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A study to determine the relationship between patient related factors and influenza vaccination status

A research report submitted by:

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In partial fulfilment of the requirements for the

MSc Pharmacotherapy Degree

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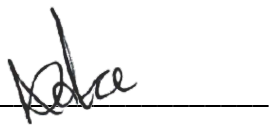
21 February 2022

Declaration

I, Dominique Kotzé, declare that this research report is my own work.

It is being submitted in partial fulfilment for the Degree Masters of Science in Pharmacotherapy at the University of the Witwatersrand.

It has not been submitted before for any degree or examination at any other university.



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ABSTRACT

Background:

Identifying and addressing the barriers to influenza vaccination can increase vaccine uptake not only through public health promotions by institutions, but also in consultations and recommendations by individual healthcare practitioners. In this study, I aim to establish the main attributing factors influencing vaccination sentiment and potential vaccine coverage in a retail pharmacy environment.

Methodology:

The study was quantitative cross-sectional and prospective in design.

Data collection was done by means of a self-administered hardcopy questionnaire adapted and tailored from previous studies.

Adult patients that brought a prescription (acute or chronic) or needed a repeat prescription to be filled (that has not been prepared beforehand) were invited to participate. The study was conducted at Clicks Pharmacy in Cresta Shopping Centre, where data collection was done from 1 April to 28 August 2020. Participants (n = 388) were mostly from the Cresta Shopping Centre catchment area (Blairgowrie, Fairland, Linden, Northcliff, Weltevreden Park, Ferndale, Greenside and Randpark Ridge) and were between the ages of 18 and 87 years. Of the 388 participants, 244 were females and 144 males.

An analytical analysis was done using the chi-square test of independence to prove links between vaccination status and the variables age, chronic conditions (HIV, respiratory conditions, diabetes and cardiovascular disease) and previous vaccinations.

Results:

A total of 152 (39%) of the participants were vaccinated and 236 (61%) were not vaccinated.

Most respondents reported getting vaccinated to avoid getting flu (87.5%) and most unvaccinated participants (40.3%) did not regard it as important. Just over a third (34.9%) of reponsdents who chose this reason fell into a category that places them in a risk group.

There is a marked increase in the probability of a patient returning to vaccinate after a previous vaccination within the last five years (2015-2019) with an Odds Ratio of 5.234 (95% confidence levels 3.352-8.174).

Conclusion:

As per the most popular reason not to vaccinate, the idea amongst patients that influenza is nothing to be concerned about became abundantly clear. Patients in risk groups were shown to consider themselves as not having any higher risk for severe influenza or complications due to influenza. This is partly due to the lack of recommendation by the healthcare providers and lack of education in this regard among patients and healthcare providers alike.

Previously vaccinated individuals were shown to be significantly more likely to be vaccinated again. Considering the higher probability for a previously vaccinated patient to return for another vaccination, establishing the reason for the first vaccination would prove vital information to formulate a strategy to increase vaccination. This would be a valuable topic for future research.

LIST OF ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
CD4	Cluster of Differentiation 4
CHAID	Chi-Square Automatic Interaction Detection
COPD	Chronic Obstructive Pulmonary Disease
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
H1N1	Hemagglutinin1 Neuraminidases1
LSM	Living Standard Measure
MMR	Measles, Mumps and Rubella
PCR	Polymerase Chain Reaction
WHO	World Health Organization

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CHAPTER 1: INTRODUCTION

1.1 Background

In recent years an anti-vaccination sentiment has grown in communities around the world. This was partly due to a paper published in the United Kingdom in 1998 claiming a link between the measles, mumps and rubella vaccine and autism. Younger (2016) called the correction of this misunderstanding, the biggest challenge for public health educators at the end of the 20th century in the UK.

Paget et al. (2019) estimated an average of 389,000 respiratory deaths associated with influenza every year in their study conducted between 2002 and 2011 (excluding the pandemic year of 2009) in the five World Health Organization (WHO) regions. In this study they found a yearly average of 43,096 respiratory deaths associated with influenza in South Africa.

Wong et al. (2016) established that influenza infections account for 43-67% of outpatient doctor visits by South Africans during influenza season. This study also estimated that 340 deaths per 100,000 population occur in South Africans over 65 years of age due to pneumonia and influenza, and 570 per 100,000 population pneumonia and influenza deaths in young adults with acquired immunodeficiency syndrome in South Africa. In 2018 Lancet Laboratories reported that a total of 49,482 specimens were received for respiratory virus polymerase chain reaction (PCR) testing (more than 3,000 specimens every month from March until October) of which 14,470 were for influenza.

Jorgenson et al. (2017) highlighted the complicated and exceedingly context-specific nature of the contributing factors affecting influenza vaccine hesitancy. Jorgenson et al. (2017) attribute the declining vaccine uptake in the WHO European Region to low trust in the safety and effectiveness of the vaccine, low perceived need to vaccinate, inadequate healthcare practitioner recommendation and general decline in trust in public health institutions after the 2009 Hemagglutinin1 Neuraminidases1 (H1N1) swine flu pandemic.

The perception that influenza is a low priority disease is also seen in the results of the study by Sagor and Al Alteeq (2018) in Saudi Arabia where 34.3% of participants responded that

influenza is a simple disease that does not deserve preventative measures. Most participants (49.7%) reported their desire to avoid medication as reason not to get vaccinated and 42.3% reported concern about the side effects even though only 7.7% reported side effects experienced with previous vaccinations.

In California, Rogers et al. (2018) found that 49.4% of respondents believed that the vaccine gives them influenza, while 30.4% fear dangerous side effects.

Wong et al. (2016) determined in the study conducted in Soweto and Klerksdorp that the most prevalent reasons people were not willing to get the influenza vaccine were the belief that the vaccine will not prevent influenza (19% of respondents in both Soweto and Klerksdorp) and for safety concerns (17% in Soweto and 10% in Klerksdorp).

1.2 Problem statement

Jorgensen et al. (2017) described that despite the WHO's goal to increase influenza vaccination coverage of at-risk patients to 75% by 2010 in the member states of the European Region, many countries reported a decline in the vaccine uptake. They reported as low distribution as 6.1 vaccines per 1,000 population in lower-middle income countries.

In a study conducted in Saudi Arabia between May 2017 and October 2017, Sagor and Al Alteeq found that even though most participants had a chronic disease, most did not receive the influenza vaccine (Sagor & Al Alteeq, 2018). This was surprising, since those with a chronic condition have an increased risk for severe disease and hospitalisation (Jorensen et al., 2017).

The picture seems to follow a similar trend in the rest of the world. Dal Negro et al. found in an Italian study in 2017 that even though more than 70% of subjects consider vaccination important, only 14% received the influenza vaccination yearly and almost 60% had never been vaccinated against influenza (Dal Negro et al., 2017).

As outlined by Jorgensen et al. (2017) influenza vaccination programmes differ from all other vaccination programmes because of the heterogeneity of its target populations as well as the

variety of healthcare facilities providing vaccinations which also complicate recordkeeping. Lower vaccine procurement in limited-resourced countries in the European Region was attributed by Jorgensen et al. (2017) as suggestive of the low-priority disease influenza seems to be.

According to Wong et al. (2016) there is a high prevalence of high-risk medical conditions (like HIV and tuberculosis) contributing to higher influenza associated mortality in South Africa. Despite mortality rates shown in the studies by Wong et al. (2016) and Paget et al. (2019) it seems that many patients entering into a private community pharmacy in South Africa do not consider influenza a threat to their health dismissing it as only an inconvenience.

