Forecasting branded and generic pharmaceuticals

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ABSTRACT

We forecast UK pharmaceutical time series before and after the time of patent expiry. This is a critical point in the lifecycle, as a generic form of the product is then introduced into the market, while the branded form is still available for prescription. Forecasting the numbers of units of branded and generic forms of pharmaceuticals dispensed is becoming increasingly important, due to their huge market value and the limited number of new ‘blockbuster’ branded drugs, as well as the imposed cost for national healthcare systems like the NHS. In this paper, eleven methods are used to forecast drug time series, including diffusion models (Bass model & RPDM), ARIMA, exponential smoothing (Simple and Holt), naïve and regression methods. ARIMA and Holt produce accurate short term (annual) forecasts for branded and generic drugs respectively, while for the more strategic horizons of 2–5 years ahead, naïve with drift provides the most accurate forecasts.

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1. Introduction

Marketing professionals and academics alike should strive to become more socially aware (Andreasen, 1978); and to that end, forecasting plays a major role in increasing the relevance of marketing. It is included in more than 98% of companies’ marketing plans, and should be taught in all business schools as a vital marketing tool (Armstrong, Brodie, & McIntyre, 1987). However, despite its importance, most managers do not appear to use forecasting effectively, as was evident from a survey of marketing managers that found that the self-reported forecast accuracy did not exceed 47% for new category entrants, and 40% for products that were new to the world (Kahn, 2002).

The introduction of new products changes the existing industry, as it adapts to include them (Darrock & Miles, 2011) and affects how forecasting managers perform. Many companies cite the forecasting of genuinely new products as one of the most difficult forecasting problems they face, given that new product forecasting is a leap into the unknown, with little or no historical information being available, which can cost the sales forecasting team substantial time, hurt its credibility through poor forecasting accuracy, and reduce its morale (Mentzer & Moon, 2005).

In this study, we forecast pharmaceutical life cycles before and after the time of patent expiry. This is a critical point in a product’s lifecycle, as a generic form of the product can be introduced to the market for the first time, while the branded form is still available for prescription. From an economic and financial point of view, assessing the numbers of units of the branded and generic
forms of pharmaceuticals dispensed becomes increasingly important, due to their huge market value and the limited number of new ‘blockbuster’ branded drugs. As a result, pharmaceutical companies make every effort to extend the commercial life of each of their branded products and to forecast their sales into the future. On the other hand, public health institutes seek insights for effective governance, as the use of a branded drug is quite costly when a generic form is available.

The rest of this paper is structured as follows: Section 2 summarizes the background literature, and Section 3 the pharmaceutical sector. Section 4 describes the dataset used for the empirical forecasting evaluation, and Section 5 discusses the forecasting models that were evaluated (with more details in the respective appendices). Section 6 provides the empirical results and a short discussion, while Section 7 elaborates more on the optimal drift. The last section concludes the study and provides avenues for future research.

2. Background literature

This study contributes to the existing body of literature by applying forecasting methods to the life cycles of pharmaceutical drugs and assessing the numbers of units dispensed. Previous studies by Cox (1967) and Easingwood (1987) modelled pharmaceutical life cycles but did not incorporate the forecasting element. This research aims to update and extend the existing work, with a specific focus on the life cycles of branded drugs, for which sales decline as soon as generic alternatives enter the marketplace.

In this context, successful forecasts and assessments of the numbers of units dispensed enable marketing managers to implement strategies that allow them to modify a product’s life cycle advantageously in order to increase sales and profitability, and decrease losses. If managers know how products are likely to perform at the yearly level, they can use this information to construct annual budgets and respective plans. They can also employ proactive strategies in order to slow down the decline of the drug, or look at introducing alternatives.

Many models have been used to predict new product sales, but previous studies have been limited to consumer goods, and have not addressed pharmaceuticals (Wind, Mahajan, & Cardozo, 1981). Models considering pharmaceutical drugs specifically have been proposed (Lilien, Rao, & Kalish, 1981) and subsequently adjusted, and their predictive abilities have been tested using pharmaceutical data (Rao & Yamada, 1988). The traditional (Bass, 1969) model, like other methods that are used to predict consumer goods, may not be suitable for pharmaceutical products. The applicability and predictive ability of diffusion models have received limited empirical testing with mixed results; however, complicated forecasting techniques do not always generate the most accurate results, and simpler approaches can be more effective in some situations (Makridakis & Hibon, 2000).

3. The pharmaceutical market

The pharmaceutical industry is one of the UK’s largest manufacturing sectors. In 2009, it was ranked 8th in the world, with an income of £7 billion. The UK pharmaceutical market is equally lively, with drugs entering the market continually. This fact creates a particular interest in the study of the interactions between the branded and generic versions of these drugs, as generic versions of branded drugs can cause pharmaceutical companies their greatest loss of revenue (according to the Association of the British Pharmaceutical Industry (ABPI)\(^1\)). On the other hand, healthcare agencies and regulating bodies may wish to make life-saving drugs available to the entire population at an affordable price through some form of regulation (Verniers, Stremersch, & Croux, 2011).

Two types of drugs tend to be available in a given market: branded drugs and their generic equivalents. At times, these may both be owned by the same pharmaceutical company, although it is more common for them to be owned by competing companies. A branded drug is generally protected by a patent that prevents the introduction of cheaper alternatives until the patent has expired. A patent is granted when the molecule is developed initially, and lasts for approximately 20 years. This means that the drug is protected through the pre-clinical and clinical trials, the approval process, and finally the introduction to the market. This introduction may occur 10–15 years after the drug was first developed, and thus, the drug is protected in the marketplace for only a limited amount of time. Generic equivalents are able to enter the market quickly upon the expiry of the patent, as they are not subject to the same lengthy development and approval process as the branded drug. Though equivalent to the branded drugs in terms of their bio-activity, generics can differ from the brands in their colour, shape, and packaging, as well as price.

When a generic drug enters the market, the number of prescriptions written for the branded version declines and the number of generic prescriptions increases at the same rate (or even faster). It was found that the persuasive role associated with detailing is responsible for GPs (general practitioners) switching between brands that contain the same active ingredient; thus, detailing should not be limited as this is likely to limit the learning rate of GPs (Ching & Ishihara, 2012). On the contrary, detailing is most effective as an acquisition tool (Montoya, Netzer, & Jedidi, 2010). Detailing should be targeted and combined with journal advertising in order to have a positive influence on an individual GP’s adoption of a new drug (Liu & Gupta, 2011).

