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A 6-Week Time Period May not be Sufficient to Identify Potential Adverse Events Following COVID-19 Vaccination

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ABSTRACT

Background. Messenger RNA (mRNA) vaccines have been widely used as the main sanitary measure destined to fight the COVID-19 pandemic. Rapidly purported as being "safe and effective", this new generation of vaccines is radically different from those developed traditionally and for which potentially associated adverse events (AEs) are considered through a standard 6-week post-vaccination period.

Hypothesis. Here, we posit that the reporting period for AEs related to the COVID-19 vaccines may need to be longer.

Method. In this retrospective, observational study, we aimed to assess the chronology of new/worsening ailments occurring after the administration of COVID-19 vaccines based on the changes to the participants' pharmacological records. Patients vaccinated against COVID-19 and experiencing health-related events during the study period (between September 30, 2021 and July 15, 2022) were included and the changes to their pharmacological records were analyzed.

Results. One hundred and twelve (112) adult patients (63 men, 49 women; 67.54 ± 14.55 years-old; mean ± standard deviation) have reported changes to their pharmacological record following health-related events, which occurred 11.57 weeks (median; range 0.04-47.14) following their last COVID-19 injection of 3 doses (median; range 1-4). The most frequent medical ailments that appeared or worsened were cardiovascular diseases (CVD; N=61), cancer (N=31), respiratory diseases (RD; N=22) and zona (N=10), half of which occurred after the second dose. Nineteen (19) patients (10 men, 9 women; 78.2 ± 11.4 years-old) died on average 17.14 weeks (SD 13.71) after their last injection.

Conclusion. Most (76.1%) of the health-related events experienced by patients vaccinated against COVID-19 occurred beyond the 6-week period prescribed by the health authorities. Our findings call for further investigations and an extension of the post-vaccination AE reporting period.

Keywords: *adverse event reporting, cancer resurgence, cardiovascular diseases, pharmacological records, respiratory disease, sanitary measures for COVID-19, varicella zoster symptoms, zona after vaccination*

I- INTRODUCTION

Messenger RNA (mRNA) and adenoviral vaccines expressing the SARS-CoV-2 spike protein have been widely promoted by pharmaceutical companies, government officials, medical associations and the worldwide media as the main sanitary measure destined to fight the COVID-19 pandemic (Kis et al., 2021). The publicity campaigns rapidly purported this new generation of vaccines, authorized for emergency use, as being "safe and effective" against COVID-19. Currently in phase 3 clinical trials, which are available for public consultation here (and the Pfizer/BioNTech protocol is available here), the safety and efficacy of these injections remain to be confirmed, as their short, medium, and long-term beneficial and side effects remain to be thoroughly documented and their link to the injections established and independently investigated (Fraiman et al., 2022).

Several hurdles remain to portray the precise nature and true incidence of the adverse events (AEs) associated with COVID-19 vaccination, including the guidelines of the professional orders, the awareness of the medical community, the passive surveillance of AEs and their reporting (Lazarus et al., 2010), which may constitute the blind spot of the COVID-19 crisis (Provost, 2023). According to Tom Shimabukuro of the Atlanta CDC and co-authors, the underreporting rate can be lower than 1% depending on the type of AE and the type of vaccine (Shimabukuro et al., 2015). Once reported by a member of the medical staff to the Quebec's Public Health Agency, the "Institut national de santé publique du Québec (INSPQ)", AEs are then screened for follow-up and those occurring more than 6 weeks after vaccination are not considered, based on what is known about traditional vaccines.

The recommended duration of follow-up for adverse events of vaccines in general and COVID-19 in particular is very poorly defined and often conflicting between references. The Brighton Collaboration, which is responsible for monitoring the safety profiles and benefit/risk ratios of vaccines, has published a guide for monitoring selected adverse events of vaccines in general. Most documents refer to vaccines prior to COVID-19 and primarily to pediatric vaccines. Follow-up times are sometimes specified (28 days for Guillain-Barré, 10 days for vasculitis, 28 days after a pneumococcal vaccine, 42 days for Kawasaki, 28 days for hearing loss) and are in some cases left unspecified (Bell's palsy, thrombosis and thromboembolism). In the recently updated documents, for vaccine-associated enhanced disease (VAED) and vaccine-associated enhanced respiratory disease (VAERD), which are phenomena of aggravation of the infection by the vaccine, the follow-up can be up to 2 years; for myocarditis, the follow-up can be up to 42 days. Yet, published studies only consider 28 days of follow-up after COVID-19 vaccination for myo/pericarditis (see the PDF in the following link, Safety Platform for Emergency vACcines SO2- D2.5.2.2 — AESI Case Definition Companion Guide for 2nd Tier AESI Myocarditis and Pericarditis, May 2022).

The Ontario Public Health Standards (Requirements for Programs, Services and Accountability Infectious Disease Protocol Appendix 1: Provincial Case Definitions for Diseases of Public Health Significance Adverse Events Following Immunization (AEFIs) Effective: May 2022 (PDF here) recommends a follow-up time for vaccines of 2-42 days for AEs in general and 42 days for Guillain-Barré; a supplementary guide for COVID-19 vaccines is reported, but the web link is not provided and we were unable to find it.

According to an FDA COVID-19 vaccine pharmacovigilance study (Wong et al., 2022) published in December 2022, vaccinated individuals are followed for up to 42 days (for only 28 days for the following adverse events: acute myocardial infarction, deep vein thrombosis, pulmonary embolism, disseminated

intravascular coagulation, and stroke, and for 42 days for immune thrombocytopenia, myo/pericarditis, Guillain-Barré syndrome, Bell's palsy, encephalomyelitis, transverse myelitis, narcolepsy, and appendicitis). It is stated in this study that references for the duration of these windows could not be found in the literature and are instead based on clinician input.

It is important to consider that mRNA and adenoviral vector vaccines have a content and mechanisms of action (i.e., pharmacodynamics) very different from that of traditional vaccines, and there is no precedent of an optimal minimal period of surveillance post-vaccination necessary to capture AEs related to these new vaccine technologies. The novelty of these approaches alone, now applied to the population on a global scale, should call into question the 6-week post-vaccination reporting period to consider the occurrence of a new or worsening ailment as a potential AE worth investigating. The consideration of a relatively short period of 6 weeks precludes the possibility of detecting slowly developing, or more insidious health problems that take longer than 6 weeks to become symptomatic, and that could affect patients in the long term. If new/worsening ailments that occur later than 6 weeks post-vaccination are systematically discarded by health agencies, they may go unnoticed and leave scientists unable to perform any observational and descriptive analysis, and, if necessary, alert the authorities.

Consequently, we explored an alternative source of health data, recorded by pharmacists following the reception of new prescriptions or modifications of previous prescriptions related to the occurrence of a new ailment or worsening of an existing one. Our rationale to consider this source of data is the following: people who are worried about their health and/or experience significant changes in their health condition usually consult their physician or visit a health care facility or hospital. The patients are then given a diagnosis and, depending on whether the existing and/or new ailment can be treated pharmacologically or not, a new drug prescription, or modification of an existing one (e.g., changes in the dose of a drug) is then transmitted to their local pharmacy. Therefore, this peripheral component of the Quebec health care system represents a valuable source of health information provided indirectly by practicing physicians and used by pharmacists, which may yield a unique perspective in the descriptive analysis of post-vaccination AEs.

The present study aims to present the incidence of new and/or worsening ailments, recorded through a pharmacy's prescriptions of new drugs, or modifications of existing prescriptions, in relation to the vaccination dates. We hypothesized that an important number of new/worsening ailments may manifest beyond the currently used 6-week time period after vaccination against COVID-19.

II- METHODS

2.1- Study design

Our study is a retrospective, observational analysis that aimed to assess the chronology of new/worsening ailments occurring after the administration of COVID-19 vaccines.

2.2-Participants

We used a convenience sample of patients of a community pharmacy located in the Bas-St-Laurent-Gaspésie region of the province of Quebec, Canada, who had new prescriptions or modifications of existing prescriptions because of the diagnosis of a new ailment or worsening of an existing ailment, as well as patients who had their pharmacy files closed following death. The study period considered was between

September 30, 2021 and July 15, 2022. A written informed consent was obtained from all the patients or from their legal representatives.

2.3-Variables of interest

We considered the following variables: age, sex, type of vaccine received, number of doses received, number and type of a new/worsening ailment (as per new/modification of drug prescription), time elapsed between last vaccination date and date of start of new/worsening ailment, number of comorbidities, PCR or antigenic COVID-19 testing results, diagnosis (i.e., type of disease) of a new/worsening ailment and cause of death.

All the variables were collected from the pharmaceutical records, the Quebec Health System (faius.santepublique.rtss.qc.ca) to record COVID-19 vaccine lot numbers, the death certificates' information, and from the patients themselves or their closest relative or legal representative.

2.4- Statistical analysis

We used descriptive statistics to present all quantitative variables, as either mean and standard deviation (SD), or median and range, according to their distribution, and all qualitative variables as proportions. We used the standard *t*-test to compare demographic quantitative variables, *chi-square* (χ^2) test to compare the frequency of events, Mann-Whitney and Kruskal-Wallis tests to assess differences of quantitative variables across categories, Spearman's correlation coefficient to explore correlations, and a generalized linear model to assess associations with specific variables of interest.

All the statistical analyses were corrected for multiple comparisons using Bonferroni correction and were performed using SPSS statistics software (26.0.0 version).

III- RESULTS

3.1- Participants

One hundred and twelve (112) adult patients who reported new or worsening ailments following vaccination against COVID-19 were included in this study, comprising 63 men (56.25%) and 49 women (43.75%) (Supplementary Table S1). The mean age of the population was 67.54 years-old (y.o.), SD 14.55, and there was no significant difference in the mean age of men (mean 66.40, SD 12.93) and women (mean 69.04, SD 16.45).

3.2- COVID-19 vaccine administration

All patients received at least one dose of a COVID-19 vaccine, but not all received the complete series of two doses or continued to receive a third or fourth dose (Note: we have used throughout this manuscript third and fourth dose instead of first and second booster, just to better depict the chronology of the administrations). At the end of the observation period, 2 patients had received only one dose (1.8%), whereas the majority (N=110, 98.2%) received at least 2 doses: thirty-five (35) patients received 2 doses (31.3%), 62 patients received 3 doses (55.4%), and 13 patients received 4 doses (11.6%).

The patients received at least one of the following vaccines: Pfizer/BioNTech (pb; N=76), Moderna (mod; N=55) or AstraZeneca (AZ; N=7)/CoviShield (CS; N=2). Patients received one (N=2), two (N=35), three

(N=62) or four (N=13) doses of the same vaccine (N=88; 78.6%), and two (N=22; 19.6%) or three (N=2; 1.8%) doses of different vaccines.

Forty-nine (49) different vaccine lots were administered to these patients, the most frequent representative being Pfizer/BioNTech #EW3344 (N=20), Moderna #3001658 (N=14) and 043D21A (N=14), AstraZeneca #MT0056 (N=5) and CoviShield #4120Z003 (N=2) (Supplementary Table S2).

