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Thèse

pour le

Diplôme d'État de Docteur en Pharmacie

IMPACT DU COVID-19 SUR LA COUVERTURE VACCINALE ANTI-GRIPPALE EN 2020-21 EN FRANCE

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IMPACT OF COVID-19 ON THE INFLUENZA VACCINE COVERAGE IN 2020-2021 IN FRANCE

Etude ICOVAG

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Plan

Liste des abréviations

OMS	Organisation mondiale de la santé
WHO	World Health Organization
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SNDS	French National Health Data System (Système national des données de santé)
SPF	National Health Agency (Santé Publique France)
Covid-19	Coronavirus Disease 2019
CNIL	National Commission for Liberty and Informatics (Commission Nationale de l'Informatique et des Libertés)
LTD	Long-Term Disease
ICD-10	International Classification of Diseases, 10th Revision
ATC	Anatomical Therapeutic Chemical
Gp	General Practitioner
DRSM	Regional Directorate of Medical Service (Direction Régionale du Service Médical)
IV	Influenza Vaccination
CPP	Ethics Committee (Comité de Protection des Personnes)
HCP	Health Care Professional

Introduction

Micro-organisme bien connu depuis plusieurs siècles, à l'origine de dix mille décès chaque année[1] en France (jusqu'à dix-huit mille morts en 2014-15[2]), la grippe est un virus qui s'attaque à tous et menace les plus fragiles d'entre nous.

La découverte du mécanisme de vaccination et la mise au point du tout premier vaccin (contre la variole) au XVIIIe siècle par Edward Jenner, permet par la suite la création, par Jonas Salk, du premier vaccin contre la grippe dans les années 1940[3]. La science semble avoir trouvé un moyen facile et à portée de tous pour se prémunir contre le virus de la grippe. Seulement, la vaccination est un sujet sensible en termes d'acceptation, en France comme à l'étranger. A ce jour, plus de 80 ans après le déploiement de la vaccination antigrippale, la couverture vaccinale souhaitée par les instances de santé françaises et mondiales est encore loin d'être atteinte. Pourquoi tant d'hésitation de la part du grand public envers la vaccination antigrippale ? La défiance ne se limite par ailleurs pas à la seule vaccination antigrippale mais touche également les autres vaccins proposés à la population. La problématique est donc de taille et est suffisamment préoccupante pour motiver des publications de la part de l'Organisation Mondiale de la Santé (OMS). De nombreuses études pointent du doigt les difficultés freinant les populations dans l'acceptation de la vaccination[4]. Un groupe de travail affilié à l'OMS (WHO EURO Vaccine Communications Working Group) propose un modèle dit les « 3 Cs » : Confidence, Complacency, Convenience[5]. Il est ainsi reconnu que les défiances envers la vaccination sont caractérisées par un manque de confiance sur l'efficacité et l'innocuité des vaccins, une évaluation défavorable de la balance bénéfice-risque, et une problématique d'accessibilité au sens large.

Le vaccin antigrippal voit sa composition adaptée chaque année. En effet, trois types de virus de la grippe co-existent (A, B et C), et présentent différents variants, nommés selon les combinaisons des antigènes de surface appelés Hémagglutinine et Neuraminidase[6]. Tous les ans, des prévisions sont réalisées par l'OMS pour déterminer l'identité des souches qui circuleront la saison hivernale suivante[7]. La composition des vaccins change ainsi annuellement suivant ces données.

En France, les recommandations vaccinales concernent notamment les personnes âgées de 65 ans et plus, car c'est dans cette catégorie d'âge que le plus de victimes est déploré chaque année. Malgré cela, trop de personnes

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[1] Grippe [Internet]. Institut Pasteur. 2015 [cited 2022 Dec 30]. Available from: https://www.pasteur.fr/fr/centre-medical/fiches-maladies/grippe

[2] La grippe en 2015 : plus de morts, moins de personnes vaccinées [Internet]. [cited 2022 Dec 30]. Available from: http://www.mesvaccins.net/web/news/7003-la-grippe-en-2015-plus-de-morts-moins-de-personnes-vaccinees

[3] Vaccins d'hier à aujourd'hui [Internet]. [cited 2022 Nov 28]. Available from: https://vaccination-info-service.fr/Generalites-sur-les-vaccinations/Histoire-de-la-vaccination/Vaccins-d-hier-a-aujourd-hui

[4] Sallam M. COVID-19 Vaccine Hesitancy Worldwide: A Concise Systematic Review of Vaccine Acceptance Rates. Vaccines (Basel) [Internet]. 2021 Feb 16 [cited 2022 Dec 30];9(2):160. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7920465/

[5] MacDonald NE. Vaccine hesitancy: Definition, scope and determinants. Vaccine [Internet]. 2015 Aug 14 [cited 2022 Dec 30];33(34):4161–4. Available from: https://www.sciencedirect.com/science/article/pii/S0264410X15005009

[6] Hutchinson EC. Influenza Virus. Trends in Microbiology [Internet]. 2018 Sep 1 [cited 2023 Jan 6];26(9):809–10. Available from: https://www.cell.com/trends/microbiology/abstract/S0966-842X(18)30131-8

[7] Composition recommandée des vaccins anti grippaux pour la saison grippale 2023 dans l'hémisphère sud [Internet]. [cited 2023 Jan 7]. Available from: http://www.mesvaccins.net/web/news/19968-composition-recommandee-des-vaccins-anti-grippaux-pour-la-saison-grippale-2023-dans-l-hemisphere-sud

ne se sentent pas à risque de développer des complications, facilement évitables pourtant par la vaccination (lorsque les souches virales composant le vaccin sont en adéquation avec la ou les souches circulantes).

Dans ce contexte général, l'apparition d'un nouveau virus découvert dans une province chinoise, semble à même de bousculer certaines opinions et croyances. En janvier 2020, les gouvernements occidentaux commencent à évoquer ce virus découvert en Chine à peine quelques mois plus tôt. Il s'agit d'un nouveau coronavirus nommé Sars-CoV-2 pour Severe Acute Respiratory Syndrome Coronavirus 2. L'émergence de ce micro-organisme sur le territoire français conduit le Gouvernement français à placer le pays en confinement pendant plusieurs semaines initialement, confinement qui durera finalement plusieurs mois. Les nouvelles sont inquiétantes : le virus est à l'origine de nombreux décès, sature les services hospitaliers dans tout le pays et se propage rapidement. Les « mesures barrières » sont mises en place, des mesures que bientôt toute la population française connaitra par cœur : pas d'embrassades, pas de rassemblement de population, port du masque, désinfection des mains au gel hydroalcoolique, etc… La population, le Gouvernement, les professionnels de santé, tous sont mobilisés contre la propagation de ce virus redouté, dont les symptômes les plus évocateurs sont proches de ceux ressentis lors d'une infection grippale. Il n'est pas si difficile pour le grand public de faire sinon l'amalgame, la comparaison entre ces deux virus. Malgré des similitudes entre ces deux virus, la population semble s'émouvoir plus facilement du covid-19 que de la grippe ; les médias relayant des informations massivement sur le sujet de la pandémie de covid-19, au détriment peut-être de l'importance du vaccin antigrippal.

En mars 2020, au tout début de cette désormais pandémie de covid-19, la question se pose d'anticiper l'impact éventuel de ce nouveau virus sur la prochaine campagne vaccinale antigrippale débutant en octobre 2020. Il est important de rappeler que les pharmacies d'officine sont intégrées à l'effort de vaccination antigrippale depuis la campagne 2019-20 (9° de l'article L. 5125-1-1 A du Code de la Santé Publique). Chaque pharmacie doit, en amont de cette campagne vaccinale, pré-commander les vaccins antigrippaux. Or, au printemps 2020, la situation est incertaine. Dans ce contexte de pandémie, faut-il s'attendre à une plus forte demande de la part des patients ? Ou au contraire, à une baisse de la vaccination antigrippale ?

Ce projet de thèse s'inscrit ainsi dans ce contexte nouveau, prégnant dans les problématiques actuelles de santé publique et de gestion des instances de santé. Le pharmacien est de plus en plus placé au centre du système de santé, et voit ce phénomène accéléré depuis la pandémie de covid-19.
Les objectifs de ce travail sont d'évaluer l'impact de la pandémie de covid-19 sur la couverture vaccinale antigrippale parmi la population de 68 ans et plus des Pays de la Loire, d'identifier les raisons de l'hésitation vaccinale au moyen d'un questionnaire, et de décrire et commenter l'évolution de la couverture vaccinale au fil des campagnes antigrippales. Notre hypothèse s'est rapidement formulée en faveur d'un impact positif de la pandémie de covid-19 sur la couverture vaccinale antigrippale en 2020-21. Afin de répondre à cette problématique, un double travail de recherche a été mené. Le premier est une étude de données extraites de la base SNDS (Système national des données de santé), rassemblant des informations telles que les couvertures vaccinales antigrippales estimées depuis la campagne 2017-18 jusqu'à la campagne 2021-22. Le deuxième est une étude multicentrique réalisée en parallèle auprès de pharmacies recrutées dans le Maine et Loire (49). Dans cette étude, un questionnaire a été proposé aux patients âgés de 68 ans et plus au comptoir, dans le but de recenser les motivations en faveur ou en défaveur de la vaccination antigrippale [Annexe 1]. L'âge minimum de 68 ans a été choisi pour avoir un recul d'au moins 3 campagnes vaccinales sur la question des habitudes de

vaccination. En effet, la vaccination antigrippale en France est systématiquement recommandée à partir de 65 ans. Cette recherche non interventionnelle a été menée du 1er février 2021 au 28 février 2021, après un travail préliminaire durant lequel l'autorisation d'un Comité de Protection de Personnes a été obtenue [Annexe 2]. Ce projet de recherche est présenté sous la forme d'un article scientifique rédigé dans un format de publication adapté au journal anglophone *Vaccine*.

Article

Impact of Covid-19 on *influenza* vaccine take-up in 2020-2021 in France

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Abstract

Background: Take-up of the influenza (flu) vaccination in France is assessed every year by Santé Publique France (SPF), a national health agency. In 2020, the pandemic of Covid-19 took place all over the world. With several symptoms known to be similar between flu and Covid-19, we expected to observe a positive impact on people's choice to also take the flu vaccine injection.

Methods: Data regarding the flu vaccination for people aged 65 and over were extracted from the French National Health Data System (Système National des Données de Santé – SNDS). A non-interventional multi-center survey in the department of Maine et Loire, an area in the west of France, was used for a qualitative analysis.