In addition, GPs have a tendency to switch to cheaper generic alternatives as they become available (Frank & Salkever, 1997; Kvesic, 2008), which can occur even before the patent has expired. Moreover, not only does generic entry lead to the expected decrease in the prescription of the branded molecule bioequivalent to the generics, it also unexpectedly benefits other non-bioequivalent branded drugs, as detail-sensitive physicians switch from the contested molecule to other branded alternatives (Gonzalez, Sismeiro, Dutta, & Stern, 2008). However, conflicting evidence suggests that some GPs do not switch

\(^1\) http://www.abpi.org.uk/industry-info/Pages/default.aspx.
immediately, supporting the idea that generics are not perfect substitutes for the branded versions (Ferrándiz, 1999). When a GP prescribes a drug in the UK, the pharmacist dispenses what is written on the prescription. The only exception to this rule occurs when a patent still exists; in this case, if the GP prescribes the patented drug using its generic name, the branded version will be dispensed (Stern, 1994, 2002).

3.1. Pharmaceutical life cycles

The study of brand life cycles has a long history, dating back to Polli and Cook (1969) and, more recently, Bauer and Fischer (2000). However, there has been limited research on forecasting the life cycles of both the initial branded pharmaceuticals and their subsequent generic alternatives (Levitt, 1965).

The present study aims to develop this specific area of research by considering the interactions between the life cycles of branded and generic pharmaceuticals, as these cycles can be extremely unstable within the UK data, experiencing both seasonal variations and trends. Easingwood (1987) modelled product life cycles using a diffusion model but stopped short of the forecasting phase, while Cox (1967) produced six polynomial variations of the pharmaceutical life cycle, of which Type 1 is the only life cycle variation that follows the normal parabola curve of the product life cycle.

Therefore, the ability to forecast the number of prescriptions for a given medicine ultimately allows us to decide whether we want to allow the drug to decline at its current rate or to introduce measures to slow that decline, or perhaps do both while creating a new, innovative variation of the same product. Thus, this gives companies time to develop alternative strategies in order to limit the amount of revenue lost. However, the lack of studies of the application of forecasting techniques to such an area left a gap, which this study now addresses.

Product life cycles have four key stages – introduction, growth, maturity, and decline – all of which can be modelled and forecasted. The uptake of the product is generally low during the introduction stage, with most of the marketing costs incurred during this period (Masterson & Pickton, 2014). Once the product enters the growth phase, its sales begin to increase rapidly, and repeat purchasing starts. The end of this phase sees the introduction of imitation products that rival the initial one. These imitators are often cheaper and better than the original product. In the maturity phase, product sales peak and then begin to level off. The brands that remain in the market at this stage compete for market share (Bayus, 1994). As products mature, there is a decline in the number of technological advances or innovations that may have taken place in the introduction and growth phases, while the final phase is mainly the decline and withdrawal phase, when sales and profits start to fall (Agarwal & Gort, 2002).

Managers are becoming increasingly aware of their need to understand sales patterns and change their strategies to address these patterns (Golder & Tellis, 2004).

However, in our case, this traditional aforementioned lifecycle for the branded drug is interrupted – and therefore prevented from materialising fully – by the entry of the generic alternative. Hence, what we are actually facing is a compound DGP as a result of the superposition and interaction of the product lifecycles: the branded first and then the generic. Thus, one could argue that a single combined life cycle model could therefore be deemed appropriate, and, from a theoretical point of view, this makes good sense.

However, from a practical point of view, branded and generic pharmaceuticals are usually traded by different companies, and as such, forecasting a single compound, and combined time series is not beneficial for either of the parties; instead, separate forecasts for the two competing products are required.

This gives us further motivation for the current study, which focuses on the separate life cycles that exist at different points in time and the important crossover point after the date of patent expiration, when the number of units of the branded drug dispensed starts declining, while that of the generic form increases.

3.2. Reasons for peak sales

The demand for a new drug comes from new adoptions and repeat prescriptions written by GPs, as the sales for most drugs exhibit a peak before tailing off. This holds for both the branded drug and its generic equivalents when they enter the market (Fischer, Leeﬂang, & Verhoef, 2010). Fischer et al. (2010) posit a number of reasons why products, and pharmaceuticals in particular, exhibit sales peaks. First, sales appear to be driven more by new prescribers than by repeat prescriptions, due to the lack of switching behaviour among GPs when a drug that works for a patient is identified; however, this really depends on the therapeutic area.

Second, marketing efforts by pharmaceutical companies tend to be focused on the first two years following product launch (Osinga, Leeﬂang, & Wieringa, 2010), thus causing an increase in the numbers of prescriptions written by GPs. However, sales may actually decline when the pharmaceutical companies’ marketing efforts begin to tail off (Osinga et al., 2010). Fischer et al. (2010) also note that there is a limit to the final number of consumers of the drug, because each drug is only relevant for patients who are in need of a specific treatment for a specific problem; however, this also depends on the therapeutic area. Finally, when the patent on a branded drug expires and generic alternatives enter the market, competition increases and branded drug sales generally decline (Aronsson, Bergman, & Rudholm, 2001; Fischer et al., 2010; Jain & Conley, 2014).

The ability to forecast the entire life cycles of branded and generic pharmaceuticals is important, as it allows pharmaceutical companies to prepare and implement the relevant marketing strategies if sales are forecast decline or increase over a given time period. These strategies can include applying for a patent extension to cover a new medical indication, introducing over-the-counter forms and different strengths of the drug, changing the drug’s price, or implementing promotional strategies to meet the change in demand. These strategies can be applied to both the branded and generic drugs at different points in their life cycles. Thus, forecasting is important for both pharmaceutical companies and forecasting practitioners.
3.3. The critical forecasting horizon for the pharmaceutical industry

There is often a great deal of speculation with regard to the critical forecasting horizon within the pharmaceutical industry. It was therefore necessary to contact people who work within the pharmaceutical industry in order to gain an accurate picture. Judy Cooke is the Head of Business Intelligence at Janssen (a subsidiary of Johnson and Johnson). Cooke, in a private email communication, stated that, at a local (UK) level, forecasts are generally produced 3–5 years ahead. The ABPI also supported this by stating that, on a global scale, most companies would produce 10-year forecasts, though these are not expected to be very accurate initially. At an individual country level, forecasts are then produced for up to around five years. Sources from the Office for Health Economics also provided support for the 3–5-year critical forecasting horizon within the pharmaceutical industry, stating that a single 10-year forecast is often produced when the product is being introduced to the global market, then 1–5-year-ahead forecasts are produced continually as market conditions evolve. Sources from Novartis stated that 12–18-month forecasts are produced for financial forecasting and budget planning, after which 18-month to 5-year forecasting is conducted for production planning. Finally, 5-year forecasting is undertaken for strategic planning. As this paper focuses on forecasting the numbers of sales at a local level, the critical horizons considered in this paper are one, three and five years.

