempting to identify when specific new products would be launched (which would be extremely time consuming and subject to unavoidable errors in predicting which ones will fail in the R&D process before reaching the market) an analysis of the world pipeline for medicines in development was undertaken. The data supporting this analysis is based on the IMS Lifecycle R&D Focus, which is a proprietary comprehensive database that tracks progress of R&D of medicines by molecule and indication. It provides data on the current phase of the R&D process of the medicine and indication and the ATC therapeutic area for that indication. An extract of the complete database was taken in March 2012. The number of projects at each stage of the R&D pipeline was collected and matched to an ATC therapeutic area. In order to estimate the number of new products launched per projection year per therapeutic area, we used information provided by Paul and colleagues (Paul, et al., 2010) on attrition rates and development times by phase. By applying these to the collated pipeline data, we estimated the number of launches for each therapeutic area per year for the forecast period. These projected launch rates then were compared with recent rates of launches and further validated by clinical experts. Table 2 shows our estimates of new launches per projection year to 2015. Estimates of future launches per year to 2018 are in the appendix.

**Table 2. Estimates of future launches per year**

	<b>2012e</b>	<b>2013e</b>	<b>2014e</b>	<b>2015e</b>
Products launched per year	27	27	26	26

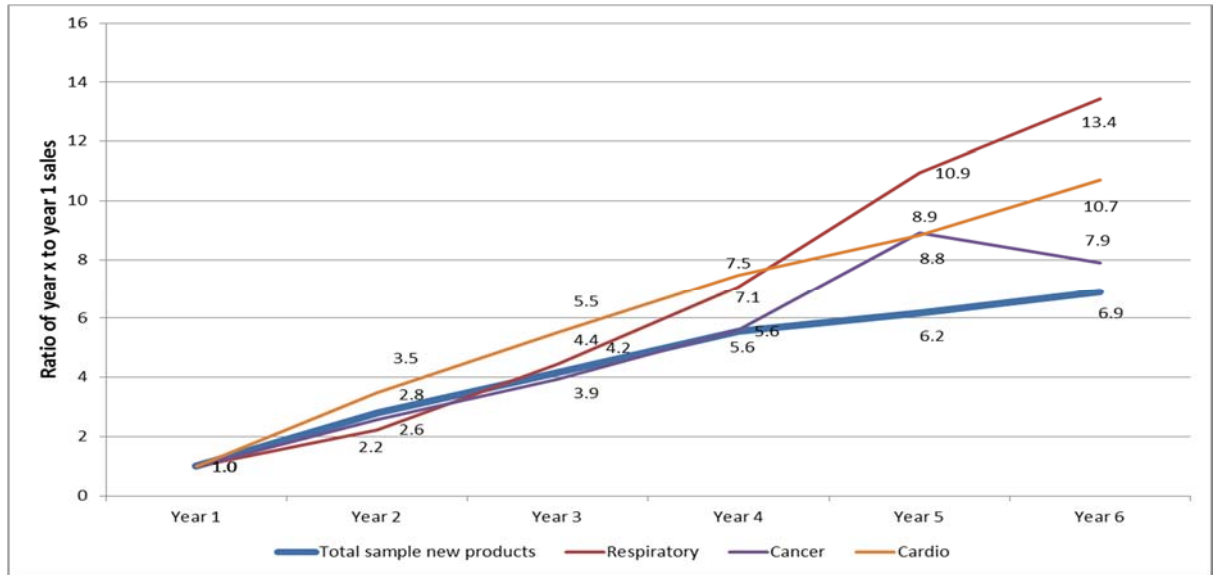
Source: Authors’ estimates from IMS Lifecycle R&D Focus (extracted March 2012) and industry expert input

To generate assumed uptake curves for these future launches, we analysed IMS data for past new launches in the period 2003–2010. Uptake curves were estimated both across the whole sample and at therapeutic level for particular core therapeutic areas and subsets: alimentary, anti-infectives HIV, cancer, cardiovascular, central nervous system and respiratory. Disease-specific uptake curves for key classes were also validated with experts, but none was changed as a result.

Uptake curves represent the ratio of each subsequent year’s sales (by value) with respect to the first year of sales after launch. For instance, the ratio in year 2 (denoted as  $r_2$ ), would be equal to year 2 sales divided by year 1 sales; ratio in year 3 would be equal to year 3 sales divided by year 1 sales, and so forth. Thus, if the ratio  $r_2 = 2$  this indicates that year 2 sales are twice as high as year 1 sales. We calculated these ratios up to year 6.

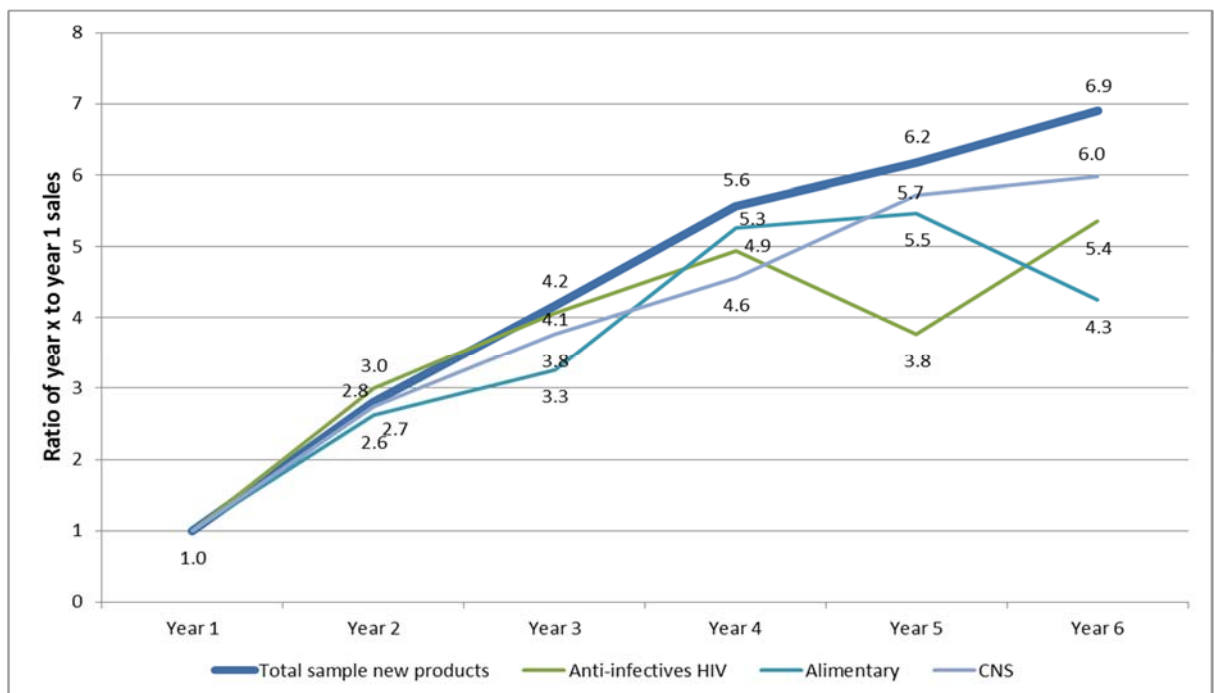
The results of this analysis are plotted in Figures 3 and 4. Figure 3 identifies classes where the ratios were greater than the average rates for the total sample of products. Figure 4 shows classes where uptake was slower than the total sample.

**Figure 3. 2003–2010 average UK uptake curves for all new products and for those classes where relative uptake was greater than the average for all new products**



Source: Authors' estimates from IMS BPI and HPAI 2002–2011 data

**Figure 4. 2003–2010 average UK uptake curves for all new products and for those classes where relative uptake was less than the average for all new products**



Source: Authors' estimates from IMS BPI and HPAI 2002–2011 data



Note that for a number of classes (cancer in Figure 3 and anti-infectives and alimentary in Figure 4), we can observe some declines in years 5 and 6. We have not explored the reasons for these.

Given that our uptake analyses uses year 1 sales as the anchor point, the final component of the new product analysis was to estimate the (average) first year sales of recent historical launches, by therapeutic area. This was achieved using the data generated to calculate uptake curves. These first year figures were also validated by therapeutic area experts; as a result of their feedback, some subclasses were excluded from the analysis as they were deemed outliers and including them would skew the results for future launches. The values used in the model are detailed in Table 3.

**Table 3. Year 1 sales values used in model**

<b>ATC1 Class</b>	<b>Average year 1 sales per product (£000s)</b>
<b>A</b>	2,518
<b>B</b>	1,030
<b>C</b>	663
<b>D</b>	783
<b>G</b>	134
<b>H</b>	562
<b>J</b>	417
<b>L</b>	3,226
<b>M</b>	876
<b>N</b>	1,655
<b>R</b>	432
<b>S</b>	2,773

Note: Does not include products launched in certain sub-classes that were outliers (A10, A16, B01, B02, C10, G04, J05, J06) as including them would skew the results for future launches.

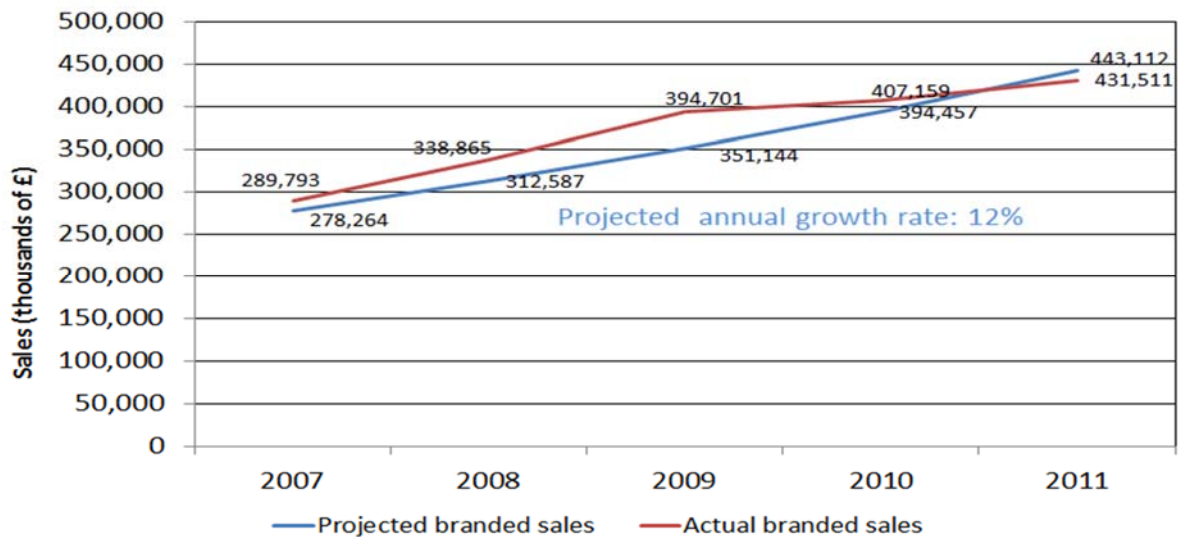
Source: Authors' calculations based on IMS BPI and HPAI 2002–2011 data

We also explored whether sales of new products wholly or partially replace sales of existing medicines, i.e. whether they substitute for older medicines or are additional sales. The extent to which substitution for existing medicines occurs varies by therapeutic class and will be influenced by factors such as response rates in subgroups of patients, side effects, ease of administration of new products and price differences. To explore this substitution effect, we undertook a historical analysis in four therapeutic

areas that have had few new launches in recent years: HIV, diabetes, multiple sclerosis and epilepsy. We followed the same methodology across these four areas to explore whether sales of new products can be deemed to be fully additive or replace older products. For each disease area, we estimated the average annual growth rate for the period 2003–2006 for branded medicines. Using this linear growth rate, we projected 2007–2011 sales as if new launches did not happen for this period and held all other things constant. We then compared our 'projected' sales with actual sales (for the period 2007–2011) to explore the degree of additional sales caused by new launches; in essence, the difference between the two curves could be thought of as the effect of new launches between 2007 and 2011.