3.3- Post-vaccination occurrence of new/worsening ailments

The most frequent medical conditions that appeared or worsened in vaccinated patients were cardiovascular diseases (CVD; N=61), cancer (N=31, including two pending biopsy confirmation), respiratory diseases (RD; N=22) and zona (N=10, including two bilateral cases). Other medical conditions (N=10) included intense fatigue, infection, lymph node inflammation, or hemorrhage.

Most patients experienced one new/worsening ailment (N=100, 89.3%) and 10 patients (8.9%) experienced 2 new/worsening ailments, 1 patient (0.9%) experienced 3, and 1 patient (0.9%) experienced 4. There was no significant difference in the number of new/worsening ailments occurring in men and women (Figure 1).

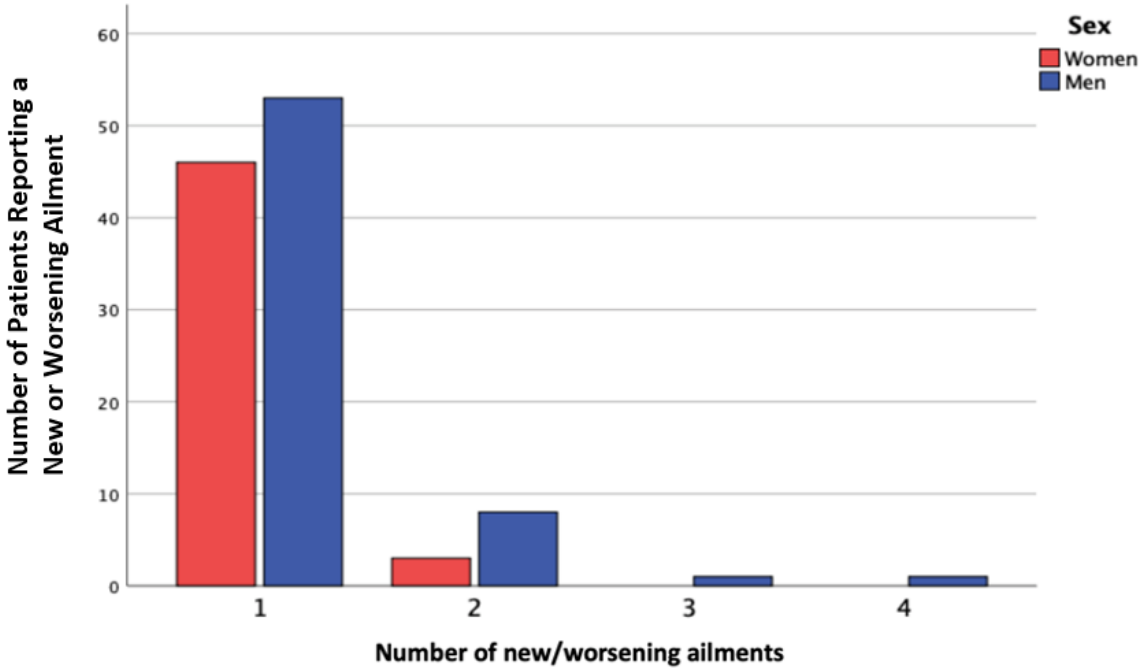

Figure 1. Bar chart presenting the number of new/worsening ailments occurring in men and women following COVID-19 vaccination.

The median time elapsed between the last administered dose and the occurrence of the first new/worsening ailment was 11.57 weeks (range 0.04-47.14). The majority of patients (N=83, 76.1%) experienced the occurrence of the new/worsening ailment after 6 weeks post-vaccination, and only 26 (23.9%) before 6 weeks. In the group of patients experiencing the new/worsening ailment after 6 weeks postvaccination, the median time elapsed was 15.0 weeks (range 6.43-47.14), and in the group experiencing the new/worsening ailment before 6 weeks postvaccination, the median time elapsed was 4.28 weeks (range 0.04-5.57).

There was not a significant difference in age between the patients with a first new/worsening ailment starting before 6 weeks post-vaccination (mean 66.64, SD 16.90) and those with a first new/worsening ailment starting after 6 weeks post-vaccination (mean 67.61, SD 13.99). There was not a significant difference in the proportion of men and women experiencing a first new/worse ailment before or after 6 weeks post-vaccination (Figure 2).

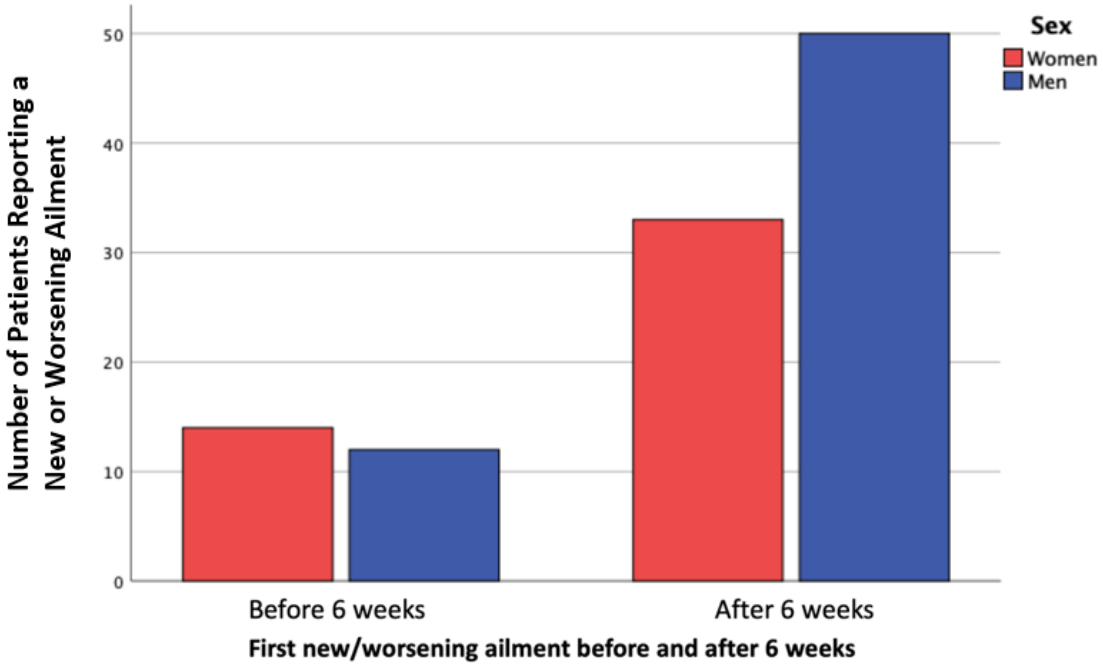

Figure 2. Bar chart presenting the number of men and women experiencing a first new/worse ailment before or after 6 weeks post-vaccination.

The median time elapsed between the last administered dose and the occurrence of the second new/worsening ailment was 18.21 weeks (range 8.57-60), all of them occurring after 6 weeks post-vaccination. The mean age of these patients was 68.83 (SD 11.85), and 75% were men (N=9) and 25% were women (N=3). One 61 year-old man experienced a third new ailment, which occurred 30 weeks post-vaccination, and one 82 year-old man experienced a fourth new ailment 21.43 weeks post-vaccination (Note: when referring to post-vaccinations, we always refer to the latest administered dose).

The number of doses administered before the occurrence of a first new/worsening ailment was 1 dose to 14 patients (12.5%), 2 doses to 64 patients (57.1%), 3 doses to 24 patients (21.4%), and 4 doses to 7 patients (6.3%) (Figure 3).

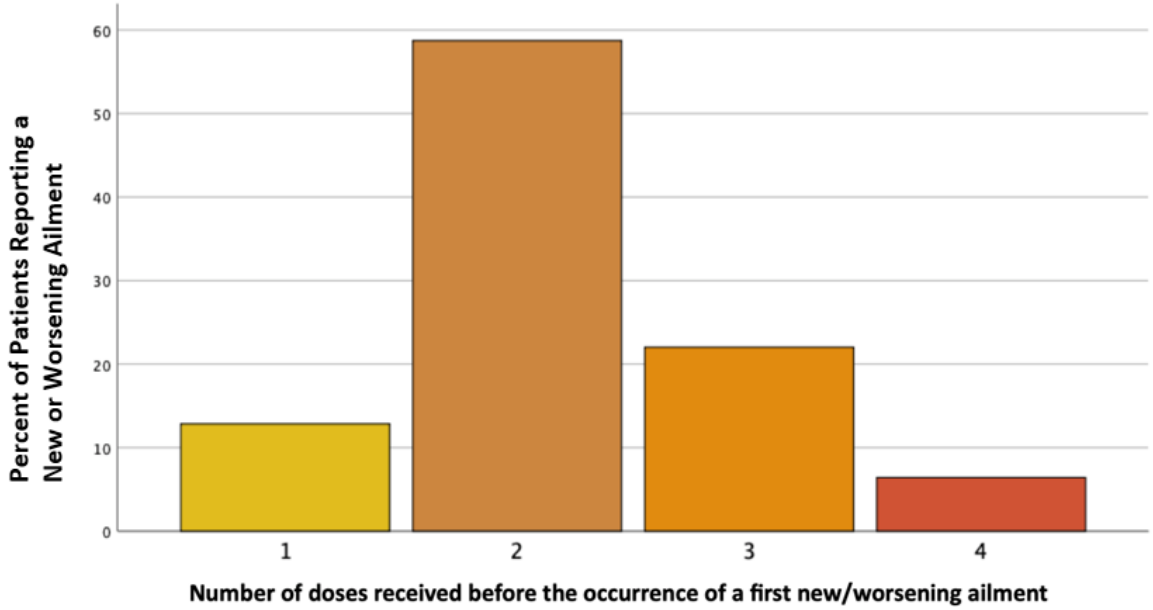

Figure 3. Bar chart presenting the number of COVID-19 vaccine doses administered before the occurrence of a first new/worsening ailment.

Additionally, 6 patients (5.3%) experienced a second new/worsening ailment after receiving 2 doses, and 5 patients (4.5%) after receiving 3 doses. The patient experiencing a third new/worsening ailment received 3 doses, and the patient experiencing a fourth new/worsening ailment received 4 doses. The number of new/worsening ailments occurring before 6 weeks was significantly higher in patients receiving four doses, while most new/worsening ailments in people receiving two and three doses occurred after 6 weeks (*chi square* 12.97, $p < 0.001$ after Bonferroni correction) (Figure 4).

Regarding the number of new/worsening ailments that occurred in patients receiving 1, 2, 3 or 4 doses, we found no significant differences across groups.

When assessing the number of new/worsening ailments per vaccine type, we did not find any significant difference. Also, the number of weeks until the occurrence of a first or second new/worsening ailment was not significantly different across vaccine types.

