THE ASSOCIATION BETWEEN METEOROLOGICAL PARAMETERS AND THE PRESCRIPTION PATTERNS FOR ASTHMA AND ALLERGIC RHINITIS, AS OBSERVED IN PRETORIA DURING A ONE-YEAR PERIOD

BY

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DECLARATION

I hereby declare that this dissertation presented to the University of Pretoria for the Masters Science in Clinical Epidemiology degree is my own work and has not been presented previously to any other tertiary institution for any purpose.

JH Retief

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Authorship and Co-workers

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ABSTRACT

The association between meteorological parameters and the prescription patterns for asthma and allergic rhinitis, as observed in Pretoria during a one year period

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Background: Can the high incidence of allergic diseases be linked to changes in weather patterns, and can these changes then be used to predict increases in the usage of medications? This could lead to better patient awareness, as well as an improved utilization of resources.

Objectives: The hypothesis was tested that treatment rates (as evidenced by the amount of prescriptions) were associated with meteorological determinants, namely temperature, rainfall, humidity, barometric pressure, and wind speed.

Setting: Medical prescriptions as received by a General Practitioner organization from 22 practices, reflecting disease codes for Asthma an Allergic Rhinitis, and geographically representing a part of eastern Pretoria, were used. These were matched on a day-to-day basis with meteorological parameters (as mentioned above) obtained from a nearby weather station over a period of one year.

Study design: A cross-sectional, ecological study was done to determine the relationship between the two databases. To take cognizance of seasonal influences, a period of one year was analyzed.

Methods: For investigating the relationship between allergic symptomology and environmental conditions, a time series analysis, utilizing a STATA package was used. Hereby trend and seasonality could be described, in order to identify and forecast future values. An Autoregressive integrated moving average (Arima) analysis provided both moving averages and lag analyses. The model was also evaluated in an appropriate manner, including testing of residuals.

Results: After analysis, and using alpha values of 10% for level of significance, it was found that rainfall and wind speed do not influence prescriptions for asthma, but temperature and humidity do have a significant influence, with p-values of 0.050 and 0.097 respectively. Concerning allergic rhinitis, none of the above parameters were found to influence prescriptions.

Conclusion: Certain weather parameters were shown to have an influence on prescriptions for asthma, but not for allergic rhinitis. The confounding effects of pollution and allergens were not studied.

ABSTRAK

Die assosiasie tussen weerkundige parameters en die voorskrifpatrone vir asma en allergiese rhinitis, soos waargeneem in Pretoria oor 'n een jaar tydperk

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Agtergrond: Daar is dikwels gevra of die hoë insidensie van allergiese siektes gekoppel kan word aan veranderinge in weerpatrone en of hierdie veranderinge gebruik kan word om toenames in medikasiegebruik te voorspel. Dit kan lei tot verbeterde pasiënt bewustheid, asook meer optimale gebruik van hulpbronne.

Doelstellings: Die hipotese is getoets dat voorskriffrekwensie (soos reflekteer deur die aantal voorskrifte) assosieerd is met weerparameters, naamlik temperatuur, reënval, humiditeit, barometriese druk en windspoed.

Plasing: Mediese voorskrifte, soos ontvang vanaf 22 praktyke uit die oostelike voorstede van Pretoria deur 'n algemene praktykorganisasie, is gebruik. Hierdie is gekoppel aan daaglikse weerparameters (soos bo vermeld), verkry oor 'n een jaar periode vanaf 'n nabygeleë weerstasie.

Studie ontwerp: 'n Deursnit, ekolgiese studie om die verhouding tussen die twee databasisse te bepaal, is gedoen. Om voorsiening te maak vir seisoenale invloede, is 'n periode van een jaar ontleed.

Metodes: Om die verhouding tussen allergiese simptome en omgewingsfaktore te bepaal is 'n tyd series analise, wat 'n STATA packet behels, gebruik. Hierdeur kon neigings en seisoenaliteit beskryf word, sodat toekomstige gebeure voorspel kan word. 'n Outoregressiewe integreerde bewegende gemiddelde analise verskaf beide bewegende gemiddeldes en vertragings analyses. Die model is ook vir akkuraatheid getoets op verskeie maniere.

Resultate: Na analise en gebruik van toepaslike (10%) alfa-waardes vir die vlak van betekenisvolheid, is gevind dat reënval en windspoed voorskrifte vir asma nie beinvloed nie, maar wel temperatuur en humiditeit (p-waardes 0.050 en 0.097 respektiewelik). Dieselfde kon nie gevind word met allergiese rhinitis, waar geen van bogenoemde betekenisvol was nie.

Gevolgtrekking: Sekere weerparameters het 'n invloed op voorskrifpatrone vir asma, maar nie allergiese rhinitis nie. By laasgenoemde speel ander omgewingsfaktore soos allergene en lugbesoedeling waarskynlik 'n belangriker rol.

CONTENTS

PART ONE: PRESCRIPTIONS FOR ASTHMA

PART TWO: PRESCRIPTIONS FOR ALLERGIC RHINITIS

CHAPTER ONE

1.1 INTRODUCTION

With the very high incidence of allergic diseases in the general population (especially younger children), the question is often asked if meteorological changes, such as variance in temperature, rainfall, barometric pressure and other factors have an influence on the prevalence of these diseases.

If so, can these weather parameters then be used as markers of disease, as evidenced by an increase in prescriptions written by doctors?

1.2 LITERATURE REVIEW

In a study in Israel done by Garty et al in 1998, a positive correlation between emergency room (ER) visits of asthmatic children and high barometric pressure, and a negative correlation with O_2 concentration and temperature were demonstrated. Sudden rainstorms and a sudden fall in temperature, have also led to epidemics of asthma: this is explained by the release of large numbers of airborne pollen or mould spores.[1]

The inhalation of cold air is known to induce intrapulmonary airway obstruction in sensitive asthmatic patients and this is a condition often ascribed to heat and water losses from the airway mucosa. According to Millqvist (1999), cold air stimulation at the nose induces a decrease in airway conductance and FEV1 and warm air stimulation has the opposite effect.[2]

The association between air pollution and various signs and symptoms of asthma is well described. These include pulmonary function decrements, increased bronchial hyper-responsiveness, visits to emergency departments, hospital admissions, increased medication use and symptom reporting, inflammatory changes, interactions between air pollution and allergen challenges, and immune system changes.[3]

There has also been an increased tendency, at least in the United Kingdom, to use weather forecasts to help health care providers plan and give early warning of increases in illnesses that may be linked to changes in the weather -- such as myocardial infarction, strokes, respiratory diseases, infectious diseases, and fractures. "Health weather forecasts" are thus currently being piloted in five regions of England.[4]

This seems to reflect what Hippocrates said more than 2000 years ago:
"Whoever wishes to investigate medicine properly, should proceed thus: In the first place consider the seasons of the year, and what effects each of them produces, for they are not all alike, but differ much from themselves in regard to their changes".[4]
Respiratory allergic diseases (rhinitis, rhinosinusitis, bronchial asthma and its equivalents) appear to be increasing in most countries, and subjects living in urban and industrialized areas are more likely to experience symptoms. This increase has been linked, among various factors, to air pollution. The most abundant air pollutants in urban areas with high levels of vehicle traffic are respirable particulate matter, nitrogen dioxide (NO_2) and ozone. Besides acting as irritants, airborne pollutants can modulate the allergenicity of antigens carried by airborne particles. Pollutants also overcome the mucosal barrier and so facilitate the allergen induced inflammatory responses.[5]

Short-term NO_2 exposure from indoor and outdoor sources has been associated with non-specific respiratory symptoms and decreased lung function, particularly in children with pre-existing asthma. Chronic exposure to respirable particles, sulphur dioxide (SO_2) and NO_2, leads to an up to three-fold increase in non-specific chronic respiratory symptoms. Truck traffic and diesel exhaust fumes lead to significant increases in respiratory symptoms and decreases in lung function.[6]

