IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 24, Issue 2 Ser. 5 (February. 2025), PP 01-10
www.iosrjournals.org

Needle-Free Injection System: An Italian Study During The Covid-19 Vaccination Campaign

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Abstract
Background: *The real "weapon" that changed the fate of the challenge to SARS-CoV-2 was the vaccine. Vaccination is done by injection, usually in the deltoid muscle. Alongside the classic method of administering vaccines, it is possible to use the "needle free" technique. This technology consists in the administration by means of a high-speed jet, which completely replaces the use of the needle and therefore of the traditional puncture, guaranteeing total absorption of the drug injected intramuscularly. The "FAST & SAFE" experimentation is part of the perspective of enhancing the results obtained in a very short time thanks to the search for solutions that could allow the vaccination campaign to be optimized.*
Methods: *The study is based on the monitoring of 100 subjects divided into two randomized groups of 50 individuals each. Then 50 subjects received the administration of the vaccine with the classic needle method, the remaining 50 subjects with the needle-free method.*
Results: *The analysis of the results was divided by type of antibody tested, distinguishing between the first and second dose and by type and frequency of adverse events. In general, there are no statistically significant differences between needle and needle-free vaccines.*
Conclusions: *There are no statistically significant differences on average both as regards the development of immunity after two doses of vaccine, and as regards pain at the injection site, and as regards the development of possible side effects.*
Keywords: *Needle free, vaccination, SARS-CoV-2, Covid-19, Sicily, Italy, Vaccine.*

Date of Submission: 12-02-2025 Date of Acceptance: 22-02-2025
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I. INTRODUCTION

SARS-CoV-2 (Severe Acute Respiratory Syndrome COronaVirus 2) is a new strain of coronavirus that was first identified in China in December 2019 and has since spread ubiquitously around the world, severely testing both the economic systems and the healthcare systems of the various nations, from the most developed to the backward ones.

Particularly during the first wave, SARS-CoV-2 was responsible for a very high mortality rate. The rapidity and ease of diffusion of the virus have been facilitated by its intrinsic characteristics, and by its main pathogenicity factors, which allow it to use the upper airways and mucous membranes in general as entry routes. [1]

Naturally, the airborne spread, by means of aerosols and droplets, the high number of infected but asymptomatic subjects, the absence of previous immunity, have contributed in a fundamental way to the rapid circulation of the virus, leading to a rapid and widespread expansion of the disease.

The health emergency plans and strategies implemented by the various nations were in some cases similar to each other, but in general insufficient to contain, in the first and tragic phases of the pandemic, the spread of the virus, hospitalizations and, above all, the deaths.

The emergency plan implemented by Italy was characterized to a large extent by restrictive measures, put in place in order to reduce interpersonal contacts as much as possible in order to limit the spread of the virus. The real turning point in contrasting the SARS-CoV-2 pandemic was certainly given by the availability of effective vaccines. Vaccination has the objective of leading to the development, in a subject receptive to a specific infectious disease, of active immunity, causing the humoral and tissue modifications necessary to ensure the specific defense of the organism against the agent of the infection itself.

As mentioned, the real "weapon" that changed the fate of the challenge to SARS-CoV-2 was the vaccine, and in order to achieve this objective, exceptional measures were implemented which allowed, albeit with an enormous effort, the commercialization of vaccines against COVID-19 in practically record time. The European Commission took the field by making 2.7 billion euros available as European Structural and Investment Funds (ESIF) in order to stipulate contracts between the member states and the pharmaceutical manufacturing companies. By exploiting these mechanisms, member states have had the advantage of being effective contractors for vaccines and pharmaceutical companies of having funds immediately available for research and large-scale production.

The health emergency triggered by the COVID-19 pandemic has forced to speed up the production and marketing times of vaccines. In addition to the reduction in approval times, the shortening of development times was fundamental, which made it possible to put the vaccines for COVID-19 on the market already in 10-12 months from the start of the experimentation.