Finally, we assessed the number of comorbidities (e.g., hypertension, diabetes, hypercholesterolemia, etc.), finding a median number of comorbidities of 4 (range 0-11), with a significantly higher number of comorbidities in women (median 4, range 0-9) than men (median 3, range 0-11) ($p = 0.04$). The number of comorbidities was also significantly higher in participants developing a first new/worsening ailment before 6 weeks post-vaccination (median 5, range 0-11) than after 6 weeks post-vaccination (median 3, range 0-9). We also find a small but significantly negative correlation (Spearman's rho correlation coefficient: -0.3; $p = 0.02$) between the number of comorbidities and the number of new/worsening ailments of the participants, which was confirmed using a generalized linear model, correcting for sex, age, and vaccine type ($p = 0.01$).

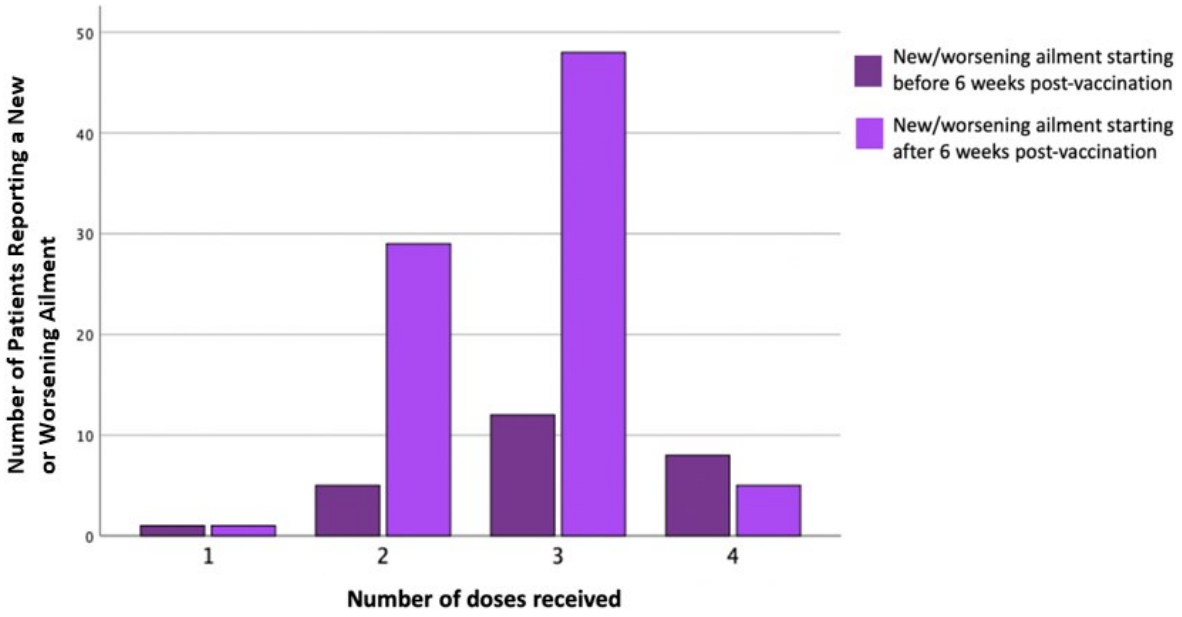

Figure 4. Bar chart showing that the greater number of new/worsening ailments in people receiving two and three doses of a COVID-19 vaccine occurred after 6 weeks.

3.4- COVID-19 test results

Among the 112 patients included in the study, 33 tested positive to a COVID-19 PCR or antigenic test during the study period, 48 were negative and 31 did not provide the information (unknown).

Of the 38 health-related events that occurred in 33 patients who tested positive for COVID-19, 26 (68.4%) occurred after vaccination but before COVID-19 infection, whereas 12 (31.6%) occurred after vaccination and infection.

3.5- Deceased patients

Nineteen (19) patients with a mean age of 78.2 y.o. (SD 11.4) (10 men, 9 women) died on average 17.14 weeks (SD 13.71) after their last injection. The known causes of death were cancer (N=9) or cardiovascular diseases (N=8). One patient died after a hip fracture, and the probable cause of death of one patient is not available. Only two of the 19 deceased patients tested positive for COVID-19 in the month preceding their death (Supplementary Table S3).

IV- DISCUSSION

Our study aimed to characterize the chronology of new and/or worsening ailments that occurred post-vaccination and that could be considered as potential AE. We explore these characteristics in a group of men and women without significant differences in age, who had received at least one dose of an approved COVID-19 vaccine.

The health authorities have assumed that COVID-19 vaccination-associated AEs would occur as shortly as with traditional vaccines. Our results suggest that, whereas some AEs do occur within 6 weeks, most AEs

do not, proving this assumption is wrong and would need to be revisited. The current use of the narrow 6-week time window, which was implemented for traditional vaccines, leaves a majority (76.1%) of potential AEs beyond the scope of any investigations, thereby justifying the need to extend that time window, so that (i) it encompasses most, if not all, health-related events possibly related to COVID-19 vaccination, (ii) it is specifically designed for this new generation of vaccines, and (iii) it allows thorough investigation of the relationship between health-related events and COVID-19 vaccination.

It is important to consider that, compared to traditional vaccines approved for regular use after years of development and clinical testing, and for which health-related events have been documented, the COVID-19 vaccines developed in a matter of months and whose phase 3 clinical study is still underway may be associated with serious, unexpected health-related events that could not have been documented as thoroughly and that may affect risk-benefit evaluation after their authorization of use. Some undesirable effects proven to be particularly serious may lead to the discontinuation of the marketing of the offending drug once the link between the drug and the health-related events has been established, with a delay that will always seem, in retrospect, to have been much too long.

4.1- Observational time window

Our data showed that the median time for a first new/worsening ailments to appear was 11.57 weeks after the last COVID-19 injection. This is two times later than the 6-week period that is currently used by the Quebec's Public Health Agency, the "Institut national de santé publique du Québec (INSPQ)", which neither considers nor investigates AEs reported beyond that period. Notably, less than a quarter (23.9%) of the new/worsening ailments that we documented occurred within 6 weeks and could be used to establish a possible relationship, if any, to the COVID-19 vaccines. With the current 6-week reporting period, post-vaccination AEs might be underestimated at least by a factor of 4, provided that they are systematically declared to the authorities and investigated, which is very unlikely for several reasons discussed elsewhere (Provost, 2023).

The 6-week reporting period may be far from adequate considering that mRNA vaccination stimulates robust lymph node germinal centers containing vaccine mRNA and spike antigen for at least 8 weeks after vaccination. Also it is worth noting that that the duration of spike protein being expressed in recipients of the vaccine was not tested beyond 8 weeks (Röltgen et al. 2022).

In addition, the overall AE underreporting may be much more impactful than we have suggested because of the fact that the assessment of VAERS database by Lazarus et al. found that fewer than 1% of vaccine AEs are reported to the Food and Drug Administration (2010).

In our study, the median time elapsed to the occurrence of a first new/worsening ailment that was happening after 6 weeks post-vaccination was 15 weeks, with a range between 6 and 47 weeks. Also, the time elapsed to the occurrence of a second new/worsening ailment was 18 weeks, with a range between 8 and 60 weeks. These delays would then justify extending the reporting time window to record new/worsening ailments as potential AEs to at least 15 to 18 weeks, up to a maximum of 60 weeks, to provide a picture closer to the reality of the COVID-19 vaccines.

Our study also assessed the potential differences between the participants developing a new/worse ailment before and after 6 weeks post-vaccination, since this information could influence the time window during

which people with certain characteristics are followed to record potential AEs. We did not find any difference in the age nor sex of participants developing new/worsening ailments before or after 6 weeks post-vaccination. However, we did find a significantly higher number of new/worsening ailments occurring before 6 weeks, in participants receiving their 4th dose, and in participants with a higher number of comorbidities. If this observation is reproduced in larger cohorts of vaccinated participants, it could be used to optimize the follow-up period of people with fewer comorbidities.

Most participants, either men or women, receiving any number of doses of any vaccine type, experienced only one new/worsening ailments. Interestingly, we found a small, albeit significant correlation between the number of new/worsening ailments and the number of comorbidities, which was confirmed when applying a generalized linear model correcting for age, sex, and vaccine type ($p = 0.01$). This suggests that patients with an increased number of comorbidities, who are deemed at higher risk of complications to COVID-19, are also more susceptible to experience post-vaccination AEs.

4.2- Causal relationship of post-vaccination AEs

Assessment of the whether or not there is a causal relationship (or absence of any such relationship) between COVID-19 vaccines and the occurrence of new/worsening ailments requires thorough investigation, the success or failure of which directly depends on the amount and quality of the data collected and analyzed. This is why as much information as possible needs to be collected for the longest period of time, reported to the authorities, processed, filtered, sorted, and thoroughly analyzed until the safety profile of this new generation of vaccines is fully determined. The importance of doing such work is emphasized by the case of an 18-year-old adolescent diagnosed with a multisystem inflammatory syndrome more than 10 weeks after vaccination (Buchhorn et al., 2021). The importance of researching such cases makes sense for drugs in general, but especially for vaccines that are supposed to modulate the body's immune systems. Indeed, unlike many drugs with classical dose/exposure/toxicity relationships, therapeutics that are supposed to impact the immune systems can trigger pathological processes that evolve independently of the initiating exposure and can be result later on, for instance, following a "second hit" by an antigen similar to the one in the vaccine (Kostoff et al., 2020; Lyons-Weiler, 2020; Nunez-Castilla et al., 2022; Vojdani & Kharrazian, 2020; Vojdani et al., 2021).

If proven to be similar to traditional vaccines, then the observational period would be deemed appropriate. If not, then we would need to consider that the underlying mechanism(s) at play may be different from traditional vaccines and that the observational period should be adjusted/extended accordingly. This is instrumental, as the occurrence, nature, severity and persistence of the symptoms directly influence the evaluation of the risk-benefit ratio of the injections — not to mention the long-term side effects, the unknown in this equation, that will need to be monitored and taken into account. This influence may be such that, for a population in which the vaccination has only limited benefits, e.g., in healthy children (Hughes, 2021; Banoun, 2022), the recognized risks may tilt the balance away from vaccination, which may also involve ethical considerations (Kraaijeveld et al., 2022). If the risks are such that the risk-benefit ratio becomes unfavorable to the vaccination of young or healthy individuals, then more specifically targeted vaccination campaigns would make more sense. If the risks are found to weigh even more, then the application of mRNA technology as a vaccine platform may need to be reconsidered.

4.3- Vaccine lot-to-lot variations

We did not attempt an analysis regarding the association between specific vaccine lots and the number and/or type of new/worsening ailment because of the small number of patients per vaccine lot in our sample, which precludes a valid statistical analysis.

Nevertheless, COVID-19 vaccine lot-to-lot variations have been reported previously (www.howbadismybatch.com), suggesting that some lots may be more problematic than others. Some batches are associated with several health-related events, whereas others are not. Some of the discrepancies between vaccine lots may be due to their accelerated production by different suppliers as well as their storage time and conditions, leading to variable quality and control issues.

