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Addressing Clinical Governance issues of Covid-19: analysis and solutions for the Italian health system

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ABSTRACT

This thesis addresses the main criticalities affecting Clinical Governance during the Covid-19 pandemic. The two areas of analysis are the RT-PCR tests and the vaccination campaigns: the two protagonists of the fight against the new virus.

RT-PCR tests are the diagnostic tool adopted to control the spread of the infection; an in-depth study of the process has been fundamental to increase their reliability and limit false results. In particular, potential sources of risks were found out, collected, and analyzed through an ad-hoc FMECA toolkit. It consists of a sources document containing all the information to fill a second file, the FMECA tool. The sources of information come from literature, experts, and incident reporting provided by the Lombard laboratories. The final output is a 134 events database for which causes, consequences, effects on the patient, and mitigation actions have been associated with coverages respectively of 96%, 15%, 16%, and 49%. The toolkit is reserved for the use of all the Lombard laboratory facilities, which will take advantage of a standardized tool for risk assessment. In this way, they will be able to reduce the most frequent errors and improve the RT-PCR process.

Vaccines represents the worldwide selected strategy to prevent the further spread of the pandemic; States rushed to prepare adequate massive vaccination plans for coping with the situation, which turned out to be different in several aspects. For this reason, the study aims at evaluating the main characteristics of the vaccination campaigns, comparing them, and determining which one had the best results. The analysis is limited to Italy, and the selected regions are Lazio, Liguria, Lombardy, and Piedmont. The methodology concerns the creation of a framework as the baseline of analysis. It needs to consider: the context elements, the key elements of the plans (demand management, operating model, governance, IT services, and communication plan), and operational and health performances. The web open sources constitute the input data for the filling of the framework. The degrees of coverage obtained are 45% for Lazio, 44% for Liguria, 55% for Lombardy, and 49% for Piedmont. After singularly analyzing and comparing the regions, Lombardy results to be the most efficient in vaccine administration.

The study enhances the standardization and facilitates the management of critical resources, which are two of the main Clinical Governance issues of the COVID-19 pandemic.

SOMMARIO

La tesi è volta a studiare le maggiori problematiche affrontate dalla Governance Clinica durante la pandemia Covid-19. I due ambiti di analisi sono i RT-PCR tests e i piani vaccinali, i due protagonisti per la lotta contro il nuovo virus.

I RT-PCR tests sono lo strumento diagnostico adottato per controllare la diffusione della pandemia; per aumentarne l'affidabilità e limitare i falsi risultati, è stato svolto uno studio approfondito del processo. In particolare, le potenziali fonti di deviazione di processo sono state collezionate ed analizzate tramite un FMECA toolkit, creato ad-hoc. Il toolkit è costituito da un file sources contenente le informazioni da inserire in un secondo file, la FMECA tool. Le fonti di informazione sono costituite da letteratura, esperti e segnalazioni di incidenti derivanti dai laboratori lombardi. L'output finale è un database di 134 eventi ai quali sono stati associati cause, conseguenze, effetti sul paziente e azioni di mitigazione con coperture rispettivamente del 96%, 15%, 16% e 49%. Il toolkit è riservato a tutte le strutture laboratoriali lombarde, le quali potranno usufruire di uno strumento standardizzato per la valutazione del rischio. In questo modo, sarà possibile ridurre gli errori più frequenti e migliorare il processo.

I vaccini rappresentano la strategia scelta a livello globale per prevenire l'ulteriore diffusione della pandemia; gli stati si sono precipitati a preparare dei piani vaccinali adeguati, i quali sono risultati essere differenti per diversi aspetti. Lo studio mira a valutare le principali caratteristiche dei piani, confrontarle e determinare quale campagna vaccinale ha avuto i risultati migliori. L'analisi è limitata all'Italia e le regioni approfondite sono Lazio, Liguria, Lombardia e Piemonte. La metodologia consta nella definizione di un framework di analisi formato da elementi di contesto, elementi chiave del piano (gestione della domanda, modello operativo, governance, servizi IT e piano di comunicazione) e prestazioni operative e sanitarie. Il framework è stato compilato tramite le fonti web disponibili e i gradi di copertura ottenuti sono 45% per il Lazio, 44% per la Liguria, 55% per la Lombardia e 49% per il Piemonte. Dalla analisi sia individuale sia comparativa tra le regioni, la campagna lombarda è risultata la più efficace.

In conclusione, lo studio incrementa la standardizzazione e facilita la gestione delle risorse critiche, i quali sono due dei maggiori problemi della Clinical Governance rispetto la pandemia di COVID-19.

EXECUTIVE SUMMARY

In December 2019, an outbreak of infection of a severe respiratory syndrome was detected in Wuhan, China. The virus, now known as COVID-19, was announced by the World Health Organization (WHO) on January 20 2020, and became a global pandemic. The Global research community faced urgent calls to develop rapid diagnostic tools, effective treatment protocols, and most importantly, vaccines against the infection. The RT-PCR test process aims at detecting viral SARS-Cov-2 RNA sequences through nasopharyngeal swabs. Looking at the increasing number of deaths and new cases, the only way to defeat the virus was to develop vaccines. The thesis will focus on these two tools; they have a crucial role in the fight against this infection.

The first part will deal with the reactive method, the identification of positive cases through the RT-PCR test process. The analysis will concentrate on the laboratorial structures located in Lombardy; the group work is composed of a task force, comprehensive of two representatives of “Regione Lombardia”, two doctors coming from the hospitals of Mantova and Professor Paolo Trucco.

The study will be conducted thanks to four sources of information: the scientific literature, incident reports, expert interviews, and two case studies. This part aims at drafting the risk assessment of the overall PCR test process. The final output will be a standardized toolkit leveraging the Failure Mode Risk Analysis (FMECA) methodology. Thanks to this product, the laboratorial structures will receive significant help when assessing and improving the criticalities of the PCR testing process. On the 22nd of June, a network was held involving the risk managers of the Lombardian hospitals. The aim is to make them aware of the potentiality of the tool and explain how to use it. All this thanks to the support of the two cases of Mantova and Brescia.

The second part will treat the proactive approach to deal with the current pandemic i.e., the design and management of the vaccination campaigns. This study will be disclosed by a comparison of different Italian regional vaccination plans. The sources that will be analyzed are official documents of the public domain, found on the websites of Italian regions, and online databases reporting updated data and statistics. The aim is to define a detailed framework of analysis that will be the baseline for evaluating Covid-19 regional vaccinations plans. In

this case, the group work received the initial support of Sham, the Italian health assurance, for the definition of the framework of analysis.

The COVID-19 pandemic introduced several hustles in its management, and Clinical Governance is one of the main aspects, which has been impacted. Clinical Governance (CG) is defined by ISS as "the organization and performance of the activity of a healthcare facility, aimed at empowerment and participation, in strategic and management choices, of all those involved in the provision of healthcare services". Specifically, Sheila Gopal Krishnan and Azanna Ahmad Kamar inside "Bioethics and COVID-19: Guidance for Clinicians" (2020) identified five main technical components from Clinical Governance that should be applied during a pandemic. Health, Safety, and Staff management (1), Risk/Crisis management (2), Strategic opportunities (3), Aftermath & Audit (4), and Ethics and Clinical Governance (5).

It is clear how the investigation interacts with the concept of Clinical Governance and more specifically with Clinical Risk Management, in the first part of the study, and with guidelines concerning the vaccination campaign analysis.

In particular, this thesis will analyze two of the main problems that can affect CG during a crisis: the lack of resources and the difficulty of standardization. They will be treated from the point of view of the RT-PCR procedure with its sources of risks and from the vaccination campaigns perspective.

Part 1 - Clinical risk Assessment of the PCR test process

Clinical risk management is the approach through which the RT-PCR test process has been analyzed. The analysis concentrates on identifying the main sources of risk, classify, and prioritize them, defining mitigation actions to reduce their effects, and finally performing a monitoring step to evaluate if the action is working well or if some adjustments are required.

Given the growing demand, the laboratories are facing many challenges in terms of staff, logistics, and equipment. Indeed, the risk of erroneous results can be a lever for the propagation of the disease. Hence, laboratories need to be aware of their limits and optimize the testing process.

The FMECA is nowadays the most applied proactive risk analysis methodology, also in the health care industry. The main steps to be followed imply: the decomposition of the overall process into elementary sub-processes,

identification of the failures which occur within each sub-process, and classification of them into failure modes, causes and effects. Then a ranking of the failure modes should be defined by calculating the risk priority number (RPN) as the product between the probability of occurrence (P), the severity of the consequences (S), and the detectability before it may occur (D). Having obtained a quantitative value of the RPN, it is possible to rank all the failure modes, from the highest RPN to the lowest, and define some mitigation actions for the most critical. The last two phases, the assessment of RPN and the creation of remedial action, could be iteratively repeated once the corrective actions have been executed to verify their efficiency. If the corrections were designed and implemented accurately, then a decrease in the RPN value should emerge.

Practically speaking, the starting point has been the definition of the process mapping for the diagnostic test. The process is composed of four main stages: demand generation, pre-analytical, analytical, and post-analytical. A FMECA template has been created with 134 failure modes for which should be searched the potential causes, the consequences, the effects on the patient, and the corrective measures. Going on with the template, a risk analysis is present: the first section regards the actual RPN, while the second part states the residual risk i.e., the amount of criticality that potentially remains after the implementation of additional mitigating countermeasures. In the same file, also the assessment scales are presented to support the calculation of the RPN. In the end, the template received the name of "tool" considering the use for which is designed.

The output is the FMECA toolkit, comprehensive of the FMECA tool, and the FMECA sources file. This last one contains the three sources used to fill the tool: the literature, the experts, and the incident reporting. The literature consists of 41 documents from which relevant statements about causes and mitigation actions are derived and assigned to a specific code B followed by a sequence of two numbers. For what regards the expert source, the information had to go through a preliminary step, the interviews, that is the method with which the knowledge of the expert Sabrina Buoro was extrapolated. The outcome of this analysis is a list of possible causes defined with the code EXP followed by an increasing number. The incident reporting come from the Lombardy laboratories. They describe real events that happened and how they were managed; relevant statements about causes, effects, consequences, mitigation actions, and even new failure modes

have been collected and translated into codes starting with IR and followed by an increasing number. Once all the sources have been collected and coded, it is the moment to populate the FMECA tool: report the codes present in the sources file into the tool; they could appear in the potential causes, consequences, effects on the patient, and possible correction actions.

The coverage obtained for the FMECA tool is not homogeneous. In particular, the causes have a final coverage index of 96%, mainly provided by literature and experts information; the consequences and the effects respectively of about 15% and 16%; finally, the mitigation actions have coverage of the 43% thanks to the literature and incident reporting.

The FMECA toolkit will be distributed in the regional structures of Lombardy to help them in the risk assessment of the PCR test process and consequently its improvement. The suggested usage is to start from the FMECA template, look at the possible events that may happen, and understand them through causes, consequences, and effects thanks to the codes and the FMECA sources. At this point, compute the RPN to identify the area of highest priority, leveraging on the pre-defined scales. If for these items there are no preventive actions already in place, adjust the mitigation strategy.

Part 2- Evaluation of COVID-19 vaccination campaigns: national benchmarking

The vaccination plans are to be repeated for the following years, and it is evident that there are many planning discrepancies between the Italian regions and between the different states.

The framework of analysis is composed of key elements, context factors, and performances. The formers correspond to the main items to describe the campaigns, context factors provide a general frame for the analysis, and performances are necessary to assess the results and effects.

Five key elements have been pointed out: the operative and organizational model, the governance model, the infrastructures, the demand management, and, lastly, the communication plan. The operational model investigates the integration of all the processes designed to create and sell products. To assess all the different entities involved in the design, planning, and execution of the vaccination campaigns it is relevant to keep track of the governance structure.

The infrastructures cover all the system and IT services deployed for the provision and distribution of the vaccines. The demand management looks at the way the population to be vaccinated is sorted and the segmenting criteria. The communication plan, instead, understands how the different regions have made people aware of the vaccination.

The descriptive variables or context factors are the elements that do not describe the vaccination campaigns but can impact them. In this regard, the management of the Covid-19 pandemic occupies a central role. In particular, the containment rules which have been applied. The second important context factor consists in knowing the structure of the Italian health system. It is to be said that the qualities and performances of the system change from region to region due to demographic and economic status; this could definitely impact the vaccination campaigns.

The performance can be split into two categories: operational performances, and health benefits. The opening of the monitor period corresponds to the end of December 2020 and terminates on the 31 of July 2021. The performances tracked are the peak and the average productivity for each region, the measurement of the duration of the campaigns. On the other hand, health benefits represent the pandemic pattern against the progression of the vaccination campaigns and the reflection of their results. To this end, the collection regards data about the number of deaths and the number of swabs tested; the average value of the Rt index, and the admission of the vaccination campaign. All the presented variables will be kept as indicators in the analysis and comparison of the vaccination campaigns.

In order to enrich the framework, some articles have been red relatively to well-known past pandemics: Smallpox, Measles, and Ebola have been deeply analyzed for what regards the vaccine delivery plans. From the study of how the governments organize the vaccination distribution, some takeaways arose.

- Stocks must be kept at a certain level to reduce the risk of stock out.
- The urban areas suffered more with respect to the rural areas.
- Epidemiological studies are crucial to finding out the disease factors.
- The severity of the contagions depends on environmental and human factors.
- The first to get the vaccine were high-risk groups.

- Socio-economic and cultural factors are strictly related to a higher vaccination uptake around the globe.
- Strong political commitment to manage the vaccine campaigns is necessary.
- The importance of having an appropriate communication and education strategy.
- Ensure procurement mechanisms to define future vaccine stocks.
- The creation of a team of experts.

The final template for the key variables is reported in *annex G,* and it is the base upon which the Italian regions selected are modeled. The idea is to represent the five pillars previously identified in an intuitive way in order to collect the data and easily compare them. For this reason, Excel was adopted, creating a visual tool organized respecting the main characteristics to be traced.

To validate the template has been used only one official document, "UK COVID-19 vaccines delivery plan" (UK Department of Health & Social Care, 2021), reporting the main features of the UK campaign. The results of the completion of this special case are reported in *annex H*.

The methodology that will define whether the degree of coverage is adequate or not is looking for the "pieces of information" the template asks. It is not fundamental for the purpose of this study to have a high degree of coverage.

Since the template has been validated is now the moment to fill in with information. In this first completion seven regions have been analyzed, Emilia-Romagna, Lazio, Liguria, Lombardy, Piedmont, Puglia, and Veneto. Successively, the same analysis performed for the UK case has been replicated for the Italian vaccination plans, comparing the degree of coverage of all the seven regions. The most problematic region was Puglia with total coverage of 29%, for this reason it was immediately eliminated from the analysis, as well as Veneto. Four regions survived the selection process: Lazio, Liguria, Lombardy, and Piedmont. Four is an adequate sample dimension for the study. All the information collected in the regions' templates is reported in *annexes J*, *K*, *L*, *M*, respectively for Lazio, Liguria, Lombardy, and Piedmont.

The regions are investigated singularly and through a cross-case comparison, touching the main commonalities and differences among the regions. The single case study tackles as main issues the capacity of the massive centers, in order

to assess which region has the higher potential to perform the vaccine administration; how regions should approach a possible transition from massive centers to pharmacies: for example, Liguria is the most advantaged region since already implemented the delivery through pharmacies and the ratio total pharmacies/MMG/PLS available over total population is the best one, especially if compared with Lombardy and Lazio cases; how the booking system and the communication campaign could have affected the adhesions; finally the composition of the vaccination staff, the ratio nurses on doctors to determine the presence or not of queues in the process. In this case, Piedmont turned out to have the best mix with a ratio higher than 1, while Lombardy and Lazio, with rates equal to 1, indicating potential queues in the anamnesis phase.

On the other hand, the main commonalities of the campaigns are symptoms of the fact that the central government set some features. The priority criteria are an example. About the operative model, the distribution of the vaccination centers follows a distributive model in all the regions; the location of the centers reflects the population density. The second point of equality is the distribution model of vaccines to the vaccination points, which is ASL-centric. As the last commonality, the possibility to speed up the overall vaccination process by means of the pre-anamnesis.

Now that the communal characteristics of the regional campaigns have been defined, it is necessary to shed light on what differentiates them.

For what regards the campaign elements, small differences emerge between the regions. For example, talking about the enlistment modalities, Piedmont is the only one that adopted the adhesion-call approach. Another distinction comes from Liguria; the region decided to involve the pharmacies in the campaign since its earliest phases. This condition could result in a fundamental advantage for the next development of the vaccination.

However, the most relevant diversities derive from a comparison of the performances of the campaigns. First of all, an analysis can be carried out on the percentage of the population that received at least the first dose in the reference period. This is a significant information because it reflects the rapidity of the regions during the observed campaign duration, which is equal to 216 days. Lombardy, although is the most populated, obtained the best performance while the last classified, Piedmont, did not keep pace with others.

Another element of interest is to observe the peak productivity of the four cases and particularly to define when it occurred: the regions with a better organization should have reached the peak earlier. The figures are associable with the concept of agility. Piedmont and Lombardy promptly reacted to the pandemic touching the maximum capacity at the end of April. Concerning the other two regions, the adapting capability to the emergency is definitely lower. Indeed, the peaks occurred more or less one month and a half later.

To understand the speed and the effectiveness of the vaccination campaign is also possible to look at the effects on the contagions, analyzing the Rt figures. All four regions exhibit similar curves in the first phase of the campaign, at least until the end of February and the beginning of March. Then, Liguria seems to take a different direction. Lazio, Lombardy, and Piedmont get to the highest Rt value on 25/02/21 and from there start a linear decrease; Liguria on the other side arrives at the peak 5 weeks later. While at the earlier stages the vaccination campaign proceeded cohesively across the four regions, between March and April, Liguria slowed down.

A further consideration arises from the merge of two elements: the level of services offered by the booking platforms of the regions and the grade of compliance to the vaccination campaign, distinct by age group. Lombardy is slightly ahead of Piedmont in all age groups; this could be the evidence of a poor correlation between the number of platform services offered and the grade of compliance because the two regions are at the extremes of the service extent. Liguria presents similar values except for the one regarding people in their 70s. In this case, it is perfectly equal to the grade of the immediately older group (93,10%), while in the other cases is always lower. Concluding, there are no indications of a strong correlation between the grade of compliance to the vaccine and the dimension of the functional services range. About the ratio administered on delivered doses, all the regions overcome the threshold of 90%. Lombardy is the only region able to keep a high level for the whole monitored period. This kind of data provides hints for further investigation; the useful index Inventory Turnover can be derived as the ratio between number of total administered doses on the total regional stocks. Piedmont and Lazio obtained similar IT ratios; they completely rotate their inventory in about one week. From the ranking point of view, this locates them still behind Lombardy with Inventory Turnover twice

bigger. Liguria takes the last position. Its ratio indicates a stock renewal only every two weeks that is by far the worst performance.

At this point, the AHP procedure can be exploited to define a final ranking.

The evaluation scale adopted goes from a maximum of 4 (best performance) to a minimum of 1 (worst performance). To determine the vaccination speed has been used as proxies the percentage of administered doses on the delivered, the date of the peak productivity, the average capacity normalized, and the peak capacity; by doing a weighted average of these performances is possible to assign 4 points to Lombardy, 3 to Lazio, 2 to Liguria and 1 to Piedmont. Secondly, has been used the number of patients that each pharmacy /PLS/MMG should cope with, in case of closing of massive centers. The most talented region, in this case, is Liguria, followed by Piedmont, Lazio, and Lombardy. The last three variables employed are: the number of over 80 vaccinated, range of services offered by the booking platform, and ratio number of first doses on the number of region inhabitants. The final AHP table ranks Lombardy as the best region.

Final conclusions

The goal of the study outcomes is to improve the performances of the two tools used to fight against the Covid-19 pandemic. The diagnostic instrument, RT-PCR tests, will be helped by the FMECA toolkit. It will be sent to all the Lombardy risk managers, who will use the tool to prevent errors and improve their processes. In conclusion, the toolkit is a base of knowledge upon which all the institutions can integrate information from their personal experience.

The second outcome provided by the thesis is the definition of a framework of analysis that can be applied to compare different vaccination campaigns. The template should be filled with the data of the object of interest and, at that point, will be easy to perform a standardized comparison. The coverage indexes for the four tables are about 45% for Lazio, 44% for Liguria, 55% for Lombardy, and 49% for Piedmont. The thesis also offers suggestions to interpret the data and derive considerations about the vaccination campaigns.

By looking at the results from the Clinical Governance perspective, they definitely address the two proposed problems. As highlighted, many issues and difficulties could arise both from the RT-PCR diagnostic procedure and the creation of vaccination campaigns. However, thanks to the conducted study and its

outcomes, it is now possible to have in your hand simple tools which could be applied to better face these situations. Anyway, it is relevant to develop research and studies to analyze the conditions and derive possible ways out. In this case, standardization is the key to success. The instruments born from the analysis can be applicated, modified, or further implemented to investigate the current pandemic and not only.

The innovation degree of the study is high; no previous works about the RT-PCR test process and evaluation of vaccine campaigns exist. In addition, when the pandemic broke out in Italy, the last pandemic plan updated date back to 2006.

The researcher who approaches the analysis done on the comparison of vaccine campaigns will be offered a more recent point of view on how to manage a pandemic. What is more, he or she will be able to model, basing on the template created, analyze, and evaluate different pandemic plans leveraging a substantial breadth of contents.

Thanks to the two analyses developed in the thesis, the hospitals, and regional healthcare facilities can rely on a set of tools intuitive and easy to apply.

On the one hand, the FMECA toolkit's object is to help the laboratorial structures in Lombardy in the risk assessment of the RT-PCR test process and its optimization. On the other hand, the vaccine campaigns comparison provides regional healthcare infrastructures with a new way to model, evaluate, and describe a plan.

FMECA method had been time-consuming, and it will be a limitation also for the hospitals when they start using the toolkit. Instead, the main restriction regarding the vaccination campaigns template is the collection of proper and updated data.

Anyway, there are possible further developments for the analysis. The FMECA should be renewed every year with new incident reporting coming from the laboratory structures of Lombardy to increase the information coverage degree.

The FMECA analysis could also cover all Italian territory to increase the standardization procedure at a national level. There is also the possibility to create a panel of experts to increase the population of the FMECA sources.

For what regards the evaluation of the vaccine campaigns, the analysis applies to all the Italian regions to understand the most talented ones and take helpful hints to improve the regional plans. Moreover, the national campaign can be evaluated and benchmarked with other nations.

Last thing last, the objectives of the first part of the study are achieved without critical obstacles. For what concerns the second part, unfortunately, the lack of data and the Covid presence still widespread in Italy slowed down the work forcing a resettling of the scope of analysis: instead of providing guidelines for the future plan, the study will concentrate on an in deep comparison between vaccination campaigns.

Chapter 1- INTRODUCTION

1.1 Covid-19 pandemic outbreak

In December 2019, an outbreak of infection of a severe respiratory syndrome (SARS-Cov-2) was detected in Wuhan, China. This virus, now known as COVID-19, was announced by the World Health Organization (WHO) on January 20, 2020 and became a global pandemic. The alarming factor was the speed at which the infection was spreading, causing until now millions of deaths.

To follow are reported two dashboards provided by the WHO about the distribution of the cases (*figure 1*) and deaths (*figure 2*) around the world (the data are referring up to the 7th of May 2021).