4. The data: prescriptions and dispensers in the UK

The data form part of the JIGSAW database, a commercially operated panel of GPs that was donated by Synovate for the purposes of academic research. The database was established by ISIS research in 1985. The time series associated with the current research are taken from a much larger database that contains 2570,000 prescription records from 1506 GPs across the United Kingdom. The time series run from 1987 to 2008. The most-prescribed chemical substances were selected from this database, resulting in seven substances that exceeded the ad-hoc threshold of 10,000 total prescriptions. These chemical substances were initially circulated as branded drugs, but once the patents expired, both a branded and a generic version of each substance was available on the market. Thus, over 10,000 prescriptions, in either the branded or generic form, were recorded for each of the seven selected substances between 1987 and 2008 (Table 1).

Each of these drugs exhibited a branded-generic crossover, with sales of the branded version initially increasing, before reaching a peak, then beginning to decline. Upon patent expiry, the number of generic prescriptions increased, reached a peak, and then began to decline, as new prescription medicines are always being released.

These newer drugs are definitely cheaper to produce, and may (or may not) have fewer side effects for the patient. If there is such an improvement, then GPs may switch the patient to the newer medicine. This is the primary life-cycle pattern exhibited by the branded and generic versions of a given pharmaceutical drug (Kvesic, 2008).

4.1. Prescribed versus dispensed

The dataset records the drugs that were actually prescribed by GPs. If the drug is protected by a patent, then the brand name must be dispensed, regardless of whether the GP writes a branded or a generic name on the prescription (Stern, 1994). Therefore, if a GP prescribed a generic drug before patent expiry, then the branded version would have to be dispensed.

However, after patent expiry, the generic version would have to be dispensed instead, and the branded version would only be dispensed if a GP prescribed it explicitly. Fig. 1 illustrates an example (generic: Ranitidine) that depicts the differences between the drugs that were prescribed initially by the GPs and those that were actually dispensed by the pharmacists.

We point out to the reader the differences between the numbers of prescriptions written and dispensed for Zantac and Ranitidine. The number of prescriptions dispensed for Zantac is higher, because, although some GPs prescribed Ranitidine earlier, the prescriptions were dispensed as Zantac until 1997, when the patent expired.

Fig. 1 makes it clear that the life cycles are actually closely connected. A large proportion of physicians prescribe the generic version of Ranitidine. Until the generic Ranitidine is available, pharmacists dispense Zantac. When generic Ranitidine becomes available, sales are high immediately (instead of going through an introduction or growth stage first).

Thus, the product life cycle of introduction, growth, maturity and decline holds only for the combined sales of brand and generic. For the UK market, it does not seem appropriate to assume separate four-stage life cycles for the brand and the generic drugs, and as such, the theoretical grounding of diffusion models does not seem to apply fully in this setting, meaning that there is room for experimentation on the forecasting abilities of more data-driven methods, such as smoothing and ARIMA models.

5. Forecasting models

In this study, the operation research (OR) forecasting paradigm is adopted and applied to the pharmaceutical industry in the UK. The aforementioned paradigm promotes competition between different forecasting techniques via a holdout period in which various forecasting horizons are evaluated simultaneously and in a rolling fashion, in order to determine the most accurate ones.

We model and forecast annual pharmaceutical time series up to five years ahead, using benchmark models including naïve and moving averages, the Bass diffusion model (Bass, 1969), the repeat purchase diffusion model (Lilien et al., 1981; Rao & Yamada, 1988), three basic regression models, and two exponential smoothing (ES)
Table 1
Basic information on the seven most-prescribed substances in the database.
Source: MPA Services, Espacenet and Patent Archives.

<table>
<thead>
<tr>
<th>Branded drug</th>
<th>Generic drug</th>
<th>Therapeutic class</th>
<th>CAS number</th>
<th>Patent number</th>
<th>Patentee</th>
<th>Year patent granted</th>
<th>Year of patent expiration</th>
<th>Supplementary protection certificate (SPC)</th>
<th>Total number of prescriptions (Rx) between 1987 and 2008</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobic</td>
<td>Meloxicam</td>
<td>Analgesic/Anti-inflammatory</td>
<td>71 125-38-7</td>
<td>EP0002482</td>
<td>Boehringer Ingelheim</td>
<td>1979</td>
<td>1998</td>
<td>2003</td>
<td>13276</td>
<td>MPA Services, Espacenet, Boehringer Ingelheim</td>
</tr>
<tr>
<td>Tenormin</td>
<td>Atenolol</td>
<td>Hypertension</td>
<td>29122-68-7</td>
<td>GB 1285038</td>
<td>ICI</td>
<td>1972</td>
<td>1990</td>
<td>NA</td>
<td>54297</td>
<td>MPA Services, Patent Archives, MPA Services, ESPACENET, Derwent Index</td>
</tr>
</tbody>
</table>
approaches for non-trended (simple ES) and trended data (Holt ES).

We do acknowledge the benefits of analysing higher frequencies of data as well, that is, quarterly, monthly or even weekly data; however, we have not done so here, as such detailed information was not available during the initial stages of the research project. Furthermore, we can also see the benefits of trying seasonal adjustments to the data at these higher frequencies; however, we believe that any improvement in accuracy in such cases would be coming mostly from the seasonal decomposition mechanism itself, rather than the extrapolation. This was also evident in the M3 competition where seasonal indices were provided a priori for monthly and quarterly series reducing the value of seasonal models such as Holt–Winters (Makridakis & Hibon, 2000).