Part of the problems may lie in lot-to-lot variations in the mRNA intactness (Gutschi, 2022). Regulatory agencies (FDA, Health Canada and EMA) had major concerns over unexpectedly low quantities of intact mRNA in batches of the vaccine developed for commercial production, but no threshold – in terms of percentage mRNA integrity they consider acceptable for vaccines against COVID-19 – has been specified by Pfizer, Moderna, and CureVac, as well as several regulators (Tinari, 2021). Obviously, the complete, intact mRNA molecule is essential to its potency as a vaccine, as even a minor degradation reaction, anywhere along a mRNA strand, can severely slow or stop proper translation performance of that strand and thus result in the incomplete expression of the encoded antigen (Crommelin et al., 2021). Therefore, one may speculate that the lack of efficacy or increased AEs associated with certain vaccine lots may be related, respectively, to mRNA degradation or the presence of mRNA fragments, some of which may encode for truncated forms of the antigen with different bioactivity and properties. In this regard, the detection of mutant spike S1 peptides in patients who experience post-acute sequelae of COVID-19 (PASC)-like symptoms more than 4 weeks post-vaccination (Patterson et al., 2022) also raises concerns regarding the authenticity of the vaccine mRNA sequence and the fidelity of its translation into spike proteins.

4.4- Post-vaccination AEs

In Canada, as of October 28, 2022 (with data up to and including October 14, 2022) (https://health-infobase.canada.ca/covid-19/vaccine-safety/), there has been a total of 51,714 reports of AEs (57.1 reports per 100,000 doses administered), of which 10,501 (20.3%) were considered serious (life-threatening; 11.6 reports per 100,000 doses administered). A total of 382 reports with an outcome of death were reported following vaccination. The prevalence of AEs following immunization for females was 77.1 reports per 100,000 doses administered, compared to 31.1 per 100,000 doses administered for males. The combined rate of AEs totaled 108.2 reports per 100,000 doses administered, i.e., ~1 report per 1,000 doses and ~1 serious report per 5,000 doses, which is substantial. This rate of post-vaccination AEs may be largely underestimated since – as suggested by the results of the present study – most AEs may occur beyond the limited 6-week time window during which the occurrence of a new/worsening ailment is currently being considered by the authorities. To the timeframe factor, we may also add the lack of patients' awareness, the self-treatable nature of new/worsening ailments, and the lack of reporting by physicians, as discussed elsewhere (Provost, 2023). The authentic rate of AEs, either non-serious or serious, may thus reach a level that can hardly be ignored, especially since long-term AEs remain unknown.

4.5- Post-vaccination cardiovascular AEs

The most frequent medical ailment that appeared or worsened among the participants of our study was cardiovascular diseases. In Canada, cardiac complications, such as myocarditis/pericarditis, account for 1.53 reports of AEs of special interest (AESI) per 100,000 injections, and complications of the circulatory system total 1.65 per 100,000 injections (Table 1; https://health-infobase.canada.ca/covid-19/vaccine-safety/). Together, the cardiac/circulatory (cardiovascular) complications account for half (3.18 or 50.8%) of the 6.26 reports per 100,000 injections for all AESI categories. This proportion is very similar to that observed in our study (61 reports of a total of 136; 44.8%), despite the relatively small number of patients. The similarity between these two proportions is in favor of attributing the causality of the observed AEs to the vaccine, regardless of the time elapsed since vaccination. This relatively high proportion of cardiovascular complications may be related to the drainage of the vaccine components from the injected site into the bloodstream and their contact with the vasculature. Further investigations, such as blood analyses (e.g., troponin levels), histological and immunohistochemical analyses of tissue biopsies, and autopsies, should be conducted to confirm or infirm any causal link with COVID-19 vaccination (Maiese et al., 2022). Analysis of the US Vaccine Adverse Events Reporting System (VAERS) and of the European Database of Suspected Adverse Drug Reaction (EudraVigilance) found, for an equivalent number of individuals vaccinated, a risk of cardiovascular AEs that is 154 higher for COVID-19 vaccines compared to influenza vaccines (Montano, 2022).

In France in 2021, the difference in myocarditis rate with 2019 and 2020 coincided with the vaccination campaign in young individuals (Boudemaghe et al., 2022). In a retrospective Israeli study based on a cohort of 196,992 adults, no increased incidence of pericarditis or myocarditis was observed after COVID-19 infection (Tuvali et al., 2022). In a cohort of 23 million people, in men over 12 years of age, the incidence of myocarditis/pericarditis in the unvaccinated was 0.261/100,000 people and shown to vary according to the vaccination schedule: between 0.322/100,000 people (1 dose of Moderna) and 2.402/100,000 people (1 dose of Pfizer followed by one dose of Moderna) (Karlstad et al., 2022). A similar or higher prevalence of post-vaccination myocarditis/pericarditis was reported elsewhere: in 2021, the CDC reported a rate of 3.23/100,000 injections for 18-39 years in the Vaccine Safe Datalink (Klein, 2021) and a study from Israel reported a rate of 3.83/100,000 men of all ages after their 2nd dose (Mevorach et al., 2021), whereas recent public health data from Ontario, Canada, reported a rate of 13 per 100,000 injections, all ages combined (Buchan et al., 2022). The real incidence of post-vaccination myocardial lesions, however, may be as high as 2.8% (as estimated by increased troponin levels), which is 800 times more than the 0.0035% of myocarditis reported in retrospective studies.

4.6- Window of vaccinal protection

We noticed that a patient (#41; Supplementary Table S1) tested positive for COVID-19 and was hospitalized ten days after his 4th dose of Pfizer-BioNTech vaccine. This case is compatible with the hypothesis of a reduced protection from the disease in the first 14 days following injection and highlights the need to constitute a distinct group of patients (0 to 14-day post-vaccination) for use in comparative analyses to other groups of non-vaccinated and vaccinated patients. Antibody-dependent enhancement (ADE) may be involved in facilitating or worsening a COVID-19 infection occurring within days of vaccination (Shimizu et al., 2022; Sridhar et al., 2022).

4.7- Limitations

The longer delay before the occurrence of the AEs (11.57 weeks instead of 6) makes it more difficult to establish a causal link with the COVID-19 injections. This may be circumvented by increasing the number of vaccinated patients and by including a control group of non-vaccinated patients in a larger retrospective study that would also cover a similar pre-COVID-19 and/or pre-COVID-19 vaccination period to correct for changes that may have occurred in the absence of vaccination.

Only patients with symptomatic AEs or major health-related events that led to changes in their prescriptions were included in our study. Patients who experienced changes in their health or medical condition following vaccination against COVID-19 that went unnoticed, were minor, could be self-treated or did not require changes to their medications or pharmacy record could not be identified and were not included in this study, thereby contributing to AE underreporting.

During the Spring of 2022, PCR testing became restricted to health care workers and patients had to be registered to the "Régie de l'assurance-maladie du Québec" (https://www.ramq.gouv.qc.ca/en) to obtain an antigenic COVID-19 detection kit. Therefore, we cannot exclude the possibility that some of our patients may have had COVID-19 without testing positive for it or without knowing it (asymptomatic).

V- CONCLUSION

The main finding of our study is that most of the health-related events, as recorded as changes in patients' pharmaceutical records, occurred beyond the 6-week observational period, which is currently used by the Quebec's Public Health Agency, the "Institut national de santé publique du Québec (INSPQ)", thereby calling for an extension of that period and a review of the guidelines set for post-vaccination AE reporting and analyses.

Association between COVID-19 vaccination and the ensuing occurrence of AEs does not necessarily equal causation. However, the new/worsening ailments that we observed in vaccinated patients of a Quebec pharmacy, the period of time after which they occurred and their faster occurrence in association with the number of doses received and the number of comorbidities, raise public health issues that are serious and important enough to warrant wider, larger and more thorough collaborative investigations by independent groups of pharmacists and researchers. Independent research funding opportunities should be launched to promote well-controlled, retrospective studies aimed to characterize the nature, occurrence and severity of the AEs associated with this new vaccine generation, and hopefully determine any possible causal link, if any, before their use is expanded even further to fight COVID-19 variants and other infectious diseases.

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VII- AUTHOR CONTRIBUTIONS

Conceptualization, P.P.; methodology, P.P.; formal analysis, P.P.; supervision, P.P.; writing — original draft preparation, P.P.; writing — review and editing, H.B., P.P.; approved submission, all authors. Both authors have read and agreed to the published version of the manuscript.

VIII- CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

IX- FUNDING

This research was not funded.

X- DATA AVAILABILITY STATEMENT

All data presented in this study are included in this published article and are available in the accompanying Supplementary Information files.

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XII- SUPPLEMENTARY INFORMATION

In the three supplementary tables that follow, all of the data used in the present study are provided. Table S1 summarizes the medical symptoms presented by the 112 patients of the study. Table S2 concerns data about manufacturers, lot numbers, and observed changes. Table S3 gives data concerning the 19 patients who died during the course of the study.

12.1- Supplementary Table S1. Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

12.2- Supplementary Table S2. Number of times a vaccine lot was injected before a change in medical condition was observed.

12.3-Supplementary Table S3. Characteristics of the 19 deceased patients of whom there were 10 males and 9 females.

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
1	M	47	19-05-2021 mod 3002331	28-6-2021 mod 043D21A			2mod	Alcoholism, depression, insomnia, pain, dyspepsia, smoking	24-10-2021: Deceased (myocardial infarction).	4	2	CVD	Negative
2	M	82	18-03-2021 mod 3001176	25-06-2021 mod 043D21A			2mod	COPD, asthma, glaucoma, insomnia, hypertension, hypercholesterolemia	29-11-2021: Deceased (cerebral aneurism).	5	2	CVD	Negative
3	F	81	Administered	22-07-2021 pb (lot no. NA)			2pb	COPD, depression, dyspepsia, insomnia, type 2 diabetes, osteoporosis, angina, constipation, pulmonary embolism	24-09-2021: Deceased (unknown cause).	2	2	NA	Negative
4	F	80	26-03-2021 pb ER1742	17-06-2021 pb FA9093			2pb	Angina, hypothyroidism, hypertension, restless legs syndrome	27-08-2021: +Nitroglycerin pump. 07-09-2021: Deceased (under plavix and aspirin).	2.7	2	CVD	Unknown
5	M	70	10-04-2021 pb EW3344	29-06-2021 pb FA9091			2pb	Pain, depression, hypercholesterolemia, hypertension, dyspepsia	01-09-2021: Deceased. No autopsy. Found dead at home.	2	2	CVD	Negative
6	M	78	26-03-2021 pb ER1742	17-06-2021 pb FA9093	18-12-2021 pb FF5109		3pb	Restless legs syndrome, asthma, idiopatic pulmonary fibrosis	20-11-2021: Brain cancer, underarm cancer mass. 22-06-2022: Influenza.	5	2	Cancer	Unknown
7	F	59	15-05-2021 pb EW1099	11-07-2021 pb FA9099	09-01-2022 mod 063H21A		2pb+mod	Hypothyroidism, depression, restless legs syndrome, dyspepsia, insomnia, pacemaker	19-10-2021: Tachycardia (140 per min) and fatigue. +Bisoprolol.	3.25	2	CVD	Negative
8	M	84	09-04-2021 pb EW3344	22-06-2021 pb FA9093	22-12-2021 pb FF5109		3pb	Hypertension, dyspepsia, insomnia, macular degeneration	01-11-2021: +Eliquis. 06-11-2021-: Atrial fibrillation, pulmonary oedema. 11-11-2021: +Amiodarone (ocular toxicity), bisoprolol, eliquis, lasix, aldactone.	4.5	2	CVD	Negative