Results: The flu vaccine take-up (Maine et Loire - France), among people aged 65 and over, improved since 2017 (54.36% in 2017-18 *vs* 58.12% in 2020-21). In 2020-21 (concomitant with Covid-19 pandemic), people got vaccinated earlier than the previous year (peak in the weeks 1-2 *vs* peak in weeks 5-6 in previous campaigns), before a shortage of doses interrupted the 2020-21 campaign. Of the 211 people that answered the survey, 175 were vaccinated during the 2020-21 flu vaccine campaign. Among them, 29.12% declared they were aware of Covid-19 when receiving the flu vaccine. The most cited reason for taking the vaccination was the need to feel safe from the influenza virus; the second was "awareness of the fact that a virus can be contagious and deadly".

Conclusion: Our study highlights the Covid-19 impact perceived by the elderly population (Maine et Loire) on flu vaccination rates. Despite having human consequences, the Covid-19 pandemic was beneficial to flu vaccine take-up, and positively changed people's beliefs and behaviors towards flu vaccination.

Keywords: Covid-19; flu vaccine; vaccine behavior; Covid-19 impact

Abbreviations

SPF: National Health Agency (*Santé Publique France* in French)

SNDS: French National Health Data System

WHO: World Health Organization

Covid-19: Coronavirus Disease 2019

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2

CNIL: National Commission for Liberty and Informatics

LTD: Long-Term Disease

ICD-10: International Classification of Diseases, 10th Revision

ATC: Anatomical Therapeutic Chemical

Gp: General Practitioner

DRSM: Regional Directorate of Medical Service

IV: I*nfluenza* Vaccination

CPP: Ethics Committee

HCP: Health Care Professional

1.1. Introduction

Influenza symptoms due to influenza virus infection appear suddenly, and include cough, fever, chills and muscle pain, as well as fatigue that can last up to 10 days[2,3]. These symptoms are well known by the French population as they affect between 2 and 8 million citizens in France each year [1]. If these symptoms usually result in some days in bed for most of the affected population, it can lead to a lot of complications notably for newborns, pregnant women, people aged 65 and over, as well as people suffering from chronic diseases such as heart failure, respiratory failure, or diabetes. The major risk is of a secondary bacterial infection, generally located in the lungs. This has to be seriously taken into consideration, as it may cause death when occurring in frail persons[4]. That is why the influenza (flu) vaccination is strongly recommended in France for people aged 65 and over, due to an increased risk of complications. Indeed, France counted 3,700 deaths in 2018-19, attributed to the influenza virus[5]. At the end of this flu seasonal vaccination, 45% of the at-risk population was vaccinated, as well as 52% of people aged 65 and over[6]. This level of vaccine take-up is far from the target set by the World Health Organization (WHO), which recommends that 75% of the elderly population should be vaccinated[7], even though the flu vaccine is completely free of charge for the at-risk population in France. Vaccine hesitancy is generally explained by four themes which are concerns over safety, lack of trust, lack of need for vaccination and cultural reasons[8]. Vaccine hesitancy is not only a French behavior: it appears to be one of the ten priorities of the WHO in 2019, identified as a threat to global health. The influenza virus itself is also present in this ten-priority list. Indeed, a global flu pandemic is awaited, and brings concern as we do not know when it may happen, nor how serious it could be[9].

In 2019, a new coronavirus called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) lead to a global pandemic [10]. Several symptoms of Covid-19 are similar to those of the flu. Both viruses lead to cough, fever and muscle aches. Covid-19-infected people can also experience loss of taste and sense of smell, asthenia, and chest pain. Complications can be hypoxia and pulmonary secondary infection, sometimes leading to death[11].

The influenza virus is transmitted through respiratory droplets when an infected person coughs, sneezes or talks, through close contact, and on inert surfaces, where the virus can survive several days[3]. The same modes of transmission are observed for the SARS-CoV-2[11]. This makes another similarity between these two viruses and protection against Covid-19 by wearing a mask is also a protection against flu. The SARS-CoV-2 is contagious 2 to 3 days before the first symptoms, and up to 8 days after and can be transmitted by asymptomatic patients[12]. On April 1st 2020, the virus has infected 4.74 million people in France, and among them 95,961 people have died from it[13]. The people who died from Covid-19 were mostly people aged 65 and more[14].

At the beginning of the 2020 flu vaccination campaign in France, no vaccine was available against the Covid-19 infection. Co-infection between influenza virus and Covid-19 was feared by specialists, as Alosaimi B. *et al* showed a rise in mortality when infected with those two viruses[15]. This is not only an issue for the health of the population, but also for the organization of the health care system, already weakened in several countries, with issues such as the deprioritization of non-covid-19 care[16]. France is not immune to these issues. This Covid-19 pandemic was also a pandemic of panic: populations were experiencing anxiety, led on by contradictive data or information from media or even governments themselves. People were indecisive about whether to wear a mask, which specialist to believe, and which medicine should improve or worsen the disease etc[17].

Some recent studies have reported that the Covid-19 pandemic might have had an impact on people's choices regarding flu vaccination. In a study conducted in Italy on 599 patients from September to November 2020, Gerussi V. *et al* reported, that among Covid-19 patients that had been hospitalized, the flu vaccine hesitancy was significantly lower than among all the other Covid-19 patients[18]. In addition, Sturm L. *et al* established, in a study conducted on 3,502 patients from the United States in May 2020, that the intention of getting vaccinated against flu was higher when people considered Covid-19 as a problem for their community[19]. On July 31st 2020 in the UK, Bachtiger P. *et al* questioned 6,641 persons eligible for the flu vaccination about their intention to get vaccinated the next year. They then identified a change of behavior among people not routinely vaccinated against flu. Finally, when asked if they had the intention to get vaccinated in 2020-21, 56.7% answered yes, increasing the vaccination rate in the entire previously eligible cohort from 79.6% to 91.2% [20]. Similarly, an Italian survey conducted on 2,543 Italians from the general population by Domnich A *et al,* showed that people not routinely vaccinated were "significantly more likely to be influenced by the Covid-19 for next flu vaccine season" [21].

A meta-analysis and systematic review recently discussed the effect of the Covid-19 pandemic on flu vaccination intention, including data from all over the world. The review reported an increased intention of getting the flu vaccine among different categories of people, that could be partly explained by the pandemic of Covid-19 [8].

These studies [8,18–21] registered the patients' intention of getting the flu vaccine, but can however not be extrapolated to an effective behavior. Moreover, people questioned were of all ages, and only one study focused on people targeted by the flu vaccine recommendation [20]. In this context, we expect to see a change in flu vaccination take-up in France during the same period.
The present study was based on patients after the 2020-21 flu vaccine campaign, to make sure they actually did or did not get the flu vaccine, in the context of Covid-19 pandemic. It also targeted a vulnerable population by including only people aged 68 and more in France. The objectives were to assess the impact of the Covid-19 pandemic on the take-up of flu vaccinations, at a local level (Pays de la Loire, France) and among people aged 68 and more, to identify reasons for vaccine hesitancy by questioning their vaccine behaviors, and to describe the evolution of their flu vaccine take-up over time.

1.2. Material and methods

1.2.1. DESCRIPTIVE DATA ON THE IMPLEMENTATION OF VACCINATION IN THE PAYS DE LA LOIRE (FRANCE)

a) Data analysis

Data were extracted from the French National Health Data System (SNDS) of Pays de la Loire area in accordance with the National Commission for Liberty and Informatics (CNIL) laws. SNDS is a pseudonymized data warehouse collecting reimbursement data derived from the main insurance schemes. The French national claims database (SNDS), includes information on all healthcare expenses, including outpatient visits, dispensed medication, procedures, chronic conditions, as well as hospital admission diagnoses and procedures. Data acquisition is permanent, from birth to death, whatever the socioeconomic or employment status, and inclusive, with data for over 98.8% of the French population.

The SNDS data were extracted from September 1st, 2017, to March 31st, 2022. The following socio-demographic patient data were extracted: date of birth, date of death, gender, address (city code, area), department of residence (Pays de la Loire area is composed by 5 departments, respectively: Loire Atlantique, Maine et Loire, Mayenne, Sarthe, Vendée) and eligibility for 100% health insurance coverage for serious and costly long-term disease (LTD) coded according to the International Classification of Diseases, 10th Revision (ICD-10). The department of Maine et Loire was selected because of its similarities with the population of France. This department is regularly used as a national reference base. It is indeed representative of the French population in terms of demographic parameters such as sex[i,ii] (France: 51.6% female *versus* Maine et Loire: 51.4%) and age[i,iii] (France: 27.15% people aged 60 and more *versus* Maine et Loire: 27.8%).

The data extraction allowed tracking of all drugs dispensed (including flu vaccine) in pharmacies for all patients registered with a mandatory health insurance scheme in the Pays de la Loire area (France), and living in this area, regardless of prescriber (physician prescriber in or outside the area) while the pharmacy where flu vaccines were dispensed was located in the Pays de la Loire area.

Dispensed drugs (flu vaccine) were identified in the SNDS at the 4th level of the Anatomical Therapeutic Chemical (ATC) classification (J07BB). Other drug information extracted were dispensing date (index date), dispensing pharmacy, coding, and fee for service according to French health insurance classification.
Health professional information extracted were medical (general practitioner [GP], midwife, pharmacist) or paramedical (nurse) status, dates of intervention to the patient during each annual flu vaccine campaign and a fifteen day-time-window following the end of annual flu vaccine campaign (March 31th).
Each annual flu campaign was defined as follow: from year N (i.e: 2017) October 1st to year N+1 (i.e: 2018) March 31th.
In France, since April 2019, pharmacists were authorized to vaccinate patients against flu. Before that date, only general practitioners, nurses and midwifes were able to vaccinate patients against flu. To identify who vaccinated the patient, two different strategies were used according to the annual flu campaign:

- From 2017-2018 flu campaign to 2018-2019 flu campaign: the vaccinator was defined as the first health professional (GP, nurse and midwife) who made intervention to the patient in a fifteen day-time-window following the index date (flu vaccine dispensing date).
- From 2019-2020 flu campaign to 2021-2022 flu campaign, we used a two-step procedure: the vaccinator was defined as the pharmacist if there was a specific pharmacist « flu vaccine » fee for service in the SNDS, or if not, the first health professional (GP, nurse and midwife) who made intervention with the patient in a fifteen day-time-window following the index date (flu vaccine dispensing date).

The number of patients participating in different flu campaigns was assumed as the sum of flu vaccines dispensed during the study period (2017-2022). Flu vaccination rates in the workplace, supported by employers or in nursing homes with in-house pharmacy are not available in the SNDS.