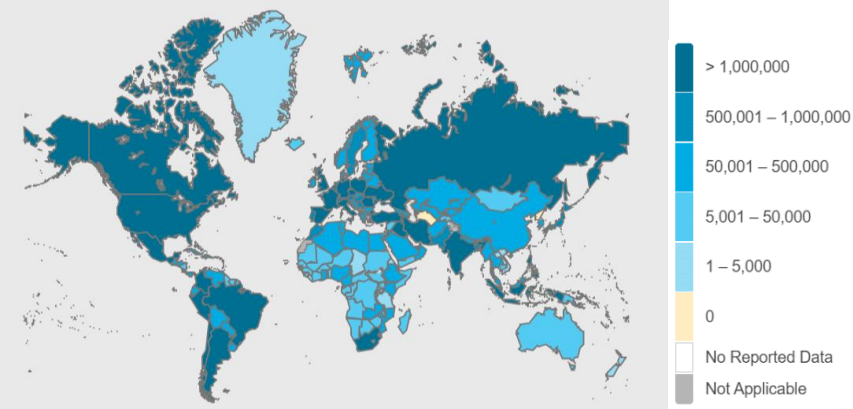


Figure 1- Distribution of cases around the world

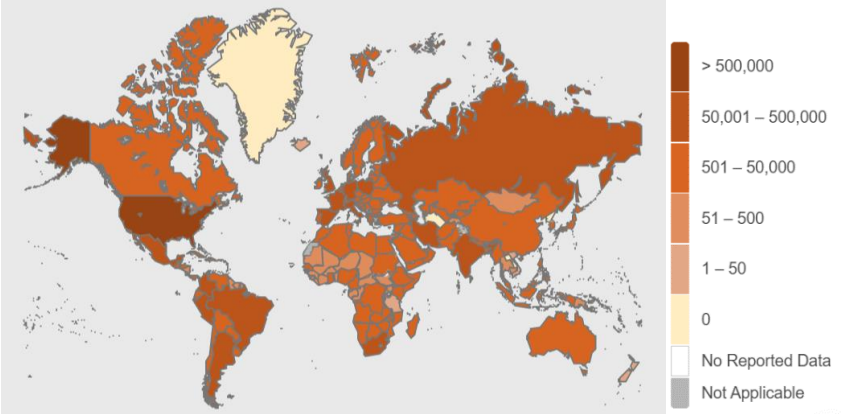


Figure 2- Distribution of deaths around the world

Globally, up to the 7th of May, there have been **155.506.494 confirmed cases** of COVID-19, including **3.247.228 deaths**, reported by WHO.

An unprecedented worldwide spread of the SARS-CoV-2 has imposed severe challenges on healthcare facilities and medical infrastructures. The global research community faced urgent calls for the development of rapid diagnostic

tools, effective treatment protocols, and most importantly, vaccines against the infection. Sreepadmanabh M, Sahu AK and Chande A. (COVID-19: advances in diagnostic tools, treatment strategies and vaccine development, 2020) published an article about diagnostic tools, treatment strategies, and vaccine development. They classified those three elements as the pillars to fight against Covid-19 spread; each of them can be implemented using different tools, described in the same article. (*Figure 3*)

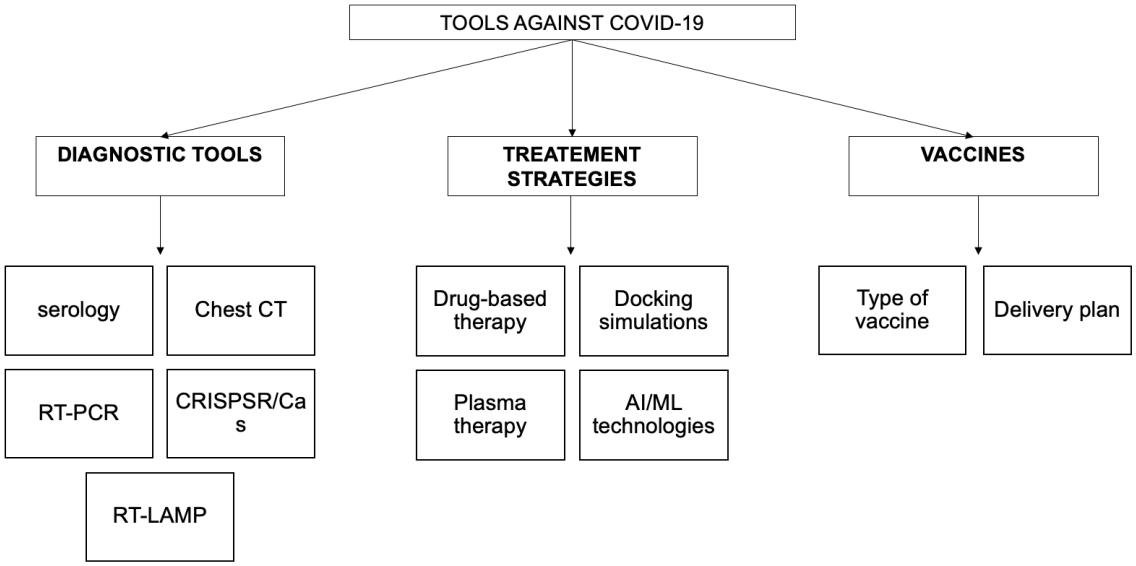


Figure 3 – tools against COVID-19

The **diagnostic tools** are methods to discover the pathogen presence. They are classified into five main instruments: serology to detect the presence of IgM and IgG antibodies; Chest scan which has very excellent accuracy, but it is inappropriate in case of mass testing; RT-PCR aims at detecting viral SARS-Cov-2 RNA sequences in nasopharyngeal swabs; CRISPSR/Cas to spot the nucleic acid, however nowadays is still an emerging technology; RT-LAMP as a way to amplify the sequences of viral RNA in one single step.

The **treatment strategies** highlight the different possibilities to take care of the patients infected by the virus. The most common strategies are the administration of drug therapy, as an example antiviral chloroquine and its derivative hydroxychloroquine have received much attention during the pandemic. At the same time, docking simulations can be carried out to identify the potential inhibitors of the SARS-COV-2 protease. Plasma therapy means adopting blood plasma obtained from recovered patients as an adaptive immune therapy for critical cases. Artificial Intelligence and machine learning techniques can be

applied to get dynamic monitoring of patients in real-time, enabling critical evaluation and optimization of the treatment protocols in an efficient manner.

The last but not least tool against the pandemic is for sure the development and distribution of **vaccines**. Their importance is stated by the high degree of protection they provide against Covid-19. The two main pillars of vaccinations strategies are the right selection of vaccine type and the delivery plan to make vaccines available to all the population.

Traditionally, vaccine development takes years, even decades: from about 40 years for Polio to 5 years for Ebola. The trial for vaccines, indeed, consists of several steps which need to be conducted systematically. The race for Covid-19 vaccine discovery and development led to many candidates, just a few of them received the final approval from the pharmaceutical institutions.

In Italy, just four of them are currently used: **mRNA-1273** by Moderna, **BNT162** by Pfizer-BioNtech, **ChAdOx1** by AstraZeneca and **Jhonson&Jhonson** by Janessen. The first two are based on the principle of messenger RNA, while the ChAdOx1 and J&J are vectorial vaccines. The main features, available on the ISS (*Istituto Superiore di Sanità*) website, referring to the 5th of July, are reported and synthesized in the following table (*table 1*).

	PFIZER-BIONTECH	**MODERNA**	**ASTRAZENECA**	**JANSSEN (J&J)**
FEATURES				
Type of vaccine	Messenger RNA (mRNA)	Messenger RNA (mRNA)	Vector vaccine	Vector vaccine
Doses	2 doses with 28 days of distance	2 doses with 28 days of distance	2 doses with 4-12 weeks of distance	1 dose

Table1- Vaccines' characteristics

As vaccine capacity ramps up, the challenge is to ensure inclusive, safe, and sustainable distribution to reach frontline healthcare workers, the risky groups, and eventually all people around the world. The creation of suitable delivery plans is the main issue of governments that have to deal with and organize the vaccination network.

1.2 Objectives of the study

When the Covid-19 outbreak, the primary goal of epidemic containment was to reduce disease transmission by lowering the number of infected people or the reproductive index (R_0). Given the lack of effective vaccines, the only available method was to reduce transmission by isolating people who were contagious.

The priority was the necessity of a rapid mass screening system to map the cases, therefore an effective diagnostic testing process to identify infected people is central to control the global pandemic of Covid-19. For that purpose, the WHO selected the real-time reverse transcription method, known for short as RT-PCR, as the standard methodology in laboratories. The RT-PCR test process is aimed at detecting viral SARS-Cov-2 RNA sequences through nasopharyngeal swabs. Clinical laboratories were in the front line when it came to implementing this policy of mass screening and testing.

Looking at the increasing number of deaths and new cases, the only way to give away with the virus was to develop vaccines. The creation of vaccines gives the possibility to get protection against the disease, developing an immune response to the virus. Reaching immunity is a victory for all the world, which enables to escape from the illness and its injurious consequences.

Since RT-PCR and vaccines have a crucial role to fight against the infection, the thesis will be focused on them. (*Figure 4*)

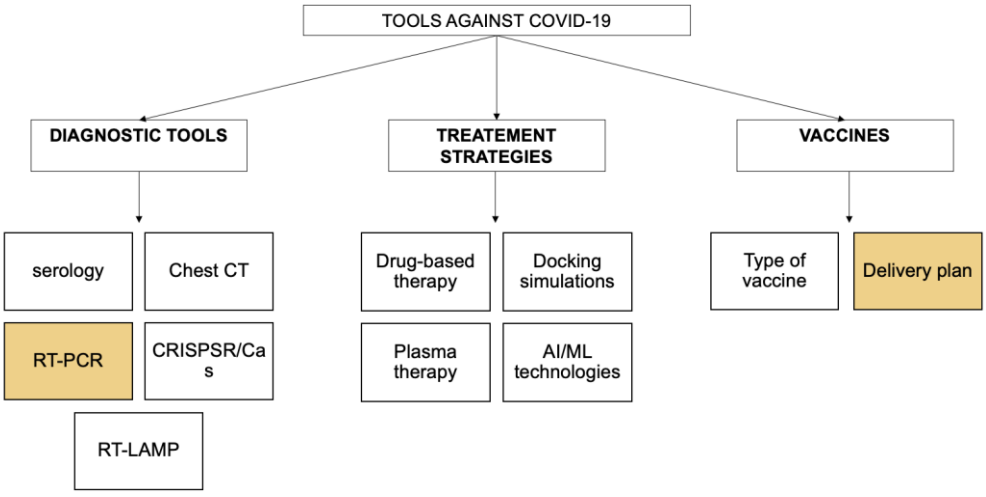


Figure 4 –The objects of the thesis

Real-time PCR is a complex method comprising several stages. To ensure the reliability of test results it is important to manage risks that could arise at each

stage of the process, from the first contact with the patient to the delivery of the final report.

For that reason, the first object of this thesis is to classify any possible source of risk that can affect the quality of the tests' results and construct a Failure Mode and Effects Criticality Analysis (FMECA), comprehensive of adverse events, causes, effects and mitigation actions. The idea is to create a tool that can be shared among all the laboratorial structures, in order to be used as a standardised approach to risk assessment. By providing the laboratorial structures with a standard FMECA, it will be possible to trace and reduce errors during the overall process.

About the vaccines, all the vaccination plans are different from country to country, but also within the single states. Due to the immediate necessity of delivering vaccines, plans have been developed rapidly and therefore are more vulnerable to problems and limitations. The creation of an ad hoc distribution system is a relevant issue that concerns all the states. Indeed, in order to reach global immunity, the population should repeat the vaccination for the following years.

For the reasons just described, the second and last object of this thesis is the comparison between the different vaccination plans developed by the Italian regions, to determine which region designed and executed the best administration campaign and get precious hints of it.

1.3 Thesis structure

The thesis will follow the scheme represented in *figure 5*.

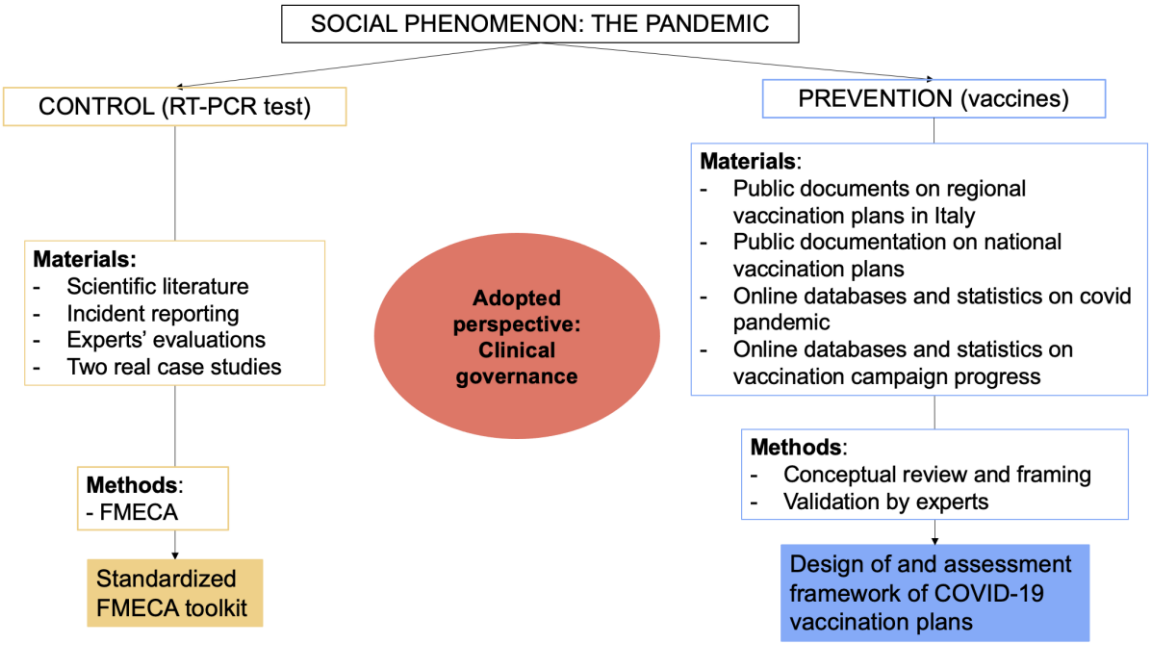


Figure 5 - The thesis structure

At the top of the scheme is reported the problem to mitigate: the pandemic, as a social phenomenon. Indeed, it is an event that is affecting the structure and the organisation of the society, by changing the habits and behaviour of the population. Because of the pandemic the different organisations had to design specific tools and methodologies to cope with it.

The perspective that will guide the reasonings along the whole thesis is the one of clinical governance which will be discuss in chapter 2.

The two main leverages to eradicate the problem under investigation are the previously anticipated tools: diagnostic tests with PCR and vaccines. They are two faces of the same coin: on the one hand, tests are used ex-post to detect, and isolate infects. On the other hand, vaccines are essential to address the problem a priori creating antibodies to fight against the virus.

In this thesis, the two action leverages selected will be treated in two different sections.

The first part will be about the reactive method, reported in chapters 3 and 4, that is the control and management of the pandemic through the identification of positive cases: the PCR test process. In this section, the analysis will be focused on the laboratorial structures located in Lombardy and the study will be conducted thanks to four major sources of information: the scientific literature, incident reports of the regional structures that will be examined to keep track of real failures occurred in the process, experts interviews and two case studies of the

structures of Mantova and Brescia. The aim of this part is to draft the risk assessment of the overall PCR test process, focusing on the main subprocesses: generation of the demand, pre-analytical, analytical, and post-analytical phases. The final output will result in the definition of a standardised toolkit leveraging the FMECA methodology. The toolkit will show the main deviations of the process, the causes that induced them, the consequences, the effects on the patients and the mitigation actions. Thanks to this product the laboratorial structures will receive crucial help when assessing and improving the criticalities of the RT-PCR testing process.

The second part will address the proactive approach to deal with the current pandemic i.e., the design and management of the vaccination plans. This study will be disclosed by a comparative study of different Italian regional vaccination plans. The sources that will be analysed are official documents of vaccination plans of the public domain, found on the official websites of Italian regions. Moreover, online website reporting updated data and statistics of the ongoing pandemic situation and about the vaccination results will be consulted.

Each source of information of this part will be critically reviewed and a validation process will also be required, in order to define a detailed model of analysis that will be used for evaluating future Covid-19 vaccinations plans. To this end, the selected vaccination campaigns will be studied both singularly and together to find out which characteristics result to be better in such context.

Chapter 2 – CLINICAL GOVERNANCE

The COVID-19 pandemic introduced several hustles in its management. This is caused by an unknown virus and the necessity has been the creation of ad hoc measures to cope with the emergency and new clinical processes and paths to provide care to acute COVID-19 patients. Accordingly, new and difficult challenges have evolved under both organizational and clinical points of view. While central and local governments deal with the former, the latter is entrusted to the general principle of clinical governance. Clinical governance (CG) is defined by ISS as "the organization and performance of the activity of a healthcare facility, aimed at empowerment and participation, in strategic and management choices, of all those involved in the provision of healthcare services"[1]. It is nothing less than a strategy aimed at controlling and improving the performances of healthcare services. CG must encompass three key principles which are, high standard of care (1), transparent responsibility and accountability for those standards (2), and constant dynamic improvement (3)[2]. Which means that, besides providing help to assist the health benefits, it is also a dynamic tool that should be revised and optimized when new information is available. The clinical governance framework is made up of different kinds of tools, but ISS highlights 8 1main categories as the most important for the Italian health system. They are guidelines; information and involvement of citizens and patients; Essential Levels of Assistance (LEA); patient classification system; Clinical Risk Management (CRM); evidence-based medicine, health impact assessment and Health Technology Assessment (HTA). These are the sectors that are identified as crucial for the Italian CG, offering a complete spectrum to analyze and describe the quality of the clinical frame. In particular, they look at two main perspectives, the first is external oriented, looking at the grade of the information offered to people and the way how the population is segmented, while the other one takes care of the internal performances and processes of healthcare institutions. Given this second aim, Clinical Risk Management, Health

[1] https://www.iss.it/web/iss-en/clinical-governance-national-guidelines-system-snlg-and-hta1

[2] Gopal K. S. & Ahmad Kamar A., Clinical Governance and Ethics During a Pandemic, In Tan H. S. & Tan M. K. M. (Eds.), "Bioethics and COVID-19: Guidance for Clinicians", *Malaysian Bioethics Community*, 2020, 1st Ed., pp. 7-9.

Technology Assessment, and guidelines take a central position. Indeed, CRM investigates and define the clinical procedures and guidelines to improve them through the identification and resolution of the main risk causes. On the other hand, HTA is a set of methodologies created to assess the value of health technologies during the stages of their life. The term “health technologies” involves a broad set of elements, such as drugs, devices, tests, medical procedures but also measures for the prevention and rehabilitation from diseases, and organizational and support systems in which health care is provided.

Finally, the category “guidelines” refers to a compilation of suggested measures, actions, and tools to be applied when dealing with certain conditions.

This is the general baseline in which the analysis is constructed. In particular, from the given definitions, it is clear how the investigation interacts with the concept of clinical governance and more specifically with Clinical Risk Management, in the first part of the study, and with guidelines concerning the vaccination campaign analysis.

2.1 Clinical Governance issues of Covid-19 pandemic

Even if the concept of clinical governance is nowadays well established and known among the health systems worldwide, in special conditions, as the one addressed in this thesis, it is essential to understand if some modifications have been introduced on the baseline reference framework. To this end, some scientific literature has been consulted to pull information about the clinical governance approaches adopted during the Covid-19 pandemic and also about the main issues that could affect the CG strategy under such unpredictable conditions.

As introduced above, CG can be practically implemented through a set of tools which may assume different levels of importance under specific contextual conditions. Specifically, Sheila Gopal Krishnan and Azanna Ahmad Kamar (2020) inside “Bioethics and COVID-19: Guidance for Clinicians” identified five main technical components from clinical governance that should be applied during a pandemic.

1. Health, Safety, and Staff management: the establishment and communication of containment measures aimed at protecting the staff wellbeing. Ensure service continuum, mitigating the impact of quarantine absences and balancing demand-offer through proper planning. Act with accountability and transparency by declaring all the possible effects on staff and guarantee that protection standards will be applied.
2. Risk/Crisis management: verify whether an updated, well-designed, and sufficient crisis management plan is in place. It should contain contingency plans, thoughtful communications, accurate clinical documentations and data sources and person risks and emergency succession plans.
3. Strategic opportunities: be sure to keep track of the data and events and conduct research because they could be useful for future pandemic plans.
4. Aftermath & Audit: study and evaluate the changes which had to be introduced during the pandemic because they could be a potential improvement even in stable conditions. Define the lessons learned to create incentives for continuous improvement and be more prepared for the next crisis.
5. Ethics and Clinical Governance: define figures and roles able to connect good governance and ethical values since in these special contexts with resource-constrained health service is essential to translate them into actions.

Having defined the key CG elements that need to be considered is now relevant to understand what are the possible implications and issues that may be encountered during severe pandemics such as the Covid-19 one.

First of all, the lack of resources. This is the most likely hustle, and it encompasses different aspects that could be problematic for the management of the emergency. Indeed, clinical governance must guarantee the availability of the needed resources to ensure the continuity of the healthcare systems; therefore, it is of paramount importance to tackle the what, the how and the why of all the tasks to be performed to develop a proper action plan. The most important asset to be managed is human resources. People working in healthcare facilities must follow correct scheduling and must be trained effectively. To manage the current pandemic, as already stated in chapter 1, other two typologies of resources are necessary, the ones enabling the

diagnostic tests and the vaccines. For what regards the protection policy it is important to ensure the highest possible levels of vigilance and responsiveness, in order to do so the diagnostic procedures must be carried out smoothly. In this specific case, the process chosen as standard is the RT-PCR method, which could hide many pitfalls. For this reason, is necessary to deep dive into the whole process, identify the main sources of risks and deal with them. As concerning vaccines distribution and administrations the major cause of problems is lack of resources. Only a few of the 150 candidates[3] are currently available and therefore all the governments must compete for a limited number of doses. In addition, once the doses are ensured to the population is necessary to develop an action plan to define time, money, materials, and human resources.

"Clinical governance is about promoting continuous improvement as well as establishing baseline standards."[4] This sentence makes explicit a further objective of CG, to create formats and made them available to enable the monitoring of all the healthcare structures. This view could be however compromised during pandemics and crisis in general. The context contains a high degree of unknown and uncertainty and consequently, it is not simple to have a clear vision of what should be the best standard approach nor if it will work.

Moreover, it is of paramount importance to highlight what are the most appropriate primary care indicators that need to be collected and analyzed. However, since the events and implications may rapidly change this kind of selection requires time and trials.

During extraordinary conditions one element that cannot be underrated is the collection and reutilization of information. Indeed, it is fundamental to record all the data and events in order to create a base of knowledge that could furnish a great help for the future. Even if this is the goal, pandemics totally mess up the ordinal performances of health care systems, people find

[3] The Lancet, "Global governance for COVID-19 vaccines", *The Lancet*, 20 June 2020, Vol. 395 (10241), pp. 1883

[4] Huntington J, Gillam S, Rosen R., "Organisational development for clinical governance", *BMJ,* 16 September 2000; Vol. 321, pp. 681

themselves overwhelmed by urgent tasks and may neglect the traditional recording procedures such as the completion of incident reporting.