1.3 Purpose of the study

Maintaining a high vaccination coverage is important because of the relatively low effectiveness of the influenza vaccine and not everyone can be vaccinated where severe allergic reactions to vaccine ingredients or socio-economic circumstances may prevent vaccination (Logan et al., 2018). At least 70% of a community needs to be vaccinated to prevent outbreaks and to benefit the community (Logan et al., 2018).

Olatunbosun et al. (2017) highlighted the lack of published studies in South Africa on influenza vaccine uptake in particular high-risk groups. They also identified the need for further studies on vaccine uptake in areas where the vaccine is readily available. Because Olantunbosun et al. (2017) conducted their study in two government hospitals, cost implications of the vaccine was not explored. Both of these limitations identified by Olatunbosun et al. (2017) were addressed by my study as the Vaxigrip quadrivalent influenza vaccine was readily available on-site at a cost of R79.

Wong et al. (2016) also identified the hypothetical acceptability of the influenza vaccine as a limitation to their study due to their methodology of interviews conducted at the participants' residences. They recognised that their participants' responses might change when faced with a real decision where the vaccine is readily available. Wong et al. (2016) only inspected the

reasons given for vaccine hesitancy, but did not investigate the reasons for willingness to vaccinate, including recommendation by a healthcare provider.

Identifying and addressing the barriers to vaccination can increase vaccine uptake not only through public health promotions by institutions, but also in consultations and recommendations by individual healthcare practitioners like myself.

1.4 Aim and objectives of the study

Aim:

Establish main attributing factors influencing vaccination sentiment and potential vaccine coverage in a Johannesburg suburban retail pharmacy environment.

Objectives:

- Determine the factors reported by patients that cause vaccine refusal or vaccine postponement.
- Determine the relationship between chronic conditions (HIV, diabetes, cardiovascular conditions and asthma), advanced age and previous vaccinations and vaccine uptake.
- Document the incidences of self-reported adverse reactions experienced by patients after influenza vaccination.

1.5 Summary of Chapter 1

With their 2019 study where Paget et al. estimated a yearly average of 43,096 respiratory deaths associated with influenza for South Africa, it became clear that influenza has a serious effect on mortality in South Africans. Even though influenza is a vaccine-preventable disease, Wong et al. (2016) determined in their study conducted in Soweto and Klerksdorp, that most people were not willing to get the influenza vaccine due to the belief that the vaccine will not prevent influenza (19% of respondents in both Soweto and Klerksdorp), and for safety concerns (17% in Soweto and 10% in Klerksdorp). Wong et al. (2016) also highlighted the fact

that there is a high prevalence of high-risk medical conditions (like HIV and tuberculosis) contributing to higher influenza associated mortality in South Africa.

Olatunbosun et al. (2017) pointed out the lack of published studies in South Africa on influenza vaccine uptake in high-risk groups in particular. This is why it is of value to review the data available on these high-risk groups in Chapter two of this study and establish (in Chapter three) the relationship between risk conditions and vaccine uptake.

1.6 Overview of chapters

Chapter one discussed the background regarding the influenza burden worldwide and in South Africa and outlined the problem of low vaccine uptake among patients with chronic diseases that leaves them at higher risk for complications due to influenza.

In Chapter two a literature review is done on the risk for influenza complications in patients that are HIV positive, asthma patients, diabetics, patients with cardiovascular diseases and elderly patients. Chapter two concludes with a short discussion on the history of vaccine hesitancy.

In Chapter three the methodology used to establish the main attributing factors that influence vaccination sentiment is discussed. The study design and procedure, sample population, data collection tool, analysis and ethics are explained and reasoning behind this methodology outlined.

In Chapter four the results rendered by the questionnaire are specified and presented in various tables and a figure. The results rendered by the chi-square analysis done on the relationship between the high-risk chronic conditions and vaccination status are outlined.

In Chapter five the results retrieved are discussed and compared with previous studies. The encouraging finding that most vaccinated individuals understand the benefit to their health is discussed. The need for public education is discussed with most unvaccinated individuals regarding vaccination as unimportant. This is reiterated in the discussion regarding patients with high-risk chronic conditions revealed to have low vaccination rates. The significantly

higher vaccine uptake among previously vaccinated individuals is discussed and compared to previous studies.

In Chapter six the conclusion is drawn that the main attribution factor influencing vaccination is a previous vaccination, which leads to the recommendation for future study into the reason for a first vaccination.

CHAPTER 2: LITERATURE REVIEW ON AT-RISK PATIENTS AND THEIR VACCINE UPTAKE

As stated by Jorgensen et al. (2018) people with comorbidities including immunosuppression, lung diseases, diabetes, and cardiovascular diseases as well as the elderly have a particularly higher risk of severe influenza and hospitalisation. According to Jorgensen et al. (2018) these groups should be prioritised for influenza vaccination.

Veerapandian et al. (2018) did a systemic literature review of epidemiological reports on hospitalisation of asthma patients during the influenza pandemic of 2009 and found, as depicted in Figure 1, that comorbidities like immunosuppression, cardiovascular disease and metabolic diseases exacerbate influenza.

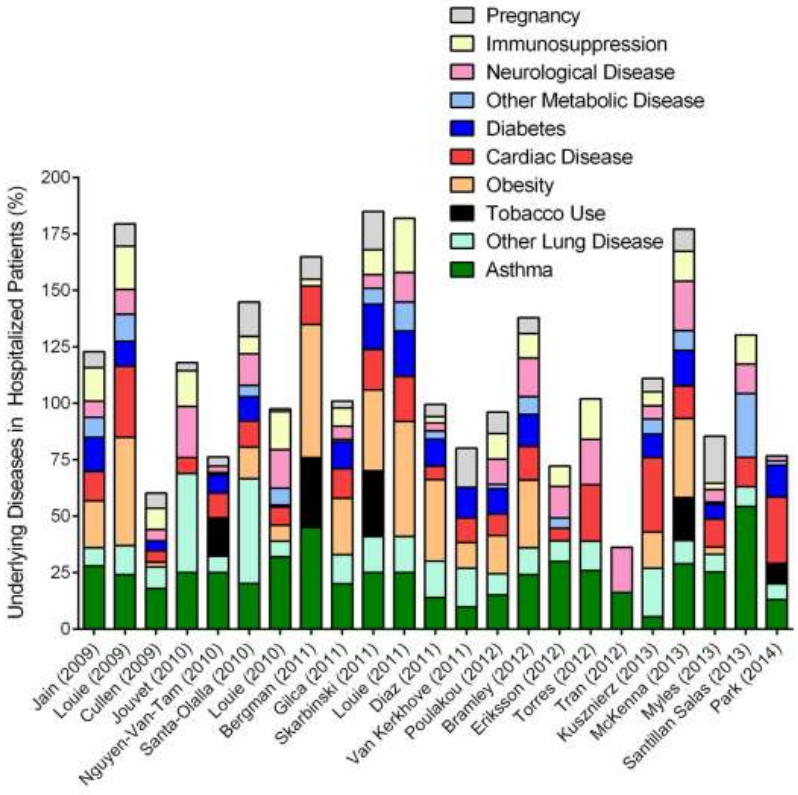

Figure 1: An overview by Veerapandian et al. (2018) of epidemiologic reports in asthma patients in the 2009 influenza pandemic

In the following chapter the literature will be reviewed on the influenza disease burden and vaccine uptake in high-risk patients with the following conditions: human immunodeficiency virus, asthma, diabetes, cardiovascular diseases and the elderly. These are the patients most represented by the risk groups described by Jorgensen et al. (2018) in the retail pharmacy environment explored in my study. The databases used were PubMed, Cochrane Library and HHS Digital Library.

2.1 Human immunodeficiency virus

Cohen et al. (2015) found that one of the highest influenza associated mortality rates in South Africa is in adult HIV positive patients. This is apparent in the twenty times higher influenza-associated mortality rates in HIV infected individuals compared to HIV uninfected individuals estimated in their study. They found that the risk for influenza-related hospitalisation in HIV positive individuals is four to eight times greater.