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
9	F	41	12-06-2021 pb EY0578	19-07-2021 pb FA9099			2pb	Depression/anxiety, dyspepsia, insomnia, smoking	14-07-2021: Cerebral aneurism (suspected), intense headache. Hypertension (uncontrolled). +Aspirin, elavil, mavik, flexeril.	1	1	CVD	Negative
10	M	39	14-08-2021 pb FD7208	18-09-2021 pb FD0810			2pb	No previous medical history	03-12-2021: Stroke (suspected). +Aspirin, lipitor. Intense headache and fatigue. 31-01-2022: +Nitroglycerin spray. 14-06-2022: Informed by cardiologist and neurologist to stop all medication.	2.5	2	CVD	Positive in February 2022 (PCR)
11	M	71	22-04-2021 pb EW3344	01-07-2021 mod 045D21A	09-01-2022 mod 063H21A		pb+2mod	Hypertension, benign prostatic hypertrophy, pain	03-12-2021: De novo atrial fibrillation. +Lixiana.	5	2	CVD	Positive in May 2022 (antigenic)
12	F	76	09-04-2021 pb EW3344	21-06-2021 pb FA9093	22-12-2021 pb FF5109		3pb	Glaucoma, hypertension, Cal-vitD	02-12-2021: De novo atrial fibrillation. +Xarelto, bisoprolol.	5.3	2	CVD	Negative
13	M	78	28-04-2021 pb EY4825	22-07-2021 pb FD7206	04-01-2022 pb FM2952		3pb	Type 2 diabetes, benign prostatic hypertrophy, hypercholesterolemia, gout, atrial fibrillation, heart failure, pain	19-11-2021: Bladder tumor (benign).	4	2	Cancer	Positive in August 2022 (antigenic)
14	F	51	19-05-2021 mod 3002331	08-07-2021 mod 043D21A			2mod	Smoking (in the past)	30-09-2021: Appendicitis (operated). August 2022: Breast cancer (suspected; under investigation).	2.7	2	Other	Positive in July 2022 (antigenic)
										14	2	Cancer	

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
15	F	46	22-05-2021 pb EW0216	01-07-2021 mod 045D21A			pb+mod	No previous medical history	22-12-2021: Breast cancer. +Pertu-trestu, paclitaxel, dexamethasone, emend-tri-pack, grastofil, stemetil, ativan, trazodone.	5.7	2	Cancer	Negative
16	M	66	29-04-2021 mod 3001658	21-06-2021 mod 043D21A	30-12-2021 mod 062H21A		3mod	No previous medical history	10-05-2021: Cancer diagnosis. 30-06-2021: Chemotherapy for advanced cancer (initiated). 04-09-2021: Pulmonary embolism. 12-02-2022: Deceased. +Lixiana, midodrine, sinequan, melatonine, grastofil, dexamethasone, fragmin, emend-tri-pack, stemetil, largactil, rince-bouche magique, zyprexa.	2.5	2	RD	Negative
										2.5	3	Cancer	
17	M	65	20-04-2021 mod 3001658	15-06-2021 mod 3002182	15-11-2021 mod 093D21A		3mod	Cardiac problems, dyslypidemia, pain	07-10-2021: Cancer (multiple myeloma). +Cybord	3.7	2	Cancer	Negative
18	M	73	09-04-2021 pb EW3344	21-07-2021 pb FD7206	09-01-2022 mod 063H21A		2pb+mod	COPD, hypertension, benign prostatic hypertrophy, vitD, smoking	26-10-2021: Pulmonary embolism. 21-05-2022: Emergency for respiratory distress, swollen legs, problem urinating. Diagnosis (unknown). 30-05-2022: Emergency with similar symptoms. +Eliquis. Diagnosis (unknown).	3	2	RD	Negative

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
										4.5	3	RD	
19	F	82	18-03-2021 mod 3001176	19-08-2021 mod 092D21A			2mod	Anxiety, hypercholesterolemia, hypertension	05-07-2021: Pulmonary embolism, diverticulite. +Xarelto, two antibiotics.	3.5	1	RD, Other	Unknown
20	F	79	09-04-2021 pb EW3344	23-06-2021 pb EW0221	28-12-2021 pb FF5109		3pb	Joint pain (tylenol for arthritis)	12-08-2021: De novo atrial fibrillation. +Bisoprolol, eliquis.	1.7	2	CVD	Positive in April 2022 (antigenic)
21	M	58	03-05-2021 mod 3002179	03-07-2021 mod 093D21A	13-01-2022 mod 079J21B		3mod	Heart failure, aspirin, hypercholesterolemia, dyspepsia	25-06-2021: Pulmonary embolism under aspirin. +Xarelto.	1.7	1	RD	Negative
22	M	61	20-04-2021 mod 3001658	15-06-2021 mod 3002182	13-01-2022 mod 063H21A		3mod	Smoking (past), hypothyroidism, dyspepsis, hypercholesterolemia, pain	29-09-2021: Zona (+prednisone, valtex). 13-10-2021: Double pneumonia (+cefzil, +doxy). Early August 2022: Zona. Days later: lower legs (red, pain and heat). Morning after, emergency: Both legs full of bruises. Diagnosis (unknown).	3.5	2	Zona	Unknown. Very sick in January 2020.
										4	2	RD	
										7	3	Zona	

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
23	F	51	12-05-2021 mod 3002331	08-07-2021 mod 043D21A	09-10-2021 mod 092D21A	24-01-2022 mod 020E21A	4mod	Anxiety, dyspepsia, arthritis, pain, restless legs syndrome, allergies	09-08-2021: Bilateral zona. +Valtrex, paxlovid (20-04-2022, 14-05-2022, 08-07-2022).	1	2	Zona	Positive in April (antigenic), on May 13 (PCR) and on July 8 (antigenic) 2022
24	M	61	12-04-2021 AZ MT0056	04-07-2021 mod 093D21A	18-12-2021 mod 062H21A		AZ+2mod	Smoking, kidney failure, dyspepsia, hypercholesterolemia, hypertension, pain	10-09-2021: Strokes (2) under aspirin (80 mg). 07-05-2022: Blood glucose at 52 (not known to be diabetic). Blindsighted. +Plavix, insuline.	2.25	2	CVD	Unknown
25	M	65	22-04-2021 mod 3001658	01-06-2021 mod 3002182	xx-xx-2022 mod 079J21B		3mod	Hypertension, hypercholesterolemia, aspirin, insomnia, COPD, hypothyroidism	17-06-2021: Stroke. +Plavix, lipitor to 80mg.	0.5	2	CVD	Negative
26	M	64	21-04-2021 mod 3001658	15-06-2021 mod 3002182	09-01-2022 mod 063H21A		3mod	Type 2 diabetes, hypertension, aspirin, vitB12, arthritis	04-10-2021: +Stent left carotid artery. Days later, transient cerebral ischemia. +Plavix, ramipril to 5 mg.	3.7	2	CVD	Positive in March 2022 (antigenic)
27	F	79	29-04-2021 mod 3001658	21-06-2021 mod 043D21A	23-01-2022 pb FM2952		2mod+pb	Hypothyroidism, hypertension, dyspepsia, non-steroidal anti-inflammatory drug (PRN)	11-08-2021: Stroke (suspected). +Aspirin. Brain aneurism discovered. 26-03-2022: Emergency: Palpitation, left-side paralysis. Diagnosis: anxiety. +Aspirin, crestor, trazodone.	1.7	2	CVD	Negative

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
										2	3	CVD	
28	F	79	22-04-2021 mod 3001658	01-06-2021 mod 3002182			2mod	Arthritis, glaucoma, hypertension, dyspepsia, angina	20-10-2021: Lymphoma. +Chemotherapy (ABVD). 21-10-2021: Nitroglycerin spray, stemetil, dexa, allopurinol, cefzil, vanco. 04-11-2021: +Invanz (iv) for several weeks. 30-01-2022: Deceased.	4.7	2	Cancer	Positive in January 2022
29	M	58	01-06-2021 mod 3002182	08-07-2021 mod 043D21A			2mod	Hypertension, Avamys	24-11-2021: Myocardial infarction. +Stents, aspirin, brilinta, lipitor, pantoloc, nitroglycerin spray.	4.5	2	CVD	Unknown. Unwell in June 2022, but not tested
30	M	65	20-04-2021 mod 3001658	15-06-2021 mod 3002182	20-01-2022 mod 079J21B		3mod	Arthritis (plaquenil+methotrexate), hypertension	15-12-2021: Lung cancer. Chemotherapy (Docetaxel). +Lapelga, dexa, effexor, zyprexa, stemetilstatex, ativan. 30-08-2022: Deceased.	6	2	Cancer, RD	Negative
31	F	38	05-05-2021 pb EW0193	22-07-2021 pb FD7206	04-01-2022 pb FM2952		3pb	Lupus, migraine, pericarditis, psoriasis, dyspepsia, pain, smoking	03-07-2021: Stroke or transient cerebral ischemia (suspected). Collapse of the left side (arm, mouth). Vision and memory loss. + Aspirin. Under investigation.	2	1	CVD	Positive in May 2022 (antigenic)
32	M	68	12-05-2021 mod 3002331	28-06-2021 mod 043D21A			2mod	COPD, hypertension, gout, hypercholesterolemia, dyspepsia, smoking	13-09-2021: Pulmonary oedema, a lot of difficulty breathing. +Lasix. Under	2.5	2	RD	Negative

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
									investigation since July 2021.				
33	F	35	27-04-2021 pb FD7206	12-06-2021 pb EY0578			2pb	Migraine, dyspepsia, eczema	28-07-2021: Pulmonary embolism. +Fragmin.	1.5	1	RD	Positive in February 2022 (antigenic)
34	M	45	29-05-2021 pb EW0216	07-08-2021 pb FD7028			2pb	Eczema, hypertension, hypercholesterolemia. Had stopped taking medication.	19-07-2021: +5 cardiac stents. January 2022: Ophtalmic zona. +Plavix, coversyl, pantoloc, aspirin.	1.7	1	CVD	Positive in April 2022 (antigenic)
										5	2	Zona	
35	F	74	18-03-2021 mod 3001176	01-07-2021 mod 045D21A	29-12-2021 mod 062H21A		3mod	Depression, pain, insomnia, dyspepsia	29-10-2021: Breast cancer. +Letrozole, then tamoxifen.	4	2	Cancer	Negative
36	M	71	26-03-2021 pb ER1742	30-06-2021 pb FA9091	13-11-2021 pb FF2595		3pb	Depression-anxiety, insomnia, dyspepsia, hypertension, angina	28-01-2022: Bladder cancer. Urinary infection. Antibiotics (cipro, fospho, macrobid). 17-08-2021: +Bisoprolo. 2-6-2021: Nitroglycerin spray. June 2022: +Dilaudid, redesca.	2.5	3	Cancer	Unknown
37	M	68	07-04-2021 pb EW3344	21-07-2021 pb FA9099	28-12-2021 pb FF5109		3pb	Pain, hypercholesterolemia, type 2 diabetes, dyspepsia	13-05-2021, 15-06-2021 and 30-06-2021: Hospitalized for cardiac problems. 14-04-2022: Transient cerebral ischemia under aspirin+plavix. +Pantoloc, seroquel, metoprolol, lasix, jardiance, lipitor, lyrica.	1.25	1	CVD	Negative

