UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Influenza Pandemic Modelling for South Africa with an Analysis of the Predicted Impact on the Healthcare Sector

Glenn Staples

A research project submitted to the Gordon Institute of Business Science, University of Pretoria, in partial fulfillment of the requirements for the degree of Master of Business Administration.

November 2006

Abstract

The predicted impact of a potential future influenza pandemic was modelled for South Africa using a multi-state Markov transition model based on key parameters from the pandemics of the twentieth century. The number of individuals falling into each of the following categories was predicted for each week in the pandemic: healthy (uninfected); infected (no treatment); infected (out-patient treatment); infected (hospital admission); infected (ICU admission); healthy (flu recovery) and dead. Four scenarios were modelled. The Mild and Severe Pandemic Scenarios were then applied to estimations of current hospital and ICU bed spare capacity in each province to provide a prediction of the impact of a pandemic on hospital capacity.

The Mild Pandemic Scenario, based on the 1957 and 1968 pandemics, showed a 9.1% total infection rate and a 0.13% mortality rate. Hospital bed capacity is stretched close to capacity, but does not exceed capacity in any province. ICU bed capacity is exceeded for all provinces during the peak of the pandemic (3-7 weeks).

The Severe Pandemic Scenario, based on the 1918 pandemic, had a 22% total infection rate with a 2.5% mortality rate. Hospital and ICU bed capacities were exceeded in all provinces for much of the pandemic.

Declaration

I declare that this research project is my own work. It is submitted in partial fulfillment of the requirements for the degree of Master of Business Administration at the Gordon Institute of Business Science, University of Pretoria. It has not been submitted before for any degree or examination in any other University.

Glenn Staples

November 2006

Acknowledgements

I would like to thank Dr Raj Raina for his advice in supervising this research project.

Sincere thanks also go to Emile Stipp, Jaco van der Merwe and Cassie Hamman for their expert advice and assistance in respect of the actuarial modelling requirements for the research.

Further thanks must go to Dr Cheryl Cohen from the National Institute of Communicable Diseases for her advice and guidance in the conceptual stages of the research.

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

TABLE OF CONTENTS

Chapter 1: Introduction to the Research Problem

The world's population suffered under the effects of three influenza pandemics during the nineteenth century; 1918, 1957 and 1968. The most devastating of these was the "Spanish Flu" of 1918 and 1919 which killed between 40 and 50 million people worldwide (Brainerd and Siegler 2003). According to Brainerd and Siegler (2003), the extent of this disaster has only been approximated by three other epidemics in world history: the Justinian Plague of the sixth century, the Black Death (Bubonic Plague) of 1348 to 1351 and the current AIDS pandemic.

Influenza is caused by a group of related orthomyxoviridae which are spread by human contact and respiratory droplet spread (Kingsbury and Wagner 1990). They infect the nasal mucosa and upper respiratory tract causing a spectrum of disease from being entirely asymptomatic to causing respiratory failure and death.

The viruses are categorized into influenza A, B and C according to the antigenic properties of their surface proteins. Type C usually only causes a mild illness, while A and B may cause epidemics. Influenza A causes the most serious form of disease (Kingsbury 1990).

The reason for the seasonal epidemics of influenza experienced by populations is that there is a very high rate of immunological variation which occurs within

the above mentior human body's ability to recognize the virus as foreign and therefore limits immunity against the virus.

This variation is caused by alterations in surface glycoproteins called haemaglutinin and neuraminidase. The first strain isolated from a human in 1933 was designated H_0N_1 on the basis of its antigenic structure. There are two types of antigenic variation, namely antigenic drift and antigenic shift. Antigenic drift is a gradual stepwise mutation of the surface antigens.

Antigenic shift is a sudden large change in antigenicity usually resulting from recombination of a human and an animal strain of influenza whilst the viruses were co-infecting the same host. Antigenic shift is the most common cause of epidemic or pandemic influenza due to the fact that the human population has very little immunity to the new virus (Kingsbury 1990).

Influenza has a very high infectivity rate as well as a short incubation period. These two factors result in a very rapid rate of spread across a population with limited immunity and in fact the Spanish Flu of 1918 spread across the globe within 3 months (Crosby 2003).

Influenza is typically not a life threatening infection to healthy individuals. It does, however, typically cause life threatening illness in the elderly or the very young, or in people who have compromised immune systems.

Twentieth Century

The Spanish Flu of 1918 was by far the most destructive of the three pandemics of the twentieth century with between 40 and 50 million fatalities. The subsequent pandemics of the twentieth century were fortunately not as severe as the Spanish Flu. Asian Flu (1957) is estimated to have killed about 2 million people, while the Hong Kong Flu (1968) killed around 1 million (World Health Organization 2005a).

Avian Influenza and the Current Pandemic Risk

In 2003 the World Health Organization published a warning that there was an increased risk of another influenza pandemic (World Health Organization 2003). This warning was based on a number of key observations and an improved understanding of influenza pandemics.

There are three pre-requisites for the start of a world-wide influenza pandemic, namely:

1. The mutation of a new influenza virus to which the human population has no, or very little immunity
2. The infection of humans by such a virus causing severe disease
3. The ability of this virus to spread efficiently and effectively from human to human (WHO 2005a)

The first two of these [illegible]en accomplished, leaving one further step before a pandemic will occur.

Motivation for Research

With the above introduction in mind, it is clear that there is more than a reasonable likelihood of an influenza pandemic afflicting the global population some time in the next few years. Unfortunately, an actual prediction of the probability of this occurrence, or of the timing of a pandemic is impossible due to the random nature of viral mutations.

Much activity has occurred recently around the planning for a possible influenza pandemic involving individuals, organizations and governments alike (Shortridge 2006) (Sleath 2006). It is clear from the description of the Spanish Flu Pandemic of 1918, that a recurrence of such a pandemic would have a dramatic effect on the world from many different perspectives.

In the light of this, it is essential that South Africa is involved in a meaningful influenza pandemic planning process. This has been recognized by the Ministry of Health as evidenced by the establishment of an Influenza Pandemic Planning Committee and the publishing of a draft Flu Pandemic Plan (South African National Department of Health 2006).

Unfortunately, plan red by the lack of any specific predictions of the impact which such a pandemic will have on South Africa. The healthcare sector, in particular, has a real need for predictions, based on proper modelling techniques, of the effects with particular reference to:

- Total patient load
- Predicted hospital admissions
- Predicted deaths
- Effect on staffing capacity

Predictions of the broad economic effects of an influenza pandemic on the healthcare sector would also be very valuable to healthcare managers and policy makers in assisting with targeted and proactive planning.

Purpose of the Study

The purpose of this study is two-fold:

1. To provide the most accurate prediction possible, given the quality of available data on influenza pandemics, of the expected extent of an influenza pandemic for South Africa in order to assist all interested and relevant parties in preparing for the possibility.
2. On the basis of the predictions in 1 above, to predict, on very high level terms, the effect which an influenza pandemic may have on South African hospitals. Once again, the purpose of this prediction is to

empower the aspects of the healthcare sector (service providers, funders, government) in the process of meaningful planning for a possible pandemic.

There are a number of critical aspects of influenza pandemic planning which are virtually impossible to make meaningful decisions on in the absence of the above predictions. The list below includes some of the key decisions which need to be made from a healthcare sector point of view:

- The possible stock-piling of anti-viral drugs including the quantities keeping in mind the considerable cost implication attached to this.
- The stock-piling of personal protective equipment (PPE) (masks etc)
- The sourcing of vaccine (if available) and in what quantities
- The rational distribution of drugs, PPE and vaccine during a pandemic
- The designation of treatment facilities and volunteer staff should the existing treatment capacity be exceeded.
- The allocation of sufficient, but affordable funds to prepare for all of the points above.

More general economic and socio-political decisions will also have to be made, including:

- Whether or not to close the country's borders
- Whether or not to enforce personal quarantine
- Allocation of drugs, vaccine etc to vital services staff (police, power generation, water provision, healthcare etc)
- Allocation of budget in preparation for a pandemic

The results of this study will facilitate more skillful decision-making in preparation for an influenza pandemic and hopefully, should a pandemic strike the country in the near future, limit the economic and social impact which it will have.

Chapter 2: Literature Review

A number of key research areas were identified which formed the framework for the literature review. The literature review will be discussed under these key areas.

Influenza

As a full description of viral structure and biology is beyond the scope of this report, only background information which is pertinent to the topics covered later in the report are discussed below.

Virology

Influenza infection is caused by a group of viruses, classified as Orthomyxoviruses. As viruses, they have the following unique characteristics of relevance:

1. They are obligate intracellular parasites (they rely entirely on plant and animal cells in order to survive; they replicate only inside animal cells, making use of animal nuclear proteins)
2. They have only one type of nucleic acid (either DNA or RNA) (Kingsbury and Wagner 1990)

Viruses are composed of central nuclear proteins (the DNA or RNA mentioned above) which are encapsulated by a viral envelope. The viral envelope consists

of a lipid bi-layer ar imal cells). The capsular proteins consist of:

1. Glycoproteins

   Which extend externally from the viral envelope, may contain enzymes, and are essential for viral infectivity (facilitate entry to host cells)

2. Matrix Proteins

   Form a structural layer at the inner surface of the viral envelope (Kingsbury and Wagner 1990).

Influenza viruses are classified into three distinct types; Type A, B and C dependent on their nuclear proteins and their matrix proteins. All three types cause clinical infection in humans, although of varying severity:

- Type A causes the most severe disease. It is the most common cause of epidemic influenza and the only type known to cause pandemic influenza
- Type B may cause from mild to severe disease and has caused epidemics in the past
- Type C causes mild disease and has not been implicated in epidemics or pandemics (Hunt 2006).

Within each type, influenza viruses are further classified according to the characteristics of the surface glycoproteins which they exhibit from their viral envelopes, namely:

- Haemaglutinnin (H) which causes agglutination of red blood cells
- Neuraminidase (N), an enzyme used in cell adherence and cleaving

The different haemaglutinin glycoproteins are given designated numbers as they are isolated and characterized. The first influenza virus isolated in 1933 was given the designation H0N1 (Hunt 2006).

Mutation and Immunity

In the course of a human infection with an influenza virus, the human body produces antibodies to the specific influenza virus (mainly to the haemaglutinin and neuraminidase glycoproteins) which then protect the individual from future infections by that particular influenza virus species (Roitt 2002). Influenza viruses, however, mutate frequently to produce new variants with different H and N glycoproteins in order to evade host immune responses.

There are two distinct types of mutation which influenza viruses undergo in order to evade host immune responses, namely antigenic drift and antigenic shift.

Antigenic drift is a process of minor mutations which occurs over a period of time. Antigenic drift is the most common cause of the seasonal influenza epidemics which the world's population experiences each winter. There is usually some degree of residual immunity within the human population due to the elements of the virus which have not changed during the drift. While the common current understanding holds that influenza viruses mutate by a process of mostly positive Darwinian selection, recent evidence has suggested

that this understanc Viboud, Holmes, Koonin and Lipman 2006).

Antigenic shift, on the other hand, is the sudden, dramatic change in the antigenic structure of the virus which creates a virus to which the human population has little or no immunity. These antigenic shifts occur infrequently and usually result in an influenza pandemic. Antigenic shift is usually the result of recombination of human and animal influenza viral genes. This occurs when there is co-infection of the same animal with both human and animal influenza viruses. Antigenic shift is thought to occur most commonly in pigs (Flint 2004). According to Capua and Alexander (2002), there have been four antigenic shifts in the past century, all of them causing influenza pandemics, namely:

1. H1N1 1918
2. H2N2 1957
3. H3N2 1968
4. H1N1 1977

Treatment and Prevention

The vast majority of cases of human influenza are treated only symptomatically, using analgesics and anti-pyretics to control the unpleasant symptoms of pain and fever (Berkow, Fletcher and Beers 2000). There are, however, specific antiviral drugs which are effective in reducing the severity and duration of influenza. While a full discussion of the treatment of influenza is beyond the scope of this report, a brief discussion of the recommended drugs for pandemic influenza will be undertaken.

The Neuraminidase inhibit the neuraminidase glycoproteins (see previous section) and thereby effectively inhibit viral replication, are the most effective therapeutic agents available for the treatment of influenza (Aoki, Macleod, Paggiaro, Carewicz, Sawy, Wat, Griffiths, Waalberg and Ward 2003).

Neuraminidase Inhibitors (Oseltamivir and Ranamivir) have been shown to be effective in preventing spread and reducing the duration of the clinical effects of influenza in household contacts of influenza infected patients. It is also well tolerated (Welliver, Monto, Carewicz, Schatteman, Hassman and Hedrick 2001). While the Neuraminidase Inhibitors have been shown to be effective in reducing the duration and severity of disease in human and avian influenza if administered within the first 48 hrs after onset of symptoms, there is some concern as to whether or not it is cost effective for use in the general population as a preventative measure (Cram, Blitz, Monto, Fendrick 2001). Oseltamivir has been shown to be 70-90% effective in preventing influenza in household contacts of influenza infected patients. It has also been shown to reduce the duration of illness by 24 to 72 hours if administered within the first 48 hours of infection (Uhnoo, Linde, Pauksens, Lindberg, Eriksson and Norrby 2003) (Aoki et al 2003).

It has been recommended that the neuraminidase inhibitors be used as the first-line therapeutic agents for the initial phases of an influenza pandemic (i.e. prior to the production of a specific vaccine) in high-risk patients and for prophylaxis

in critical staff (e.g. practitioners etc) (World Health Organization 2004).

Vaccination

Human influenza vaccination was first pioneered in the 1940's, representing a breakthrough in the struggle against influenza. Current influenza vaccines are produced using inactivated virus grown on hen's eggs. The World Health Organization selects the two Type A strains and one Type B strain which are used in the production of the annual vaccine (Uhnoo et al 2003).

While anti-viral agents have shown some efficacy in treating and preventing influenza, vaccination remains the gold standard in the prevention of the disease (Uhnoo *et al* 2003). Recent research has shown that current influenza vaccines are 73% effective in preventing disease from the influenza types which have been included in the vaccine production process. They are, however, only 37% effective in preventing influenza-like illness in the general population. This is as a result of the choice of candidate strains for the vaccine not adequately covering the strains which eventually afflict the population (Jefferson, Bianco and Demicheli 2002).

Despite the relatively low efficacy in preventing influenza-like illness, vaccination is still recommended for high-risk patients (elderly and patients with co-existing chronic diseases) as it has been shown to reduce admission to hospital by 50% and mortality by 68% in this group (Uhnoo et al 2003).

While early research on Avian influenza showed some effectiveness of vaccines in reducing the severity and infectivity of Avian Influenza in birds, the effectiveness for prevention of the disease was poor (Swayne, Beck, Garcia and Stone 1999). More recent research suggests that emergency vaccination campaigns for birds can be successful in controlling Avian Influenza outbreaks if combined with biosecurity (control of bird movements) measures (Capua and Marangon 2003).

The only effective means of preventing a future influenza pandemic is the vaccination of a significant proportion of the world's population with a specific influenza vaccine. The most concerning problem in this regard is the fact that global vaccine production capacity is limited and will fall many billions of doses short of the requirement should a pandemic strike in the near future (World Health Organization 2006c). The World Health Organization's "Global Pandemic Action Plan to Increase Vaccine Supply" (2006c) states that the Global Vaccine Action Plan will take 5 years and between US $ 3 billion and US $ 10 billion before vaccine production can meet the demand for an influenza pandemic.

Some of the important issues which will need to be addressed in the event of a future influenza pandemic regarding vaccination are as follows:

- What proportion of the population should be vaccinated, assuming access to sufficient vaccine?
- Which population groups should be preferentially vaccinated?
- What is the economic impact of such a vaccination programme?

A large amount of research work and modelling is ongoing in an attempt to answer some of the questions posed above. Most current Influenza Pandemic plans have targeted high-risk individuals and vital services personnel as the population groups which will receive priority in the allocation of vaccine when it becomes available (World Health Organization 2004)(Cox, Tamblyn and Tam 2003)(Mabuya, Singh and Masilo 2005) (South African National Department of Health 2006).

Some debate, however, exists as to the targeted proportion of the population which should be vaccinated. Patel, Longini and Halloran (2005) demonstrated in their Influenza Pandemic Model that there was little improvement in case rates and mortality rates for population vaccination rates above 40%. Meltzer, Cox and Fukuda (1999) in their economic predictions of an influenza pandemic in the United States, predicted that a vaccination campaign which vaccinated 60% of the population demonstrated the greatest net economic saving to the country.

There is currently little evidence to suggest that HIV positive patients have poorer outcomes with influenza infections although most concensus seems to suggest that patients who are already classified as suffering from AIDS will have a higher incidence of complications and death from influenza (Skiest, Kaplan, Machala, Boney and Luby 2001).

Epidemic/ Pandemic Modelling

Classical epidemic disease modelling involves a bottom-up approach of predicting the spread of the infection within a given theoretical population based on assumptions concerning the characteristics of the specific infection and the population (Giesecke 1994). The following specific characteristics are required as assumptions or predictions for the modelling process:

1. The probability that an infected individual will transmit the infection to a susceptible contact
2. The rate of such contacts within the population
3. The duration for which the infected individual remains infectious
4. The proportion of the population which is susceptible at that time.

The basis of this modelling process relies heavily on a knowledge or prediction of the Basic Reproductive Number (R0). R0 is defined as the average number of infectious cases which result from each primary infectious case within a population (assuming that the entire population is susceptible) (Giesecke 1994). R0 is therefore a theoretical value only, as the only time that an entire population is susceptible to an infection is for the first case of an entirely new infection (i.e. no prior immunity in the population). There is a high correlation between the value of R0 for an influenza epidemic/ pandemic and the severity of such an epidemic (Viboud, Tam, Fleming, Handel, Miller and Simonsen (2006).

