



Swansea University
Prifysgol Abertawe



Cronfa - Swansea University Open Access Repository

This is an author produced version of a paper published in:

Cronfa URL for this paper:

<http://cronfa.swan.ac.uk/Record/cronfa43655>

Conference contribution :

Buxton, S., Nikolopoulos, K., Khammash, M. & Stern, P. (2014). *Forecasting Pharmaceutical Life Cycles*.

This item is brought to you by Swansea University. Any person downloading material is agreeing to abide by the terms of the repository licence. Copies of full text items may be used or reproduced in any format or medium, without prior permission for personal research or study, educational or non-commercial purposes only. The copyright for any work remains with the original author unless otherwise specified. The full-text must not be sold in any format or medium without the formal permission of the copyright holder.

Permission for multiple reproductions should be obtained from the original author.

Authors are personally responsible for adhering to copyright and publisher restrictions when uploading content to the repository.

<http://www.swansea.ac.uk/library/researchsupport/ris-support/>



Prifysgol Abertawe
Swansea University

US University
of Sussex



UNIVERSITY OF
EXETER

FORECASTING PHARMACEUTICAL LIFE CYCLES

By

Dr Samantha Buxton

Dr Marwan Khammash

Professor Philip Stern

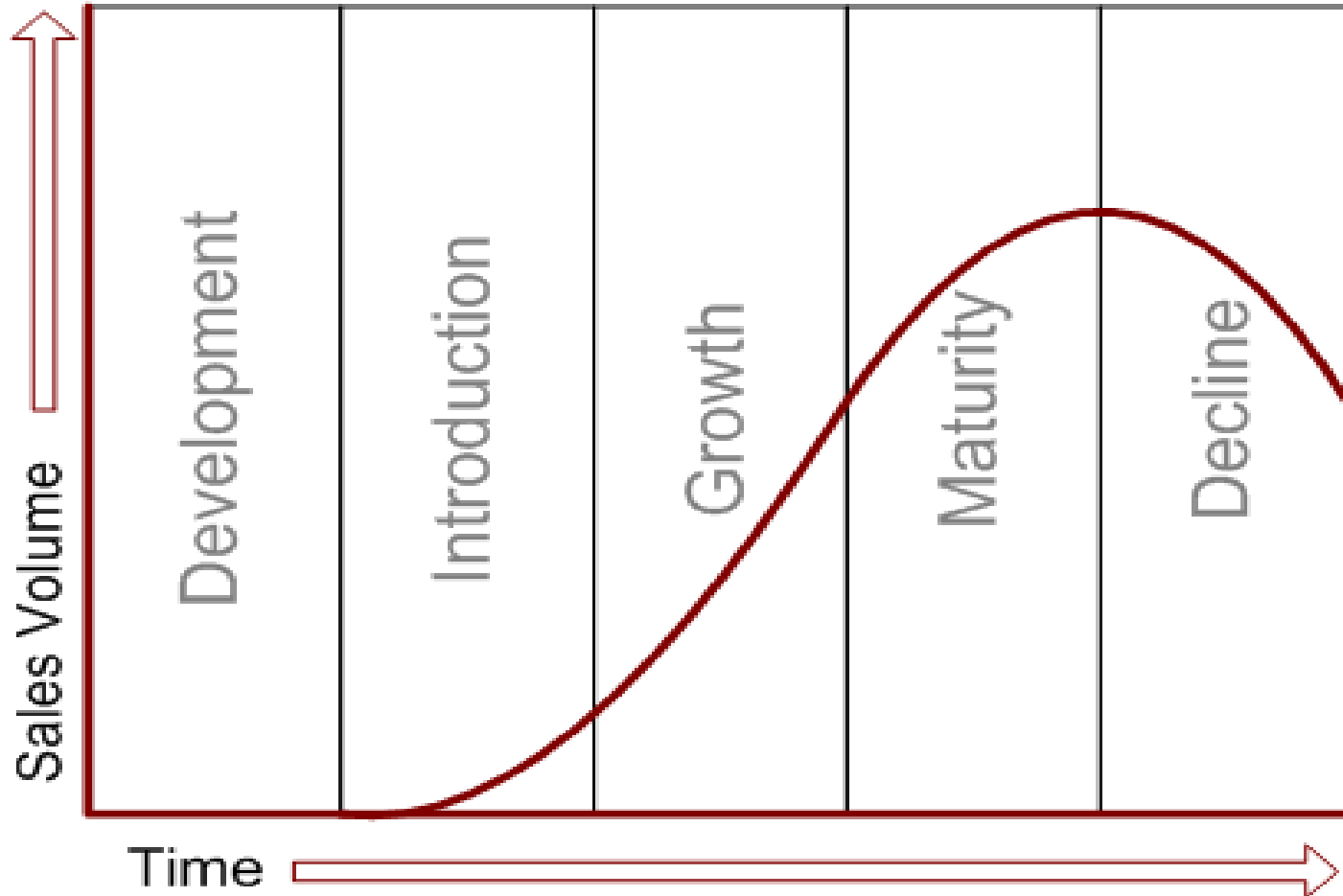
&

Professor Kostas Nikolopoulos

Presentation Structure

- Previous Research – Product Lifecycle
- Pharmaceutical Market
- Research Project – Aims
- Research Project - The Data
- Preliminary Results
- Graph Categories
- Next Steps

Previous Research - Product Life Cycle



Pharmaceutical Market