In the United States, Gallagher et al. (2007) found vaccination coverage in HIV infected patients increased from 28.5% to 34% between 1990 and 1992, but then declined to 21.4% in 1995, and reached a high of 41.6% again by 2002. During the pre-highly active antiretroviral therapy (HAART) period (1990-1995) Gallagher et al. (2007) noticed that patients with a higher cluster of differentiation 4 cell (CD4 T-cell) count were less likely to be vaccinated, but patients on antiretroviral (ARV) treatment during the HAART period showed higher vaccination rates (46%) irrespective of their CD4 T-cell count (2007). This could be because patients on ARVs are likely to make more visits to a healthcare facility. This reaffirms the importance of the healthcare provider's recommendation to vaccinate, where the providers, like the pharmacist, are in an optimal position to improve coverage, even if it is only one patient at a time.

2.2 Asthma

Dharmage et al. (2019) stated that around 300 million people around the world have asthma. Keenan et al. (2007) highlighted the particular vulnerability of asthma patients to the complications of influenza, but found the vaccine uptake in their British study to be only 40% amongst asthma patients and it did not increase in recent years as for other risk groups. Similarly, Jimenez-Garcia et al. (2010) found only 38% of asthmatics vaccinated against influenza in Spain in 2006.

Concern that the influenza vaccine may cause asthma exacerbations could possibly explain the low vaccine coverage, but this was disproven by studies by Jimenez-Garcia et al. (2010) and Cates and Rowe (2013).

Mertz et al. (2013) proved a higher risk for admission to hospital, intensive care units and ventilation support in patients with chronic lung disease. They found asthma patients had a higher risk to contract pneumonia and chronic obstructive pulmonary disease, as such this showed a greater need for ventilation support (Mertz et al., 2013).

Asthma was shown as an unquestionable risk factor in the swine flu pandemic with 10-20% of hospitalised patients worldwide being asthmatics and 25% of hospitalised patients in the USA (Veerapandian et al., 2018). They demonstrated similar frequencies of hospitalisation and death between seasonal and pandemic influenza with comparative analysis.

Veerapandian et al. (2018) suggested that the differences in behaviour of asthmatics when seeking healthcare could be the cause of increased hospitalisation which creates more opportunity for preventative recommendations like vaccination by the healthcare provider.

2.3 Diabetes

Diabetes is estimated to have contributed up to 1.5 million deaths globally in 2015. It is the 3rd biggest illness causing death in South Africa with a 7% prevalence in South African adults in 2014 (Olatunbosun et al., 2017).

Diabetics are three to six times more likely to be admitted into hospital due to influenza complications and the death rate increases by 5-15% among diabetics during an influenza epidemic (Olatunbosun et al., 2017).

A reduction of 79% in hospital admissions amongst diabetics have been seen after receiving the influenza vaccination and yet Olatunbosun et al. (2017) found vaccine coverage of only 16.9% in South African adult diabetics in 2005.

However, Remschmidt et al. (2015) found a lack of influenza vaccination associated safety outcomes in diabetics in previous studies, and could not identify any experimental studies to establish the effects of the vaccine in a large group of diabetics.

This highlights the need for particular attention to this high-risk patient group during every visit to the healthcare facility as well as the need for further studies in this regard.

2.4 Elderly and cardiovascular disease

Paget et al. (2019) estimated that 2% of the yearly respiratory deaths between 2002 and 2011 (excluding 2009) in the five WHO's regions were related to influenza infections and that as much as 67% were people 65 years and older. Paget et al. (2019) also found, in patients over the age of 65, a twenty-six times higher influenza-related mortality rate globally and eighteen times higher in South Africa.

Elderly vs. non-elderly delivered an odds ratio of 4.65 (95% confidence interval of 1.74-12.41) for hospital admissions and a 2.95 odds ratio (1.53-5.70) for all case mortality in a meta-analysis on risk populations for severe influenza (Mertz et al., 2013).

Almost without exception most elderly patients have comorbidities of which cardiovascular is the most frequent. Mertz et al. (2013) found that cardiovascular conditions increase the mortality risk in severe influenza with an odds ratio of 1.97 (95% confidence interval 1.06-3.67).

These increased mortality rates in the elderly as well as the presence of cardiovascular comorbidities emphasise the greater burden of influenza in this patient group and the importance for prevention of seasonal influenza.

2.5 History of vaccine hesitancy

Even from before the development of what is considered the first vaccine by Dr Edward Jenner in 1798, people have been sceptical about vaccines (Callender, 2016). Variolisation was then often done unsafe by poorly qualified practitioners and corrupt individuals were promoting practises of unnecessary deep cuts and extreme bloodletting in an effort to increase profits (Callender. 2016). Although vaccines and vaccination practices have improved vastly in recent history, Callender (2016) has reiterated the constant need for the record to be straightened because the public does not obtain knowledge from proper medical and scientific publications. In addition public figures like Donald Trump, have continued to sow seeds of doubt by expressing belief in Andrew Wakefield's disproven research on autism causing vaccines (Callender, 2016).

Callender (2016) also found that concerns about the influenza vaccine and Guillian-Barré syndrome still exists among vaccine hesitant individuals. Initial evidence of an association between the influenza vaccine and Guillian-Barré syndrome was first reported in 1976 (Soni et al. 2020). Hesitancy persists even though the current influenza vaccination formulation has never been proven to have an association with Guillian-Barré syndrome (Callender, 2016).

2.6 Conclusion of Chapter 2

HIV positive patients, asthmatics, patients with cardiovascular disease, diabetics and elderly patients clearly show an increased risk for severe influenza or complications due to influenza. This increased risk should serve as motivation for these patients to vaccinate and thus show an increased vaccination rate among these patient groups. Unfortunately, this does not seem

to be the case when referring to studies done by Gallagher et al. (2010), Keenan et al. (2007), Jimenez-Garcia et al. (2010) and Olatunbosun et al. (2014).

Therefore, in Chapter 3, the methodology used to explore the relationship between these risk factors and vaccination status of the participants of my study, is explained.

CHAPTER 3: METHODOLOGY

3.1 Introduction

In order to establish a relationship between influenza vaccination status and patient-related factors, a questionnaire was used to collect information to assist in demonstrating an association between patient factors and vaccination status. The methodology to establish this is discussed in more detail in this chapter by describing the study design, discussing the sample population, explaining the study procedure, discussing the data collection tool, explaining the analysis done on the collected data, and finally discussing the ethics surrounding my study.

The research hypothesis asked:

Will a particular reason have a larger impact on the patient's decision to vaccinate or not to vaccinate? Similarly, will advanced age and concurrent chronic conditions show increased vaccination rates? This also leads to the question if previously vaccinated individuals are more likely to be vaccinated again?

3.2 Study design

The study was quantitative, cross-sectional and prospective in design.

The study utilised a self-administrated hardcopy questionnaire. This data collection tool was used due to its suitability to the timeframe of the study. The timeframe of the study was dictated by the annual flu season (from April until August) when influenza vaccine demand by patients in the retail pharmacy occur. This study design also promoted easy access to the information required to meet the objectives of the study and keep the financial cost of the study low.

3.3 Sample population

The study was conducted at Clicks Pharmacy in Cresta Shopping Centre, where data collection was done from 1 April to 28 August 2020.

According to a research summary supplied by Cresta shopping centre management, the catchment area has a population of approximately 540,000 people. This population is mostly middle-class to affluent with 78% of customers being of the South African Living Standard Measure (LSM) 8-10 (10 being the highest on this scale). Although comprehensive on customers, this research summary by Cresta centre management did not include employees working in the centre or patients collecting ready parcels sent by the Department of Health for collection at the pharmacy. These patients also entering the pharmacy may fall into a different LSM group.