5.1. Diffusion models

5.1.1. Bass diffusion model

Diffusion models have been employed in several areas of marketing, including consumer behaviour, marketing management, and marketing science research (Mahajan, Muller, & Bass, 1990). The generalised Bass model is popular in both normative and descriptive applications (Fruchter & Van den Bulte, 2011). Researchers have contributed to the diffusion theory by developing forecasting techniques associated with diffusion models, which were initially described by Bass (1969).

The Bass diffusion model explains the adoption of new products as an interaction between users and potential users. This theory of adoption and diffusion was first developed conceptually by Rogers (1962), who stated that individuals can decide to adopt a product independently of other influences. These people are generally known as the innovators of a product.

The model developed by Bass (1969) implies exponential growth followed by a peak and then a decline. The model generally provides good predictions for the products to which it is applied, and, according to Bass, is useful in providing a basic rationale for long-range forecasting (Bass, 1969). Since its inception, there have been many extensions of the original Bass diffusion model.

(For more details on the technical aspects of the Bass model, refer to Appendix A.1.)

5.1.2. Repeat purchase diffusion model (RPDM)

A three-step methodology was proposed by Lilien et al. (1981) for predicting the sales of new drugs as they enter the market, with little or no prior data being available. The steps proposed were as follows.

1. The model represents a repeat purchase diffusion process, using historical time series data associated with prescription drug introductions to develop sales models as a function of the total number of GPs in the target market and a number of other marketing variables, since GPs tend to repeat-prescribe new drugs.
2. A model is then produced to forecast the sales of the new drug prior to entering the market. It is suggested that this model be parameterised on a drug that management deems “similar” to the new drug being introduced to the market.
3. The final step aims to use early sales data for the product to update the model via a Bayesian regression, in order to make it more accurate. This approach is valid when no prior data are available, but if sales data are available, the RPDM can be used to produce accurate one-step-ahead forecasts (Rao & Yamada, 1988). This model provides the best fit for pharmaceutical data when the decay factor is removed.

(For more details on the technical aspects of the RPDM model, refer to Appendix A.2.)

5.2. Regression models

For the sake of comparisons with diffusion models, three simple regression models have been tested:

• regression over \( t \);
• introducing a lag with a regression over \( t - 1 \);
• robust regression with the number of prescriptions, number of GPs and year as explanatory variables.

Robust regression is an alternative to least squares regression when the data potentially include outliers. The basic idea is to weight the observations differently, and STATA’s \( rreg \) command implements a version of OLS regression where data with large absolute residuals are down-weighted.
Table 2
Data points available for forecasting.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Data points</th>
<th>Forecasting points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sertraline</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Lustral</td>
<td>19</td>
<td>14</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Zantac</td>
<td>22</td>
<td>17</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td>Tagamet</td>
<td>22</td>
<td>17</td>
</tr>
<tr>
<td>Atenolol</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Tenormin</td>
<td>22</td>
<td>17</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Mobic</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>Naproxen</td>
<td>21</td>
<td>16</td>
</tr>
<tr>
<td>Naprosyn</td>
<td>22</td>
<td>17</td>
</tr>
<tr>
<td>Ramipril</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Tritace</td>
<td>22</td>
<td>17</td>
</tr>
</tbody>
</table>

5.3. Other popular forecasting models

Consistent with the OR paradigm, a number of basic benchmarks and models that have been popular in previous forecasting competitions (e.g., Makridakis & Hibon, 2000) have also been included in the competition, being implemented, automatically initialised and optimised in STATA 11, namely:

- the naïve model;
- a moving average of three periods, which is a common choice for annual data, especially when the data have limited history available;
- simple exponential smoothing;
- Holt exponential smoothing;
- ARIMA.

Obviously, there was no need to include seasonal methods or apply a classical seasonal decomposition to the aforementioned methods/models, as the dataset we analysed consisted of yearly data.

6. Empirical results and discussion

With twenty-one years of data available for each drug, the first data points are used to estimate the model; however, some products have fewer data points, due to the patent expiry date. This is a direct result of the large number of branded pharmaceuticals for which patents expired in the 1990s, which meant that once the five-point hold-out period was included, there would not be enough data points available for accurate forecast comparisons.

The models were estimated using the statistical software STATA, and a non-linear approach was conducted for the RPDM and Bass diffusion models. Table 2 shows the total numbers of annual data points and observations for forecasting available for each drug time series. For three of the seven pairs (branded and generic versions), the generic alternative had a very limited history. This is because Sertraline, Meloxicam and Ramipril were released quite close to the final year in the database, with three, five and four annual observations, respectively. As a result, there were very few data points available for initialising a forecasting model, and these three generics were therefore excluded from the forecasting evaluation.

Table 3
Diffusion models: model fitting.

<table>
<thead>
<tr>
<th>Drug</th>
<th>RPDM</th>
<th>Bass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lustral</td>
<td>0.78</td>
<td>0.78</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>0.93</td>
<td>0.89</td>
</tr>
<tr>
<td>Zantac</td>
<td>0.88</td>
<td>0.80</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>0.90</td>
<td>0.92</td>
</tr>
<tr>
<td>Tagamet</td>
<td>0.85</td>
<td>0.74</td>
</tr>
<tr>
<td>Atenolol</td>
<td>0.98</td>
<td>0.67</td>
</tr>
<tr>
<td>Tenormin</td>
<td>0.80</td>
<td>0.73</td>
</tr>
<tr>
<td>Mobic</td>
<td>0.72</td>
<td>0.73</td>
</tr>
<tr>
<td>Naproxen</td>
<td>0.75</td>
<td>0.75</td>
</tr>
<tr>
<td>Naprosyn</td>
<td>0.98</td>
<td>0.74</td>
</tr>
<tr>
<td>Tritace</td>
<td>0.70</td>
<td>0.71</td>
</tr>
</tbody>
</table>

The chosen models were applied to the data describing the dispensed rather than prescribed pharmaceuticals. The first five data points of the time series were used to forecast the sixth, the sixth was used to produce the seventh, and so on.

As in a typical forecasting competition setup, where we compare the performances of various forecasting models/methods, we are interested primarily in three characteristics of the forecasts:

- **Bias**, that is, whether there is a systematic tendency to over- or under-forecast the actual values;
- **Accuracy**, in terms of how close the provided forecasts are to the actual values;
- **Uncertainty**, in terms of the size of the average deviation of the provided forecasts from the mean forecast.