The home environment can also play an important role in asthma and related diseases. Airborne allergens such as those from house dust mites may be important, as well as factors like pollution from particulate materials associated with combustion and smoking, e.g. chemical vapours and gases including the above mentioned, NO_2, SO_2 and volatile organic compounds, including also passive smoking.[7]

The effect of thermally induced asthma and airway drying, has been extensively studied.[8] Technical difficulties associated with measuring expired air temperature and water loss led to a mass of inconsistent data and the abandonment of this technology: there were local differences in water flux in different regions along the tracheo-bronchial tree.[9] Direct measurements of airway surface fluid (ASF) osmolality revealed that cool dry air does increase ASF osmolality during and after hyperventilation, and these changes correlate with the development of airway obstruction in a canine model of exercise-induced asthma.[10]

Of the pollen spores Ambrosia pollen counts demonstrated the strongest correlation with allergic rhinitis and asthma symptoms, with a lag period of up to 7 days. A nonlinear relationship was found between the clinical measures and pollen counts; the clinical consequences of a given pollen load also increased as the season progressed, probably due to a priming effect.[11]

Concerning the burden of disease: the annual cost of asthma in the United States has been estimated to exceed 6 billion U.S. dollars. The average cost of an outpatient visit (1999) was $188, but was $3812 for a hospital admission. It was found that a substantial portion of asthma costs results from the use of inpatient or urgent emergency services that may represent failure of preventive management and treatment. Here an Education and Prevention Programme may help to increase awareness and reduce costs.[12]

1.3 RELEVANCE

The relevance of this study lies in the ability to predict increases in symptoms amongst a population requiring drug treatment for allergic diseases. This will lead to better patient awareness, as well as a better ability to plan and provide a cost effective service to patients.

CHAPTER TWO

2.1 METHODS

2.1.1 Hypothesis

The hypothesis will be tested that treatment rates (as evidenced by the amount of prescriptions) are associated with meteorological determinants, namely temperature, rainfall, humidity, barometric pressure, and wind speed.

Due to constraints in measurement of certain confounders (e.g. air pollution and pollen counts), these factors will not be adjusted for in the analysis.

2.1.2 Identifying Variables

(a) Domain:

Medical prescriptions as received by GPNet (a general practitioner organization representing up to 40% of all General Practitioners countrywide) are used. A duplicate copy of the prescription given to the patient is sent to the organization for documentation and statistical purposes. Prescriptions identified by the International Statistical Classification of Diseases (ICD) code J45 ("Asthma"), and code J30 ("Allergic rhinitis") are used. Medications by name are not used, due to possible overlap in usage for certain diseases (see also: possible bias). Only those doctors who were present and participated both within the start and end of study dates' data were used for compilation of data. A group of 22 medical practices were thus identified, and their data used in the study. A geographical area encompassing certain Eastern Suburbs in Pretoria was used in order to correlate data within a 2.5 km. radius from a nearby weather station.

(b) Determinants:

Meteorological parameters, including temperature, rainfall, humidity, barometric pressure, and wind speed are used. These are documented and measured at the Botanic Gardens Weather Station, and verified by the Agricultural Research Council (ARC) (Institute for soil, climate and water research).

Temperature and relative humidity are measured at height 1.2 to 1.4 meters within a Stevenson screen, where a free flow of air, and shade are assured. Arma Therm thermometers are used, and replaced if inaccurate.

Temperature readings are measured with a maximum and minimum thermometer, and controlled by a Thies thermohydrograph, where readings are constantly monitored and recorded graphically. These instruments are calibrated twice yearly.

Rainfall is measured at height 1.2 meters in a standard 127mm SA Weather Bureau rain meter.

Wind speed is measured at height 2m, with a wind totalisator, manufactured by Casella of London.

2.2 STUDY DESIGN

The study is a cross-sectional, ecological study, which examines the relationship between the above- mentioned meteorological data, and frequency of prescriptions in a defined population. Data given by the Agricultural Research Council and the Weather Bureau are compared with the number of prescriptions for allergies as evidenced by allergic rhinitis and asthma, as documented by GP Net in a specific geographical area. To take cognizance of seasonal influences, a period of one year is analyzed.

2.3 ETHICAL CONSIDERATIONS

The project has been submitted and approved by the Ethical Committee of the Faculty of Medicine, University of Pretoria.

Consent was given by the General Practitioner Association (GPNet) for use of their prescription data, which was extracted on an anonymous basis.

No patient or animal was in any way harmed during the execution of this study.

2.4 DATA COLLECTION

1. AGRICULTURAL RESEARCH COUNCIL: A time period of more than 365 days (or one year) was determined from March 2002 to April 2003, to collect the following data on a daily basis:
    (A) Rainfall (quantity) in mm.
    (B) Wind speed in meters / second (m/s).
    (C) Temperature (Maximum – Minimum) in ^{0}C.
    (D) Humidity (Maximum – Minimum), as a percentage (%)

2. GPNet: Over the same time period as above, data was collected by GPNet on a daily basis as mentioned before

   Number of prescriptions for allergic rhinitis: > 170 cases could be identified (see analysis later)

   Number of prescriptions for asthma: > 400 cases could be identified (see analysis later)

The two databases were then matched for dates and analyzed.

CHAPTER THREE

3.1 STATISTICAL ANALYSIS

3.1.1 Introduction

For investigating the relationship between allergic symptoms and environmental conditions, **a time series analysis** is used, utilizing a STATA package.

In a time series analysis data, that is, sequences of measurements follow non- random orders. The assumption is that successive values in the data file represent consecutive measurements taken at equally spaced time intervals. The data consist of a systematic pattern, and random noise (error). The latter is filtered out to some degree.

Time series patterns describe two components, namely trend and seasonality. Trend represents a general systematic linear or nonlinear component that changes over time and does not repeat, whereas seasonality may have a formally similar nature, but repeats itself in systematic intervals over time.

Two main goals of time series analysis are to identify the nature of the phenomenon represented by the sequence of observations, and forecasting of future values. Once a pattern is established, it can be interpreted and integrated with other data. Extrapolation can then follow to predict future events.

An Autoregressive integrated moving average (ARIMA) analysis procedure is used to provide both moving averages and lag results: a moving average will show vertical fluctuations in the amount of prescriptions for asthma and rhinitis, whilst a <u>lag analysis</u> will show the period between successive fluctuations.

Two common processes are thus in place:

- An autoregressive process (**AR**), where each observation is made up of a random error component, and a linear combination of prior observations.
- A moving average (**MA**) process where each element in the series can also be affected by the past error, that cannot be accounted for by the autoregressive component.

In STATA, ar () and ma () are thus used to specify the lags of autoregressive and moving-average terms respectively.

The Autoregressive Integrated Moving Average model thus includes three parameters in the model, namely the autoregressive parameters, the number of differencing passes, and the moving average parameters.

The **ARIMA** (p, d, q) procedure in STATA is thus used to explain the relationship between a time- dependent outcome variable Y, and a set of k predictor variables X1, X2, …, Xk.

Distributional assumptions must be made about 3 important parameters that determine the pattern of the variation of Y as a function of the k predictor variables through time. These 3 parameters are the number of lags (p), the number of times Y and each of the X's are differentiated (d), and the number of lags of moving averages (q). Estimation (where the parameters are estimated by means of minimizing the sum of squared residuals) and forecasting (where values are first integrated) are the next steps.

3.1.2 Structural equations for a time series analysis

The structural equation of a time series model containing a first order autoregressive process **AR**(1) and a first order moving average **MA**(1) is given by the following equation:

$\underline{Y_t = X_t\beta + \mu_t}$ where $\mu_t \sim N(0, \delta^2_t)$ (1.1)

In the above expression, the variance δ^2_t is expressed as a function of lagged disturbances. In the above model, it is assumed that the true mean μ_t is normally distributed with mean 0 and constant variance δ^2_t.