In order for this to be achievable, the various phases were combined, conducting studies in parallel, for example phase I/II or II/III, testing the vaccine directly on a population of hundreds of individuals. Another very useful expedient to shorten the times was the implementation of the staff both to analyze more rapidly the results of the studies, but also to be able to increase production, while maintaining the appropriate quality standards. [2-3]

The vaccines against COVID-19 approved by AIFA to date belong to different categories: mRNA (messenger ribonucleic acid) vaccines (BTN1 62b2 Comirnaty, from Pfizer and Spikevax COVID-19 Vaccine from Moderna), viral vector vaccines (Vaxzevria, formerly AstraZeneca COVID-19 vaccine and Jcovden ex Janssen COVID-19 vaccine), those with protein subunits ("Nuvaxovid", recombinant, adjuvanted, from the pharmaceutical company Novavax), those with inactivated virus ("Valneva", inactivated, adjuvanted, from the pharmaceutical company Valneva). [4]

All vaccines currently under study have been developed to induce a response that blocks the Spike protein and therefore prevents cell infection.

In order to deal with the health emergency and buffer the very high number of victims of the first 9 months of the pandemic, the Strategic Plan for the anti-SARS-CoV2/COVID-19 vaccination (DM 2 January 2021), divided the population into categories and gave an order of priority.

In a primary phase, the goal was to reduce morbidity and mortality, trying to keep essential services constantly active; while in a second phase the focus had been shifted to reducing the transmission of the virus, with the aim of reducing the number of infections and their socio-economic impact as much as possible. Almost three years after the start of the pandemic, the vaccination plan has undergone numerous changes.

Regardless of the type of anti-COVID-19 vaccine used, vaccination is carried out with a special disposable sterile syringe, equipped with a needle locking system associated with disposable sterile needles.

Vaccination is performed by qualified personnel, doctors, nurses or pharmacists, trained and experienced in vaccination techniques. Staff training is very important especially for the Comirnaty since it needs a particular treatment before being dispensed. [5]

As for the physical administration of the vaccine, it is carried out by injection, usually at the level of the deltoid muscle. Alongside the classic method of administering vaccines, it is possible to use the "needle free" technique. This technology consists in the administration by means of a high-speed jet, which completely replaces the use of the needle and therefore of the traditional puncture, guaranteeing total absorption of the drug injected intramuscularly. [6]

The device uses the "nozzle", a syringe without needle, sterile and disposable (accidents related to accidental punctures are among the most frequent and with high costs associated with treatment), capable of administering the vaccine into the arm through a microhole of 0.15 mm which allows entry into the body in less than 100 milliseconds and is a system compliant with Directive 2010/32/EU, implemented with Legislative Decree no. 19 of 19/02/2014. [7]

This method of administration could guarantee greater compliance on the part of patients, in which the anxiety associated with the presence of the needle (*belonephobia*) is reduced, with the possibility of using it also in the pediatric age. [8-9]

Finally, the risk of accidentally pricking oneself and the possible transmission of infectious diseases is eliminated for the healthcare professional. The device is very simple to use and uses a particular mechanism thanks to which the drug is released through a 0.15 mm micro-hole, at high speed, in less than 100 ms, practically creating a "fluid needle". The diffusion is subcutaneous and occurs following the "sputtering" model. In the context of the administration of SARS-CoV-2 vaccines, it is associated exclusively with mRNA vaccines.

The "FAST & SAFE" experimentation is part of the perspective of enhancing the results obtained in a very short time thanks to the search for solutions that could allow the vaccination campaign to be optimized.

This technology used for the first time in Europe, in this case at the Messina vaccination hub (with testing started on 07/28/2021), is called NFIT (Needle Free Inject Technology) and the medical device used is class IIb, known by the name "*Comfort-in*", CE certified and supplied by the Catania company Gamastech s.r.l.