Another important issue that clinical governance may undergo during healthcare emergencies is a decrease in the availability and quality of ordinary primary care services. In fact, all the care facilities turn their business accordingly to the ongoing situation and this leads to a reduction in the execution of ordinary activities. This is of course a relevant disadvantage for clinical governance because it impacts the overall performance and the continuity objective.

These are the major typologies of problems that clinical governance is called to face during a pandemic. In particular, in this thesis will be analyzed the first two points which will be seen from the point of view of the RT-PCR procedure and its main sources of risks and from the vaccination campaign which need to be organized managing a wide set of resources.

PART ONE

Clinical risk Assessment of the PCR test process

Chapter 3- STUDY METHODOLOGY

3.1 Clinical risk management

Clinical risk management (CRM) can be defined as ‘‘an approach to improving quality in healthcare which places special emphasis on identifying circumstances which put patients at risk of harm, and then acting to prevent or control those risks. The aim is to both improve safety and quality of care for patients and to reduce the costs of such risks for health care providers” (Walshe and Dineen, 1998). From a more practical point of view, it has been defined as ‘‘the system of guidelines, protocols, steps, organizational and clinical procedures adopted by a hospital to reduce the probability that events and actions, that might potentially produce negative or unexpected effects on the health of patients, occur” (Floreani,2005).

The incidence of adverse events in the health industry has increased in the past years. This has pushed the governments to set up institutions to guarantee safety protection and quality of healthcare. For instance, the United States, UK, Australia and Canada have all created patient-safety institutions since 1999. These measures are meant to identify the risks that could arise and neutralize them to improve the overall perfomances.

One possible classification of clinical risks divides them into the following categories (Ministero della Salute, 2004):

– Errors in the use of pharmaceuticals: prescription, preparation, transcription, distribution, administering, and monitoring.

– Surgical errors: surgery on the wrong part or side of the body, unnecessary surgery, incorrect management of the patient and so on.

– Errors in the use of equipment: malfunctioning caused by technical problems during manufacturing, malfunctioning caused by the person using the equipment, equipment utilization in inappropriate conditions, inadequate maintenance, inadequate instructions, incorrect cleaning, use beyond the stated life cycle of the equipment.

– Diagnostic exams or procedures: not carried out, planned but not carried out, carried out inadequately or incorrectly, carried out correctly but on the wrong patients.

– Timing errors: delays in pharmaceutical treatments, delays in carrying out surgery, delays in diagnosis, and other organizational, management, or logistical tasks.

Now that is clear what CRM is and which are the main risks that a healthcare structure can suffer, the next step is to define how the risk management process works. The process of risk management is determined by a first phase of identifying risks, a second phase of risk evaluation and quantification, and then a third of risk treatment in which the measurements and tools for management and mitigation actions are planned. The cycle ends with the implementation of a control program to be applied on the process. (*Figure 6*)

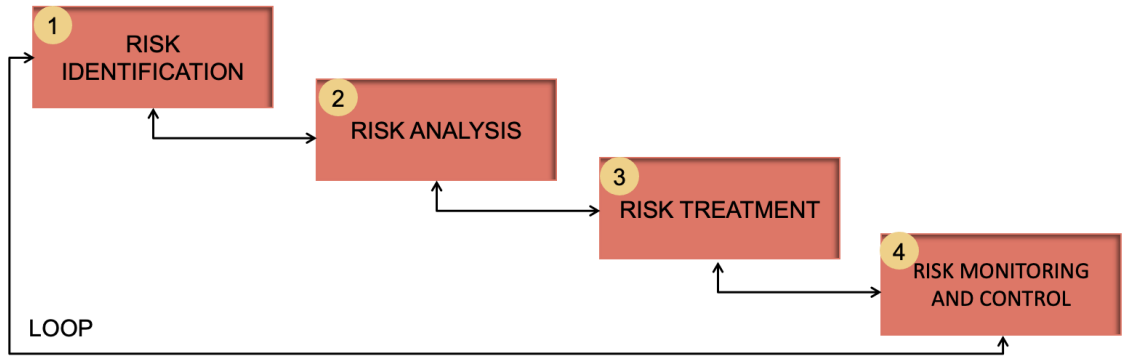


Figure 6 – phases of the process

In order to properly manage and control risks it is of paramount importance to have a clear and detailed picture of the hazards that may have an impact on the environment of analysis. This is the aim of the **risk identification** phase; it basically consists of creating a list of possible events describing their sources and consequences. Once the possible risks are mapped it is essential to dip dive them in the **risk assessment** phase, which purpose is to perform a detailed consideration of uncertainties, risk sources, consequences, likelihood, events,

scenarios, controls, and their efficiency. What is important is to arrive at a prioritization of the identified risks, which will be used as an input for the last phase, the **risk treatment.** When approaching the treatment step the purpose becomes to create and apply mitigation plans to reduce the effects of risks. Since the execution of these programs is not for free but it requires the use of resources, time, and money, it is essential to keep priorities in mind. The **monitoring and control** phase gives a push forward to the continuous improvement of the clinical disciplines; the idea is to periodically check the strategy in use iteratively repeating the first three steps in order to see if some adjustments are required.

The organizational theories used to deal with problems in healthcare contexts are mainly based on human reliability and the human factors methods. Among them, the well-known model developed by James during the 90s, called "*swiss cheese*" represents how to deal with such problems. (*Figure 7*)

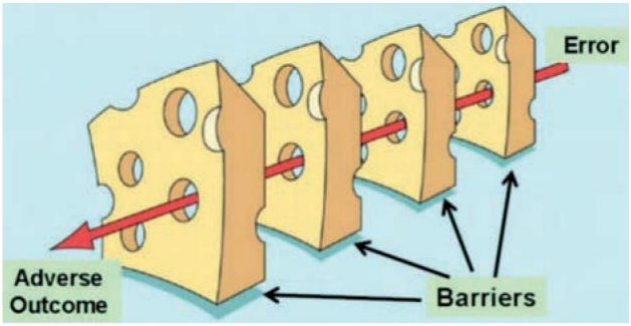


Figure 7 - Swiss cheese model

To prevent downside, institutions set up different barriers (represented by the slices of cheese); they can be of many types, among procedures, standards, control, and safety features. However, these defensive measures could be deficient due to process' failures or errors that can weaken them; the holes inside the cheese slices reproduce these treats. Since the healthcare system is dynamic, the barriers can and must be modified, upgraded. When this occurs, there is the possibility that the holes will line up. It generates a chain of conditions that can lead to adverse events occurring.

The role of a risk manager is to reduce the probability of occurrence of an adverse event (prevention) and, at the same time, reduce the severity of the impact when an event occurred (protection). The operator should have the means to execute a reactive and proactive analysis to identify and eliminate a process's criticality. The investigation should focus on the overall process, identifying the critical

activities with the final aim to project safer healthcare systems. A risk manager must have in its package of knowledge both reactive and proactive tools. The following scheme reports the main ones of the two categories. (*Figure 7*)

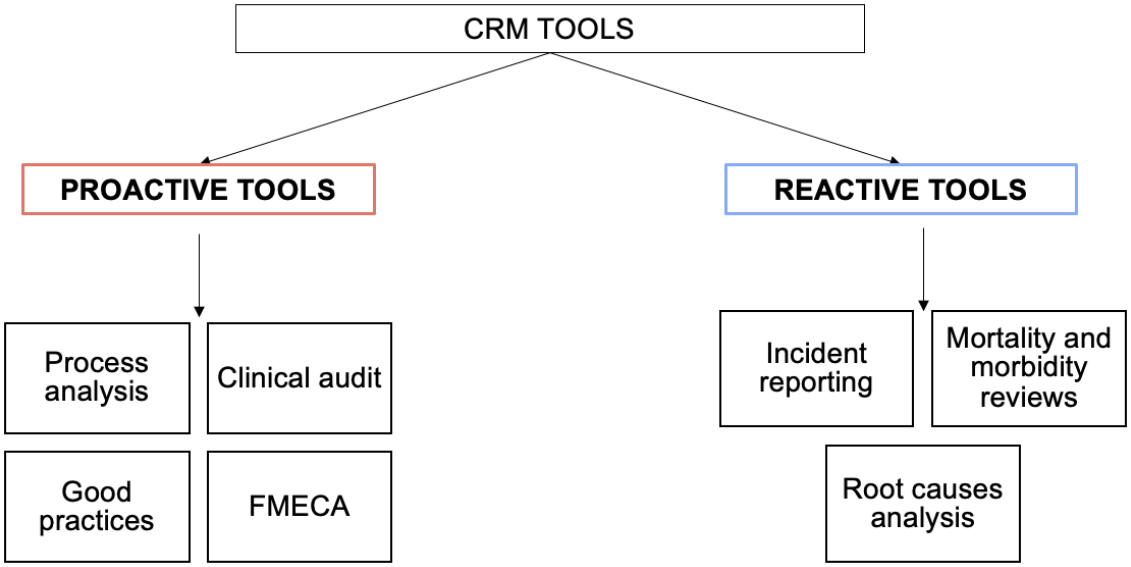


Figure 8 – CRM tools

In general, the tools can be used singularly or coupled to obtain more robust and complete results. Usually, proactive methods are highly suggested because they enhance the preparedness in case of failures. Anyway, in difficult and unpredictable situations, such as the Covid-19 pandemic, the capability of developing and implementing reactive tools effectively and suddenly is without any doubts of paramount importance for any kind of business.

The two following figures provide a brief description of all the identified tools (*figure 8-9*).

PROACTIVE TOOLS			
Good practises	Clinical audit	Process analysis	FMECA
Practices with demonstrated success and can be replicated. (i.e., disinfection of the areas, correct identification of patients, filling check lists)	Carried out by an interdisciplinary team, with the aim of identifying organizational criticalities and the related suggestions of improvement.	Map the overall process flow. Analyse process subprocess and activities through indicators to assess their efficiency and effectiveness.	Failure mode risk analysis, is a way to assess the critical activities, prioritize them, and intervene with mitigation actions.

Figure 9 – Proactive tools

REACTIVE TOOLS		
Incident reporting	Root causes analysis	Mortality and morbidity reviews
The tracking of adverse events inside the organisation. Is an easy way to map risks inside the healthcare structures.	Technique aimed at defining the primary cause of an adverse event. Known also as ishikawa diagram or fishbone diagram.	A periodical discussion of the cases that have had an unexpected outcome or whose management was particularly difficult.

Figure 10 – Reactive tools

After having defined how to approach risk management in healthcare infrastructure, is now possible to start with the assessment of PCR test process and vaccine plans.

3.2 Clinical setting

The rapid outbreak of Covid-19 disease has forced countries to develop systems for the vastest possible testing of their citizens. The World Health Organization (WHO) pushed countries to carry out as many tests as possible to track and isolate cases. The preponderance of the laboratories implemented the RT-PCR (reverse transcription- Polymerase Chain Reaction) test method for the diagnosis, indicated by the WHO. This technique was discovered by Mullins in 1985, allowing him to earn the Nobel Prize in Chemistry in 1993. SARS-COV-2 is an RNA virus meaning that it can be detected using that kind of approach.

The demand for diagnostic tests with the spread of the pandemic was extremely high. The consequence affected the laboratories that met many challenges in terms of staff, equipment, and logistics.

Adapting to this situation, the clinical laboratories had to: reduce their usual activities to concentrate their efforts in PCR testing, recruit and train new staff to carry out the test, select and implement tests, manage stocks and orders while facing reagent shortage.

The risk of erroneous results, which could be either false positive or false negative, is real. The reliability of the tests depends on many factors. An example is the quality collection of the sample, its transportation, or even directly the performance of PCR kits. All these elements contribute to elevating the difficulty level of the process. For those reasons is of paramount importance for

laboratories to be aware of their limits and adjust their practices to optimize the testing process. In order to do so, it is relevant to determine the main features of the process to be able to classify each event in a specific stage of the process.
The medical diagnostic test is a complex process carried out in four main stages: demand generation, pre-analytical, analytical, and post-analytical, as figure 11 shows. They are successive and strictly dependent: the quality of the output at each phase influences the successive one. Therefore, while analyzing all the possible problems affecting the single step, it is crucial to assess the impact on the downstream stages.

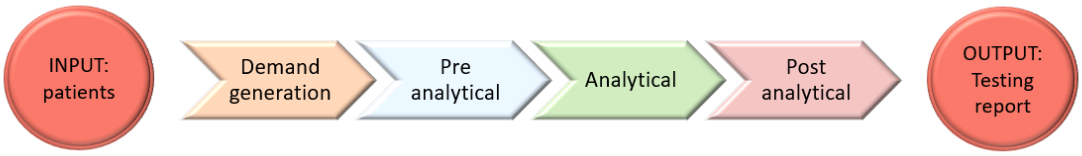


Figure 11 – process map

The input of the overall process is the customer, in this case patient who need a diagnostic test. The output, instead, is the result of the test in form of reporting.
To conclude, the object of this chapter is to identify and analyze the principal risks encountered with the SARS-Cov-2 detection process and to suggest some alternatives to deal with them.

3.3 Sources

This study took place from the urgency of creating a standard template to assess the main criticalities in the testing process and to highlight possible ways out. To this end, different perspectives and backgrounds are necessary. A task force was created to gather people coming from different environments. Liviana Scotti and Enrico Burato as representatives of Lombardy Region were part of the work group. At the same time, Dr. Sabrina Buoro and Enrico Comberti assisted with their expertise in the testing process. The team was then coordinated by Prof. Paolo Trucco for what regards the risk management methodology to be applied.
The sources of information used in this analysis are three. The first one is the literature collected from online libraries (Pubmed and Scopus principally), which is made up of 41 documents between scientific articles, opinion papers, reviews, case reports, and letters to the editor. Then there is the incident reporting

documents furnished by hospitals and structures located in Lombardy. This source comes from the request of the region to keep track of unsuccessful events and, or problems verified during the processes. Last but not least the judgments of experts, will be relevant in the analysis to cover the topics not covered by the other two sources. The professionals' knowledge will be extrapolated through interview sessions.

3.4 FMECA in laboratory medicine

3.4.1 introduction to FMECA method

In the most recent ten years, many methodologies and tools traditionally belonging to the industrial risk management have been readapted in the clinical contexts, as Onofrio et al. (2015) tell in their work, “Failure Mode, Effects and Criticality Analysis (FMECA) for Medical Devices: Does Standardization Foster Improvements in the Practice?”. As a result, the FMECA (Failure Mode Effects Analysis) methodology, and its most recent implementation, the HFMECA (Healthcare Failure Mode Effects Analysis) are nowadays the most applied proactive risk analysis methodologies in the health care industry. Specifically, FMECA has been proven as reliable for detecting risks in a process involving medical appliances, while HFMECA is more geared to deal with clinical processes.

FMECA is an inductive, bottom-up approach aimed at evaluating a specific process under analysis in terms of potential failures and their impacts, providing a criticality ranking. Failure must be intended as any typology of deviation from the expected outcome of the process. The FMECA objective can be achieved following five main steps defined by Clemente et al. (2019).

a. Definition of a multidisciplinary team,
b. Identification of sub-processes and main activities,
c. Identification of failures,
d. Scoring of the failures,
e. Suggestion of corrective actions.

Once the team is composed the selected process must be fragmented into elementary sub-processes in order to facilitate the analysis. Moreover, it is also significant to highlight the connections between the activities which form the

procedure. At this point, it is of paramount importance to identify the failures which could occur within each sub-process and describe them according to their failure modes, causes, and effects.

- *Failure mode: the way a failure manifest itself.*
- *Failure cause: primary motivation that makes the failure happen.*
- *Failure effect: the consequence of the failure, associated with a severity.*

It is now the moment of the scoring of the highlighted potential failures. The risk management team will have to leverage its experience and process knowledge to assign the score. The traditional procedure suggests computing the RPN (Risk Priority Number), an index expressing the criticality level for each failure. It is calculated by the multiplication of three factors: the probability of occurrence (P) which is the likelihood to happen of a failure, the severity of consequences (S) measuring the seriousness of the possible risk effects and the detectability (D), the capability to detect a failure before it may occur. The RPN assessment is carried out at first with qualitative scales and then converted into quantitative evaluations. Onofrio et al. (2015) identify as the most used ranges between 1 and 5 or alternatively between 1 and 10. However, the scales can be empirically defined by the team of experts.

In the table below is presented an example of the RPN computation.

ITEM	P	S	D	RPN
sub-process1	P1	S1	D1	P1*S1*D1
sub-process2	2	5	3	30

Table 2- Example of RPN calculation

The ranking based on the RPN will highlight which are the most critical failures and therefore should be held in high regard. Furthermore, a threshold could be selected as has been done in the study “Critical failures in the use of home ventilation medical equipment” (Clemente et al., 2019); this will easily allow determining which is the last element of the analysis to be assigned to the extreme level of criticality.

The last step of the FMECA procedure implies investigating some corrective measures for the listed failures modes. Inside this phase, the expertise of the ones involved in the analysis assumes a particularly crucial role. It must be used to create a list of specific countermeasures to limit the effect of the risks.

Actually, the last two phases, the assessment of RPN and the creation of remedial action, could be iteratively repeated once that the corrective actions have been executed to verify their efficiency. If the corrections were accurately designed and implemented, then a decrease in the RPN value should emerge. If this is the situation and some rank reversals have been obtained the elements belonging to the next level of risk can be addressed. If not, the suggestion is to find out new alternative solutions to improve the situation.

Figure 12 reports the possible appearance of the FMECA tool.

Rewew team:				Process stakeholders:								Date			
Supplier:				Key project dates:							Tollgate 1 completed:				
Product:											Tollgate 2 completed:				
											Tollgate 3 completed:				
												Anticipated results due to proposed action(s)			
Item and Function	Potential Failure Mode	Effects of Failure	Projected Severity at 1st ship Rank 1 - 10	Cause(s) or Mechanism(s) of Failure	Projected Probability of Occurrence at 1st ship Rank 1 - 10	Key Process or Product Characteristic Yes/No	Current Design Controls	Projected Probability of Detection at 1st ship Rank 1 - 10	Ranking or Priority Number (Calculated 4X6X9)	Proposed Action(s)	Responsibility and Planned Completion Date	Severity Rank 1 - 10	Probability of Occurrence Rank 1 - 10	Probability of Detection Rank 1 - 10	Ranking or Priority number (Calculated 13X14X15)
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Part and/or Product															
Liability									0						0
New Technology									0						0
Process Complexity (Delivery Performance)									0						0
Process Complexity (Cost)									0						0
Specifications (Incoming quality)									0						0
Business															
Core Competency									0						0
Ownership									0						0
Capacity									0						0
Quality System									0						0
Financial									0						0
Environmental									0						0
Facilities									0						0
EDI/TradeWeb									0						0
Relationship															
Segmentation									0						0
Finished Goods									0						0
Sole/Single/ Multi Source									0						0
Lead Time									0						0
Logistics									0						0

Figure 12 - Example of FMECA

3.4.2 State of the art on FMECA in laboratory medicine

This chapter will be dedicated to the detailed analysis of a FMECA application with respect to the PCR test processing conducted in the document “Reliability of RT-PCR tests to detect SARS-CoV-2: risk analysis” by Clément Bezier *et al.* (2020). This investigation will be helpful to understand the level of details and the elements to be included in the final output of the study: the standardized FMECA toolkit. In this specific case, an undesirable event can be either the incorrect result of the test (false positive or false negative) or an exceeding in the reasonable delivery time limits of the result report. In order to track all the possible risks in this context is relevant to have a transversal vision of the laboratorial processes,

by looking at both technical and organizational issues. In *figure 13* is the definition of the scales used to perform the FMECA analysis.

Rating	Frequency	Severity	Non-detection
1	Less than once in 14 000 tests (1 month)	No direct consequences on result No lost time for laboratory No extra costs	Problem can be seen directly
2	Once in 14 000 tests (1 month)	No direct consequences on result Loss of time (But can be overcome internally)	Problem can be detected within the hour through simple verification (IT, rapid)
3	Once in 3500 tests (1week)	No direct consequences on result Loss of time and resources Risk of deadline failure	Investigation needed to identify failure, may be several hours before it is detected
4	Once in 500 tests (1day)	Indirect consequences on result possibly leading to a false result Loss of time and resources Risk of deadline failure	Problem difficult to detect, involves extra costs (Observation by a technician, contamination tests)
5	Once in 42 tests (1series)	Potentially direct consequences on result Loss of time and resources High risk of deadline failure	Problem almost impossible to detect

Figure 13 - P, S and D scales

The team decided to categorize as most critical the items with the maximum possible value for the severity (5) plus the ones overcoming an arbitrary RPN threshold equal to 75. The analysis has focused only on the analytical macro-phase, decomposed in extraction, mix preparation, amplification, and validation of results. The level of details is high in order to assess all possible failures deriving from a specific activity in the process, for this reason some of the stages just outlined can be split into more than one function. In total for the analytical phase have been extracted 103 risks, out of these only the 18% belongs to the extreme criticality category. In the table below (*figure 14*) is presented the number of identified risks per each stage, the amount of these falling into the first priority level before and after the application of countermeasures.

Stage of analytical process	Number of risks analyzed	Number of initially identified critical risks	Number of critical risks after application of measures
Viral inactivation	19	0	0
Extraction of nucleic acids	25	5	2
Preparation of mix	24	5	2
Amplification	15	2	1
Validation of results	19	4	4

Figure 14 - Identified risks per each analytical stage

One specific event which has been detected many times through the process is the possibility of contamination. Even though its occurrence is high the RPN totalized 64, which is lower than the defined threshold, because being a well-known possible event in a laboratorial context many preventive actions are

already in place, lowering the severity. This is a relevant example to highlight the importance of also evaluating the preventive measures.

As it appears, the stages characterized by the highest quantity of prioritized risks are the extraction and mix preparation, equal to 5, while none for the inactivation, then 2 and 4 respectively for amplification and validation of results. From the table is also understandable that after having applied some specific corrective measures some of the critical risks remain. The meaning is that the actions proposed were not able to solve those criticalities and therefore new solutions are needed to tackle them.

Summing up, the “lesson learned” from this example of FMECA of PCR test process are:

1. The level of detail must be high, decompose the phase of the process until the elementary activities are reached.
2. Look for all the possible sources of risk, from operational to technical to human errors etc.
3. Select proper scales for the RPN identification and criteria for the determination of the most critical risks.
4. Map also the preventive measures in use, they could explain the level of consequences of a determined effect.
5. Conduct a reassessment of the risks after the implementation of corrective measures to check their efficiency.

3.5 Standardised FMECA for the PCR test process

3.5.1 Standardised process mapping

As anticipated in paragraph 3.2, the process of diagnostic testing is composed of four stages: demand generation, pre-analytical, analytical, and post-analytical (*figure 11*). Now there will be a deepening in the specific of those sub-processes to assess the main activities that compose them.

The demand generation is a sort of introductory step for the following three ones. In the literature, it is not treated as an independent stage, but in this will be unbundled and will have the same weight as the others. In this first phase the aim is to collect the patients’ requests coming in and to process them tracking all the patients’ identifiers.

In the following flux diagram (*figure 15*), the decomposition in two main steps is visible and described.