While it is common for epidemiologists to calculate R0 for known infections, it is impossible to calculate such a value for an infection which does not yet exist. Consideration was given to the possible use of R0 from previous influenza pandemics for the modelling of a future pandemic. The R0 for influenza epidemics ranges between 1.2 and 1.8. The epidemic of 1951 had an R0 of 2.1 (2.2 in Liverpool) which was equivalent to that of the 1918 Spanish Influenza Pandemic (Viboud et al 2006).

As can be seen, there is a wide range of possible predictions for R0 for a future influenza pandemic. This inability to accurately predict R0 for a future pandemic raises serious concerns around the validity of any models which are based on the classical epidemic modelling approach.

A number of generic influenza pandemic models have been devised for a number of countries. The majority of these models have followed the approach of modelling the basic characteristics of a future pandemic on the same basic characteristics as calculated for the major pandemics of the past century (Patel et al 2005)(Meltzer et al 1999)(Longini and Halloran 2004)(Hagenaars, Van Genugten and Wallinga 2003).

Solomon and Isham (2000) suggest that disease surveillance and clinical data collection are vital components in the process of epidemic disease modelling. They propose a number of possible mathematical models including the Susceptible-Infected-Removed (SIR) Model and the Susceptible-Infected-

Susceptible (SIS) M relevant for influenza on the basis that infected individuals either die or survive and become immune (i.e. they are no longer susceptible).

As mentioned previously, the prediction of the clinical behaviour of an influenza pandemic based on knowledge of the current Avian Influenza characteristics is limited due to the likelihood that the virus will lose some pathogenicity in the process of mutation to enable for effective human to human spread (Rambon 2004).

Past Influenza Pandemics

Spanish Flu (1918)

The devastating influenza pandemic of 1918-19 was dubbed “Spanish Flu” in the mistaken belief that it originated in Spain. This mistaken belief resulted from the fact that the Spanish media were the first to publicize its existence due to the fact that they were one of the few countries at the end of World War 1 which had few restrictions on the media (Tognotti 2003).

The first recorded cases of the pandemic in fact occurred at a military camp in Kansas, USA in March 1918 (Brainerd 2003). It spread to Europe within a couple of weeks aided by the large movement of military troops to Europe as a result of World War 1. The rapid spread and high mortality rate are believed by some authors to be the result of the poor and cramped living conditions to which

the soldiers were su 05). It had further spread to Australia, New Zealand and India by June 1918.

A second, more deadly wave started simultaneously in France, Sierra Leone and Boston in September 1918 and spread rapidly around the world. This was later followed by a third, less severe wave in early 1919 limited to certain parts of the world only.

One of the distinctive characteristics of the 1918 pandemic was the fact that it caused a peculiarly high mortality rate amongst young healthy individuals in the age group 15 to 40 years. This resulted in a “W” shaped mortality curve instead of the typical “U” shaped curve seen with the very young and elderly being worst affected (Philips and Killingray 2003). There appears to have been a social bias to the effects of the Spanish Flu (Mamelund 2006).

Crosby (2003) reports that the first wave of illness typically lasted 3-4 days followed by recovery. A proportion of people then were afflicted by a second wave of illness which was severe, resulting in shortness of breath and rapid death. Autopsies performed on the deceased revealed thick fluid throughout the lungs.

Some recent evidence suggests that the Spanish Flu may in fact have arisen in a military camp in France as a result of the mixture of humans, animals and noxious gases (Oxford, Lamblein, Sefton, Daniels, Elliot, Brown and Gill 2005).

Asian Flu (1957) and Hong Kong Flu (1968)

The Asian and Hong Kong influenza pandemics were substantially milder in their overall impact than the Spanish Flu. Although their total infection rate was as high, or even higher, than that of the Spanish Flu, the disease was not nearly as virulent and thus had mortality rates dramatically lower than the 1918 pandemic. The Spanish Flu killed 40-50 million people while the Asian and Hong Kong Pandemics killed approximately 2 million and 1 million people respectively (WHO 2005).

The table below represents infection rates and mortality rates as predicted for the Asian and Hong Kong Pandemics (Patel *et al* 2005).

Age Group	0-4	5-18	19-50	51-64	>65
Asian infection rates	35.2%	55.4%	24.6%	19.9%	13.9%
Hong Kong infection rates	34.8%	34.8%	34.6%	32.2%	30.5%
Deaths/ 10000 illnesses	0.263	0.210	2.942	2.942	199.8

Avian Influenza

As discussed in Chapter 1, the reason for the heightened alert around Influenza Pandemic preparedness globally, is the presence and behaviour of the current Avian Influenza (H_5N_1).

The new virus is the a Virus (H_5N_1) which was first isolated in Gaundong Province, China in 1996 (WHO 2006b). The second pre-requisite for an influenza pandemic (ability to cause severe disease in humans) was met in 1997, and then again in 2003 when human infections with H_5N_1 were recorded in South East Asia with severe disease and a high mortality rate.

H_5N_1 has spread rapidly amongst wild birds in Asia and is now spreading via the birds' migratory routes to many other parts of the world. This spread within the avian population has resulted in further human infections in other parts of the world (World Health Organization 2005a).

The probability of the H_5N_1 virus accomplishing the final mutation to enable efficient human to human spread is increased by contact with current human influenza virus. Such contact can occur in either humans or pigs which are infected with both viruses simultaneously. Thus, as the incidence of human infections increases, so the probability of the H_5N_1 virus making the final mutation increases.

One of the major reasons for the extent of concern about an imminent pandemic is the fact that the current H_5N_1 is particularly virulent. Current mortality rate for human infections of H_5N_1 is 59% with 258 cases of infection and 153 deaths from 2003 until the present (WHO 2006).

While there are oth ılating presently amongst birds involving other serotypes of the virus (H_7N_1; H_7N_3), none have caused human infection to date and are thus not of particularly great concern from a human health perspective (Dundon 2006).

While an understanding of the current avian influenza is very important in planning for a pandemic, the major limitation of this relates to the inability to accurately predict the clinical behaviour of the virus once it has mutated to efficiently transfer from human to human. The virus is predicted to lose some of its virulence in the mutation process (i.e. mortality rate is unlikely to remain as high as 59% above) (WHO 2005a). This determines the proposed methodology of making use of parameters from the previous influenza pandemics to drive the proposed model as opposed to using predictors from the current H_5N_1.

South African Demographics

Demographic information for South Africa is a vital component of the modelling process. The basic model used is adjusted for the demographic and population statistics for each province. The most recent available population prediction from Statistics SA is used (Stats SA 2006). Table 1 below is a brief summary of the population estimates per province for mid-2005 from Statistics SA.

Table 1

SA Population Mid 2005		
Province	**% of Population**	**Population**
Eastern Cape	15.0%	7.0
Free State	6.3%	3.0
Gauteng	19.2%	9.0
KwaZulu Natal	20.6%	9.7
Limpopo	12.0%	5.6
Mpumalanga	6.9%	3.2
Northern Cape	1.9%	0.9
North West	8.2%	3.8
Western Cape	9.9%	4.6
Total	100.0%	46.9

Chapter 3: Research Questions

1. What will be the predicted effect of a potential influenza pandemic on South Africa with respect to number of cases, number of hospital admissions, number of ICU admissions and number of deaths?

2. What will be the predicted effect of a potential influenza pandemic, as modeled in question 1 above, on the healthcare sector with respect to incremental hospital and ICU admissions as compared with current spare capacity per province?

Chapter 4: Research Methodology

The two major components involved in this research were the documentary research required to provide the parameters for the modelling process, and a predictive study, utilizing the above mentioned documentary research in order to provide predictions for the country and the healthcare sector. A breakdown of the components has been listed below:

1. Documentary Research, in the form of case study research, provided the basic parameters required for the modelling process (Welman and Kruger 2001). The three most recent pandemics of the twentieth century were studied in an attempt to find the most likely predictions of key parameters in order to model a future pandemic, namely:
    1. Influenza attack rates:
        - The proportion of the global population which is estimated to have been infected by the pandemic influenza virus in each of the previous pandemics.
    2. Incubation period:
        - The duration of time between exposure to the virus and a patient showing signs of disease and becoming infectious.
    3. Rate of hospital admission
        - The proportion of the influenza infected population which will require hospital admission due to the effects of the influenza.
    4. Rate of intensive care unit (ICU) admission

- admitted patients which require admission to an intensive care unit due to the severe effects of the influenza infection.

5. Mortality rate
    - The proportion of the total population which died due to the influenza pandemic.
6. Demographic data for South Africa per province in order to model the pandemic more specifically, in particular the population estimates per province.
7. Healthcare Sector information to enable a prediction of the impact on the sector:
    1. Number of hospital beds per province
    2. Number of ICU beds per region
    3. Current capacity utilization figures (i.e. spare capacity at present)

Due to the inability to accurately predict the behaviour of a future pandemic (as discussed more fully above), four separate models were created based on the key parameters from the three previous twentieth century pandemics (1918, 1957 and 1968). This has created a range of possibilities which constitute the most likely predictions for the behaviour of a future pandemic.

The model was extended down to provincial level within South Africa in order to predict the case load for hospitals within each province. Case loads were then compared with current predictions of hospital spare capacity in order to predict

the point at which cı oaded and the number of influenza patients which would be denied necessary treatment due to the lack of capacity within the hospital sector.

Actuarial Modelling of the Impact on South Africa

The spread of the influenza pandemic was modeled using a statistical technique referred to as a Multi-state Markov Transition Model. This technique assigns each life in the population being modeled to a particular state, which indicates the health status of the life under consideration. States are defined in a mutually exclusive manner such that a life can fall into only one particular state at a given point in time. Transfer rates between the various states are then computed in order to ascertain the flow of the lives in the population between the various states. In a typical basic Markov model with three states (Healthy, Sick and Dead) a life would typically start off in the Healthy state, make a number visits to the Sick state with subsequent return to the Healthy state and then ultimately end up in the Dead state. Once the life has entered the Dead state it will remain there for the duration of the modelling process. A state such as the Dead state from which a life cannot leave is termed an "absorbing" state (Chang, Krinik, Randall and Swift 2006).

The lives in each state were split according to a number of demographic features such as Age, Province and AIDS status. A unique set of transition probabilities was computed and hence the modelling of the movement between

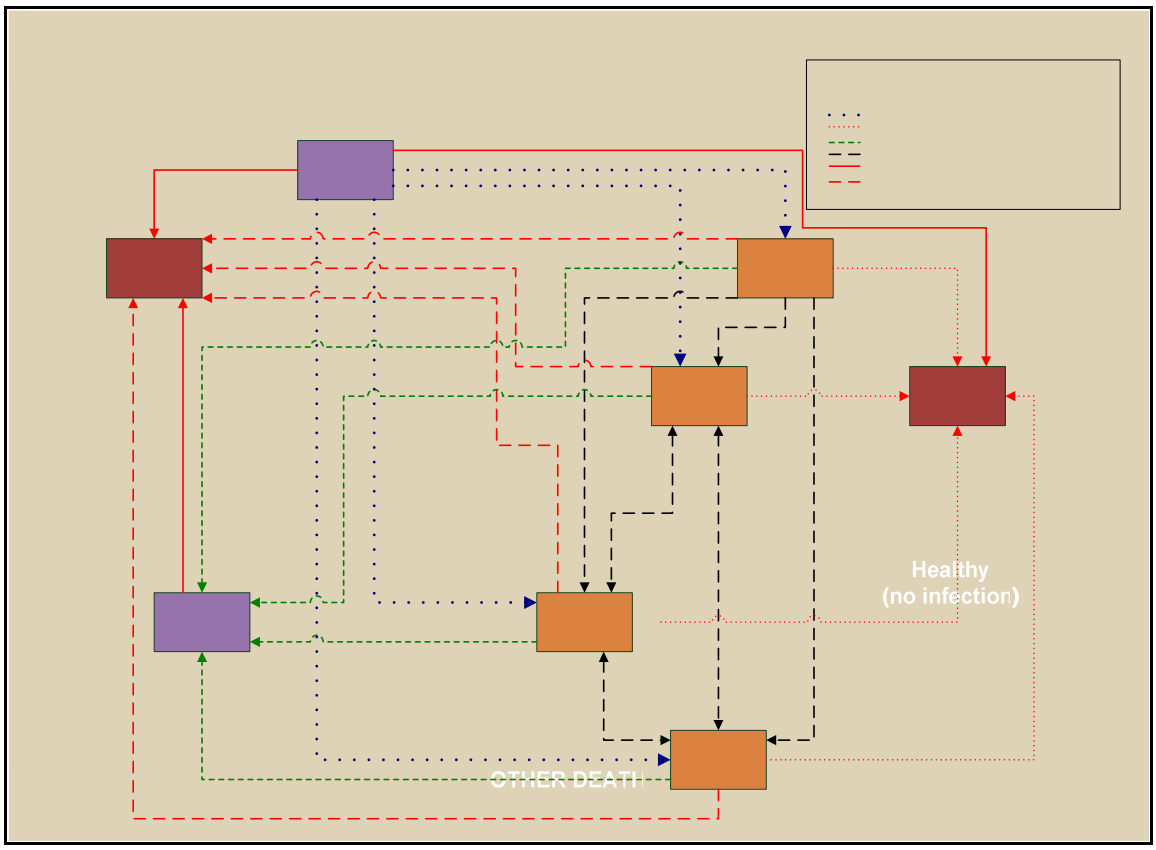
the various states for each of the unique combinations of the above-mentioned demographic factors. It was assumed that, given the fairly short expected duration of the pandemic, the movement of lives between the various demographic groups (e.g. individuals changing AIDS status during the epidemic) will be negligible. Similarly new entrants into the population due to either births or migrations during the modelling timeframe are not considered.

A multi-state modelling process was chosen as the best means of providing the specific predictions required for each of the required states of being. The following is a list of the possible states chosen for the model:

1. Healthy (uninfected)
2. Influenza infected but receiving no treatment
3. Influenza infected requiring out-patient treatment
4. Influenza infected requiring hospital admission for treatment
5. Influenza infected requiring ICU admission for treatment
6. Healthy (recovered from influenza)
7. Dead (from influenza or other causes)

The Markov property was used for the model, dictating that the future value of a process is independent of the past if the current value of the process is known. The resultant Markov Chain is graphically represented by the transition graph below (Figure 1):

Figure 1



In the Transition Graph above, the states are represented by the block diagrams and each arrow represents a possible transition. For example, assuming that an individual is healthy at a point in time; that individual has a probability of being in one of the following states in the next time period:

- Remains healthy (“Healthy”)
- Becomes infected but elects not to seek medical treatment (“Flu Sickness; Symptomatic”)
- Becomes infected and seeks medical treatment as an out-patient (“Flu Sickness; Out-of-hospital”)
- Becomes infected requiring hospital admission due to condition (“Flu Sickness; In-hospital”)

- Becomes infe t (ICU) admission due to condition (“Flu Sickness; ICU”)
- Dies from influenza (“Flu Death”)
- Dies from other causes (“Other Death”)

The multi-state transition model then relies on the assignment of probabilities to each of the transitions stated in the graph above. These transition probabilities then determine the movement of people between the relevant states from one time unit to the next.

The time unit chosen for the model was one week. The reasons for this decision are the following:

1. Due to the fact that the pandemic is likely to last for at least six months (evidence from previous pandemics), a daily unit time would have made the model very complex whilst adding little additional value in terms of predictions.
2. A unit of time greater than one week would have reduced the accuracy of the model as many of the probable transitions would not have been accounted for by the model (see explanation in next paragraph)

One of the weaknesses of this modelling approach is the fact that the model only predicts the state which an individual is in at the end of each week. The model ignores those individuals who make more than one transition in a week.

For example, a hea /eek could fall ill, recover from the illness and die from causes other than flu within a week. This model only captures the move from the healthy state to death at the end of the week. This results from the use of discrete time intervals.

Ideally the model should allow for changes in states in continuous time. Such a model is known as a Markov jump process and the parameterisation of such a model involves integrals and differential equations. The differential equations in a two or three state Markov jump process are reasonably easy to derive. However, in an eight state model such as this, the solving of such differential equations is complex. On the grounds that this model was based on empirical as opposed to actual data, the introduction of the additional complications of a Markov jump process was not considered necessary.

The Base Transition Matrix

The base transition probabilities used in our model are contained within the matrix below (Table 2).

Table 2

	Uninfected	Flu Recovery	Flu No Treatment	Flu Out-patient	Flu In-patient	Flu ICU	Flu Death	Other Death
Uninfected	99.630%	0.000%	0.250%	0.075%	0.020%	0.005%	0.010%	0.010%
Flu Recovery	0.000%	99.990%	0.000%	0.000%	0.000%	0.000%	0.000%	0.010%
Flu No Treatment	0.000%	24.640%	50.000%	25.000%	0.250%	0.050%	0.050%	0.010%
Flu Out-patient	0.000%	43.590%	0.000%	55.000%	1.000%	0.250%	0.150%	0.010%
Flu In-patient	0.000%	9.240%	0.000%	40.000%	45.000%	0.750%	5.000%	0.010%
Flu ICU	0.000%	1.490%	0.000%	3.500%	10.000%	35.000%	50.000%	0.010%
Flu Death	0.000%	0.000%	0.000%	0.000%	0.000%	0.000%	100.000%	0.000%
Other Death	0.000%	0.000%	0.000%	0.000%	0.000%	0.000%	0.000%	100.000%

The percentage in each cell reflects the probability of an individual moving from the state in the row heading to the state in the column heading. For example, the probability of an individual moving from the state “Flu No Treatment” to the state “Flu In-patient” in any week is 0.25% (3rd column; 5th row).