The experimental study, which takes the name of FAST & SAFE, was performed in compliance with the European Union's Standards of Good Clinical Practice [10] and with the Declaration of Helsinki on human experimentation [11], then notified and approved by the Messina Intercompany Ethics Committee report n. 10 session of 12 October 2021.

Participation in the trial is on a voluntary basis and patients who decide to participate can decide to revoke their consent at any time during the trial, without needing to provide explanations on the matter, but having to simply notify the scientific manager of the study.

The aim of the study is to evaluate the antibody response to the SARS-CoV-2 vaccine by comparing the classic needle method and the needle-free method.

The secondary objective is to evaluate the possible onset of adverse effects, in particular pain at the vaccine inoculation site, by comparing the hypothetical differences between the two methods, with and without a needle. It is important to point out that based on the data available in the literature, a large portion of the population, around 5-10%, suffers from *belonephobia*, i.e. the fear of needles, classified in the DMS 5 as a specific phobic disorder, i.e. an experience of anxiety and irrational fear linked to exposure to needles, pins or sharp objects and to any procedure involving their use, such as vaccinations.

Needle-free jet injectors have had a significant impact on drug and vaccine delivery, occupying a prominent place in history as an important component of mass immunization programs. However, they have not yet reached their full potential due to several factors, such as occasional pain or local reactions. [12]

II. METHODS

The study is based on the monitoring of 100 subjects divided into two randomized groups of 50 individuals each. Then 50 subjects received the administration of the Pfizer vaccine with the classic needle method, the remaining 50 subjects with the needle-free method of the same vaccine.

Inclusion criteria: over 18 years of age, ability to understand and want and to provide personal data and to sign the informed consent autonomously. Furthermore, to be included, subjects must not have previously contracted SARS-CoV-2 infection and must be willing to undergo a full vaccination course (to evaluate this, the presence of IgG antibodies against the capsid of the virus was evaluated (if negative, the value had to be equal to or less than 23 BAU/ml).

Time 0 of the study was March 1, 2022, on that date at the "Hub Fiera di Messina" in Messina (city in Sicily, Italy), vaccination center for the COVID-19 vaccination campaign, they were recruited by extracting randomly, through the random extraction function of the Microsoft Excel program, from the list of booked 100 people who met the study inclusion criteria. All 100 selected people agreed to be part of the study.

As regards the timing: subjects will be enrolled in month 1; in months 1 and 2, both doses of the vaccine will be administered, with the serological test being performed 10 days after each administration, while 3 days after the administration, data relating to pain and any adverse effects will be collected.

At the time of enrollment of patients, the following will be collected at the same time:

- epidemiological data, such as age and gender;
- past and present pathological history;
- drug history;

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randomly, through the random extraction function of the Microsoft Excel program, from the list of booked 100 people who met the study inclusion criteria. All 100 selected people agreed to be part of the study.

The data were processed according to the provisions in force pursuant to EU regulation 679/2016 (GDPR, General Data Protection Regulation) and Legislative Decree 196/2003, and were completely anonymized and entered into a database on Microsoft Excel, with particular reference to the antibody response for each IgG component related to the various portions of the spike protein, in particular anti-S1 (S1 subunit of Spike protein) IgG, anti-S2 (Spike protein S2 subunit) IgG and anti-RBD (Receptor Binding Domain) IgG.
Serum analysis was performed using MFI (Multiplex Flow Immunoassay) technology.
For the analysis of the samples, the BioPlex 2200 system (Bio-Rad, CA) was used.
The cut-offs used are described below.
Cut-offs [13]:

- Sars-Cov-2 RBD IgG ≤12 Negative, >12 Positive Unit of measurement BAU/ml;
- Sars-Cov-2 S1 IgG ≤21 Negative, >21 Positive Unit of measurement BAU/ml;
- Sars-Cov-2 S2 IgG >10 Positive Unit of measurement U/ml;
- Sars-Cov-2 Capsid IgG ≤23 Negative, > 23 Positive Unit of measurement BAU/ml.