- Moss (2008) states that research has focused on consumer products and brands disregarding other products and brands such as pharmaceuticals.
- Highly competitive non assembled global industry
- In 2007 the top 10 pharmaceutical companies had a combined sales of just under £150 billion and commanded 45% market share
- 2 of these were UK companies – AstraZeneca and GlaxoSmithKline

Pharmaceutical Market continued

- In 2008 £4 billion was spent on R&D however this was expected to decrease due to the financial climate
- Patent Expiration – Major Problem
- UK patents last for 20 years from application
- 5 year extension can be applied for
- Generics enter the market
- NHS and other health/government organisations always looking at ways to curb the rising cost of healthcare

Pharmaceutical Market continued

- **A branded drug** is one made by a specific pharmaceutical company and is therefore given a name. The generic is the key compound that makes up the drug. In some cases the company can market both the branded and generic to appeal to a wider audience. An example is Sertraline.
- Brand name – Lustral by Pfizer
- Generic name – Sertraline.

Research project - aims

- Aims

1. To classify the patterns that are exhibited during the product lifecycle of pharmaceutical drugs
2. Model these patterns
3. Forecast the patterns
4. This will allow us to discover which forecasting methods forecast the lifecycle better depending on the different stages
 1. Introduction
 2. Growth
 3. Maturity
 4. Decline

Research Project – The Data

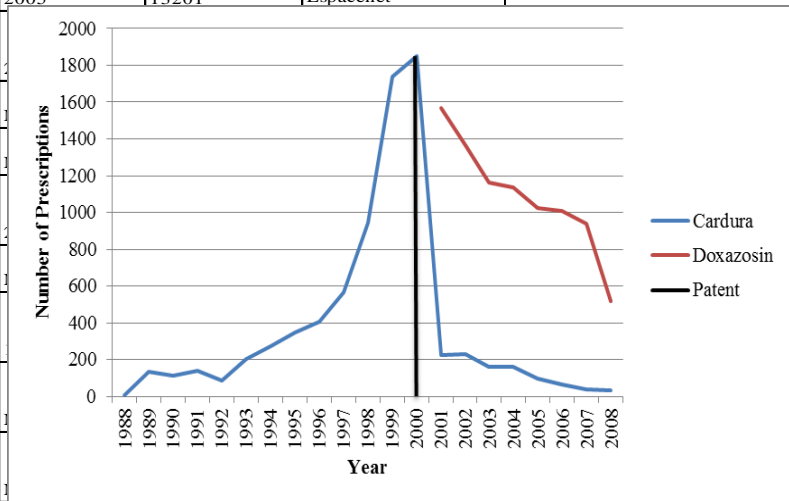
- JIGSAW database
- Established in 1985 by ISIS research for the purposes of academic research
- Data from 1987 -2008
- 2.57 million script records
- Self Report Questionnaires from GP's
- Data is specifically relating to what drugs are prescribed