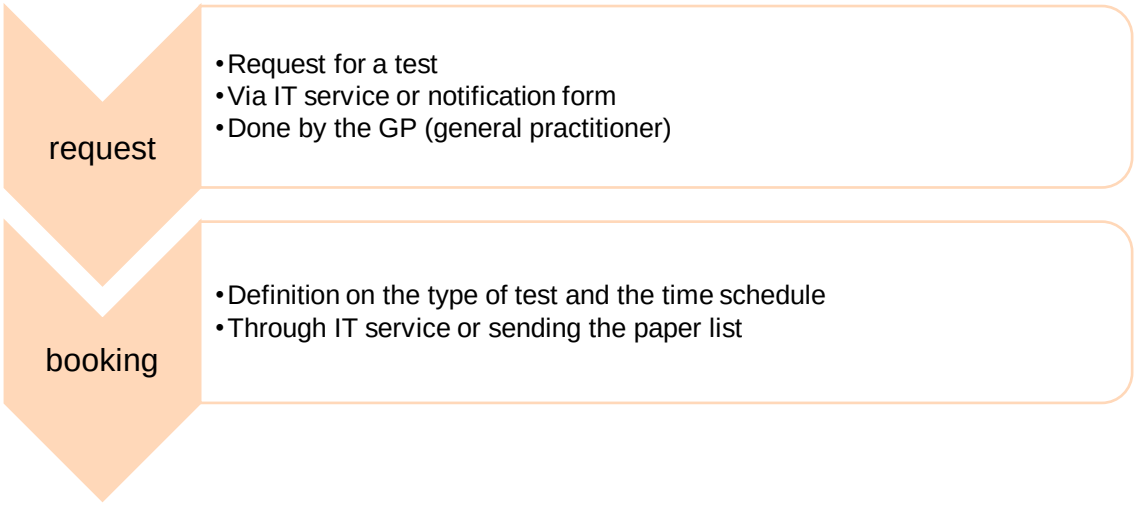


Figure 15 - Demand generation steps

After the generation of demand there is the pre-analytical phase, made up of five microphases that are described as follows (*figure 16*). This is the part of the process where the swab is actually performed on the patient and then the sample is prepared to be sent to the laboratories where it will be analysed in the next phase.

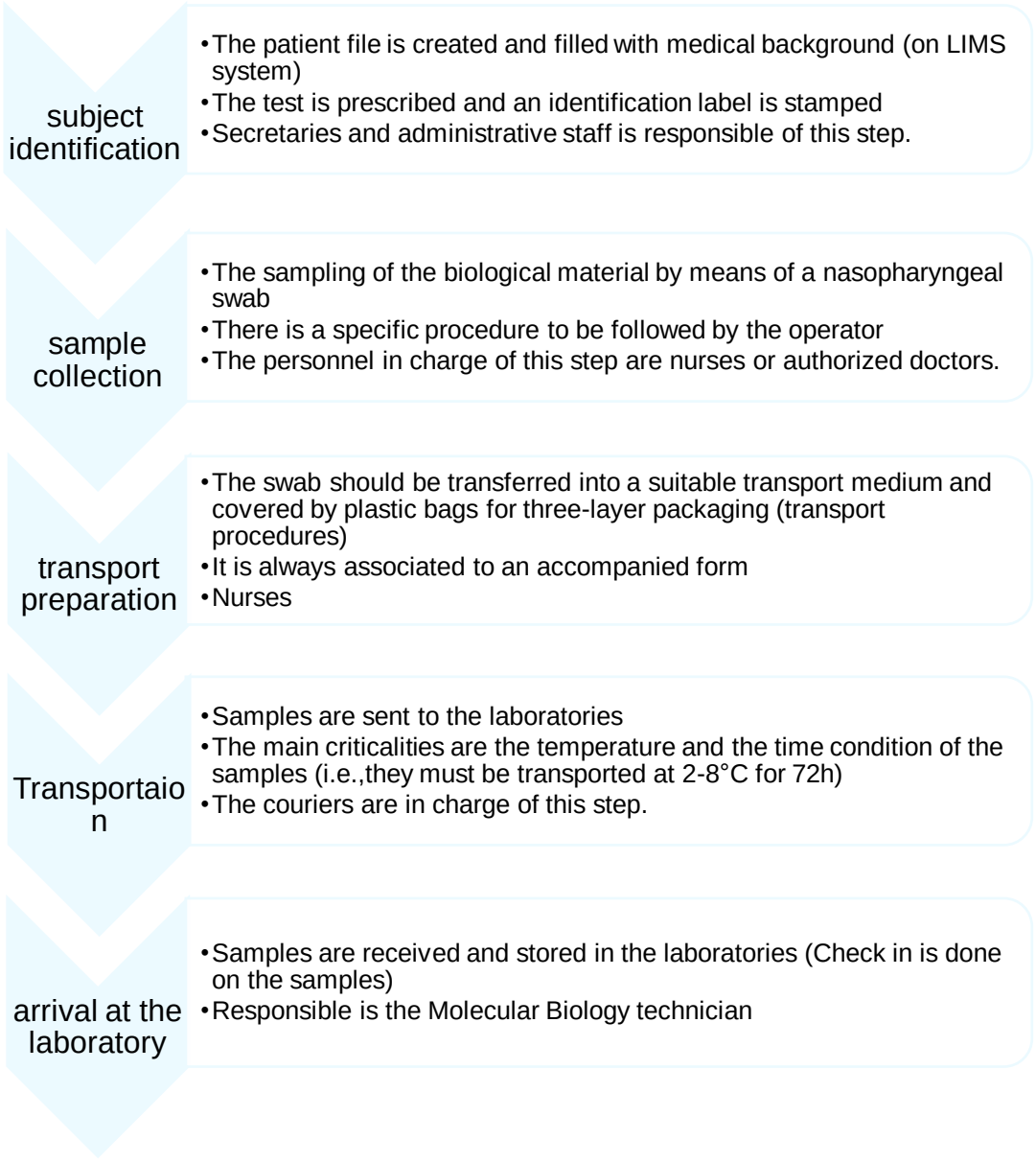


Figure 16 - Pre-analytical steps

When the pre-analytical phase ended, it is the turn of the most crucial part of the analysis of swabs, the analytical phase. In this part the main issue is to analyze the samples to discover if they are infected or not. The central activities of the analytical sub-process are extraction and amplification, which enables the complete detection of swabs. As the previous step, it is composed of five microphases. All of them are carried out in the laboratories by technicians. The process is step by step analyzed in *figure 17.*

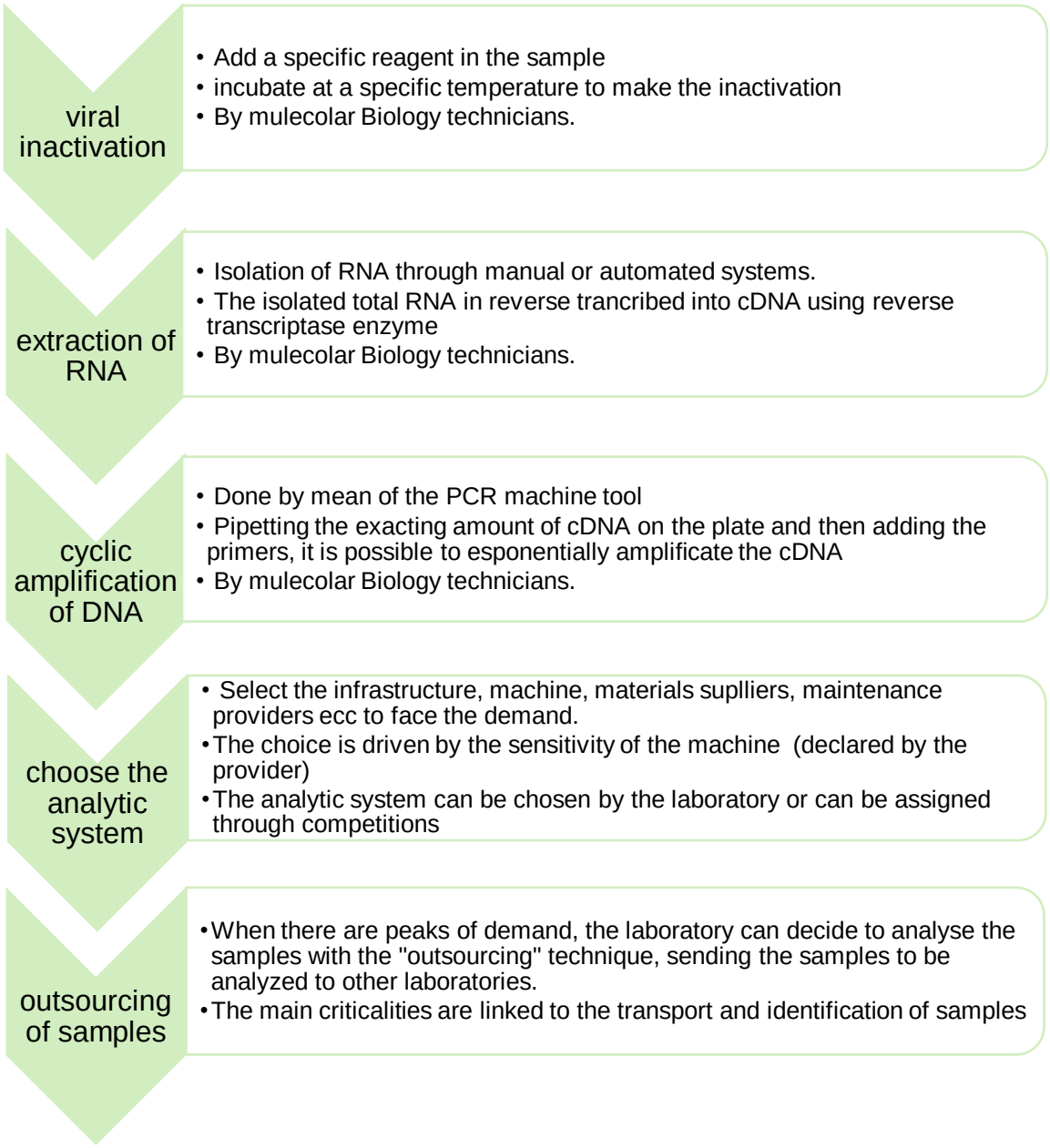


Figure 17 - Analytical steps

The tail of the overall process is represented by the post-analytical. This part aims at linking the test outcome with the patient and alert the ATS in case of positives. The main issue related to the post-analytical is the robustness of the results. Since the false negative is one of the main levers of the Covid-19 pandemic diffusion, it is crucial to reduce the errors to the minimum. *Figure 18* describes the main activities of post-analytical phase.

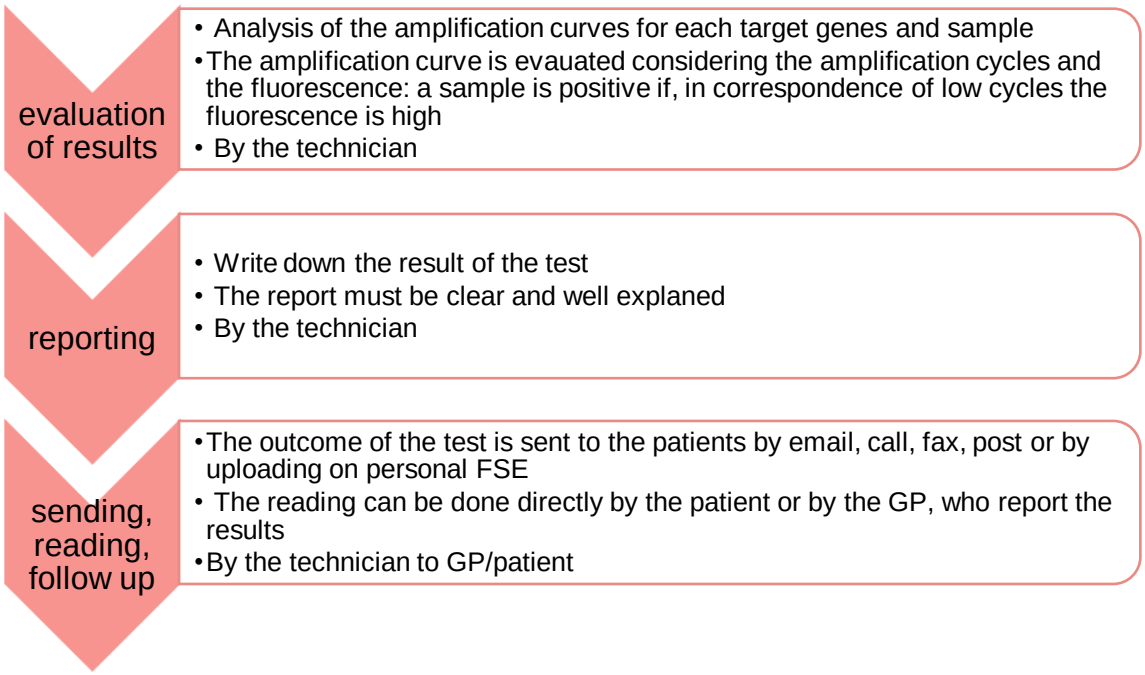


Figure 18 - Post-analytical steps

3.5.2 FMECA template

In the case under examination the FMECA was organized following the decomposition of the process in four main phases previously stated and investigated (demand generation, pre-analytical, analytical, post-analytical). These four sub-processes were divided in their turn into specific activities, each one is identified by a progressive code recording the phase (from F1 to F4) and the numerical order inside that specific phase (from A1 to An). In addition, each activity has a dedicated space for the description of elemental steps and resources to be used in terms of material, tools, and type of personnel. The activities were selected and listed by Dr. Sabrina Buoro who has full knowledge of the process.

At this point, as the following screenshots of the template (*figure 19*) reveal, from every single activity depart many events (i.e., deviations from the process) that may occur while performing. These new rows represent the base elements of the FMECA; They should be finalized with the potential causes, the possible consequences, the final effects, and the corrective measures already in place. With this last name are intended all the norms that must be present in the current process and therefore should be detailed by normative references.

Going on with the template, a risk analysis is presented. The first section regards the actual criticality for each event expressed by the RPN. Consequently, a space for the criticality level is left in order to write down the ranking. The second part of the risk analysis states the residual risk i.e., the amount of criticality that potentially remains after having applied additional mitigating countermeasures. Those possible solutions are outlined in between the comparison actual-residual risk.

Finally, the FMECA should also report some administrative and control invoices which editable in the final columns of the template. In this case it is necessary to assign who is responsible for the control of a specific event and related countermeasures, the monitoring periodicity, the enhancement of the activity and the final efficiency.

Was then decided to assign to this template the name of “tool” considering the future use for which it is designed. It will be an instrument that should be used by health facilities in case of adverse events or as a preventive goal.

An extract of the template used is shown as follows (*figure 19*), the integrated version can be found in *annex A*. In particular, is shown the macro-phase of the request generation as an example.

ID FASE	FASE DEL PROCESSO	ID ATTIVITA'	ATTIVITA'	DESCRIZIONE ATTIVITA' (attività elementari, materiali e metodi, personale, ...)	POSSIBILE EVENTO (Cosa può accadere?)
F1	**Generazione della richiesta**	F1A1	richiesta prestazione informatica o con scheda di notifica: Tampone Molecolare per SARS CoV-2		errata (incompleta?)
					errata: anagrafica soggetto
					prescrizione errata per scelta del tipo campione es. BAL anzichè tampone orofaringeo
					inappropriatezza prescrittiva
					tempistica prescrizione errata rispetto al momento presunto di esposizione al contatto positivo
		F1A2	prenotazione prestazione con trasmissione lista cartacea o via informatica		non effettuata
					errata per anagrafica soggetto
					indicazione errata del luogo di prelievo al soggetto
					blocco o mal funzionamento informatico

POTENZIALI CAUSE (Da cosa può essere indotto?)	POSSIBILI CONSEGUENZE (Cosa ne può derivare?)	TIPO DI EFFETTO (clinico, di processo, economico, privacy ecc.)	MISURE DI CONTROLLO GIA' IN ESSERE (Oggi cosa stiamo facendo per evitare e contenere l'evento?) RIFERIMENTI NORMATIVI	Rischio attuale					
				G	vP	R	vPXR	IR	Priorità
	ritardo esecuzione o mancata erogazione prestazione		Protocollo G1.2021.0003182 del 20/01/2021 Oggetto : Aggiornamento della definizione di caso COVID-19 e strategie di testing-----Protocollo G1.2021.0016859 del 17/03/2021 Oggetto : Indicazioni sorveglianza covid ----0000705-08/01/2021-DGPRE-DGPRE-P OGGETTO: Aggiornamento della definizione di caso COVID-19 e strategie di testing.-----Rapporto ISS COVID-19 n. 2/2020 Rev------0005616-15/02/2021-DGPRE-DGPRE-P OGGETTO: Aggiornamento sull'uso dei test antigenici e molecolari per la rilevazione di SARS-CoV-2.				0	0	
	risultato errato						0	0	
	falso negativo						0	0	
	risultato errato		Ministero della Salute, "Test di laboratorio per SARS CoV-2 e loro uso in sanità pubblica", 30.10.2020						
	falso negativo						0	0	
	ritardo esecuzione o mancata erogazione prestazione						0	0	
	risultato errato						0	0	
	ritardo esecuzione o mancata erogazione prestazione						0	0	
	mancata o ritardata erogazione della prestazione						0	0	

EVENTUALI AZIONI DI CONTROLLO AGGIUNTIVE (Mitigazione del rischio attuale)	Rischio residuo							RESPONSABILE	STATO AVANZAMENTO ATTIVITA'	PERIODICITA' MONITORAGGIO	VERIFICA EFFICACIA
	G	vP	R	vPXR	IR	IR_var	Priorità				
				0	0	0					
				0	0	0					
				0	0	0					
				0	0	0					
				0	0	0					
				0	0	0					
				0	0	0					
				0	0	0					

Figure 19- Extract of the template

3.5.3 Assessment scales

As anticipated in paragraph 2.3.1, the RPN is the baseline to assess the level of criticality related to a specific event. Before computing it, the elements which compose the RPN must be defined. As previously stated, they are the level of severity, probability, and detectability. The assessment scales used for the development of the FMECA tool are linked to the clinical risk. Therefore, the effects on the patients are the base upon which the quantitative rankings are determined. In *table 3* is shown the severity, as the seriousness of the effects on the patient after a failure happened. In *table 4* is shown the probability, as the likelihood to happen of a failure. Finally, in *table 5*, there is the definition of detectability, representing the capability to detect a failure before it may occur.

SEVERITY		
Scale	**Level**	**Description**
1	No damage	The event does not cause any damage to the patient or just higher monitoring to him
2	Slight damage	The event causes temporary damage to the patient and makes necessary interventions/additional treatments o an increasing of the hospitalization
3	Medium damage	The event causes temporary invalidity to the patient and makes necessary to increase the hospitalization
4	Sever damage	The event causes permanent invalidity to the patient, or it generates an event near the death
5	Death	The patient dies

Table 3- Severity scale

PROBABILITY		
Scale	**Level**	**Description**
1	Remote	It can occur less than 1 time every 20.000 tests
2	Low	It can occur 1 time every 2.000-20.000 tests
3	Medium	It can occur 1 time every 200-2.000 tests
4	High	It can occur 1 time every 20-200 tests
5	Very high	It can occur more than 1 time on 20 tests

Table 4- Probability scale

DETECTABILITY		
Scale	**Level**	**Description**
5	Remote (almost impossible to be detected)	It does not exist any method to detect the event before the effects are produced.
4	Low (low probability to detect the error)	The error can be detected by just one observation before the effect occurs.

3	Medium (medium probability to detect the error)	The error can be detected by more than one observation before the effect occurs.
2	High (high probability to detect the error)	The detection is done through direct observation of behaviour blocking the process.
1	Very high (the error is always detected)	The detection is done through automatized alert systems.

Table 5 - Detectability scale

Chapter 4- RESULTS

The following chapter is going to show the different sources (scientific literature, incident reporting, experts' evaluations) covering the elements of the FMECA in order to assess the completeness of the final toolkit obtained.

The procedure adopted for the analysis of the PCR test process to obtain the final toolkit is reported in *figure 20*. As shown in the figure, the final toolkit will be composed of the FMECA sources (that will be analysed in paragraph 4.1) and the FMECA tool (as described in paragraph 3.5.2) to be filled by each user. In addition, two applications of the FMECA will be presented during a network to give further hints and suggestions to use this method. The two real cases examples have been developed in two structures located in Mantova and Brescia, however the results will not be delivered together with the toolkit for privacy reasons.

4.1 FMECA sources

The definition of the FMECA sources is critical since they represent the input data of the FMECA template. The sources are grouped in three main categories: the literature, the experts, and the incident reporting. The process through which the sources have been investigated is visible in the figure below.

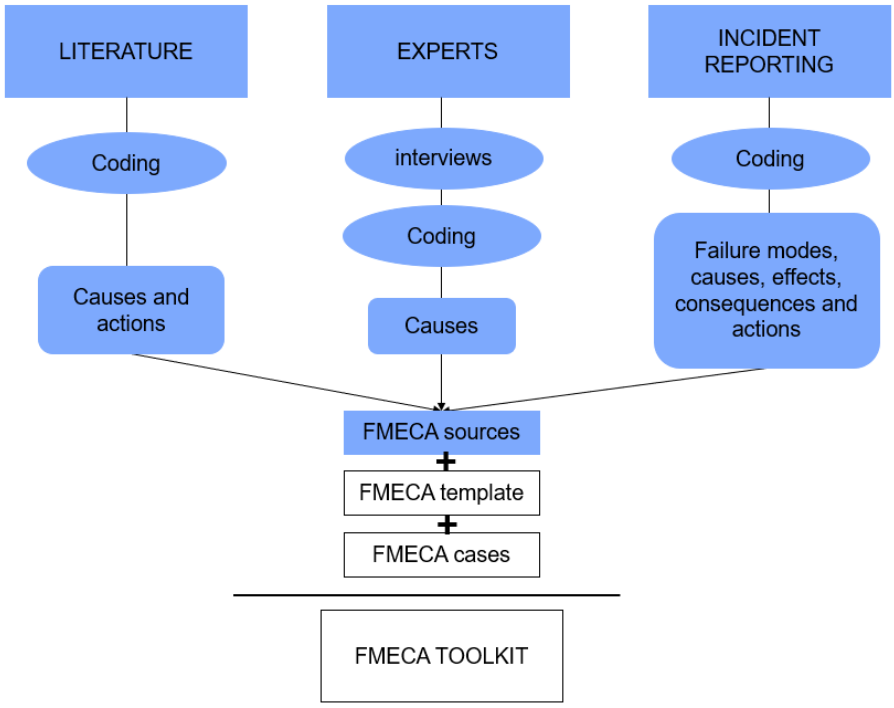


Figure 20 – Process flow

For what regards the expert source, the information had to go through a preliminary step. The knowledge of the expertise of Dr. Buoro was extrapolated through interviews. The doctor was asked direct questions related to some topics of the FMECA template not covered by the literature. The outcome of this analysis is a list of possible causes defined with the code EXP followed by an increasing number; *annex B* reports all the information obtained.

The other two sources will be treated deeply in the next two sub-paragraphs.

Once the sources are all coded and put in order, the FMECA sources file is ready. Summing up, it consists of an Excel file reporting the extracted and coded information articulated in three sheets, one for each typology of the source.

4.1.1 Literature review

The literature archive was approached following a priority order furnished by Dr. Buoro. The different papers were investigated according to the typology, the publication dates, and the editor; the result was a 3-class prioritization level structure: high, medium, or low.

After the primary reading 8 out of the 41 papers were discard since they did not report relevant information for the study. An element has been considered relevant if it provides valuable knowledge related to any of the categories reported in the FMECA template *(for instance: possible causes, effect, corrective measure, etc.).* Anything that could be useful has been extracted from the documents and cataloged in an appropriate Excel sheet. From the literature analysis have been identified several causes for the failure modes and possible countermeasures, none of the other categories of information.