As far as pain assessment is concerned, the subjects were contacted by the investigators who, using the Numerical Rating Scale (NRS, a numerical scale that evaluates pain one-dimensionally, i.e. the intensity perceived by the patient), evaluated the presence of pain, its possible intensity and, contextually, the occurrence of adverse events.

NRS is an 11-point pain rating scale and requires the operator to ask the patient to select the value that he thinks best identifies her condition. The values range from 0-10, where 0 indicates the absence of pain, 10 the worst possible pain and values between 1-9 the worsening presence of pain. In particular:

- 0 absence of pain;
- between 1-3 we speak of mild pain;
- between 4-6 intermediate;
- 7-10 severe.

Statistical Analysis

The data analysis was performed with the STATA statistical software, version 14 (StataCorp. Stata Statistical Software. In: Station C, editor. StataCorp LP; 2015.). [14]

Categorical data were reported using frequencies and percentages, whereas continuous data were reported using mean (and standard deviation, SD). Both absolute and relative frequencies were calculated for all qualitative variables; Pearson's chi-square test ($\chi 2$) was used to analyze categorical variables, t-test was used to analyze continuous variables. Lastly, ordered logistic regressions were used to estimate the association between NRS and tipology of vaccine (no needle/needle), yielding Odds Ratios (OR) and 95% Confidence Intervals (95% C.I.). The regression models were adjusted for age and gender. Lastly, a stratification by tipology of vaccine (no needle/needle) was also performed in order to detect any differences among tipology. Associations with $p < 0.05$ were considered statistically significant in two-sided tests.

III. RESULTS

The sample is composed of 100 (42 women and 58 men) subjects, 50 participants were subjected to the vaccine using the needle-free method, and 50 participants using the classic method. Of the participants who received the needle-free vaccine, 19 (38%) were women and 31 (62%) were men; among the participants who underwent a vaccine using the traditional method, 23 (46%) were women and 27 (54%) were men (Table 1).

The analysis of the results was divided by type of antibody tested, distinguishing between the first and second dose and by type and frequency of adverse events with a specific focus on pain assessment.

Below are the graphs (Figure 1, Figure 2, Figure 3) and the tables (Table 1, Table 2, Table 3) relating to the t-tests to test the mean difference in the antibody titer for the first and second dose, between the two methods of administration object of the study. The figure 1 shows that the median relative to the distribution of RBG IgG antibody titer dosages are higher in the needle-free mode than in the classic mode. The interquartile range as well as the whiskers is wider in the second distribution, with the presence of more outliers. The distribution of the dosages of the S1 IgG antibody titers in both groups is symmetrical, as is the median. The whiskers are wider in the second distribution, with the presence of more outliers (Figure 2).

The distribution of the dosages of the S2 IgG antibody titers is asymmetric with the median shifted upwards in favor of the administration without a needle; the whiskers are wider in the second distribution, with the presence of more outliers. In general, there are no statistically significant differences between needle and needle-free vaccines.

Fig.1. Box-plot distribution of dosages of RBG IgG antibody titer. **No ago: needle free; ago: needle**.

Fig.2. Box-plot distribution of dosages of S1 IgG antibody titers. **No ago: needle free, ago: needle**.
Fig.3. Box-plot distribution of dosages of S2 IgG antibody titers. **No ago: needle free, ago: needle**.