A sample size of 385 was calculated using Formula 1 below, but 390 questionnaires were collected to compensate for questionnaires that had to be disregarded.

$$n = \frac{z^2 \times \hat{p}(1-\hat{p})}{\varepsilon^2}$$

$$n = \frac{1.96^2 \times 0.5(1-0.5)}{0.05^2} = 384.16$$

n = Sample size

z= Confidence level (set at 95% with a standard value of 1.96)

p= Standard deviation

e= margin of error

Formula 1: Sample size calculation

Inclusion criteria:

- Adults (over the age of 18 years).
- Patients that bring in a prescription or need a repeat to be filled (that has not been prepared beforehand).
- Patients that request a flu vaccine prior to being offered the vaccine.

Exclusion criteria:

- Patients with allergies to any of the ingredients in the flu vaccine preparation, such as eggs, chicken protein, neomycin, formaldehyde and octoxynol 9.

3.4 Study procedure

Upon approach at the dispensing counter of the researcher, a patient that complied with the inclusion criteria was invited to participate in the study anonymously. Adult patients that brought in a prescription (acute or chronic), and patients that needed a repeat prescription to be filled (that has not been prepared beforehand) were invited by the researcher to participate.

The aim, objectives and methodology of the study were verbally explained to the patient. A patient information leaflet (Appendix 2) was given to every patient to read and take home. After ample consideration and opportunity to ask questions, if the patient agreed, he/she was asked to sign the consent form (Appendix 3) and complete the paper questionnaire (Appendix 1). A unique identification number was assigned to each questionnaire to protect the identity of the patient.

After completion of the questionnaires, the data was inserted into an Excel spreadsheet to enable analysis.

3.5 Data collection tool

Data collection was done by means of a hardcopy questionnaire adapted and tailored from previous studies, Dal Negro et al. (2018), Rogers et al. (2018), Logan et al. (2018), Sagor and Al Alteeq (2018) and Olantunbosun et al. (2017), all of whom used validated questionnaires. In addition Sagor and Al Alteeq (2018) and Logan et al. (2018) used their questionnaires in smaller pilot studies to ensure validity and reliability. The tailored questionnaire used in my study was

scrutinised and ultimately approved in May 2019 by the protocol assessors appointed by the University of Witwatersrand.

Data fields to be completed by the patient include age, gender, residential area and reasons for either getting vaccinated or not getting vaccinated, vaccination history for the past five years, concurrent chronic condition, adverse effects experienced and smoking habits. To satisfy the quantitative nature of the study design, the questionnaire consisted of mostly closed-ended questions and multiple-choice questions.

3.6 Data analysis

An analytical analysis was done using the chi-square test of independence to prove a relationship between vaccination status and the variables age, chronic conditions (HIV, respiratory conditions, diabetes and cardiovascular disease) and previous vaccinations. The chi-square test was chosen as analysis due to its functionality when analysing cross tabulations generated from the questionnaire responses. Software used for the analysis was SPSS version 26.

The Null hypothesis (H_0) is that there is no correlation between vaccination status and any variables enquired in the questionnaire, thus no factor has an influence on a patient's decision to vaccinate. The alternative hypothesis (H_1) is that a particular variable does have a significant influence on the patient's decision to get vaccinated.

3.7 Ethics

Approval to conduct this study was granted by the Human Research Ethics Committee at the University of Witwatersrand, which issued a clearance certificate in this regard (Appendix 4).

An approved patient consent form (Appendix 3) and patient information leaflet (Appendix 2) was given to each participant. If the patient agreed, he/she was asked to complete the paper questionnaire (Appendix 1) which was also approved by the Ethics Committee. A unique

identification number was assigned to each questionnaire to protect the identity of the patient.

When the data was captured into an Excel document, no patient-identifying information was included, but regardless of this, the document is kept digitally in a password protected file. The hardcopy questionnaires and patient consent forms were separated from each other to protect the identity of the participant, and is kept in a locked cupboard.

Approval was also granted to collect data at Clicks pharmacy in Cresta by both the responsible pharmacist (Appendix 5) and area manager (Appendix 6).

CHAPTER 4: RESULTS

Of the 390 questionnaires, two questionnaires were disregarded having only two data fields completed thus 388 participants were included in the study. There were 152 (39%) vaccinated participants and 236 (61%) unvaccinated participants. Age and gender distribution (Table 1) of participants mostly reflected the expected distribution as outlined by the customer research summary provided by Cresta Shopping Centre management. Females accounted for 244 of the participants, of which 96 were vaccinated (63.2% of vaccinated individuals).

Participants that reported having a comorbidity that places them into one of the risk categories (HIV, asthma, diabetes or cardiovascular disease) came to 124 out of the 388 respondents and 58 elderly respondents participated. Elderly was defined as participants 65 years and older (Mertz et al. 2013).

Table 1: Demographics and comorbidities of respondents

	Frequency	Respondents (%)
Age distribution		
18-29	76	19.6
30-39	91	23.5
40-49	87	22.4
50-59	57	14.7
60-69	38	9.8
70+	39	10
Total	388	100.0
Gender		
Female	244	62.9
Male	144	37.1
Total	388	100.0
Comorbidities		
HIV	15	7.7
Asthma	29	14.9
Diabetes	20	10.3
Cardiovascular disease	84	43.3
Elderly (>65years)	58	14.9
None	182	46.9
Total	388	

4.1. Factors reported by patients that cause vaccine refusal or vaccine uptake.

Just over a third of patients (152; 39%) indicated that they were vaccinated, with the majority of those participants (133; 87.5%) indicating the need to avoid getting the flu as the reason for getting vaccinated. Partcipants were allowed to select more than one reason, but 60 (39%) of the vaccinated respondents chose “to avoid getting flu” as the only reason for vaccine uptake. Other reasons specified by participants included, to achieve herd immunity, working in a high-risk enviroment, the desire to “keep the immune system strong”, influenza vaccination is a work requirement, vaccination was paid for by the participant’s employer and one repondent listed her asthma as reason to be vaccinated.

Table 2: Reasons given for getting vaccinated

Reason for getting the vaccine	n	Number of times this reason was chosen	Percent (%)
Other	152	6	3.9
Recommended by pharmacist	152	9	5.9
Recommended by friends/family	152	15	9.9
Loyalty points	152	16	10.5
Got very sick	152	25	16.4
Corona virus scare	152	36	23.7
Recommended by doctor	152	41	27.0
Avoid getting flu	152	133	87.5

A total of 236 (61%) of respondents did not get vaccinated. Most listed that they did not think it is important (95; 40.3%) and 82 (34.7%) of the respondents gave this reason as the only reason for vaccine hesitancy. Other reasons for hesitancy specified by respondents included the desire to avoid going into a mall during the COVID-19 pandemic, the belief that taking vitamins will offer enough protection against influenza and simply that the respondent has never been vaccinated against influenza before.

Table 3: Reasons given for not getting vaccinated

Reason for not getting the vaccine	n	Number of times this reason was chosen	Percent (%)
Other	236	3	1.3
Too expensive	236	4	1.7
Was unavailable when I wanted it	236	4	1.7
Never got it before	236	10	4.2
Friends/family said it is bad for me	236	16	6.8
Forgot	236	17	7.2
Does not work	236	17	7.2
I do not need it	236	28	11.9
Gives me flu	236	29	12.3
Previous bad experience	236	37	15.7
Did not think it is important	236	95	40.3

4.2 Chronic conditions and age of respondents in relation to vaccine uptake

Half of the respondents (194) indicated that they have one or more chronic condition. As shown in Table 4, only 81 (41.8%) of the participants that have a chronic condition were vaccinated. The chi-square analysis done on concurrent chronic conditions indicates an insignificant result with evidence for H_1. This is also highlighted in Table 5 by an Odds Ratio of 1.242 (95% confidence levels 0.825-1.868). This indicates that having a chronic condition in general did not persuade a patient to vaccinate.