Every piece of information should be easily accessible from the future users of the FMECA. For this reason, the code was constructed indicating the progressive number of the analyzed document and the numerical order of the information in that document.

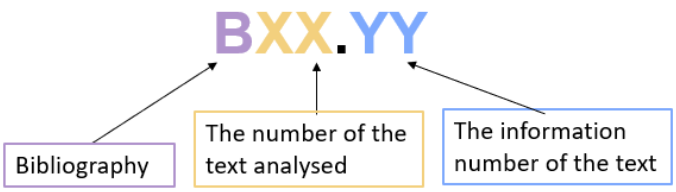


Figure 21 –Codification of the bibliography

Example: B01.02 stands for information number two coming from document number one belonging to the bibliography archive.

It is essential to stress the codes' definitions since they will all be reported in the FMECA template and from there it must be fast and intuitive to arrive at the meaning of each code. As for this regard, another element of paramount importance is the clarity of the sentences reporting the information; with this aim a colour code was inserted in the bibliography data table for each line, reminding the belonging to the specific macro-phase of the process. Light red is associated with the demand generation, light blue to the pre-analytical, green to the analytical, and red to the post-analytical. These are the same colors that the FMECA template exploits, hence this choice increases the degree of consistency of the source.

The list of the literature used is reported in *annex C* and a screenshot of the overall table with the related information is shown in *annex D*.

4.1.2 Ex-post analysis of events

Going on with the incident reporting source, the mindset has been subject to a small change. Indeed, the documents described real events that happened in the structures across Lombardy. The approach, in this case, should start from these events and disclose them through the FMECA voices. This section of the process was particularly relevant because it made it possible to amplify the current version of the FMECA template by adding new events which were not previously considered. In order to accomplish this goal, however, it has been vital to give a careful reading to the reports. Be sure to not miss some data and correctly associate the events already present in the template with the new ones, not to create useless redundancies. Some of the furnished documents were of no importance for this analysis; since the structures did not report adverse events during the Covid period, or they were dealing with non-conformities. The focus here is to understand how laboratories reacted in front of problems, therefore some reports describing potential risk analysis of the process or anomalies were not used for this purpose. The incident reporting documents were recorded in different formats; sometimes a precise form was attached with the event its possible cause and effects, and possible mitigating solutions; other times was

found only a rough description of what happened. The nomenclature chosen for this part was IR (*Incident Reporting*) coupled with an increasing number, each one associated with an event. The pieces of information collected are presented in a designated Excel sheet in the form of a FMECA, this will increase the easiness of the association of the codes in the tool. The events have been assigned to one of the macro-phases and each of them has four descriptive columns: cause, consequences, effects on the patient and possible corrective actions. The results are visible in *annex E*.

The codes must be reported in the FMECA template and could appear in the potential causes, consequences, in the effects on the patient and in the suggested countermeasures all at once, depending on the amount of information given. In addition, also the new events coming from this analysis, which were not inserted in the first version of the FMECA template have been included following the four macro-phases division.

4.2 Synthesis of results

Once the sources file and the template have been defined, the next step is to link the two of them to create the final toolkit. It will act as a synthetic tool to be used easily by risk managers. In order to do so, the focus should be on improving the fluency and readability of the tool and the clarity of the overall statements.

The first step implies reporting all the codes in the **FMECA template**. In particular, the Bs will be positioned in the column of causes or in the actions, EXPs only in the causes while the IR codes could be found in the same event i.e., in the same row, more than one time depending on the information retrieved from that failure mode. When this operation will be over the FMECA template is ready. This document is made up of 5 sheets (excluding the front page). The number one reports the detailed instructions to fill the FMECA and the steps of the procedure, then there is the FMECA template followed by a sheet called FMECA activities. This last one gives free space in case the user will desire to develop a deeper analysis. The last two sheets need to be used for the assessment of the RPN and the evaluation of risk categories. Indeed, the first one includes the assessment scales to determine the quantitative values of P, S and D which have been discussed in chapter 2.4.3. While the last one represents the risk matrix using as

axes probability of occurrence and severity of the effects, in this way the final user has also a visual instrument to understand the criticality of each failure mode.

4.2.1 Obtained results and gaps

The final FMECA filled with the source information is reported in *annex F*.

What attracts the attention while looking at it, is the heterogeneity of the process data coverage. In particular, the FMECA can be divided into different zones, depending on the level of coverage: low (effects/consequences), medium (preventive actions) or high (causes column). The degree of coverage is strictly related to the consistency of the sources of information analysed; in particular, the literature is the source for a great number of causes and few mitigation actions, the incident reporting source provides information also for the effects on the patients and the consequences. At last, the expert statements are present mainly in the causes to cope with literature gaps.

To enable a clear understating of how the different sources are distributed in the different phases of the process, three graphs were developed to show the coverage for causes, effects/consequences, and mitigation actions.

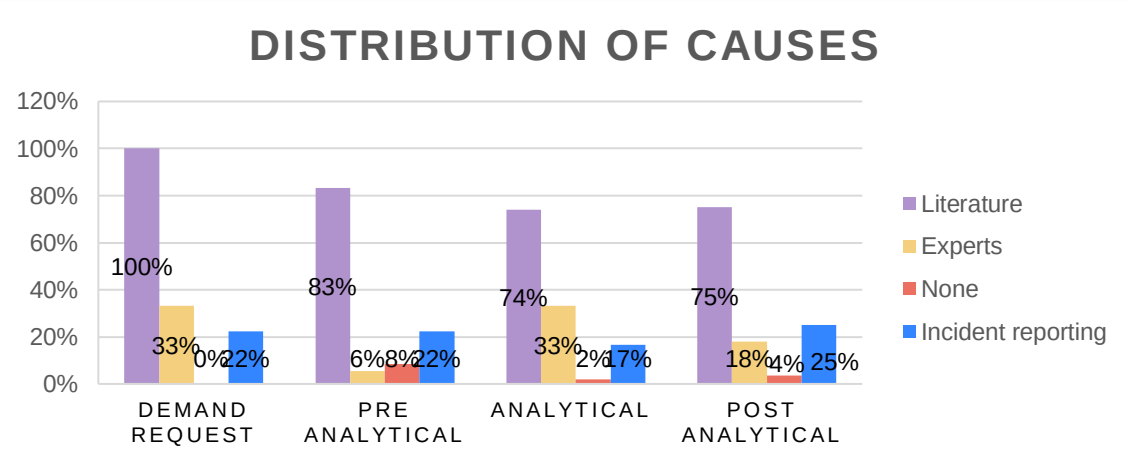


Figure 22 – Distribution of causes

About the causes the higher contribution is given by the literature, covering the 100% of causes for the demand request, the 83% for the pre-analytical, the 74% for the analytical and the 75% of the post-analytical. The incident reporting coverage instead is very poor, going from a minimum of 17% (analytical phase) to a maximum of 25% (post-analytical phase). The experts provide most of the information for what regards the demand generation and the analytical part, which were the poorest if considering the other two sources already described. In the

end, there are few blank spaces, 5 in total. In general, there is a quite homogeneity for what regard the causes. (*Figure 22*)

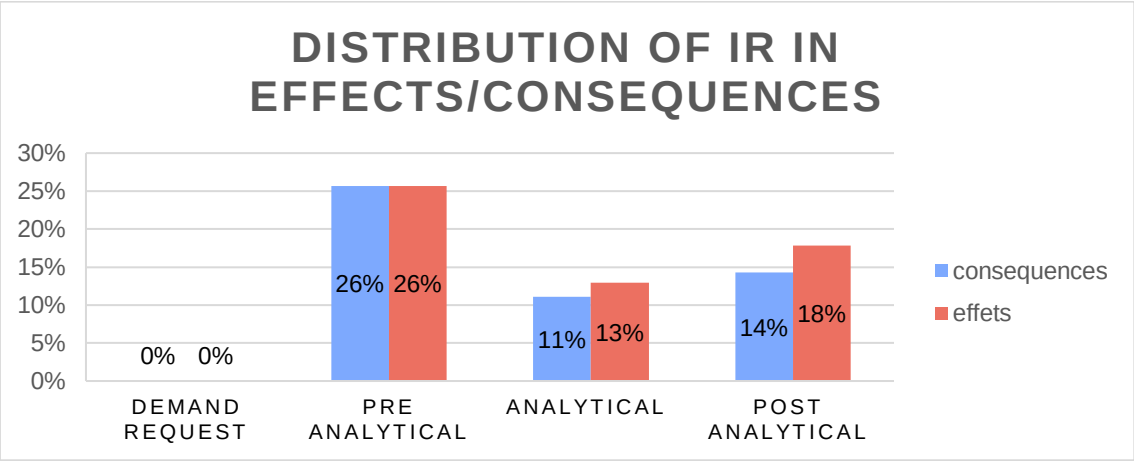


Figure 23 – Distribution of effects and consequences

Looking at the consequences and the effects on the patients, only the incidents reporting was useful to find information about them. *Figure 23* describes the coverage of the incident reporting on the different phases of the process. The most problematic phase is the demand generation, for which was not possible to derive consequences and effects. At the same time, the richest one is the pre-analytical phase with a coverage of 26% for both consequences and effects. Those percentages must be divided to obtain the values for the analytical phase. In general, these two parts are very missing information.

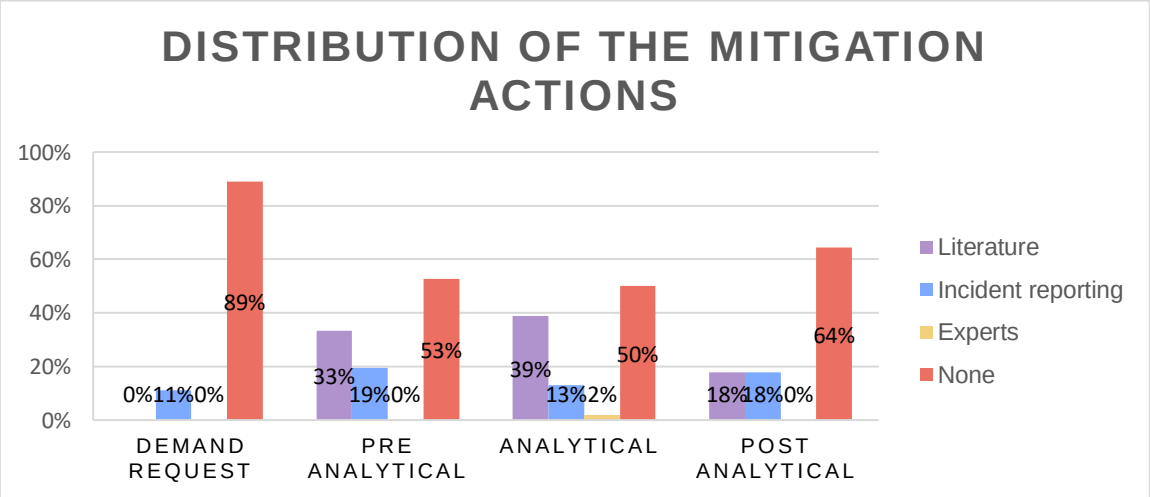


Figure 24 – Distribution of the mitigation actions

The mitigation actions have a not homogeneous coverage: 11% for the demand request, 52% for the pre-analytical, 54% for the analytical and 36% for the post-analytical. The demand request is the most critical one since very few of the

contacted institutions reported actions to cope with problems related to that phase. (*Figure 24*)

In conclusion:

- Almost all the events are associated with causes.
- Literature mainly defines the causes of the events instead of effects/consequences and actions.
- Blank spaces are mostly associated with consequences and effects of the events.
- Mitigation actions have a total of 48% of coverage and are mainly provided by incident reporting.

The level of coverage achieved is definitely a good starting point, of course, it needs to be constantly updated and revised. In conclusion what has been developed through the toolkit is a base of knowledge upon which all the institutions can integrate information from their personal experience. The more their involvement is, the more powerful the toolkit will become.

4.3 Development of a Risk Assessment Toolkit for hospitals

The output of the study is a standardized FMECA toolkit to be distributed in the regional structures of Lombardy with the aim of helping them in the risk assessment of the PCR test process and consequently its improvement. The composition of the final toolkit is represented in *figure 25*.

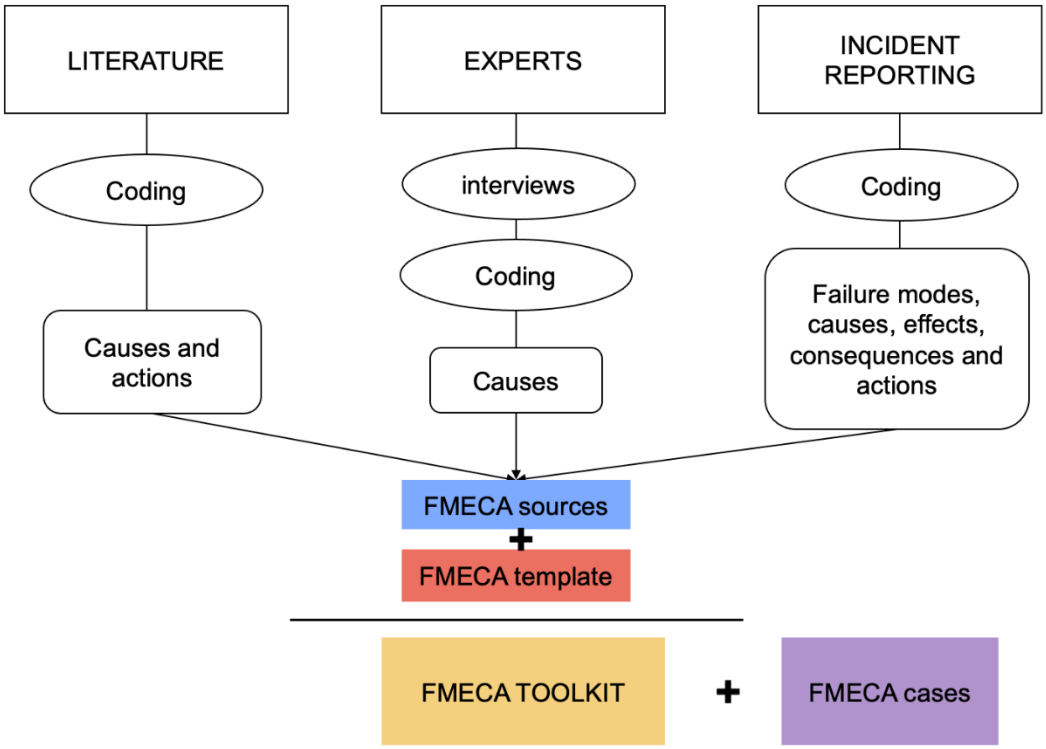


Figure 25- FMECA toolkit composition

The laboratories will have in their hands two different elements of knowledge, the FMECA sources (1) and the FMECA template (2). These two documents, each one delivered in an Excel format, compose the standardised toolkit. The idea is to leverage the given information to perform a risk assessment of the process, deeply analyse it and identify possible areas of improvement. Furthermore, the Excel files will be full access, therefore each user will have the possibility to change and/or adapt the data to the specific needs, enriching them with time.

The suggested usage is to start from the FMECA template, look what are the possible events that may happen and understand them through causes, consequences, and effects thanks to the codes and the FMECA sources document. At this point compute the RPN to identify the area of highest priority, leveraging on the pre-defined scales. If for these items there are no preventive actions already in place, adjust the mitigation strategy to understand which intervention could be useful.

Additional help has been given by two FMECA cases. They are the application of the standardized toolkit on two laboratories located in Brescia and Mantova. Although these two specific documents will not be directly shared with the structures for privacy reasons they have been used as a clarification. On the 22^{th} of June 2020 has been organized a network involving all the risk managers of the

Lombardian structures where the two FMECA cases have been presented. This event has been a huge opportunity because it allowed seeing for the first time how the tool will look like and understand how the methodology works and should be applied to laboratorial processes.

In conclusion, thanks to this analysis the laboratorial structures of Lombardy will have in their hands a powerful tool, the FMECA toolkit, that not only will help them in achieving better individual results in the PCR testing process but will also enhance a kind of standardisation throughout the region.

PART TWO

Evaluation of covid-19 vaccination campaigns: a national benchmarking

Chapter 5- STUDY DESIGN

The second part of the thesis will focus, as previously stated, on the vaccination campaigns. The vaccination plans will be repeated for the following years, and it is evident that there are many planning differences, between the Italian regions and the different states as well. What the states are searching for are solid plans sustainable in the long run. For that reason, the analysis that will be presented in this thesis aims at evaluating the structural, operational, and performance characteristics of the different vaccination campaigns to determine the most efficient. Secondly, by comparing the regional Covid-19 vaccination campaigns will be possible to achieve a final assessment of their quality and take hints from the most talented one.

The process to be developed needs to follow four principal phases, shown in *figure 26*.

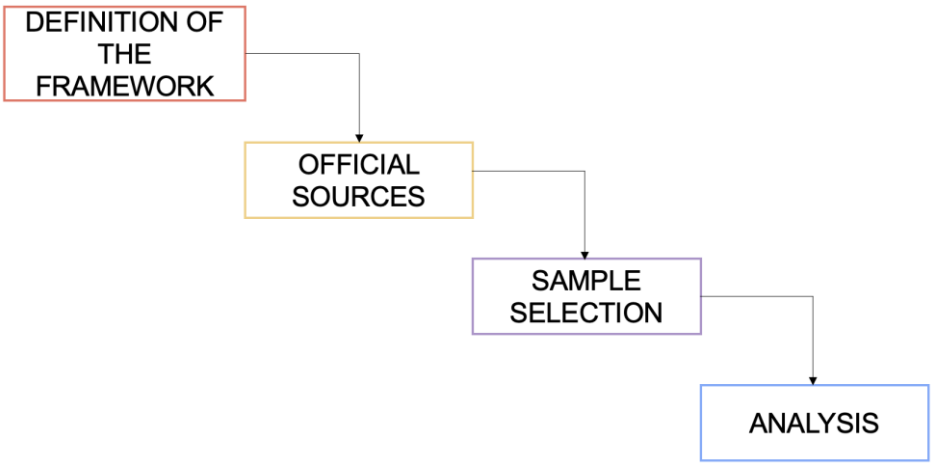


Figure 26- The process

The first step consists of the definition of the assessment framework, i.e., the delineation of reference points to describe the context factors, the main characteristics of the vaccination campaigns, and the relative performances.

Once the main structure has been identified, the next phase consists of filling it with data. In this case, the initial completion has been carried out leveraging available documents on the internet together with official communications of the regions and online articles. Looking at the collected data, some regions resulted richer in terms of information with respect to the others. Therefore, for some of them would be difficult to conduct a proper analysis. For this reason, the objects of study must pass through a selection; only some of them will be kept in the sample for comparison while the others will be discarded.

Finally, it is possible to analyze them by considering the operational performances and the health benefits. It will be conducted individual analysis for each region and a final comparison among all the selected regions. The final aim is to identify the keys features of the vaccination campaign assessment framework.

5.1 Definition of the assessment framework

The origin of the study coincides with the disclosure of the crucial vaccination campaigns elements. All this information together gives life to the framework of the analysis. The data should be sufficient to describe the regional context factors and the characteristics of the campaigns. Moreover, the framework has to allow the evaluation of the vaccination plans through performance indicators.

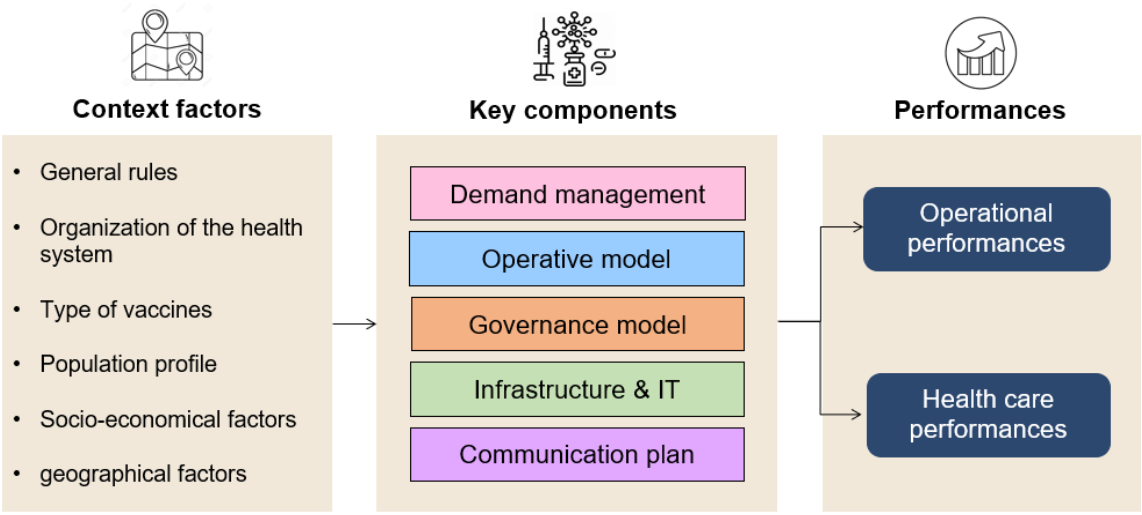


Figure 27- Framework components

In particular, the framework is composed of the so-called key elements, context factors, and performances. The formers are the main elements to describe the campaigns (demand management, operative model, governance model, infrastructures and IT, and the communication plan). Instead, performances are

necessary to assess the results and effects, while the context factors provide a general frame for the analysis.

To arrive at the final framework different steps should be followed, *figure 28* shows them.

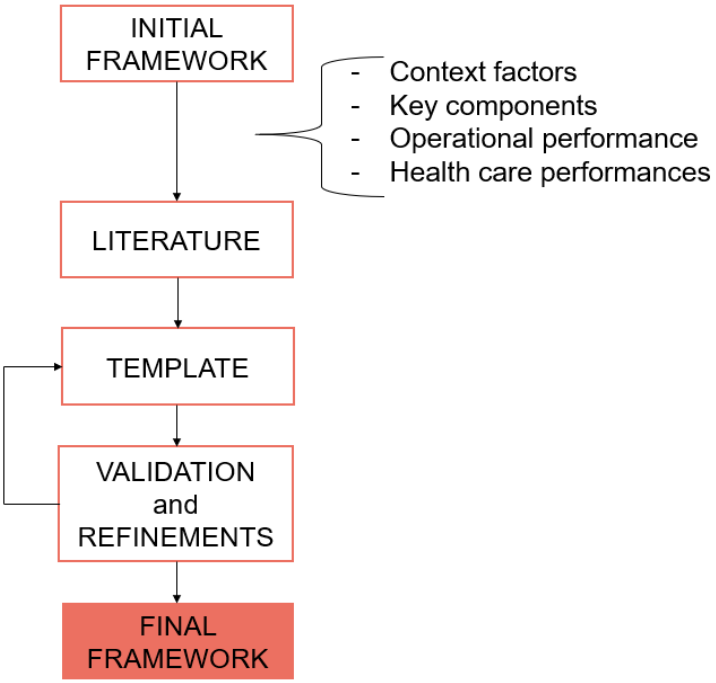


Figure 28 – Definition of the framework process

The starting point is a rough draft of the pillars of the framework. Once these general elements have been designed it is essential to validate them and understand if something needs to be removed, added, or adjusted. To do so, the literature acted a principal role.

As will be discussed in paragraph 5.1.2 some open sources articles regarding past epidemics and relative vaccination campaigns have been traced and used as comparisons for the initial framework.