Table 1. Descriptive characteristics of the sample

Variable		N	% or SD
Gender	Female	42	42.00
	Male	58	58.00
Tipology	Needle-free	50	50.00
	Needle	50	50.00
Vaccine	Moderna	2	2.00
	Pfizer	98	98.00
Age	mean (±SD)	43.1	±11.98
NRS dose 1	mean (±SD)	0.56	±1.22
NRS dose 1	Absent	76	76.00
	Slight	19	19.00
	Moderate	5	5.00
	Severe	0	0.00
RBD dose 1	mean (±SD)	13.26	±104.46
S1 dose 1	mean (±SD)	9.29	±55.42
S2 dose 1	mean (±SD)	3.69	±6.56
Capsid dose 1	mean (±SD)	0	±0
NRS dose 2	mean (±SD)	0.72	±1.75
NRS dose 2	Absent	77	77.00
	Slight	15	15.00
	Moderate	5	5.00
	Severe	3	3.00
RBD dose 2	mean (±SD)	3716.04	±3503.68
S1 dose 2	mean (±SD)	4019.68	±3258.17
S2 dose 2	mean (±SD)	52.82	±82.68
Capsid dose 2	mean (±SD)	0	±0
At least 1 adverse event (dose 1)	No	73	73.00
	Yes	27	27.00
At least 1 adverse event (dose 2)	No	46	46.00
	Yes	54	54.00

Table 2. Bivariate analysis stratified by type of vaccine (Needle-free /needle). Used Pearson's chi-squared test for categorical variables and t-test for continuous variables.

Variable		Needle-free (% or SD)	Needle (% or SD)	*p-value*
Gender	Female	19 (38.00)	23 (46.00)	0.418
	Male	31 (62.00)	27 (54.00)	
Vaccine	Moderna	0 (0)	2 (4.00)	0.153
	Pfizer	50 (100)	48 (100.00)	
Age	mean	44.52 (±13.00)	44.52 (±10.81)	0.881
NRS dose 1	mean	0.54 (±1.28)	0.58 (±1.16)	
NRS dose 1	Absent	40 (80.00)	36 (72.00)	0.422
	Slight	7 (14.00)	12 (24.00)	
	Moderate	3 (6.00)	2 (4.00)	
	Severe	0 (0)	0 (0)	
RBD dose 1	mean (±SD)	1.67 (±1.27)	24.86 (±147.54)	0.135
S1 dose 1	mean (±SD)	2.65 (±1.67)	15.93 (±78.19)	0.116
S2 dose 1	mean (±SD)	2.74 (±2.08)	4.63 (±8.99)	0.076
Capsid dose 1	mean (±SD)	0 (±0)	0 (±0)	-
NRS dose 2	mean (±SD)	0.66 (±1.75)	0.78 (±1.76)	0.367
NRS dose 2	Absent	41 (82.00)	36 (72.00)	0.471
	Slight	5 (10.00)	10 (20.00)	
	Moderate	3 (6.00)	2 (4.00)	
	Severe	1 (2.00)	2 (4.00)	

RBD dose 2	mean (±SD)	3189.84 (±2053.76)	4242.24 (±4474.28)	0.067
S1 dose 2	mean (±SD)	3661.02 (±2204.89)	4378.34 (±4040.29)	0.137
S2 dose 2	mean (±SD)	59.04 (±107.49)	46.60 (±46.67)	0.227
Capsid dose 2	mean (±SD)	0 (±0)	0 (±0)	-
At least 1 adverse event (dose 1)	No	36 (72.00)	37 (74.00)	0.822
	Yes	14 (28.00)	13 (26.00)	
At least 1 adverse event (dose 2)	No	22 (44.00)	24 (48.00)	0.688
	Yes	28 (56.00)	26 (52.00)	

Legend: SD: Standard Deviation; %: percentage

Table 3. Logistic regression model (adjusted by age and sex).

	Dependent variable: At least 1 adverse event (dose 1)		
Independent variable	**adjOR**	**C.I. 95%**	***p-value***
Needle-free	*ref.*		
Needle	1.54	0.57-4.12	0.392
	Dependent variable: At least 1 adverse event (dose 2)		
Independent variable	**adjOR**	**C.I. 95%**	***p-value***
Needle-free	*ref.*		
Needle	1.59	0.61-4.13	0.344

Legend: adjOR: adjusted Odds Ratio

IV. DISCUSSION

Spike protein is one of the peculiar characteristics of the coronavirus family, giving it the characteristic crown appearance. It is a trimer and each monomer consists of two subunits, S1 and S2.