The standard metrics for measuring the aforementioned characteristics are as follows: mean error (ME) for the bias, mean absolute error (MAE) for the accuracy, and mean squared error (MSE) for the uncertainty (Makridakis & Hibon, 2000). A more intuitively appealing choice for the evaluation of the forecasting accuracy is to use a relative metric instead, such as the relative absolute error (RAE), which is just the MAE of an evaluated method divided by that of a benchmark method, in this instance, the naïve method for the one-year-ahead forecast. The reason for the popularity of this specific metric is that the results are very easy to interpret; if the value for a given method is less than that for the benchmark method, then the evaluated method forecasts better than the benchmark, and vice versa.

In our forecasting evaluation, we do not believe that one size fits all, and as such, we run two separate forecasting evaluations: one for the seven branded drugs and one for the seven generic ones. We take the same approach as far as forecasting horizons are concerned, and therefore perform separate evaluations for short-term (one year ahead), mid-term (2–3 years ahead) and long-term (4–5 years ahead) forecasts. The results were supportive of this approach, as different “horses for courses” were identified, consistent with the recommendations of Petropoulos, Makridakis, Assimakopoulos, and Nikolopoulos (2014).

6.1. Forecasting using the diffusion models

Table 3 presents the results for the model’s goodness of fit using Pearson’s $R^2$ correlation coefficient for the pharmaceuticals actually dispensed.
The $R^2$ values for both the RPDM and the Bass (1969) diffusion model provide significant results for the eleven pharmaceuticals that were forecast. The lowest $R^2$ value in the RPDM was for Tritace (0.70); in the Bass model, it was for Atenolol (0.67). Two illustrative examples of forecasts from the models are presented in Figs. 2 and 3 respectively.

6.2. Forecasting branded pharmaceuticals

Branded pharmaceuticals are expected to follow the classical product lifecycle curve until this is interrupted by the expiry of the patent, at which point alternative products become available in the market, and therefore a very steep descent in demand is expected. As such, there is no preconception as to the kind of models that might be most appropriate, given that it is not known a priori what the exact phase of the lifecycle will be when the patent is about to expire. The results of our evaluation are presented in Tables 4–6.

Table 4 presents the average forecasting errors for the branded drugs across the seven drugs and the respective time series, for each of the models used in the study. The error results in Table 4 show clearly that the ARIMA model was the most accurate for forecasting the time series of branded drugs for the immediate one-year-ahead forecasting horizon. The results remain the same across the three performance metrics of bias, accuracy and variance (ME, RAE and MSE).

Table 5 presents the average forecasting errors for the branded drugs for each of the models used in the study.
results across the three performance metrics are the same. The model is again Holt’s exponential smoothing model. The drugs, and show clearly that the most accurate forecasting term forecasting horizon of 2–3 years ahead for the generic (ME, RAE and MSE).

The results presented in Table 7 clearly show that, on average, Holt exponential smoothing was the most accurate method for forecasting the respective time series of generic drugs. The results remain the same across the three performance metrics of bias, accuracy and variance (ME, RAE and MSE).

Table 8 presents the forecasting errors for the mid-term forecasting horizon of 2–3 years ahead for the generic drugs, and shows clearly that the most accurate forecasting model is again Holt’s exponential smoothing model. The results across the three performance metrics are the same.

Finally, Table 9 presents the long-term forecasting errors for the generic drugs for each of the models used in the study, and Holt’s exponential smoothing model is the most accurate one once again, with the naïve model coming second. The results remain the same across the three performance metrics.

6.4. On the shortfalls of diffusion models for forecasting the real data series

Following the illustrative examples in Figs. 1–3, the poor performances in Tables 4–9, and our earlier discussion emphasising the fact that we are not facing a pure product lifecycle, but the superposition and interactions of two (branded first and then generic entry), one could argue immediately that the Bass and RPDM models are not appropriate for forecasting the branded and generic drugs considered. Hence, it may not be quite clear why we need further empirical evidence.

Nevertheless, we do believe that such an analysis is necessary, since, if we had not included results from diffusion models in our empirical forecasting competition, many scholars would still be sceptical about the validity of our results, despite acknowledging that diffusion models may not be appropriate in this context, given the compound DGP that we are trying to model. Thus, we decided to let the empirical results add another, admittedly rather small, corroborative insight to that end.

A further theoretical argument that could explain the poor performance of the Bass model is the fact that our data do not follow specific patients. GPs prescribe medicines to patients in a process that can take place either once, if the patient recovers rapidly and does not need the medication.
any more, or on a repeated basis, if the patient is suffering from a long-term illness. Thus, repeat purchases do not necessarily apply to a given patient, but come from GPs prescribing the drug again (possibly to different patients). Hence, adoption refers to the adoption of the drug by the physician, not by the patient.

7. On the (empirical) quest for an optimal drift

Given the success of trended models in the empirical investigation presented in the previous section, especially for the generic drugs, we would like to investigate this aspect further. One avenue of investigation is to try find the optimal trend by adding a gradually increasing trend to the naïve model. There is also some scope for doing the same for branded drugs, as trended models could capture the growth and steep decline phases of the respective time series.

These trended extrapolation models tend to capture the medium- to long-term trends; however, these did not usually produce forecasts that were any better than those from the naïve model; the same applies for the trended version of exponential smoothing models, such as Holt exponential smoothing and the Theta model (Assimakopoulos & Nikolopoulos, 2000; Makridakis & Hibon, 2000).

Our next step was to add a term (called the drift) which is the difference between the last two known actual observations, in order to capture the very short-term trend in the data. Given the dominance of the naïve model in our empirical competition, it was decided to add just a drift to this model, giving the naïve with drift model, with the forecasting equation:

\[ F_{t+1} = Y_t + d_t, \quad \text{where the drift is} \quad d_t = Y_t - Y_{t-1}. \quad (1) \]

If we want to use only a portion of the drift, our model becomes:

\[ F_{t+1} = Y_t + \alpha d_t, \quad d_t = Y_t - Y_{t-1}, \quad 0 < \alpha < 1. \quad (2) \]

Tables 10 and 11 show the forecasting performance of the naïve with drift model for forecasting horizon 1, where \( \alpha \) is introduced in 10% increments. Table 10 shows that the ME of the branded pharmaceuticals decreases as the percentage of drift increases, while the RAE and MSE increase as the percentage of drift increases. These results suggest that for branded pharmaceutical life cycles, the most appropriate forecasting method is naïve + 20% drift. This drift has been selected because it has the lowest ME and MSE, while still having a RAE of 0.98, showing that the method has a high level of forecasting accuracy.

