FORECASTING PHARMACEUTICAL LIFE CYCLES: A CASE STUDY OF HOW PHARMACEUTICALS ARE PRESCRIBED IN THE NHS IN THE UK

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ABSTRACT

This paper is a case study on how pharmaceuticals are prescribed on the NHS in the UK. The paper discusses the modelling and forecasting of pharmaceutical life cycles, specifically around after the time of patent expiry. In this situation one of two things can occur the branded pharmaceutical sales remain high while the generic are low, the alternative is when the branded drug declines and stays low while the sales of the generic drug are high.. Understanding the patterns of brand decline (and the associated generic growth) is increasingly important because in a market currently worth over £7bn in the UK, the number of new 'blockbuster' drugs continues to decline. As a result pharmaceutical companies make efforts to extend the commercial life of their brands, and the ability to forecast is important in this regard. Second, this paper provides insights for effective governance because the use of a branded drug (when a generic is available) results in wasted resources. Five methods are used to model and forecast these life cycles: Bass Diffusion, Repeat Purchase Diffusion Model (RPDM), Naïve, Exponential Smoothing and Moving Averages. The empirical evidence presented here suggests that the use of the Naïve model incorporating drift provided the most accurate and robust method of modelling both types of prescribing, with the more advanced models being less accurate.

Keywords*:* Forecasting; Diffusion Models; Pharmaceutical Lifecycles; Branded drugs; Generic drugs.

INTRODUCTION

Over the past three decades, marketers have been encouraged from both within and outside the Marketing profession to become more socially relevant by broadening their viewpoints and extending their research into areas not traditionally associated with marketing (Churchill, 1999). Andreasen (1978) has reported that marketing professionals and academics alike should strive to become more socially aware. Secondly, Armstrong, Brodie, and McIntyre (1987) found that forecasting was included in more than 98% of companies' marketing plans and argued that forecasting should be taught in business schools. Despite the importance of forecasting, managers do not appear to use the technique effectively. Khan's (2002) survey of marketing managers found self-reported forecast accuracy of just 47% for new category entrants, and only 40% for products that were new to the world.

This paper describes an approach for forecasting pharmaceutical life cycles. The model specifically focuses on the life cycle of branded and generic drugs in which the sales of branded drugs decline and prescriptions for generic alternatives increase or vice versa. In this arena, successful forecasting enables marketing managers to implement strategies that allow them to advantageously modify a product's life, and we therefore demonstrate an application of practical use to managers.

Wind, Mahajan, and Cardozo (1981) reviewed the many models used to predict new product sales, but they were limited to consumer goods and did not address pharmaceuticals. Lilien, Rao, and Kalish (1981) proposed a model that specifically considers pharmaceutical drugs. Rao and Yamada (1988) made a number of changes to this model and tested its predictability again using pharmaceutical data. Rao and Yamada (1988) posited that like other methods used to predict consumer goods, the traditional Bass (1969) model cannot be applied to pharmaceutical products. The application and predictability of diffusion models have received limited empirical testing with mixed results; however, as shown by Nikolopoulos et al (2007) complicated forecasting techniques do not always generate the most accurate results, and in some situations, simpler approaches can be more effective. The OR forecasting paradigm allows competition between different techniques to determine the best solution. Nikolopoulos *et al*. (2007) used this approach in the marketing field and Bamiatzi, Bozos, and Nikolopoulos (2010) conducted research using financial data. In this study, the OR forecasting paradigm is applied to the pharmaceutical industry, highlighting the changing nature of prescription drugs when generic alternatives enter a market previously dominated by branded versions of the same drug.

The study contributes to the existing body of literature by applying forecasting methods to the life cycles of pharmaceutical drugs. 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 literature by applying forecasting techniques to the data, with a specific focus on the life cycles of branded drugs that decline as soon as generic alternatives enter the marketplace.