The S1 subunit, which is very flexible, in turn contains the epitopes RBD and NTD (N terminal domain), which represent the most immunogenic sites. [14]

The Spike protein, through the RBD receptor, binds to the converting enzyme ACE2 (Angiotensin-converting enzyme 2) located on the host's pulmonary epithelial cells, which allows it to enter the cell, practically acting as a gateway.

Once the fusion between the membranes has occurred, the RNA is released so as to exploit the organelles of the host cell for the production of viral, structural and non-structural proteins, causing the virus to replicate, leave the host cell by lysis, propagating, in the last instance, the infection.

The neutralizing antibodies are those against the RBD epitope in the S1 region of Spike glycoprotein. They are able to prevent the binding of the virus to the ACE2 enzyme and therefore are effective in protecting us from infection. The production of these antibodies is stimulated by vaccines, so the dosage of anti-RBD antibodies by means of serological tests allows us both to evaluate the occurred seroconversion approximately 10-15 days after the administration of the vaccine, and to monitor the antibodies over time.

The study made it possible to evaluate the differences in the results obtained in the group that performed the vaccination with the needle-free method of administration compared to the group that received the vaccine with the classic administration, with a needle.

Following the first blood sample, performed 10 days after the administration of the first vaccine dose, none of the subjects vaccinated with the needle-free method of administration developed an antibody titer such as to be defined as positive according to the cut-offs taken into consideration. After the second sample, also in this case performed 10 days after the second dose of vaccine, all patients developed an antibody titer such as to be defined as positive according to the cut-offs taken into consideration.

Focusing on the mean values relating to the antibody titers developed following the first dose, the data suggest a better performance with administration of the vaccine with the traditional method, however, no statistically significant differences are found on average.

Focusing on the data relating to the antibody titers developed following the administration of the second dose of vaccine with both methods (classical and needle-free), no statistically significant differences are found on average.

The FAST&SAFE study takes into consideration further variables, defined as secondary objectives of the experimentation, namely the evaluation of the onset of adverse events and the subjective evaluation of pain 3 days after the administration of the vaccine.

As regards the assessment of the type and frequency of adverse events following the inoculation of the vaccine, given that no serious events have been reported, there are no substantial differences in terms of prevalence in absolute terms between the two methods of administration. It should also be highlighted the increase in the prevalence of adverse events following the administration of the second dose regardless of the technique.

With regard to the specific focus on pain assessment at the injection site, there are no substantial differences in terms of prevalence between the two methods of administration in absolute terms.

A separate consideration must be made in relation to the biological risk in the healthcare personnel responsible for administering the vaccine, although it was not included among the objectives of the study.

Biological risk is the possibility of contracting an infectious disease following occupational exposure to biological agents.

This risk is present in all those work activities which may involve, even potentially, exposure to biological fluids (in particular blood) or which in any case involve the use of sharp and sharp tools.

Biological risk represents, in health and social health work environments, one of the priorities for prevention, as it is a potential cause of injury and occupational disease.

Legislative Decree 9 April 2008, n. 81 (Consolidated Law on the protection of health and safety in the workplace, implementation of article 1 of the law of 3 August 2007, n. 123) and subsequent amendments. Includes in the assessment of the risks to be taken into consideration, exposure to biological agents, with particular reference to Title X. The Legislative Decree 81/2008 defines a biological agent as "any microorganism, even if genetically modified, cell culture and human endoparasite, which could cause infection, allergy or intoxication" in personnel exposed to such microorganism. [15]

Occupational infections, i.e. those transmitted from patient to healthcare professional and from healthcare professional to other healthcare professional, and nosocomial infections represent problems of great importance for healthcare and social-healthcare structures due to the consequences that may arise in terms of liability, both relating to the safety of workers, and relating to the potential harm suffered by patients.