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[i] Estimations de population par sexe et âge au 1er janvier 2022 | Insee [Internet]. [cited 2022 Nov 7]. Available from: https://www.insee.fr/fr/statistiques/2012692#titre-bloc-1

[ii] Population par sexe | Insee [Internet]. [cited 2022 Nov 7]. Available from: https://www.insee.fr/fr/statistiques/2381466#tableau-figure1

[iii] Population par sexe et groupe d'âges | Insee [Internet]. [cited 2022 Nov 7]. Available from: https://www.insee.fr/fr/statistiques/2381474

b) 2.1.2 Statistical analysis

All statistical analyses were carried out with SAS software, version 7.15 (SAS institut Inc., Cary, NC, USA).

c) 2.1.3 Ethics statement

In accordance with data protection legislation and the French regulation, the authors cannot publicly release the data from the French National Health Data System (Système National des Données de Santé—SNDS). However, any person or structure, public or private, for-profit or non-profit, is able to access SNDS data upon authorization from the French Data Protection Office (CNIL), in order to carry out a study, research or an evaluation in the public interest (https://www.snds.gouv.fr/SNDS/Processus-d-acces-aux-donnees and https://www.indsante.fr/). CNAM has permanent regulatory access to the data from the French National Health Data System (SNDS) via its constitutive bodies DRSM (Regional Directorate of Medical Service)-CNAM. This permanent access is given in accordance with the French Decree No. 2016–1871 of December 26, 2016 relating to the processing of personal data called the "National Health Data System", and French law articles Art. R. 1461–13 and 14. All requests in the database were made by duly authorized people, all methods were carried out in accordance with relevant guidelines and regulations and the study was conducted in accordance with the Declaration of Helsinki. In accordance with the permanent regulatory access granted to DRSM-CNAM, this present work did not require the approval from the French Data Protection Authority (CNIL). The study was registered on the study register of DRSM Pays de la Loire - CNAM concerning studies from SNDS data. Given that data are anonymous, no informed consent to participate was required.

1.2.2. ANALYSIS OF PATIENTS' MOTIVATIONS FOR FLU VACCINATION IN MAINE ET LOIRE (FRANCE): IMPACT OF COVID-19

a) Description of the study

This study is non-interventional, multi-center, and was carried out by interviewing people aged 68 and over *via* a questionnaire. The questionnaire was proposed in pharmacies by the pharmacy team to all people aged 68 and over. This age limit was chosen because the recommendation for *influenza* vaccination (IV) begins at 65 years of age: setting the minimum age at 68 years allows a three-year hindsight on previous flu vaccine campaigns since the vaccination was recommended.

b) Recruitment of participants

When visiting one of the participating pharmacies and whatever the reason they were visiting for, if the persons met the selection criteria of the study, the questionnaire was offered at the counter and was to be filled out on the spot. The protocol received a favorable opinion from the independent French Ethics committee CPP SO3 - Sud-Ouest et Outre-Mer III on 12/16/2020 (#20111639621).

c) Research dates and locations

The study was set up from February 1st, 2021, for a duration of one month. It was held after the 2020-2021 *influenza* vaccination campaign to obtain reliable vaccination data from study participants.

d) Endpoints

The primary endpoint was the vaccination rate in 2020-21 and previous years. The secondary endpoints were the flu vaccination habits, the reasons given for flu vaccination (favorable or unfavorable) and the perceived influence of Covid-19 on flu vaccination (self-declaration).

e) Statistical Analyses:

For the description of the sample as well as to meet the primary and secondary objectives, we used tools inherent to descriptive statistics, namely:

- Quantitative variables were characterized by their mean and standard deviation if normal distribution.
- The qualitative variables were reported in numbers and percentages with their 95% confidence intervals.

Excel® and R® software were used for these analyses.

First, the pharmacies were sorted according to their topographical characteristics (shopping center, neighbourhood, downtown). These groups of pharmacies were compared following the responses to different items of the questionnaire (flu vaccination in 2020-21, influence of Covid-19 (self-declaration), vaccination habits), in order to know whether to interpret the results according to topography or not.

1.3. Results

1.3.1. DESCRIPTIVE DATA ON THE IMPLEMENTATION OF VACCINATION IN THE PAYS DE LA LOIRE (France)

The SNDS data extraction gathered 792,000 persons from 65 to 109 years old. The mean age was 76.21 (*Table I*). The sex ratio (male/female) was 0.77 in 2017-18; 0.78 in 2018-19; 0.78 in 2019-20; 0.78 in 2020-21; and 0.79 in 2021-22.

Table I: Age and sex characteristics of the study population in Maine et Loire, for people aged 65 and over in 2017 that got vaccinated at least once in the five last campaigns.

Seasons 2017-18 to 2021-22	**Age**
Minimum	65
Maximum	109
Mean	76.21
Median	75
1st Quartile	69
3rd Quartile	82

a) Vaccination rate by frequency over the last 5 years for the patients aged 65 and more in 2017

The participation rates of the five last vaccination campaigns included data from the 2017-18 campaign to December 31st, 2021. Thus, each patient could take part in 5 campaigns at most, as shown on the vertical

axis*(Fig.1)*. Among the 119,395 vaccinated persons, 46,103 received the flu vaccine 5 times in 5 campaigns, whereas 15,938 to 23,437 persons received 1 to 4 flu vaccines in 5 campaigns.

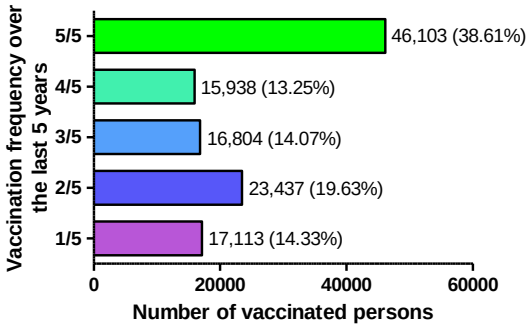

Figure 1: Vaccination rate by frequency over the last 5 years for the patients aged 65 and more in 2017. On the ordinate: Number of influenza vaccinations between the 2017-18 season and the 2021-22 season.

b) *Influenza* vaccination coverage in people aged 65 and more in Maine et Loire

Flu vaccine take-up sorted by age, for the people of Maine et Loire aged 65 and more *(Fig. 2),* follows an increasing trend over time. The flu vaccine take-up by patients aged 80 and more is more constant over time than for younger age groups investigated. It reached its highest rate in 2020-21, with 59.06% of vaccinated persons. The older are the people, the better is the flu vaccine take-up rates. Flu vaccine take-up increased between 2017-18 and 2020-21 for patients aged 65 years old and patients aged 66- to 69-years old. Take-up of the flu vaccine by the latter increased by 3.9 percentage points between 2019-20 and 2020-21, reaching 58.81% in 2020-21. It increased by 5.9 percentage points in four campaigns. At the end of the 2020-21 campaign, the 65-year-old patients have a flu vaccine take-up rate 8.02 percentage points higher than in 2017-18.

The improvement of flu vaccine take-up is especially strong in the 66- to 69-year-old age-group between the 2019-20 and the 2020-21 campaigns, coinciding with the outbreak of the Covid-19 pandemic.

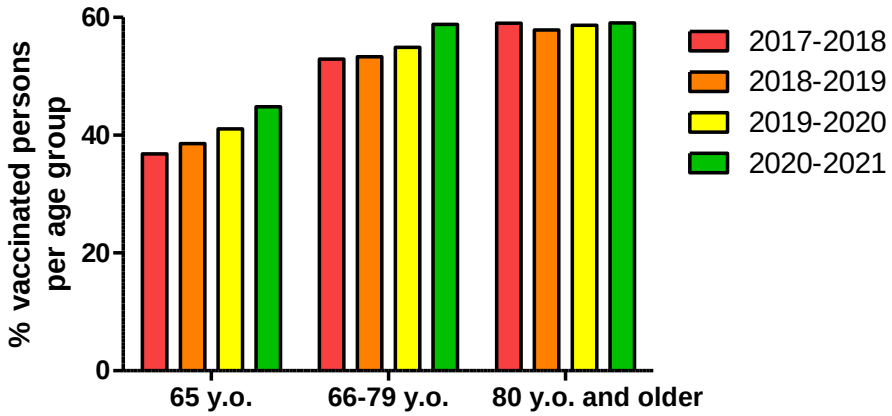

Figure 2: *Influenza* vaccination coverage in people aged 65 and more in Maine et Loire. Percentage values are calculated by dividing the number of persons vaccinated by the total number of persons in the age group.

c) Impact of the entry of pharmacies in flu vaccination and distribution of the vaccinations according to the health care professional

The time-distribution of vaccinated people *(Fig. 3)* confirms an improvement of the flu vaccine coverage over time.

Then, the distribution of vaccinated people according to the health care professionnel (HCP) indicates that nurses vaccinated a little less in 2019-20 than in the previous years with the highest vaccination rate in 2020-2021, with up to 34,036 vaccinated patients.

General practitioners (GP) observed more change during the 2 last campaigns, for which they vaccinated fewer patients compared to 2017-18 and 2018-19. However, they still are the HCP the patients see more frequently to get vaccinated against the flu. The 2019-20 campaign allowed 19,332 people aged 65 and older to be vaccinated in pharmacies, and 33,224 people in the following campaign.

Finally, in 2020-21, there are 34,160 additional vaccinations in the population aged 65 and older compared to 2017-18. The people aged 65 and over were 138,165 in 2017-18 in Maine et Loire, while 187,997 in 2020-2021, resulting in a positive difference of 49,832 people.