Pharmaceutical Life Cycle types

- Based on the current research there are three types of pharmaceutical life cycle including both a branded and a generic strand.
- Branded then Generic
- High Branded Low Generic
- High Generic Low Branded

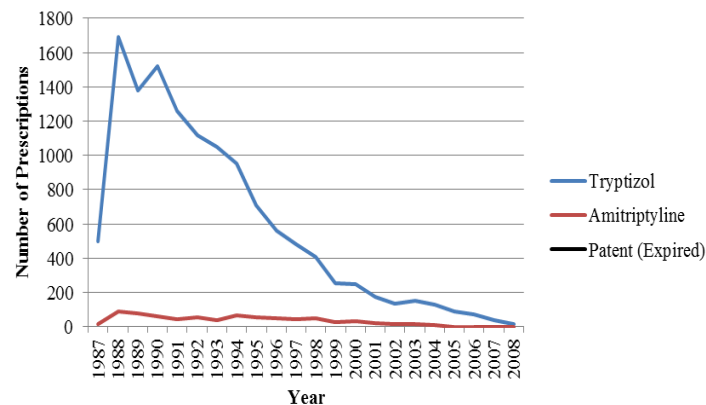
Branded Then Generic

| 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 | Lofepamine | 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 | | | |
| Naprosyn | Naproxen | Anti-inflammatory | 22204-53-1 | GB 1291386 | Syntex | 1972 | 1988 | | | |
| Prothiaden | Dosulepin** | Anti-depressant | 113-53-1 | GB 1013574 | Spofa | 1965 | 1978 | | | |
| Prozac | Fluoxetine | Anti-depressant | 54910-89-3 | GB1493961 | Lilly and Co | 1977 | 1995 | | | |
| Serevent | Salmeterol | Asthma | 89365-50-4 | GB2176476 | Glaxo | 1987 | 2004 | | | |
| Seroxat | Paroxetine | Anti-depressant | 61869-08-7 | GB1422263 | Ferrosan | 1976 | 1994 | | | |
| Tagamet | Cimetidine | Acid reflux | 51481-61-9 | GB1338169 | SmithKline & French | 1971 | 1992 | | | |
| Tenormin | Atenolol | Hypertension | 29122-68-7 | GB 1285038 | ICI | 1972 | 1990 | | | |
| 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 |
| | Lansoprazole | Proton Pump Inhibitor | 103577-45-3 | EP174726 | Nippon Chemipar | 1986 | 2001(non-payment of fees) | NA | 37264 | USPTO, Espacenet |