The specific probabilities within the matrix were formulated as a combination of empiric data (where available) and input from medical experts within the field of infectious diseases whilst at the same time adhering to the predicted parameters derived from the case studies of the previous pandemics. The accuracy of this model will thus be greatly improved following the outbreak of the next pandemic due to the fact that these predicted probabilities will be replaced with probabilities from observational studies on the pandemic itself. As discussed in detail in Chapter 2, however, the disease does not currently exist

and therefore such a [illegible]ble. Further to this, due to the dramatic impact which the next influenza pandemic is likely to have on the human population, combined with the amount of time necessary to plan adequately for its occurrence, the luxury does not exist to delay predictive modelling until the virus has mutated.

Table 3 below summarizes the predicted mortality rates of the past pandemics studied:

Table 3

Pandemic	Est Death Toll	World Population	Mortality Rate
1918	50 million	1.8 billion	2.500%
1957	3 million	2.9 billion	0.050%
1968	1 million	3.6 billion	0.025%
2007	1.6 million	6.5 billion	0.025%
2007	162 million	6.5 billion	2.500%

Population Vector

The Base Transition Matrix probabilities (as per Table 2 above) were then used to calculate the number of people in each state at the end of each future week.

Firstly, the number of people in each state was expressed as a vector with each entry corresponding with the states in the Base Transition Matrix. Assuming that all individuals are healthy at the start of the pandemic, then the population vector at the start of the pandemic can be expressed as:

$$\overline{X}_0 = \begin{bmatrix} \text{Everybody} \\ \text{healthy} \end{bmatrix} \quad 0 \quad 0 \quad 0 \quad 0 \quad 0 \quad 0 \quad 0 \quad \ldots (1)$$

The population vector *X* at any time *n* is then given by the following formula:

$$\overline{X}_n = \overline{X}_{n-1} \bullet P \qquad \ldots (2)$$

The population vector at the start defined by (1) was then used together with the relationship with the Base Transition Probability Matrix given in (2) in order to determine the number of people in each state at the end of each future week.

The relationship given in the Base Transition Matrix (2) greatly simplifies the analysis of the movement of people between different states. However, the following very important features from the Base Transition Matrix should be noted:

- Either of the death states (Flu or Other) are by necessity permanent (i.e. individuals will remain in this state with a probability of 1).
- All individuals who move into the “Healthy Flu Recovery” state are deemed to be immune and therefore cannot contract the infection again. This is in keeping with current understanding of influenza (see Chapter 2). The individual could therefore either stay healthy or die from causes other than flu death. Although the recovery from influenza does not confer absolute immunity, the immunity conferred approaches 100% and therefore this assumption is deemed adequate for modelling purposes.

Adjustments to the

A simple Base Transition Matrix as described above is not capable of allowing for other variables which may have an influence on the specific transition probabilities. Due to the fact that a number of other factors have an influence in an influenza pandemic, the Base Transition Matrix was modified to take these other variables into account as follows:

- The probability of each individual within the population becoming infected will increase in the early stages of the pandemic due to the fact that there are an increasing number of infected individuals from whom to catch the infection. Thus these probabilities increase each week in the early stages of the pandemic.
- As discussed in Chapter 2, the infectivity rate in a population decreases in proportion to the size of the susceptible portion of that population. Therefore, as the number of individuals within the population who have recovered from influenza, and are thus immune, increases, so the infectivity rate decreases. This process continues until the epidemic/ pandemic burns itself out. In order to adequately account for the increasing infectivity during the initial stages as well as the decreasing infectivity due to progressive immunity, the Transition Matrix was adjusted for each successive week in the pandemic as per the Herd Immunity Factor (described below).
- The Base Transition Matrix does not allow for variations within the demographics of the population. Further variables were therefore introduced to cater for the following demographic variables:

  - Mortal npared with young adults and children
  - Mortality rates in AIDS sufferers is likely to be higher than the general population

- The Base Transition Matrix assumes that all individuals who require hospital admission and ICU admission will be admitted to the respective facilities. This is obviously not true due to the limited spare capacity of hospitals and ICU's in South Africa. The model was further developed to adjust the basic transition matrix probabilities as soon as capacity within the respective service was exceeded. For example, in the event that a patient, admitted to hospital with influenza, required ICU admission but could not be admitted due to capacity constraints, this patient's probability of death increased from 50% to 90%.

The transition matrices were adjusted for the demographic variables on the following basis:

- Sixteen age categories
- AIDS status
- Province

The data for the respective demographic variables were drawn from the latest publications of Statistics South Africa (2006).

Herd Immunity Fac

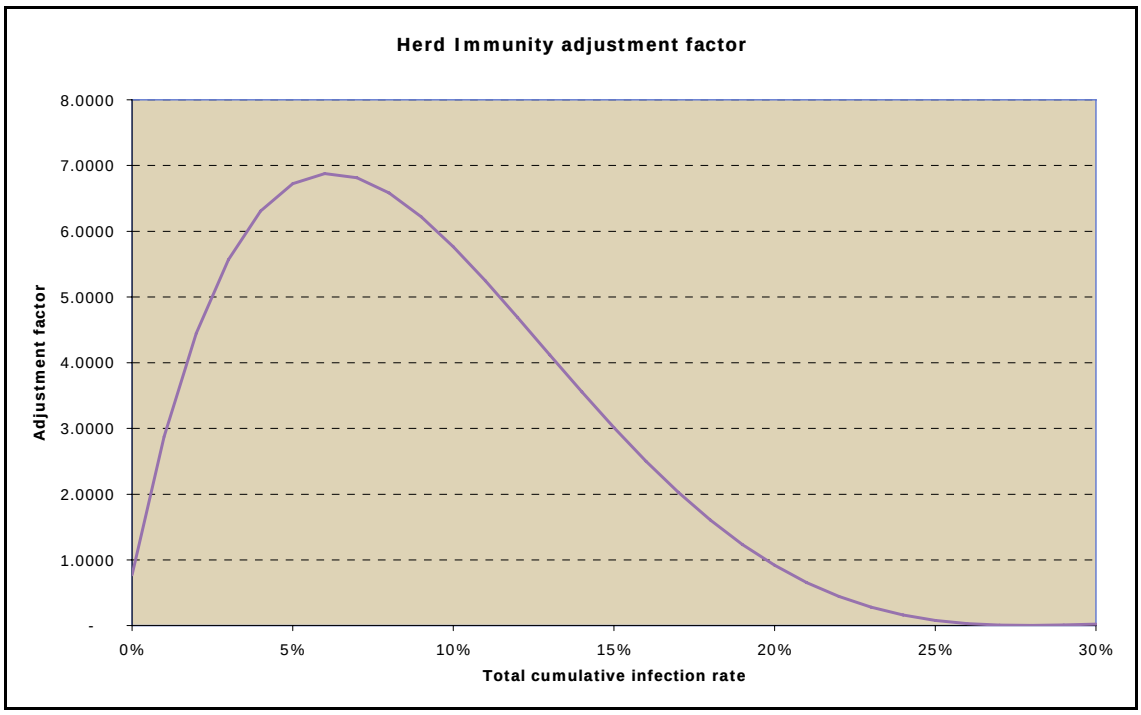
The Base Transition Matrix was adjusted to cater for the increasing immunity of recovered individuals by applying a factor to the rate of new infections at the start of each future week. Based on evidence from the literature (see Chapter 2) it was assumed that there would be no new infections once 30% of the population were immune (Herd Immunity).

Further to this, the probability of each individual becoming infected initially increases as the infection spreads in the population (i.e. there is an increasing force of infection). At some point this probability will start to decrease as the population approaches herd immunity.

This variability was achieved by adjusting the probability of moving from an initial healthy state (not infected) to one of the four flu states. This adjustment factor was started at 1 at the beginning of the pandemic and increased to a maximum adjustment factor of 7.0 when approximately 7% of the population had been infected. This implies that the infection rate will be seven times higher compared to the start of the pandemic. From this point the adjustment factor was progressively reduced to 0 at the point where the overall infection rate of the population reaches 30% (Herd Immunity; i.e. no new infections are expected).

Figure 2 below shows the adjustment factor for different levels of cumulative infection rate within the population:

Figure 2



With the adjustment variables built into the Base Transition Matrix, a very large number of specific transition matrices are created for each demographic component and for each week in the pandemic. One such matrix has been included below (Table 4) for a specific category, namely:

- Age over 70 years
- AIDS sufferer
- 10% of the population has been infected

Table 4

	Uninfected	Flu Recovery	Flu No Treatment	Flu Out-patient	Flu In-patient	Flu ICU	Flu Death	Other Death
Uninfected	87.257%	0.000%	5.474%	3.284%	2.627%	1.095%	0.088%	0.175%
Flu Recovery	0.000%	99.800%	0.000%	0.000%	0.000%	0.000%	0.000%	0.200%
Flu No Treatment	0.000%	4.256%	34.546%	25.909%	0.432%	0.173%	34.546%	0.138%
Flu Out-patient	0.000%	5.014%	0.000%	37.958%	1.150%	0.575%	55.211%	0.092%
Flu In-patient	0.000%	0.073%	0.000%	1.266%	3.562%	0.119%	94.974%	0.006%
Flu ICU	0.000%	0.002%	0.000%	0.017%	0.124%	0.866%	98.990%	0.001%
Flu Death	0.000%	0.000%	0.000%	0.000%	0.000%	0.000%	100.000%	0.000%
Other Death	0.000%	0.000%	0.000%	0.000%	0.000%	0.000%	0.000%	100.000%

An analysis of the matrix reveals that the individual's chance of being infected is higher than the Base Transition Matrix and the probability of an adverse outcome from the disease is dramatically higher. This is consistent with the expected outcome of a 70 year old AIDS sufferer who is infected at this stage of a pandemic.

Limited Hospital Bed and ICU Bed Capacity

As previously discussed, the model was designed to take account of the limitations which currently exist in South Africa with respect to hospital bed and ICU bed spare capacity.

In order to accomplish this, the total number of hospital beds was estimated using published data (Stander 2004). This included 130 000 public and 25 000 private hospital beds.

The most extensive ity within the healthcare sector in recent years was completed by Broomberg (2006) for the research report into the viability of a potential Low Income Medical Scheme (LIMS). This analysis was used as the basis for the prediction of spare capacity. The report indicates that private hospitals currently operate at 59% average occupancy, whereas public hospitals operate at approximately 90% average occupancy. There are about 130 000 public hospital beds and about 25 000 private hospital beds in total. Therefore, using the occupancy assumptions of 59% and 90% for private and public hospitals respectively, this indicates availability of between 20 000 and 25 000 hospital beds for influenza patients, assuming that current capacity is maintained during a pandemic.

A similar process was followed for ICU beds. Approximately 2700 ICU beds are registered within the private sector, with an occupancy exceeding 80%. Reliable statistics concerning ICU bed numbers and occupancy within the public sector was not available. While the public sector is known to have significantly more ICU beds than the private sector, the occupancy rates are also significantly higher. With these factors in mind, an assumption was made that the public sector had the same number of ICU beds available as the private sector, taking the total available beds to 1500.

The model demonstrates that the available ICU beds are very rapidly fully occupied in the event of a pandemic. As such, the assumption was made that a

dramatically increas vent that individuals who require ICU facilities could not access them due to capacity constraints.

No provision was made for the establishment of temporary hospital facilities due to the fact that no such contingency planning exists currently and the effectiveness of such facilities in improving patient outcomes is difficult to predict.

A further variable which has not been addressed in the model is the substantial effect which the pandemic will have on healthcare staff due to absenteeism as a result of illness or paranoia. While it is still possible to estimate this effect, it is very difficult to estimate the extent of “voluntary quarantining” which un-infected healthcare staff will impose (i.e. stay away from work) in order to protect themselves and their families (Blendon, Benson, Wellman and Herrman 2006). Despite the fact that it has not been modelled, the effect which absenteeism and disrupted basic services (e.g. water, electricity) will have on healthcare service delivery in a devastating pandemic is likely to be pronounced. With this in mind, the current bed capacity may be exceeded with non-influenza (due to a reduction in staffed available beds) patients before even taking the influenza patients into account.

Population and Demographic Assumptions

The total South African population at the start of the pandemic is 47 390 900, based on the most current available estimate from Statistics South Africa (Statistics SA 2006).

The population was then further stratified into other demographic groups as per statistics derived from Statistics SA (2006) and the Actuarial Society of South Africa (2005), namely age, province and AIDS status.

Age

The population can be split as per Table 5 below for the different age categories:

Table 5

Age	Population Size
0-14	15 189 364
15-19	5 267 500
20-24	4 540 879
25-29	4 160 667
30-34	3 532 552
35-39	3 247 987
40-44	2 769 730
45-49	2 207 127
50-54	1 731 983
55-59	1 274 408
60-64	1 126 404
65-69	833 127
70-74	667 691
75-79	388 626
80-84	286 489
>84	166 365
Total	**47 390 900**

AIDS Status

The population can be split as follows between those currently living with AIDS and those who are HIV negative or HIV positive but not yet defined as having AIDS (Actuarial Society of South Africa 2005).

Table 6

AIDS Status	Population
AIDS	837 726
Non-AIDS	46 553 174
Total	**47 390 900**

Province

The population split according to province is shown in Table 7 below:

Table 7

Province	Population
E. Cape	6 806 012
Free State	2 862 053
Gauteng	9 344 125
KZN	9 966 752
Limpopo	5 576 164
Mpumalanga	3 302 148
North West	3 879 846
N. Cape	869 922
W. Cape	4 783 878
Total	**47 390 900**

The four scenarios produced during the first section of the modelling process as described above, were used as a basis for making more specific predictions regarding the burden which will be placed on the South African hospitals. This modelling was based specifically on the South African hospitals and the impact which an influenza pandemic is predicted to have on bed capacity and occupancy levels.

In order to achieve this, more detailed information was required concerning the number of hospital and ICU beds which are available and their relative occupancy levels. From this, the spare capacity within the current system was estimated, per province, and the results used in predicting the implications for an influenza pandemic. The South African hospital sector is divided into public hospitals and private hospitals with differing statistics between the two groups.

Data Collection and Estimation

Detailed and reliable data in respect of hospital and ICU beds and occupancy levels for the whole country is not available. Data that was available was used, and in instances where specific data was lacking, generalizations were used based on the reliable data available. The specific details of the process followed are summarized below.

All hospital beds i stered with the National Department of Health. This registry therefore represents the most accurate source of hospital bed numbers and was used as the source for this research (Stander 2004). The bed numbers are further categorized according to province and split between public and private.

Occupancy Levels

Extensive research was performed in respect of spare capacity within the private hospital sector as part of the Consultative Investigation into Low Income Medical Schemes (Broomberg 2006). This is the only reliable, industry wide, analysis of spare capacity in the hospital sector and as such was used in the modelling process.

This analysis showed that private hospitals in South Africa operate at an average occupancy level of 58.8%. This occupancy level was then extrapolated across the private hospital bed numbers in each province to arrive at an average spare capacity within each province.

Published public hospital occupancy levels were only available for four provinces, namely the Free State, Gauteng, KwaZulu Natal and North West Province (Day and Gray 2005). An average of these four occupancy levels was used as a proxy when estimating the spare capacity in the remaining provinces.

The total hospital be current spare capacity are contained in Table 8 below.

Table 8

Province	HOSPITAL BEDS					
	Private			Public		
	Total beds	Occupancy	Beds available	Total beds	Occupancy	Beds available
Eatern Cape	2,251	58.8%	929	14,280	70.0%	4,284
Free State	2,417	58.8%	997	5,176	63.0%	1,915
Gauteng	15,174	58.8%	6,259	18,405	80.0%	3,681
KZN	3,816	58.8%	1,574	29,067	65.0%	10,173
Limpopo	311	58.8%	128	11,207	70.0%	3,362
Mpumalanga	513	58.8%	212	5,347	70.0%	1,604
Northern Cape	746	58.8%	308	2,117	70.0%	635
NW Province	1,438	58.8%	593	7,037	58.0%	2,956
Western Cape	3,917	58.8%	1,616	10,224	70.0%	3,067
Total	**30,583**	**58.8%**	**12,615**	**102,860**	**69.2%**	**31,678**

Intensive Care Unit bed occupancy levels are known to be at 80% for one of the large private hospital groups in the country. The three large private hospital groups comprise 85% of the total registered private beds in the country. Due to the great similarity between the operating environments of the private hospital groups, the 80% occupancy level mentioned above was deemed to be the best proxy for occupancy levels across the private hospital sector.

Data with respect to occupancy levels within public hospitals was not available. Anecdotal evidence and consultations with numerous public hospital ICU physicians suggested that public hospital ICU occupancy exceeded that of the 80% in the private sector. As a result of this, the average public hospital ICU occupancy level was taken as 90% for the purposes of the model.

The total ICU beds capacity are contained in Table 9 below.

Table 9

Province	ICU BEDS					
	Private			Public		
	Total beds	Occupancy	Beds available	Total beds	Occupancy	Beds available
Eatern Cape	228	80.0%	46	1,447	90.0%	145
Free State	245	80.0%	49	524	90.0%	52
Gauteng	1,537	80.0%	307	1,865	90.0%	186
KZN	387	80.0%	77	2,945	90.0%	294
Limpopo	32	80.0%	6	1,135	90.0%	114
Mpumalanga	52	80.0%	10	542	90.0%	54
Northern Cape	76	80.0%	15	214	90.0%	21
NW Province	146	80.0%	29	713	90.0%	71
Western Cape	397	80.0%	79	1,036	90.0%	104
Total	**3,098**	**80.0%**	**620**	**10,421**	**90.0%**	**1,042**

These estimations of spare capacity within the hospital sector per province were then modeled against the predicted number of hospital and ICU admissions per province for both the Mild and Severe Pandemic Scenarios and displayed as a percentage of total occupancy for each province.