Table 4: Concurrent chronic conditions and vaccination status

	Vaccinated	Not vaccinated
Concurrent chronic condition (n=194)	81 (41.8%)	113 (58.2%)
No other chronic condition (n=194)	71 (36.6%)	123 (63.4%)

The chi-square analysis (Table 5) done on HIV as factor influencing vaccination status indicates an insignificant result with evidence for H_0, but only three of the 15 HIV-infected participants indicated that they were vaccinated and 12 did not get vaccinated. HIV could possibly be underreported and the size of the sample needs to be larger to render a more reliable result.

The chi-square analysis done on respiratory conditions as a factor influencing vaccination status indicates a significant result with evidence for H_1. Of the 29 respondents with asthma, 17 (58.6%) were vaccinated. This indicates that patients with asthma were more prone to be vaccinated against influenza, but a larger sample size will render a more reliable result.

The chi-square analysis done on diabetes as a factor influencing vaccination status indicates an insignificant result where H_0 is true. Half of the diabetic respondents (10 respondents) indicated that they were vaccinated, but with only 20 respondents being diabetics, a larger sample size will render a more reliable result.

The chi-square analysis done on cardiovascular disease as an influencing factor for vaccination indicates an insignificant result where H_0 is true. This shows that patients with cardiovascular disease do not consider their disease sufficient reason to be vaccinated against influenza. Less than half of the cardiovascular patients were vaccinated (36 of the 84, or 42.9%).

Vaccine hesitancy was shown to be more prevalent in participants younger than 49 years, with Figure 2 showing a decreasing hesitancy after the age of 50 years, but the chi-square analysis done on the different age categories showed an insignificant result.

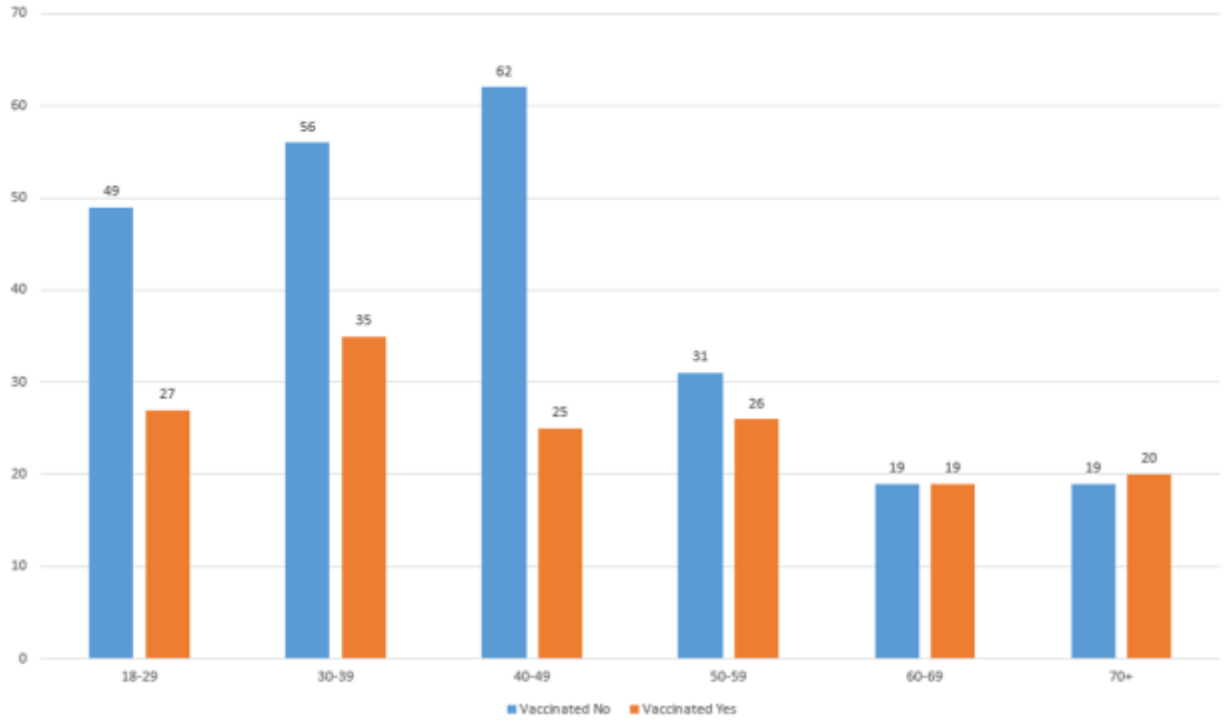

Figure 2: Age categories and vaccination status

The chi-square analysis done on participants older than 60 years of age as an influencing factor for vaccination indicates a significant result with evidence for H_1. This means that participants older than 60 years were more prone to vaccinate. In this study 77 participants were older than 60 years and 39 (50.6%) participants were vaccinated.

Table 5: Chi-square analysis of risk factors

Chi-Square Tests	Value	df	p-value
Analysis on concurrent chronic conditions			
Pearson chi-square	1.082	1	0.298
Fisher's exact test			0.349
N of valid cases	388		
Analysis on HIV			
Pearson chi-square	3.163	1	0.075
Fisher's exact test			0.102
N of valid cases	194		
Analysis on respiratory conditions			
Pearson chi-square	3.989	1	0.046
Fisher's exact test			0.065
N of valid cases	194		
Analysis on diabetes			
Pearson chi-square	0.624	1	0.43
Fisher's exact test			0.478
N of valid cases	194		
Analysis on cardiovascular disease			
Pearson chi-square	0.074	1	0.785
Fisher's exact test			0.883
N of valid cases	194		
Analysis of age categories			
Pearson chi-square	9.683	5	0.085
N of valid cases	388		
Analysis of age 60 years and older			
Pearson chi-square	5.308	1	0.021
Fisher's exact test			0.026
N of valid cases	388		

4.3 Adverse reactions reported by patients after influenza vaccination.

Most patients that were vaccinated did not report any side effects. Only 30 (19.7%) of the 152 participants that were vaccinated reported side effects. Of the side effects reported, pain at the site of the injections (as expected) was reported the most (36.7%). Other adverse reactions reported by respondents included a rash and severe bronchitis.

Table 6: Frequency of side effects experienced

Side effects	n	No	Yes	Percent (%)
Other	30	28	2	6.7
Fatigue	30	27	3	10.0
Nausea	30	26	4	13.3
Mild cold/flu symptoms	30	25	5	16.7
Headache	30	24	6	20.0
Muscle ache	30	23	7	23.3
Fever	30	20	10	33.3
Swelling/pain at injection site	30	19	11	36.7

4.4 Previous vaccinations and vaccine uptake

The chi-square analysis done on previous vaccination as an influencing factor for vaccination (Table 7), indicates a highly significant result with strong evidence for H_1. An Odds Ratio of 5.234 (95% confidence levels 3.352-8.174) highlights the fact that a person that had the vaccination in previous years were most likely to return for a vaccination.