From here, it is possible to derive a basic template for the key components. It is composed of the main building blocks of the model, i.e., a visual representation of the five pillars that can be furtherly break down to reach a higher level of detail. All the elements will be described in sub-paragraph 5.1.4 where will be developed an accurate description of the template.

About the performances instead, no template has been created for them, they are just used as a database containing the main performances about the Covid-19 evolution and treatment.

The template should go through a validation step to ensure its efficiency for the study of the collected data. To verify this condition has been created an example based on an international vaccination campaign, the one belonging to the United Kingdom. The decision to use a case outside the boundaries of Italy has been a strategic choice because if the validation process will result positively, it would mean that the model can be applied on a larger scale. After this process is over the objective has been achieved, the model of analysis is now defined.

5.1.1 Detailed description of the key components of the framework

The creation of the baseline of the analysis started from the definition of the main pillars describing the vaccination campaigns, the key components. Five basic elements have been pointed out: the infrastructures, the operative and organizational model, the demand management, the governance model, and, lastly, the communication plan. They offer a complete perspective of the campaigns starting from different points of view but remaining deeply correlated among themselves.

These blocks can be generally classified in two subcategories assimilable with the concepts of back and front office. The back office refers to all the functions which are not directly seen by the final customer but are crucial to the fulfillment of the products and/or services. On the other hand, the front office is defined as the set of organizational structures which establish a straight relationship with the client.

Applying these notions to the key components the result, visible in *figure 29*, is that the back office is composed of the operative model, the infrastructures, and the governance while the communication plan and the demand management represent the front office.

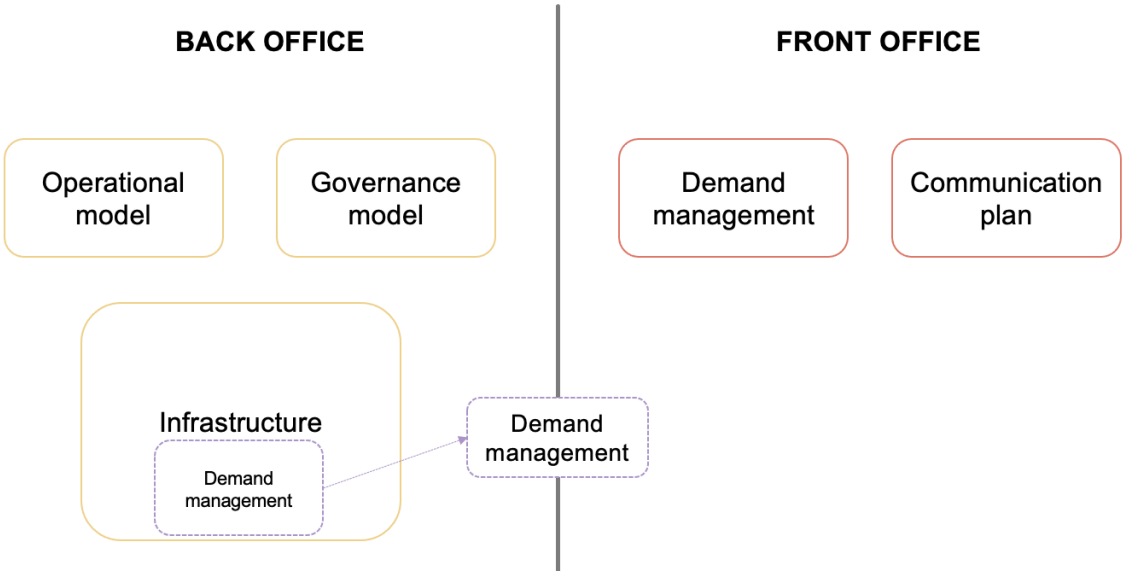


Figure 29- Categorization of the key components

The first three blocks are, indeed, internally managed. The operational model investigates the integration of all the processes designed to create and sell products. In this specific case are searched the typologies of vaccination centers, their number, characteristics and, location; the logistics, and, also, how the human resources are employed.

To assess all the different entities involved in the design, planning, and execution of the vaccination campaign it is relevant to keep track of the governance structure. Since events such as the current pandemic are unpredictable, its management needed extraordinary measures which may appear in the governance structure with the creations of new figures and roles, therefore it is an essential element to be recorded.

The infrastructures cover all the system and IT services deployed both for the provision and the distribution of the vaccines. It is significant to define and compare the technological level of the regions involved. In this block, there is a particular anomaly; besides other elements, it regards the typologies of platforms and, in general, channels through which the target population performs the registration to the vaccine. Clearly, this is a “grey” component: it can be properly placed on the boundary between front and office because it is managed internally but requires external interactions.

Passing to the front office two main features deserve attention: the demand management and the communication plan. The former looks at the way the population to be vaccinated is sorted, searches information regarding the criteria

used to segment people assigning them to different priority groups. The latter, instead, is fundamental for reaching the high effectiveness of the vaccination campaign. This element intends to understand how the regions have made people aware of the vaccination. Therefore, which channels have been used, as well as who is in charge of announcing official notices. The communication plan, if present, can give a big push to the demand for vaccines; otherwise, can slow down the campaign.

5.1.2 Enrichment of the framework through literature

Starting from the blocks previously described, the main concern now is to confirm and enrich the framework and complete it. The final one will set the base for the analysis. In order to do so, some articles have been red relatively to well-known past pandemics: Smallpox, Measles, and Ebola have been deeply analyzed for what regards the vaccine delivery plans. From the study of those historical pandemics, some takeaways have been selected and applied. They are helpful not only to complete the framework but also to validate it.

About Smallpox

Smallpox has been known since ancient times. Edward Jenner described smallpox as "the most dreadful scourge of the human species." The exact numbers of deaths were not recorded but it has been estimated on average 400 million people in the 20th century. Even the discovery of the vaccine by E. Jenner in 1796 did not stop its diffusion. The resolution of the disease came in 1967 when the Intensified Smallpox Eradication Program started and brought to its eradication, officially declared by the WHO on the 8th of May 1980. [5]

The main issues considered for the model enrichment are:

- Stocks must be kept at a certain level to reduce the risk of stock out.
- The urban areas (usually with a higher density of population) suffered more from the disease with respect to the rural areas.
- Epidemiological studies were carried out to dip dive into the most relevant factors of the disease.

About Measles

[5] Hermann Meyer, Rosina Ehmann and Geo_rey L. Smith "Smallpox in the Post-Eradication Era", *Viruses*, Vol. 12, 24 January 2020, pp.138.

Before the introduction of the measles vaccine in 1963, the epidemics occurred approximately every 2 to 3 years. It is also estimated that 30 million cases of measles and more than 2 million deaths occurred globally each year, and that by the age of 15 years, more than 95% of individuals had been infected with the measles virus.[6]

The most relevant takeaways related to this epidemic are:

- The severity of the contagions depends on the environmental factors (density, urban/rural, malnutrition) and human factors (pathologies, age).
- Determine the target population in order to determine prioritization for the vaccine administration. The first to get the vaccine were high risk groups (HIV children, pregnant women, health-care workers).
- Socio-economic and cultural factors are strictly related to a higher vaccination uptake around the globe.
- Strong political commitment to manage the vaccine campaigns is necessary.

About Ebola

The 2014–2016 West African Ebola virus outbreak was the largest ever wave of the disease. It resulted in more than 28,000 confirmed cases, and more than 11,000 deaths in Guinea, Liberia, and Sierra Leone. The outbreak was widespread and difficult to control due to multiple systemic factors including healthcare system capacity, lack of resources, challenges related to international coordination, and communication and community resistance to prevention measures.[7]

The main hints acquired from the Ebola case are the following ones:

- The importance of having an appropriate communication and education strategy, supported by more channels as possible to avoid misinterpretation and confusion between people.
- Ensure procurement mechanisms to define future vaccine stocks.

[6] SAGE, "measles vaccine: WHO position paper*", Weekly epidemiological report* Vol.17, 28 April 2017.

[7] Jenny A. Walldorf, Emily A. Cloessner, Terri B. Hyde, Adam MacNeil, CDC Emergency Ebola Vaccine Taskforce "Considerations for use of Ebola vaccine during an emergency response", *Vaccine*, Vol. 37(48), 15 November 2019, pp. 7190.

- The creation of a team of experts prepared to coordinate the outbreak of the disease.

The reading of documents about how Smallpox, Measles, and Ebola were deleted, thanks to the vaccine introduction, is for sure a supportive way to design the model for the Covid-19 vaccine plans. In particular, it was possible to validate some aspects of the initial framework and enrich it with new elements not considered in the preliminary drafting.
In the following figure *(figure 30)* the adjusted framework is presented in a schematic way. In particular, the aspects not touched by the literature are presented in black character, the elements added with the knowledge extracted from the literature contribute are highlighted in red, while the validated ones are light blue.

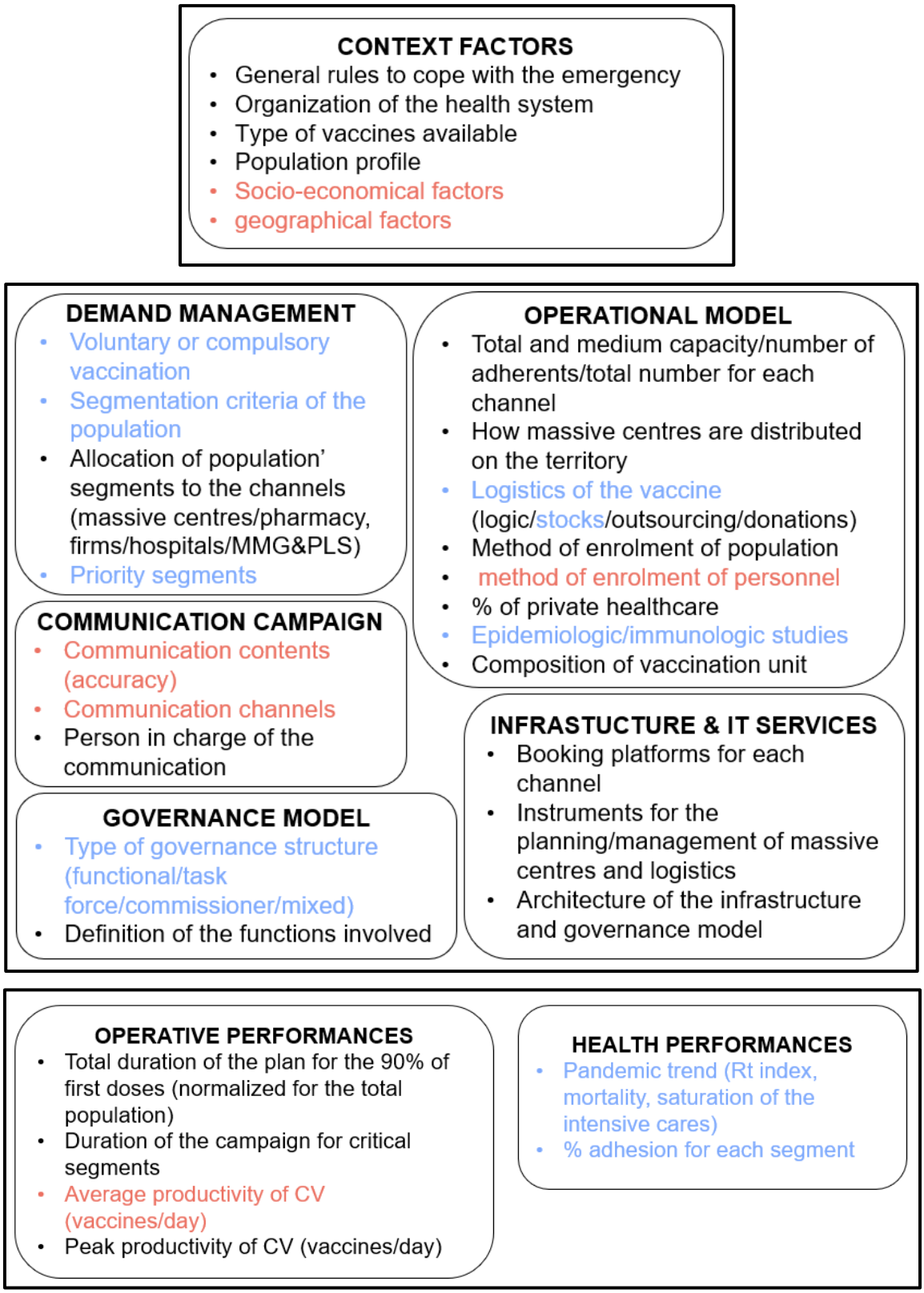


Figure 30-Validation and enrichment of the framework through literature

As it is visible, the literature was fundamental to validate some aspects of the framework, to confirm that it touched the main elements of previous pandemic strategies and therefore that the initial vision was correct (in particular, the

demand management, the operational model, the governance, and health care performances). Instead, just a few points have been added: first, the context factors are enriched with socio-economical and geographical factors. Then, the method adopted for personnel selection was added to the operational model, and finally, the accuracy and reliability of contents and the channels used were included in the communication campaign. No information was found in the literature about the infrastructure and IT systems since many years ago the states did not rely on technologies as today. About the operative performances, the average productivity of the vaccination centers, measured as the number of vaccines per day, was introduced.

The next step is the modeling of both the key components and the performance indicators (on Excel sheet) to be filled for each region. The creation of a unique tool to collect all the information is crucial to make a standardized analysis and provide more reliable results.

5.1.3 Descriptive and performance variables

The descriptive variables or context factors are the elements that do not describe the vaccination campaigns but can impact them. The management of the Covid-19 pandemic occupies a central role in this view and, in particular, the containment rules which have been applied. The Italian government established the general directives through DPCMs. Inside those documents are reported the rules to deal with the development of the pandemic. Several ad hoc measures were created. Initially, a complete lockdown was announced in March 2020. During the second wave, specifically on the 6th of November 2020, Italian regions have been divided into three criticality levels corresponding to three colors: red, orange, and yellow. The containment measures were changing from region to region depending on the color code. In the riskiest zones, the movements outside their own municipality were permitted only for health, work, or special necessities and, the auto-certification must be always completed. Moreover, the schools of any order and grade were closed in the red zone. The only shops and business activities open were the ones classified as vital for the community, such as pharmacies, supermarkets, etc. Going on with the orange level, the movements here were allowed inside the boundaries of the municipalities, even for visiting

friends and family, only once a day. About the schools, they are open for the youngest until the first class of middle school; the remaining with a presence percentage from 50% to 75%. Shops of all types could stay open. Finally, in the yellow regions, the ones collocated in the lowest level of risk, people could move around all the regional territory. The situation of the schools did not change, but the upgrade refers to bars and restaurants that could start serving at the tables, while in the other two zones, only take-away and delivery were allowed.

Every week the results of the monitoring were communicated: regions could change the zone color whether in better or worse. Above all this, Italy was also under curfew from 10 p.m. to 5 a.m. Regions had only the possibility of embittering the restrictions into their territorial competencies.

Specifically talking about the vaccine, the government defined the main guidelines that all the regions must be respected. Vaccination must be on a voluntary basis except for doctors, nurses, and all people employed in health structures.

The second important context factor consists in knowing the structure of the Italian health system. In 1979 has been established the SSN (Servizio Sanitario Nazionale), the head of a stratified network made of 20 regions, subdivided into 650 USL, which are the fulcrum of the health service. The qualities and performances of the system change from region to region due to demographic and economic status; this could definitely impact the vaccination campaigns.

Following the last report about the Italian inhabitants published by ISTAT (15 December 2020), the average age is 45,2, which defines a quite old population; considering the type of virus and its effects this feature could determine a disadvantage for the containment.

Finally, the last element to consider is the type and mix of vaccines available for the Italian vaccination campaign. Here the regions do not have any power; the provisions are managed by the government which is subdued to the European Commission. Italy receives and administrates, until now, four vaccines: Jannsen, Moderna, Pfizer/Biontech, and AstraZeneca for a total of 255,029 million doses up to the second trimester of 2022.

About the performance variables, they can be split into two categories operational performances and health benefits. First of all, it is essential to define the time horizon of the analysis; it has been decided to start from the very beginning of

the campaigns, end of December 2020/January 2021, and go on until the 31 of July 2021. The former kind of performance aims at collecting the results reached under determined context and conditions and, it is interesting to monitor more than one aspect. The performances that have been tracked are the peak and the average productivity for each region in the considered period. These data have to be normalized for 100.000 inhabitants. The normalization occurred to ensure the comparability of the performances independently by the population density. Besides that, it is needed the measurement of the duration of the campaigns since they will not be concluded in the period of the study a proper estimate ought to be defined. The best way is to rely only on the administration of the first doses to conduct an equal comparison. Considering that it is not achievable to have the 100% of the population vaccinated, due to disapproval or medical issues, 90% of first doses is the target to compute the campaign duration. Whether the objects of the study do not reach it, it will be considered the achieved percentage on the 31st of July 2021.

On the other hand, health benefits are selected to represent the pandemic pattern against the progression of the vaccination campaigns and the reflection of their results. With this scope, regional data about the number of deaths and the number of swabs tested have been collected for all the days in the monitoring period. In addition, the average value of the Rt index has been traced weekly; it indicates how many people could be infected by only one positive person. It is a fundamental indicator of the progression of the pandemic, has to be analyzed. The last element that has been considered is the level of the admission of the vaccination campaign. It changes depending on the age ranges, and it gives a good approximation of how well the vaccination campaigns performed.

All the presented variables will be kept as key indicators in the analysis and comparison of the vaccination campaigns.

5.1.4 Design of data acquisition template

The final template is reported in *annex G,* and it is the base upon which the Italian regions selected are modeled. The idea is to represent the five pillars previously identified in an intuitive way, in order to easily collect the needed data and make

them comparable. For this reason, Excel was adopted creating a visual tool organized respecting the main characteristics to be tracked.

The five sections that make up the template will be exploded below concerning the types of information needed for each of them.

1. Demand Management

1.1 Adhesion

The population can decide to adhere to the vaccination plan on a voluntary or mandatory basis. In case of mandatory, for which segment of the population has been activated that rule.

1.2 Population segmentation criteria

What are the main segmentation criteria used to define the priorities of vaccinations distribution (age/pathologies/profession/place of residence/other) and inside each distinction what are the specific segments.

1.3 Allocation of the population to the delivery channels

This sub-area is represented using a matrix, which axes are the segments and the distribution channels (surgeries, massive centers, MMG/PLS, pharmacies, companies, or domicile). The aim is to show which channel is chosen for each segment criteria. Finally, for each channel is possible to determine the total number of people for whom is reserved.

1.4 Vaccination priority

In this case, a matrix has been created similarly to the previous one. The difference is that now the goal is to show for each segment criteria their allocation through the different channels. Indeed, each segment has to be colored in order to show the priority of each of them, employing a scale color.

2. Operational model

2.1 Dispensing capacity

Definition of the total capacity (maximum capacity installed), the average capacity, and the number of members (numbers of structures for each channel operating as vaccination points). Then, just for the MMG/PLS and pharmacies could be relevant for the analysis to represent the total number in the regional territory.

2.2 Logistics management model

In this part, there is the classification of the network model, provided by Prof. Perego Alessandro from Politecnico di Milano.

He defined four types of logistic network (graphically presented in *figure 31*): hierarchical model, meaning that the regional hub is at the top and it is in charge of the distribution to the ATS hubs, which themselves distribute to the vaccination units; ATS-Centric model, in which the regional hub is a "virtual" one and so the first level is directly composed of the ATS hubs, which themselves distribute to the vaccination units; extreme distributed model, the logistic operator distributes stocks from the transit points directly to the vaccination units dislocated in the territory; mixed distributed model, in which the logistic operator is in charge for the main vaccination centers (the bigger ones) and for the ATS hubs, which themselves are responsible for the distribution to the smallest vaccination units.

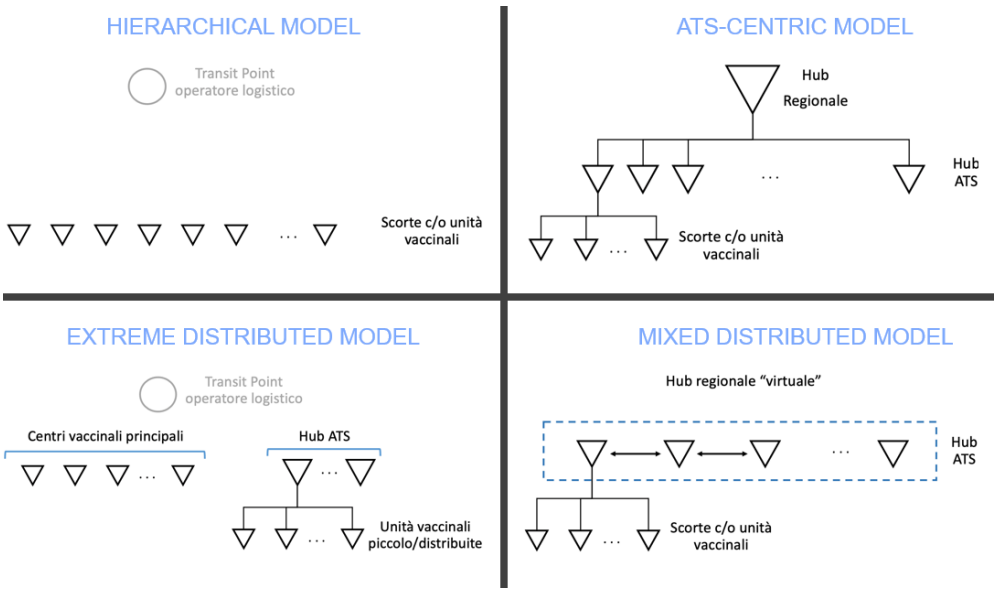


Figure 31 – Classification of the logistic network

The logistic management model also includes the definition of the number of the cycle inventory and the security inventory. In addition, the level of the logistic outsourcing (if any) and if it concerns the transport of vaccines and/or the warehouses.

The region could take advantage of some donations from private or public institutions to support the vaccination campaign. They can

represent donations in personnel, equipment, sites, infrastructures, or others and their level is an indicator to be considered for the analysis.

2.3 How to enlist

Three different enlisting methodologies have been defined: adhesion-booking (by means of platforms it is possible to complete the adhesion and, if the platform allows it, book directly the vaccine date), adhesion-call (the person first decide to compile the request for the vaccine and then it is called for the booking), call-adhesion (the person first receive a call in which it is offered the possibility to the get vaccine and then decide to do it). The template of this section is organized through a matrix, showing the enrolment modality for each segment of the population. Indeed, not all segments are enrolled with the same modality. Usually, people belonging to the riskiest group, such as the elderly and patients with acute diseases, are engaged through calls.

Finally, to shorten the procedure time at the vaccination point, it is possible to compile the self-evaluation sheet to be given to the doctor when the person arrives at the vaccination point. It is a questionnaire with general questions about the patient's conditions (prescribed medicines, allergies, diseases, pregnancy, etc.). In the matrix should be indicated the segments that fill in the self-evaluation.

2.4 Vaccination unit

The vaccination unit is the functional unit responsible for administering the vaccine to a single subject in the unit of time. Furthermore, the vaccination unit is in charge of recording the vaccination in the information system.

It is composed of different figures: doctors, who are responsible for the unit of reference and support the acceptance point; nurses, who prepare, administrate the vaccine, and perform the preparatory activities (i.e., check fridges, manage the wastes, etc.). In many cases, a nurse is elected just for the dilution of the vaccine only. Administrative operators, who perform the acceptance and registration phases; OSSs, who perform the cleaning and disinfection activities. Other figures can be employed depending by region to region. It is relevant to identify the mix corresponding to the vaccination unit and

the number of units requested to support each inoculation line. The inoculation line is defined as the station for the administration of the vaccine to a subject in the unit of time. [8]

2.5 Private health

Private health is supporting the vaccine campaign. In the analysis is requested to establish in which channels it has been used and in which percentage.