Research Limitations

Many of the research limitations have already been mentioned in the course of this chapter. The limitations are summarized below.

The modelling process is significantly limited in its predictive accuracy by the fact that the disease being modeled does not currently exist, and as such, parameters relating to its behaviour can only be predicted based on other

similar diseases. In this limitation, parameters from the previous pandemics of the twentieth century were used to provide the ranges of likely probability.

The relevance of the research is further limited by the inability to predict with any degree of certainty when the next influenza pandemic will start, and in fact whether or not the currently recognized H_5N_1 threat will become that reality. This results from the fact that a chance mutation is required in the H_5N_1 virus for a pandemic to become a reality. The probability of this chance mutation occurring is impossible to predict with any degree of certainty. Having said this, the probability is rapidly increasing as a result of the dramatic spread of Avian Influenza in birds and the increasing numbers of human cases of Avian Influenza. This scenario creates increasing opportunities for the virus to mutate.

The model methodology (Multi-state Markov Transition Model) is limited by the time intervals chosen, allowing certain transitions to be missed if they occur within the week interval.

Certain of the inputs for the model required predictive judgement on the basis that specific data were not available (e.g. numbers of ICU beds and occupancy levels in public hospitals). Hospital bed and ICU bed capacity were also modeled on the assumption that there will be no geographical mismatch between demand and supply i.e. patients requiring hospital beds are able to move freely in order to find available beds in the country. This is certainly not the case in reality and will place further strain on actual patient outcomes.

The effect of staff absenteeism due to illness or paranoia was not adequately accounted for in the predictions of hospital and ICU bed capacity. While it will almost certainly have a dramatic effect, it is very difficult to predict with any certainty and was thus not included in this model.

In summary, therefore, there are a large number of limitations to this predictive model and caution must be exercised in interpreting the outputs. Despite the limitations, however, the model is very valuable to a great variety of decision makers in business, the government and the healthcare sector in guiding the decision-making process in planning for the next influenza pandemic.

Chapter 5: Results

Predicted Flu Pandemic Model for South Africa

A number of different models were created for the purposes of the research, namely:

1. A Basic Scenario
2. Limited Capacity Scenario
3. Mild Pandemic Scenario
4. Severe Pandemic Scenario

All models were displayed up to 25 weeks from the start of the pandemic due to the fact that the run-off after 25 weeks is rather prolonged and adds little to the final predicted parameters.

Basic Scenario

The Basic Scenario utilizes the Base Transition Matrix as defined in Table 2, adjusted for herd immunity and demographic factors. The basic parameters are based on a severe pandemic as per the Spanish Flu Pandemic of 1918. Unlimited hospital bed and ICU bed capacity is assumed for the Basic Scenario. Due to multiple variables not accounted for in the Basic Scenario, it must not be considered a realistic prediction of possible outcomes, but has been included to highlight the logical flow of the modelling process.

The overall results a

Percentage of population infected	20.3%
Overall Mortality Rate	1.5%

Figure 3 shows the number of new infections at the beginning of each week.

Figure 3

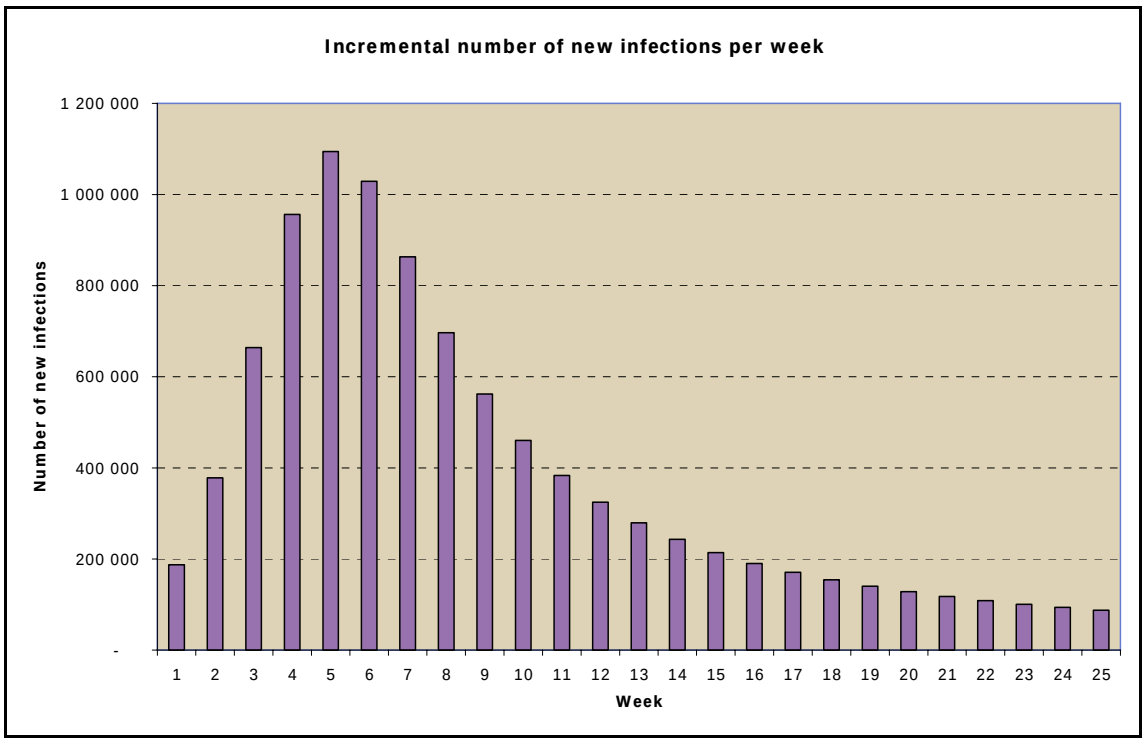


Figure 4 below shows the ill population at the beginning of each week. The ill population can be defined as the sum of the number of people in each of the flu infected states in a particular week. From the graph it can be seen that the ill population peaks at 7 weeks with 2.9 million sick people before the number starts to diminish. After week 25 we still expect a small number of people being

sick, although the le ilar to levels experienced within a normal seasonal influenza epidemic.

Figure 4

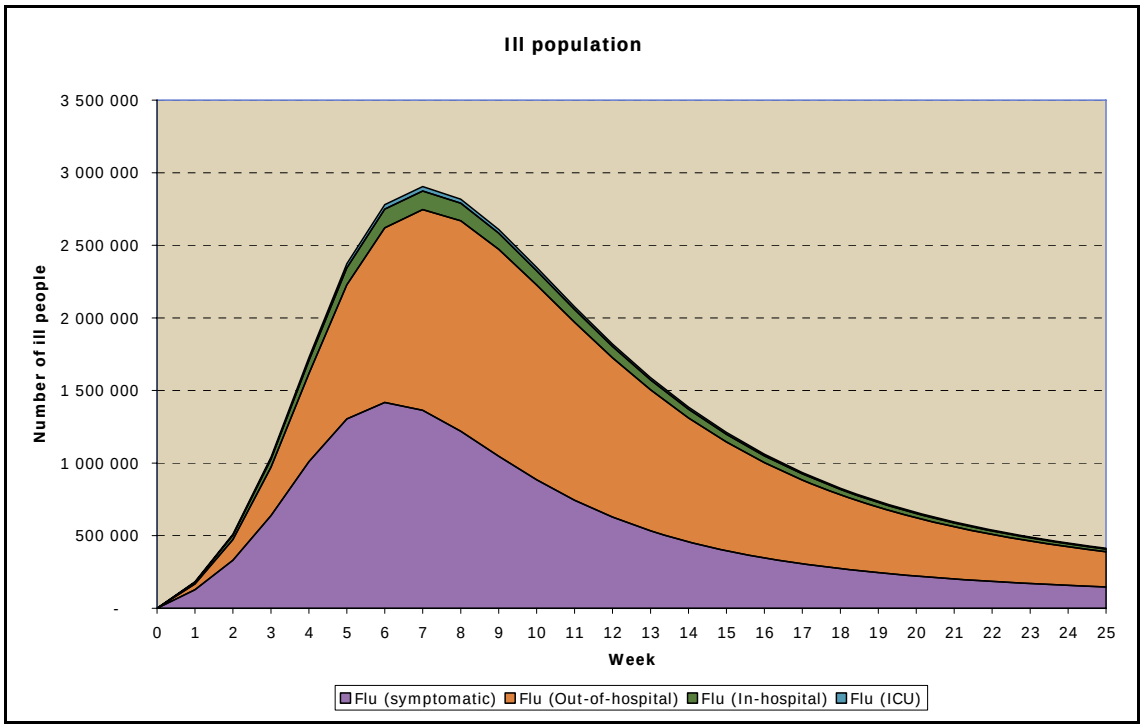
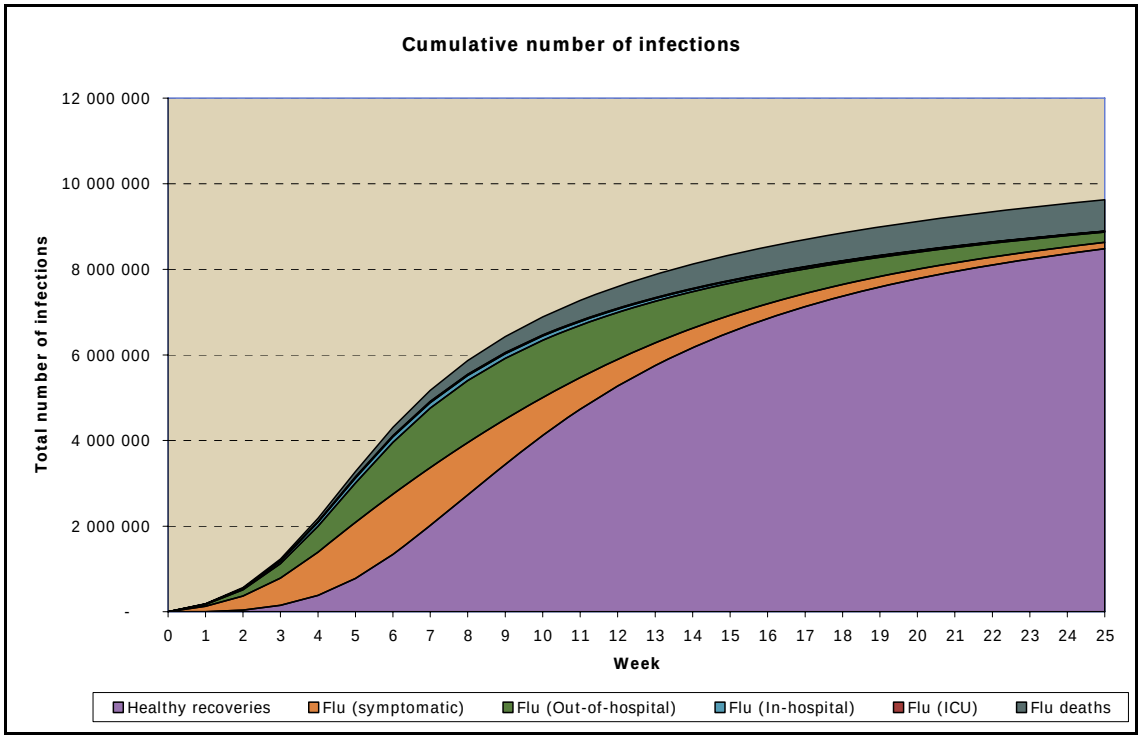


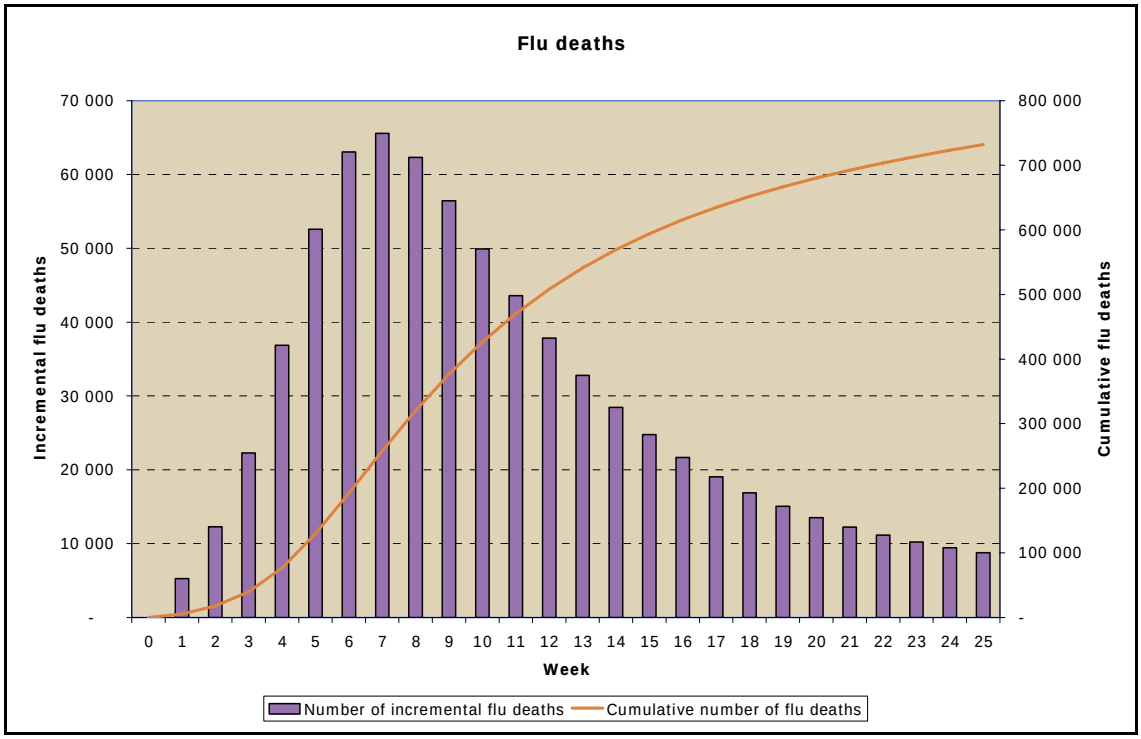
Figure 5 below shows the cumulative number of infections as at the beginning of each week. The cumulative number of infections is determined as the sum of the healthy recoveries, all current flu illnesses and flu deaths as at the beginning of that week. At the end of week 25 there are 9.6 million people that have been infected with influenza, which equates to the 20.3% expressed above.

Figure 5



The following graph ( ) influenza-related deaths per week and includes a graph of the cumulative death toll for the pandemic. The pandemic deaths peak at 7 weeks with total deaths settling at just over 700 000 for the 25 week period.

Figure 6



Limited Capacity Scenario

The Basic Scenario was used as a baseline from which to determine the Limited Capacity Scenario. Current hospital bed and ICU bed spare capacity constraints were then placed on the Basic Scenario. All patients requiring hospitalization or ICU admission following capacity exhaustion were allocated worse outcomes as discussed in Chapter 4.

The overall results a

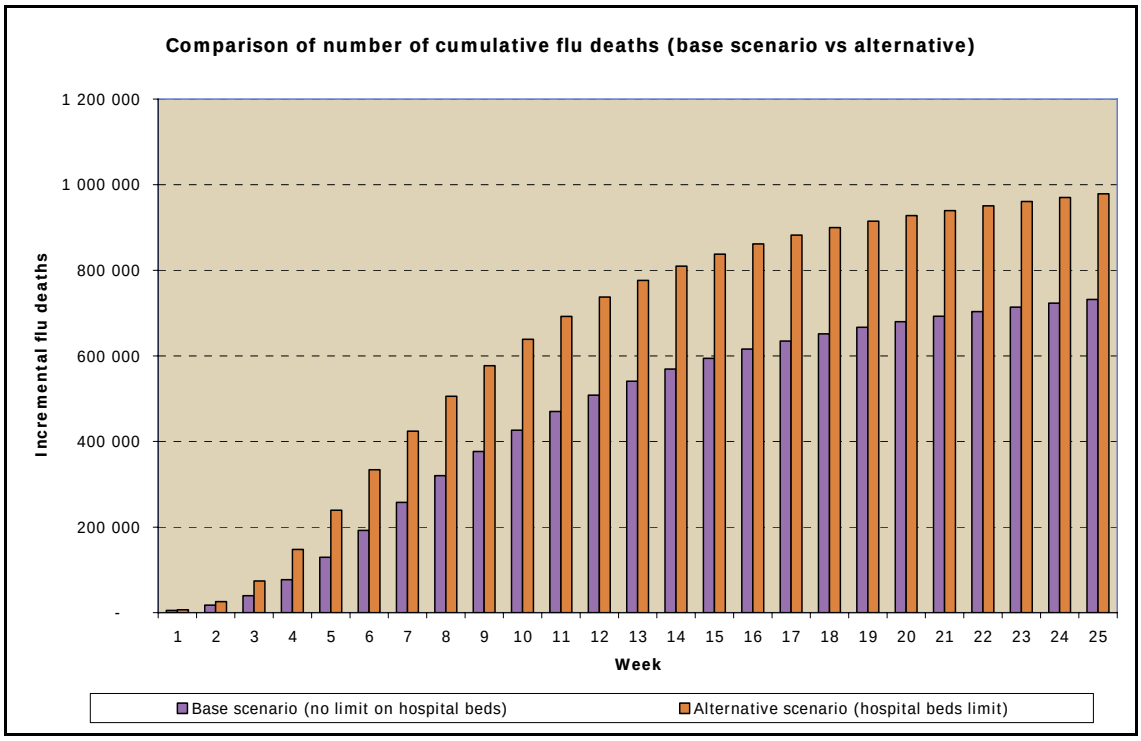
Percentage of population infected	20.3%
Overall Mortality Rate	2.1%

Figure 7 shows a comparison between the Basic Scenario and the Limited Capacity Scenario in respect of the number of incremental flu deaths over the investigation period

Figure 7

The effect of the li further illustrated by the number of cumulative deaths over the investigation period as shown in Figure 8 below.