If a first order autoregressive AR(1) estimate and a first order moving average MA(1) have to be done, the following structural equation would be suitable:

$Y_t = X_t\beta + \mu_t$ where

$\mu_t = \rho\mu_{t-1} + \theta\,\varepsilon_{t-1} + \varepsilon_t$ where

ρ = first order autocorrelation parameter

θ = first order moving average parameter

$\varepsilon_t \sim NID(0,\sigma^2)$ are white noise disturbances

In the study and analysis interpretations can thus be made as follows:

Prescriptions for asthma: a time- dependent variable that is affected by the predictor variables rainfall, wind speed, temperature and humidity.

AR (1) (also called the Markov process) indicates that autoregressive terms or lags of order 1 are included in the time series regression model. This means that the process is similar to a multiple linear regression model, but X_t is regressed past values of X_t and not on independent variables. In this study, due to fairly stationary time series data sets, the order of past values of the predictor variables that affect the dependent variables is only 1.

MA(1 4) indicates that the residuals are assumed to have white noise disturbances, and that a quarterly moving average effect is added. Although the data set in this study is not quarterly data, the time series plots of the set show that it resembles quarterly time series data. In addition to an autoregressive term and a moving average (1) term, a seasonal moving average (4) term at lag 4 is included to account for the remaining quarterly effect.

3.1.3 Evaluation of the model

The following can be looked at to evaluate the model:

1. Parameter estimates for example appropriate t values, are computed from the parameter standard errors.
2. Accuracy of the forecasts: includes a parsimonious model (least parameters and greatest number of degrees of freedom) and the production of statistically independent residuals where the autocorrelogram of the residuals should show no serial dependency between the residuals.
3. Analysis of the residuals: The analysis of the residuals constitutes an important test of the model. They should not be (auto)-correlated, and be normally distributed.
4. Possible bias (As applicable to the study):

   (a) Selection bias:

   - People not taking treatment for disease, presenting late, taking follow up medication for a diagnosis made earlier, or taking over-the-counter prescriptions (not reflected in prescriptions received at GPNet).
   - Late submissions of prescriptions.

   (b) Information Bias:

   - Misclassification of disease (wrong diagnosis) by doctor.
   - Presence of an infective epidemic, e.g. influenza, precipitating further disease.
   - Other climatic variables not measured at present (e.g. pollution).
   - Patients admitted in hospitals, or treated by specialists (not reflected in the database).

3.2 RESULTS OF THE TIME SERIES ANALYSIS

3.2.1 List of variables in the data set

- Year
- Month
- Day
- Rain = quantity of rainfall in mms
- Wind = wind speed in meters per second
- Prh = number of prescriptions for allergic rhinitis (dependant variable)
- Pas = number of prescriptions for asthma (dependant variable)
- Temp = maximum temperature – minimum temperature (degrees Celcius)
- Hum = maximum humidity – minimum humidity (as a %)

The above variables (on a y-axis) are listed against time (365 daily columns, on the x-axis)

3.2.2 Calculation

403 observations were used, as well as the following variables namely year, month, day, rain, wind, prescriptions for asthma, prescriptions for allergic rhinitis, temperature and humidity.

Time was then generated, a t –set done, and an **ARIMA** process done namely

ARIMA pas rain wind temp humidity ar (1) ma (1 4).

Parameter estimates were obtained by Maximum Likelihood estimation; an **ARIMA** regression was then done (See Table one for values).

Part 1:

ARIMA regression for prescriptions for asthma

Sample: 01mar2002 to 07apr2003 n = 403

Wald chi2(7) = 453.95

Log likelihood = -800.0464 Prob > chi^2 = 0.0000

Since STATA does not give multiple R-squared values for ARIMA procedures, SPSS calculations were done to determine the Akaike Information Criterion (AIC) and the Schwarz Bayesian Criterion (SBC). The small values of 1228.3898 and 1256.365 obtained respectively, indicated that the fitted models are parsimonious.

Table 1 Parameter estimates obtained from a Time Series Regression

pas	**Coefficient.**	**Standard Error.**	**z**	**P>|z|**	**95% Confidence Interval**	
rain	.000446	.0010305	0.43	0.665	-.0015737	.0024656
wind	-.000366	.0008255	-0.44	0.658	-.0019839	.001252
temp	-.0011625	.0005927	-1.96	0.050	-.0023241	-8.95
hum	.0004675	.0002817	1.66	0.097	-.0000847	.0010197
cons	1.195743	.1128314	10.60	0.000	.9745977	1.416889
ARIMA						
L1 (Lag#1)	.7674467	.0812798	9.44	0.0000	.6081413	.9267522
L1	-.8103576	.0826385	-9.81	0.000	-.9723262	-.6483891
L4 (Lag#4)	-.0895653	.0475581	-1.88	0.060	-.1827775	.0036469
/sigma	1.761126	.1017455	17.31	0.000	1.561708	1.960543

Interpretation of results from the regression of prescriptions for Asthma on rainfall, wind speed, temperature range and humidity.

The regression coefficients at lags 1 and 4 are different from each other. The results show that the regression coefficients of AR and MA are significant at lag number 1, but not at lag number 4. This is to be expected, due to the fairly stationary time series data.

Prescriptions for asthma was regressed on rain, wind, temp and humidity.

An α- value of 10% represents the maximum probability of making a Type-I error, viz. wrongfully rejecting a parameter under the null hypothesis. In the context of an

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AR- model, as used in this dissertation, α denotes the first-order parameter in the model. In practice the estimate of this parameter is usually 0.30 or lower.

A p-value, or probability of obtaining a result as extreme (or more) than the one observed (if the null hypothesis is true), was obtained after the statistical test has been performed. Estimated parameters with p-value <0.05 are deemed statistically significantly different from zero, and should remain in the model.

At the $\alpha = 10\%$ level of significance:

Rainfall does not influence prescriptions for asthma since $p = 0.665 > \alpha$.
Wind speed does not influence prescriptions for asthma since $p = 0.658 > \alpha$.
Temperature influences prescriptions for asthma since $p = 0.050 < \alpha$.
Humidity influences prescriptions for asthma since $p = 0.097 < \alpha$.

Concerning **residuals:**

Residuals are the differences between estimated results and true values. Large values will indicate incorrect estimations, and small values of the residuals indicate accurate estimations. STATA standardizes the residuals, and plots a normal probability plot of residuals. Ideally it should be a straight line, but if it resembles an S- shape (as in this study: see probability plot), it means that the white noise assumption is satisfied, and hence the time series has achieved a state of equilibrium.

$\hat{\beta}_{AR(L1)} = 0.7674467$ with $p = 0.000 < \alpha = 0.05$.

Since $p < \alpha$, there is a statistically significant first order autocorrelation in the disturbances.

$\hat{\beta}_{MA(L1)} = -0.8103576$ with $p = 0.000 < \alpha = 0.05$.

Since $p < \alpha$, there is a statistically significant first order moving average.

$\hat{\beta}_{MA(L4)} = -0.0895653$ with $p = 0.060 > \alpha = 0.05$.

Since $p > \alpha$, there is no significant fourth order moving average.