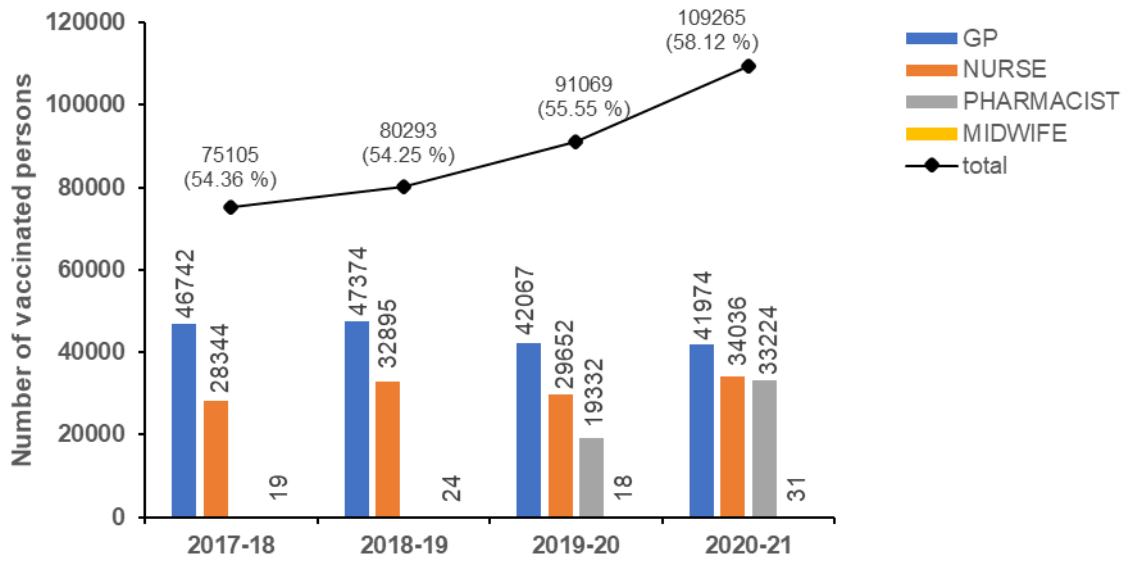

Figure 3: Distribution of flu-vaccinated people aged 65 and over according to the health care professional, for each season, in Maine et Loire. Total: vaccinated persons aged 65 and over for each flu vaccine season.

d) Distribution of vaccinations by week for each flu vaccine campaign

The *influenza* vaccine campaigns began on October 6th for the 2017-18 and 2018-19 campaigns (week 40), October 15th for the 2019-20 campaign (week 42), and October 13th for 2020-21 (week 42). They all ended on January 31st, excepted for the 2020-21 campaign, which was extended to February 28th, notably due to the pandemic context of Covid-19. The first three campaigns observed in figure 4 show a common trend on the vaccination kinetics. From 2017-18 to 2019-20, the number of vaccinated patients gradually increased from the first week, leading to a main peak by weeks 5 and 6. The number of vaccinated patients per week then decreased

in a homogeneous way between the three campaigns mentioned above until the end of the vaccination campaign. However, an important and early increase of the number of vaccinated patients was observed in 2020-2021 at week 2 which then decreases until week 4 and increases again at week 5. The distribution of vaccinated people by week and by vaccine campaign *(Fig. 4)* reveals an early peak of flu vaccinations in the 2020-21 campaign.

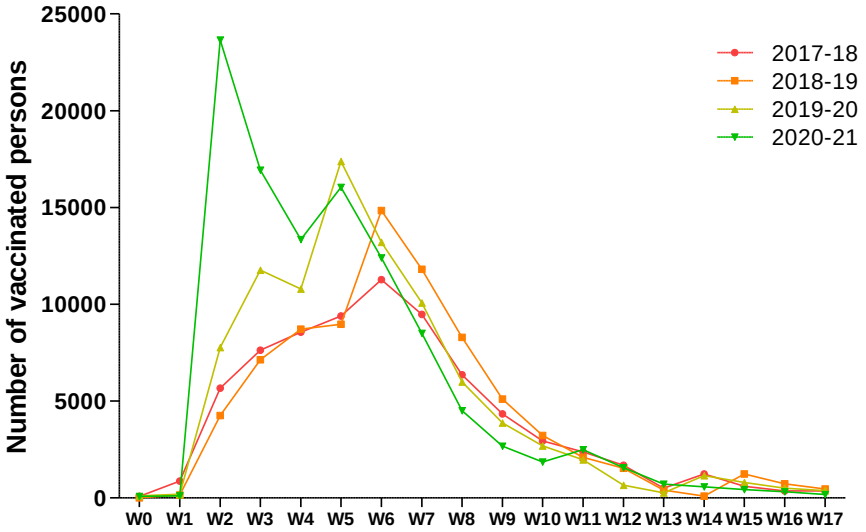

Figure 4: Distribution of vaccinations for people aged 65 and more, by week and for each flu vaccine season. "W1" is the launch week of each campaign for flu vaccination.

1.3.2. ANALYSIS OF PATIENTS' MOTIVATIONS FOR FLU VACCINATION IN MAINE ET LOIRE: IMPACT OF COVID-19

a) Description of the centers and the participants

To investigate the precise the reasons for vaccine hesitancy in the population, a questionnaire was designed and sent to different community pharmacies in the Maine et Loire department. Among the 47 community pharmacies invited, 11 agreed to take part in the research and were able to include 211 participants from February 1st 2021, to February 28th 2021. They were divided into 3 different groups according to precise criteria (*Table II*). Patients from pharmacies belonging to the "neighbourhood group" are less influenced (self-declaration) by Covid-19 than patients from the other groups (*Table II*). In the "neighbourhood group", patients are usually more vaccinated than the other patients. They are 82.61% to declare being vaccinated every year or almost, against 73.07% and 75.31% for the "shopping center" and "downtown" groups respectively.

Among all 211 participants, 25.12% said to be influenced by Covid-19 (self-declaration).

Table II: Characteristics of the participating community pharmacies

	« Shopping center » group	« Downtown » group	« Neighbourhood » group	Total
Number of investigative centers	4	4	3	**11**
Total size	26 (12.32%)	162 (76.78%)	23 (10.90%)	**211 (100%)**
Average number of patients included per center	6.5	31.5	7.7	**/**
Minimum	1	5	3	**/**
Maximum	14	80	12	**/**
Number of vaccinated people (%) in 2020-21	23 (88.46%)	132 (81.48%)	20 (86.96%)	**175 (82.94%)**
Number of always or almost every year vaccinated people (%)	19 (73.07%)	122 (75.31%)	19 (82.61%)	**160 (75.83%)**
Number of never vaccinated or sometimes vaccinated people (%)	7 (26.92%)	40 (24.69%)	4 (17.39%)	**51 (24.17%)**
Impact of Covid-19 (self-declaration)	7 (26.92%)	45 (27.78%)	1 (4.35%*)	**53 (25.12%)**

Total size: total number of inclusions per pharmacy category; Impact of covid-19 (self-declaration): number of participants who felt influenced by Covid-19 when they decided whether to take the *influenza* vaccine in 2020-21.
« Shopping center » group: community pharmacy belonging to a shopping center or being less than 80 meters far from a supermarket.
« Downtown » group: community pharmacy less than 600 meters away from the geographic downtown of a city.
« Neighbourhood » group: community pharmacy more than 600 meters away from the geographic downtown of a city.

Among the 175 participants vaccinated during the 2020-21 season, 51 said they were influenced by Covid-19 when choosing to receive the flu vaccination *(Fig. 5)*. The participants were 36 to refuse the flu vaccination, with 2 of them saying they were influenced by Covid-19.

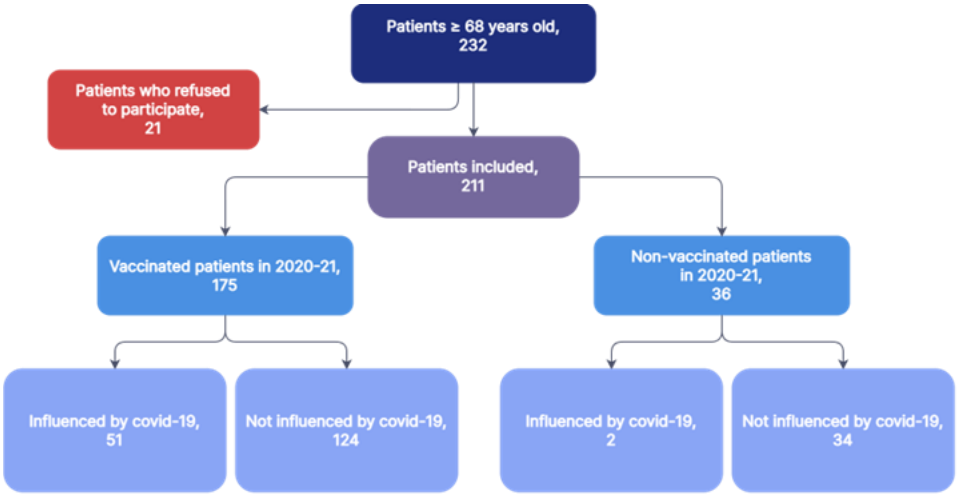

Figure 5: Flow chart of the study conducted from February 1st 2021 to February 28th 2021.

Most of the participants (75%) were aged between 68 and 81 years old, and only a quarter of the participants were 81 or older (*Table III*). The sex ratio (male/female) is 0.61.

Table III: Age of the ICOVAG participants

ICOVAG Participants	Age
Minimum	68
Maximum	94
Mean	77
Median	75
1st Quartile	72
3rd Quartile	81

b) Vaccination behavior and reasons for or against the flu vaccine

There is a gap between the proportion of people getting vaccinated every year (74.93%), and all the others, who get vaccinated almost every year (10.90%), sometimes (9.00%), or never (15.17%) (*Fig. 6.A*).

Then, we collected the reasons explaining the flu vaccination or its refusals. The main three reasons explaining the acceptance to get vaccinated against the flu (*Fig. 6.B*) are "not to be sick" (77.50%), "because your doctor recommended you to do it" (44.38%) and "not to contaminate others" (41.25%).

On the other hand, the main reasons why patients tend to refuse the flu vaccination (*Fig. 6.C*) are the "fear of adverse effects" (37.28%), and a "distrust in vaccines" (27.43%). Other reasons were brought by the patients themselves (19.61%) and mostly related to the experience of adverse effects (long lasting flu-like symptoms), and even a death of friend/family member attributed to a flu vaccine complication.