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
										3.5	3	CVD	
38	M	75	15-04-2021 pb EX0438	17-06-2021 pb FA9093			2pb	Hypertension, hypercholesterolemia, angina, COPD, asthma, dyspepsia	04-10-2021: Metastatic oesophagal cancer (chemotherapy: folfiri). 12-04-2022: Double pneumonia. 12-07-2022: Deceased.	3.5	2	Cancer	Unknown
										10	2	RD	
39	M	35	26-05-2021 pb EW0216	23-07-2021 pb FD7206			2pb	No previous medical history	27-01-2022: Left side paralysis. Chest pain. +Pantoloc.	6	2	CVD	Positive in April 2022 (antigenic)
40	F	64	20-04-2021 mod 3001658	15-06-2021 mod 3002182			2mod	Hypertension, pain, dyspepsia	22-06-2021: Lymph node inflammation. Cluster of lymph nodes in the neck, on the side of the injection. Cluster of lymph nodes still present and visible to the naked eye. Diagnosis (unknown). Under investigation.	0.25	2	Other	Positive in July 2022 (antigenic)

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
41	M	82	09-04-2021 pb EW3344	23-06-2021 pb EW0221	28-12-2021 pb FF5109	11-04-2022 pb FN7934	4pb	Dyspepsia, hypertension, hypercholesterolemia, COPD, asthma, insomnia, vitB12, osteoporosis, pulmonary embolism (coumadin)	20-05-2021-: Hospitalized for respiratory problems (7 times). Under coumadin. 24-02-2022: Ophtalmic zona (+valtrex, cipro) and respiratory infection (cipro). 21-04-2022-24-04-2022: Hospitalized for COVID-19. Changed coumadin for lixiana. +Doxycycline, prednisolone, clavulin, levaquin. 12-07-2022: Paxlovid. 07-09-2022: Hospitalized for pneumonia. Lung Cancer.	1.3	1	RD	Positive on April 21 (PCR) and on July 11 (PCR) 2022
										2	3	Zona	
										0.33	4	Other	
										5	4	Cancer	
42	M	72	Received (details NA)	Received (details NA)	Received (details NA)		Received (details NA)	Arthritis, dyspepsia, angina, vertigo, smoking	29-05-2021: Brain cancer with metastases. 17-06-2021: Deceased.	NA	NA	Cancer	Negative
43	F	62	22-04-2021 pb EX2294	12-08-2021 pb FD7208	06-01-2022 pb FM2952		3pb	No previous medical history	14-10-2021: Zona. +Valtrex, lyrica.	2	2	Zona	Negative
44	F	39	24-09-2021 mod 3001658	22-05-2021 pb EW0216			mod+pb	Type 2 diabetes, hypercholesterolemia, hypothyroidism, hyperpilosity, anxiety, dyspepsia, atrial fibrillation, heart failure, pacemaker	05-11-2021: Zona. +Valtrex.	5.5	2	Zona	Positive in Spring 2022 (antigenic)

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
45	M	60	12-05-2021 pb EW0199	07-07-2021 pb FA9091	07-01-2022 pb FM2952		3pb	No previous medical history	01-10-2021: Zona. +Valtrex.	3	2	Zona	Negative
46	F	45	22-01-2021 pb EL1406	10-05-2021 pb EW0193	20-12-2021 pb FF5109		3pb	Pain, dyspepsia, transient cerebral ischemia	15-05-2021: Tachycardia. +Bisoprolol.	0.16	2	CVD	Negative
47	M	88	28-03-2021 pb ER1742	23-06-2021 pb EW0221	04-01-2022 pb FM2952		3pb	Type 2 diabetes, kidney failure, hypertension, pancreatic insufficiency, atral fibrillation (coumadin)	15-12-2021: Hospitalized for pulmonary oedema. 01-06-2022: Lasix from 40 mg bid to 120 mg (am) and 80 mg (pm).	5.7	2	RD	Negative
48	M	78	09-04-2021 pb EW3344	27-06-2021 pb FA9091	10-01-2022 pb FM2952		3pb	COPD, asthma, dyspepsia, hypercholesterolemia, smoking (past)	05-10-2021: Lung cancer (+dilaudid, lyrica) and cardiac problems (changed metoprolol for bisoprolol, lipitor from 20 mg to 80 mg, aspirin). 07-04-2022: Hospitalized for a double pneumonia. +Prednizolone, azithroclavulin, doxycyclin.	3.3	2	Cancer, RD, CVD	Negative
49	M	59	29-05-2021 pb EW0216	24-07-2021 pb FD7206	04-10-2021 pb FD0810		3pb	Smoking	12-07-2021: Cancer. Chemotherapy (capecitabine). Permanent stoma. +Morphine, stemetil, largactil, dexamethasone, ativan, famotidine, lapelga, immodium, flomax, fragmin, acet, pantoloc, acet, seroquel, atasol, trazodone.	1.5	1	Cancer	Negative

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
50	F	82	09-04-2021 pb EW3344	21-06-2021 pb FA9093			2pb	Pain, hypertension, insomnia, anxiety, osteoporosis	End october 2021: Emergency for respiratory problems and tachycardia. +Invanz (iv). 13-11-2021: Deceased.	4.25	2	CVD	Negative
51	M	66	20-04-2021 AZ MT0056	10-07-2021 mod 045D21A	27-12-2021 mod 062H21A		AZ+2mod	Unknown	10-12-2021: +Nitroglycerin spray. 2022-05-18: Out of cardiology unit after four coronary artery bypasses.	5	2	CVD	Unknown
52	F	53	13-05-2021 pb EW0199	10-08-2021 pb FD7208	24-01-2022 pb FM2952		3pb	Menopause, herpes labialis	08-01-2022: Vaginal hemorrhage.	5	2	Other	Positive in April 2022 (antigenic)
53	F	91	11-03-2021 pb ER1742	17-05-2021 pb EW0199	09-11-2021 pb FF2595		3pb	Unknown	07-01-2022: Angina. +Nitroglycerin patches.	2	3	CVD	Unknown
54	F	75	24-04-2021 pb EX2294	07-07-2021 pb FA9091	15-01-2022 mod 020E21A		2pb+mod	Breast cancer, dyspepsia, tachycardia, insomnia, eczema, cosentyx	February 2022: Lung cancer. 01-06-2022: Atrial fibrillation. +Amiodarone, eliquis, aspirin.	1	3	Cancer, RD	Negative
55	M	54	01-06-2021 mod 3002182	08-07-2021 mod 043D21A	16-01-2022 mod 020E21A		3mod	Psychiatric condition, hypertension, smoking	18-02-2022: Myocardial infarction. +Aspirin, plavix, coumadin (3mo), lasix, entresto, aldactone, metoprolol, crestor, ezetrol.	1	3	CVD	Negative
56	M	85	09-04-2021 pb EW3344	21-06-2021 pb FA9093	19-12-2021 pb FF5109		3pb	Hypothyroidism, hypertension, dyspepsia, pain, urinary incontinence, type 2 diabetes	23-02-2022: Hospitalized for 10 days. Diagnosis (unknown). Hemato-oncology (under investigation). +Dexamethasone, venofer,	2	3	Cancer?	Negative

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
									statex, fer, metamucil, laxaday.				
57	F	76	18-03-2021 mod 3001176	08-07-2021 mod 045D21A	27-12-2021 mod 062H21A		3mod	Unknown	13-08-2021: De novo atrial fibrillation. +Eliquis.	1.16	2	CVD	Unknown
58	F	83	09-05-2021 pb EW0193	26-07-2021 pb FD7206	23-02-2022 pb FN7934		3pb	Unknown	11-02-2022: Occluded femoral artery. Aspirin added to xarelto. 18-03-2022: Lasix increased, +potassium. 13-04-2022: Hospitalized again. 14-04-2022: Deceased.	6.5	2	CVD	Unknown
59	F	75	31-03-2021 pb EW3344	14-06-2021 pb EY0578	28-12-2021 pb FF5109		3pb	Dyspepsia, hypercholesterolemia, hypertension, vitD (10,000 I.U./week), smoking (past; for 30 years)	08-12-2021: Lung cancer and lung resection. +Lyrica.	5.75	2	Cancer, RD	Negative
60	M	64	28-04-2021 pb ET0384				pb	Heart problem (past)	06-11-2021: Four coronary artery bypasses. +Aspirin, plavix, monocor, crestor, nitroglycerin spray. 05-06-2022: Angina. Pain in the back and legs.	6.25	1	CVD	Negative
61	F	59	22-05-2021 mod 3002538	20-07-2021 mod 092D21A	19-01-2022 mod 079J21B		3mod	Diabetes, hypercholesterolemia, hypothyroidism, Ursodiol	23-02-2022: Heart failure. +Carvediol, aspirin, lasix, aldactone, jardiance, diovan, vitB12.	1	3	CVD	Negative

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
62	F	86	11-03-2021 pb ER1742	17-05-2021 pb EW0199			2pb	Tye 2 diabetes, hypertension, hypercholesterolemia, dyspepsia, pain, anxiety, insomnia	03-03-2022: Heart failure. +Entresto, aldactone, aspirin, plavix.	9.5	2	CVD	Unknown
63	F	67	08-04-2021 pb EW3344	27-06-2021 pb FA9091	13-09-2021 pb FD7208	26-01-2022 pb FF5109	4pb	Rhumatoid arthritis, pain, hypothyroidism, hypertension, dyspepsia, angina	10-03-2022: Respiratory problems. +two antibiotics. Diagnosis (unknown). 08-04-2022: Atypical pneumonia.	1.5	4	RD	Positive in July 2022 (antigenic)
64	M	85	24-04-2021 pb EX2294	01-07-2021 mod 045D21A	03-01-2022 mod 062H21A	04-04-2022 mod 079J21B	pb+3mod	Hypertension, pain, insomnia, benign prostatic hypertrophy, hypercholesterolemia, atrial fibrillation, dyspepsia, asthma	06-08-2021: +Nitroglycerin patch. Plavix added to eliquis.	1	2	NA	Unknown
65	F	67	02-04-2021 mod 3001658	15-06-2021 mod 3002182	27-12-2021 mod 062H21A		3mod	Breast cancer, dyspepsia, restless legs syndrome, asthma, pain, constipation, hypercholesterolemia	07-03-2022: De novo atrial fibrillation. Diltiazem to 240 mg, +flecainide, eliquis.	2.3	3	CVD	Positive in May 2022 (antigenic)
66	M	58	15-05-2021 pb EW1099	20-07-2021 pb FA9099	18-01-2022 pb FM2952		3pb	Hypercholesterolemia, triglycerides, hypertension, type 2 diabetes, dyspepsia	08-10-2021: Heart failure. +Entresto, bisoprolol, jardiance, lipitor chanegd for crestor 40 mg.	2.5	2	CVD	Unknown
67	F	71	18-03-2021 mod 3001176	25-06-2021 mod 043D21A	03-01-2022 mod 062H21A		3mod	Unknown	04-04-2022: Hospitalized for cardiac problems.	3	3	CVD	Unknown
68	M	64	06-05-2021 pb EW0193	22-07-2021 pb FD7206	11-01-2022 pb FM2952		3pb	Cardiac problems (atrial fibrillation, angina), pain	12-04-2022: Several lymph nodes in the groin.	3	3	Other	Positive in February 2022 (antigenic)