This research models and forecasts pharmaceutical life cycles using the Bass Diffusion model (1969), the Repeat Purchase Diffusion Model proposed by Lilien *et al*. (1981) and the adaptations proposed by Rao and Yamada (1988), and benchmark models including the Moving Average, Exponential Smoothing, and Naïve Models. As this is a working paper, the results gathered will be available at the conference.

MATHEMATICAL MODELS

Diffusion Model literature

Mahajan, Muller, and Bass (1990) demonstrate that Diffusion Models have been employed in several areas of marketing, including consumer behaviour, marketing management and marketing science research. In the field of marketing science, researchers have contributed to the diffusion theory by developing forecasting techniques associated with Diffusion Models.

Bass Diffusion Model

Diffusion Models were initially developed by Frank Bass (1969). The Bass Diffusion Model describes how new products are adopted as an interaction between users and potential users. This theory of adoption and diffusion was first developed conceptually by Rogers (1962.

Individuals can decide to adopt a product independently of other influences. These people are generally known as the innovators of a product. Bass (1969) highlights five classes of adopters: (1) Innovators; (2) Early Adopters; (3) Early Majority; (4) Late Majority and (5) Laggards. Rogers (1962) describes groups (2) through to (5) as imitators. Imitators make decisions based on information gained from other individuals in the same social group, such as friends or family. Rogers (1962) describes innovators as daring and notes that they have a tendency to interact with other innovators. These consumers are not influenced by the timing of purchases made by other members of their social group, and their pressure to adopt a product does not increase as the number of people adopting the product grows. The pressure of adoption is only felt by consumers in groups (2) through group (5), not by group (1) (Rogers, 1962).

The two main assumptions of the Bass Diffusion Model (1969) are as follows:

a) During the life of a product, there will be *m* initial purchases of that product. When replacement purchases are made, sales combine both the replacement and the initial purchases leading to the second assumption, 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:

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

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

$$F(T) = \int_0^T f(t)dt \quad (2)$$

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*:

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

$$S\,(t) = m\frac{(p+q)^2}{p}\frac{e^{-(p+q)t}}{(1+\frac{q}{p}e^{-(p+q)t})^2} \quad (3)$$

The time of peak sales *t** is

$$t^* = \frac{\ln q - \ln p}{p+q} \quad (4)$$

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 the coefficient of imitation, word-of-mouth effects, and internal influences (Bass, 1969).

The behavioural justifications behind these two assumptions are outlined here:

I. Initial purchases of any product are generally made by both imitators and innovators. The underlying distinction between the innovator and the imitator is how the purchaser comes to be influenced to purchase the product. Innovators are not influenced by the number of people in their social groups that have purchased the product, while imitators are. Innovators have greater importance 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 0.3-0.5. This also demonstrates that on average, the coefficient of imitators is greater than the coefficient of innovators.

The regression analysis and model performance must then be analysed, allowing long-range forecasts to be produced. The model developed by Bass (1969) implies exponential growth followed by a peak and then a decline. The model provides good predictions for the products to which it was applied and, according to Bass, it is useful in providing a basic rationale for long-range forecasting (Bass, 1969).

The Bass Model has been influential in both marketing and management science, and the 1969 paper is one of the most frequently cited in the management science literature. There have also been many extensions of the original Bass Diffusion Model; the model used in this paper is Lilien et al's. (1981) Repeat Purchase Diffusion Model, which has also been used to model the sales of ethical drugs.

Repeat Purchase Diffusion Model (RPDM)

Lilien et al. (1981) proposed a three-step methodology to predict the sales of new drugs when they enter the market when little or no prior data are available. The steps Lilien et al. (1981) propose are as follows:

1. To use 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. Because GPs have a tendency to repeat-prescribe new drugs, the model represents a repeat purchase diffusion process.
2. A model is then produced to forecast the sales of the new drug prior to entering the market. Lilien et al. (1981) have suggested that this model is parameterised on a drug that the management deem "similar" to the new drug being introduced to the market.
3. The final step aims to use early sales data gathered to update the model to make it more accurate using Bayesian regression. As Rao and Yamada (1988) note, this approach is valid when no prior data are available, but if sales data are available, the RPDM can be used accurately to produce one-step-ahead forecasts.