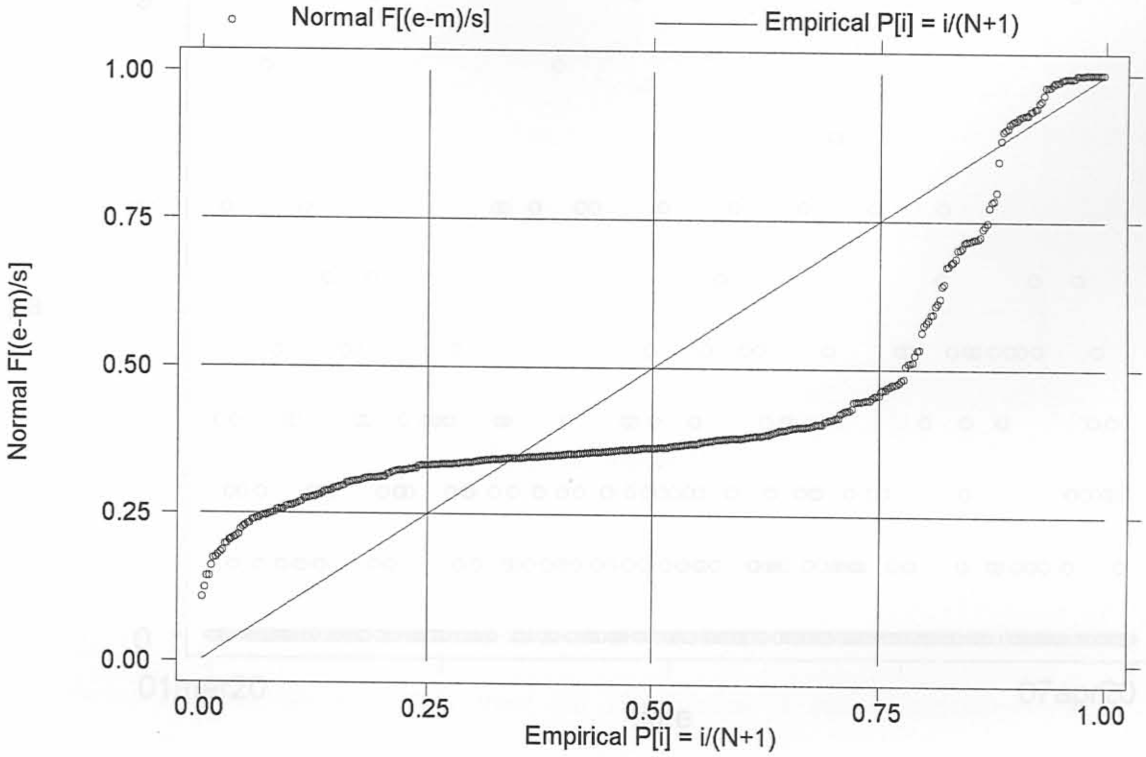

Figure 1 Normal Probability Plot of Residuals

The S- shaped normal probability plot indicates a violation of the normal assumption of the error structure. The S- shape indicates that a distribution with lighter tails than the normal distribution fits the residual series.

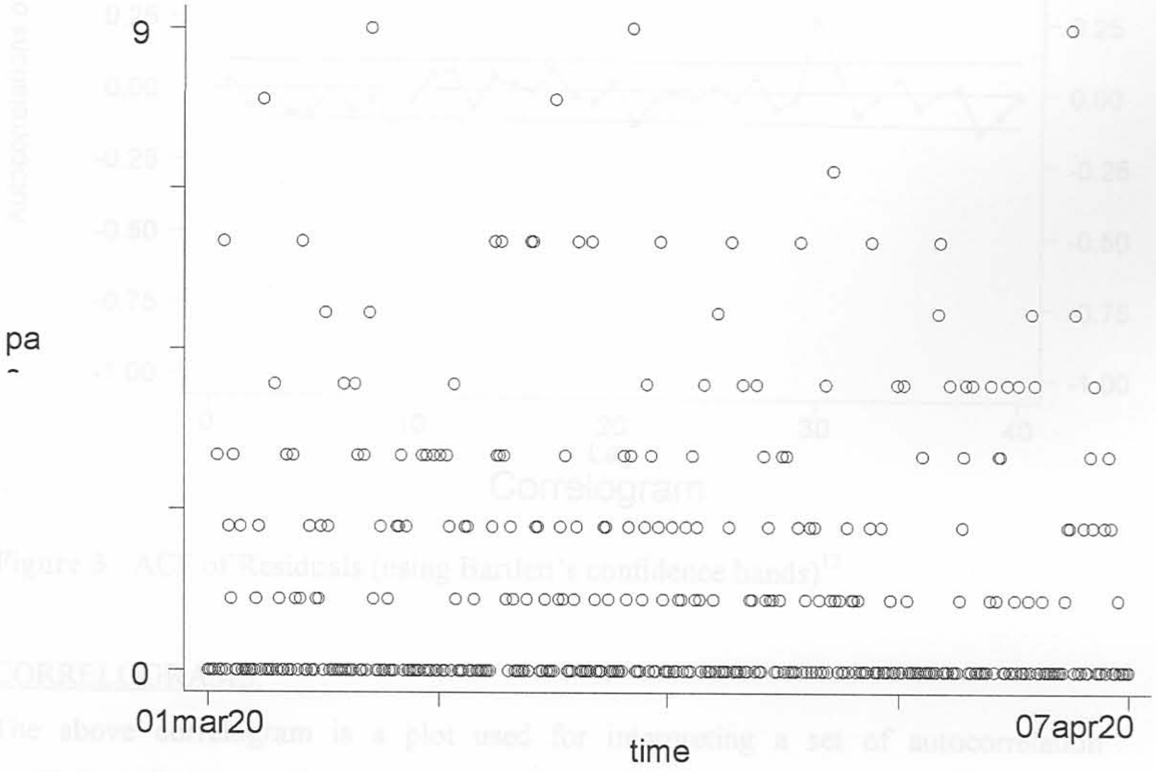

Figure 2 Time Series Plot of Asthma Prescriptions

The above graph shows the trend followed by prescriptions for asthma as time varied from 01 March 2002 to 07 April 2003. (Y- axis shows amount of prescriptions on a daily basis, from 0 to 9; X- axis shows the time, divided into 4 quarters).

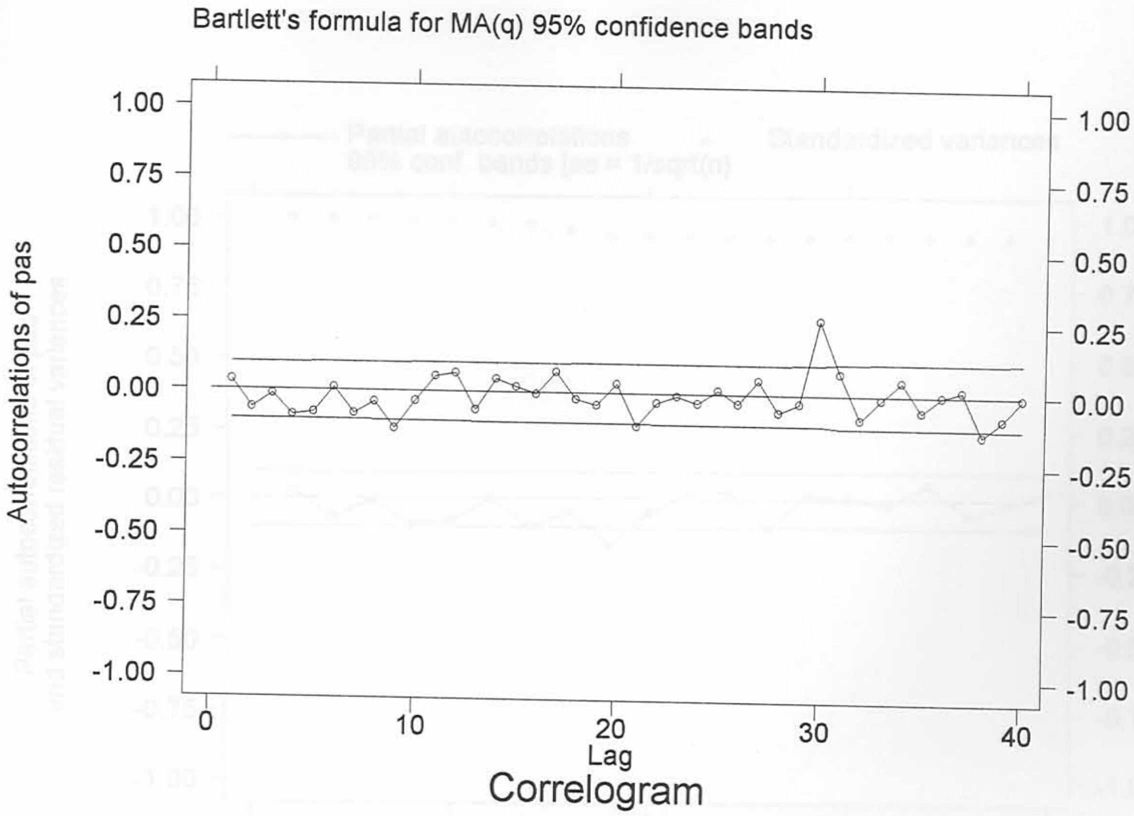

Figure 3 ACF of Residuals (using Bartlett's confidence bands)[13]

<u>CORRELOGRAMS:</u>

The above correlogram is a plot used for interpreting a set of autocorrelation coefficients. It is a graph of $\mathbf{r}_k$ versus lag k.