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
69	M	67	10-04-2021 pb EP6017	14-06-2021 pb EY0578	29-01-2022 pb FF5109		3pb	Hypertension, myocardial infarction, dyspepsia, hypercholesterolemia, anxiety/depression	13-01-2022: Deep venous thrombosis and pain in both legs (under aspirin).	7	2	CVD	Positive in March 2022 (antigenic)
70	M	68	07-04-2021 pb EW3344	27-06-2021 pb FA9091	10-01-2022 mod 063H21A 1.5		2pb+mod	Hypertension	09-06-2021: +Bisoprolol, aspirin, crestor 40 mg. 23-02-2022: Nitroglycerin patches. 12-04-2022: Angina. 06-05-2022: Open heart surgery. +Lasix, aldactone, flomax.	2	1	CVD	Negative
										3	3		
71	M	62	17-03-2021 CS 4120Z003	08-06-2021 AZ ABX3120	28-03-2022 pb FN7934		CS+AZ+pb	Atrial fibrillation, chronic pain, hypertension, hypercholesterolemia, dyspepsia, insomnia	01-07-2021: Cancer (subcutaneous, near the nose). Date of diagnosis uncertain.	0.7	2	Cancer	Positive on January 13, 2022 (PCR)
72	M	64	06-05-2021 pb EW0193	24-07-2021 pb FD7206	22-01-2022 mod 020E21A		2pb+mod	Pain, hypertension, hypercholesterolemia	11-04-2022: De novo atrial fibrillation (under aspirin). +Eliquis.	2.7	3	CVD	Negative
73	F	61	19-05-2021 pb FA8721	01-08-2021 pb FD7208	12-01-2022 mod 063H21A		2pb+mod	Atrial fibrillation, hypercholesterolemia, pain, dyspepsia	After 01-08-2021: Lost 40 pounds before 3rd dose. Three coronary arteries partially occluded. Physician suspects post-vaccination side effects. Eliquis.	NA	2	CVD	Unknown

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
74	M	77	16-04-2021 mod 3001657	03-07-2021 mod 093D21A	15-01-2022 mod 020E21A		3mod	Type 2 diabetes, gout, hypertension, hypercholesterolemia, dyspepsia, anemia, insomnia, pain, pulmonary embolism (coumadin), COPD, asthma	02-03-2022: Scrotum surgery to remove a possibly cancerous mass. 21-04-2022: Hospitalized, positive for COVID-19.	1.5	3	Cancer?	Positive on April 21, 2022 (PCR)
75	F	94	11-03-2021 pb ER1742	17-05-2021 pb EW0199	09-11-2021 pb FF2595	06-04-2022 mod 079J21B	3pb+mod	Unknown	22-04-2022: Cancer (lymphoma or breast cancer) and aspiration pneumonia. 19-05-2022: Deceased.	0.5	4	Cancer, RD	Unknown
76	M	94	16-04-2021 mod 3001657	03-07-2021 mod 093D21A	07-03-2022 pb FN7934		2mod+pb	Unknown	13-04-2022: Hospitalized for liver/pancreatic cancer and kidney failure. In the following days: Deceased. No autopsy.	1.2	3	Cancer	Unknown
77	M	64	20-04-2021 mod 3001658	15-06-2021 mod 3002182	19-12-2021 mod 062H21A		3mod	Pain, constipation, anxiety, hypertension, dyspepsia, eczema	22-04-2022: Mass in the thyroid gland (possibly cancerous).	4	3	Cancer	Negative
78	F	70	16-04-2021 mod 3001657	26-06-2021 mod 043D21A	30-12-2021 mod 062H21A	30-04-2022 mod 079J21B	4mod	Type 2 diabetes, hypertension, hypercholesterolemia, vitB12, dyspepsia, one lung only	End April 2022 (before 4th dose): Aspirin changed for Plavix. Leg pain. Deep venous thrombosis suspected.	3.5	3	CVD	Unknown
79	F	69	24-04-2021 pb EX2294	28-06-2021 pb FA9091	13-01-2022 mod 063H21A		2pb+mod	Smoking	End April 2022: Myocardial infarction (stent installed). +Brilinta, aspirin. 28-06-2022: Emergency for chest pain and numbed back and arms. Later, cardiac	3.5	3	CVD	Negative

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
									problem and coma (stroke suspected).				
80	M	56	29-04-2021 mod 3001658	28-06-2021 mod 043D21A			2mod	Cardiac problems, dyslypidemia	17-02-2022: Intense chest pain treated with nitroglycerin spray. +Imdur. 03-05-2022: Emergency for chest pain. Nitroglycerin spray 4-5 times a day. Under investigation.	7.7	2	CVD	Positive in April 2022 (test not specified)
81	M	55	11-05-2021 pb EW0193	09-08-2021 pb FD7204			2pb	Pain	March 2022: Operated for the knees. 30-04-2022: Deep venous thrombosis. +Xarelto.	8.5	2	CVD	Negative
82	F	42	03-04-2021 pb EW3344	17-05-2021 pb EW0199	13-01-2022 mod 063H21A		2pb+mod	Hypertension, hypothyroidism	22-05-2021: Strokes (3). +Aspirin, lipitor. Elle veut attendre de parler avec son md de famille. 04-05-2022: +Plavix.	0.16	2	CVD	Negative
83	M	70	03-04-2021 pb EW3344	30-06-2021 pb FA9091	27-12-2021 pb FF5109		3pb	Arthritis, hypertension, dyspepsia, osteoporosis (prevention), asthma (light), atrial fibrillation (Eliquis)	09-05-2022: Strokes (10; 7 minor + 3 major). Coma. 09-05-2022: Deceased. 21-05-2022: 18 strokes. Unknown disease involving deregulated platelet function. Under investigation.	4.3	3	CVD	Positive on April 10, 2022 (PCR)

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
84	M	81	31-03-2021 pb EW3344	23-06-2021 pb EW0221	03-01-2022 pb FF5109		3pb	Angina, hypercholesterolemia, Aspirin (80 mg)	11-05-2022: Tachycardia (under eliquis). +Toloxin. 21-05-2022: Respiratory problem. 28-05-2022: Heart failure. +lasix, entresto. 06-06-2022: Lung cancer. 13-06-2022: Deceased (from cancer).	4.25	3	CVD	Negative
85	M	74	07-04-2021 pb EW3344	16-06-2021 pb EY0578	19-12-2021 pb FF5109	09-04-2022 pb FN7934	4pb	Asthma, hypertension, hypercholesterolemia, dyspepsia, eczema, pain	10-05-2022: Operated for a lung cancer. +Dilaudid, redesca.	1	4	Cancer, RD	Positive on April 19, 2022 (PCR)
86	F	84	18-03-2021 mod 3001176	08-07-2021 mod 093D21A	01-02-2022 mod 020E21A		3mod	Atrial fibrillation, hypothyroidism, hypercholesterolemia, pain, dyspepsia, asthma	16-05-2022: Transient cerebral ischemia (4 in the last month). Under pradaxa (1x/day instead of 2x/day, because of bruises). Changed pradaxa for eliquis.	3.5	3	CVD	Positive on April 8, 2022 (PCR)
87	M	60	13-04-2021 AZ MT0056	08-07-2021 mod 093D21A	05-01-2022 mod 062H21A		AZ+2mod	Pain, Naproxen (PRN)	19-04-2022: Atrial fibrillation. +Lixiana, bisoprolol.	3.5	3	CVD	Positive on March 15, 2022 (antigenic), asymptomatic
88	M	56	26-05-2021 pb EW0216	09-08-2021 pb FD7208			2pb	Pain, osteoarthritis, dyspepsia	10-08-2021: Extreme fatigue, heavy legs, excessive perspiration, runny nose. Blood analysis clear. 17-06-2022: Under investigation.	0.03	2	Other	Negative

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
89	M	58	19-05-2021 mod 3002331	28-06-2021 mod 043D21A			2mod	Renal dialysis, depression-anxiety, gout, hypertension, dyspepsia, hypercholesterolemia, pain, asthma, smoking	29-04-2022: Deep venous thrombosis under aspirin. +coumadin.	10	2	CVD	Negative
90	M	45	21-05-2021 mod 3002187	20-08-2021 mod 052C21A			2mod	Insomnia, ophtalmic zona	25-04-2022: Cancer (non-resectable melanoma). Chemotherapy (ipilimumab-nivolumab). +Dilaudid, lyrica, acet, duricef, HC-Contin, cefazolin iv, ertapenem iv, clavulin, napro, pantolol, elavil, gabapentin, cymbalta, methadone, fentanyl, statex, cesamet. Pain (12/10).	8	2	Cancer	Positive on January 24, 2022 (PCR)
91	M	56	21-02-2021 pb EP6017	07-06-2021 pb EW0221			2pb	Pain, epilepsia, anxiety	09-06-2021: Breathing difficulties. Diaphragm paralysis. Patient suspects post-vaccination side effects. +respiratory pumps (2). 04-07-2022: Bursitis on right side.	0.07	2	RD	Unknown
92	F	88	26-01-2021 pb EL1406	14-05-2021 pb (lot unknown)			2pb	Vertigo (occasional), vitB12, vitD, acetaminophen	27-04-2021: Emergency for pain. +Pantoloc, HC-Contin, ativan, dilaudid. June 2021: Deceased. From lung cancer.	3	1	Cancer, RD	Negative
93	F	60	05-05-2021 pb EW0193	22-07-2021 pb FD7206	04-01-2022 pb FM2952		3pb	Arthritis, dyspepsia, pain	01-06-2022: Breathing difficulties for several weeks now.	4	3	RD	Positive on April 26, 2022 (PCR)