Table 11 also shows that the ME of the generic pharmaceuticals declines as the percentage of drift increases. Both the RAE and MSE decline as the drift increases to 70%, after which they start to increase again. This shows that the best forecasting method for the generic pharmaceutical life cycle is naïve + 70% drift. This shows that branded and generic pharmaceutical life cycles need different levels of drift in order to maximise the forecast accuracy. To visualise this optimum drift, we can graph the way in which the error (RAE) changes depending on the \( \alpha \) parameter selected, as in Fig. 4.

Tables 12 and 13 show the forecasting performance of the naïve with drift model for a forecasting horizon of 2–3 years ahead.

The tables show that the ME, RAE and MSE values of the branded and generic pharmaceuticals decrease as the percentage of drift increases. The results suggest that the most appropriate forecasting method for a 2–3-year-ahead
forecast for a branded drug is naïve + 100% drift. This drift has been selected because it has the lowest ME, MSE and RAE values. The same method is also the most accurate for the generic drugs at a forecast horizon of 2–3 years. The results show that the branded and generic pharmaceuticals can both use the same forecasting method for a forecast horizon of 2–3 years. Fig. 5 provides a visualisation of the optimum level of drift plotted against the RAE.

Tables 14 and 15 show the forecasting performance of the naïve with drift model for a forecasting horizon of 4–5 years ahead.

Table 14 shows that the ME, RAE and MSE values of the branded pharmaceuticals decrease as the percentage of drift increases. The results suggest that the most appropriate forecasting method for a 4–5-year-ahead forecast for a branded drug is naïve + 100% drift. This drift is selected because it has the lowest ME, MSE and RAE results. Table 15 shows that the same holds for the generic drugs at a 3-year-ahead forecast horizon. The results show that the branded and generic pharmaceuticals can both use the same forecasting method at a forecast horizon of 4–5 years. Fig. 6 provides a visualisation of the optimum level of drift plotted against the RAE.

Given the nature of the data series and the steep growth and decline phases of the branded ones, as well as the steep increase of the newly introduced generic ones, it is not surprising that a certain level of drift can always provide a superior forecasting performance; however, it is not always the same level of drift.

**Table 10**
Forecasting horizon 1, naïve + drift, branded drugs.

<table>
<thead>
<tr>
<th>Benchmark</th>
<th>Drift</th>
<th>Naïve</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
<th>60%</th>
<th>70%</th>
<th>80%</th>
<th>90%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ME</td>
<td></td>
<td>−90.13</td>
<td>−81.42</td>
<td>−72.73</td>
<td>−63.99</td>
<td>−55.28</td>
<td>−46.56</td>
<td>−37.78</td>
<td>−29.13</td>
<td>−20.42</td>
<td>−11.71</td>
<td>−2.99</td>
</tr>
<tr>
<td>RAE</td>
<td>1.00</td>
<td>0.98</td>
<td>0.98</td>
<td>1.01</td>
<td>1.04</td>
<td>1.07</td>
<td>1.10</td>
<td>1.14</td>
<td>1.25</td>
<td>1.34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSE</td>
<td></td>
<td>188.674.93</td>
<td>181.978.42</td>
<td>179.087.22</td>
<td>180.001.33</td>
<td>184.720.76</td>
<td>193.245.50</td>
<td>205.576.84</td>
<td>221.710.91</td>
<td>241.651.59</td>
<td>265.397.58</td>
<td>292.948.87</td>
</tr>
</tbody>
</table>

**Table 11**
Forecasting horizon 1, naïve + drift, generic drugs.

<table>
<thead>
<tr>
<th>Benchmark</th>
<th>Drift</th>
<th>Naïve</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
<th>60%</th>
<th>70%</th>
<th>80%</th>
<th>90%</th>
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</tr>
</thead>
<tbody>
<tr>
<td>ME</td>
<td></td>
<td>−178.32</td>
<td>−163.33</td>
<td>−148.34</td>
<td>−133.35</td>
<td>−118.36</td>
<td>−103.37</td>
<td>−88.38</td>
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<tr>
<td>RAE</td>
<td>1.00</td>
<td>0.93</td>
<td>0.87</td>
<td>0.80</td>
<td>0.74</td>
<td>0.70</td>
<td>0.68</td>
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<tr>
<td>MSE</td>
<td></td>
<td>97.114.84</td>
<td>87.054.64</td>
<td>78.756.63</td>
<td>72.220.82</td>
<td>67.447.19</td>
<td>64.435.75</td>
<td>23.019.66</td>
<td>63.699.45</td>
<td>65.974.58</td>
<td>70.011.91</td>
<td>75.811.42</td>
</tr>
</tbody>
</table>

**Table 12**
Forecasting 2–3 years ahead: naïve + drift, branded drugs.

<table>
<thead>
<tr>
<th>Benchmark</th>
<th>Drift</th>
<th>Naïve</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
<th>60%</th>
<th>70%</th>
<th>80%</th>
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<tbody>
<tr>
<td>ME</td>
<td></td>
<td>−179.74</td>
<td>−170.06</td>
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<td>−150.70</td>
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<td>−131.34</td>
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<td>−102.30</td>
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</tr>
<tr>
<td>RAE</td>
<td>1.81</td>
<td>1.73</td>
<td>1.66</td>
<td>1.59</td>
<td>1.53</td>
<td>1.48</td>
<td>1.43</td>
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<td>1.35</td>
<td>1.32</td>
<td>1.29</td>
<td></td>
</tr>
<tr>
<td>MSE</td>
<td></td>
<td>389.146.11</td>
<td>366.131.46</td>
<td>345.056.91</td>
<td>325.922.46</td>
<td>308.728.10</td>
<td>293.473.84</td>
<td>280.159.67</td>
<td>268.785.59</td>
<td>259.351.62</td>
<td>251.857.73</td>
<td>246.303.94</td>
</tr>
</tbody>
</table>