For a large sample, $\mathbf{r}_k$ is approximately normally distributed with expected value 0 and variance 1/N. An approximate 95% confidence interval for $\mathbf{r}_k$ is therefore given by [-2/sqrt(N); 2/sq(N)]. In this study, N=403, and an approximate 95% confidence interval for r_k is hence given by [-0.0996; 0.0996].

40 Lag periods were used: 0 staring at the start of study period, and 40 denoting the end of study period.

The above correlogram shows a fairly stationary time series pattern for prescriptions for asthma, with a break-out at lag number 30, reflecting an increase in prescriptions during the rainy season (November and December).

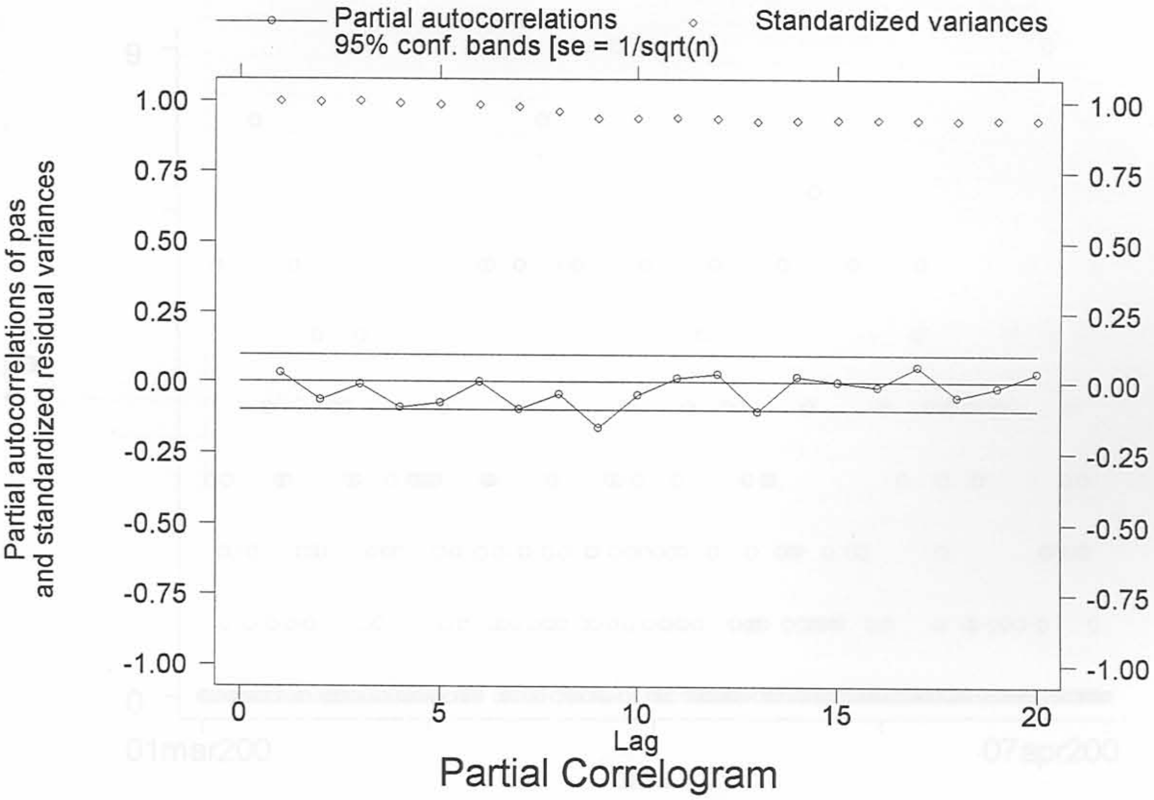

Figure 4 PACF of Residuals

PARTIAL CORRELOGRAMS:

The above partial Correlogram gives a plot of partial autocorrelations and standardized residual variances versus lag periods, very similar to the correlogram. It is however more precise, as it gives a 95% confidence band for autocorrelations. Again it is shown that the time series for prescriptions for asthma is fairly constant, with no outliers.

20 lag periods were used in the above to rule out the presence of unexpected significant results at higher lag periods.

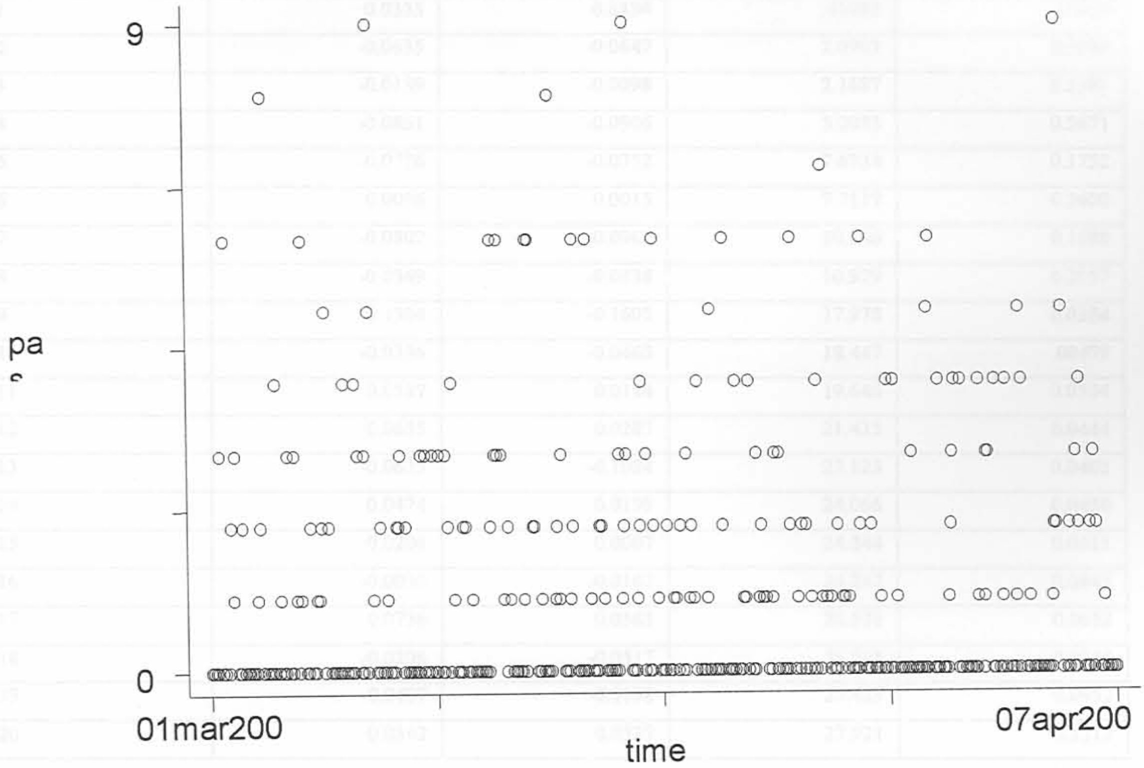

Figure 5 Time Series Plot of Asthma Prescriptions

Table 2 : Autocorrelation Function (ACF) and Partial Autocorrelation Function (PACF) for 20 lags