2.6 Epidemiological studies

List of all the epidemiological studies carried out in the regional territory concerning the Covid vaccines and define from which bodies have been organized.

2.7 Network topology

The CVs (vaccination centers) are distributed along with the regional territory following two possible logics: distributive or selective. The former means that the CVs are distributed according to the density of the population, usually the concentration is higher in the urban centers and lower in the rural areas. On the other hand, a selective logic refers to a distribution that is independent from the density of the population. To be able to establish the topology type in the template is requested to compare the regional map about the population density with the map showing the CVs distribution.

To give an example, *figures 32-33* are reporting the maps about density and CVs distribution for Lombardy. It is visible that in correspondence of Milan (higher rate of population density) the number of CVs is increasing, while in the mountain areas (with a very low population density) the number of CVs is very small. In this case, the logic followed by Lombardy is a distributed one.

[8] Regione Lazio, “Approvazione del piano regionale vaccinazione anti sars-cov2: prima fase”, 29 December 2020, pp.17-18.

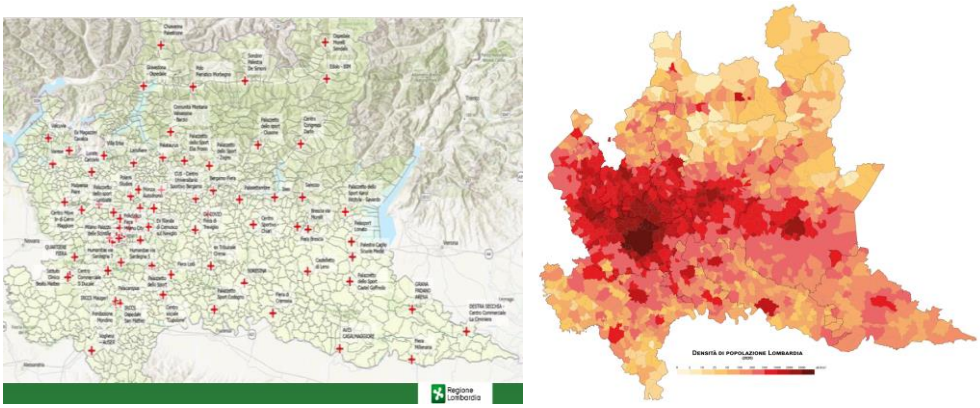


Figure 32-33 – The distribution of CV and density of population in Lombardy

2.8 Organizational model

The organizational model explains the modality for the personnel (doctors, nurses, or administrative staff) recruitment. The main ways of recruitment are the following: ad hoc, meaning that staff is hired and trained for the specific tasks to be performed; by detachment, the personnel of the health facilities is reassigned to support the vaccination activities; by selecting MMG/PLS and pharmacists.

Finally in this section should be defined the head of the CV, that could be directly the region, the territorial companies like ATS or others.

3. Governance model

3.1 Decisional model

The governance structure that manages the regional plans can be chosen among the following classification logic: functional, task force, commissioner, and mixed.

In the functional model, the vaccination plan is managed only through the structures and functions already present within the health system.

The task force instead is an ad hoc structure composed of a set of people nominated to cover specific tasks and it is coordinated by the regional health system.

Also, the commissioner model consists of a team of people selected ad hoc, but differently from the task force, it is coordinated directly by the government.

The mixed one is a combination of the just described models.

3.2 Functional perimeter

Inside the governance structure, different figures are selected with precise managerial functions, such as medical management, pharmacovigilance and risks management, logistic/operational management, epidemiological studies, demand management, and IT system management. In the template, this part is represented with a matrix to be filled with the main actors operating in the region and the relative function covered.

4. Infrastructures and IT services

4.1 Demand management

The regions have adopted different platforms to manage the vaccines requests and to allow a rigorous booking system. In Italy, two main vaccines booking modalities are active: the regional platforms developed by each region for their citizens, or the national platform developed by Poste Italiane, that counts 6 regions adherents till now (Marche, Abruzzo, Basilicata, Calabria, Sicily, Lombardy, and Sardinia).

4.2 CV management

In order to have proper management of the vaccination centers spread along with the territory, some IT systems have been developed at the regional level to facilitate and speed up the stream of the process. They can involve the planning part or the logistic part of the CVs. In the template, it is requested to write all of them to establish which region has developed the stronger IT system.

4.3 Infrastructure and governance IT

This section aims at defining the logic of the architecture behind the informatics systems and who and how is managing them. The template asks for a brief description of how the used IT services are constructed, and the model followed to manage them.

5. Communication campaign

5.1 Contents

The effectiveness of the campaign adhesion is strictly correlated to how the information is provided in terms of accuracy and reliability. For that purpose, the indicator chosen to quantify the correctness of the contents is the number of FAQs present on the official website of the

region. The more the quantity of frequently asked questions, the more a region is considered solid in providing answers to all the persons' doubts and necessities.

5.2 Channels

The regions have activated different channels to communicate with people about the main issues linked to vaccinations. The channels can be distinguished between radio, websites, social networks, online advertising, television, newspapers, OOH media and ads, and others. Each channel is targeting a specific segment of the population, for example, social media are mainly directed to engage the youngers while television and newspapers are for elder people.

5.3 Who communicates

Who are the persons in charge of the communication campaign in the region. The choice could be different, it could be a politician, a spokesman, or other actors. For example, some regions decided to leverage on VIP to enlarge the campaign adhesion.

5.1.5 Validation and refinement of the framework against the UK case

As previously explained once the framework has been constructed and its template has been developed a validation process is needed for ensuring the quality of the study. In this case, the reference object chosen is the UK's vaccination plan. In order to accomplish the scope has been used only one official document, "UK COVID-19 vaccines delivery plan" (Department of Health & Social Care, 2021). The results of the completion of this special case are reported in *annex H*.

Having the templated filled with available information it is visible that there is no homogeneity between the five different sections: for instance, the demand management is rich in data, but looking at the communication plan the situation is different, the lack of knowledge is evident. For what concerns the whole study it is important to have a baseline from which to start the investigation.

What should now demand all the attention is the methodology through which it will be defined whether the degree of coverage is adequate or not. After several

reasoning and attempts, the best way to execute it seemed to look for the “pieces of information”. The basic concept is to understand how many data the template asks for. The matrix of the allocation of the population to the delivery channels formerly described can be taken as an example. The aforementioned table is now reported.

ALLOCAZIONE DELLA POPOLAZIONE AI CANALI DI EROGAZIOE							
Segmento	Ambulatori ospedalieri	Centri massivi	MMG/PLS	Farmacie	Aziende	Domicilio	Totale
Età							
Patologie/fragilità							
Professione							
Luogo di residenza							
Totale							

Table 6- Matrix of allocation of the population to the delivery channels

In this specific case counting all the cells as pieces of information would not have been meaningful since following the pre-explained logic only some of them will have to be selected. Therefore, the only solution is to figure out for each singular element how much information needs to be tracked. In this example, it is necessary to assess for each distribution channel the allocation of the population, which makes the pieces of information equal to 6, one for each channel. For what regards the row and the column called “totale” the same reasoning could be applied. The comprehensive result is 16 pieces of information for this matrix.

Applying this methodology for all the elements of the template the outcome in terms of the number of information sought for each section is 30 for the demand management, 43 for the operative model, 7 for the governance model, 10 for the infrastructures, and 3 for the communication campaign.

Now the same logic can be used only on the pieces of information which have been actually completed leveraging the quoted document data. Carrying out this task, results the number of information obtained which even in this case can be cataloged according to the 5 sections of the template.

The outcome of the UK case is reassumed in the following table.

COVERAGE DEGREE			
	Number of information sought	Number of information obtained	Information coverage %
Demand management	30	24	80%
Operative model	43	13	30%
Governance model	7	7	100%
Infrastructure and IT services	10	5	50%
Communication campaign	3	1	33%
TOT.			**54%**

Table 7- Information coverage degree for the UK case

Looking at the table it is clear that the level of information is high for the demand management and the governance model. The level is intermediate for infrastructures and IT services, while the two remaining sections are the most problematic. Indeed, both the operative model and the communication campaign scored a coverage degree of about the 30%.

For what regards the former, the most plausible answer is that the operative model contains much information about the logistics issues or in general data that are not always shared on public domain documents.

However, as earlier stated, it is not fundamental for the purpose of this study to reach the template completeness. Using this assumption, it can be derived that the total coverage, which has been settled on 54%, is more than sufficient.

In conclusion, the result of this investigation is definitely positive; it means that independently of the society, geographical location, and strategies the model is a proper tool to compare the vaccination plans.

5.2 Identification and selection of the sample

Since both the framework and the template have been validated is now the moment to fill in the latter with information. In particular, in this first completion seven regions will be analyzed: Emilia-Romagna, Lazio, Liguria, Lombardy, Piedmont, Puglia, and Veneto. Online research has been carried out in order to gather all the documents available and to keep track of the website reporting statistical data on the vaccine administrations. These two sources of information are reported in *annex 9*, divided according to the Italian regions.

After a careful reading, the data have been extrapolated and located in the proper section of the template. At first sight, is clear that the distribution of information is changing from region to region, reflecting the completeness of the found sources. For instance, it has been difficult to retrieve official information about Puglia and as consequence, a big percentage of the template remained empty.

Successively the same analysis performed for the UK case has been replicated for the Italian vaccination plans, comparing the degree of coverage of all the seven studied regions. The results are reported in the following table (*table 8*).

COVERAGE DEGREE									
Region	**Emilia-Romagna**			**Lazio**			**Liguria**		
	# of information sought	# of information obtained	Information coverage %	# of information sought	# of information obtained	Information coverage %	# of information sought	# of information obtained	Information coverage %
Demand management	30	13	43%	30	16	53%	30	20	67%
Operative model	43	16	37%	43	21	49%	43	17	40%
Governance model	7	7	100%	7	2	29%	7	1	14%
Infrastrcutres and IT	10	0	0%	10	2	20%	10	2	20%
Communication campaign	3	2	67%	3	1	33%	3	1	33%
TOT.			**41%**			**45%**			**44%**
Region	**Lombardy**			**Piedmont**			**Puglia**		
	# of information sought	# of information obtained	Information coverage %	# of information sought	# of information obtained	Information coverage %	# of information sought	# of information obtained	Information coverage %
Demand management	30	19	63%	30	18	60%	30	15	50%
Operative model	43	20	47%	43	22	51%	43	8	19%
Governance model	7	6	86%	7	1	14%	7	2	29%
Infrastrcutres and IT	10	4	40%	10	2	20%	10	1	10%
Communication campaign	3	2	67%	3	3	100%	3	1	33%
TOT.			**55%**			**49%**			**29%**
Region	**Veneto**								
	# of information sought	# of information obtained	Information coverage %						
Demand management	30	14	47%						
Operative model	43	18	42%						
Governance model	7	6	86%						
Infrastrcutres and IT	10	2	20%						
Communication campaign	3	1	33%						
TOT.			**44%**						

Table 8- Italian regions' coverage degree analysis

As it appears the most problematic region is Puglia with total coverage of 29%, for this reason it is immediately eliminated by the analysis. Going on, it is visible that the left cases present quite high degrees, all included between 40% and 60%. Emilia-Romagna occupies the last position, even if the overall condition is sufficient the voice infrastructure and IT services totalized 0. This could be a relevant issue when it comes to analyze and compare the regions, in addition no informants are available and therefore Emilia-Romagna is left behind as Puglia. Next In line there are Liguria and Veneto with the same percentage, equal to 44. However, the result of Veneto is given by the high contribution of the governance model, which reached 86% of coverage, while all the other values are really similar to Liguria. For the aim of the analysis the governance model has not the

same importance as the other blocks meaning that normalizing the data Liguria overcomes Veneto in terms of helpful information degree. Using this consideration, four regions survived the selection process: Lazio, Liguria, Lombardy, and Piedmont. Four is a satisfactory sample dimension for the study which will be successively developed.

Chapter 6- FINDINGS

In this chapter will be deeply described the templates of the chosen regions according to the building blocks of the proposed framework.

6.1 Lazio

All the information regarding the Lazio region is reported in the *annex J*.

6.1.1 Demand management

The President of the Italian Republic established the obligation for Covid-19 vaccines. He stated that the vaccine is voluntary for the population, except for some categories for which it is mandatory: the health professions and the operators of the health sector. This law is valid not only in Lazio but also in all the other Italian regions.

The segmentation criteria adopted in Lazio regards the population age, the presence or not of pathologies or fragilities, the profession, and the site of residence. The main channels through which people get vaccinated are hospitals, the massive vaccination centers, the MMG/PLS, the pharmacies, and at the end the domicile. The four aforementioned segments can be allocated to the different channels in different ways: the segments with pathologies can take the vaccine in hospitals, massive centers, MMG/PLS, or, in case of moving problems, directly at domicile. The people living in protected places of residence can have the vaccine dose at their homes. The professions like professors and school staff, the service operators (police, civil protection, etc.), and the health staff are vaccinated in hospitals or massive centers. Finally, the rest of the population can be allocated to all the dispensing channels, including pharmacies.

For sure inside each segment, there are some sub-segments prioritizations. The higher priority is reserved for the elderly living in residential structures, their staff, and all the workers of the health sectors, which are obliged to get vaccinated. Then, it is the turn of the population affected by severe pathologies, persons with an age of 80 years or more and high priority professionals. The third wave of vaccinations is reserved for the service workers, low priority professors, and moderate pathological persons. After them, aggregation sites like prisons and

recovery centers are made immune. For the remaining population, the order to be followed is age-based, from the older people to the youngers.

6.1.2 Operative model

About the operative model, the gathered information is quite limited for all the regions. Specifically, it is known that Lazio initially installed a capacity of 7.356 administrations per day per each massive center. This figure is intended as the total capacity while there are no data about the average capacity nor the capacities of any other channel. Regarding the number of vaccination points only two figures are recorded in official documents: 20 Hubs which are the massive centers that also support the storage of doses and their distribution towards other points, and the number of participant pharmacies, more or less 1000 on a total of 1612. The vaccine administration through MMG and PLS will hopefully start by September; therefore, the only information regards the cumulative regional figure of 6528 MMG/PLS.

Data about logistic management is difficult to be found on public sources. As regards the Lazio case, the only aspect which could be derived is the ASL-centric model adoption since the structure is composed by the Hub's middle level. As previously explained, the network topology could be selective or distributed. In this specific case, the result is a distributed repartition of the vaccination centers meaning that the region chose to locate the vaccination points following the population density. This characteristic facilitates the transportation of both provisions and people.

The method to enlist people for the vaccine is linear for almost all segments of the population. You have to adhere to the campaign and after it is possible to book your appointment. Special treatment has been reserved for the extremely fragile category who received direct phone calls. Overall, everyone who accepted the vaccine must complete an auto-evaluation form, reporting the medical condition and history of the patient.

The regional epidemic department gave rise to a study aimed at defining the vaccination effects on the over 80s segment while another study conducted by SIGG (Società Italiana di Gerontologia e Geriatria) tried to establish the duration and effectiveness of the vaccination of the care homes.

Finally, it is known the composition of the vaccination unit. Lazio chose to dedicate equal resources for the main roles: one doctor, one nurse, one administrative, and one social health worker. In addition, this basic team has been flanked by a local operations manager with a coordination role. This is the overall vaccination mix, four of them need to be assigned to each vaccination line.
This is all for Lazio, therefore two sub-blocks remained totally blank: private health and organizational model.

6.1.3 Governance model

The head of the civil protection department of Lazio, Carmelo Tulumello, is supported by a technical-scientific committee, nominated on the 5th of February 2020. It is made up of 7 members and has the role of supporting the coordination of all the activities required for coping with the Covid-19 emergency.

6.1.4 Infrastructures and IT services

Lazio developed a regional platform from which it is possible for citizens to book their vaccination slots.

6.1.5 Communication campaign

The communication campaign in Lazio is mainly aimed at increasing knowledge on the different types of vaccines available, defining the priority groups and the beginning date for their booking. The most important issues are published on the website of the region, where the citizens can find all the information needed about the vaccination campaign. A list of FAQs is also present with 42 typical questions. For sure the second source of information is characterized by the presence of doctors/nurses, who make people aware of the vaccine efficacy and answer to any doubt.

6.2 Liguria

The screenshot of the Ligurian template with data is visible in *annex K*.

6.2.1 Demand management

Like the Lazio case, also in Liguria, the obligation for the vaccine regards the health sectors. For pharmacists, OSSs, doctors, and professional studies the vaccine is compulsory.

The segmentation criteria adopted in Liguria regards the population age, the presence or not of pathologies or fragilities, the profession, and the place of residence. The main channels through which people get vaccinated are the hospitals, the massive centers, the MMG/PLS, the pharmacies, the companies, and at the end the domicile. The segments are allocated to the channels following different rules: people with diseases can get vaccinated at hospitals, massive centers, or, in case of mobility limitations, directly at home. The health professions are allocated to the hospitals, the service operators to the hospitals or MMG/PLS and in this region, some companies can act as vaccination centers and guarantee vaccines for their workers. The people working in protected residence centers are vaccinated at domicile by the vaccination squads. The remaining population is allocated to massive centers, MMG/PLS, pharmacies, or domicile.

The sub-segments with number one priority are persons with more than 80 years old, hospices hosts and their staff, health operators and people with severe pathologies. The priority two sub-segments are the 75-79 years old people. Then moderate disease affected people, professors and school staff, and the 70-74 years old people. To follow the service operators, the 65-69 people. The rest of the population is vaccinated with age basis in descending order.

6.2.2 Operative model

The Ligurian operative model is generally poor; three out of the seven categories of information are void and are vaccination unit, private health, and epidemiologic studies. The remaining elements are at least partially completed.

Starting from the dispensing capacity, it can be easily found that 20 regional Hubs have been appositely created to satisfy the uprising vaccine demand. In

particular, the maximum capacity is installed in a Hub located in Genova, able to provide for 2.800 administrations per day. Furthermore, also the pharmacies highly contribute to the Ligurian vaccination campaign, overall are 105 structures involved. Their contribution is fundamental; they should guarantee 6.000 administrations per week.

The logistic net model is ASL-centric, and in this case, there are also some data about the donations. In particular, the region launched a fund-raising campaign aimed at helping the management of the current pandemic. The regional Liguria website states, that the collected sum will be operated on improving the condition of doctors, nurses, and all the personnel involved in the health structures, which are fighting the emergency.

Looking at the locations of the vaccination points, it seems that Liguria followed a distributive logic trying to match higher administration capacity with high population density.

For almost all segments, there are two main ways for enlisting for the vaccine, adhere and then book the appointment or receive a phone call for the adhesion. The exception is the extremely fragile segment which can leverage only the call model. As for Lazio, the “to be vaccinated” must complete a pre-anamnesis form. In the organizational model, it is known that MMG, PLS, and pharmacists are called to the vaccination centers. Lastly, the responsibility of the vaccination centers belongs to territorial authorities.

6.2.3 Governance model

The region has set up a task force to tackle the second phase of the campaign. The reason why it was created is to develop all the measures and the protocols to be adopted, allowing the regional economy to restart, and prevent the contagious curve to rise again. It is made up of 27 experts, taken by the main scientific and educational institutions.

6.2.4 Infrastructures and IT services

Liguria region developed a regional platform for vaccinations booking. It is possible for the citizens to confirm a booking online through

“prenotovaccino.regione.liguria.it”, pharmacies or by calling the number 800 938 818.

6.2.5 Communication campaign

The main information about the Ligurian regulations is given on the official website as well as newspapers and conferences by politicians. About the first source cited, the effectiveness of the vaccination booking is guaranteed by the presence of a tutorial explaining how to perform the booking online. The weakness is given by the FAQ, not specific for the region but reporting to the Italian government.

6.3 Lombardy

Annex L shows the Lombardy case filled in with the available information.

6.3.1 Demand management

In Lombardy, like the other Italian regions, the vaccines are compulsory just for people belonging to the health workers group.

The vaccination criteria adopted in Lombardy are age, pathologies, profession, and place of residence.

The vaccination channels employed are the hospitals, massive centers, MMG/PLS, companies, and domicile. Pharmacies have not yet been activated.

The ways the segments are allocated to the channels are: the fragile people can get vaccinated at hospitals, massive centers, MMG/PLS, or, domicile, in case of patients with moving problems; the workers are directed to hospitals, massive centers or in the firm they work; the patients living in protected structures, like hospices, are vaccinated in the structure site.

The prioritization is following the segmentation criteria, and it involves first the over 80, the health staff and the hospices and their staff. The second group to be vaccinated is composed of 75-79 years old, severe pathological patients, the service operators, professors, and school staff. The remaining population is prioritized considering the descending age and the presence of minor clinical issues.

6.3.2 Operative model

The description of the operative model of Lombardy could start from the dispensing capacity here, states that the number of massive centers installed across the region is 76 for a total capacity equal to 144.000 administrations a day. Moreover, it is also known that the remaining channels, excluded the pharmacies, are meant to guarantee a total capacity of 30.000 administrations per day. About the MMG, PLS, and pharmacies, unfortunately, the number of participants is missing, at the moment, is only available the totals which are respectively 8.821 (MMG and PLS) and 3.089.

Going on with the logistic management model, once again the net is governed by an ATS-centric model as in the two previous cases. Even for Lombardy, there is no information regarding the way stocks are managed. However, some materials about logistic outsourcing and donations have been collected. Concerning the former, the region rented some furnishings and equipment for stocking and storing the vaccine provisions. While the donations coming for Lombardy have been deployed to equipment and personnel.

Comparing the two maps, the one reporting the population density and the other with the vaccination centers distribution, it is visible that Lombardy adopted a distributive approach. This is the same strategy implemented by Lazio, collocate more vaccination points where the housing density is more elevated.

The population segments defined by age or profession in Lombardy can accede to the vaccination program by confirming their intent, book their appointment, and finally completing the auto-evaluation sheet. On the other hand, people affected by pathologies should receive a phone call from their doctor in order to be signed for the vaccination, but in this case, it is not known if they still need to fill in the pre-anamnesis or not. No data have been retrieved for the segment of the population distinct by the place of residence.

Some epidemiologic studies have been conducted inside the regional boundaries. In particular, the one already quoted of SIGG taking care of the care homes vaccination duration and effectiveness and another one cured by DG Welfare and Università Bicocca. This last one aimed at assigning an indicator of vulnerability for each citizen, making it possible to create a proper prioritization and segmentation of the population.

About the organizational model, what is sure is that the responsibility of the centers is assigned by territorial authorities while there is no information of how the medical staff has been enlisted.
Lombardy also furnishes a complete vision of the vaccination unit; the mix, which will be soon presented will be valid for a total of four lines. The composition is the following: one doctor, one nurse, at least one administrative figure, and two social health workers. No additional roles are inserted in this case.
As it appears, the only cells that remained completely blank are the ones concerning private health.

6.3.3 Governance model

The governance structure of Lombardy has been defined as commissioner. Indeed, an executive committee guided by Guido Bertolaso has been created for the coordination of the vaccination campaign. The executive committee responds directly to the steering committee, headed by the president Attilio Fontana.