Figure 8



Mild Pandemic Scenario

This scenario is based on the basic parameters more closely resembling those of the 1957 and 1968 pandemics. Due to the fact that these two pandemics were significantly milder in their total impact (particularly on mortality), this scenario provides a milder prediction of a future pandemic's impact. Hospital bed and ICU bed capacity constraints were included in this scenario.

The transition matrix is shown in Table 10 below:

Table 10

	Uninfected	Flu Recovery	Flu No Treatment	Flu Out-patient	Flu In-patient	Flu ICU	Flu Death	Other Death
Uninfected	99.832%	0.000%	0.125%	0.025%	0.003%	0.001%	0.001%	0.010%
Flu Recovery	0.000%	99.990%	0.000%	0.000%	0.000%	0.000%	0.000%	0.010%
Flu No Treatment	0.000%	24.839%	50.000%	25.000%	0.150%	0.001%	0.001%	0.010%
Flu Out-patient	0.000%	44.485%	0.000%	55.000%	0.500%	0.005%	0.001%	0.010%
Flu In-patient	0.000%	4.975%	0.000%	50.000%	45.000%	0.010%	0.005%	0.010%
Flu ICU	0.000%	2.490%	0.000%	5.000%	27.500%	40.000%	25.000%	0.010%
Flu Death	0.000%	0.000%	0.000%	0.000%	0.000%	0.000%	100.000%	0.000%
Other Death	0.000%	0.000%	0.000%	0.000%	0.000%	0.000%	0.000%	100.000%

The overall results as at the end of 25 weeks show:

Percentage of population infected 9.1%

Overall Mortality Rate 0.13%

Figure 9 shows the i ginning of each week.

Figure 9

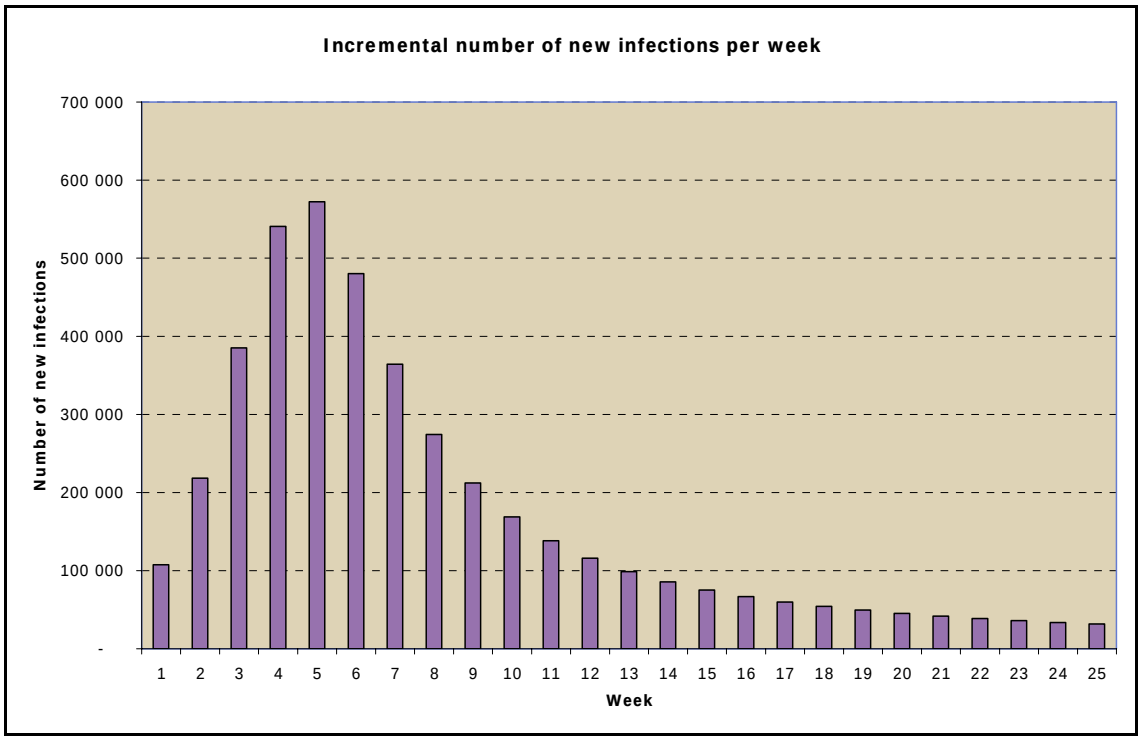


Figure 10 shows the [illegible] ach week.

Figure 10

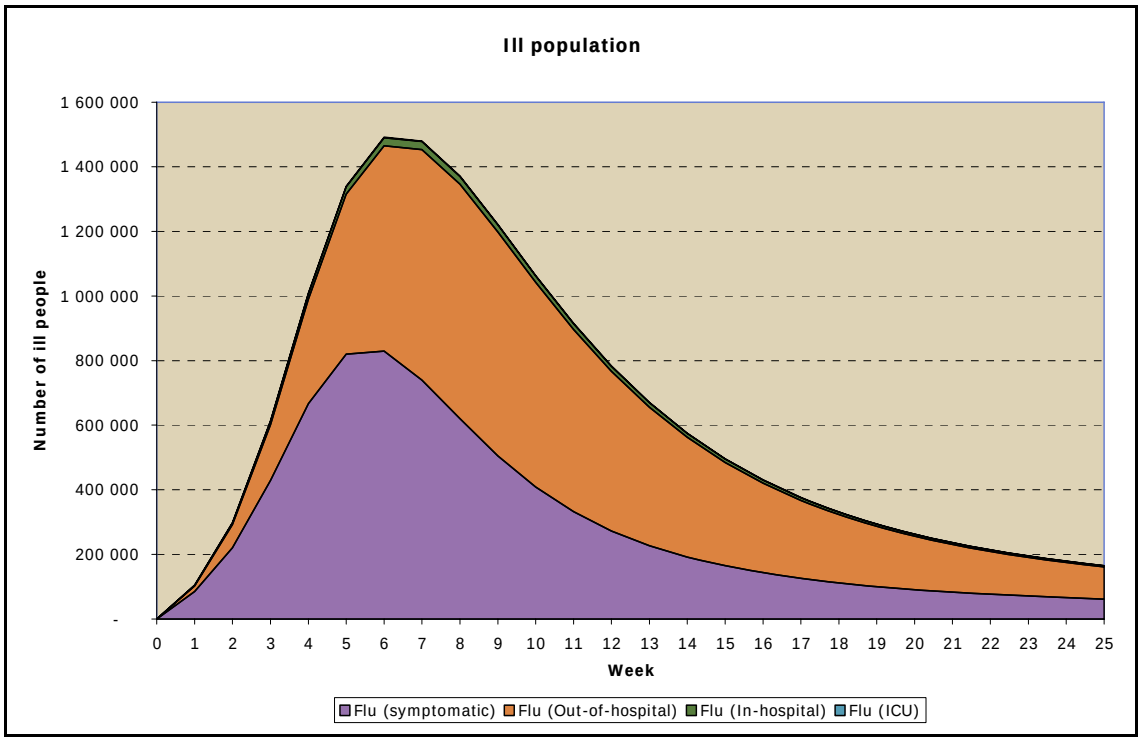
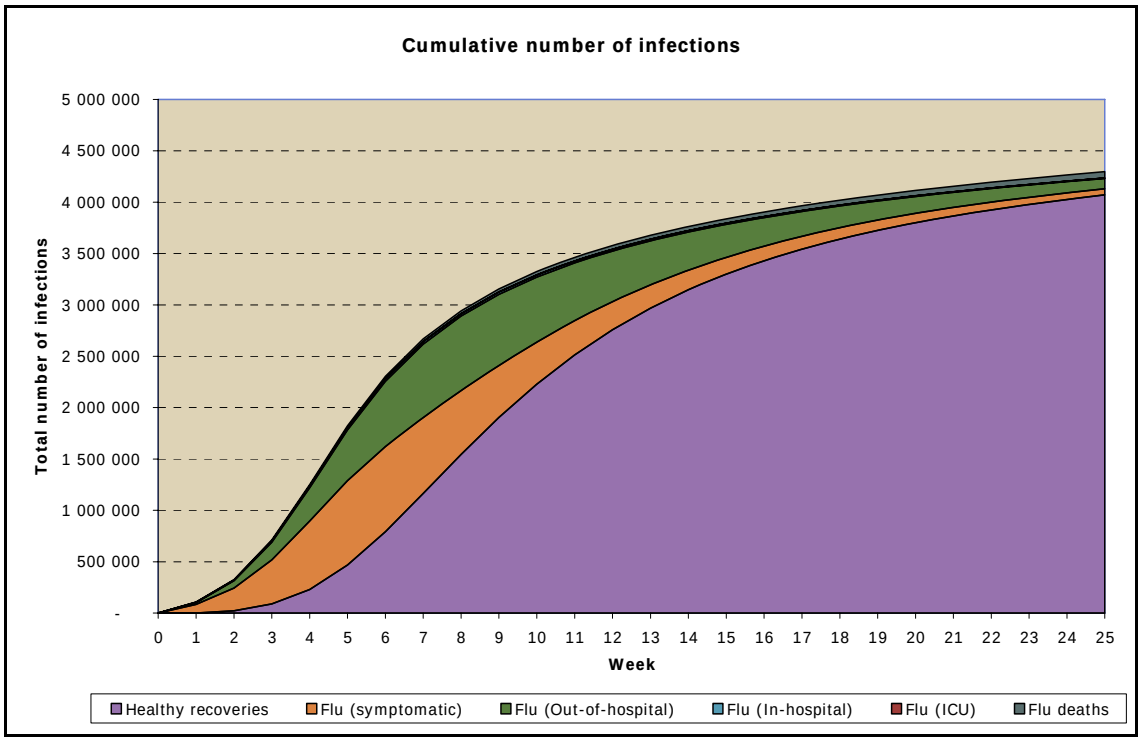


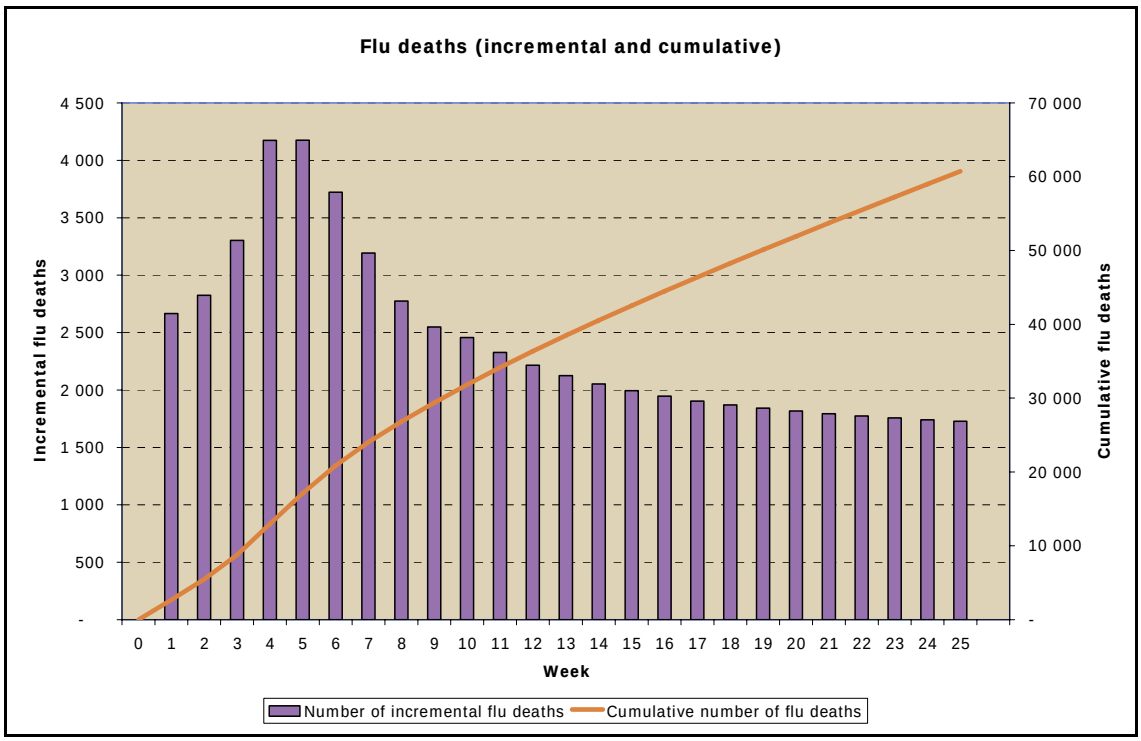
Figure 11 below sho ctions as at the beginning of each week. At the end of week 25 there are 4.3 million people that have been infected with influenza, which is equal to the 9.1% stated above.

Figure 11



The following graph shows the number of influenza-related deaths develops over the investigation period. The pandemic deaths peak at five weeks while the cumulative number of influenza-related deaths settles at just over 60 000.

Figure 12



Severe Pandemic Scenario

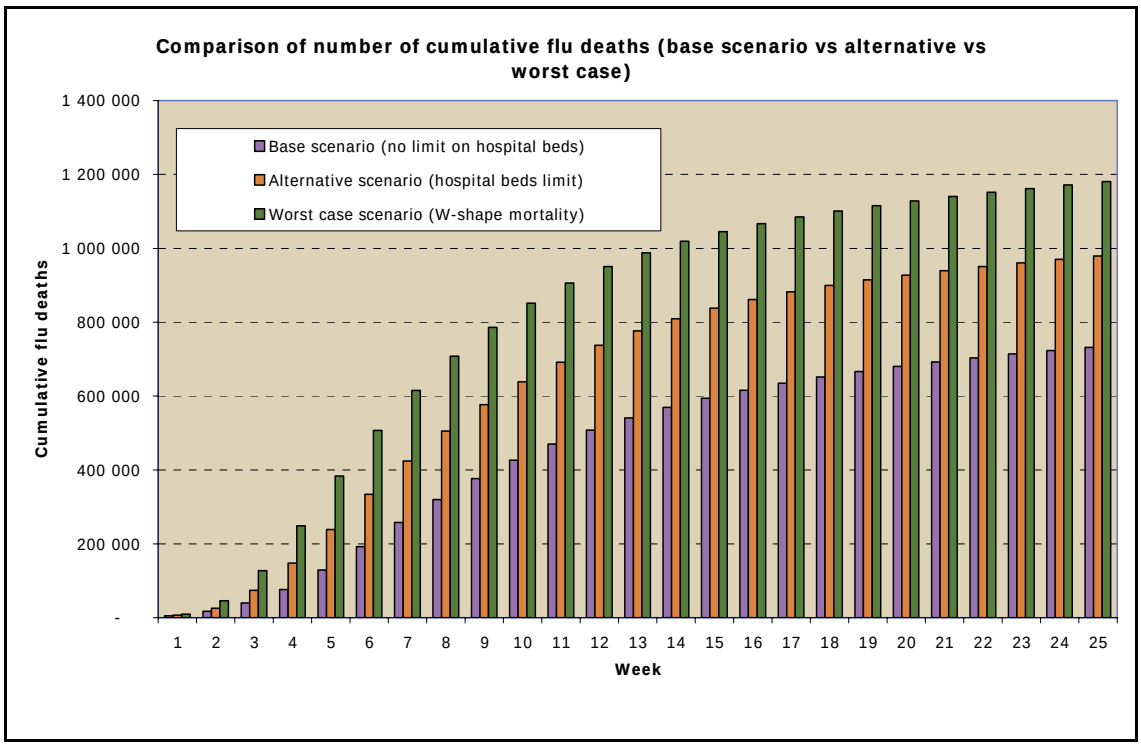
The shape of the mortality curve experienced during the Spanish Flu Pandemic of 1918 was unusual in that mortality for young adults was dramatically higher than that for seasonal influenza epidemics, which has higher mortality in the very young and the elderly. This scenario has been based on the re-occurrence of such a “W-shaped” mortality curve (Brainerd and Siegler 2003).

The overall results a

Percentage of population infected	22%
Overall Mortality Rate	2.5%

Figure 13 shows the comparison between the Basic Scenario, the Limited Capacity Scenario and the Severe Pandemic Scenario for the number of cumulative influenza-related deaths over the investigation period.

Figure 13



The table below represents a summary of the attack rate (% of the population infected) and mortality rate results for all four scenarios (Table 11).