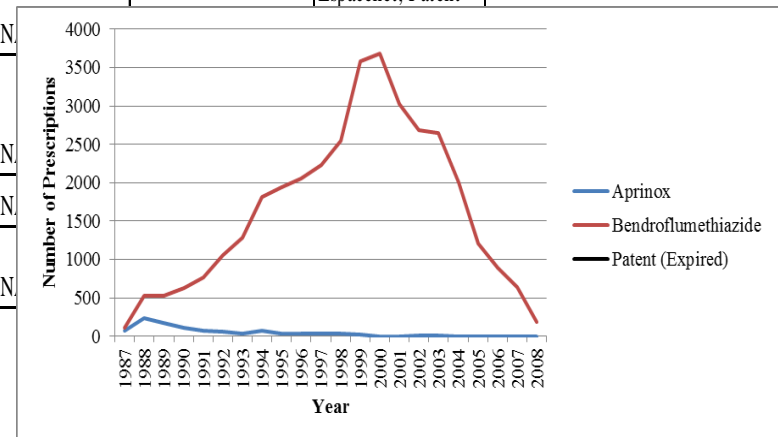
High Branded Low Generic

| 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 Sneider, 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 | | | |
| Oruvail | Ketoprofen | Anti-inflammatory | 22071-15-4 | GB1164585 | Rhone Poulec SA | 1969 | 1989 | | | |
| Prempak | Oestrogens + Progesterone (Norgestrel) | Hormone Replacement Therapy | 82115-62-6 | US2565115 | Squibb & Son | 1951 | Expired | | | |
| | | | 57-83-0 | US2379832 | Schering Corp | 1945 | Expired | | | |
| Ponstan | Mefenamic acid | Anti-inflammatory | 67861-88-7 | GB989951 | Parke Davis and Co | 1965 | 1985 | | | |
| Traxam | Felbinac | Anti-inflammatory | 5728-52-9 | FR798941 | IG Farbenindustrie AG | 1936 | Expired | | | |
| Tryptizol | Amitriptyline | Anti-depressant | 50-48-6 | GB858187 | Hoffman and La | 1961 | Expired | | | |
| Intolin | Salbutamol | Asthma | 18559-94-9 | GB1200886 | Allen & Hanbury's | 1970 | 1987 | | | |



High Generic Low Branded

| 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 | | Espacenet, Patent |
| Lasix | Furosemide | Loop Diuretic - water retention | 54-31-9 | GB936417 | Hoechst AG | 1963 | 1983 | NA | | |
| Panadol | Paracetamol | Analgesic | 103-90-2 | US2998450 | Warner Lambert | 1961 | Expired | NA | | |
| Zydol | Tramadol | Analgesic | 27203-92-5 | GB997399 | Chem Gruenthal GMBH | 1964 | 1984 | NA | | |



Models used in the current research

- Naïve Model
- Moving Average Model
- Single Exponential Smoothing (SES)
- Repeat Purchase Diffusion Model (RPDM)
- Bass Diffusion Model

Results – Branded then Generic

Forecasting Bias, Accuracy and Variance (ME, RAE, MSE) of Branded Drugs

| Branded | Benchmark | EWMA | | Diffusion | |
|------------------|-----------|-----------------------|----------------|------------|------------|
| | Naïve | Exponential Smoothing | Moving Average | Bass | RPDM |
| ME(Bias) | -83.11 | -134.94 | -127.28 | -334.33 | -327.50 |
| RAE(Accuracy) | 1.00 | 1.53 | 1.58 | 4.21 | 4.40 |
| MSE(Uncertainty) | 261458.16 | 371854.37 | 419259.71 | 1092619.18 | 1237103.57 |

Forecasting Bias, Accuracy and Variance (ME, RAE, MSE) of Generic Drugs

| Generic | Benchmark | EWMA | | Diffusion | |
|------------------|-----------|-----------------------|----------------|------------|------------|
| | Naïve | Exponential Smoothing | Moving Average | Bass | RPDM |
| ME(Bias) | -82.12 | -134.75 | -87.81 | -56.58 | -5.21 |
| RAE(Accuracy) | 1.00 | 1.48 | 1.51 | 3.49 | 3.73 |
| MSE(Uncertainty) | 198214.64 | 341448.32 | 404526.49 | 1347374.97 | 1663575.54 |

Results – High Branded Low Generic

Forecasting Bias, Accuracy and Variance (ME, RAE, MSE) of Branded Drugs

| Branded | Benchmark | EWMA | | Diffusion | |
|------------------|-----------|-----------------------|----------------|-----------|-----------|
| | Naïve | Exponential Smoothing | Moving Average | Bass | RPDM |
| ME(Bias) | -58.47 | -123.74 | -122.43 | -365.81 | -309.11 |
| RAE(Accuracy) | 1.00 | 1.85 | 1.78 | 4.81 | 4.80 |
| MSE(Uncertainty) | 155842.58 | 229410.24 | 357958.64 | 599272.17 | 703422.40 |

Forecasting Bias, Accuracy and Variance (ME, RAE, MSE) of Generic Drugs

| Generic | Benchmark | EWMA | | Diffusion | |
|------------------|-----------|-----------------------|----------------|-----------|----------|
| | Naïve | Exponential Smoothing | Moving Average | Bass | RPDM |
| ME(Bias) | -7.48 | -9.38 | -10.15 | -17.05 | -2.23 |
| RAE(Accuracy) | 1.00 | 1.21 | 1.40 | 2.40 | 2.61 |
| MSE(Uncertainty) | 6350.14 | 7285.49 | 13739.63 | 17616.17 | 21974.55 |