The WHO estimates that over 3 million accidents occur worldwide every year caused by sharp and/or sharp tools contaminated with HIV or hepatitis B and C viruses, and that at least 83,000 infections a year are attributable to occupational exposure, of the percutaneous type, linked to infected biological materials. Globally, these incidents cause up to 37% of hepatitis B, up to 39% of hepatitis C and up to 4.4% of HIV infections contracted by healthcare workers, according to the WHO. According to the Atlanta CDC, the chance of acquiring an infection following an accidental puncture with a contaminated needle is 0.3% for HIV, 2.7% to 10% for HCV, and 2% to 40% for HBV.

In the literature data emerge that overlap with those of the WHO: it is estimated that percutaneous occupational exposure causes 37% of hepatitis B, 39% of hepatitis C and 4.4% of HIV infections considering the reference population that of health professionals. [16]

In Europe, accidental sharps or needlestick injuries are estimated at about 1 million a year.

In Italy, the estimate of these harmful events is around 100,000 units and they represent one of the most frequently reported injuries among healthcare workers, thus configuring a real "occupational risk".

Based on the data of a survey conducted by the Italian Association of Health Prevention and Protection Services Managers (AIRESPSA), it was highlighted that exposures to biological risk in healthcare workers are very frequent, representing about 40% of all reported injuries. The most representative data of the Italian situation derive from the "Italian Study on Occupational Risk from HIV" (SIROH10, of the National Institute for Infectious Diseases "Lazzaro Spallanzani"). The data collected through this study have allowed us to have a deep scientific knowledge not only of the frequency, causes and methods that lead to occupational exposure, or of the risk of contracting an infection, but also of the preventive measures that can be implemented. More specifically, 75% of exposures are of the percutaneous type, i.e. they are caused by accidental punctures caused by needles or other sharp objects contaminated with blood. The remaining 25% consists of mucocutaneous exposures, i.e. accidental contact of potentially infected biological material with the operator's mucous membranes or non-intact skin. Therefore, all those maneuvers that are performed daily by healthcare personnel that involve the handling of possibly contaminated tools, objects and materials are to be considered "potentially risky activities". [17]

Today risk assessment in the health sector, particularly in hospitals, represents a strategic process in the corporate security system, as it leads to the identification of all the risks and dangers associated with the work activity, allowing on the one hand maximum protection of the worker and on the other a potential optimization of resources, considering that protecting the worker in the best possible way from potential occupational pathologies deriving from biological risk means indirectly preventing potential retaliatory actions against the employer and the company where he works service.

In consideration of these premises, all preventive measures are put in place, which can be of an ergonomic, technical, organizational, hygienic-sanitary type aimed at protecting the healthcare operator.

In this case, as regards the handling of needles, scalpels and sharps, the operator is recommended to handle them with extreme care in order to prevent accidental injuries, not to recap them, disengage them and/or bend or break them.

In addition, needles, scalpels and sharps must be disposed of using special resistant, rigid, waterproof containers with an airtight final closure and disposed of as special waste.

In this sense, the introduction by the Legislator of the new Title Xbis of Legislative Decree 81/2008 entitled "Protection of cuts and sharps wounds in the hospital and healthcare sector".

The Legislative Decree of 19 February 2014, n. 19 provides for the introductory six articles (from 286-bis to 286-septies).

Particularly relevant is the provisions of Art. 286-ter, in which the legislator meticulously indicates what is meant by "specific prevention measures" or "measures adopted to prevent injuries and the transmission of infections in the context of the provision of services and the performance of activities directly connected to assistance hospital and healthcare, including the use of equipment deemed technically safer in relation to the risks and methods of disposal of sharps medical devices, such as sharps medical devices equipped with a protection and safety mechanism, able to protect the hands of the user operator during and at the end of the procedure for which the device itself is used and to ensure a permanent protective action in the phases of collection and final disposal". [18]

Referring to the possibility of reducing the biological risk for the healthcare worker from handling needles, scalpels and sharps by taking into account the most advanced technologies, the use of needle-free, sterile and disposable syringes, with non-statistically significant differences in terms of efficacy, represents a chance.