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

$$Y(t) = Y(t-1) + f(t)[a_1 d(t-1) - a_2 d^2(t-1)] \times [N - Y(t-1)] + a_3[Y(t-1) - Y(t-2)] \times [N - Y(t-1)] - a_4 \bar{d}(t-1) Y(t-1) \quad (5)$$

Where

Y*(t*) is the number of prescriptions written at time *t*;
d(t) is the firm's detailing effort at time *t*;
$\bar{d}(t)$ 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)* will decline as *t* increases;
N is the total potential number of prescribers multiplied by the average prescription rate;
A_i $i = 1,\ldots 4$ are constants.

Rao and Yamada (1988) show how the Lilien *et al* (1981) model could be updated when new sales data for the drugs being researched become available, and given the research objectives and the data available, their model was deemed appropriate. The Rao and Yamada (1988) model is as follows:

$$Y' = \big(Y(3), Y(4), \ldots, Y(T)\big) given\ Y(1) and\ Y(2):$$

$$Y(t) - Y(t-1) = [a_1 d(t-1) - a_2 d^2(t-1)] \cdot [N - Y(t-1)] + a_3[Y(t-1) - Y(t-2)] \cdot [N - Y(t-1)] - a_4 \bar{d}(t-1) \cdot Y(t-1) + u(t)$$

$t = 3,4,\ldots,T,$ (6)

Rao and Yamada (1988) found that the Lilien et al. (1981) model provides the best fit for pharmaceutical data when the decay factor is removed. For this reason, in the Rao and Yamada (1988) version, *f(t)* is set to 1. In addition, in the Rao and Yamada (1988) version, the parameters *N* and a_1, a_2, a_3, a_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. Consistent with the OR paradigm, a number of other basic benchmark models are also used, including the Naïve Model, Exponential Smoothing and Moving Average techniques.

THE DATA

The time series associated with the current research are taken from a much larger database that contains 2,570,000 prescription records from 1,506 GPs all over the United Kingdom. The time series run from 1987-2008. As pharmaceuticals can be prescribed in two forms branded and generic, it allows the research to use three different data sets. They are branded then generic, high branded and low generic and high generic and low branded.
The branded then generic category is where the branded drug is prescribed first then due to generic entry declines while there is an increased number of prescriptions written for then generic drug. Table 1 show the data used in this sample.