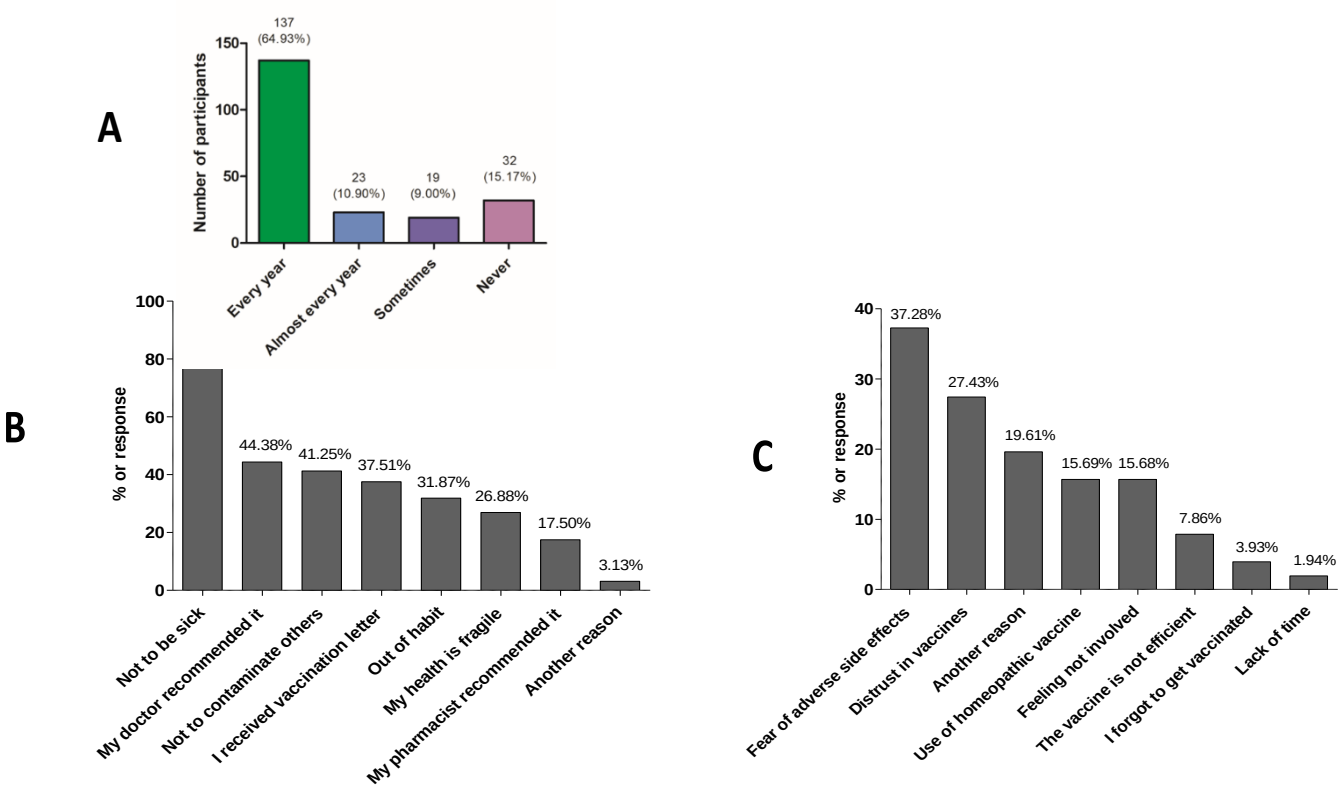

Figure 6: Description of the vaccination behavior. A) Previous vaccinations. B) Reasons in favor of the vaccination. C) Reasons not in favor of the vaccination.

c) Influence (self-declaration) of Covid-19 and vaccination habits compared to 2020-21

In 2020-21, 29.14% of vaccinated participants were influenced by Covid-19 (self-declaration) (*Table IV*). Among the non-vaccinated participants, 5.56% reported they were influenced by Covid-19 when deciding to refuse the flu vaccine.

The vaccinated participants in 2020-21 represent 82.94% of the included patients of the present study. People who usually get vaccinated every year represent 77.71% of the vaccinated patients in 2020-2021. People who get vaccinated almost every year represent 12.57%, and those who get vaccinated sometimes account for 8.57%. The non-vaccinated participants in 2020-2021 are mostly represented by those who were never vaccinated (83.33%).

Table IV: Characteristics of vaccinated and non-vaccinated persons in 2020-21

	Vaccinated in 2020-21	**Non-vaccinated in 2020-21**
n (%[1])	175 (82.94%)	36 (17.06%)
Vaccinated every year(%[2])	136 (77.71%)	1 (2.78%)
Vaccinated almost every year (%[2])	22 (12.57%)	1 (2.78%)
Vaccinated sometimes (%[2])	15 (8.57%)	4 (11.11%)
Never vaccinated (%[2])	2 (1.14%)	30 (83.33%)
Influence of covid-19 (self-declaration) (%[2])	51 (29.14%)	2 (5.56%)

(%[1]): row percentage (%[2]): percentage related to n

d) Reasons for feeling influenced by Covid-19

The participants who received the flu vaccine and declared to be influenced by Covid-19 (self-declaration) were asked to explain the reasons why they felt this impact (*Fig. 7*). The first most chosen reason was the "need to feel safe from the virus" (66.05%). The second and third ones were the "awareness on the fact that virus can be contagious and deadly" and a need to "contribute to protect others" (50.96%).

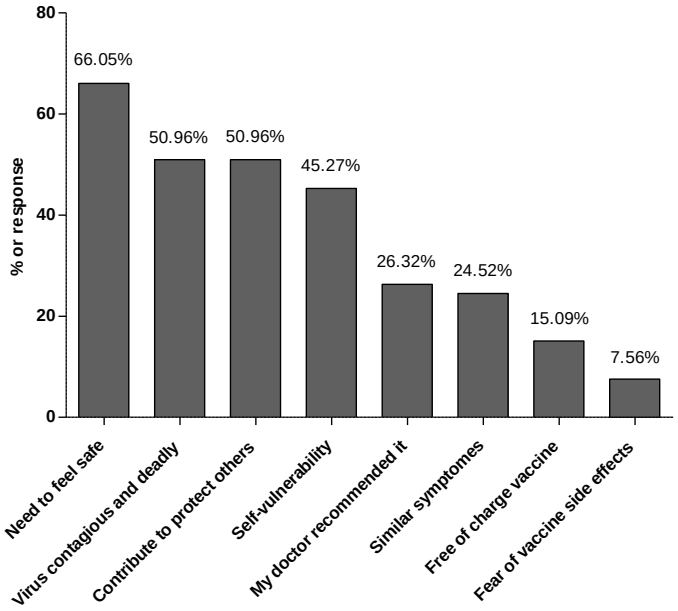

Figure 7: Reasons for taking the flu vaccine because of Covid-19 impact in 2020-21

e) Influence (self-declaration) of covid-19 according to flu vaccine habits

The participants who got the most influenced by Covid-19 were the ones getting vaccinated against the flu sometimes (63.16%) and almost every year (43.48%) (*Table V*). The non-influenced participants are represented the most by people that systematically either received of refused the flu vaccine.

Table V: Influenced persons (self-declaration) according to usual vaccine behavior

	Influenced (self-declaration)	**Non-influenced (self-declaration)**	**Total**
Vaccinated every year (%)	29 (21.16%)	108 (78.83%)	137
Vaccinated almost every year (%)	10 (43.48%)	13 (56.52%)	23
Vaccinated sometimes (%)	12 (63.16%)	7 (36.84%)	19
Never vaccinated (%)	2 (6.25%)	30 (93.75%)	32

(%): row percentage

f) Details of the vaccinations impacted by Covid-19 (self-declaration)

Concerning the 19 persons getting flu-vaccinated "sometimes," they explain their choice (*Table VI*) by usually not feeling involved, having distrust in vaccines, fearing the adverse effects, or even having experienced some already, and/or thinking the flu vaccine is not needed for them. Among this category of participants, the ones who decided to receive the flu vaccine in 2020-21 are the ones who previously thought to be not involved, and who distrusted the vaccination in general. For almost every one of them, Covid-19 was one of the reasons why they got the flu vaccine in 2020-21.

Table VI: Details of the vaccinations impacted (self-declaration) by Covid-19

Reason justifying a vaccination « sometimes »	Number of participants who chose this/these reason(s)	Number of participants vaccinated in 2020-21	Vaccinated in 2020-21 because of an impact of Covid-19 (self-declaration)
Feeling not involved	5	5	5
Distrust in vaccines	6	5	4
Fear of the adverse side effects	5	2	2
Not needed	2	2	2
By oversight	1	1	1
Side effects experience	3	1	1
Homeopathy	2	2	0

Each participant could choose several answers when asked about the reasons explaining their choice to get vaccinated «sometimes». These propositions of answer were showed only to participants that use to get vaccinated "sometimes" or "never".

g) Description of the influence (self-declaration) felt by patients vaccinated « sometimes » or « almost every year »

This change of minds and behavior towards the *influenza* virus and its vaccine is explored in more detail in *Table VII*. The need to feel safe from the virus and the awareness of their vulnerability were the two reasons chosen by 66.67% of the patients vaccinated "sometimes". The third most chosen reason was the discovery that a virus can be contagious and deadly, reason chosen by half of the patients vaccinated "sometimes". "Awareness of your vulnerability" was the most chosen reason among patients that are vaccinated "sometimes" because they usually did not feel involved, distrusted the flu vaccine, and feared the adverse effects.

The second category of patients who were influenced by Covid-19, is represented by the patients who are vaccinated almost every year (n=23) (*Table V*). When deciding to receive the flu shot while impacted by Covid-19 (self-declaration), 70.00% of them wanted to feel safe from the virus, 50.00% of them became aware of the virus possibly being contagious and deadly, 40.00% of them wanted to protect others, and another 40.00% became aware of their own vulnerability.

Table VII: Description of the influence (self-declaration) felt by patients taking the flu vaccine "sometimes" or "almost every year"

		n	Vaccinated persons in 2020-21 (%[1])	Vaccinated persons in 2020-21 influenced (self-declaration) by covid-19 (%[1])	Reasons justifying the influence of Covid-19 (self-declaration) among vaccinated persons in 2020-21.				
					Similar symptoms (%[2])	Awareness on your vulnerability (%[2])	Contagious and deadly virus (%[2])	Need to feel safe from the virus (%[2])	Contribute to protect others (%[2])
Persons taking the vaccine "sometimes"		19	15/19 (78.95%)	12/19 (63.16)	3/12 (25.00%)	8/12 (66.67%)	6/12 (50.00%)	8/12 (66.67%)	5/12 (41.67%)
Reasons for a vaccination "sometimes"	Feeling not involved	5	5/5	5/5	1/5	3/5	2/5	5/5	1/5
	Distrust in vaccines	6	5/6	4/6	1/4	3/4	2/4	0	2/4
	Fear of the adverse side effects	5	2/5	2/5	1/2	2/2	1/2	0	1/2
	Not needed	2	2/2	2/2	0	1/2	1/2	2/2	1/2
	By oversight	1	1/1	1/1	0	0	0	1/1	0
	Side effects experience	3	1/3	1/3	1/1	1/1	1/1	1/1	1/1
Persons taking the vaccine "almost every year"		23	22/23 (95.65%)	10/22 (43.48%)	3/10 (30.00%)	4/10 (40.00%)	5/10 (50.00%)	7/10 (70.00%)	4/10 (40.00%)

(%[1]): percentage related to n; (%[2]): percentage related to Vaccinated persons in 2020-21 influenced (self-declaration) by Covid-19

1.4. Discussion

In this study, we assessed the impact of the Covid-19 pandemic on the decision (for people aged 65 and more) to get vaccinated against the flu during the 2020-21 season. The first part of this study evidenced earlier take-up of the influenza vaccination during the campaign 2020-2021 compared to previous ones for people aged 65 and over in the department of Maine et Loire, a region in the west of France. These results also described a gap in the vaccination frequency between people who are vaccinated every year compared to the others.