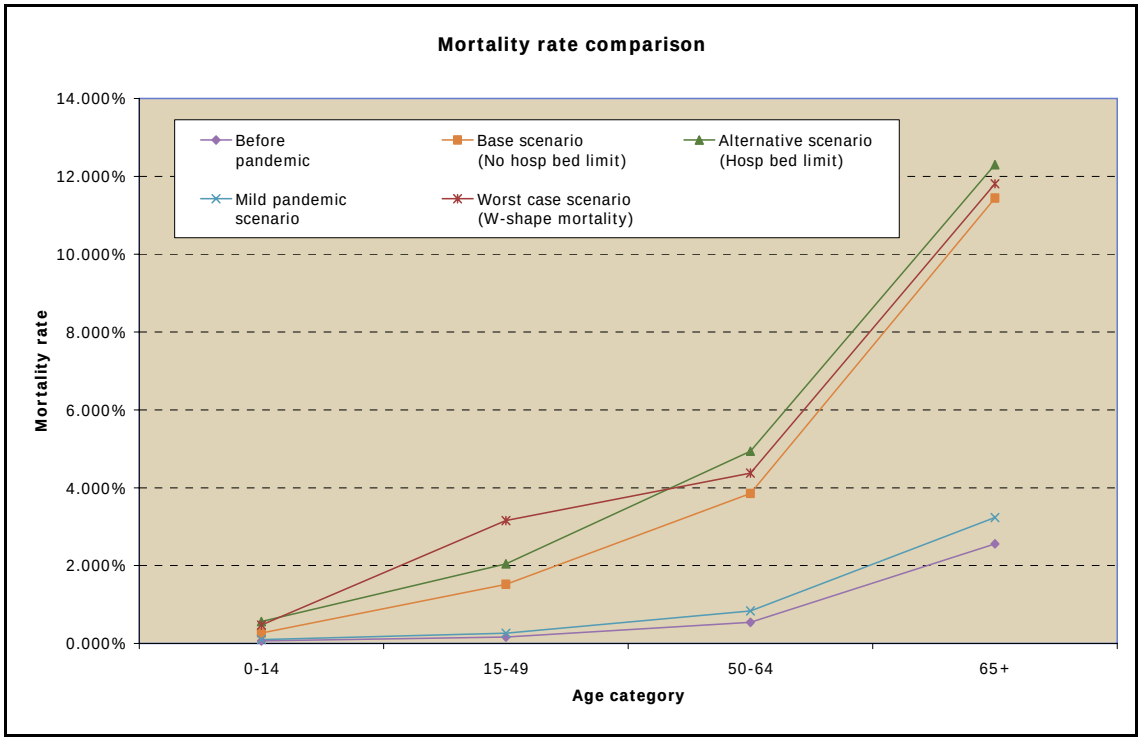
Table 11

Scenario	% Population Infected	% Mortality
Basic	20.30%	1.50%
Limited Capacity	20.30%	2.10%
Mild Pandemic	9.10%	0.13%
Severe Pandemic	22%	2.50%

Demographic Impact

As discussed in Chapter 4, the model was adjusted for age categories as per the latest available statistics concerning the South African population. The graph below (Figure 14) demonstrates the differences in mortality rate for different age categories and compares the pandemic scenarios with the pre-pandemic state.

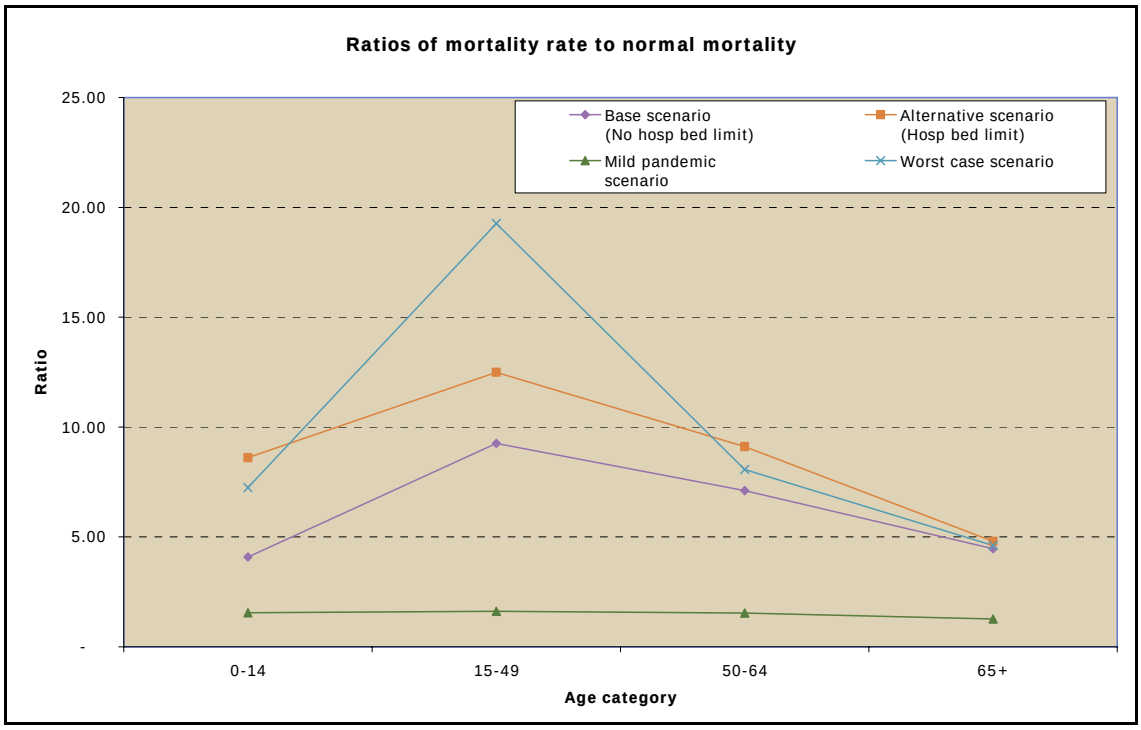
Figure 14



Mortality rates in the respective scenarios were then compared with normal mortality rates in each age category. Figure 15 below graphically demonstrates

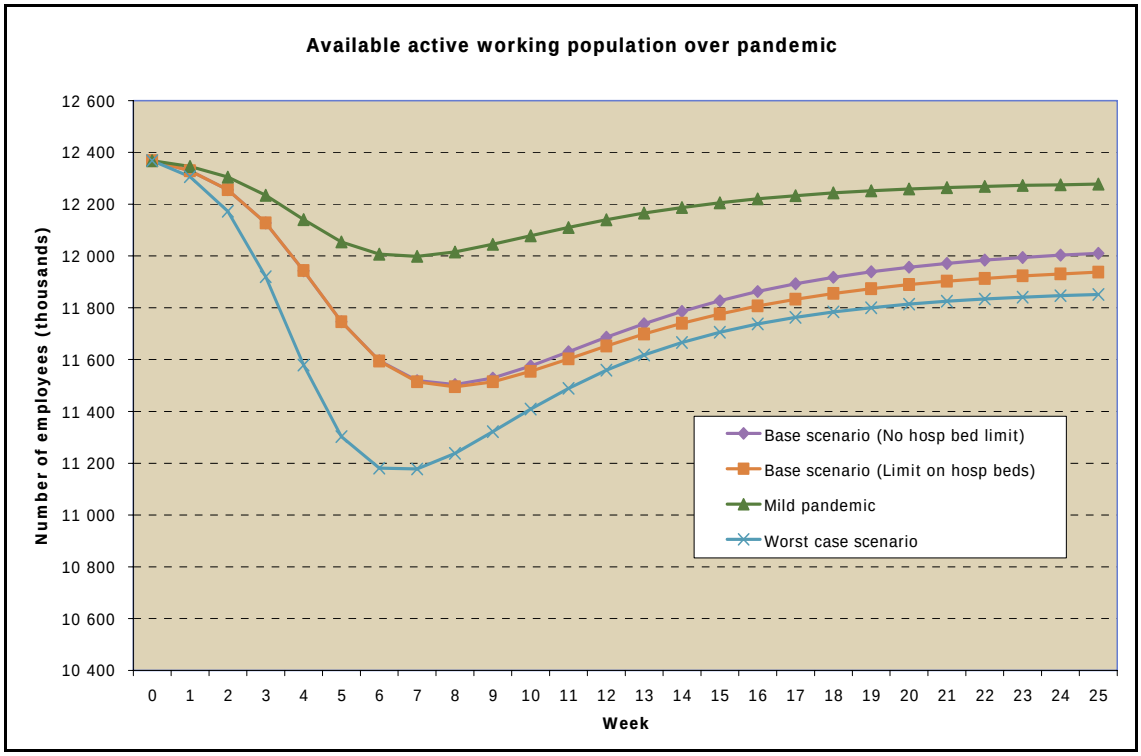
the relative mortality rtion of the pre-pandemic baseline level.

Figure 15



Using this information and results from our models, we are able to estimate the number of people actively in employment at the beginning of every week as all the healthy individuals (i.e. not sick or dead). The following graph (Figure 16) shows the active employed population for each of the four pandemic scenarios.

Figure 16

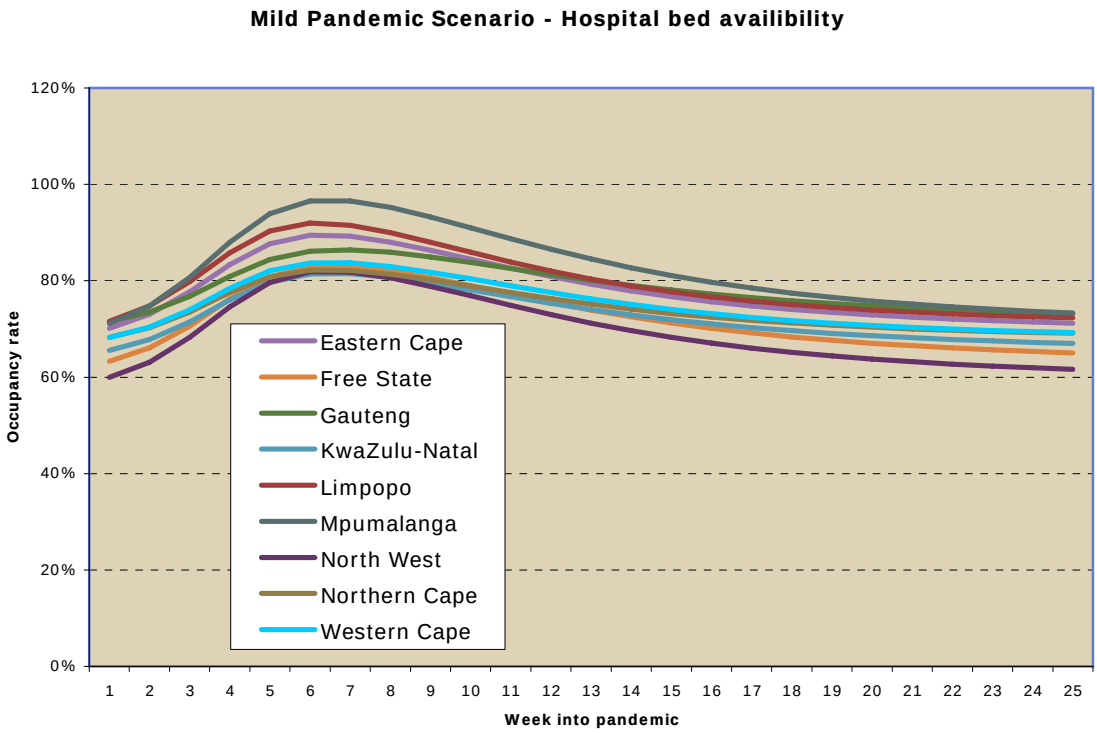

Available active working population over pandemic
Number of employees (thousands)
12 600
12 400
12 200
12 000
11 800
11 600
11 400
11 200
11 000
10 800
10 600
10 400
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Week
Base scenario (No hosp bed limit)
Base scenario (Limit on hosp beds)
Mild pandemic
Worst case scenario

Effect on the Healthcare Sector

Hospital Bed Occupancy: Mild Pandemic Scenario

Figure 17 below represents a graph of the general hospital bed occupancy levels predicted for all nine provinces for the duration of the Mild Pandemic Scenario as modeled in section 1.

Figure 17



Hospital Bed Occupancy: Severe Pandemic Scenario

Figure 18 below represents a graph of the general hospital bed occupancy levels predicted for all nine provinces for the duration of the Severe Pandemic Scenario as modeled in section 1.

Figure 18

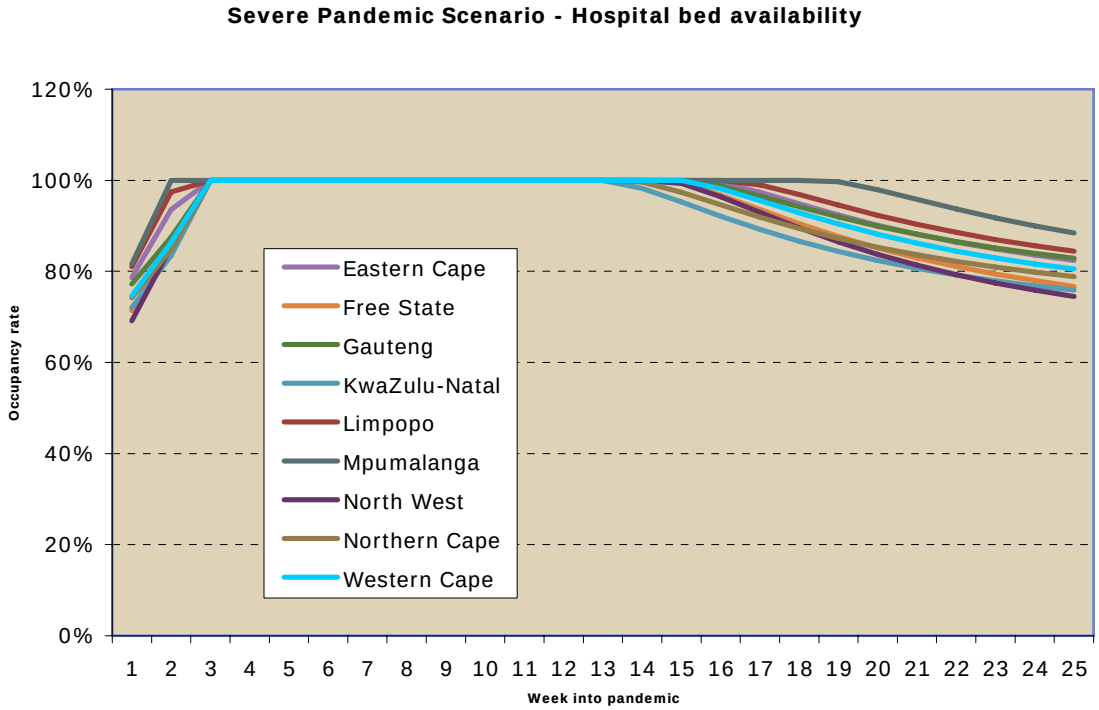
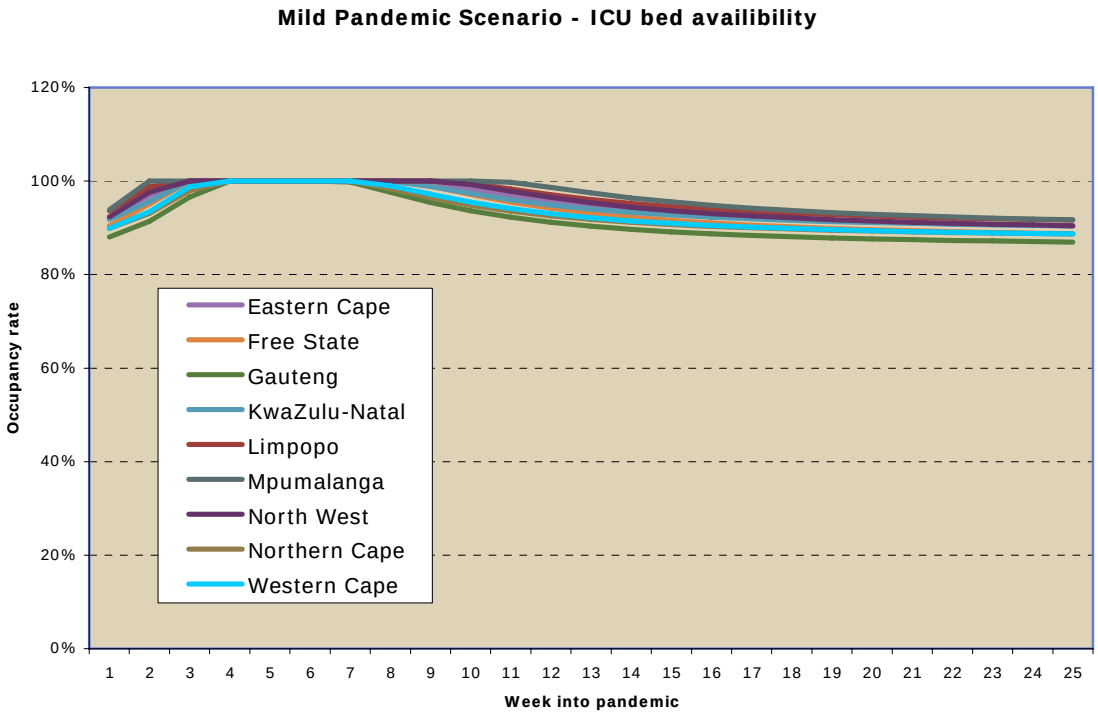

Severe Pandemic Scenario - Hospital bed availability
120%
100%
80%
60%
40%
20%
0%
Occupancy rate
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Week into pandemic
Eastern Cape
Free State
Gauteng
KwaZulu-Natal
Limpopo
Mpumalanga
North West
Northern Cape
Western Cape

Figure 19 below represents a graph of occupancy levels of ICU beds for all nine provinces for the duration of the Mild Pandemic Scenario.