TABLE 1
Basic Information of the Branded then Generic Prescription Sample

Branded Drug	Generic Drug	Therapeutic Class	CAS Number	Patent Number	Patentee	Year of Patent Granted	Year of Patent Expiration	Supplementary Protection Certificate (SPC)	Total Number of Prescriptions (Rx) between 1987 and 2008	Sources
Cardura	Doxazosin	Hypertension	74191-85-8	US4188390	Pfizer	1980	2000	NA	17990	Merck Index, Espacenet
Defanac	Diclofenac	Anti-inflammatory	13307-86-5	GB 1132318	Geigy	1968	1983	NA	167190	Espacenet, Patent Archives
Gamanil	Lofepramine	Anti-depressant	23047-25-8	GB 1177525	Leo	1970	1984	NA	17767	Espacenet, Patent Archives
Innovace	Enalapril	Angiotensin Converting Enzyme (ACE)	7475847-73-3	EP12401	Merck and Co	1983	1995	NA	16410	Espacenet
Losec	Omeprazole	Acid Reflux	73590-58-6	EP5129	Haessle AB	1979	1999	2005	47751	USPTO, Espacenet, MPA services
Lustral	Sertraline	Anti-depressant	79617-96-2	EP 30081	Pfizer	1981	2000	2005	13201	MPA Services, Espacenet
Mobic	Meloxicam	Analgesic/Anti-inflammatory	71125-38-7	EP0002482	Boehringer Ingelheim	1979	1998	2003	13276	MPA Services, Boehringer Ingelheim, Espacenet
Naprosyn	Naproxen	Anti-inflammatory	22204-53-1	GB 1291386	Syntex	1972	1988	NA	65817	MPA Services, Espacenet
Prothiaden	Dosulepin**	Anti-depressant	113-53-1	GB 1013574	Spofa	1965	1978	NA	45982	Espacenet, MPA Sernices
Prozac	Fluoxetine	Anti-depressant	54910-89-3	GB1493961	Lilly and Co	1977	1995	2000	42813	Espacenet, MPA services, Patent Archives
Serevent	Salmeterol	Asthma	89365-50-4	GB2176476	Glaxo	1987	2004	NA	10995	Merck Index, Espacenet
Seroxat	Paroxetine	Anti-depressant	61869-08-7	GB1422263	Ferrosan	1976	1994	1999	30448	Espacenet, MPA services, Patent Archives
Tagamet	Cimetidine	Acid reflux	51481-61-9	GB1338169	SmithKline & French	1971	1992	NA	41033	Espacenet, Patent Archives, Derwent Index, MPA Services
Tenormin	Atenolol	Hypertension	29122-68-7	GB 1285038	ICI	1972	1990	NA	54297	MPA Services, Espacenet, Patent Archives
Tritace	Ramipril	Hypertension	87333-19-5	EP79022	Hoechst AG	1983	2002	2004	27898	USPTO, Espacenet, MPA services
Zantac	Ranitidine	Peptic Ulcer Disease	66357-35-5	GB 1565966	Allen & Hanburys	1980	1997	NA	46673	MPA Services, Espacenet, Patent Archives
Zestril	Lisinopril	Angiotensin Converting Enzyme (ACE)	83915-83-7	EP12401	Merck & Co	1980	1999	2002	30642	Merck Index, Espacenet, MPA Services
Zocor	Simvastatin	Controls Hyperlipidemia	79902-63-9	EP33538	Merck and Co	1981	2001	NA	34216	Espacenet, MPA services
Zoton	Lansoprazole	Proton Pump Inhibitor	103577-45-3	EP174726	Nippon Chemipar	1986	2001(non-payment of fees)	NA	37264	USPTO, Espacenet

The high branded and low generic data set refers to the pharmaceuticals that are no longer protected by a patent and both the branded and generic drug can be prescribed at the same time and the number of branded prescriptions written is higher than the number of generic prescriptions written. Table 2 shows the data used in this sample.

TABLE 2
Basic Information of the High Branded and Low Generic Prescription Sample