Table 7: Chi-square analysis of previous vaccinations (2015-2019)

Chi-Square Tests	Value	df	p-value
Pearson chi-square	56.586	1	0.000
Fisher's exact test			0.000
N of valid Cases	388		

Table 8: Number of previous vaccinations and vaccination status

Observed frequency		Got flu vaccine		
		No	**Yes**	**Total**
Number of previous vaccination	1	50	24	74
	2	17	15	32
	3	3	19	22
	4	4	13	17
	5	2	38	40
	Total	76	109	185

4.5 Smoking habit of participants

Only 53 participants reported as being smokers. This could have been underreported due to the perceived risk of judgement by the researcher in the healthcare facility setting. The ban on the sale of tobacco products imposed by government during the level five lockdown regulations of the COVID-19 pandemic response, during most of the data collection period, could have added to underreporting of the smoking habit. As illustrated in Table 9, most (45; 84.9%) of those that reported as smokers, did not get the influenza vaccine. This is an apparent difference to the 144 (43%) of non-smokers that did get vaccinated.

Table 9: Smoking habit and vaccination status

Smoking habit	**Vaccinated**	**Not vaccinated**
Smoker (n=53)	8 (15.1%)	45 (84.9%)
Not smoker (n=335)	144 (43%)	191 (57%)

CHAPTER 5: DISCUSSION

5.1 Introduction

This study aimed to establish the main attributing factors influencing vaccination sentiment and potential vaccine coverage. The factor that proved to be the most influential on vaccine uptake was previous vaccinations. A chronic condition did not motivate the respondents to get vaccinated, with the exception of asthmatics that showed a better vaccine uptake. As with asthmatics, respondents older than 60 years of age also showed a higher vaccine uptake.

The finding of 39% (152 of the 388 participants) vaccination coverage is in line with the 45.6% estimated for the United States in 2015 by Logan et al. (2018).

In this chapter follows a discussion on the results found on factors reported by patients that cause vaccine refusal or vaccine uptake, chronic conditions and age of respondents in relation to vaccine uptake, adverse reactions reported by patients after influenza vaccination and previous vaccinations and vaccine uptake.

5.2 Factors reported by patients that cause vaccine refusal or vaccine uptake

Most respondents reported getting vaccinated to avoid getting the flu (87.5%). This was in line with the 80% of participents in the study by Dal Negro et al. (2018) and higher compared to the 47.6% of the respondents in the study done by Logan et al. (2018), where most respondents also identified preventing the flu as the main reason for vaccination. This was in contrast to just earn loyalty points (like Discovery Vitality points) which only 10.5% of repondents confessed to (and not a single respondent chose only getting the vaccine to earn points). This was an encouraging finding in the thought patterns and decesion-making of these patients in general which indicate that most respondents who were vaccinated, understood the health benefits that prevention of influenza can provide.

Just over a third (34.9%) of reponsdents who chose this reason (to avoid getting flu), fell into a category that placed them in a risk group. Most other respondents that fell into a risk category reported that they were vaccinated by their doctors' recommendation. This highlights the importance of recommendation by a healthcare provider. Recommendation by the pharmacists at only 5.6% highlighted the need for educating the pharmacists about the risks of severe influenza and burden of influenza in general. This argument is strenghened by the results found by Logan et al. (2018) that showed 23.1% of the respondents that were vaccinated did so because of recommendation by a healthcare provider.

Most patients did not regard it as important to be vaccinated against influenza (40.3% or 95 of the 236 participants). This is in contrast to the findings by Wong et al. (2016) where only 3% of Sowetan participants and 8% of Klerksdorp participants responded that they regarded the vaccine as unimportant. Of the 95 respondents that did not regard vaccination important, 30 (31.6%) fell into a risk group for severe influenza or complications. This was a major concern regarding the way these at-risk patients view their health in general and/or the lack of understanding of the risk posed to them as risk patients. This also pointed to the dire need for public education on the different aspects of influenza as a disease as well as aspects of the vaccine. A better understanding by the patients and heathcare providers alike will increase trust in the vaccine and decrease reluctance towards it.

The 15.7% of people stating that they had a previous bad experience is in contradiction to the 80.3% of people that reported vaccination without any side effects.

5.3 Chronic conditions and age of respondents in relation to vaccine uptake

5.3.1 HIV

Only 20% of HIV infected individuals in this study reported as vaccinated. This rate was found to be below the estimated 30% of vaccinated HIV positive patients in the study by Gallagher et al. (2007). This rate could be lower compared to Gallagher et al. (2007), due to underreporting and a small sample size.

All three respondents that were vaccinated chose the “to avoid getting flu” option, with one adding that the doctor recommended it and another adding Coronavirus fear as a reason to vaccinate. All three were also vaccinated in the previous years. Four respondents that did not get vaccinated chose that they did not think it was important. These responses were not unique to the condition but rather followed the overall trend occurring as with other respondents. In contrast, 11 of the 15 unvaccinated respondents were vaccinated during the last five years, which deviates from the trend to return after an initial vaccination. Previous recommendation explains the higher vaccination rate in the past five years when, as highlighted by Gallager et al. (2007), vaccination rates increase with a higher frequency of medical visits when the diagnosis is initially made. However, the concern that these patients were not returning for annual vaccination highlights the lack of repeated recommendation which is contributing to the idea that it was not important.

5.3.2 Asthma

Asthma patients showed a slightly higher probability to be vaccinated with 58.6% of asthmatic respondents vaccinated, which was higher than the 40.1% found by Keenan et al. (2007). Most of these individuals kept to the trend and chose “to avoid getting flu” as the reason to get vaccinated, but more individuals also responded that it was recommended by their doctor. The increased probability of vaccination in asthmatics, is attributed to asthmatic patients being

more aware of their state of health due to fear of an asthma attack and thus being more prone to seek medical attention when concerned and taking preventative measures.

Keenan et al. (2007) found that 66% of their asthmatic respondents declined vaccination due to the belief that influenza does not pose a serious risk for them. In contrast with the majority of non-asthmatic respondents in my study who also thought of vaccination as unimportant, most unvaccinated asthmatics, responded that they had a bad past experience. This brings to mind the theory that the vaccine can cause asthma exacerbations. According to Cates and Rowe (2013), this theory was proven wrong but the possibility exists that exacerbations that occurred could have wrongly been attributed by healthcare providers and patients in this risk group to the vaccine because of the misconception created by this theory.

5.3.3 Diabetes

Although the 50% vaccine uptake among diabetics in my study is higher than the 28.8% found by Olantunbosun et al. (2017), diabetes was not an influencing factor for vaccine uptake. Half of the diabetics (10 respondents) in the study were vaccinated despite the fact that 14 of the 20 diabetics, also had other chronic conditions that placed them even further at risk for complications due to influenza. The fact that diabetes has very little influence on a patient's decision to vaccinate, was reiterated by the fact that the reasons for vaccine hesitancy followed the trend presented in the rest of the respondents, with most (6 of the 10 unvaccinated diabetics) also choosing not to be vaccinated because they did not think it is important. In the study by Olantunbosun et al. (2017) 6.9% of their diabetic respondents also felt influenza vaccination is unimportant and 28.4% responded that they are unsure of the importance of vaccination. One diabetic that did not vaccinate had a vaccination in a previous year, but nine of the ten who were vaccinated took the vaccine in the previous years.

The lack of previous large-scale studies on influenza and influenza vaccination in diabetics and the fact that the diabetic participants in my study did not display any refined approach to preventative care, highlights the need for enhanced study and education in this risk group.

5.3.4 Cardiovascular disease and the elderly

Only 36 of the 84 (42.9%) participants with a cardiovascular disease were vaccinated. Elderly patients accounted for 36 of the participants that have cardiac diseases and 21 (58.3%) of these participants (elderly with a cardiac condition), were vaccinated.