Results – High Generic Low Branded

Forecasting Bias, Accuracy and Variance (ME, RAE, MSE) of Branded Drugs

| Branded | Benchmark | EWMA | | Diffusion | |
|------------------|-----------|-----------------------|----------------|-----------|-----------|
| | Naïve | Exponential Smoothing | Moving Average | Bass | RPDM |
| ME(Bias) | -36.79 | -102.30 | -79.08 | -292.06 | -276.98 |
| RAE(Accuracy) | 1.00 | 2.15 | 1.73 | 5.35 | 5.59 |
| MSE(Uncertainty) | 21199.25 | 108823.30 | 46540.67 | 348546.20 | 353349.73 |

Forecasting Bias, Accuracy and Variance (ME, RAE, MSE) of Generic Drugs

| Generic | Benchmark | EWMA | | Diffusion | |
|------------------|-----------|-----------------------|----------------|------------|------------|
| | Naïve | Exponential Smoothing | Moving Average | Bass | RPDM |
| ME(Bias) | -50.81 | -51.68 | -68.75 | -26.79 | 105.53 |
| RAE(Accuracy) | 1.00 | 1.23 | 1.53 | 2.59 | 2.86 |
| MSE(Uncertainty) | 190881.37 | 206286.76 | 509913.82 | 1300270.10 | 1700203.04 |

Discussion – Branded then Generic

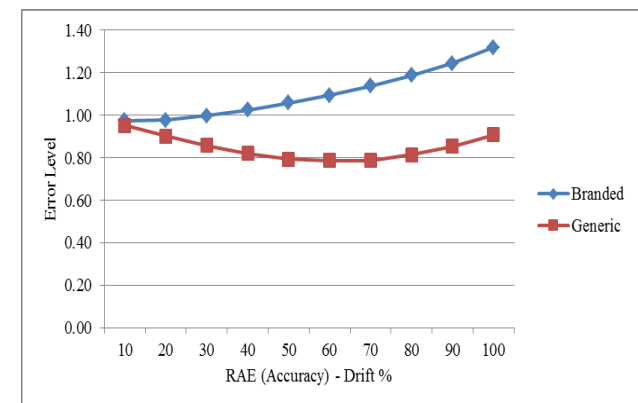
Naïve + Drift Errors of Branded Drugs for the BTG Category

| Branded | Benchmark | Drift | | | | | | | | | |
|------------------|-----------|-----------------|------------------|-----------------|-----------------|-----------------|-----------------|------------------|------------------|------------------|-------------------|
| | | Naïve+10% drift | Naïve+20% %drift | Naïve+30% drift | Naïve+40% drift | Naïve+50% drift | Naïve+60% drift | Naïve+70% %drift | Naïve+80% %drift | Naïve+90% %drift | Naïve+100% %drift |
| ME(Bias) | -83.11 | -76.01 | -68.93 | -61.81 | -54.71 | -47.61 | -40.48 | -33.42 | -26.32 | -19.22 | -12.12 |
| RAE(Accuracy) | 1.00 | 0.98 | 0.98 | 1.00 | 1.02 | 1.06 | 1.09 | 1.14 | 1.19 | 1.24 | 1.32 |
| MSE(Uncertainty) | 261458.16 | 257314.60 | 258543.24 | 265144.09 | 277117.15 | 294462.41 | 317180.53 | 345269.56 | 378731.44 | 417565.53 | 461771.83 |