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
94	M	93	28-03-2021 pb ER1742	24-06-2021 pb EW0221	28-12-2021 pb FF5109		3pb	Unknown	End September 2021: Angina. 5-10-2021: +Imdur.	3	2	CVD	Unknown
95	F	90	29-03-2021 pb ER1742	21-06-2021 pb FA9093	06-01-2022 pb FM2952	09-04-2022 pb FN7934	4pb	VitD (10,000 I.U./week)	06-06-2022: Myocardial infarction. 08-06-2022: Deceased of an advanced liver cancer.	2	4	CVD, Cancer	Negative
96	F	62	22-04-2021 mod 3001658	21-06-2021 mod 043D21A	26-01-2022 mod 062H21A		3mod	Hypothyroidism, pain, auto-immune hepatitis, hypertension, eczema, vitB12, aspirin	23-02-2022: Partially (70%) occluded femoral arteries (2 stents installed). +Aspirin, plavix, crestor, ramipril, nifedipine, pantoloc.	1	3	CVD	Unknown
97	M	59	13-04-2021 AZ MT0056	10-07-2021 mod 045D21A	23-01-2022 pb FM2952		AZ+mod+pb	No previous medical history	06-06-2022: Advanced intestinal cancer and important pain. +Statex.	4.5	3	Cancer	Positive on April 7, 2022 (PCR)
98	F	86	Received (details NA)	Received (details NA)			2pb	Unknown	21-10-2021: Deceased. After suffering a hip fracture treated with comfort care (refused the operation). Vaccine doses (2) deduced from the vaccination mandates at her residency.	NA	NA	Other	Unknown
99	M	87	29-03-2021 pb ER1742	19-07-2021 pb FA9099	09-01-2022 pb FM2952	10-05-2022 pb FM3444	4pb	Unknown	08-06-2022: Emergency for a stroke. Carotid arteries 80% occluded.	1	4	CVD	Unknown
100	F	62	19-05-2021 pb FA8721	27-07-2021 pb FD7206			2pb	Hypercholesterolemia, hypertension, hypothyroidism, Cal-vitD, vitB12, insomnia	02-05-2022: Stroke. Constant loss of balance. +Plavix, aspirin, lipitor to 20 mg, telmisartan to 80 mg.	9	2	CVD	Positive in February or March 2022 (antigenic)

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
101	M	68	08-04-2021 pb EW3344	26-06-2021 pb EW0221	28-12-2021 pb FF5109	30-04-2022 pb FN7934	4pb	Hypercholesterolemia, hypertension, type 2 diabetes, asthma, calcium supplements, pain	25-06-2022: Bladder or renal cancer (suspected). 04-07-2022: Mass on the left kidney. Under investigation.	2	c	Cancer	Negative
102	M	82	10-04-2021 pb EW3344	22-07-2021 pb FD7206			2pb	Hypothyroidism, urinary incontinence, hypercholesterolemia, constipation, aspirin	01-11-2021: Black plaque under left foot. +Bactroban. January 2022: Operated to remove cancerous mass under left foot. Since then, loss of balance and important weight loss.	3	2	Cancer	Negative
103	F	93	26-02-2021 pb EP6775	01-06-2021 pb EW0216	08-11-2021 pb FF2595	06-04-2022 mod 079J21B	3pb+mod	Hypertension, hypothyroidism, anxiety, insomnia, angina, pain	31-03-2021: Atrial fibrillation. +Eliquis, amiodarone.	1	1	CVD	Positive on December 30, 2021 (PCR)
104	F	87	11-03-2021 pb ER1742	17-05-2021 pb EW0199	09-11-2021 pb FF2595	06-04-2022 mod 079J21B	3pb+mod	Unknown	06-07-2022: Suicidal thoughts. Moved to a residence for seniors.	3	4	Other	Unknown
105	F	84	18-03-2021 mod 3001176	08-07-2021 mod 093D21A	30-12-2021 mod 062H21A	07-05-2022 mod 079J21B	4mod	Arthritis, hypertension, hypercholesterolemia, type 2 diabetes, pain, asthma, dyspepsia	04-06-2022: Angina (under plavix). +Aspirin, imdur. Hospitalized for influenza. Pulmonary oedema.	1	4	CVD	Unknown
106	F	84	16-03-2021 CS 4120Z003	04-06-2021 AZ ABX3120			CS+AZ	Alzheimer's disease, hypothyroidism, hypertension, anxiety, dyspepsia, vertigo, asthma, angina, pain	29-04-2022: Atrial fibrillation (+amiodarone) and heart failure (+aldactone). 30-06-2022: Zona.	11	2	CVD	Unknown
										13	2	Zona	

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
107	M	45	11-05-2021 AZ MT0056				AZ	Depression	For several days following vaccination: Intense fatigue and incapable of functioning. Episode of intense fatigue until September 2021. Physician suspects post-vaccination side effects. Patient from another pharmacy.	0.1	1	Other	Positive in January 2022 (antigenic)
108	F	52	05-02-2021 pb EJ1686	28-05-2021 pb FA8721	23-12-2021 pb FM2952		3pb	Unknown	23-12-2021: Pericarditis. In the days before AE, the axillary nodes on the side of the injection were swollen. January 2022: Two strokes while on vacation abroad. Craniectomy to reduce intracranial pressure. Pneumothorax. Meningitis following craniectomy. Left hemiplegia, with facial paralysis. Patient from another pharmacy.	0.01	3	CVD	Unknown

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
109	M	74	15-04-2021 pb EX0438	30-06-2021 pb FA9091			2pb	Arthritis, cancer, pain, several surgeries for a work accident	Mid-August 2021: Emergency for a bilateral zona. Three weeks later: Emergency for extreme fatigue and shoulder pain. 16-02-2022: Breathing difficulties. 28-02-2022: Fever, intense pain and breathing difficulties. Hospitalized for 5 days. Pneumonia suspected. April 2022: Emergency for breathing difficulties (pulmonary oedema). 07-05-2022: Fever, swollen legs. Pneumonia persisted after iv antibiotics in February. Patient from another pharmacy.	2	2	Zona	Unknown
										7.5	2	RD	
110	M	62	06-05-2021 pb EW0193	02-08-2021 pb FD7208	15-01-2022 mod 020E21A		2pb+mod	Pain (occasional), some bone fractures practicing sports (past), excellent physical condition	March 2022: Emergency for intense abdominal pain. Intestinal mass and abdominal aneurism. Intestinal cancer (a foot of intestine removed). Three of 46 lymph nodes are problematic. 06-07-2022: Chemotherapy initiated. Patient from another pharmacy.	1.5	3	Cancer	Negative

12.1- Supplementary Table S1.
Characteristics of the 112 patients included in the study (abbreviations: Cardiovascular disease, CVD; Respiratory disease, RD; Pfizer/BioNTech, pb; Moderna, mod; AstraZeneca, az; CoviShield, cs; Not available, NA; date format, day-month-year).

Patient #	Sex	Age	1st dose	2nd dose	3rd dose	4th dose	Vaccine Maker	Medical history	Changes in past year	Months from last vaccine to change	Doses before change	Condition	COVID-19 test
111	F	NA	05-07-2021 mod 3002179	06-09-2021 mod 052C21A			2mod	Unknown	08-09-2021: Pericarditis. Fatigue remains. 05-01-2022: Suicide attempt. Patient from another pharmacy.	0.07	2	CVD	Unknown
112	M	44	13-05-2021 pb EW0199	06-08-2021 pb FD7206			2pb	Anxiety, depression, alcoolism (moderate)	05-04-2021 to 08-04-2021: Hospitalized for myocarditis/pericarditis. Patient from another pharmacy.	8	2	CVD	Negative
Mean	**63 M; 49 F**	**67.5**	**112**	**110**	**75**	**13**	**76 pb; 55 mod; 7 AZ; 2 CS**			**3.5**	**2.3**	**61 CVD; 31 Cancer (2 probable); 22 RD; 10 Zona; 10 Other; 2 NA**	**33 positive; 48 negative; 31 unknown**
Median		**67.0**								**3.0**	**2.0**		
SD		**14.5**								**2.7**	**0.8**		
SEM		**1.4**								**0.2**	**0.1**		

12.2-Supplementary Table S2.
Number of times a vaccine lot was injected before a change in medical condition was observed.

Maker and lot number	Doses administered before change observed
Pfizer/BioNTech EW3344	**20**
Moderna 3001658	**14**
Moderna 043D21A	**14**
Moderna 3002182	**12**
Pfizer/BioNTech FD7206	**11**
Pfizer/BioNTech ER1742	**10**
Pfizer/BioNTech FA9091	**9**
Pfizer/BioNTech FA9093	**8**
Pfizer/BioNTech EW0193	**8**
Moderna 062H21A	**8**
Pfizer/BioNTech FF5109	**7**
Pfizer/BioNTech FM2952	**7**
Moderna 045D21A	**7**
Moderna 3001176	**7**
Pfizer/BioNTech FD7208	**7**
Pfizer/BioNTech EW0199	**7**
Pfizer/BioNTech EW0221	**6**
Pfizer/BioNTech EW0216	**6**
Moderna 093D21A	**6**
Moderna 020E21A	**6**
Moderna 3002331	**5**
Pfizer/BioNTech EY0578	**5**
AstraZeneca MT0056	**5**
Pfizer/BioNTech FN7934	**5**
Pfizer/BioNTech FF2595	**4**
Pfizer/BioNTech EX2294	**4**
Pfizer/BioNTech FA9099	**4**
Moderna 063H21A	**3**
Moderna 079J21B	**3**
Pfizer/BioNTech FA8721	**3**
Moderna 3001657	**3**
CoviShield 4120Z003	**2**
AstraZeneca ABX3120	**2**

12.2-Supplementary Table S2.
Number of times a vaccine lot was injected before a change in medical condition was observed.

Maker and lot number	Doses administered before change observed
Pfizer/BioNTech EL1406	**2**
Pfizer/BioNTech EX0438	**2**
Moderna 052C21A	**2**
Pfizer/BioNTech EP6017	**2**
Pfizer/BioNTech EW1099	**2**
Moderna 3002179	**2**
Pfizer/BioNTech FD0810	**1**
Moderna 3002187	**1**
Pfizer/BioNTech EP6775	**1**
Pfizer/BioNTech FM3444	**1**
Pfizer/BioNTech EJ1686	**1**
Pfizer/BioNTech FD7204	**1**
Moderna 3002538	**1**
Pfizer/BioNTech ET0384	**1**
Moderna 092D21A	**1**
Pfizer/BioNTech EY4825	**1**

12.3-Supplementary Table S3.
Characteristics of the 19 deceased patients of whom there were 10 males and 9 females.

Patient #	Sex	Age	Months from between last dose to death	Probable cause of death	COVID-19 test results
1	M	47	4	CVD	Negative
2	M	82	5	CVD	Negative
3	F	81	2	CVD	Negative
4	F	80	2.7	CVD	Unknown
5	M	70	2	CVD	Negative
16	M	66	1.5	Cancer	Negative
28	F	79	8	NA	**Positive**
30	M	65	7.3	Cancer	Negative
38	M	75	13	Cancer	Unknown
42	M	72	NA	Cancer	Negative
50	F	82	4.7	CVD	Negative
58	F	83	1.7	CVD	Unknown
75	F	94	1.5	Cancer	Unknown
76	M	94	1.3	Cancer	Unknown
83	M	70	4.5	CVD	**Positive**
84	M	81	5.3	Cancer	Negative
92	F	88	1	Cancer	Negative
95	F	90	2	Cancer	Negative
98	F	86	NA	(hip fracture)	Unknown
Summary Data	**Mean**	**78.2**	**4.0**	**8 CVD**	
	SD	**11.4**	**3.2**	**9 Cancer**	**11 Negative**
	SEM	**2.6**	**0.8**	**1 Other**	**2 Positive**
	n	**19**	**17**	**1 NA**	**6 Unknown**

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