**Table 13**
Forecasting 2–3 years ahead: naïve + drift, generic drugs.

<table>
<thead>
<tr>
<th>Benchmark</th>
<th>Drift</th>
<th>Naïve</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
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<th>80%</th>
<th>90%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ME</td>
<td></td>
<td>−354.96</td>
<td>−338.63</td>
<td>−322.31</td>
<td>−305.99</td>
<td>−289.66</td>
<td>−273.34</td>
<td>−257.02</td>
<td>−240.69</td>
<td>−224.37</td>
<td>−208.05</td>
<td>−191.72</td>
</tr>
<tr>
<td>RAE</td>
<td>1.68</td>
<td>1.61</td>
<td>1.53</td>
<td>1.46</td>
<td>1.38</td>
<td>1.31</td>
<td>1.24</td>
<td>1.18</td>
<td>1.11</td>
<td>1.05</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>MSE</td>
<td></td>
<td>234.023.33</td>
<td>213.011.11</td>
<td>193.336.09</td>
<td>174.998.27</td>
<td>157.997.64</td>
<td>142.334.20</td>
<td>128.007.97</td>
<td>115.018.93</td>
<td>103.367.09</td>
<td>93.052.44</td>
<td>84.074.99</td>
</tr>
</tbody>
</table>

**Fig. 4.** Level of drift for forecasting horizon 1 (in terms of RAEs) for branded and generic pharmaceutical life cycles.

**Fig. 5.** Level of drift for forecasting 2–3 years ahead (in terms of RAEs) for branded and generic pharmaceutical life cycles.
Table 14
Forecasting 4–5 years ahead: naïve + drift, branded drugs.

<table>
<thead>
<tr>
<th>Benchmark Drift Naïve</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
<th>60%</th>
<th>70%</th>
<th>80%</th>
<th>90%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ME</td>
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<td>−281.34</td>
<td>−272.18</td>
<td>−263.02</td>
<td>−253.85</td>
<td>−244.69</td>
<td>−235.53</td>
<td>−226.37</td>
<td>−217.21</td>
<td>−208.05</td>
</tr>
<tr>
<td>RAE</td>
<td>2.51</td>
<td>2.43</td>
<td>2.35</td>
<td>2.28</td>
<td>2.20</td>
<td>2.13</td>
<td>2.07</td>
<td>2.00</td>
<td>1.95</td>
<td>1.89</td>
</tr>
<tr>
<td>MSE</td>
<td>607 225.93</td>
<td>581 862.49</td>
<td>557 758.49</td>
<td>534 913.94</td>
<td>513 328.82</td>
<td>493 003.15</td>
<td>473 936.92</td>
<td>456 130.14</td>
<td>439 582.79</td>
<td>424 294.89</td>
</tr>
</tbody>
</table>

Table 15
Forecasting 4–5 years ahead: naïve + drift, generic drugs.

<table>
<thead>
<tr>
<th>Benchmark Drift Naïve</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
<th>60%</th>
<th>70%</th>
<th>80%</th>
<th>90%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ME</td>
<td>−465.52</td>
<td>−449.67</td>
<td>−433.83</td>
<td>−417.98</td>
<td>−402.13</td>
<td>−386.29</td>
<td>−370.44</td>
<td>−354.59</td>
<td>−338.75</td>
<td>−322.90</td>
</tr>
<tr>
<td>RAE</td>
<td>2.24</td>
<td>2.17</td>
<td>2.10</td>
<td>2.04</td>
<td>1.97</td>
<td>1.90</td>
<td>1.84</td>
<td>1.77</td>
<td>1.70</td>
<td>1.64</td>
</tr>
<tr>
<td>MSE</td>
<td>371 033.22</td>
<td>349 229.60</td>
<td>328 294.83</td>
<td>308 228.90</td>
<td>289 031.82</td>
<td>270 703.58</td>
<td>253 244.19</td>
<td>236 653.64</td>
<td>220 931.94</td>
<td>206 079.09</td>
</tr>
</tbody>
</table>

Fig. 6. Level of drift for forecasting 4–5 years ahead (in terms of RAEs) for branded and generic pharmaceutical life cycles.

8. More thoughts, conclusions and further research

This paper has aspired to provide the first empirical forecasting competition of pharmaceutical time series (to the best of our knowledge), especially given the separate treatment of the branded and generic drug series.

In this context, diffusion models would seem a natural choice, such as the RPDM previously used, though only in a limited evaluation, by Rao and Yamada (1988). The results of the comparisons between RPDM and the Bass model show that the pharmaceutical life cycle can be modelled effectively using both models, but that the performance is rather mediocre when it comes to out-of-sample forecasting.

One could argue that this latter result is to be expected, to some extent, as the Bass model is aimed at the modelling of adoptions, not sales or related measures. In a situation where each new adopter buys once, the number of new adopters would equal sales. On the other hand, if each new adopter keeps on purchasing at a fixed rate, one could use the cumulative number of adopters to proxy sales. In the setting studied here, neither situation seems to apply: most physicians prescribe more than once, while the steep decline in brand sales is not consistent with a fixed repeat purchase rate combined with the cumulative number of adopters. The RPDM model does not alleviate the problems described above, since it does not allow explicitly for a steep decline after patent expiration.

Thus, there is a need to investigate different avenues for finding more appropriate forecasting models for pharmaceutical data, which brings the discussion back to the holy grail of forecasting: a ‘horses for courses’ approach (Petropoulos et al., 2014).

Branded pharmaceuticals are expected to follow the classical product lifecycle curve (introduction, growth, maturity, decline) until it is interrupted by the patent expiry, at which time alternative products become available on the market, in the form of generics. As such, there is no consensus as to what kind of model might be most appropriate, given that is not known a priori what exact phase of the lifecycle will be prevailing at the time when the patent expires.

The results support this idea, as, on average across the seven series, the most accurate, least biased and least volatile one-year-ahead forecasts are provided by a quite adaptive method: ARIMA, which allows different models to be used for each series (though within the generic Box–Jenkins framework still). For longer horizons of up to five years, the naïve model with various levels of drift does the job.

On the other hand, generic pharmaceuticals are expected to grow rapidly immediately after the patent expiry of the branded alternative, and as such, trended models might have an advantage in this forecasting evaluation. This expectation is met in our evaluation, as a trended model, Holt’s exponential smoothing model, provides the best one-year-ahead forecasts across the three dimensions of accuracy, bias and uncertainty. Yet again, for longer horizons of up to five years ahead, the naïve model with various levels of drift does the job.