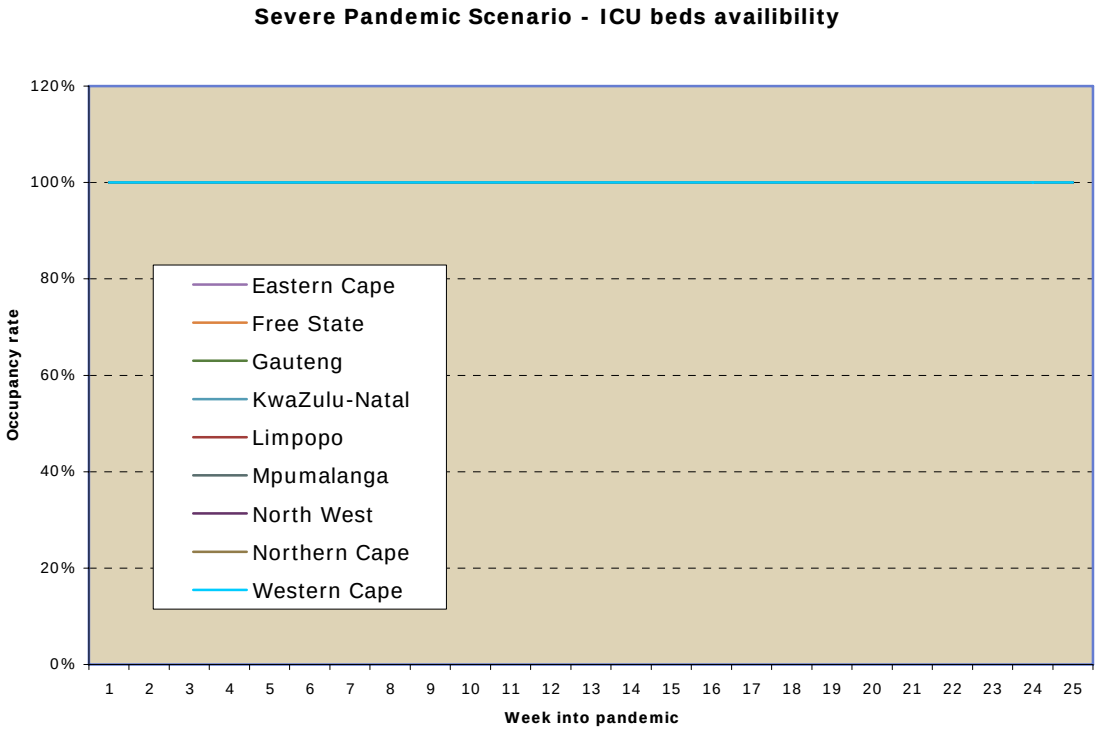
Figure 19



ICU Bed Occupanc

Figure 20 below represents the ICU bed occupancy levels in all nine provinces for the duration of the Severe Pandemic Scenario.

Figure 20



Chapter 6: Discussion of Results

Predicted Model for South Africa

The influenza virus which will cause the next global influenza pandemic does not currently exist. The virus will arise by means of a mutation from a combination of genes from the currently existent influenza viruses (both human and animal). Due to the fact that the virus does not currently exist, it is impossible to predict, with any degree of certainty, what the characteristics of this new virus will be and how it will behave.

It is clear from the analysis of the previous influenza pandemics, that their impact on the human population was dramatic and on a truly global scale. All of these pandemics swept through the globe within eighteen months and caused major disruptions to society. The disruptions caused include the following:

- Social disruptions due to significant illness and death
- Economic disruptions due to deaths, absenteeism and the numerous behavioural adaptations adopted by the human population in an attempt to mitigate the effects of the pandemic (e.g. travel restrictions, self-quarantine).

With the above factors in mind, and considering the extent of planning which will be required in order to adequately mitigate the effects of a future pandemic, it is vital that specific influenza pandemic planning is undertaken on a global, regional and local scale before the next influenza pandemic starts.

In order to facilitate meaningful planning for a future influenza pandemic, predictions regarding the overall impact and behaviour of such a pandemic are necessary.

The task of predicting the behaviour of a disease which does not currently exist has numerous pitfalls. An analysis of the current thinking in respect of influenza pandemic modelling revealed that the best predictions are based on existing key parameters from the past pandemics which have been studied. No current influenza pandemic models exist for South Africa.

Four different scenarios were modeled for South Africa in order to provide a full spectrum of valid predictions for a future influenza pandemic. An analysis of available literature concerning the previous influenza pandemics of the twentieth century (1918; 1957 and 1968) revealed a high degree of variability in the key parameters determining the impact of each pandemic, namely:

- Attack rates (proportion of population infected)
- Mortality rates (both total and within age categories)
- Rate of spread

Basic Scenario

The Basic Scenario was modeled on the key parameters of the Spanish Flu of 1918, whilst making use of the Base Transition Matrix adjusted for the Herd Immunity Factor and the demographic factors. The Basic Scenario is not a

realistic scenario, as the fact that it assumes a limitless supply of available hospital and ICU beds which is not realistic. It has been included in the report for the purpose of facilitating an understanding of the logical process involved in arriving at the realistic scenarios discussed later.

The total infection rate within the entire population is at 20.3% for this scenario at the end of the 25 week period. This is slightly below those estimates of the Spanish Flu (25-30%), on the basis that, with the use of anti-viral drugs and the possibility of a vaccine halting the second wave of a future pandemic, the full attack rate as experienced in 1918-1919 is less likely.

The cumulative mortality rate for the 25 week period is at 1.5%. This is expected to be below the 2.5% rate for the Spanish Flu for two reasons:

1. Advances in medical therapy for influenza are likely to reduce the total mortality rate
2. This scenario ignores hospital capacity constraints and thereby spuriously reduces the total mortality rate.

The number of new infections in the entirely susceptible population rises dramatically over the first five weeks of the pandemic. It reaches its highest rate in the fifth week with approximately 1.1 million new infections during that week. From this point onward, the number of new infections per week reduces progressively until week 25. This progressive reduction is due to the fact that, as the proportion of influenza recovered healthy individuals who are immune to the disease rises, so the rate of new infections within the population falls. This is

consistent with the diseases modelling and herd immunity (Meltzer *et al* 1999) (Patel *et al* 2005).

As can be seen from Figure 4 the total influenza-sick proportion of the population rises until it reaches a peak at 7 weeks with 2.9 million people ill. It is further worth noting that peaks for Out-patient, In-patient and ICU categories occur progressively later in the pandemic. This phenomenon is explained due to the fact that patients will tend to move progressively further up the chain of disease severity with time.

Figure 5 illustrates the progressive increase in patients in each state as the pandemic progresses. Note the lag in peaks of the various states from the Infected, no Treatment state through to the Flu ICU state. Note also that the Flu Death and Healthy Recovered states continue to increase in size throughout the pandemic. This results from the fact that they are absorbing states, which means that individuals who move into these states cannot exit.

The peak incidence of Flu Deaths occurs in week 7 with 65 000 new deaths and the total mortality increases to 720 000 by the end of the 25 week period (Figure 6).

Limited Capacity Scenario

The Limited Capacity Scenario is an adjustment of the Basic Scenario discussed above to allow for capacity constraints within hospital bed and ICU bed numbers. This scenario then represents a more realistic model due to the fact that individuals who require certain healthcare services, but cannot access them due to capacity constraints, will have worse outcomes than if they had full access to these services.

A comparison with the Basic Scenario reveals that the total infection rate within the population is unchanged whilst the mortality rate increases from 1.5% to 2.1%. The overall infection rate is logically consistent as a limitation in hospital and ICU bed availability is unlikely to have an impact on the total number of infections within the population.

The increased mortality rate reflects the aggravated outcomes of those patients who require healthcare services but cannot access them. The total mortality rate of 2.1% is slightly below the estimated mortality of the Spanish Flu (2.5%) consistent with the likely outcome considering improved medical treatment capabilities and improved access to healthcare for the world's population when compared with 1918.

It is important to note that the increase in mortality rate from 1.5% for the Basic Scenario to 2.1% for the Limited Capacity Scenario represents an increase of 270 000 deaths taking the total from 720 000 to 990 000 (Figure 8).

Mild Pandemic Sce

As is evident from the scenario outputs, this scenario has a significantly smaller impact, proportional to the relative impact which the 1957 and 1968 pandemics had on the world in comparison to the Spanish Flu of 1918.

The outcome analysis reveals an overall infection rate of 9.1% as compared with 20.3% for both the Basic and Limited Capacity Scenarios. This parameter outcome must be considered a shortfall of this particular scenario model as it is inconsistent with evidence from the lesser pandemics of 1957 and 1968 which showed infection rates in excess of 30% (Brundage 2006). These infection rates were even greater than those experienced during the Spanish Flu of 1918.

As a result of this short-coming, caution must be exercised in making use of the predictions in this scenario for the purposes of absenteeism predictions and overall economic impact analyses.

Despite this short-coming, however, the hospital admission, ICU admission and mortality rates remain consistent with parameters from the 1957 and 1968 pandemics and thus are highly relevant. These predictions will be of great value to the healthcare sector, comprising the most critical aspects of a healthcare sector response to an influenza pandemic.

The upward swing in the cumulative mortality curve at three weeks (Figure 12) captures the point at which all available hospital beds are occupied. There is

therefore an increas enza-related deaths from this point onward. Additional hospital beds become available again after seven weeks, which results in downward swing and stabilisation of the cumulative mortality graph.

It is important to note that the spare capacity within the South African healthcare system for both hospital and ICU beds is exceeded within two to three weeks of all of the other scenarios (Basic, Limited Capacity and Severe Pandemic) and remain exceeded until beyond 25 weeks in each instance.

Severe Pandemic Scenario

The Severe Pandemic Scenario is very similar to the Limited Capacity Scenario with the addition of an increased mortality rate for young adults as per the behaviour of the Spanish Flu of 1918. The mortality rate predictions were taken from research performed in the USA during the 1918 Pandemic (Brainerd and Siegler 2003).

The total infection rate for the population increased from 20.3% (Basic Scenario) to 22%. The mortality rate for the population increased from 2.1% (Limited Capacity Scenario) to 2.5% which is similar to that experienced for the Spanish Flu Pandemic. This increase in mortality translates into a further 200 000 deaths, taking the total death toll to just short of 1.2 million for the 25 week period.

Table 12

Scenario	Infection Rate	Mortality Rate	Validity	Observations
Basic	20.30%	1.50%	Unrealistic; Included as part of logical process	For modelling process purposes only
Limited Capacity	20.30%	2.10%	Valid	Capacity exceeded very early; mortality increases dramatically
Mild Pandemic	9.10%	0.13%	Valid except total infection rate which is underestimated	Capacity exceeded for 4 weeks; mortality much lower; economic impact much lower
Severe Pandemic	22%	2.50%	Valid	High mortality; High economic & social impact due to death of young adults

A comparison of all four scenarios as summarized in Table 12 above reveals much regarding the relationship between the variables involved. There is a substantial increase in mortality rate, translating into 270 000 deaths, in comparing the Basic Scenario with the Limited Capacity Scenario due to the limitation on availability of hospital and ICU beds. Consideration must be given to the fact that, in a real influenza pandemic, the hospital and ICU bed capacity is likely to be even further reduced due to absenteeism of staff. This significant absenteeism will be due to staff illness, illness of family members and self-quarantining behaviour as a means of avoiding infection. In the light of this, the mortality estimate should be considered as conservative due to the fact that further deaths will result should there be an incremental limitation on capacity.

The Mild Pandemic Scenario, in comparison, shows a significantly reduced mortality rate and hospitalization rate when compared with the preceding scenarios. To keep it in perspective, however, it must be borne in mind that the

hospital capacity is even in the Mild Pandemic Scenario. The overall impact on society, both economic and social, will be substantially lower due largely to the lower mortality rate.

The Severe Pandemic Scenario has the highest infection and mortality rates and very closely resembles the Spanish Flu Pandemic of 1918. The economic and social impact of this scenario is magnified due to the fact that the mortality in young adults is significantly higher than other pandemics experienced in the past. Due to the fact that young adults make up the back-bone of both the economy and the social/ family structures in society, the loss of a large number of lives in this age category will be felt heavily in both spheres.

Mild versus Severe Pandemic

Much debate currently exists within the medical and epidemiological fields as to whether the next pandemic is likely to be a severe one (resembling the 1918 pandemic) or a mild one (resembling the 1957 and 1968 pandemics). There are strong arguments for both cases which are worth exploring at this point.

Arguments in favour of a milder pandemic include:

- Most previous pandemics which we have accurate knowledge of were milder in nature and resembled the latter pandemics of the twentieth century.
- If the H5N1 Avian Influenza Virus is in fact the precursor for the next pandemic, many experts believe that it will lose much of its pathogenicity

(severity) in to become a pandemic virus.

- The extent of vaccination and medical care today will tend to mitigate against a severe pandemic.

Arguments in favour of a more severe pandemic include:

- There is currently no immunity within the human population against the H5N1 virus. This is in contrast to the milder pandemics of 1957 and 1968. The total lack of immunity more closely resembles the scenario of 1918.
- The current pathogenicity of the H5N1 infections in humans is alarmingly high with 59% mortality in human cases. Such mortality rates have not been seen before in human influenza, leading many experts to believe that the next pandemic may be even more severe than the Spanish Flu.
- The fact that world-wide travel is currently so prevalent and extensive leaves many to believe that an influenza pandemic will be impossible to contain and will spread for more rapidly around the globe.

With strong arguments for both a mild and a severe pandemic it is very difficult to predict which of the two is most likely to occur. It is therefore even more important to take note of the predictions for both scenarios in planning for a possible future pandemic.

Mild Pandemic Scenario

The results of the modelling process for occupancy levels of general hospital beds for the Mild Pandemic Scenario are contained in Figure 17**Error! Reference source not found.**. A detailed analysis of the results shows that total hospital bed capacity is not exceeded in any of the nine provinces during the pandemic.

The respective provinces start with total occupancy levels of between 60% and 73% and peak at between 80% and 96% occupancy at the height of the pandemic (7 weeks), gradually declining again to end at the pre-pandemic levels at the 25 week mark. Limpopo and Mpumalanga Provinces have the highest occupancy levels and approach full capacity at the height of the pandemic. North West Province has the lowest occupancy levels throughout the pandemic.

The results for the ICU bed occupancy levels for the Mild Pandemic Scenario are contained in Figure 19**Error! Reference source not found.**. All provinces exceed their ICU bed capacities during the peak of the pandemic (3 weeks to 7 weeks). Mpumalanga Province has the most critical shortage of beds with Gauteng Province having the least critical shortage of ICU beds.

Severe Pandemic Scenario

The results of the Severe Pandemic Scenario's impact on hospital bed capacity are shown in Figure 18. The results show that hospital bed capacity in all provinces is overwhelmed from 2-3 weeks into the pandemic until 13-18 weeks into the pandemic. Mpumalanga Province is again the province with the most critical shortage of hospital beds with the North West Province and Kwa Zulu Natal having the least critical shortage.

The extent of the shortfall in capacity and the duration for which it lasts is a concerning prediction for hospitals in the case of a severe pandemic.

The results of the Severe Pandemic Scenario's impact on the ICU bed occupancy levels are illustrated in Figure 20. This striking graph shows that ICU bed capacity is overwhelmed for the entire duration of a severe pandemic in all nine provinces.

Implications for General Influenza Pandemic Planning

The purpose of this research is to provide a range of predictions for a possible future influenza pandemic in order to empower decision-makers and policy-makers in their attempts to plan for the next influenza pandemic. As influenza pandemics have occurred for as far back as there is accurate recordings of human history, one can predict with relative certainty that another influenza pandemic will occur in the future.

The major difference between past pandemics and the next potential pandemic is the fact that we have a far greater understanding of influenza pandemics and how they arise today than we had for any previous pandemic. As a result, we are in a better position than ever before to make specific preparations for the next influenza pandemic and thereby to significantly limit its overall impact.

The predictions in this model have implications for pandemic planning within multiple sectors of society:

Absenteeism

All sectors within the economy will be affected by the absenteeism relating to an influenza pandemic. With a predicted 20-22% of the population becoming infected, and being absent from work for between two days and two weeks, in the space of 25 weeks, the resultant loss of productivity will be large. All businesses and organizations will need to make contingency plans to ensure business continuity throughout this period of absenteeism. This absenteeism due to illness will be further compounded by staff who will need to take leave in order to attend to sick family members or attend funerals of family members who have died from influenza.

The effect of absenteeism and its knock-on effect on service provision within the essential services will further compound the adverse economic impact. Reductions in service delivery in the police, military, electricity generation,

telecommunications hamper productivity in the economy as a whole.

Changes in Behaviour

Changes in human behaviour are difficult to predict, but are likely to have a very large impact in the case of an influenza pandemic (Blendon *et al* 2006). It is predicted that a large proportion of the population will institute varying degrees of self-quarantine in order to limit contact with other people and thereby reduce their chances of being infected. Public places, gatherings and institutions may be stopped for the duration of a pandemic (e.g. shopping centres, schools, churches etc). In certain countries governments may mandate the limitation on public gatherings (Blendon *et al* 2006).

Self-quarantining behaviour may dramatically compound the absenteeism problem discussed above.

Mortality

The number of deaths predicted for the Mild Pandemic Scenario will have an appreciable, but limited effect on society and the economy. The death toll predicted for the Severe Pandemic Scenario, however, will have a marked effect in a number of realms.

Socially, the impact will be great, particularly in the case of a “W-shaped” mortality curve as used in the Severe Pandemic Scenario. In this instance, the

loss of life in the yo :ed economic productivity and social problems related to loss of bread-winners and parents of dependent children.

The high mortality rates could also have a crippling effect on the life insurance industry for obvious reasons. It is essential that life insurers are aware of the possibility and implications of a future pandemic and that they make specific contingency plans in this regard.

Travel

World-wide travel is likely to be severely curtailed for the duration of an influenza pandemic as both a mandated process by governments and a voluntary process on the part of individuals wishing to limit their risk of infection.

A similar scenario took place during the SARS epidemic in Asia and other affected countries with significant effects on their economies. Travel agencies and international airlines will be most severely affected and should be proactive in planning.

Overall Economic Impact

The overall economic impact for South Africa is difficult to predict, but is likely to be substantial. The World Bank has predicted the economic effects of a future influenza pandemic as being between a 2.6% and 4.4% reduction in annual GDP (World Bank 2006). With the predictions from this study, the GDP loss to

South Africa is likel the next pandemic be a severe one.