Naïve + Drift Errors of Generic Drugs for the BTG Category

| Generic | Benchmark | Drift | | | | | | | | | |
|------------------|-----------|-----------------|------------------|-----------------|-----------------|-----------------|-----------------|------------------|------------------|------------------|-------------------|
| | | Naïve+10% drift | Naïve+20% %drift | Naïve+30% drift | Naïve+40% drift | Naïve+50% drift | Naïve+60% drift | Naïve+70% %drift | Naïve+80% %drift | Naïve+90% %drift | Naïve+100% %drift |
| ME(Bias) | -82.12 | -77.98 | -73.84 | -69.71 | -65.57 | -61.43 | -56.56 | -53.15 | -49.01 | -44.87 | -40.73 |
| RAE(Accuracy) | 1.00 | 0.95 | 0.90 | 0.86 | 0.82 | 0.79 | 0.79 | 0.79 | 0.81 | 0.85 | 0.91 |
| MSE(Uncertainty) | 198214.64 | 185541.65 | 175497.55 | 168082.35 | 163296.04 | 161138.62 | 161684.64 | 164710.47 | 170439.73 | 178797.89 | 189784.94 |

Level of Drift Compared with RAE for Branded and Generic Pharmaceutical Life Cycles



Discussion – High Branded Low Generic

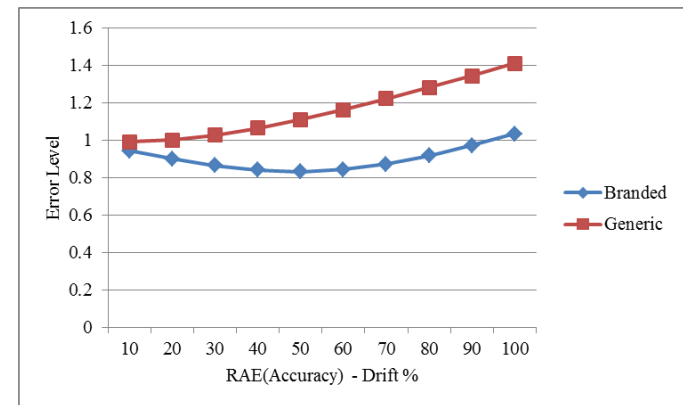
Naïve + Drift Errors of Branded Drugs in the HBLG Category

| Branded | Benchmark | Drift | | | | | | | | | |
|------------------|-----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|------------------|
| | | Naïve+10% drift | Naïve+20% drift | Naïve+30% drift | Naïve+40% drift | Naïve+50% drift | Naïve+60% drift | Naïve+70% drift | Naïve+80% drift | Naïve+90% drift | Naïve+100% drift |
| | Naïve | | | | | | | | | | |
| ME(Bias) | -58.47 | -51.89 | -45.30 | -38.71 | -32.13 | -25.54 | -18.96 | -12.37 | -5.78 | 0.80 | 7.39 |
| RAE(Accuracy) | 1.00 | 0.95 | 0.90 | 0.87 | 0.84 | 0.83 | 0.84 | 0.87 | 0.92 | 0.97 | 1.04 |
| MSE(Uncertainty) | 155842.58 | 144656.62 | 137092.54 | 133150.34 | 132830.03 | 136131.59 | 143055.05 | 153600.38 | 167767.60 | 185556.70 | 206967.68 |

Naïve + Drift Errors of Generic Drugs in the HBLG Category

| Generic | Benchmark | Drift | | | | | | | | | |
|------------------|-----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|------------------|
| | | Naïve+10% drift | Naïve+20% drift | Naïve+30% drift | Naïve+40% drift | Naïve+50% drift | Naïve+60% drift | Naïve+70% drift | Naïve+80% drift | Naïve+90% drift | Naïve+100% drift |
| | Naïve | | | | | | | | | | |
| ME(Bias) | -7.48 | -7.14 | -6.79 | -6.44 | -6.10 | -5.75 | -5.41 | -5.06 | -4.71 | -4.37 | -4.02 |
| RAE(Accuracy) | 1.00 | 0.99 | 1.00 | 1.03 | 1.07 | 1.11 | 1.17 | 1.22 | 1.28 | 1.35 | 1.41 |
| MSE(Uncertainty) | 6350.14 | 5954.06 | 5677.42 | 5520.23 | 5482.48 | 5564.18 | 5765.32 | 6085.90 | 6525.93 | 7085.40 | 7764.31 |