In this regard, a comparative assessment between increased costs and benefits could be decisive, quantifiable with the reduction of claims for compensation for occupational disease or ancillary costs deriving from access to the ED, serological investigations, vaccination prophylaxis, and any absences due to illness.

Extremely interesting in this regard, a 2013 study conducted in a Belgian hospital, for the evaluation of the economic impact linked to the replacement of conventional devices with innovative devices for needlestick injuries, demonstrating that the reduction of health costs resulting from accidents with needles and sharps would offset the increased cost of replacing conventional devices. [19]

It is estimated that every year in Italy around 36 million euros are spent on expenses resulting from accidental injuries from needle sticks and sharps among healthcare workers as well as for the need to dispose of sharps [20], significant but above all avoidable costs. [21-22]

V. CONCLUSIONS

The study has highlighted countless highly relevant insights that could form the basis of further evaluations in the field of public health management.

On the basis of the data collected, the objectives of the study of demonstrating a "non-inferiority" of the administration of mRNA vaccines for SARS-CoV-2 with the needle-free method compared to the classic administration method can be considered achieved.

In fact, there are no statistically significant differences on average both as regards the development of immunity after two doses of vaccine, and as regards pain at the injection site, and as regards the development of possible side effects (evaluated both as a number both raw and specifically).

Surely the use of the needle-free method allows a better compliance of aicmophobic/belonephobic patients, potentially allowing to widen the vaccination coverage, in this case for SARS-CoV-2 m-RNA vaccines, to all those subjects who do not get vaccinated for the fear of needles, in the adult population but also in the pediatric one.

In this regard, with a view to obtaining an increase in vaccination coverage in the general population, the FAST&SAFE study could also find interesting implications for no-COVID-19 vaccinations, guaranteed as LEA by the NHS.

A further implication is the reduction of the biological risk for healthcare personnel considering that the method does not involve the use of a needle.

The latter assessment could be of considerable importance, in the light of the fact that around 40% of the reports of occupational accidents in the healthcare sector are to be charged to damage attributable to sharp and sharp objects.

Finally, through a careful cost/benefit analysis, considering on the one hand the higher cost of the device compared to the classic syringe and on the other the savings deriving from the reduction of the disposal costs of special waste (disposal regulated by Presidential Decree 254/03, must take place according to strict procedures), the reduction in claims for compensation for occupational accidents, the possible costs of post-exposure hepatitis B vaccine prophylaxis and antibody dosages and any days of absence from work, their use could also be evaluated for usually used intramuscularly.

These considerations, supported by the relative numerical data, could be an important driver of change in public health.

Net of these considerations, what emerges with certainty from the FAST&SAFE study is reported below:

- Needle-free vaccination is a quick and easy-to-use method;
- Staff training for the use of the needle-free syringe is simple;

- In the light of the results that emerged, vaccination with a needle-free syringe has comparable efficacy compared to the traditional method of administration;
- In the light of the results that emerged, vaccination with a needle-free syringe presents adverse events of a degree and number that can be superimposed on the traditional method of administration;
- In the light of the results that emerged, the pain at the injection site level is superimposable with respect to the traditional method of administration;
- Vaccination with a needle-free syringe could make it possible to overcome resistance to vaccination for those who are afraid of the needle;
- Vaccination with a needle-free syringe totally eliminates the risk of accidental punctures;
- Vaccination with a needle-free syringe minimizes the risk of contamination from pathogens, as it does not come into contact with the patient's blood in any way.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of Provincial Health Authority of Messina (ID 4, 12st April 2022).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Acknowledgments: this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Interest: The authors declare no conflict of interest.

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