An interesting observation from the literature suggests that the economic impact of an influenza pandemic is not always negative. Brainerd and Siegler (2003) showed that, for the USA, there was a 0.15% increase in per capital GDP for every 1% increase in mortality rate from the Spanish Flu of 1918. This effect lasted for the 10 years following the pandemic. It is suggested that the loss of lives in the population exceeded the loss of economic income, thereby increasing the per capita GDP.

Implications for Pandemic Planning in the Healthcare Sector

The implications of a potential future influenza pandemic are most serious for the healthcare sector. The healthcare sector is faced with a potentially large increase in demand for its services, based on the increased number of patients, as well as the same constraints on service delivery which are common to other industries (e.g. absenteeism, disrupted essential services etc). A few of the more prominent aspects of healthcare services have been discussed below.

Hospital Capacity

As is clear from the results of this research, the current bed capacity (for both general and ICU beds) within South African hospitals will be placed under severe pressure in the case of a mild pandemic and will be completely overwhelmed in the case of a severe pandemic.

The research is particularly helpful to healthcare authorities in the respective provinces as it highlights provinces with more significant capacity constraints and may enable planning around the movement of patients between provinces in order to balance the load more evenly during a pandemic.

The predictions concerning the time distribution of patient load within a pandemic will also be very useful in facilitating specific capacity and staffing planning for different times in a pandemic.

The decision making process around increasing total hospital bed capacity in preparation for an influenza pandemic is complex in view of the high cost of increasing capacity and the lack of accurate predictions around when the next pandemic will occur.

Despite the difficulties concerned in increasing hospital bed capacity, the preparation for the provision of temporary hospital beds will prove invaluable in the case of a severe pandemic as is evidenced by the Severe Pandemic Scenario. Options available for temporary increases in capacity include:

- Postponing a ailability of existing beds
- Opening up currently unused hospital beds with the aid of extra staffing
- Designating non-hospital facilities as temporary hospitals (e.g. schools)

Mortuaries represent a further hospital related service which will be placed under substantial pressure in the case of a pandemic. While a specific analysis of current mortuary capacity was not performed, it could be readily accomplished as part of a follow-up study and the findings used to guide planning for this sector.

Hospital Staffing

Hospitals and other healthcare facilities will have similar staffing problems relating to absenteeism to those of other industries. The problem may in fact be aggravated in the healthcare sector due to the high exposure to influenza infected patients.

Based on the predictions provided, all healthcare provider organizations will have to make specific decisions regarding the provision of anti-viral drugs, personal protective equipment and vaccination (should it become available before the end of a pandemic) to their staff.

The above mentioned drugs and equipment would need to be stock-piled prior to the start of the next pandemic. It is very unlikely that large quantities of either will be readily available once the pandemic has already begun due to the

overwhelming dema ating to the stock-piling of these drugs and equipment have significant cost implications and must be informed by adequate information.

Medical Schemes

In the event of a severe influenza pandemic, the most disastrous impact is likely to be experienced within the Medical Schemes environment. The high cost of medical claims related to the treatment and hospitalization of influenza infected patients will represent a real threat to the solvency of most medical schemes.

While detailed predictions of these costs were beyond the scope of this research project, they would be very valuable and would be an ideal topic for further study.

Specific planning on the part of medical schemes, beyond generically increasing their solvency ratios (the ratio of accumulated reserves to annual claims), will remain challenging. Despite this, there is value in the Council for Medical Schemes, which regulates all medical schemes in South Africa, using the results of this study to guide policy decisions in an attempt to limit the chances of a collapse of the industry in the event of a severe pandemic.

Prioritization of Vaccine and Anti-viral Drugs

It is clear from the discussions in this research paper that there will be insufficient vaccine (if South Africa acquires any at all) and anti-viral drugs to provide prophylaxis and treatment for the whole population. These limited resources will therefore need to be rationed in the case of a pandemic.

It is important that the government and the National Department of Health have a coherent and clear plan as to the most effective prioritization of people to receive anti-viral drugs initially or perhaps vaccine in case it arrives.

Cooperative Planning

The next influenza pandemic will affect all aspects of society. It is clear from the research findings that the impact is likely to be significant across the entire country. In view of the extent of the impact, it is essential that a multi-sectoral approach is adopted in formulating a plan for the country.

The planning process should ideally be centrally controlled with involvement of all stakeholders. A case in point is the balancing of spare hospital and ICU bed capacity within the healthcare sector to most optimally meet demand. If the public and private sector hospitals do not cooperate during a pandemic, it is likely that capacity will be exceeded in some areas whilst other areas retain available beds.

Chapter 7: Conclusion

The world has been plagued by influenza pandemics at fairly regular intervals for the duration of recorded history. There were three significant influenza pandemics in the twentieth century with the Spanish Flu of 1918 being particularly severe and the latter two (1957 and 1968) being substantially milder in their overall impact.

There is considerable concern in the world at present regarding the risks of another influenza pandemic in the near future due to the H5N1 virus displaying some alarming signs, namely:

- An ability to infect humans
- A very high virulence (59% mortality to date)
- A large endemic pool within birds which is spreading globally

In an attempt to make meaningful plans for a possible pandemic, governments and other agencies are hungry for evidence-based predictions of the possible extent and impact of a future influenza pandemic. In particular, no current meaningful predictions exist for South Africa in this regard. This study has attempted to provide some of these predictions.

This study has provided predictions for the impact of an influenza pandemic on South Africa and the implications for capacity within South African hospitals based on the key parameters from the preceding three pandemics of the

twentieth century. T s have been summarized into predictions based on a Mild Pandemic compared with predictions based on a Severe Pandemic.

The Mild Pandemic Scenario closely resembles the pandemics of 1957 and 1968 and showed a total infection rate of 9.1% (although this has been discussed as being probably too low). The mortality rate was 0.13% representing 60 000 deaths. The hospital bed capacity was placed under pressure in all provinces, but not exceeded in any during the pandemic period. The ICU bed capacity, however, was exceeded in all provinces during the peak of the pandemic.

The Severe Pandemic Scenario closely resembles the Spanish Flu Pandemic of 1918 with a total infection rate of 22%. The mortality rate was significantly higher than the Mild Pandemic Scenario at 2.5% representing 1.2 million deaths. The hospital bed capacity was exceeded in all provinces for a period of approximately 10-12 weeks at the height of the pandemic and the ICU bed capacity was exceeded in all provinces for the duration of the pandemic.

The decision as to which of the two scenarios is a more realistic prediction for a future pandemic is a debatable point at this stage.

Due to the large impact which is predicted on the South African economy and healthcare sector, it is vital that all key decision-makers are informed as to the potential implications of a future pandemic, and are pro-actively involved in

planning for this p of necessity, involve all aspects of society and must be informed by valid research into the potential implications. In particular, the healthcare and health financing sectors must be pro-active in planning to mitigate the potentially disastrous effects which a severe pandemic may have on the population and the economy.

There are a number of potential future research projects which would add great value in informing the preparation process, namely:

- Prediction of absenteeism rates with the implications for the economy
- Prediction of the effects of a pandemic on out-patient healthcare services
- Financial and economic assessment of the impact on hospitals and other healthcare providers
- More detailed impact analysis for the Medical Schemes' industry in South Africa
- Should more healthcare capacity statistics become available, a more detailed prediction down to regional/ city level would be very useful in the planning process.

REFERENCES

Actuarial Society of South Africa (2005) *AIDS and Demographic Model 2003*. Available at http://www.assa.org.za/aids/content.asp?id=1000000449. (accessed on 15.7.06)

Berkow, R. Fletcher, A. Beers, M. (2000) *The Merck Manual of Diagnosis and Therapy.* 17th Edition. New Jersey: Merck Research Laboratories.

Blendon, R. Benson, J. Weldon, K. Herrmann, M. (2006) *In the Case of an Outbreak of Pandemic Flu, a Large Majority of Americans are Willing to Make Major Changes in their Lives*. Harvard School of Public Health. Available at http://www.hsph.harvard.edu/press/releases/press10262006.html. (accessed 26.10.06)

Brainerd, C and Siegler, M. (2003) The economic effects of the 1918 influenza epidemic. *Discussion Paper Series at Center for Economic Policy Research*, *No. 3791*. Available from http://www.cepr.org/pubs/dps/DP3791.asp (accessed 27/5/06)

Broomberg, J. (2006), *Consultative Investigation into Low Income Medical Schemes.* Available at http://www.sapma.co.za/assets/attachments/0223_First_Interim_LIMS_Report_Final_Draft_31_Oct_2005.pdf. (Accessed 20.07.06)

Brundage, J. (2006 uenza Pandemics in the United States. *American Journal of Preventative Medicine* 2006; 31 (3): 252-256

Byerly, C. (2005) *Fever of War: The influenza epidemic in the US Army of World War 1.* New York: New York University Press.

Capua, I. Alexander, D. (2002) Avian Influenza and Human Health. *Acta Tropica* 83; 1-6.

Capua, I. Marangon, S. (2003) The use of vaccination as an option for the control of avian influenza. *Avian Pathology* 32 (4) 335-343.

Chang, I. Krinik, A. Randall, J, Swift, A. (2006) Birth-multiple Catastrophe Processes. *Journal of Statistics and Inference*. Available at: http://www.sciencedirect.com/science?_ob=ArticleListURL&_method=list&_ArticleListID=487545633&_sort=d&view=c&_acct=C000005298&_version=1&_urlVersion=0&_userid=94552&md5=9a58659172fff06072a8ec3cf495b2d6.

Cram, O. Blitz, S. Monto, A. Fendrick, A. (2001) Influenza: Cost of Illness and Considerations in the Economic Evaluation of New and Emerging Therapies. *PharmacoEconomics* 19, 3.

Cox, N. Tamblyn, S. Tam, T. (2003) Influenza Pandemic Planning. *Vaccine*. 21, 1801-1803.

Crosby, A. (2003) *America's forgotten pandemic: The influenza of 1918.* New York: Cambridge University Press.

Day,C. Gray, A (2005). *Health Facilities Occupancy Levels*. Health Systems Trust. Available at http://www.hst.org.za/healthstats/156/data. (accessed 13.9.06)

Dundon, W. Milani, A. Catoli, G. Capua, I. (2006) Progressive truncation of the non-structural 1 gene of H7N1 avian influenza viruses following extensive circulation in poultry. *Viral Research.* 119 (2) 171-6.

Flint, S. (2004) *Principles of Virology: Molecular Biology, Pathogenesis and Control of Animal Viruses*. ASM Press.

Giesecke, J (1994). *Modern Infectious Diseases Epidemiology*. London.

Goldman, L. Ausiello, D. (2004) *Cecil Textbook of Medicine, 22nd Edition.* Massachusetts: Elsevier.

Hagenaars, T. van Genugten, M. Wallinga, J. (2003) Pandemic influenza and health care demand: dynamic modelling. *International Congress Series* 1263: 235-238.

Hunt, M. (2006) *nd Immunology Online*. University of South Carolina, School of Medicine. Available at http://pathmicro.med.sc.edu/mhunt/flu.htm. (accessed 20.9.06)

Jefferson, T. Bianco, E. Demicheli, V. (2002) Influenza vaccination in adults. *Occupational Medicine* 52 (5) 255-258.

Kasper, D. (2004) *Harrison's Principles of Internal Medicine, 16th Edition.* USA: McGraw Hill.

Kingsbury, D and Wagner, G. (1990) *Microbiology: 2nd Edition*. USA: Harwal Publishing.

Longini, I. Halloran, M. (2004) Containing pandemic influenza with antiviral agents. *American Journal of Epidemiology*, 159: 623-633.

Mabuya, N. Singh, A. Masilo, F. (2005) Roche South Africa: Influenza Pandemic Plan. *Roche SOP Manual*.

Mamelund, S. (2006) A socially neutral disease: Individual social class, household wealth and mortality from Spanish influenza in two socially contrasting parishes in Kristiania 1918-1919. *Social science and medicine, 62, 923-940.*

Meltzer, M. Cox, N mic Impact of Pandemic Influenza in the United States: Priorities for Intervention. *Emerging Infectious Diseases*. 5 (5) 659-671.

Netcare Hospital Division Overview. Network Healthcare Holdings Website. Available from: http://www.netcare.co.za/default.asp?currentpage=basemodule&id=4&level=2&subid=8 (accessed 25.5.06)

Oxford, J. Lamblein, R. Sefton, A. Daniels, R. Elliot, A. Brown, R. Gill, D. (2005) A hypothesis: the conjunction of soldiers, gas, pigs, ducks, geese and horses in Northern France during the Great War provided the conditions for the emergence of the "Spanish" influenza pandemic of 1918-1919. *Vaccine* 23: 940-945.

Patel, R. Longini, I. Halloran, M (2005). Finding optimal vaccination strategies for pandemic influenza using genetic algorithms. *Journal of Theoretical Biology,*234: 201-212

Philips, H. Killingray, D. (2003) *The Spanish Influenza Pandemic of 1918-19*. London: Routledge.

Ramdon, P. (2004) The inexact science of influenza prediction. *Lancet* 363 (9409), 583-4.

Roitt, M. (2002) *Roit* lge: Blackwell Publishing Ltd.

Shortridge, K. (2006) Influenza Pandemic preparedness: gauging from EU plans. *Lancet,* Vol 367, 1374-1375.

Skiest, D. Kaplan, P. Machala, T. Boney, L. Luby, J. (2001) Clinical manifestations of influenza in HIV infected individuals. *International Journal of STD and AIDS*; 12 (10) 645-650.

Sleath, J. (2006) Pandemic flu at the coal face. *BMJ,* 332, 913

Solomon, P. Isham, V. (2000) Disease surveillance and data collection issues in epidemic modelling. *Statistical Methods in Medical Research.* 9, 259-277.

South African National Department of Health (2006). Influenza Pandemic Preparedness Plan. Available at http://www.doh.gov.za/docs/influenza.html. (accessed June 2006)

Stander, V. (2004) *Hospital & Nursing Yearbook for Southern Africa. 44th edition*. Pretoria: Pharmaceutical Printers and Publishers.

Statistics SA (2006) *Midyear Population Estimates*, *South Africa 2005*. Available from: http://www.statssa.gov.za/publications/P0302/P03022005.pdf (accessed 30/5/06)

Swayne, D. Beck, J Garcia, M. Stone, H. (1999) Influence of virus strain and antigenic mass on efficacy of H5 Avian influenza inactivated vaccines. Avian Pathology 28 (3) 245-255.

Tognotti, E. (2003) Scientific triumphalism and learning from facts: Bacteriology and the Spanish flu challenge of 1918. *Social History of Medicine*, 16 (1), 97-110.

Uhnoo, I. Linde, A. Pauksens, K. Lindberg, A. Eriksson, M. Norrby , R. (2003) Treatment and Prevention of Influenza: Swedish Recommendations. *Scandinavian Journal of Infectious Diseases*. 35:3-11.

Viboud, C. Tam, T. Fleming, D. Handel, A. Miller, M. Simonsen, L. (2006) Transmissibility and mortality impact of epidemic and pandemic influenza, with emphasis on the unusually deadly 1951 epidemic. *Vaccine* (to be published in 2006).

Welliver, R. Monto, A. Crewics, O. Scatteman, E. Hassman, M. Hedrick, J. Jackson, H. Huson, L. Ward, P. Oxford, J. (2001) Effectiveness of Oseltamivir in Prevention of influenza in household contacts: A randomized controlled trial. *Journal of the American Medical Association* 285 (6).

Wolf, Y. Viboud, C. Holmes, E. Koonin, E. Lipman, D. (2006) Long Intervals of Stasis Punctuated by Bursts of Positive Selection in the Seasonal Evolution of

Inluenza A Virus. : at http://www.biology-direct.com/content/pdf/1745-6150-1-34.pdf. (accessed 27.10.06).

World Bank (2006) *Avian Flu: Human Pandemic*. Available at http://web.worldbank.org/WBSITE/EXTERNAL/EXTDEC/EXTDECPROSPECTS/EXTGBLPROSPECTSAPRIL/0,,contentMDK:20894257~menuPK:2466765~pagePK:2470434~piPK:2470429~theSitePK:659149,00.html. (Accessed on 26.10.06)

World Health Organization (2004) *WHO Guidelines on the Use of Vaccines and Antivirals during Influenza Pandemics.* Available from: http://www.who.int/csr/resources/publications/influenza/11_29_01_A.pdf (accessed 23/05/06)

World Health Organization (2005a) *Avian Influenza: Assessing the Pandemic Threat*. Available from: http://www.who.int/csr/disease/influenza/H5N1-9reduit.pdf (accessed 23/5/06)

World Health Organization (2005b) *Vaccine Research and Development: Current Status*. Available from: http://www.who.int/csr/disease/avian_influenza/vaccineresearch2005_11_3/en/print.html (accessed 23/05/06)

World Health Organization (2005c) *Influenza Pandemic Risk Assessment and Preparedness in Africa.* Available from:

http://www.afro.who 31_10_05.pdf (accessed 23/5/06)

World Health Organization (2006) *Cumulative Number of Confirmed Cases of Avian Influenza A (H5N1)*. Available from: http://www.who.int/csr/disease/avian_influenza/country/cases_table_2006_11_13/en/index.html. (accessed 13/11/06)

World Health Organization (2006a) *Avian Influenza: Current Status.* Available from: http://www.who.int/csr/disease/avian_influenza/country/cases_table_2006_05_29/en/index.html (accessed 30/5/06)

World Health Organization (2006b) *H5N1 Avian Influenza: Timeline*. Available from: http://www.who.int/csr/disease/avian_influenza/timeline.pdf (accessed 23/5/06)

World Health Organization (2006c) *Global Pandemic Influenza Action Plan to Increase Vaccine Supply.* Available from http://www.who.int/csr/resources/publications/influenza/CDS_EPR_GIP_2006_1.pdf. (accessed 27.10.06)