For brevity, we only include below the specific analysis for HIV and epilepsy, as these are the two extremes (results for diabetes and multiple sclerosis lie in between these two areas). Figures 5 and 6 show the analysis for HIV and epilepsy respectively.

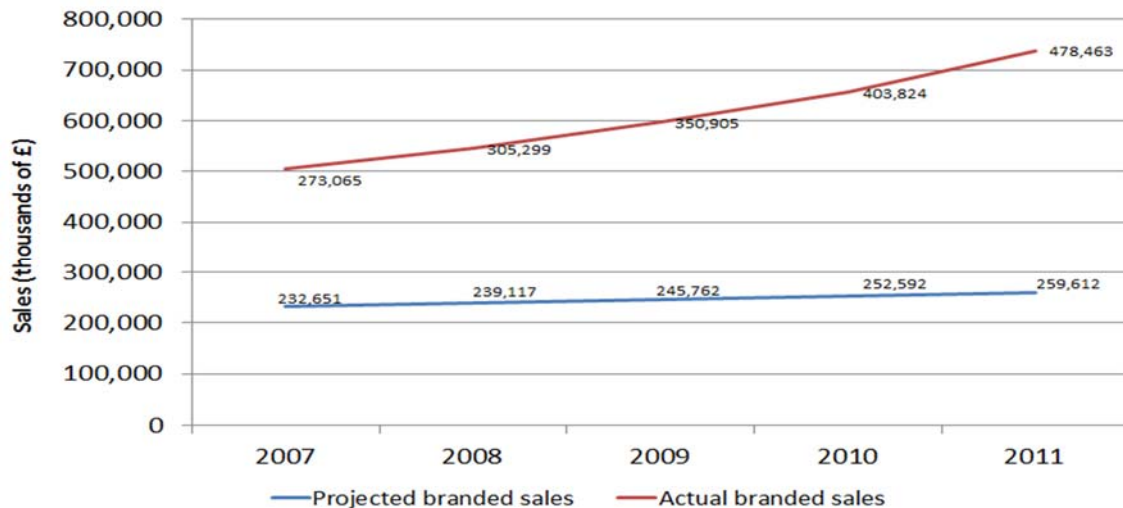
**Figure 5. Net impact of new launches: HIV case study**



Source: Authors’ calculations from IMS BPI and HPAI 2002–2011 data

The blue line represents the projections for 2007–2011 assuming no new launches in this period, based on the average annual growth rate for the period 2003–2006. The red line shows actual sales for this period. Three new products were launched in the UK between 2007 and 2011 for the treatment of HIV. Summing across 2007 and 2011, the difference between actual and projected sales was £82m, which represents 4.6% of the total projected sales. In this case, it seems that the impact of launches had a small net effect on the HIV market.

**Figure 6. Net impact of new launches: Epilepsy case study**



Source: Authors' calculations from IMS BPI and HPAI 2002–2011 data

Figure 6 should be read in the same way as Figure 5. Four new products were launched in the UK between 2007 and 2011 for the treatment of epilepsy. Summing across 2007–2011, the difference between actual and projected sales over this period was £219m, which represents 84% of the total projected sales. In this case, new products for epilepsy had an important net effect on the size of this market.

For diabetes and multiple sclerosis (details not shown here), the respective percentages were 23% and 33%. The unweighted average across the four therapeutic areas analysed is 36%, which is the same as the weighted average by 2011 actual sales. Weighting by 2007 actual sales decreases the average to 33%.

These four examples should be treated with caution when trying to gauge across-the-board substitution rates for future new launches, as the limited evidence provided here suggests that the effect of new launches is very mixed across therapeutic areas. Based on these analyses and the feedback received by our industry experts and Steering Group, we assumed in our baseline scenario that 25% of sales of future launches are additive, with the exception of cancer, where we assumed that 75% of sales of future launches are additive. The rationale of a higher percentage for future cancer products is that, when first introduced, they tend to be used in combination with existing treatments, or as third or fourth line treatments so, by definition, they will replace existing treatments relatively less often. The choice of 25%, which is slightly below the average found in our analysis, was suggested by our Steering Group as being a more realistic figure across the entire market (with the exception of cancer, as noted).

### Loss of Exclusivity

One of the key issues for projecting medicines expenditure is how generic competition affects those medicines losing patent protection between 2012 and 2018. For this purpose, we have constructed four (price and volume) erosion curves, depending on manufacturing complexity ('easy' or 'difficult') and channel (primary or secondary care), based on historical analysis of the UK market.

For the purposes of our analysis, LOE was defined as occurring (1) when an on-patent medicine loses legal protection to benefit exclusively from the intellectual property rights

associated with all patents related to the medicine and (2) when at least one other manufacturer is supplying a generic equivalent to the market. The second condition is necessary to identify actual, rather than potential, generic entry. We have detailed patent expiry dates between 2012 and 2018, based on IMS BPI and HPAI. As part of the validation process of patent expiry dates, we also asked our industry experts to validate these dates. Our patent expiry dates include PIP extensions awarded up to September 2012<sup>2</sup>. We have used the observed impact of generic competition in the UK in recent years to project the impact of future patent expiries.

### Primary Care

For primary care medicines, patent expiries over the period 2002–2011 were modelled and grouped by ATC1 class. This timeframe was thought to be long enough to capture the information needed for our modelling purposes. Formulations were identified as being either difficult or easy to manufacture<sup>3</sup> because this is a key determinant of the degree of competition from generic alternatives—higher in the case of easy-to-manufacture formulations (DH and ABPI, 2002). Indeed, as shown in Figures 2.5 and 2.6, the erosion curves are different. For some cardiovascular and anti-Alzheimer’s drugs will lose their exclusivity in the projection period, alternative curves have been applied, based on historical analysis and expert input. In particular, for these two therapeutic areas, we used more aggressive erosion curves; for cardiovascular, this was based on the actual degree of generic competition faced by simvastatin, which was the first statin to face generic competition. Simvastatin came off patent in 2002, providing abundant information on the effect of generic entry in the UK. For anti-Alzheimer’s drugs, and in particular cholinesterase inhibitors, the first of which came off-patent in late 2011, we were able to monitor the actual degree of generic competition and found it to be significantly more aggressive than the average erosion curves estimated above. As a result, we decided to use more aggressive erosion curves.

The price of a counting unit for each product in primary care is estimated by dividing the value of sales in pounds sterling by volumes in counting units. We then estimated the price erosion curve for each branded product and type of formulation (easy and difficult) as the average price of generic product(s) for a given year with respect to the price of the branded product the year before a generic enters the market. Algebraically:

$$\text{Price erosion year 1} = \frac{\text{generic price year 1}}{\text{price branded product in year before generic entry}}$$

$$\text{Price erosion year 2} = \frac{\text{generic price year 2}}{\text{price branded product in year before generic entry}}; \text{ etc.}$$

We then estimated the weighted average price erosion curve in our sample. As weights, we use sales of the branded products the year before generic entry to account for the fact that the sample is populated by products with very different levels of sales. In this

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<sup>2</sup> Details are available on request.

<sup>3</sup> Easy formulations are tablets, capsules, pastilles, retard tabs, dispersible tabs, soluble tabs, solutions, bottles. Difficult formulations were all other formulations, e.g. syringes, vials, cartridges, pens, patches, ampoules, creams, ointments, gels, suspensions, eye drops, diskhalers, accuhalers, inhalers, powders. These were determined using expert input from companies that manufacture medicines.

way, the products with greater sales have a heavier weight in the average price erosion curve.

Volume curves are estimated for each branded product and type of formulation (easy and difficult) as the proportion of sales in counting units of that molecule that is retained by the branded product for each year until year 6 of sales:

$$Volume\ erosion\ year\ 1 = \frac{\text{sales of the branded product in year 1}}{\text{sales of branded + generic product(s) in year 1}}$$

$$Volume\ erosion\ year\ 2 = \frac{\text{sales of the branded product in year 2}}{\text{sales of branded + generic product(s) in year 2}}; \text{ etc.}$$

We then estimate the weighted average volume erosion curve in our sample using the same weights as in the price erosion curve. Table 4 and Figure 7 show our results.

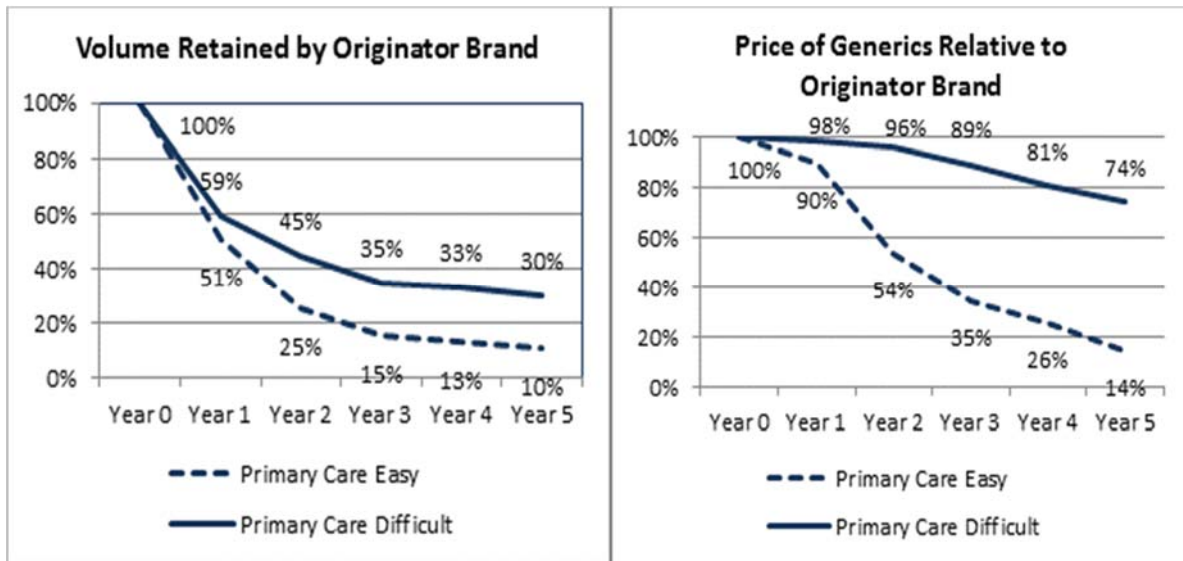
**Table 4. Volume and price erosion curves in primary care**

Retained volume by the originator						Generic price as % of originator					
Formulation	Year 1	Year 2	Year 3	Year 4	Year 5	Formulation	Year 1	Year 2	Year 3	Year 4	Year 5
Easy	51%	25%	15%	13%	10%	Easy	90%	54%	35%	26%	14%
Difficult	59%	45%	35%	33%	30%	Difficult	98%	96%	89%	81%	74%
Number of observations											
Easy	71	53	44	35	26						
Difficult	19	17	13	6	4						

Note on sample size: There were only 6 and 4 observations for year 4 and year 5, respectively, for 'difficult' formulations, and results derived for the volume erosion curve presented some anomalies. For this reason, we decided to trend for years 4 and 5, assuming 33% and 30% erosion rates respectively. For the price erosion curve, although the samples were small for years 4 and 5, the results were not anomalous (81% and 74% respectively).