Level of Drift Compared With RAE for Branded and Generic Pharmaceutical Life Cycles



Discussion – High Generic Low Branded

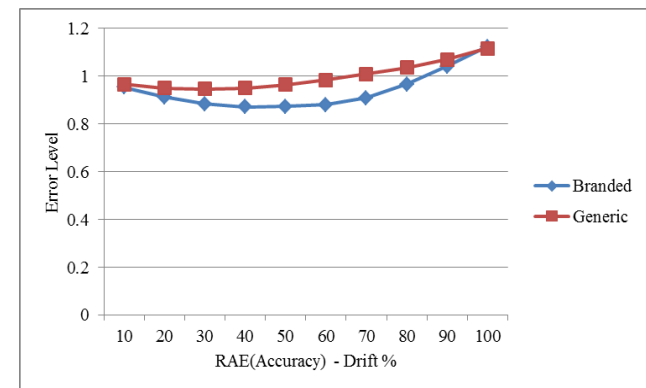
Naïve + Drift Errors of Branded Drugs for the HGLB Category

| Branded | Benchmark | Drift | | | | | | | | | |
|------------------|-----------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|---------------------|
| | Naïve | Naïve+10 %drift | Naïve+20 %drift | Naïve+30 %drift | Naïve+40 %drift | Naïve+50% drift | Naïve+60 %drift | Naïve+70 %drift | Naïve+80 %drift | Naïve+90 %drift | Naïve+100 %drift |
| ME(Bias) | -36.79 | -32.56 | -28.34 | -24.12 | -19.89 | -15.67 | -11.44 | -7.22 | -3.00 | 1.23 | 5.45 |
| RAE(Accuracy) | 1 | 0.95 | 0.91 | 0.88 | 0.87 | 0.87 | 0.88 | 0.91 | 0.97 | 1.04 | 1.12 |
| MSE(Uncertainty) | 21199.25 | 20991.79 | 21313.64 | 22164.81 | 23545.29 | 25455.08 | 27894.19 | 30862.61 | 34360.34 | 38387.39 | 42943.75 |

Naïve + Drift Errors of Generic Drugs for the HGLB Category

| Generic | Benchmark | Drift | | | | | | | | | |
|------------------|-----------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|---------------------|
| | Naïve | Naïve+10 %drift | Naïve+20 %drift | Naïve+30 %drift | Naïve+40 %drift | Naïve+50% drift | Naïve+60 %drift | Naïve+70 %drift | Naïve+80 %drift | Naïve+90 %drift | Naïve+100 %drift |
| ME(Bias) | -50.81 | -48.77 | -46.73 | -44.68 | -42.64 | -40.60 | -38.56 | -36.52 | -34.48 | -32.44 | -30.40 |
| RAE(Accuracy) | 1.00 | 0.97 | 0.95 | 0.95 | 0.95 | 0.96 | 0.98 | 1.01 | 1.04 | 1.07 | 1.12 |
| MSE(Uncertainty) | 190881.37 | 173568.10 | 159902.37 | 149884.20 | 143513.58 | 140790.50 | 141714.98 | 146287.01 | 154506.59 | 166373.72 | 181888.40 |

Level of Drift Compared with RAE for Branded and Generic Pharmaceutical Life Cycles



Conclusions

- GP's within the UK have a tendency to prescribe branded and generic drugs differently
- Simpler models forecast pharmaceutical life cycles with a greater level of accuracy than more complex ones.
- Most accurate of the current research = Naïve+%drift
- Aaker and Jacobson (1987) found that when modelling market share using the naive market share model, its predictive power was relatively high.
- Brodie & de Kluyver (1987) found that a number of econometric market share models perform no better than a 'naive' model.'

Conclusions

- This research provides a basis for the NHS in employing any cost saving techniques when looking at how different pharmaceuticals are prescribed, and forecasting how they may be prescribed in the future
- As for pharmaceutical companies this research will allow them to discover, when it is best in the life cycle of the branded pharmaceutical to introduce strategies to prolong its life cycle and slow down the number of generic prescriptions written

Thank you

Any Questions?