LAG	Auto Correlation	Partial Auto Correlation	Prob>Q	
			[Autocorrelation]	[Partial Autocor]
1	0.0333	0.0334	.45083	0.5019
2	-0.0635	-0.0647	2.0903	0.3516
3	-0.0139	-0.0098	2.1687	0.5381
4	-0.0861	-0.0906	5.2033	0.2671
5	-0.0776	-0.0752	7.6734	0.1752
6	0.0096	0.0015	7.7117	0.2600
7	-0.0802	-0.0967	10.366	0.1688
8	-0.0369	-0.0438	10.929	0.2057
9	-0.1304	-0.1605	17.978	**0.0354**
10	-0.0336	-0.0460	18.447	**00479**
11	0.0537	0.0144	19.646	0.0504
12	0.0655	0.0287	21.435	**0.0444**
13	-0.0635	-0.1024	23.123	**0.0402**
14	0.0474	0.0199	24.066	**0.0450**
15	0.0206	0.0007	24.244	0.0611
16	-0.0030	-0.0167	24.247	0.0842
17	0.0736	0.0563	26.539	0.0652
18	-0.0206	-0.0517	26.718	0.0844
19	-0.0407	-0.0198	27.423	0.0952
20	0.0342	0.0337	27.921	0.1113

Discussion:

The above table shows values of autocorrelations and partial autocorrelations for each of the 20 lags assumed for data analysis. The Q statistic is used to measure the strength of autocorrelations (AC) and partial autocorrelations (PAC) at each lag. If the p-value next to the Q statistic falls below 0.05, it means there is a significant AC and PAC at the lag. (A p-value greater than 0.05 means no significant AC and PAC at that specific lag).

The p-values for lags 9, 10, 12, 13 and 14 (printed in bold, and reflecting the time period August 2002 to December 2002) are each less than 0.05, thus significant at the 5% level of significance. It also correlates with the rainy season in Pretoria. This shows that the autocorrelations and partial correlations are statistically significant at lags 9, 10, 12, 13 and 14 at the 5% level of significance.

PREDICTING FUTURE VALUES OF PRESCRIPTIONS FOR ASTHMA (PAS)

The estimated ARIMA model for prescriptions for asthma as a function of rain, wind, temperature and humidity is given by the following equation:

$$\text{Pas} = 1.195743 + 0.000446 \times \text{rain} - 0.000366 \times \text{wind} - 0.0011625 \times \text{temperature} + 0.0004675 \times \text{humidity} \qquad (1.2)$$

SCATTER PLOT FOR PRESCRIPTIONS FOR ASTHMA (PAS) OVER TIME

n = 403

```
9 +
   |     *          *                *
   |
   |
   | *          *
   |
   |                     *
   |
   | *  *       ** * **  *  *  *  *  *
 p  |
 a  |  * *                *      *   * *
 s  |
   |  *  **   *       *  * **  *  ** ******* *
   |
   |** *  * **** *  * *** *  ***     * * **   **
   |
   | ***  ** * * ** * ** ** * ****** * * ** * *   *    ****
   |
   | * ** **  **  ** ******** ******* *** ***** **  * * ** *  *
   |
0 + ****************************************************************
   +-------------------------------------------------------------+
     1              t                 403
```

Figure 6 Time Series Plot of Predicted Asthma Prescriptions (PAS)

Part 2:

ARIMA regression for prescriptions for allergic rhinitis

```
Sample:  01mar2002 to 07apr2003          n = 178
Wald chi² (7)    =    82.53
Log likelihood  =  -593.689              Prob > chi²  =  0.0000

------------------------------------------------------------------------
            |     Semi-robust
prh         |    Coef.   Std. Err.      z    P>|z|    [95% Conf. Interval]
```

Table 3 Parameter estimates obtained from a Time Series Regression

Prescriptions for Rhinitis	Coefficient	Std. error	Z value	P > (z)	95% Conf.Interval	
Rain	-.00028	.0009787	-0.29	0.775	-.0021982	.0016382
Wind	.0005293	.0008769	0.60	0.546	-.0011894	.0022481
Temperature	.0009475	.0009261	1.02	0.306	-.0008676	.00027626
Humidity	.0003061	.0003728	.82	0.412	-.0004246	.0010367
Constant	.3699983	.1177453	3.14	0.002	.1392218	.6007749
AR(1)						
L1	-.4813308	.1592303	-3.02	0.003	-.7934164	-.1692452
MA (1 4)						
L1	.6216669	.1505346	4.13	0.000	.3266246	.9167093
L4	.1119957	.0796528	1.41	0.160	-.044121	.2681124
/sigma	1.055584	.0835694	12.63	0.000	.8917905	1.219377

Interpretation of results from the regression of prh (prescriptions for ALLERGIC RHINITIS) on rainfall, wind speed, temperature range and humidity.

At the α = 10% level of significance.

Rainfall doesn't influence prescriptions for allergic rhinitis, since $p=0.775 > \alpha$.

Wind speed does not influence prescriptions for allergic rhinitis, since $p = 0.546 > \alpha$.

Temperature does not influence prescriptions for allergic rhinitis since $p = 0.306 > \alpha$.

Humidity does not influence prescriptions for allergic rhinitis, since $p = 0.412 > \alpha$.

Examining the residuals:

$\hat{\beta}_{AR(L1)} = -0.4813308$ with $p = 0.003 < \alpha = 0.05$.

Since $p < \alpha$, there is a statistically significant first order autocorrelation in the disturbances.

$\hat{\beta}_{MA(L1)} = 0.6216669$ with $p = 0.000 < \alpha = 0.05$.

Since $p < \alpha$, there is a statistically significant first order moving average.

$\hat{\beta}_{MA(L4)} = 0.1119957$ with $p = 0.160 > \alpha = 0.05$.

Since $p > \alpha$, there is no significant fourth order moving average.

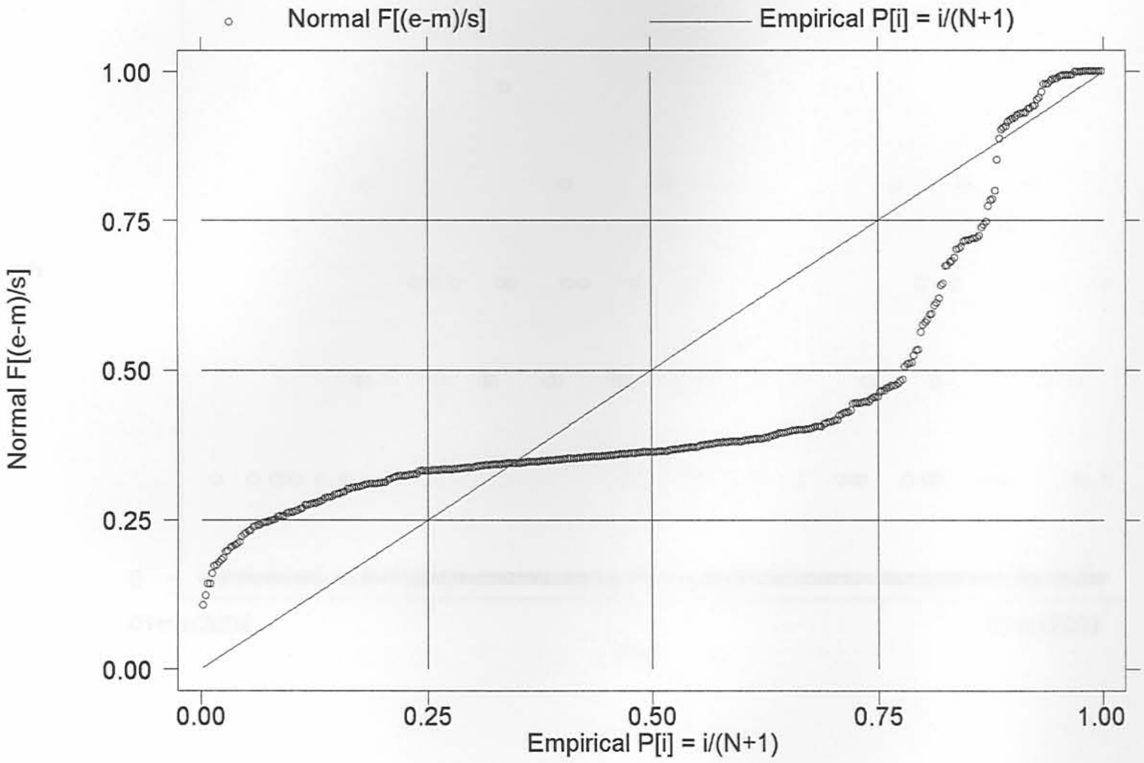

Figure 7 Normal Probability Plot of Residuals

The S- shaped normal probability plot indicates a violation of the normal assumption of the error structure. The S- shape indicates that a distribution with lighter tails than the normal distribution fits the residual series.