The participation of pharmacies in the flu vaccination (2019-20 campaign) improved overall vaccine take-up and did not negatively impact the vaccine activity of the other HCPs. Indeed, if flu vaccine take-up slightly decreased between 2017-18 and 2018-19, it showed an increase in the 2019-20 campaign and the next one, respectively impacted by the pharmacies' involvement in vaccination and the Covid-19 pandemic. Adding this to the fact that the population of Maine et Loire is getting older, leading to more people being eligible for influenza vaccination, there were more people than before that accepted to receive the flu vaccine. A positive consequence of allowing pharmacies to administer vaccines is the increased vaccination take-up rates of citizens who did not previously accept a recommended flu vaccination. It may have its weight in the improvement of the flu vaccine coverage during the season affected by Covid-19, which is the season that followed the vaccination in pharmacies. A French survey has noted that the major part of the French population is satisfied with the vaccination in pharmacies[22]. This point was not an objective of our survey, but it would be interesting to deepen it, because it would maybe show another pandemic-related influence on flu-vaccination rates. According to a 2021 study on vaccination in pharmacies (Poland) including 1,062 patients, 65.3% of them strongly agreed with the statement that "pharmacies are more accessible for patients than outpatient clinics" [23]. A large proportion of respondents reported that it saved time to go to a pharmacy for a vaccination rather than to a GPs office. This study was conducted in 2021 and responses could be influenced by the Covid-19 pandemic context, even if that was not expressed clearly by the authors. In a French 2022 study, among more than 2,000 patients (over 55 years old suffering from comorbidities) that received the anticovid-19 vaccination in pharmacies, 76.6% were previously flu-vaccinated and 47% had previously received at least one flu vaccination in the same pharmacy[22]. These two vaccines did not target the same population, explaining the different age criteria between the studies. Patients who were regularly flu-vaccinated before Covid-19, appear more likely to be vaccinated against Covid-19 and seemed to have a preference for receiving the vaccine in pharmacy rather than from other HCP. Effectively, for these patients, only 26% received the flu vaccination from another HCP.

Further evidence that Covid-19 impacted flu vaccination rates is the analysis of the flu vaccine take-up rates by week for each campaign. The 2020-21 campaign started earlier in the year and with higher take-up targets than in previous years. People usually get vaccinated during the weeks 5 and 6 of the flu vaccine campaign. This was not the case in 2020-21: most of the vaccinations occurred in the first two weeks of the campaign. There was a second peak in weeks 5 and 6, and it could have been even higher if there were more doses available. In France, community pharmacies provide all the doses for the population, except for patients and professionals from hospitals and from nursing homes that have their own pharmacies. Even though community pharmacies received their flu vaccine orders, supply of doses started to run out only a few weeks after the launch of the 2020-21 campaign. As pharmacies could not order nor receive flu vaccines anymore, the Government of France created a "*Stock Etat*", made of flu vaccines coming from foreign countries (USA, Finland). Pharmacies could use these vaccines only for at-risk patients. Inpatients from nursing homes were the first to benefit from these new flu vaccines when outpatients had to wait until the first weeks of December 2020[24]. To our knowledge, it was the first time in France that such a situation happened. The shortage of doses can be explained by the fact that too many people decided to get the flu vaccine at the same time, on the very first days after the opening of the campaign. This unregular behavior was linked to the fear of Covid-19 but was also likely relative to strong media communication. The media played an important part in the so-called pandemic of panic and may have also influenced people on their choice on receiving the flu vaccination. Many newspapers reported on the Covid-19

cases, deaths, lockdowns, closing of schools, universities, shops etc[iv, v, vi, vii]. The government itself underlined the importance of the flu vaccine in the context of Covid-19, as a co-circulation between the two viruses was feared[25]. The first vaccine against Covid-19 was made available by the end of December 2020 and targeted only frail population [26,27]. At the time of the present study, it was the beginning of the Covid-19 vaccine campaign and people were, for the most part, not vaccinated yet, allowing them to focus more on the vaccine that could protect them from the flu.

The second part of the study gathered 211 answers to a questionnaire and identified an influence of Covid-19 for 25.12% of the participants. 82.94% of them were vaccinated during the 2020-21 campaign. Their vaccination history revealed a gap between people who get routinely vaccinated every year against the flu and the others who do not. The majority of those who were hesitant to get vaccinated against the flu in previous years overcame their hesitation and were vaccinated during the 2020-21 campaign. These citizens were the most likely to say that they had been influenced by Covid-19 in making their decision (self-declaration).

In our survey, 29.14% of the respondents were influenced by Covid-19 when deciding to receive the flu vaccine in 2020-21. A similar study (targeting young population from US colleges mostly aged between 18 and 29) reported that 53% of respondents felt the Covid-19 pandemic affected their choice[28]. In this last study, 70% of the students got flu-vaccinated in 2019-20, which is important, but a number of the participants had attended *influenza* clinics. This could explain such a high rate. The divergence of influence rate between this last study and the present survey could lay in the age difference between the participants of the two studies. Indeed, younger people are not specifically targeted by the flu vaccine recommendation compared to older ones, because they are less at risk with the *influenza* virus complications. However, it appears that Covid-19 can also affect younger people, with patterns that are not fully understood yet [29].

In the first part as well as in the second, for all the flu vaccine campaigns from 2017 to 2021, a gap is observed between people vaccinated each year and the others. According to our questionnaire, people flu-vaccinated each year (self-declaration), were all vaccinated during the season 2020-21 (excepted one person who could not because of the shortage of vaccine doses), while Covid-19 was progressing. Participants from community pharmacies belonging to the "downtown group" were 64% to be vaccinated every year against the flu. Participants vaccinated every year represent 70% of the "neighbourhood group", and 65% of the "shopping center group". The pharmacies of neighbourhood gather more persons that are vaccinated every year than the other groups. There may be more proximity with the patients in this type of community pharmacies that would explain people getting vaccinated every year, maybe on the pharmacist recommendation. Downtown and shop center pharmacies are more likely to work with a more diverse patient base, with people that do not choose to go to one pharmacy only.

[iv] CHAINAY CR Solange ESTEVES et Jennifer. Coronavirus : 13 215 cas supplémentaires enregistrés en France en 24 heures, nouveau record [Internet]. Ouest-France.fr. 2020 [cited 2022 Sep 23]. Available from: https://www.ouest-france.fr/sante/virus/coronavirus/direct-coronavirus-30-millions-de-cas-dans-le-monde-israel-se-reconfine-pour-trois-semaines-6978794

[v] Covid-19: les temps forts de la semaine du 29 septembre 2020 [Internet]. Sciences et Avenir. 2020 [cited 2022 Sep 23]. Available from: https://www.sciencesetavenir.fr/sante/covid-19-les-temps-forts-de-la-semaine-du-29-septembre-2020_147767

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[vii] Le Covid-19 a fait au moins un million de morts dans le monde. Le Monde.fr [Internet]. 2020 Sep 28 [cited 2022 Sep 23]; Available from: https://www.lemonde.fr/planete/article/2020/09/28/coronavirus-le-covid-19-a-fait-un-million-de-morts-dans-le-monde_6053836_3244.html

Participants that get vaccinated every time were 81% to accept the vaccine not to be sick, when it was 57% only for participants that get vaccinated almost every year. The second most chosen reason for those vaccinated every year was the recommendation from their GP (47%) whereas it was the reception of the invitation for free vaccination, from the French national health insurance, for those vaccinated almost every year. People who said to be vaccinated sometimes against flu were also asked why but did not get the same propositions to choose. A comparison can thus not be made, although it could have enlightened a difference in mentalities between participants getting vaccinated every year and the others.

The present survey showed that the people that were the most influenced (self-declaration) by the Covid-19 pandemic were the people usually hesitant towards the flu vaccination. They feared a new unknown virus, looking like a severe kind of *influenza virus*. They became aware of their own vulnerability when facing a respiratory virus, even when they thought (before Covid-19 pandemic) they were not at risk with the flu. In our survey, a lot of them did not regularly get vaccinated against the flu because they could not see the benefit that the vaccine would provide, and only saw the potential risks of the vaccine injection. This was observed too by Chu A. *et al* in a US survey on adults over 18 years old[30]. Another reason in disfavor of the flu vaccine in this US survey was the fear of needles. This was not a reason found in our survey, possibly because people were older than in the US survey. It is reasonable to think that younger people are more afraid of needles than older people, who could have had to deal with it more regularly (ie. diabetes monitoring, blood sample …).

Both parts of the present study show an improvement of the flu vaccine take-up since 2017. It could be related to better communications from the Healthcare System in France, and to the participation of pharmacies in the flu vaccination campaign. Indeed, this improvement is occurring thanks to hesitant patients that chose this time to get vaccinated against the flu. Since pharmacists began to vaccinate against the flu, it probably seems to be easier for the frail population to get flu-vaccinated, even maybe for their first time. People that got flu-vaccinated only once or twice since 2017 were mostly vaccinated for the 2020-21 campaign or the 2021-22 campaign. This is totally consistent with the hypothesis that the Covid-19 pandemic impacted on people's choice to get the flu vaccine and is likely also linked to the pharmacists' commitment.

Several limitations can be identified in this study. Firstly, the survey gathered 211 participants, which were unevenly distributed between the 11 community pharmacies. The main limitations come from the selection of the centers and the participants, as it was based on voluntary participation and was not built on randomization. There is a bias of independence in the collection of answers, as participants answered the pharmacist at the counter, and could not benefit from a total anonymization. Data from the SNDS were extracted until the end of December 2021 and did not cover completely the last flu vaccine campaign (*Table I; Fig. 1*). This could not take into account the complete data of the flu vaccination for the campaign 2021-2022. In addition, the questionnaire could not be submitted to inpatients from nursing homes or hospitals. These data are possibly not fully representative of the whole population aged 65 and more in the Maine et Loire. However, this study was conducted for the purpose of a qualitative analysis. In this survey, participants from the "neighbourhood group" are less influenced (self-declaration) by Covid-19 than patients from the other groups. We did not consider studying the three groups apart from each other. Indeed, the "neighbourhood group" gathered only three community pharmacies, represented 10.9% of participants and did not consequently change the mean of the groups.