Among participants over the age of 65 years (regardless of any chronic conditions) 46% of individuals were vaccinated. This compares to a study done by Schattner (2020) that found only 53% of respondents 65 years and older with a cardiovascular disease intended to vaccinate. Reasons given to vaccinate or not corresponded with the trend of most other participants in my study with unvaccinated individuals stating that vaccination was not important to them, and vaccinated individuals wishing "to avoid flu". This highlighted the concern about the knowledge and attitudes in this risk group about their risk for severe influenza. This was also proven by Schattner (2020) when vaccination uptake increased to 64% after intervention.

Although vaccination rates were slightly higher in this risk group than the mean for all participants, when considering the higher risk for severe influenza, complications and even death, the need for recommendation of prevention becomes abundantly clear.

5.4 Adverse reactions reported by patients after influenza vaccination.

Side effects were reported by only 30 participants (19.7%) who were vaccinated. This is in line with the 20.1% of respondents that reported side effects in the study done by Olatunbosun et al. (2017). Swelling or pain at the injection site (37.7%) and fever (33.3%) were reported most by the respondents in my study, which was not concerning as both side effects are listed in the package insert of the vaccine as common side effects.

Most participants (22 or 73%) that reported side effects were patients that were vaccinated in the past five years. Although not specified when (current year or previous years) the side effects were experienced, this is an indication that the possibility of experiencing side effects

did not deter a patient from getting the vaccine and thus did not play a role in the patient's decision to vaccinate or not.

Other side effects elaborated on by participants included rash and nasal congestion.

5.5 Previous vaccinations and vaccine uptake

There was a marked increase in the probability of a patient returning to vaccinate after a previous vaccination in past years with an Odds Ratio of 5.234 (95% confidence levels 3.352-8.174). Out of the 152 participants who were vaccinated this year, 109 participants (71.7%) had been vaccinated at least once within the last five years. A quarter of participants (38 participants) who were vaccinated this year have been vaccinated every year since 2015. Olatunbosun et al. (2017) also found that most (81%) of their vaccinated respondents were vaccinated yearly. Logan et al. (2018) found 64% of their vaccinated participants were vaccinated annually.

Using a chi-square automatic interaction detection (CHAID) (Figure 3), analysis technique it can be expected that an individual who was vaccinated this year and in previous years has an 88.6% chance of returning for a vaccination next year.

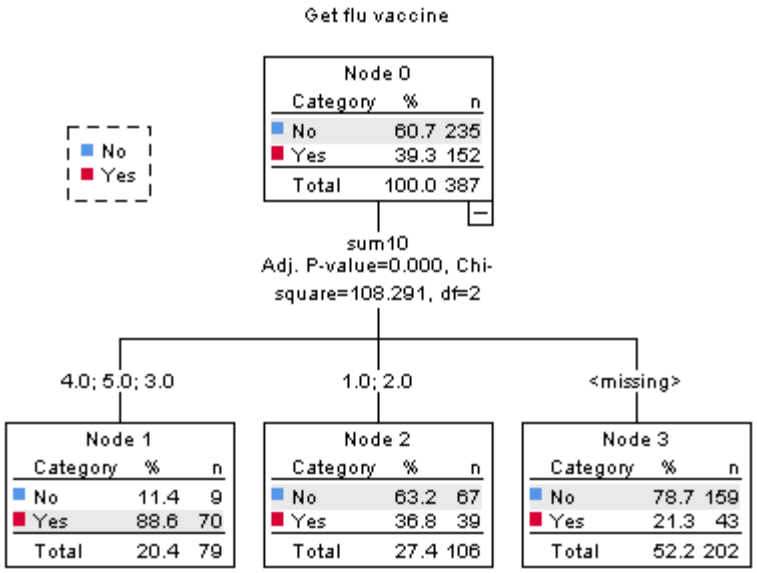

Figure 3: CHAID analysis on previous vaccinations

Although this finding could be an important tool to increase vaccination rates, it creates an impasse to get the patient to vaccinate the first time and to raise the probability of increased annual vaccination. This is especially salient for risk groups where vaccination coverage was low.

CHAPTER 6: CONCLUSION, RECOMMENDATIONS AND LIMITATIONS OF THE STUDY

6.1 Conclusion

A previous vaccination is the main attributing factor influencing vaccination uptake by patients in the Johannesburg retail pharmacy environment.

Despite the fact that patients with HIV, diabetes, cardiovascular conditions or asthma show an increased risk for severe influenza, these conditions do not provide sufficient motivation to increase vaccine uptake. Although patients older than the age of 60 showed higher vaccination rates, this increased vaccine uptake is not high enough to offer the desired protection in this patient group.

Vaccine refusal or vaccine postponement is caused by the notion that the influenza vaccine is unimportant. This highlights the need for education on the risks of severe influenza and influenza as a vaccine-preventable disease among patients and healthcare providers. Patients mostly vaccinate motivated by the desire to prevent influenza.

The incidence of self-reported adverse reactions experienced by patients after influenza vaccination was low. The most adverse reactions reported were minor and were to be expected as they are listed on the vaccine's packing insert.

6.2 Recommendations

Vaccination rates were lower than desired and especially concerning in risk groups.

As per the most chosen reason not to vaccinate, the idea among patients that influenza was nothing to be concerned about was abundantly clear. Patients in risk groups did not consider themselves as having any higher risk for severe influenza or complications due to influenza. This was partly due to the lack of recommendation by the healthcare providers and lack of education in this regard among patients and healthcare providers alike. Mertz et al. (2013)

also pointed out that there is insufficient supporting evidence with vaccine recommendations by public health institution like the World Health Organization and national government.

More research is required in the risk-group patients, especially in diabetic patients where Remschmidt et al. (2015) also identified the need for additional studies.

Considering the higher probability for a previously vaccinated patient to return for another vaccination, establishing the reason for a first vaccination would prove vital information to formulate a plan to increase vaccination. This would be a valuable topic for future research.

6.3 Limitations of the study

The sample was a convenience sample which prevents generalisation to the population. The sample was mostly taken from a high Living Standard Measure group, which narrows the perspectives of the sample. This has the implication that other reasons for not getting the vaccine, like it being too expensive, will have a larger impact on the general population.

The movements of participants were altered due to the lockdown regulations that was from level five to level two in the data collection period. As per government recommendations elderly and other risk group patients avoided going into a shopping mall in an effort to apply social distancing. Similarly, the COVID-19 pandemic has changed the way participants think about health and preventative health in general.

The sample size for the HIV, respiratory conditions and diabetes risk groups needs to be larger to render a more reliable result.

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LIST OF APPENDICES

APPENDIX 1: Flu vaccine questionnaire

To be completed by researcher

Unique Number: _____

1. Age: _____ years
2. Gender: Female ☐ Male ☐
3. Residential area (suburb): _____
4. Do you suffer from any chronic conditions? Yes ☐ No ☐

   if yes, please specify:

   _____
5. Are you a smoker? Yes ☐ No ☐
6. Are you getting the flu vaccine Yes ☐ No ☐

   If YES, please answer question 7 and 8. If NO, please skip to question 9.
7. Why are you getting the flu vaccine this year (Select the most applicable)?

   7.1 To avoid getting sick with flu ☐

   7.2 Doctor recommended it ☐

   7.3 Pharmacist recommended it ☐

   7.4 A friend or family member recommended it ☐

   7.5 To get loyalty points e.g. Discovery vitality ☐

   7.6 I got very sick in the past ☐

7.7 The Corona virus outbreak scared me ☐

7.8 Other, please specify _____ ☐

8. Did you ever get any side effects after getting the flu vaccine?

Yes ☐ No ☐ If **YES,** please choose the side effect that occurred:

8.1 Swelling/pain at injection site ☐

8.2 Headache ☐

8.3 Fever ☐

8.4 Nausea ☐

8.5 Muscle ache ☐

8.6 Other, please specify _____ ☐

9. Why did you **NOT** get the flu vaccine (Select most applicable)?

9.1 It gives me flu ☐

9.2 It is too expensive ☐

9.3 A friend or family member said it is bad for you ☐

9.4 I had a previous bad experience ☐

9.5 I forgot ☐

9.6 I didn't think it's important ☐

9.7 It doesn't work ☐

9.8 Other (Please specify)_____ ☐

10. Indicate any previous year(s) you got the vaccine (select all applicable years):

2019 ☐ 2018 ☐ 2017 ☐ 2016 ☐ 2015 ☐

APPENDIX 2: Participant information sheet

(To be retained by the participant)

A study to determine the relationship between patient related factors and influenza vaccination status

Invitation:
You are invited to participate in a study to research the reasons why a person will or will not get the flu vaccine.