Source: Authors' calculations from IMS BPI and HPAI (2002–2011)

**Figure 7. Volume and price erosion curves in primary care**



Source: Authors’ calculations from IMS BPI and HPAI (2002–2011)

Based on Figure 6, the off-patent, easy-to-manufacture, branded medicine keeps 51% of the market share in year 1, on average; the remaining 49% will go to generic equivalents. By year 5 after patent expiry, the market share retained by the originator falls to 10% (and 30% when it is a ‘difficult-to-manufacture’ molecule).

Figure 7 also shows how the price of generics relative to the originator brand’s price pre-LOE evolves. For instance, for easy formulations, we estimate that in year 1 of generic competition, the generic price is 10% lower than the originator price was pre-LOE. By year 5, this discount is 86%. For the purposes of our modelling, we have assumed that the price of the branded medicine does not change post-LOE.

### Secondary care

We had used different approach for the historical analysis of secondary care medicines facing generic competition because IMS data do not capture the discounting below list prices that takes place in secondary care markets. We constructed two case studies representing respectively:

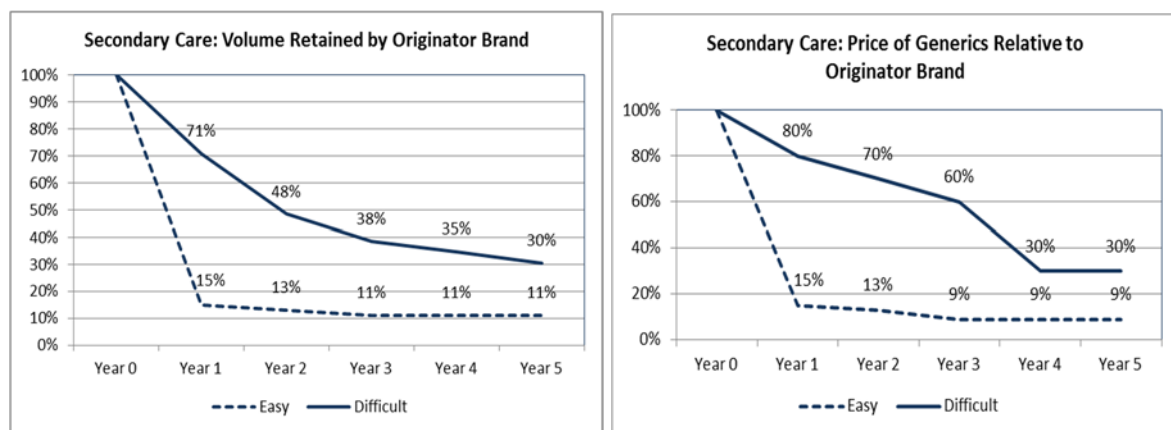
- An ‘easy to manufacture’ product
- A ‘difficult to manufacture’ product

To replicate the analysis we did for primary care, we differentiated the two case studies according to manufacturing complexity. Our Steering Group provided us with suggestions for the two case studies: the ‘easy to manufacture’ product is licensed for colorectal cancer and the ‘hard to manufacture’ to treat a number of infectious diseases. Once these two products were agreed, we asked the respective manufacturer of each branded medicine to provide us with data on real transaction prices and volumes for the off-patent brands and generics in hospitals, based on the manufacturers’ own internal data. Based on this information, we then constructed (anonymised) price and volume erosion curves.

We then used a panel of four NHS hospital pharmacists to validate our case studies via a Delphi-type process. The process was as follows. In the first round, we provided them with our preliminary erosion curves for the two case studies and asked them the following question: 'In your view, are these two case studies a reasonable representation of generic competition in the hospital market?' Based on the feedback received in the first round, we then went back to them with revised curves and asked them to validate the curves. For the 'easy to manufacture' curves, the volume erosion curves were unchanged, while the price erosion curve was slightly modified (they argued for more aggressive price competition in the first year than our original estimate and relative stability thereafter). For the 'difficult to manufacture' volume erosion curve, no change was required, as they thought our original curve was a good representation. However, regarding the price erosion curve, they argued, relatively to our original curve, for less aggressive price competition in the first three years after patent expiry, but more aggressive in the last two year years.

Figure 8 illustrates the price and volume erosion curves resulting. It should be interpreted similarly to Figure 7.

**Figure 8. Volume and price erosion curves in secondary care**



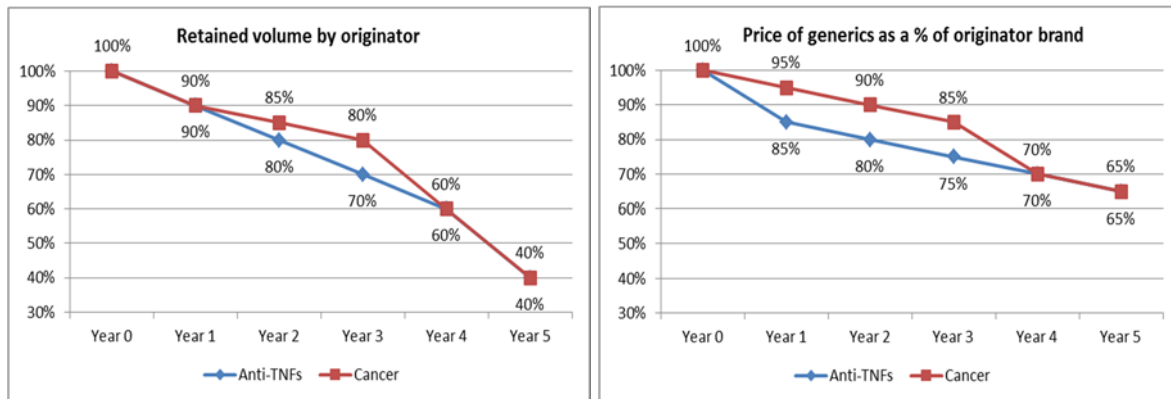
Source: authors' calculations based on expert input

### Biosimilars

Two specific classes of biological medicines in secondary care, tumour necrosis factor (TNF) inhibitors (anti-TNFs), and monoclonal antibodies for use in treating cancer, provided specific challenges for forecasting the impact of loss of exclusivity as they give rise to 'biosimilars' rather than exact-copy chemical generics. For biosimilars, we lacked suitable historical parallel examples from which to develop analogues. Even after seeking expert input, we found uncertainty about the future evolution of biosimilar competition in these markets. Although markets exist where biotechnology medicines have faced biosimilar competition—including granulocyte-colony-stimulating-factor medicines, EPOs and growth hormones—expert opinion was that these would not be suitable analogues for the two classes above. The regulatory environment is evolving and investment in biosimilar production capacity by large pharmaceutical producers is growing along with both the size of the markets involved and greater familiarity with biosimilars among prescribers. In total, the value of UK sales for anti-TNFs and monoclonal antibodies in 2011 was £1bn (based on IMS sales). Figure 9 plots the volume and price erosion curves for anti-TNFs and monoclonal antibodies used in our model.

Due to the uncertainties mentioned above, the analysis supporting the curves in Figure 9 is primarily based on our discussions with the Steering Group. We ultimately decided that the curves represented in Figure 9 are as reliable predictors as possible, based on the limited evidence available to date on the potential impact of biosimilars for anti-TNFs and monoclonal antibodies. Anticipated LOE dates for these medicines occur in 2014 and 2015 but, given the size of these markets, any significant changes in prices for these medicines could potentially have a considerable impact on rates of growth for the medicines bill as a whole after 2015.

**Figure 9. Anti-TNF and monoclonal antibodies for cancer: Volume and price erosion curves**



Source: Authors’ calculations based on expert input

To model the future impact of LOE for medicines expected to face generic entry in the projection period, each medicine by formulation was assigned an LOE date and a price and volume erosion curve. Total (branded plus generic) volumes for each product were trended through the forecast period.

### Recent Products

Sales of branded medicines follow a lifecycle. Generally, the most rapid relative growth period in the lifecycle of an on-patent medicine is the first five years post launch. Growth after that tends to slow or plateau. Hence, it would be misleading to assume that sales of recently launched medicines would continue to grow at the same percentage rates in future. To overcome this, all medicines that were launched in the last five years, i.e. between 2007 and 2011 inclusive, were placed on relevant uptake curves using the results of the analysis that generated the new product uptake curves (explained earlier). The position on the curve was determined by the number of years from launch at 2011. In particular, we use the year-on-year growth rates for values shown in Table 5, which are based on the numbers underpinning our uptake curve across the full sample (i.e. the average). As an illustration, for a product launched in 2009, sales in 2012 (which will be year 3 after launch) will be projected by growing 2011 sales by the year 3 growth rate below, 2013 sales by applying year 4 growth rate to 2012 sales, and so forth.



**Table 5. Year-on-year growth rates used for recent launch**

	<b>Year 2</b>	<b>Year 3</b>	<b>Year 4</b>	<b>Year 5</b>	<b>Year 6</b>
<b>Growth rate over preceding year</b>	173%	47%	34%	12%	11%

Source: Authors' analysis based on IMS BPI and HPAI (2003–2010)

## Older On-patent Products

For older (i.e. more than five years on the market) medicines that did not lose exclusivity in the projection period (last component of the model), projections were based on smoothed historical trends between 2008 and 2011 at ATC4 level. We used four years of historical data because we thought that would cover a long enough period to smooth out any year-on-year fluctuations.

## EXAMPLE RESULTS

We now present the results obtained for our baseline scenario where we assume no major changes in policy affecting the UK medicines market between 2012 and 2015. Table 6 summarises the key characteristics of this scenario.