This study also presents strengths, due to its structure in two complementary methods. The first one is quantitative and shows several years of evolution, which makes it quite comprehensive. The second method allowed a direct questioning of patients, which avoided transcription biases, and was conducted in not less than 11 centers.

1.5. Conclusion

This study highlights the Covid-19 impact perceived by the elderly in an area from the west of France (Maine et Loire) towards the flu vaccination. It allows us to understand better the uptake of the flu vaccine and could guide us through vaccine hesitancy to increase the participation and protection of the frailest people. Despite having severe human consequences, the Covid-19 pandemic was beneficial to flu vaccine take-up, and positively changed people's beliefs and behavior towards the flu vaccination. We indeed observed a change of opinion towards the flu vaccination, triggered by the Covid-19 pandemic, for people aged 65 and over, but also towards the perception of the *influenza virus* itself. This new perspective could be applied to future flu vaccination campaigns and may well be extended to other vaccines.

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Conflict of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Discussion générale

Alors que les pharmaciens commencent tout juste au niveau national à participer à l'effort de vaccination contre la grippe (2019-20), la pandémie de covid-19 vient bousculer les professions de santé. Le pharmacien d'officine est largement sollicité dans ce contexte sanitaire pour mener à bien des missions de santé publique. Les pharmaciens peuvent désormais effectuer des tests antigéniques en vue de dépister chez les patients le virus du covid-19 [Arrêté du 10 Juillet 2020[8]]. Sans toutefois être obligatoire, cette nouvelle mission est très attendue par les patients, souvent anxieux et éprouvés par ce contexte. Les officines ont joué le jeu pour la plupart, mettant en avant des compétences d'adaptation rapide en termes de logistique et de formation. Alors que beaucoup de commerces, écoles, lieux sportifs et culturels ferment, les pharmacies resteront ouvertes durant toutes les périodes de confinement, au même titre que les autres professionnels de santé, rendus disponibles pour faire face au covid-19.
C'est ainsi sans surprise qu'au moment du recrutement des pharmacies d'officine pour notre étude, les pharmaciens étaient surchargés de travail. Onze pharmacies officinales ont toutefois accepté de participer à notre étude et de déployer le questionnaire à destination des patients de 68 ans et plus.

La vaccination à l'officine crée un contact privilégié avec le patient. Le pharmacien bénéficie déjà d'une relation particulière avec sa patientèle, qui diffère et est complémentaire de la relation médecin-patient. Pouvoir vacciner en pharmacie renforce le lien de confiance entre le pharmacien et son patient. Cela a toute son importance, notamment en contexte de crise sanitaire, où bon nombre d'informations au sein des médias, de communautés scientifiques, et de son propre entourage sont relayées. Il est aisé de tomber dans la désinformation. Le professionnel de santé, comme le pharmacien officinal, se doit de lutter contre les fausses informations qui circulent et peuvent mettre en péril la santé de la population. Cela n'est pas un rôle facile en temps de pandémie, car les notes officielles sont très régulièrement mises à jour, et le pharmacien doit sans cesse s'informer des nouveautés publiées, pour pouvoir répondre à la demande légitime des patients en quête de renseignements. Certaines données relayées par le Gouvernement ont pu apparaitre parfois comme confuses, complexes ou même en contradiction avec les connaissances scientifiques partagées au sein de la profession pharmaceutique. Si ce n'est pas dans le rôle ni dans l'intention du pharmacien de décrédibiliser certains points du discours officiel, l'objectif n'est pas non plus de se sentir en désaccord avec l'information transmise aux patients, qui nous font confiance. Cet équilibre est sans nul doute difficile à trouver en période de crise sanitaire, où demeurent encore beaucoup d'inconnues.

La capacité des pharmaciens à vacciner est destinée en premier lieu à étendre la couverture vaccinale de la population française, en ne ciblant pas seulement les personnes fragiles mais également toutes les personnes de 16 ans et plus, avec ou sans comorbidités[9]. Notre étude montre que cette stratégie contribue en effet à augmenter la couverture vaccinale antigrippale, sans toutefois restreindre l'activité vaccinale des autres professionnels de

[8] Arrêté du 10 juillet 2020 prescrivant les mesures d'organisation et de fonctionnement du système de santé nécessaires pour faire face à l'épidémie de covid-19 dans le cadre de l'état d'urgence sanitaire - Légifrance [Internet]. [cited 2023 Jan 8]. Available from: https://www.legifrance.gouv.fr/loda/id/JORFTEXT000042106233/2020-11-04/

[9] Vaccination contre la grippe saisonnière [Internet]. [cited 2023 Jan 8]. Available from: https://www.ameli.fr/pharmacien/exercice-professionnel/delivrance-produits-sante/regles-delivrance-prise-charge/delivrance-vaccination/vaccination-grippe-saisonniere

santé. Les populations vaccinées par les pharmaciens semblent s'ajouter à celles vaccinées par les médecins, sage-femmes, et infirmières. Depuis maintenant de nombreuses années, la France fait face à une désertification médicale[10] : ce phénomène touche aussi bien les zones rurales que les zones urbaines. Les pharmacies d'officine constituent un pilier fondamental de la chaîne de soins du fait de leur maillage territorial qui permet une meilleure accessibilité des usagers aux professionnels de santé.

Au cours de discussions informelles avec des patients âgés issus de l'Est de la France (département des Ardennes), lors de séances de vaccinations antigrippales et anticovid-19, le vaccin antigrippal n'avait pas toujours été fait en 2021-22 car le vaccin anticovid-19 avait trop occupé les esprits, certains pensant même bénéficier d'une protection croisée covid-19/grippe avec le seul vaccin anticovid-19. Cela n'est pas directement comparable avec notre étude ICOVAG, qui s'intéressait à la campagne 2020-21, et au cours de laquelle le vaccin anticovid-19 était à peine déployé. Il serait cependant intéressant de croiser les données de cet article avec une recherche plus globale, mettant en comparaison les différentes régions de France, et incluant des données sur la vaccination anticovid-19.

Cette thèse aura été l'occasion pour moi d'apprendre à mettre en place un travail de recherche, de la conception du sujet jusqu'à la rédaction de l'article, ainsi que la préparation à sa publication dans un journal anglophone. Un projet comme celui-ci a nécessité un travail préliminaire de validation auprès d'un comité d'éthique. En effet, avant de pouvoir déployer le questionnaire interrogeant des patients sur des questions de santé, il a été nécessaire de contextualiser, de justifier le questionnaire et de le soumettre à un comité de protection des personnes pour validation. En parallèle de cela, s'est déroulée la phase de recrutement des pharmacies. Dans ce but, de nombreux appels/visioconférences/e-mails ont été passés, et ce en plein confinement dû au covid-19. J'ai ainsi rencontré des difficultés pour joindre et motiver les titulaires à participer à ce projet. Les étudiants de 6ème année ont beaucoup aidé à la mise en place du questionnaire dans leur pharmacie de stage.
Ce travail en collaboration avec les officines a été une expérience riche et m'a incitée à me dépasser en termes de communication. Je me sens plus à l'aise désormais à l'idée de monter un projet nécessitant une coopération avec des professionnels de santé. Ce projet m'a également permis une mise en relation avec des médecins du Service médical des Pays de la Loire, qui nous ont été d'une grande aide.

Les principales difficultés auxquelles j'ai été confrontée étaient en lien avec la phase de lancement du questionnaire auprès des officines, ainsi que les phases d'extraction de données du SNDS. En effet, tout ne dépendait plus seulement de moi et cela avait un côté frustrant. Cette expérience m'a appris à faire preuve de patience et à faire confiance à ses collaborateurs, ce qui, dans le métier de pharmacien, me parait indispensable pour travailler en équipe de manière saine et efficace. Je suis bien consciente du contexte particulier qui surmenait les officinaux depuis de longs mois. C'était par ailleurs ma crainte : que le questionnaire, proposé sur le mois de février 2021, coïncide avec un nouveau confinement. Nous avons finalement obtenu un nombre de réponses satisfaisant et suffisant pour une analyse qualitative, apportant une complémentarité avec les analyses quantitatives des données du SNDS.

[10] Lutter contre les déserts médicaux [Internet]. Ministère de la Santé et de la Prévention. 2023 [cited 2023 Jan 8]. Available from: https://solidarites-sante.gouv.fr/systeme-de-sante-et-medico-social/masante2022/lutter-contre-les -deserts-medicaux/

Si j'étais amenée à travailler sur un autre article scientifique, je pense que je serais plus efficace que je ne l'ai été pour ce projet. J'ai désormais des clés pour rédiger plus facilement et mettre en place un travail comme celui-là. Si je devais réaliser à nouveau une enquête ou un questionnaire, je réfléchirais davantage en amont au traitement et à l'analyse que je souhaite mener à l'issue de la collecte des données. En effet, pour ce projet de thèse, certains points auraient été intéressants à creuser et il aurait pu être bénéfique de disposer de plus de renseignements sur les patients. La construction du questionnaire est donc particulièrement importante et cette phase de réflexion n'est pas à négliger, car tous les résultats en découlent.

Conclusion générale

Ce projet m'aura beaucoup appris, de la mise en place d'un projet de recherche, à la construction d'un article en anglais, en passant par des présentations et des communications avec différents collaborateurs, que je souhaite remercier à nouveau pour leur implication. Rédiger cette thèse m'a fait passer par toute sortes d'émotions : du stress, de l'impatience, des phases de motivations et des phases moins productives, des déceptions parfois mais surtout de la reconnaissance vis-à-vis de ceux qui m'ont accompagnée et de la fierté d'être allée jusqu'au bout.

Pour conclure, le pharmacien d'officine a un rôle particulièrement intéressant dans la mise en place d'études cliniques, qu'elles soient axées sur le soin primaire ou sur de l'épidémiologie, car il a un contact privilégié avec le patient et ses données de santé. Son accessibilité et sa proximité avec les patients de tout type font de lui un atout dans le cadre d'études cliniques. De plus, le pharmacien d'officine est au cœur du système de santé, et peut établir le lien avec les autres membres de l'équipe de soin tel que le médecin généraliste ou encore l'infirmière. Ce type de mission offre également aux pharmaciens impliqués un nouvel axe de travail, qui permet de diversifier le quotidien et d'élargir son champ d'action et ses compétences, toujours dans l'intérêt du patient, et dans le but d'améliorer la santé de tous.