The study is being conducted by Dominique Kotzé independently. I am one of the pharmacists at Clicks Cresta pharmacy.
The study is part of a requirement in partial fulfilment of the MSc Pharmacotherapy degree that I am currently enrolled in at Wits University.

Before you decide whether or not you wish to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

1. **'What is the purpose of this study?'**

   The purpose is to investigate the reasons why people get the vaccine or why they don't get the vaccine.

2. **'Why have I been invited to participate in this study?'**

   You are eligible to participate in this study because you are an adult (older than 18 years) and does not have an allergy to the vaccine.

3. **'What if I don't want to take part in this study, or if I want to withdraw later?'**

   Participation in this study is voluntary. It is completely up to you whether or not you participate. If you decide not to participate, it will not affect your relationship with any of the pharmacy staff at the pharmacy.

   If you wish to withdraw from the study once it has started, you can do so at any time without having to give a reason.

4. **'What does this study involve?'**

   If you agree to participate in this study, you will be asked to sign the Participant Consent Form.

   This study will be conducted over five months (April – August 2020) for data collection which will then be followed by a period where analysis of the data collected will be done.

   The study will only require you to fill in a questionnaire that enquire about your age, gender, demographics, vaccination status and reasons for that specific vaccination status. Your name or contact details will not be required and confidentiality is protected.

5. **'How is this study being paid for?'**

   The study is being funded entirely by only the researcher, Dominique Kotzé, which will provide all necessary resources (e.g. paper and printing of questionnaires) and the researcher or participants will not receive any compensation.

6. **'Are there risks to me in taking part in this study?'**

   There will be no risk for participating. Only an anonymous opinion will be obtained.

7. **'Will I benefit from the study?'**

   This study aims to further medical knowledge and may improve future approaches to flu vaccine drives, however it may not directly benefit you.

8. **'Will taking part in this study cost me anything, and will I be paid?**

   Participation in this study will not cost you anything. Only a few minutes of your time will be required.

9. **'What will happen to my completed questionnaire after it has been used?'**

   The information gathered with the questionnaires will be analysed and used to compile a research report and submitted to Wits University as part of the assessment towards obtaining the MSc Pharmacotherapy degree. The completed questionnaires and signed consent forms will stay in the possession of the researcher and will be destroyed after the required five years.

10. **'How will my confidentiality be protected?'**

    You will not be asked to include your name or contact details on the questionnaire. Your signed consent form will only be kept by the researcher and will not be shared with anyone else and will be destroyed after the required timeframe.

11. **'What happens with the results?'**

    If you give me your permission by signing the consent document, I plan to use the information gathered to compile a research report that will be submitted to Wits University for assessment.

In any publication, information will be provided in such a way that you cannot be identified.

12. **'What should I do if I want to discuss this study further?'**

    When you have read this information, the researcher will discuss it with you and any queries you may have. If you would like to know more at any stage, please do not hesitate to contact her at dominiquemoolman@yahoo.com or 011 678 5436

13. **'Who should I contact if I have concerns about the conduct of this study?'**

    Please contact the researcher (Dominique Kotze) at either 011 678 5436 or on dominiquemoolman@yahoo.com

    The study has been approved by the Medical Human Research Ethics Committee of the University of the Witwatersrand. The clearance certificate number is M190465

Thank you for taking the time to consider this study.

If you wish to take part in it, please sign the attached consent form.

This information sheet is for you to keep.

APPENDIX 3: Informed consent form

I _____ hereby give consent to take part in the research project that I have been invited to by Dominique Kotzé at Clicks Cresta and will fill in the provided questionnaire regarding my age, gender, demographics, vaccination status and reasons for that status.

The study is to establish the reasons for getting or not getting the vaccine. This will contribute to increase vaccination rates and offer better protection against flu in the greater community in the future.

My personal details will be handled confidentially by the researcher, and my questionnaire will remain totally anonymous - no identifiable details will appear on the questionnaire.

I understand that:

1. I was informed by the researcher about the specific details of the study
2. My data, which does not include my name or contact details can be used for research purposes.
3. I can withdraw my consent at any time without giving a reason for my withdraw
4. There is no cost involved to me as the patient regarding the research project
5. The research does not have any effect on any of my prescribed treatment or the service/care will be exactly the same whether I participate in the study or not.

6. I have been given enough time to consider before taking part in the study and know I can ask questions about the study until I feel comfortable.
7. The study will not benefit me directly and might only contribute to future knowledge about the flu vaccine.
8. There will be no risk to me to take part in the study.

This study was approved by the Human Research Ethics Committee (Medical) of the University of Witwatersrand. The clearance certificate number is M190465

Tel: 011 717 1234

Email: HREC-Medical.ResearchOffice@wits.ac.za

In case an emergency should arise directly related to this study please feel free to contact the researcher, Dominique Kotzé, at 011 678 5436 or dominiquemoolman@yahoo.com

Patient name: _____

Patient signature: _____

Researchers' signature: _____

Date: _____

APPENDIX 4: Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Mrs Dominique Kotze

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M190465

NAME: (Principal Investigator)	Mrs Dominique Kotze
DEPARTMENT:	Pharmacy and Pharmacology Clicks Pharmacy, Cresta Shopping Centre, Randburg
PROJECT TITLE:	A study to determine the relationship between patient related factors and influenza vaccination status
DATE CONSIDERED:	26/04/2019
DECISION:	Approved unconditionally
CONDITIONS:	Change of title
SUPERVISOR:	Prof Andries Gous
APPROVED BY:	Dr CB Perry, Chairperson, HREC (Medical)
DATE OF APPROVAL:	22/06/2020 (Initial approval); 17/07/2020 (Change of title)

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report.** The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **April** and will therefore be due in the month of **April** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX 5: Letter of permission by research site (Responsible pharmacist)

To whom it may concern

I hereby give my consent to Dominique Kotzé, to conduct her research project in Clicks pharmacy Cresta, in partial fulfilment of her MSc Pharmacotherapy degree. The research may be done from April 2019 to September 2019 according to the prepared protocol, that I have read.

I am the Responsible Pharmacist at Clicks pharmacy Cresta and her direct line manager.

Kind regards

Fathima Vawda

Contact nr: 011 678 5436

Signed _____ Date: 27/3/19

HYPERPHARM CLIFFVIEW PHARMACY
P.O. Box 41
NEWLANDS
0049
Tel: 011 678 5436 / 7
Fax: 011 678 5021

APPENDIX 6: Letter of permission by research site (Area manager)

Letter of permission by research site

To whom it may concern

I hereby give consent to Dominique Kotze to conduct her research in Clicks pharmacy Cresta, in partial fulfilment for the MSc Pharmacotherapy degree.

The research will be conducted from April 2020 to August 2020 according to the protocol that has been made available to me.

I am the Area Manager for Clicks pharmacy Cresta.

Kind regards

Mirriam Gilbert

Email: mirriam.gilbert@clicksgroup.co.za

Signed  Date: 7/3/20