**Table 6. Baseline scenario: Key characteristics**

<b>Estimate range</b>	<b>New product launches – Attrition rates</b>	<b>New product launches – Uptake curves</b>	<b>New product launches – Year 1 sales</b>	<b>Extent to which sales of future launches are additive rather than substituting for existing medicines</b>	<b>LOE – Generics</b>	<b>LOE – Biosimilars (Cancer and TNFs)</b>
<b>Baseline</b>	Match count of future launches to launches during 2003–2010	Current uptake curves per therapeutic area (TA)	Current year 1 sales per TA	25% of sales of future launches are additive.  For oncology: 75% of sales of future launches are additive	Use current erosion curves	TNFs and Cancer: less aggressive than difficult secondary care.  Cancer less aggressive than TNFs (for earlier years)

As noted below, two additional illustrative scenarios (high and low) have been modelled by varying key assumptions. The model permits an infinite variety of scenarios to be tested for their impact on UK medicines expenditure. We first report on the baseline scenario and then describe how the results for the other two scenarios compare with the

baseline. For the baseline scenario, results are also presented at the different levels of analysis: by type of product (branded, generic or biosimilar), by channel (primary or secondary) and by therapeutic area.

### The Baseline Scenario

Table 7 shows the total medicines bill from 2007 to 2015 where the data for 2007 to 2011 are actual sales (based on IMS) and the sales for 2012–2015 are our baseline estimates.

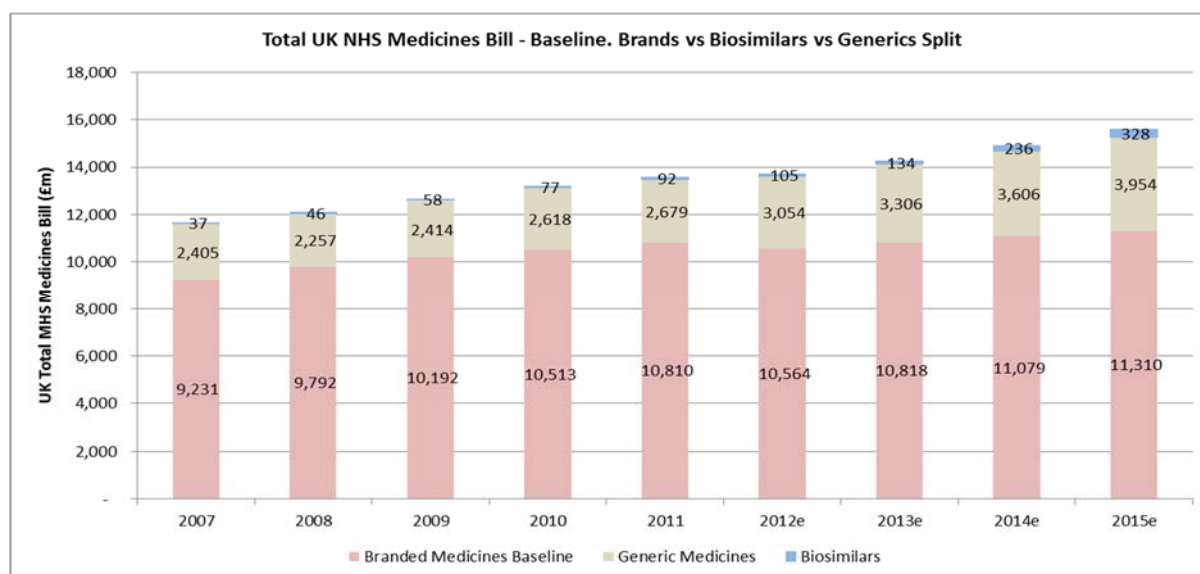
**Table 7. Total UK NHS medicines expenditure (£million): Baseline scenario**

2007	2008	2009	2010	2011	2012e	2013e	2014e	2015e
11,673	12,095	12,664	13,208	13,581	13,723	14,259	14,922	15,592

Sources: 2007–2011 are from IMS BPI and HPAI; 2012–2015 are authors’ estimates

Figure 10 shows the decomposition of total sales for branded medicines, generics and biosimilars, respectively.

**Figure 10. Total UK NHS medicines bill (£million): Baseline scenario**



Sources: 2007–2011 are from IMS BPI and HPAI; 2012–2015 are authors’ estimates

Table 8 shows the compound annual growth rates (CAGRs) for the periods 2007–2011 and 2011–2015 for the total bill and the different components of the model included in Figure 9.

**Table 8. CAGRs: Baseline scenario**

<b>CAGRs</b>	<b>2007–2011</b>	<b>2011–2015e</b>
Total medicines bill	3.9%	3.5%
Brands	4.0%	1.1%
Generics	2.7%	10.2%
Biosimilars	26.1%	37.2%

Sources: 2007–2011 are from IMS BPI and HPAI; 2012–2015 are authors' estimates

Table 9 decomposes total sales into primary and secondary care.

**Table 9. Primary care and secondary care UK NHS medicines expenditure (£million): Baseline scenario**

	<b>2007</b>	<b>2008</b>	<b>2009</b>	<b>2010</b>	<b>2011</b>	<b>2012e</b>	<b>2013e</b>	<b>2014e</b>	<b>2015e</b>
<b>Primary care</b>	8,457	8,380	8,465	8,689	8,754	8,584	8,768	9,003	9,275
<b>Secondary care</b>	3,216	3,715	4,199	4,519	4,827	5,140	5,491	5,918	6,318
<b>Total</b>	11,673	12,095	12,664	13,208	13,581	13,723	14,259	14,922	15,592

Sources: 2007–2011 are from IMS BPI and HPAI; 2012–2015 are authors' estimates

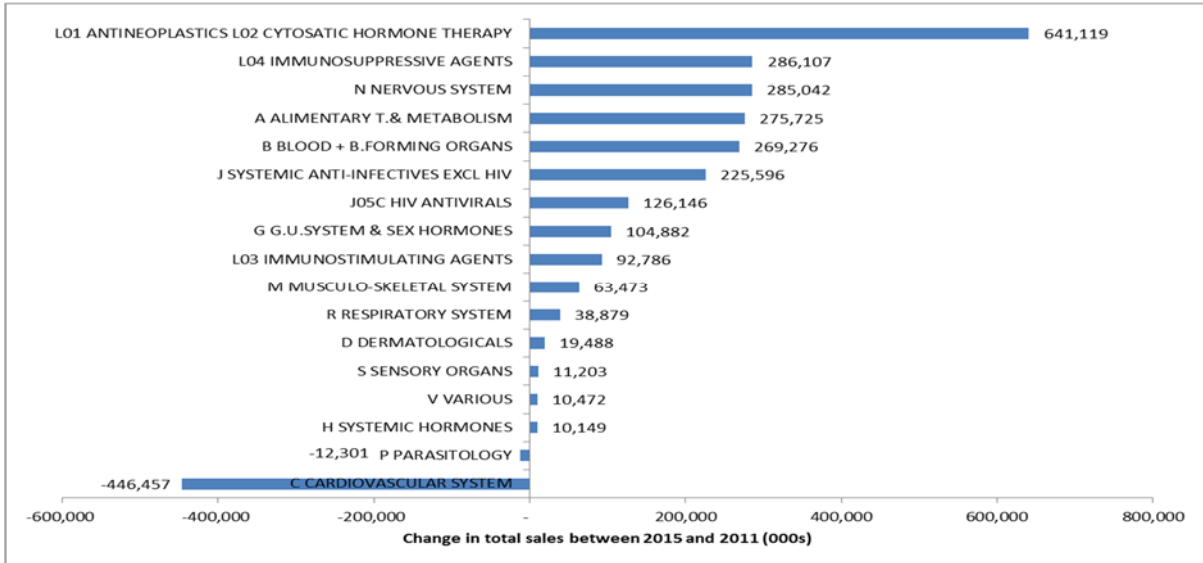
Primary care and secondary care medicine expenditures are expected to increase by 1.4% and 6.9% CAGR, respectively, between 2011 and 2015. On this basis, the share of secondary care medicines would rise from 36% of the total NHS medicines bill in 2011 to 41% in 2015.

Within primary care, sales of branded medicines are projected to decrease from £6.9bn in 2011 to £6.4bn in 2015. This is due to the impact of LOE, as nine out of the top 20 brands by sales in 2011 lose patent protection between 2012 and 2015. In 2011, this represented 26% of the total medicines bill and 33% of the branded medicines bill.

In secondary care, our model projects that sales of branded medicines will increase in the baseline scenario from £3.9bn in 2011 to £4.9bn in 2015. Expenditure on branded medicines mostly sold in secondary care increases because fewer products go off patent during the forecast period relative to brands sold in primary care and because a significant proportion of future launches are expected to be secondary care medicines.

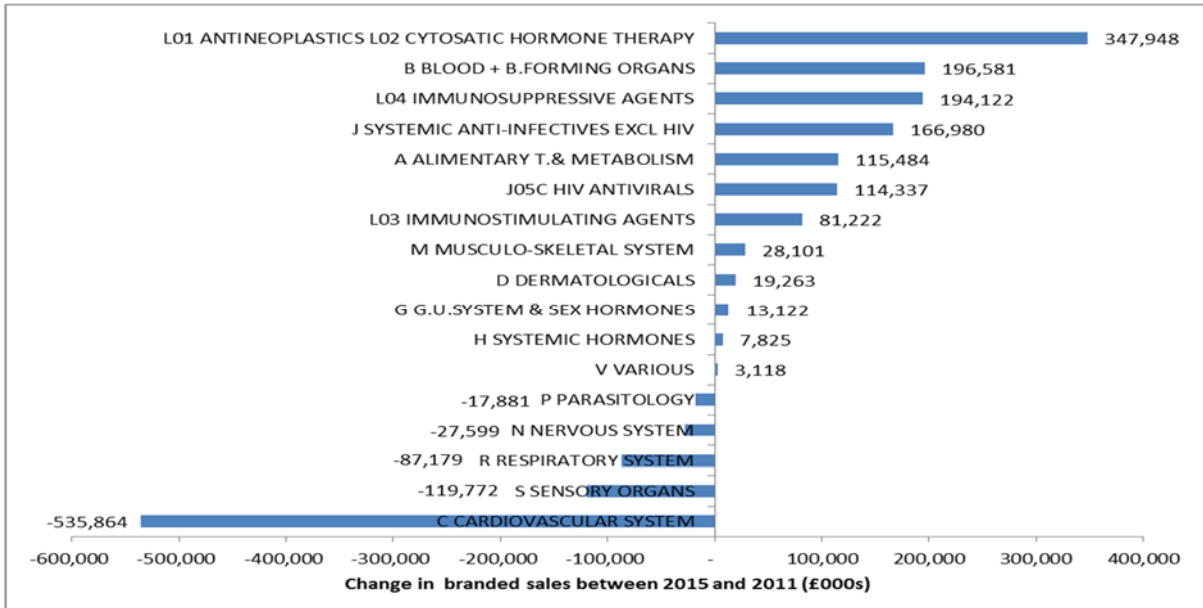
Figure 11 shows the projected change in total sales (brands, generics and biosimilars) between 2011 and 2015 in the baseline scenario by therapeutic category. Figure 11 shows the same but only for branded medicines. Figure 10 shows that the highest increase in sales over the forecast period is for cancer medicines and, from Figure 11, we can see that more than half of this increase is due to branded sales, but not much less than half goes to generics and biosimilars.