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Table des matières

Annexes

Annexe 1 : Questionnaire proposé aux patients

QUESTIONNAIRE ICOVAG

1. Quel âge avez-vous ? (éligible si âge ≥68 ans) ..... ans

2. Acceptez-vous de participer à l'étude ? ☐ Oui ☐ Non

3. Renseigner le code participant (1ère lettre du prénom et du nom et date de naissance)

Exemple : AB21081950) [.....]

4. Quel est votre sexe ? ☐ Féminin ☐ Masculin

VACCINATIONS ANTERIEURES :

5. Depuis que la vaccination antigrippale est recommandée pour vous, combien de fois vous êtes-vous fait vacciner ? ☐ Chaque année ☐ Presque chaque année ☐ Parfois ☐ Jamais

Si vous avez répondu « Parfois » ou « Jamais », pour quelles raisons ? ***(Plusieurs choix sont possibles)***

- ☐ Méfiance des vaccins de manière générale
- ☐ Vous ne vous sentez pas concerné(e)
- ☐ Vous pensez que le vaccin n'est pas efficace
- ☐ Peur des effets secondaires
- ☐ Oubli
- ☐ Manque de temps

Autre : .....

Si vous avez répondu « Chaque année » ou « Presque chaque année », pour quelles raisons ? ***(Plusieurs choix sont possibles)***

- ☐ Pour ne pas tomber malade
- ☐ Pour ne pas contaminer son entourage
- ☐ Parce que vous avez reçu un bon de vaccination
- ☐ Par habitude
- ☐ Parce que vous avez une santé fragile
- ☐ Parce que votre médecin vous l'a recommandé
- ☐ Parce que votre pharmacien vous l'a recommandé

Autre : .....

VACCINATION EN 2020 :

6. Avez-vous été vacciné contre la grippe cette année (fin 2020- début 2021) ?

☐ Oui ☐ Non

7. Si non : Souhaitiez-vous vous faire vacciner contre la grippe cette année mais n'avez pas pu à cause des pénuries de vaccins ? ☐ Oui ☐ Non

8. Le contexte dû à la pandémie de Covid 19 a-t-il impacté votre choix de vous faire ou non vacciner ?

☐ Oui ☐ Non

Si oui : en quoi la Covid 19 vous a-t-elle influencée dans votre choix ? ***(Plusieurs choix sont possibles)***

- ☐ Symptomatologie similaire entre les deux virus
- ☐ Prise de conscience sur sa propre vulnérabilité face à un virus respiratoire
- ☐ Prise de conscience qu'un virus peut être contagieux et mortel
- ☐ Besoin de se sentir protégé face au virus
- ☐ Contribuer à la protection de son entourage
- ☐ Gratuité du vaccin
- ☐ Le médecin vous l'a recommandé
- ☐ Crainte de développer un syndrome grippal à cause de la vaccination

Autre : .....

Version 1 – 12/10/2020 1/1

Annexe 2 : Validation du Comité de Protection des Personnes

COMITÉ DE PROTECTION DES PERSONNES
SUD-OUEST ET OUTRE MER III
Présidente : Madame Marie VIGUIER

NUMERO D'ENREGISTREMENT SI CNRIPH : ID 10269 N° 20.11.16.39621
NUMERO ID-RCB : 2020-A03113-36

PROMOTEUR : Docteur Samuel LEGEAY

COORDONNATEUR : Docteur Samuel LEGEAY

En date du **16 DECEMBRE 2020**, conformément aux dispositions du Code de la Santé Publique, le Comité de Protection des Personnes Sud-Ouest et Outre-mer III a examiné la recherche impliquant la personne humaine mentionnée au 3° de l'article L. 1121-1 du même code, ne portant pas sur un produit mentionné à l'article L. 5311-1 du code de la santé publique, et intitulé :

Évaluation de l'impact de la COVID-19 sur la couverture vaccinale antigrippale en 2020 chez les personnes âgées de 68 ans et plus.

Le Comité à l'unanimité des membres votants émet un

AVIS FAVORABLE

Remarque :
Concernant la sécurité et l'anonymat, il est demandé au participant de renseigner son code participant avec la première lettre de son prénom et de son nom ainsi que sa date de naissance, ce qui ne permet pas vraiment un anonymat pour les personnes travaillant dans l'officine. Il faudrait, une fois le questionnaire rempli, qu'il soit immédiatement déposé dans un endroit qui permette de garder cet anonymat.

La Présidente du Comité

Marie VIGUIER.

Conformément à l'article R. 1123-26 du code de la santé publique, si dans un délai de deux ans suivant le présent avis la recherche impliquant la personne humaine n'a pas débutée, cet avis devient caduc.

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NUMERO D'ENREGISTREMENT SI CNRIPH : ID 10269 N° 20.11.16.39621
NUMERO ID-RCB : 2020-A03113-36

DOCUMENTS EXAMINES PAR LE COMITE

- Courrier de demande d'avis de Monsieur LEGEAY en date du 16 novembre 2020 ;
- Questionnaire d'autoévaluation complété, signé et daté du 19 novembre 2020 ;
- Protocole version 1 du 16 novembre 2020 ;
- Résumé du protocole version 1 du 16 novembre 2020 ;
- Engagement de conformité à la méthodologie de référence MR-003 ;
- Lettre d'information pour le participant version 1 du 16 novembre 2020 ;
- Attestation de conformité avec les dispositions législatives et réglementaires relatives aux recherches impliquant la personne humaine en date du 16 novembre 2020 ;
- Questionnaire version 1 du 12 octobre 2020 ;
- Lettres d'engagement ;
- Curriculum vitae de M. LEGEAY et de Mme ABLINE ;
- Liste des investigateurs.

MEMBRES PRESENTS

Catégorie médecins ou personnes qualifiées dans la recherche biomédicale :
- Docteur Driss BERDAÏ (titulaire)
- Docteur Olivier MARCY - compétent en matière biostatistique ou d'épidémiologie (titulaire)
- Docteur Vincent BOUTELOUP - compétent en matière biostatistique ou d'épidémiologie (suppléant)

Catégorie médecins généralistes
- Docteur Shérazade KINOUANI (titulaire)

Catégorie pharmaciens hospitaliers :
- Mademoiselle Marie-Claude SAUX (titulaire)
- Docteur Barbara LORTAL-CANGUILHEM (suppléante)

Catégorie infirmiers
- Madame Marie VIGUIER (titulaire)

Catégorie psychologues :
- Madame Eva TOUSSAINT (titulaire)

Catégorie juridique :
- Professeur Jean-Pierre DUPRAT (titulaire)

Catégorie Représentants des associations agréées de malades et d'usagers du système de santé :
- Monsieur Michel PERDRISET (titulaire)
- Monsieur Serge ARNOULET (titulaire)

Résumé

Impact du covid-19 sur la couverture vaccinale antigrippale en 2020-21 en France

RÉSUMÉ

La couverture vaccinale contre la grippe en France est évaluée chaque année par Santé Publique France (SPF), une agence sanitaire nationale. En 2020, une pandémie de covid-19 émerge dans le monde entier. Avec plusieurs symptômes connus comme similaires entre la grippe et le covid-19, nous nous attendons à observer un impact positif sur le choix des personnes à recevoir l'injection du vaccin contre la grippe.

Les données concernant la vaccination contre la grippe des personnes âgées de 65 ans et plus ont été extraites du Système National des Données de Santé (SNDS). Une enquête multicentrique non interventionnelle dans le département du Maine et Loire a été utilisée pour une analyse qualitative.

La couverture vaccinale contre la grippe (Maine et Loire - France), chez les personnes âgées de 65 ans et plus, s'améliore depuis 2017 (54,36% en 2017-18 vs 58,12% en 2020-21). En 2020-21 (de manière concomitante à la pandémie de covid-19), les personnes se sont fait vacciner plus tôt que l'année précédente (pic en semaine 1-2 vs pic en semaine 5-6 lors des campagnes précédentes), et une pénurie de doses a perturbé la campagne 2020-21. Sur les 211 personnes ayant répondu à l'enquête, 175 ont été vaccinées lors de la campagne de vaccination contre la grippe 2020-21. Parmi elles, 29,12% ont déclaré avoir été impactées par le covid-19 au moment de recevoir le vaccin contre la grippe. La raison la plus citée était le besoin de se sentir à l'abri du virus ; la seconde était la " sensibilisation au fait qu'un virus peut être contagieux et mortel ".

Notre étude met en évidence l'impact du covid-19 perçu par la population âgée (Maine et Loire) vis-à-vis de la vaccination contre la grippe. Malgré ses conséquences humaines, la pandémie de covid-19 a été bénéfique pour la couverture vaccinale contre la grippe, et a modifié positivement les croyances et les comportements des personnes vis-à-vis de la vaccination contre la grippe.

Mots-clés : covid-19 ; vaccin antigrippal ; habitudes de vaccination ; impact du covid-19

Impact of covid-19 on the influenza vaccine take-up in 2020-2021 in France

ABSTRACT

The flu vaccination coverage in France is assessed every year by Santé Publique France (SPF), a national health agency. In 2020, the pandemic of covid-19 takes place all over the world. With several symptoms known to be similar between flu and covid-19, we expect to observe a positive impact on people's choice for the flu vaccine injection.

Data regarding the flu vaccination for people aged 65 and over were extracted from the French National Health Data System (Système National des Données de Santé – SNDS). A non-interventional multi-center survey in the department of Maine et Loire, an area from the west of France, was used for a qualitative analysis.

The flu vaccine take-up (Maine et Loire - France), among people aged 65 and over, improves since 2017 (54.36% in 2017-18 vs 58.12% in 2020-21). In 2020-21 (concomitantly to covid-19 pandemic), people got vaccinated earlier than the previous year (peak in the weeks 1-2 vs peak in weeks 5-6 in previous campaigns), and a shortage of doses disturbed the 2020-21 campaign. Of the 211 people that answered the survey, 175 were vaccinated during the 2020-21 flu vaccine campaign. Among them, 29.12% declared they were aware by covid-19 when receiving the flu vaccine. The most cited reason was the need to feel safe from the virus; the second was the "awareness on the fact that a virus can be contagious and deadly".

Our study highlights the covid-19 impact perceived by the elderly population (Maine et Loire) towards the flu vaccination. Despite having human consequences, the covid-19 pandemic was beneficial to the flu vaccine take-up, and positively changed people beliefs and behaviors towards flu vaccination.

Keywords : covid-19; flu vaccine; vaccine behavior; covid-19 impact

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