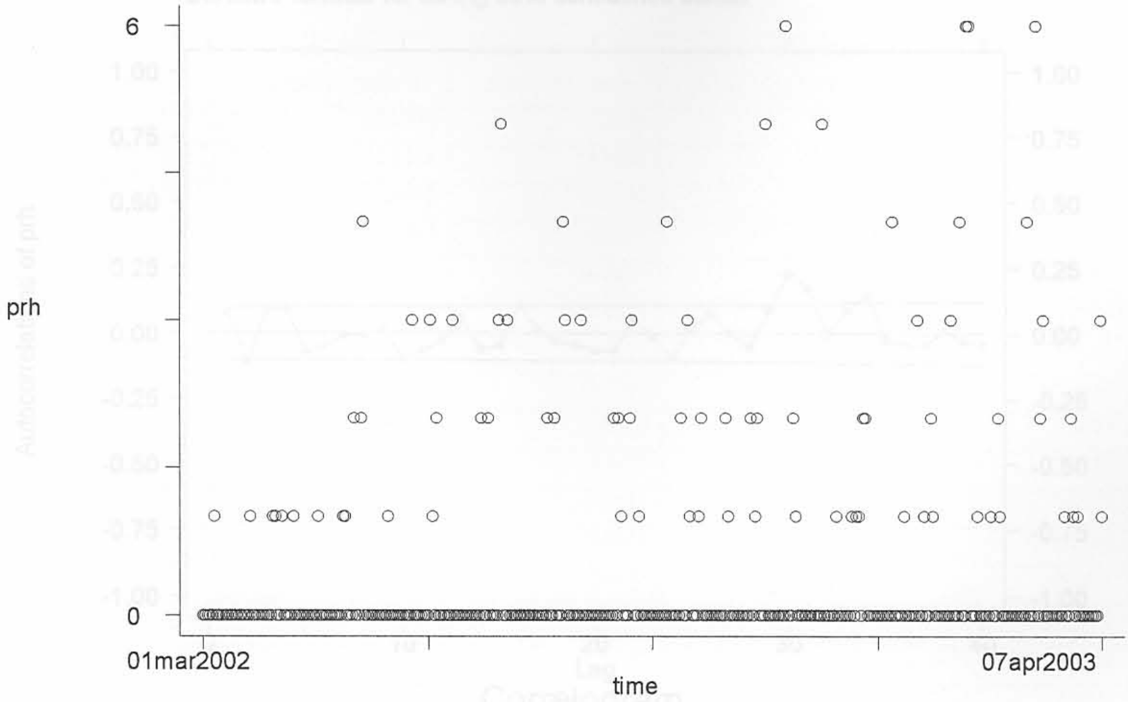

Figure 8 Time Series Plot of Allergic Rhinitis Prescriptions

The above graph shows the trend followed by prescriptions for allergic rhinitis as time varied from 01 March 2002 to 07 April 2003. (Maximum of 6 prescriptions / day noted)

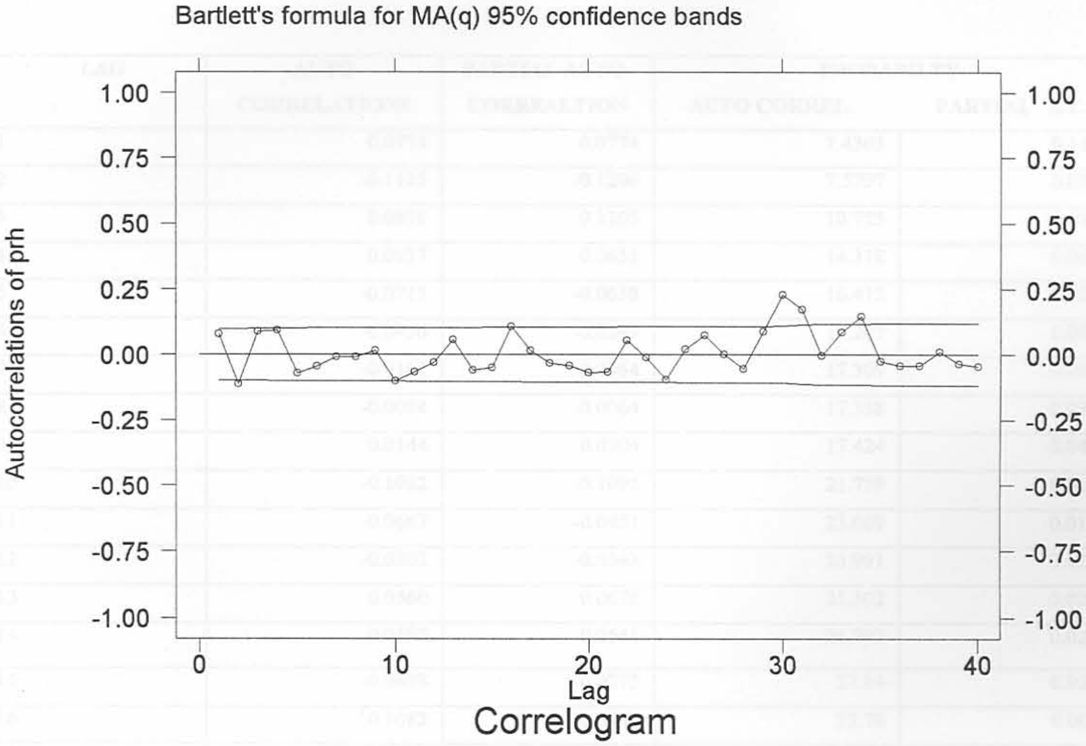

Figure 9 ACF of Residuals (using Bartlett's confidence bands)

The above graph is a plot of autocorrelations, again showing breakout during the rainy season

Table 4: ACF and PACF for 20 lags

LAG	AUTO CORRELATIONS	PARTIAL AUTO-CORREALTION	PROBABILTY	
			AUTO CORREL.	PARTIAL A.C.
1	0.0774	0.0774	2.4305	0.1190
2	-0.1125	-0.1206	7.5797	0.0226
3	0.0878	0.1105	10.725	0.0133
4	0.0937	0.0653	14.318	0.0063
5	-0.0715	-0.0658	16.412	0.0058
6	-0.0456	-0.0249	17.267	0.0084
7	-0.0101	-0.0364	17.309	0.0155
8	-0.0084	-0.0064	17.338	0.0268
9	0.0144	0.0304	17.424	0.0425
10	-0.1022	-0.1095	21.759	0.0164
11	-0.0667	-0.0451	23.609	0.0145
12	-0.0302	-0.0543	23.991	0.0204
13	0.0560	0.0679	25.302	0.0211
14	-0.0597	-0.0541	26.797	0.0205
15	-0.0498	-0.0275	27.84	0.0226
16	0.1082	0.0943	32.78	0.0079
17	0.0149	-0.0261	32.874	0.0117
18	-0.0332	0.0064	33.341	0.0152
19	-0.0442	-0.0608	34.17	0.0175
20	-0.0699	-0.1076	36.254	0.0144

The above table shows values of autocorrelations and partial autocorrelations for each of the 20 lags assumed for data analysis. The p-values for lags 2 to 20 are each less than 0.05. This shows that the autocorrelations and partial correlations are statistically significant at lags 2 to 20 at the 5% level of significance.

```
                N = 178

 6 +
   |                  *     *  *
   |
   |
   |
   |         *        *  *
   |
   |
   |    *      *   *        *  *  *
 p |
 r |
 h |      * **  *  ** *  *         * *   * *
   |
   |
   |    **   * **  *  **  ** * * *  **  *  * **
   |
   |
   |* **** *** * *      * * ** * * * ** * *  **   ** *
   |
   |
 0 + ************************************************************
   +-------------------------------------------+
      1            t               178
```

Figure 10 Time Series Plot of Predicted Allergic Rhinitis Prescriptions

The above graph shows a scatter plot of prescriptions for allergic rhinitis versus time, prescriptions varying between 0 to maximum 6 per day.