**Figure 11. Change in total sales by therapeutic area (£'000) 2011–2015: Baseline scenario**



Source: Authors' estimates

**Figure 12. Change in total sales by therapeutic area (£'000) 2011–2015: Baseline scenario**



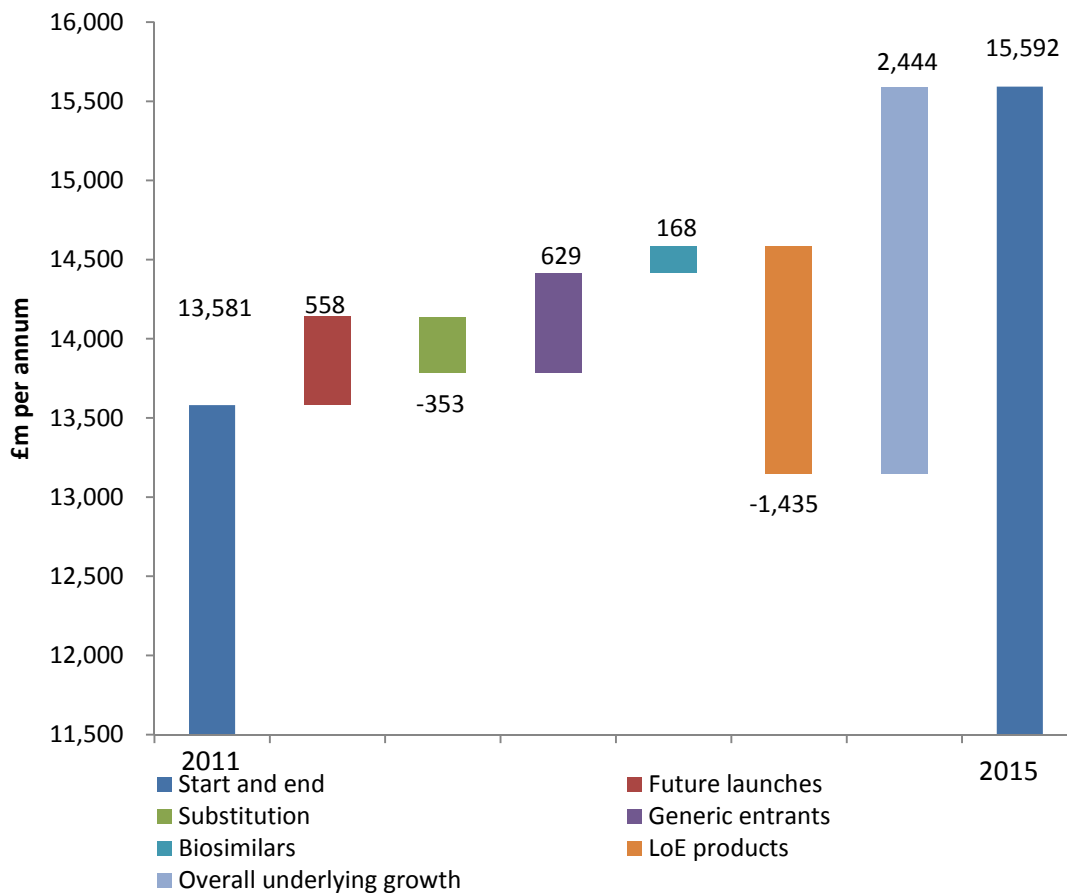
Source: Authors' estimates

From Figures 11 and 12, we can also see that the therapeutic area that suffers the greatest decline in sales from 2011 to 2015 is cardiovascular (C). This is mainly for two reasons: (1) generic versions of Lipitor® (atorvastatin) entering the UK market from July 2012 and (2) strong generic competition across the class.

Figure 13 shows the contributions of the different components of the model to the total £2 billion projected change (from £13.6 billion to £15.6 billion) in UK NHS medicines expenditure between 2011 and 2015 under the baseline scenario. Future launches between 2012 and 2015, inclusive, are projected to generate UK NHS spending of

£558m in 2015 but, given our substitution assumptions, these are projected to displace £353m of spending on medicines that already existed in 2011. Spending on generic copies of branded products that lose exclusivity between 2012 and 2015, inclusive, is expected to be £629m in 2015; spending on biosimilars of branded biologicals losing exclusivity in the same period is expected to be £168m in 2015. Annual expenditure on originator brand medicines that lose exclusivity over the period 2012–2015, inclusive, is expected to decline as a result of generic competition by £1,435m by 2015. The last-but-one block in Figure 13 (+£2,444m), shows the overall underlying growth trend in the baseline scenario once the other drivers just described have been taken into account.

**Figure 13. Elements driving the change in total medicines expenditure (£ million): Baseline scenario**



Source: Authors' estimates

### High and Low Scenarios

Two further scenarios have been modelled to illustrate the impact of changing key assumptions. Table 10 shows how these two scenarios (labelled 'high' and 'low') compare with the baseline scenario. Broadly speaking, under the 'high' scenario we assume that the uptake of new medicines improves relative to experience and that oncology biosimilars have little penetration. For the 'low' scenario, the uptake of new

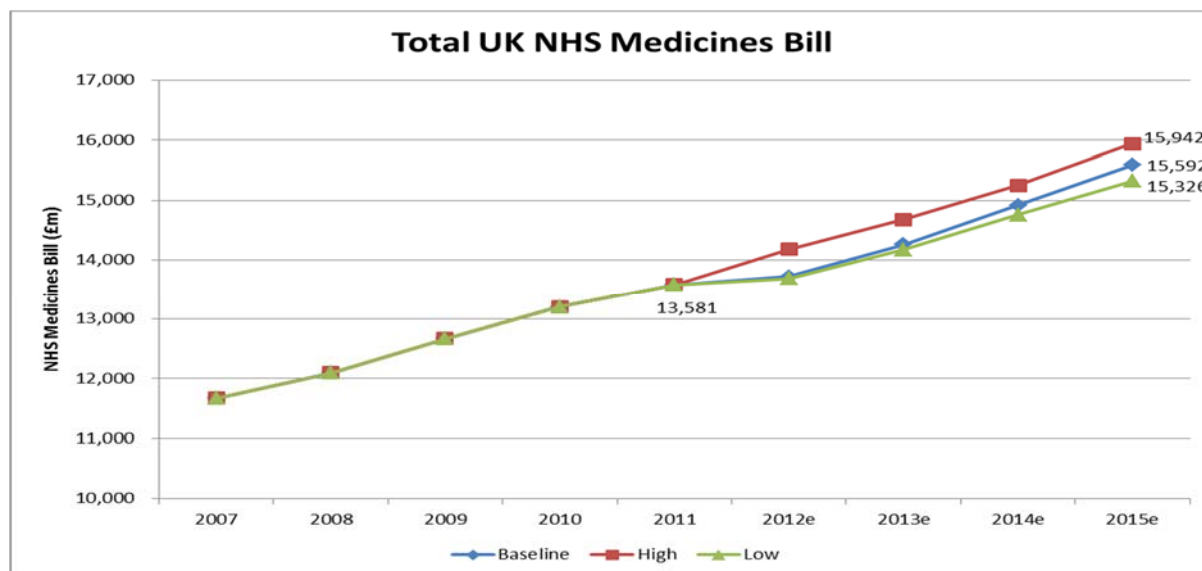
medicines worsens and there is more aggressive generic and biosimilar competition than in the baseline.

**Table 10. Scenarios**

<b>Estimate Range</b>	<b>New product launches – Attrition rates</b>	<b>New product launches – Uptake curves</b>	<b>New product launches – Year 1 sales</b>	<b>Extent to which sales of future launches are additive rather than substituting for existing medicines</b>	<b>LOE: Generics</b>	<b>LOE: Biosimilars (Cancer and TNFs)</b>	<b>Non-core areas/all therapeutic area growth</b>	<b>'Genericisation' of established products</b>
<b>Baseline</b>	Match count of future launches to launches during 2003–2010	Current uptake curves by therapeutic area (TA)	Current year 1 sales per TA	25% of sales of future launches are additive. For oncology: 75% of sales of future launches are additive	Use current erosion curves	TNFs and cancer: less aggressive than difficult secondary care. Cancer less aggressive than TNFs (for earlier years)		
<b>Low</b>	10% fewer launches relative to 2003–2010	Use 'average' uptake curves for TA with higher than average uptake curves	Current year 1 sales per TA - 10%	10% of sales of future launches are additive. For oncology: 50% of sales of future launches are additive	For TA with less than aggressive erosion curves, use 'average'	10 percentage points more aggressive than baseline for all LOE products	Both core and non-core areas growth reduced from trend by 2% p.a.	Additional 1% reduction in 'recent' branded growth for key ATC4 with generics (diabetes, CV, SSRI/SNRI)
<b>High</b>	10% more launches relative to 2003–2010	Use 'average' uptake curves for TA with lower than average uptake curves	Current year 1 sales per TA + 10%	40% of sales of future launches are additive. For oncology: 100% of sales of future launches are additive	For TA with more than aggressive erosion curves, use 'average'	Cancer: 10 percentage points less aggressive than baseline		

Figure 14 shows the projections for total UK NHS medicines expenditure across the three scenarios.

**Figure 14. Total medicines expenditure across the three scenarios**

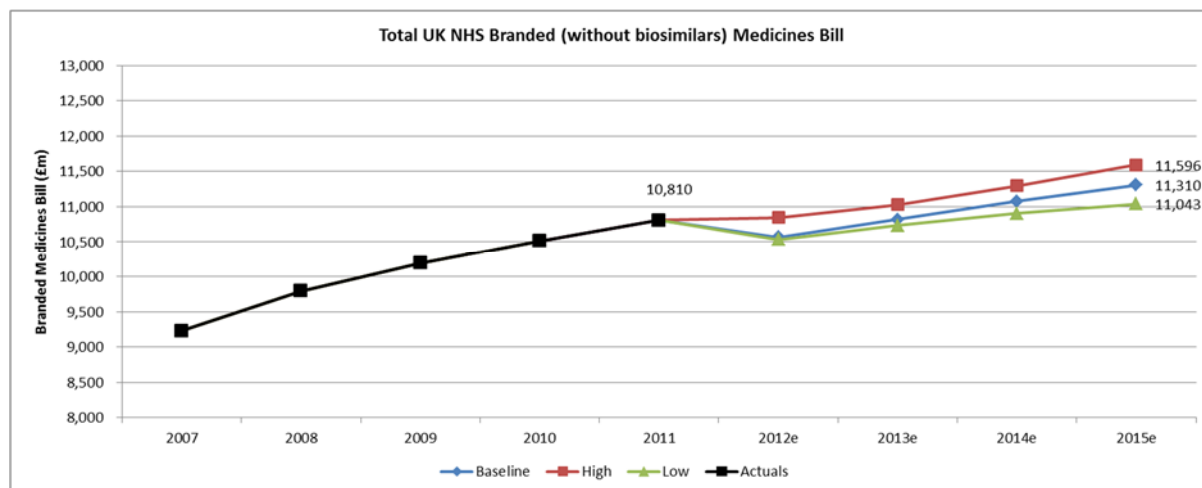


Sources: 2007–2011 IMS BPI and HPAI; 2012–2015 authors’ estimates

Under the high scenario, the total NHS medicines bill increases by a 4.1% CAGR between 2011 and 2015; the CAGR for the low scenario for the same time period is 3.1% (compared to a 3.5% CAGR for the baseline).