Overall, given the nature of both the branded and generic drug time series, and the steep growth and decline phases of the branded ones, together with the steep increase of the newly introduced generic ones, it is not surprising that a certain level of drift can always improve the forecasting performance for the longer forecasting horizons; however, it is not always the same level of drift, and as such, one size still does not fit all!

Further investigation is needed in order to determine whether pharmaceutical drugs that exhibit other life-cycle formats can also be forecasted effectively using similar methods and models. The branded and generic crossover points of many drugs can vary from those in the current study. The drugs studied here tend to adhere to the general pattern of an increase in branded sales, followed by a
decline, then a rise in generic sales, followed by an eventual decline. However, not all drugs exhibit this pattern.

A comparison of the different stages of the pharmaceutical life cycles may also be an appropriate extension to this study, as the RPDM model exhibited a higher level of forecasting accuracy when considering only the maturity stage of the life cycle, compared to the period of the drug’s decline. Another suggestion is to consider 10-year-ahead forecasts. This might not be viable for the UK market, but would be more appealing for the global market.

Another issue that would be worth investigating in future studies relates to the pharmaceutical company’s profits. It would be interesting to consider what happens to the general sales pattern in the case of drugs that do not need prescriptions and can be bought freely off the shelf, and what would be the level of revenue generated given the overall sales volume. This might shed additional light on the drug’s life cycle if and only if the prescribed and unprescribed sales of the branded drug are much higher than the prescribed and unprescribed sales of the generic drug.

Acknowledgments

We would like to thank the Handling Editor Professor Paul Goodwin, the Associate Editor and three anonymous reviewers for their comments, which helped us to revise and improve this manuscript substantially. The third reviewer in particular provided us with very useful arguments and an insightful line of thought on the shortfalls of diffusion models for coping with our empirical data.

Appendix. Diffusion models

A.1. The Bass model

The two main assumptions of the Bass diffusion model (Bass, 1969) are as follows.

(a) During a product’s life cycle, there will be m initial purchases of that product. When replacement purchases are made, sales combine the initial and replacement purchases of that product. When replacement purchases are made, sales combine the initial and replacement purchases of that product, which provides the main equation for the Bass diffusion model.

(b) The likelihood of an initial purchase at time $T$, given that no purchase has yet been made, is as follows:

$$\frac{F(T)}{[1 - F(T)]} = P(T) = p + \frac{q}{mY(T)} = p + qF(T).$$

(A.1)

where $f(t)$ is the likelihood of purchase at $T$ and

$$F(T) = \int_0^T f(t)dt.$$  \hspace{1cm} (A.2)

Therefore, sales $S(t)$ is the rate of change of the installed base (i.e., the rate of adoption) $f(t)$, multiplied by the ultimate market potential $m$:

$$S(t) = mf(t)$$

$$S(t) = m \left(\frac{(p + q)^2}{p} + \frac{e^{-p+q}t}{1 + \frac{p}{e^{p+q}t}}\right)^2.$$ \hspace{1cm} (A.3)

The time of peak sales $t^*$ is

$$t^* = \frac{\ln q - \ln p}{p + q}.$$ \hspace{1cm} (A.4)

In these equations, $f(t)$ is the rate of change based on the initial base fraction; $F(t)$ is the installed base fraction; $p$ is the coefficient of innovation, including the coefficients of innovation, advertising effects and external influences; and $q$ is the coefficient of imitation, including word-of-mouth effects and internal influences (Bass, 1969).

The behavioural justifications behind these two assumptions are as follows.

I. Initial purchases of a product are generally made by both imitators and innovators. The underlying distinction between innovators and imitators is the way in which the purchaser comes to be influenced to purchase the product. Innovators are not influenced by the numbers of people in their social groups who have purchased the product, while imitators are. Innovators are more important when the product is first launched, but this importance decreases steadily over time.

II. For successful new products, the coefficient of imitators is generally greater than the coefficient of innovators. Sales reach their maximum value when the total sales are approximately one-half of $m$. When $t$ is measured in years, the typical values of $p$ and $q$ are as follows:

a. On average, $p$ is 0.03; more often than not, it is 0.01.

b. On average, $q$ is 0.38; more often than not, it falls between 0.3 and 0.5.

This also demonstrates that on average, the coefficient of imitators is greater than the coefficient of innovators.

A.2. The repeat purchase diffusion model (RPDM)

This model is based on the assumption that there is a linear relationship between the number of prescribers and the number of prescriptions written (Lilien et al., 1981). The model can be operationalized as follows:

$$Y(t) = Y(t-1) + f(t)[a_1d(t-1) - a_2d^2(t-1)]$$

$$\times [N - Y(t-1)] + a_3[Y(t-1) - Y(t-2)]$$

$$> [N - Y(t-1)] - a_4d(t-1)Y(t-1)$$

(A.5)

where

$Y(t)$ is the number of prescriptions written at time $t$;

$d(t)$ is the firm’s detailing effort at time $t$;

$\hat{d}(t)$ is the competitive detailing effort at time $t$;

$f(t)$ is the decay rate; i.e., early prescribers tend to prescribe the most and $f(t)$ declines as $t$ increases;

$N$ is the total potential number of prescribers multiplied by the average prescription rate; and

$A_i, i = 1, \ldots, 4$ are constants.
This model can be updated as new sales data for the drugs being researched become available, and was deemed appropriate, given the research objectives (Rao & Yamada, 1988). It is explained as follows:

\[
Y' = (Y(3), Y(4), \ldots, Y(T)) \text{ given } Y(1) \text{ and } Y(2) : \\
(Y(T) - Y(t - 1)) = [\alpha_1 d(t - 1) - \alpha_2 d^2(t - 1)] \cdot [N - Y(t - 1)] + \alpha_3 Y(t - 1) - Y(t - 2) \cdot [N - Y(t - 1)] - \alpha_4 d(t - 1) \cdot Y(t - 1) + u(t) \\
t = 3, 4, \ldots, T. \tag{A.6}
\]

In Rao and Yamada’s (1988) version, \( f(t) \) is set to one and the parameters \( N \) and \( \alpha_1, \alpha_2, \alpha_3, \alpha_4 \) are unknown; \( u(t) \) is included as a disturbance term. It is assumed that the disturbances are all independently and normally distributed with a zero mean and a common variance.

**References**


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