Branded Drug	Generic Drug	Therapeutic Class	CAS Number	Patent Number	Patentee	Year of Patent Granted	Year of Patent Expiration	Supplementary Protection Certificate (SPC)	Total Number of Prescriptions (Rx) between 1987 and 2008	Sources
Adalat	Nifedipine	Hypertension	21829-25-4	GB1173862	Farbenfabriken Bayer AG	1969	1988	NA	26905	Espacenet, Merck Index, MPA services, Patent Archive
Becotide	Beclomethasone	Asthma	08/09/5534	GB912378	Merck and co	1962	1982	NA	43184	Patent Archives, Espacenet
Feldene	Piroxicam	Anti-inflammatory	36322-90-4	GB1257180	Pfizer	1971	1989	NA	30313	Espacenet, patent.ipexl.com/GB/GB1257180.html
Frumil	Furosemide/ Amiloride HCL (co-amilofruse)	Water Retention	54-31-9	GB936417 (fru)	Hoechst AG	1963	1983	NA	13889	Espacenet, Patent Archives
			2016-88-8	GB1066855 (am)	Merck and co	1967	1987			
GNT	Glyceryl trinitrate	Angina	55-63-0	NA	NA	Pre 1900	NA	NA	23520	Walter Sneader, Drug Discovery: A History. John Wiley & Sons (2005)
Maalox	Aluminium hydroxide	Acid Reflux	21645-51-2	NA	NA	NA	NA	NA	17916	Patent Archives
Maxolon	Metoclopramide	Anti-emtic/ gastroprokinetic (Nausea/Vomiting)	364-62-5	GB 994023	Ile de France	1965	1978	NA	13126	Patent Archives, Espacenet
Oruvail	Ketoprofen	Anti-inflammatory	22071-15-4	GB1164585	Rhone Poulec SA	1969	1989	NA	13963	Patent Archives, Espacenet
Prempak	Oestrogens + Progesterone (Norgestrel)	Hormone Replacement Therapy	82115-62-6	US2565115	Squibb & Son	1951	Expired	NA	51598	Merck Index, Espacenet
			57-83-0	US2379832	Schering Corp	1945	Expired	NA		
Ponstan	Mefenamic acid	Anti-inflammatory	67861-88-7	GB989951	Parke Davis and Co	1965	1985	NA	17017	Espacenet, Patent Archives
Traxam	Felbinac	Anti-inflammatory	5728-52-9	FR798941	IG Farbenindustrie AG	1936	Expired	NA	14881	Merck Index, Espacenet
Tryptizol	Amitriptyline	Anti-depressant	50-48-6	GB858187	Hoffman and La	1961	Expired	NA	24354	Patent Archives, Espacenet
Ventolin	Salbutamol	Asthma	18559-94-9	GB1200886	Allen & Hanbury's	1970	1987	NA	54961	Espacenet, Merck Index

Finally, the high generic low branded data set refers to pharmaceuticals that are also no longer patent protected and this is where the number of generic drug prescriptions is higher than the number of branded drug prescriptions. The basic information for this data set can be seen in Table 3.

TABLE 3
Basic Information of the High Generic and Low Branded Prescription Sample

Branded Drug	Generic Drug	Therapeutic Class	CAS Number	Patent Number	Patentee	Year of Patent Granted	Year of Patent Expiration	Supplementary Protection Certificate (SPC)	Total Number of Prescriptions (Rx) between 1987 and 2008	Sources
Aprinox	Bendroflumethiazide	Hypertension	78-48-3	GB 863474	F. Lund and W. O. Godtfredsen	1961	Expired	NA	42441	Patent Archives, Espacenet
Brufen	Ibuprofen	Anti-inflammatory	15687-27-1	GB971700	Boots Pure Drug Co	1961	Expired	NA	203300	Patent Archives, Espacenet
Deltastab	Prednisolone	Anti-inflammatory	50-24-8	US2837464	Schering Corp	1958	Expired	NA	29144	Espacenet, Patent Archives
DHC	Dihydrocodeine	Severe Pain Relief	125-28-0	NA	NA	Introduced 1911	NA	NA	13592	Merck Index
Flexin	Indocid	Analgesic/Anti-inflammatory	53-86-1	GB 997638	Merck and Co	1965	1978	NA	21409	Patent Archives, Espacenet
Inderal	Propranolol	Hypertension	525-66-6	GB 994918	ICI	1965	1979	NA	11778	Espacenet, Patent Archives
Lasix	Furosemide	Loop Diuretic – water retention	54-31-9	GB936417	Hoechst AG	1963	1983	NA	22037	Espacenet, Patent Archives
Panadol	Paracetamol	Analgesic	103-90-2	US2998450	Warner Lambert	1961	Expired	NA	24722	Espacenet
Zydol	Tramadol	Analgesic	27203-92-5	GB997399	Chem Gruenenthal GMBH	1964	1984	NA	14306	Patent Archives, Espacenet

RESULTS

As this is a working paper the results will be provided during the conference.

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