Figure 15 shows the projections under the three scenarios for branded medicines only.

**Figure 15. Branded medicines expenditure across the three scenarios**



Sources: 2007–2011 IMS BPI and HPAI (2007–2011); 2012–2015 authors’ estimates

Under the high scenario, the branded medicines bill increases by a 1.8% CAGR between 2011 and 2015; the CAGR for the low scenario for the same time period is 0.5% (compared to a 1.1% CAGR for the baseline).



## Comparison of Actuals and Projections for 2012

At the time of writing this paper, sales data for 2012 had just become available from IMS. This allows us now to compare our projections with 2012 actual sales for the following dimensions of the medicines bill: total medicines bill, total primary care medicines bill, total secondary care medicines bill and total branded and generic medicines bill. Table 11 shows these comparisons.

**Table 11. Actual versus projections, 2012**

<b>Growth Rates: 2012 vs. 2011</b>	<b>Actual</b>	<b>Baseline</b>	<b>High</b>	<b>Low</b>
<b>Total Market</b>	1.3%	1.0%	4.4%	0.8%
<b>Total Brands</b>	-1.5%	-2.3%	0.3%	-2.6%
<b>Total Generics</b>	12.6%	14.0%	27.4%	14.0%
<b>Total Primary Care</b>	-3.7%	-1.9%	3.2%	-2.2%
<b>Total Secondary Care</b>	10.3%	6.5%	6.6%	6.3%

Source: Actual: IMS BPI and HPAI (2012); Baseline, High and Low: author's analysis

Based on Table 11, we can highlight the following results:

- For the total market: actual sales are within our projected range
- For total brands (not including biosimilars): our baseline negative growth rate is higher than the actual (-2.3% vs. -1.5%); but, again, actual sales are within our range
- Generics: overall, we have slightly overestimated growth (14.0% in the baseline scenario vs. 12.6%)
- Total primary care: the actual negative growth rate has been higher even compared to our 'low' scenario
- Total secondary care: the actual growth rate is higher even than in our 'high' scenario

Overall, for the total market (both for brands and generics together and for brands only), the actual growth rate for 2012 lies within our ranges.

## DISCUSSION

Two broad approaches may be used to project future medicines expenditure in any health care system: bottom up or top down. A top-down approach has more modest data requirements and suits a long-term time horizon. But a top-down approach ignores a lot of information that already is known and will affect medicines expenditure over a time horizon of a few years: specifically the probable date of LOE of individual medicines already on the market and the likely impact of generic or biosimilar competition at that time; also missed is what is known about the likely launch of new medicines the short to medium term based on current R&D pipelines.

The choice of approach depends on the reason for projecting medicines expenditure. We have used a bottom-up model because we were particularly interested in exploring the impact of generic competition and new products over the medium term. A strength of this approach is that it enables and accommodates modelling of key issues that, for instance, affect top selling products and can have potentially large effects on the results.

If we were interested only in assessing the evolution of the medicines bill at a high level, one option would be to calculate historical growth rates over a long time frame and then assume that the projections will be the same as the historical evolution—i.e. using a top-down approach. For this reason, we have computed historical annual growth rates and the CAGR between 2003 and 2011 (based on IMS BPI and HPAI databases). Table 12 shows these results. The last column shows our projections for 2011–2015.

**Table 12. Historical growth rates (2003–2011) vs. projections (2011–2015)**

	<b>Average annual growth rate: 2003–2011</b>	<b>CAGR 2003–2011</b>	<b>CAGR 2011–2015e</b>
Total medicines bill	3.9%	3.8%	3.1%–4.1%
Total brands	3.4%	3.4%	0.5%–1.8%
Total generics	6.2%	5.8%	10.0%–11.0%

Source: 2003–2011 authors’ calculations from IMS BPI and HPAI (2003–2011); 2011–2015 authors’ analysis

As seen in Table 12, both the average annual growth rate (3.9%) and CAGR for the period 2003–2011 (3.8%) for the total medicines bill lie within our range for 2011–2015 (3.1–4.1%); however, our projections for brands and generics are considerably lower and higher respectively than for the 2003–2011 period. This suggests that our bottom-down approach pays off in understanding the key factors driving the evolution of the medicines bill in the short and medium term.

A top-down model does not make transparent the differential impact of various drivers of change in medicines expenditure, such as new products and loss of exclusivity. If the evolution of the medicines bill was steady then this would be less of an issue for this type of model. But the medicines bill in the UK has not evolved steadily. New classes of medicines can have a disproportionate effect; e.g. the market for medicines for macular degeneration has grown five fold in the last five years to £200m in 2011, based on IMS sales data<sup>4</sup>. Other classes have been disproportionately affected by LOE and have shrunk considerably in value over the period, such as statins and acid pump inhibitors, on which spending fell by more than half between 2008 and 2011<sup>5</sup>. Understanding the interaction of drivers within a class of medicines also can be complex, notably the degree to which newly launched medicines displace spending on older products. A bottom-up model is able to incorporate these complex interactions directly.

<sup>4</sup> Authors’ analysis based on IMS (IMS BPI and HPAI)

<sup>5</sup> Authors’ analysis based on IMS (IMS BPI and HPAI)

In addition to quantitative analyses of past trends at therapeutic level, patent dates for individual medicines and R&D pipelines to project expenditures, we have sought qualitative inputs from industry experts at the therapeutic class level and NHS pharmacists to validate assumptions. Including expert input is essential to tap into knowledge about how possible trends in the use of medicines in particular therapeutic areas might reasonably be expected to change in future. Future research could develop our model to include testing different qualitative methodologies for obtaining these important inputs. Additional analyses would be useful in developing the forecasting model: to examine 'non-core' therapeutic areas in the same degree of detail as we have analysed 'core' areas; to explore in greater detail any one of the dimensions discussed here, such as the impact of future biosimilars especially in oncology; to analyse further the uptake of newly launched medicines; and to explore the drivers and effects of generic competition in future. We also propose in future to compare projections from our model with actual sales and to analyse where the discrepancies are greatest and why.

## **SUMMARY AND CONCLUSIONS**

In this paper, we describe a method for projecting UK NHS expenditure on medicines over the medium term. The basis for our projections includes historical trends, knowledge of the unfolding lifecycles of existing medicines, published information about R&D pipelines that will produce future new medicines, and expert input. Our basic premise has been to try to ascertain when historical trends can be expected to be a good predictor of the future and when not. This is especially challenging when analysing the future impact of new launches and generic competition.

For any forecast, it is important to address the inevitable uncertainty by modelling a number of scenarios. For this reason, we created a baseline scenario and two others as illustrations. It would be possible to use the model to assess the impact of a wide range of alternative scenarios rapidly.

Taking into consideration all the issues surrounding projections, we believe that our methodology nevertheless provides a robust and comprehensive framework for projecting the medicines bill in the UK over the medium term. Parallel models could readily be developed for other countries' health care systems.

## APPENDIX. EXTENDING THE RESULTS TO 2018

The Pharmaceutical Price Regulation Scheme (PPRS) 2014 Heads of Agreement was announced on 6 November 2014 (DH and ABPI, 2013a)<sup>6</sup>. It outlines the terms of the five-year deal between the Association of the British Pharmaceutical Industry (ABPI) and the UK Government. For the first time in the UK, the PPRS caps future growth in the NHS branded medicines bill, between 2013 and 2018. OHE's model for projecting NHS medicines expenditure, based on data to 2011, was an important tool used by the ABPI and the UK Department of Health (DH) in drawing up the Heads of Agreement.

We have extended our results to cover the evolution of NHS medicines expenditure until 2018, i.e. we show additional results for the years 2016, 2017 and 2018. The purpose of this Appendix is to describe in greater detail the extended results, as well as distinguishing between gross sales (at list prices) and net sales (following discounts). We do not model the effect of the 2014 PPRS on our projections between 2014 and 2018. Our original projections to 2015 have not changed.

### Methods

Two key elements to extend the results from 2015 to 2018 involve:

1. Projecting sales for new products launched between 2016 and 2018;
2. Estimating the impact of generics and biosimilars entering the market after branded products lose exclusivity between 2016 and 2018.

For new products, we extended our pipeline analysis to estimate the count of products expected to be launched between 2016 and 2018, based on our original analysis. Table A1 replicates Table 2 in the main text, but with results for these additional three years.

**Table A1. Estimates of future launches per year**

	<b>2012e</b>	<b>2013e</b>	<b>2014e</b>	<b>2015e</b>	<b>2016e</b>	<b>2017e</b>	<b>2018e</b>
Products launched per year	27	27	26	26	22	22	18

Source: Authors' estimates from IMS Lifecycle R&D Focus (extracted March 2012) and industry expert input

To project sales of these products, we used the same uptake curves as before. For products losing exclusivity, we investigated the branded products expected to lose exclusivity between 2016 and 2018. We then applied the erosion curves used in the main text of this paper to project the sales of off-patented brands and their generic and biosimilar versions.

For recent on-patent products launched in the five years 2007 to 2011 inclusive; for older products (i.e. launched before 2007) not expected to lose exclusivity between 2012

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<sup>6</sup> The full PPRS was published on 3 December 2013 (DH and ABPI, 2013b), but the PPRS payments percentages are unchanged from the HoA.

and 2018; and for generic versions of medicines we used the same approach as in the same text.

We kept the baseline, high and low scenarios unchanged.

## Results

Table A1 shows the total medicines bill (gross sales) from 2011 to 2018. Data for 2011 are actual sales (based on IMS); sales for 2012–2018 are the baseline projections. Table A1 also decomposes total medicines expenditure between primary and secondary care channels. The results for 2011–2015 in Table A2 are the same as in Tables 7 and 9 in the main text.