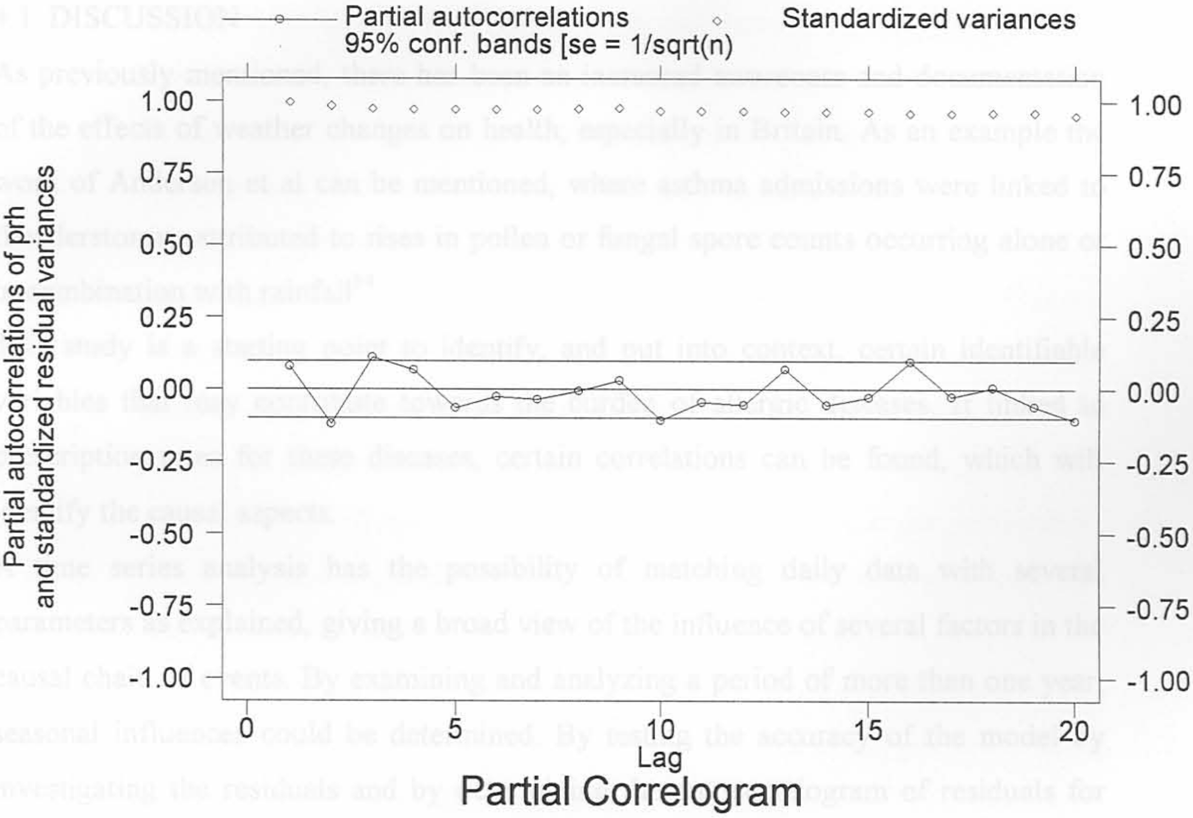

Figure 11 PACF of Residuals

The above graph shows a plot of partial autocorrelations versus lags for prescriptions for allergic rhinitis (prh). It can be seen from the correlogram plot that values of prescriptions for allergic rhinitis fluctuated during the period of study.

CHAPTER FOUR

4.1 DISCUSSION

As previously mentioned, there has been an increased awareness and documentation of the effects of weather changes on health, especially in Britain. As an example the work of Anderson et al can be mentioned, where asthma admissions were linked to thunderstorms, attributed to rises in pollen or fungal spore counts occurring alone or in combination with rainfall[14]

This study is a starting point to identify, and put into context, certain identifiable variables that may contribute towards the burden of allergic diseases. If linked to prescription rates for these diseases, certain correlations can be found, which will identify the causal aspects.

A time series analysis has the possibility of matching daily data with several parameters as explained, giving a broad view of the influence of several factors in the causal chain of events. By examining and analyzing a period of more than one year, seasonal influences could be determined. By testing the accuracy of the model by investigating the residuals and by determining the autocorrelogram of residuals for example, the model has been found to be applicable and reliable. Enough data has been found to make the deductions meaningful, since the Arima method is appropriate only for a time series that is stationary, and there should be at least 50 observations in the input data.

From the data, and with the ARIMA model, it was possible to formulate predictive equations, where possible future values for the prescriptions for asthma and allergic rhinitis can be predicted or forecasted, taking the 4 predictor variables into consideration.

This may help preparing health suppliers in coping with expected increases in prescriptions, as weather changes manifest in future.

4.2 POSSIBLE SHORTCOMINGS OF THIS STUDY

- Only weather parameters were investigated: no inclusion of allergens (for example pollen counts) was done, due to lack of sufficient data. Also were no air pollution factors accounted for, although some data (smoke, and sulphur dioxide) might have been available for at least part of the study. Concerning wind speed: this was only measured at low level, and air movement at high levels were not taken into consideration.

- Using specific drug related codes, and not disease diagnostic codes, might be more accurate and comprehensive, but could also lead to false positive findings (see also bias). The pattern of prescriptions related to the overall prescription rate (all medications) was also not investigated.
- Codes used for prescriptions reflected only visits by patients to General Practitioners at their surgeries, and excluded patients who visited Specialists, or people admitted in Hospitals (Private or Public sector). It also excluded patients who were ill, but for some reason either did not visit their usual (participating) doctor or took over-the-counter medication. Certain groups might thus not have been included in the investigation (the very ill, and the not-so-ill).
- The geographical area where data was obtained from was relatively small, due to lack of weather parameters in surrounding areas. Ideally a larger patient base and geographical area should have been used. This could then have contributed towards a more meaningful comparison between geographical areas.

4.3 SUMMARY

In a time series analysis, where data from a weather station was paired to prescriptions for allergic diseases, an analysis over a time period of one year revealed the following:

- Rainfall and Wind speed do not influence prescriptions for Asthma, as the p-values (at $\alpha = 10\%$ level of significance) are $> \alpha$
- Temperature variance (Maximum minus Minimum), and Humidity changes do influence prescriptions for Asthma, as the p- values are $< \alpha$. This fits in with previous studies where exposure to cold air triggers asthmatic attacks, as well as drying of airways.
- None of the above variables (rainfall, wind, temperature, and humidity) influences prescriptions for allergic rhinitis,_with p-values all $> \alpha$ (significantly). This is perhaps to be expected, with allergic rhinitis more

likely to be triggered by other environmental factors (allergens), which were not measured in this study.

4.4 CONCLUSION

Further work is needed to expand on what have been investigated, but meaningful insight has been acquired in the process, which will be applicable and useful to doctors and patients alike.

The findings will also be of help to the GP organization and medical aid schemes, in that better planning may be done concerning expected prescriptions, as well as insight into the pattern, and manifestations of allergic diseases.

CHAPTER FIVE

5.1 BUDGET AND FUNDING

No funding was required for the project.

CHAPTER SIX

6.1 REFERENCES

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ADDENDUM

LIST OF PLOTS, FIGURES AND TABLES

PART ONE: PRESCRIPTIONS FOR ASTHMA PAGE

PART TWO: PRESCRIPTIONS FOR ALLERGIC RHINITIS