**Table A2. Total primary and secondary care UK NHS medicines expenditure (£million): baseline scenario (gross sales)**

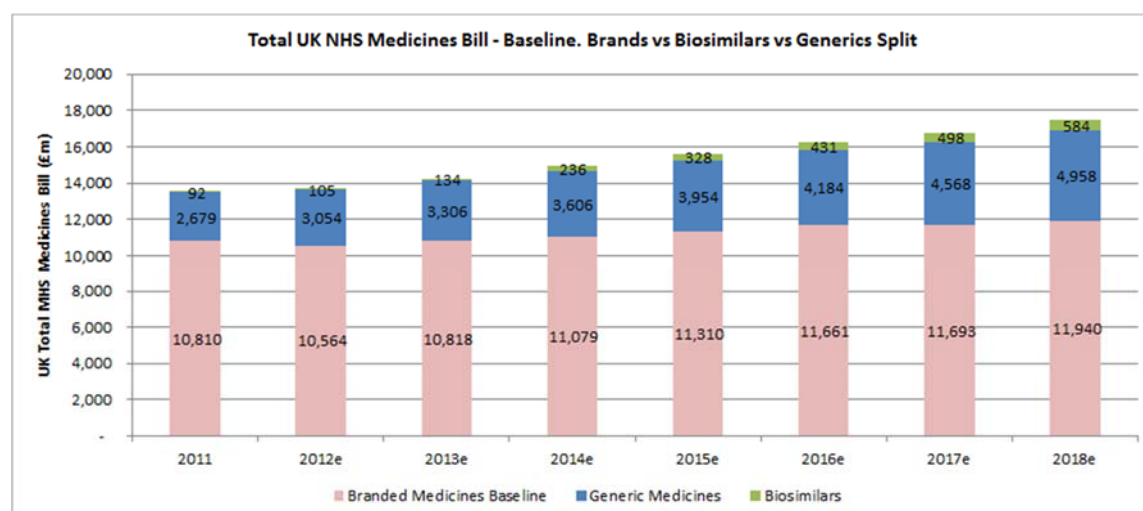
	2011	2012e	2013e	2014e	2015e	2016e	2017e	2018e	CAGR 2011-2018e
<b>Total</b>	13,581	13,723	14,259	14,922	15,592	16,277	16,759	17,481	<b>3.7%</b>
<b>Primary care</b>	8,754	8,584	8,768	9,003	9,275	9,582	9,725	10,070	<b>2.0%</b>
<b>Secondary care</b>	4,827	5,140	5,491	5,918	6,318	6,695	7,034	7,411	<b>6.3%</b>

CAGR: compound annual growth rate.

Sources: 2011 are from IMS BPI and HPAI; 2012–2018 are authors' projections

Figure A1 shows the decomposition of total sales for branded medicines, generics and biosimilars, respectively, at list prices (i.e. gross sales). Again, Figure A1 replicates Figure 10, but with new data for 2016, 2017 and 2018.

**Figure A1. Total UK NHS medicines bill (£million): baseline scenario (gross sales)**



Sources: 2011 are from IMS BPI and HPAI; 2012–2018 are authors' projections

Table A3 shows the compound annual growth rates (CAGRs) for the periods 2007–2011 and 2011–2018 for the total medicines bill and the different components of the model included in Figure A1.

**Table A3. CAGRs: baseline scenario (gross sales)**

<b>CAGRs</b>	<b>2007–2011</b>	<b>2011–2018e</b>
Total medicines bill	3.9%	3.7%
Brands	4.0%	1.4%
Generics	2.7%	9.2%
Biosimilars	26.1%	30.1%

CAGRs: compound annual growth rates.

Sources: 2011 are from IMS BPI and HPAI; 2012–2018 are authors' projections

Table A4 shows year on year growth rates from 2013 to 2018.

**Table A4. Year on year growth rates (based on gross sales)**

<b>Baseline</b>	<b>2012 – 13e</b>	<b>2013 – 14e</b>	<b>2014 – 15e</b>	<b>2015 – 16e</b>	<b>2016 – 17e</b>	<b>2017 – 18e</b>	<b>CAGR 2012- 15e</b>	<b>CAGR 2016- 18e</b>
<b>Total</b>	3.9%	4.7%	4.5%	4.4%	3.0%	4.3%	4.3%	3.6%
<b>Total PC</b>	2.1%	2.7%	3.0%	3.3%	1.5%	3.5%	2.6%	2.5%
<b>Total SC</b>	6.8%	7.8%	6.7%	6.0%	5.1%	5.4%	7.1%	5.2%
<b>Total branded (incl. biosimilars)</b>	2.7%	3.3%	2.9%	3.9%	0.8%	2.7%	2.9%	1.8%
<b>Branded PC</b>	0.2%	1.2%	0.9%	2.9%	-1.8%	1.9%	0.8%	0.0%
<b>Branded SC</b>	6.3%	6.3%	5.5%	5.2%	4.2%	3.7%	6.0%	3.9%

CAGR: compound annual growth rate; PC: primary care; SC: secondary care

Sources: Authors' projections

The total medicines bill in the last three years 2016–2018 is projected to slow compared to the period 2012–2015. This is driven primarily by a lower growth rate in 2017, where we project a 0.8% growth rate for total brands (including biosimilars) relative to 2016. There is even a nearly 2% negative growth rate for the branded segment in primary care—due to products losing exclusivity. The growth rates for branded sales in secondary care in 2017 and 2018 are also lower than in the preceding years.

The share of secondary care medicines is expected to rise from 36% of the total NHS medicines bill in 2011 to 42% in 2018. Within primary care, sales of branded medicines are projected to decrease from £6.9bn in 2011 to £6.5bn in 2018. This is due to the impact of LOE.

In secondary care, our model projects that sales of branded medicines would increase in the baseline scenario from £3.9bn in 2011 to £5.4bn in 2018. Expenditure on branded medicines mostly sold in secondary care increases because: (1) fewer products go off patent during the forecast period relative to brands sold in primary care and (2) a significant proportion of future new launches are expected to be of secondary care medicines.

Over the total projection period from 2011 to 2018 the annual NHS medicines bill is projected in the baseline scenario to increase in cash terms by +£3,900 million. This total increase over those seven years is the net result of the following changes:

- New launches add £1,445 million to annual spend. But these displace £828 million that would otherwise have been spent on older medicines for the same patients, so the net effect of the new launches is to add £627 million to annual spend by 2018
- Loss of exclusivity by existing branded medicines produces, via competition from lower priced generics and biosimilars, a cut of £1,424 million from annual spend;
- All other drivers of medicines expenditure contribute an increase of £4,697 million to annual spend
- Thus the total projected change in annual spend by 2018 compared to 2011 is (627-1,424+4,697=) £3,900 million.

Table A5 shows our projections for the sales of new products launched after 1 January 2014 as a percentage of total branded medicines sales.

**Table A5. Share of new medicines as a percentage of branded medicines sales**

	2014e	2015e	2016e	2017e	2018e
<b>Sales of new medicines as a % of total branded sales</b>	0.4%	1.8%	3.4%	5.5%	7.8%

New medicines: new active substances expected to be launched in the UK after 1 January 2014.

Source: Authors' projections

## Adjustments

As stated above, our starting point is IMS data, which are based on list prices. However, to reflect where list prices are discounted when manufacturers sell to the NHS, two adjustments have been made to allow us to also estimate net sales:

1. Value of brand equalisation deals in primary care
2. Level of discounts in the secondary care (hospital) sector.

These adjustments will affect slightly the growth rates going forward (as explained below) and represent savings to the NHS relative to IMS data.

We now explain the methods used to evaluate these two adjustments.

### **Brand Equalisation Deals in Primary Care**

Historic IMS data, as used in this study, did not track instances where originator brands are dispensed against a generic prescription and reimbursed at the generic rate. Branded volumes were priced at the branded list price. This implies there is an over estimation of the value of the medicines bill. In order to estimate the value of brands dispensed against a generic prescription (what is commonly termed in the UK as 'brands dispensed as generics (BDAG)'), we need to compare IMS data with prescription cost analysis (PCA) data.

The method used was as follows. First, using England PCA data and Department of Health coding, we identified branded medicines with a branded and generic alternative in 2011. The Net Ingredient Cost for such branded medicines was £271m. Second, we matched at pack level IMS data labels to the PCA Dictionary of Medicines and Devices, which gave us 1,300 matches. We estimated that 45% of IMS volumes of branded medicines with generic versions were dispensed against a branded prescription (weighted average for volumes), which therefore implies that the remainder of prescriptions, i.e. 55%, were dispensed against a generic prescription. Based on this analysis, we estimate an overestimation of the medicines bill value due to BDAG in 2011 of £211m. To estimate the value of BDAG for the period 2012-2018, we reduced the sales of LOE branded products by 55%.

To assess whether our brand equalisation estimate for 2011 was reasonable, we compared branded sales in our IMS baseline data to PCA data, and assumed that the difference between reported branded sales in the two audits should be explained by brands being dispensed against a generic prescription. As the two datasets are not matched in terms of coverage, assumptions had to be made to compare them: for IMS data, we adjusted for England's market share in the UK and for PCA data (which apply only to England) we excluded non-pharmaceuticals.

A range of comparisons was made between 2007 and 2011 varying the UK share of primary care attributed to England. We had three scenarios:

- Mid: we applied England's share across all primary care sales
- Low: we applied the lowest therapy class share for England
- High: we applied the highest therapy class share for England.

Table A6 shows our results.



**Table A6. Difference between IMS and PCA branded sales (three scenarios)**

<b>Year</b>	<b>Difference between IMS branded sales in model and PCA branded sales (high) £ million</b>	<b>Difference between IMS branded sales in model less PCA branded sales PCA (mid) £ million</b>	<b>Difference between IMS branded sales in model less PCA branded sales (low) £ million</b>
2007	306	5	-159
2008	256	-50	-217
2009	308	1	-167
2010	298	-13	-183
2011	449	134	-39

Source: Authors' analysis from IMS BPI and PCA data

Given the results in Table A6, we believe our 2011 estimate from the analysis of BDAG (£211m) can be considered reasonable, as it lies close to the middle of the our estimated range.

To estimate the value of BDAG for the period 2007-2011, we calculated the value of brand equalisation deals (£211m) as a share of branded sales in primary care (£6.9bn), which is equal to 3.1%, for 2011. We then applied this 3.1% to branded sales in primary care (year on year).

### **Level of discounts in the hospital sector**

We surveyed companies selling branded medicines to the NHS hospital market to ascertain the level of discounts in that sector. We asked them for annual gross and net sales for branded medicines for the period 2008 - 2011. Companies included in the survey represented 57% of the hospital market<sup>7</sup> (based on 2011 sales; source: IMS BPI (2011)). Responses were compiled by an independent auditor and we only had access to aggregated results, due to confidentiality reasons. On average, the level of discounts was constant throughout the four years, and equal to 20%. These results were also confirmed by the Delphi-type analyses used to explore the erosion curves used for secondary care in O'Neill et al. (2013). We applied this average 20% discount between 2012 and 2018 to obtain 'net' hospital sales for branded products not facing generic competition. We assume that when generics are available competition would be driving any discounts from off-patent brands.

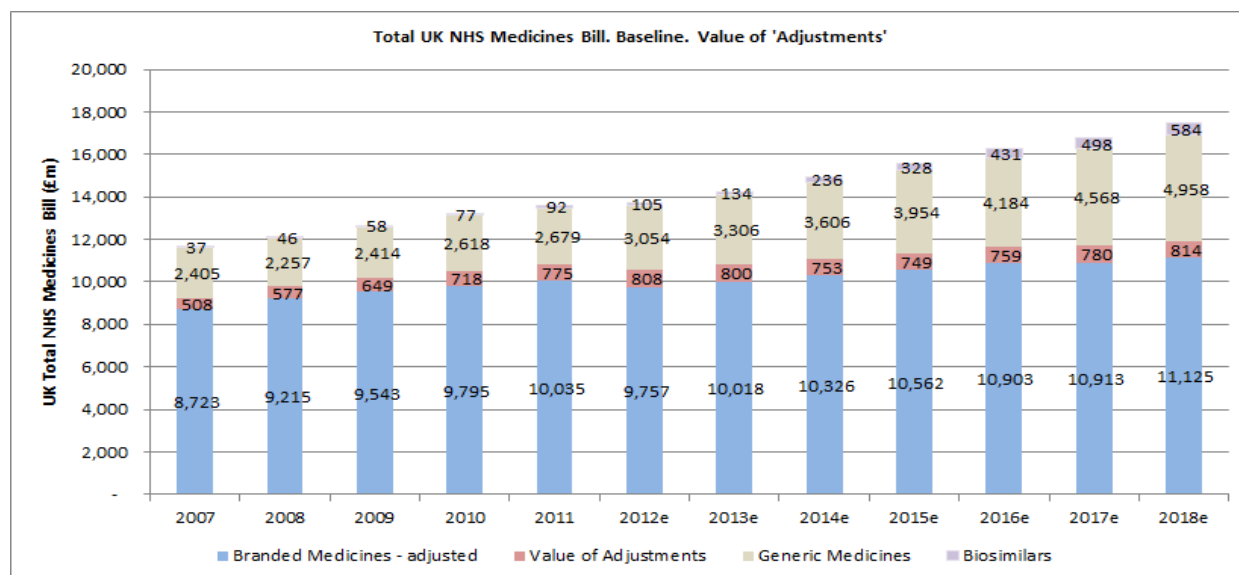
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<sup>7</sup> The companies we surveyed were members of the ABPI and the American Pharmaceutical Group (which represents the US research-based biopharmaceutical companies with a presence in the UK) with significant hospital sales (based on IMS data from BPI).

### Gross versus net sales

Figure A2 replicates Figure A1 above, but with a separate entry for the value of adjustments on aggregate.

**Figure A2. Value of adjustments from gross to net sales**



Sources: 2007 - 2011 are from IMS BPI and HPAI; 2012–2018 are authors' projections

Table A7 shows the differences in the CAGRs for 2011–2018 between the 'gross' and 'net' sales, for the different components of the model (total and branded sales respectively—as there is no effect on generic sales).

The differences between the growth rates in Table A7 for gross and net sales is because the adjustments do not apply uniformly across the entire time period; they depend on LOE dates and availability of generics—both in primary care and hospitals.

**Table A7. Comparison between CAGRs for 'gross' and 'net' sales (2011–2018)**

CAGRs 2011–2018e	Gross sales	Net sales
<b>Total</b>	3.7%	3.8%
<i>Total primary care</i>	2.0%	1.9%
<i>Total secondary care</i>	6.3%	7.1%
<b>Total branded (incl. biosimilars)</b>	2.0%	2.1%
<i>Branded primary care</i>	-0.3%	-0.5%
<i>Branded secondary care</i>	5.4%	6.3%

CAGRs: compound annual growth rates.

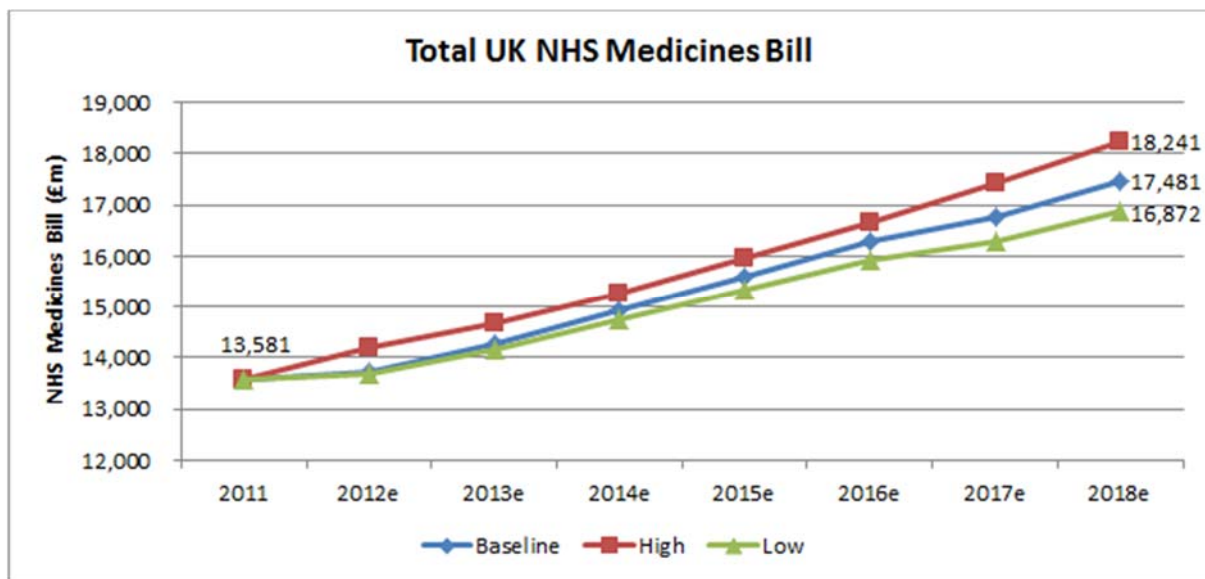
Source: Authors' projections

### Scenario Analysis: High and Low Scenarios

The same two scenarios as in O'Neill et al. (2013) have been modelled here. Broadly speaking, the 'high' scenario assumes higher uptake of new medicines relative to experience and that oncology biosimilars have little penetration and so displace fewer sales of originator medicines. For the 'low' scenario, uptake of new medicines is lower and there is more aggressive generic and biosimilar competition than in the baseline.

Figure A3 shows the projections for total UK NHS medicines expenditure across the three scenarios for 'gross' sales.

**Figure A3. Total projected NHS medicines expenditure across the three scenarios (gross sales)**

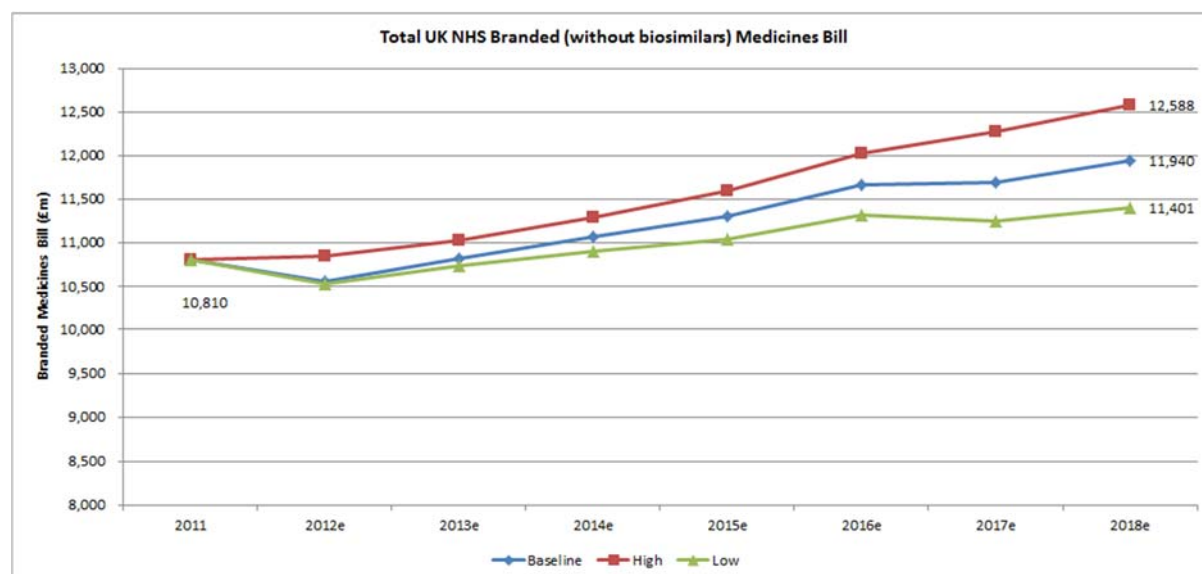


Sources: 2011 are from IMS BPI and HPAI; 2012–2018 are authors' projections

Under the high scenario, the total NHS medicines bill is projected to increase by an average 4.3% CAGR between 2011 and 2018; the CAGR for the low scenario for the same time period is 3.1%; compared to a 3.7% CAGR for the baseline scenario.

Figure A4 shows the gross sales projections under the three scenarios for branded medicines only (i.e. not including adjustments).

**Figure A4. Branded medicines expenditure across the three scenarios (gross sales)**



Sources: 2011 are from IMS BPI and HPAI; 2012–2018 are authors' projections

Under the high scenario, the branded medicines bill (at gross level) is projected to increase by an average 2.2% CAGR between 2011 and 2018; the CAGR for the low scenario for the same time period is 0.8%; compared to a 1.4% CAGR for the baseline. At net level, the CAGR between 2011 and 2018 for the branded medicines bill for the baseline scenario is 1.5%; for the high and low scenario, it is 2.3% and 0.8% respectively.

Table A8 shows projected year on year growth rates, between 2014 and 2018, for sales at net level (i.e. including discounts). For the total market (brands, biosimilars and generics), results are only shown for the baseline scenario. For brands and biosimilars, we also include the range (as driven by the low and high scenario respectively).

**Table A8. Projected year on year growth rates (net sales)**

Baseline – Growth rate (NET)	2013–14e	2014– 15e	2015–16e	2016–17e	2017–18e
<b>Total</b>	5.3%	4.8%	4.5%	3.0%	4.3%
<i>Total primary care</i>	2.7%	3.0%	3.3%	1.4%	3.4%
<i>Total secondary care</i>	9.7%	7.7%	6.4%	5.4%	5.6%
<b>Total branded (incl. biosimilars) [RANGES]</b>	4.0% [3.4 – 3.7%]	3.1% [2.2 – 3.6%]	4.1% [3.4 – 4.8%]	0.7% [-0.3 – 2.8%]	2.6% [1.7 – 3.0%]
<i>Branded primary care</i>	1.2% [0.9 – 0.3%]	0.8% [0.2 – 0.7%]	2.9% [2.7 – 3.1%]	-2.1% [-2.7 – 0.4%]	1.6% [1.0 – 1.1%]
<i>Branded secondary</i>	8.5%	6.5%	5.7%	4.5%	3.9%

<b>Baseline – Growth rate (NET)</b>	<b>2013–14e</b>	<b>2014– 15e</b>	<b>2015–16e</b>	<b>2016–17e</b>	<b>2017–18e</b>
<i>care</i>	[7.3 – 9.3%]	[5.2 – 7.9%]	[4.4 – 7.1%]	[3.1 – 5.9%]	[2.6 – 5.4%]

Source: Authors' projections

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