6.3.4 Infrastructures and IT services

From the 2 of April 2021, the Lombardy booking system is managed by the Italian post office. This system replaced the previously used ARIA system. The main advantage is that the vaccine can be reserved live, by choosing the date and the vaccination center of preference. The head of technology and operation at Poste Italiane defined it as “a dynamic infrastructure developed to manage large volumes of traffic and uses innovative programming languages and technologies to optimize the demand for vaccines”. [9]
The platform of Poste Italiane is not the only platform developed in Lombardy. SIAVR is the regional information system for vaccines; it supports both the logistic aspects and the organization of the vaccine centers.

[9] https://www.ilcittadinomb.it/stories/Cronaca/vaccini-come-prenotare-con-il-sistema-di-poste-italiane_1391481_11/

6.3.5 Communication campaign

To support the initial phase of the vaccinations, the region put in place integrated planning of communication tools to ensure a wider spread of vaccines information. In this regard, it was activated a number (800 89 45 45) that people can contact for doubts or technical assistance. The communication campaign has involved all the institutional communication channels (web portal, social media, regional call centers...). In the end, means like newspapers, radio, local TV, OOH, and social media are exploited to reach the highest number of people possible.

On the regional website are reported all the issues related to the Covid-19 vaccines and the campaign. It also presents a FAQ, which contains 17 frequent questions.

6.4 Piedmont

All the retrieved data about Piedmont can be found in *annex M*, displaced on the template.

6.4.1 Demand management

In Piedmont, like in the other Italian regions, the covid vaccine is compulsory just for the health workers.

The vaccination criteria adopted in this region are age, the pathologies, the profession, and the residence site.

The channels used to deliver the vaccines are hospitals, massive centers, MMG/PLS, pharmacies, companies, and domicile. Also for the Piedmont case, there are different allocation criteria: patients with pathologies go to hospitals or massive centers; persons with walking problems can get the vaccine at their domicile as well as the community centers, for which is possible to get vaccinated at the hospitals. The workers instead are allocated to hospitals, massive centers, or firms. For the rest of the population, another channel is activated, which is composed of pharmacies.

The first group for which was possible to get the vaccine is the over 80, hospices and staff and the health operators. The second group is composed of 60-80 years old people, severe pathological patients, high priority school staff and professors, and service operators. Then it is the turn of community centers, low priority school

staff and professors, and moderate pathological patients. In the end, the population not covered by the described prioritizations is vaccinated considering an age-based scale.

6.4.2 Operative model

Unfortunately, with the free access data is not possible to complete all the blocks of the Piedmontese operative model. Two parts of the template remain unfilled, epidemiological studies and private health.

Regarding the numerosity of the centers, by typologies of channels, from an online source, it derives that Piedmont has a total of 73 hospital dispensaries. Moreover, 735 on 4762 MMG and PLS participate in the vaccination campaign; about 500 out of the 1666 regional pharmacies are available to administrate the vaccines. About the remaining three channels, there is no numerosity information still, for the massive centers, is known the maximum capacity installed. Indeed, in the biggest structures, the highest peak that can be reached is 1.500 administrations per day.

Approaching the logistic model, there are always two constants: the ATS-centric model and the fact that data about stock management are untraceable also in this case, are confirmed. For Piedmont was not possible to retrieve any data about the donations, but on the other side, it is stated that the region leveraged on a territorial company outsourcing to it the distribution of the vaccines.

As for what regards the net topology, even, in this case, there are no surprises. Piedmont implemented a distributive strategy like all the other three regions.

About the ways people enlist for the vaccine, there are data concerning all the segmentation criteria. First of all, the entire population must complete the pre-anamnesis plus the process to get access to the vaccine is to express consent and, after that, communication will come through reporting the appointment info. In addition, for the most fragile segments: people over 80s and serious pathologies affected, it also used the call-adhesion method therefore, the ones belonging to these segments have been directly contacted.

The organizational model lacks much of the required information since the only one reported is the centers' responsibilities which is regional.

On the other hand, same as Lazio and Lombardy there is a complete frame of the vaccination unit. In Piedmont the number of vaccinal basic mix required for one line is five for the biggest structures and is composed of at least two doctors, two nurses who take care of the vaccine preparation, at least two people from administrative staff, at least two social health workers, and at least two volunteers.

6.4.3 Governance model

On 21 April 2020, a task force has been established to work alongside the regional council for the management of phase 2 of the coronavirus emergency. The coordinator of the group is Ferruccio Fazio, which worked as Minister of Health. The task force started to act immediately on the front of the territorial medicine, by a constant interaction with the health operators of the region.

6.4.4 Infrastructures and IT services

The booking platform developed for the Piedmont region is called “ilpiemontetivaccina”. It is a system based on the pre-adhesion of the patient, who will receive a confirmation message with the appointment in the following 48 hours.

6.4.5 Communication campaign

The communication campaign is initially disseminated via social media on the institutional channels of the region to furnish a base knowledge about the vaccines. Then was spread using local TV and newspapers. On the official regional website, it is present a set of 42 FAQ and a tutorial about the booking system to increase the completeness of the information. The main spokesman are politicians, but also the VIPs who are elected as ambassadors of the communication program.

Chapter 7- DISCUSSION

Done the collection of data for the four regions under analysis, it is now the turn of examining and drafting considerations about the vaccination campaigns.

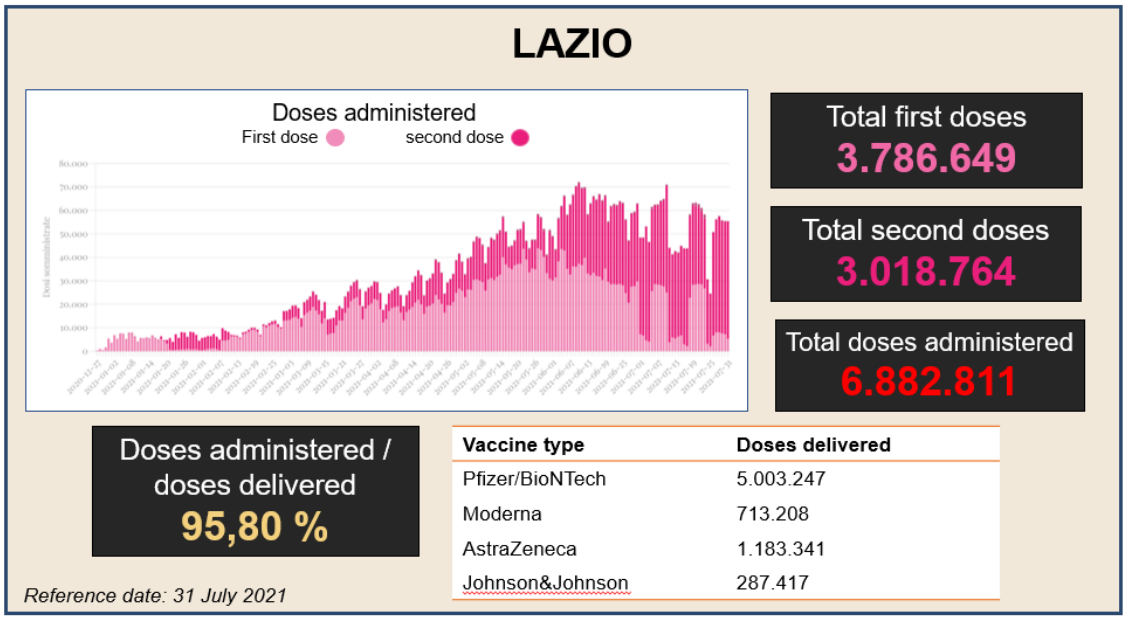
The chapter is organized in a first paragraph, in which the regions are analysed separately, then a second one in which commonalities and distinctive elements are presented through comparisons.

7.1 Single case analysis

This section considers the main information extrapolated from the regional plans; the regions will be analyzed one by one, tackling as main issues the capacity of the massive centers, how regions should approach to a possible closure of massive centers; how the booking system and the communication campaign could have affected the adhesions and finally the composition of the vaccination staff and the weak points derived.

7.1.1 Lazio

In the following figure (*figure 34*), it is presented a dashboard with the general performances of Lazio.



Vaccine type	Doses delivered
Pfizer/BioNTech	5.003.247
Moderna	713.208
AstraZeneca	1.183.341
Johnson&Johnson	287.417

Figure 34-Dashboard of Lazio

By comparing the performances with the regional plan, present in *annex J*, the following considerations are derived:

- The first regional index to be analyzed is the ratio between doses administered and doses delivered. This value assesses to 95,80%, that position Lazio as the 4th in Italy, after Lombardy, Marche, and Puglia.
  Being the value above the national average, equal to 95,6%, explains the ability of the centers to cope well with the demand for vaccines. Indeed, almost all the doses are rapidly administered to the population as soon as received. In order to reach this value of the index, the capacity installed in the vaccination points should be for sure large (the average capacity is about 31.865 doses, which normalized for the population is about 543 doses); Lazio is definitely a region where the speed has a central role, and it can support vaccinations not only to the priority segments but also fulfill the demand for the population in general.
- During the last phase of the vaccination campaign, the hypothesis of closing the massive centers in favor of pharmacies and MMG/PLS started to be evaluated. In this regard, a deeper investigation of the Lazio region is presented as follows. The total number of pharmacies, MMG/PLS in the region is about 8.140; supposing that all of them will be able to organize themselves to support the vaccination program, it is estimated that on average, for every 100.000 citizens there should be 139 vaccination points as the sum of pharmacies, MMG and PLS. As a consequence, each new CV should serve on average 721 people.
- The booking platform is created on regional basis, and it allows a set of services among which the choice of the center, the date and the vaccine type, the management of the appointment, the consultation of the booking information and the download of the pre-anamnesis module. Given the easiness and the number of services offered, the adhesion of the population may have been affected. The obtained result is 3.104.145 total adhesion since the beginning of the campaign, which correspond to the 52,92% of the population.
- Each vaccination center is organized on a regional basis for what regards the composition of the staff. In particular, the ratio between the number of doctors and nurses is 1 to1 in Lazio. Thus, for each doctor performing the anamnesis, a nurse is administering the vaccine. Since the inoculation is a very fast phase, of the duration of few minutes, this composition choice

will lead to queues at the doctor station, which duration is longer, especially if the patient did not compile the pre- anamnesis document. It is possible to affirm that the anamnesis is the bottleneck, which needs to be at least duplicated to solve the problem and make the process more rapid and fluid.

7.1.2 Liguria

In the following figure (*figure 35*), it is presented a dashboard with the general performances of Liguria.

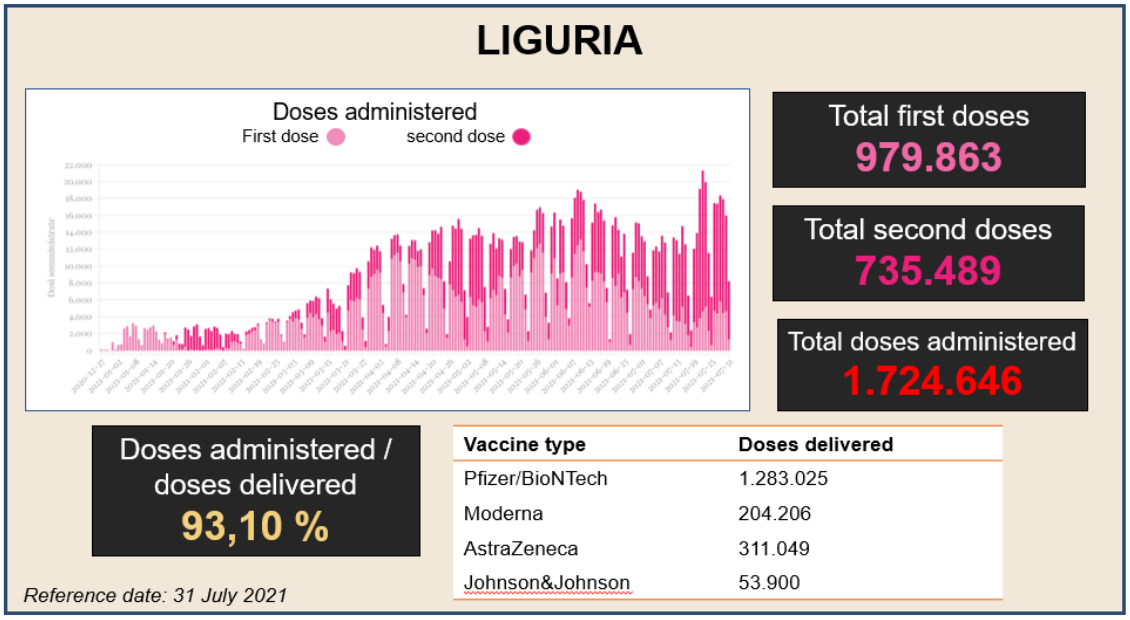


Figure 35- Dashboard of Liguria

By comparing the performances with the regional plan, present in *annex K*, the following considerations derive:

- The first index to be analyzed is the ratio doses administered on doses delivered. The value for Liguria is about 93,1%, that positions the region in the last 4 worst regions of Italy, together with Calabria and the autonomous provinces of Trento and Bolzano. Liguria is one of the slowest regions in the administration of vaccines. To support this performance index, it is possible to consider the capacity of the centers, which is low. The average productivity of massive centers is about 7984 doses, and normalized is about 517 doses. In conclusion, the region has decided to attribute higher importance to the administration of vaccines to the priority

groups (older and pathology affected patients) overshadowing the rest of the population, who received the vaccination with a slowdown.

- About the channels present in the region, Liguria has already activated the pharmacy system for the vaccine delivery, therefore should be ready and more advantageous when will come the time to close massive centers. In particular, in the region are present 612 pharmacies and 2.198 general practitioners and pediatricians. Considering the necessity to cover the total population, there should be 183 vaccination points (MMG/ PLS/ pharmacies) every 100.000 citizens. In the end, every center should have a capacity of about 550 people to vaccinate, which is a lower load if compared to the Lombardy and Lazio cases. With high probability, Liguria will be able to substitute the massive centers with the resources already in place.
- The booking system is supported by one regional platform which services are the possibility to choose the center and data, the consultation of the booking data, and the download of the pre-anamnesis module. The system is easy and simple since the number of services is essential. For that reason, the adhesions for the vaccination campaign equalized the 93,1% of the over 80, the 93,1% of the 70-79 people, the 71,6% of the 60-69 people, and the 60,3% of the 50-59 people (data registered on 25/05/2021).

7.1.3 Lombardy

In the following figure (*figure 36*), it is presented a dashboard with the general performances of Lombardy.

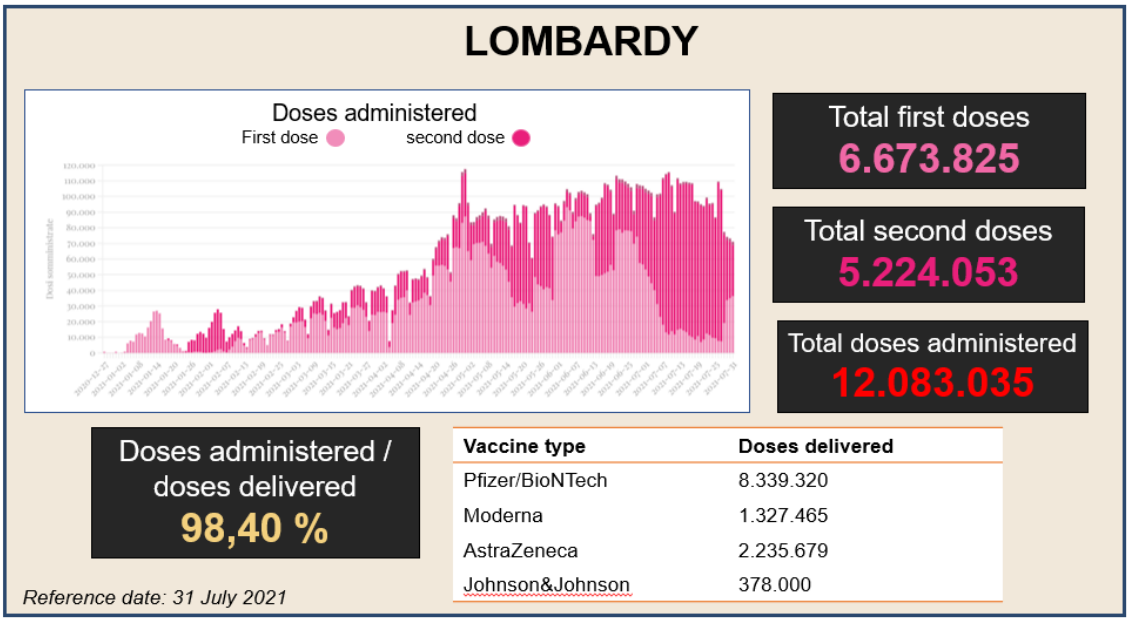


Figure 36- Dashboard of Lombardy

By comparing the performances with the regional plan, present in *annex L*, the following considerations are derived:

- The ratio doses administered on doses delivered is equal to 98,40%, putting Lombardy in first place in the Italian region by looking at this indicator. In the centers, almost all the doses received are delivered to people as fast as possible, leaving a minimum stock. As confirmation of this consideration, it is essential to consider the average productivity of the massive centers, which is about 55940 doses. This figure corresponds to 554 doses per day if normalized by the regional population. Definitely, Lombardy is the region with the highest speed in vaccinating not only the segments with high priority but all the population in general.
- Lombardy is the highest populated region in Italy. For this reason, the massive centers with their big capacity played a crucial role in the vaccination campaign. Also, for Lombardy, the most reasonable choice will be to close those centers in the short term, even if will be difficult to vaccine such a large number of citizens only using general practitioners, pediatricians and pharmacies. As a matter of fact, the total number of pharmacies, MMG and PLS for 100.000 people is 118, meaning that each new center should cope with 850 people, definitely a high number.
- The “Sistema Poste Italiane” has been adopted by the region because is able to manage a high number of bookings. The services offered by this

national platform are multiple and they include the possibility to choose the center, the data of the appointment, the consultation of the booking data and the download of the pre-anamnesis module. In addition, it offers access to the green pass; the vaccinated can download it following an easy procedure.

Furthermore, the region has put in place a structured communication plan using various channels to be able to reach all the population segments. In this way the campaign could reach a higher number of people; the percentage of adhesion by segments are 95% of the over 80, 89% of the 70-79, 84% of the 60-19, 78% of the 50-59, 66% of the 40-49, 51% of the 30-39, 21% of the 20-29 and just 8% of the 12-19 (data registered on the 28/05/2021).

- The region had autonomy for the management of the massive centers, in particular, it was able to define the staff inside each center. The chosen ratio between doctors and nurses is 1 to 1 (without considering any possible nurse in charge of dilutions). Thus, for each doctor performing the anamnesis, a nurse is administering the vaccine. As described in the section dedicated to Lazio, this configuration leads to the creation of queues at the anamnesis station, which is the bottleneck of the vaccination process.

7.1.4 Piedmont

In the following figure (*figure 37*), it is presented a dashboard with the general performances of Piedmont.

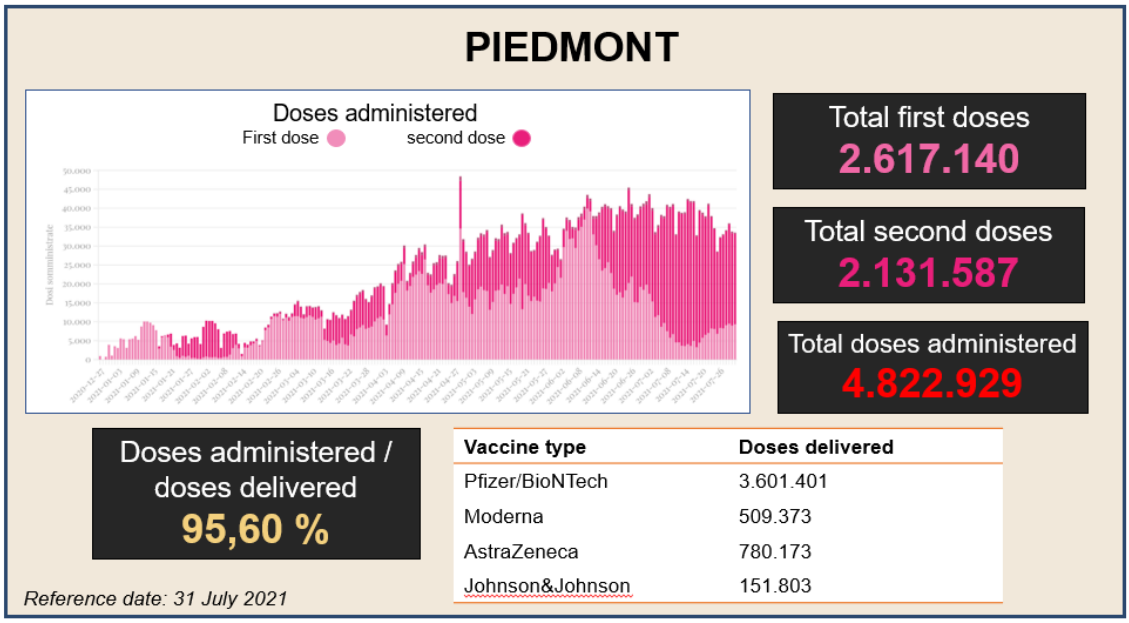


Figure 37 – Dashboard of Piedmont

By comparing the performances with the regional plan, present in *annex M*, the following considerations are derived:

- Starting with the index comparing the doses administered and the delivered doses, it is possible to obtain a value of about 95,60%, which positions the region at 5th place after Lazio. Being the value equal to the national average of 95,60%, Piedmont administers vaccines at similar rapidity at which it receives the doses. In order to reach this value of the index, the capacity installed in the vaccination points should be for sure large. The average productivity of the centers is high because they are able to administer about 22328 doses a day (514 doses normalized), meaning that Piedmont put in place a strategy based on vaccinating all the population in general, without focusing just on the priority segments (which for sure continue to be the focus).
- Piedmont has already implemented the delivery channel of pharmacies. Anyway, a prevision for the future should be done, in case of closing of the massive centers. The actual position and the result of the forecast are very similar to Liguria. Indeed, it is calculated that the total number of pharmacies, general practitioners, and pediatricians for 100.000 persons is about 151. As a consequence, the coverage for each of the aforementioned vaccination points should be at least 665 people, which is a sustainable capacity. It is a great result, especially if compared to Lazio

and Lombardy cases, which should sustain more patients in their structures.

- The booking system is characterized by the presence of one regional platform. The services offered to the population are: the possibility to make a pre-adhesion, the consultation of the booking data and the download of the pre-anamnesis module. It is a rigid system, especially if compared to the other regional platforms because the number of services is low. The disadvantage can be a negative impact of the adhesion on the population, who do not feel free to choose the data or the vaccination center location. What is more, Piedmont did not create a strong communication campaign, since it involves the use of few channels, maybe not enough to reach the majority of the population. In contrast, the number of FAQ is high and provide precise information to the citizens. The related percentage of adhesions for the region are: 90,68% for the over 80, 85,56% for the 70-79 people, 77,12% for the 60-69 people, 69,12% for the 50-59 people, 57,95% for the 40-49 people (data are registered on the 28/05/2021).
- Piedmont's strategy about the composition of staff in the massive centers concerns a not equal number of doctors and nurses. In particular, the ratio between doctors and nurses developed in the biggest massive centers is higher than 1. That involves the presence of more than one doctor for each nurse and it guarantees no queueing at the anamnesis station. Instead, the unit a fluid process and an equally distributed workload between all the personnel.

7.2 Cross case analysis

7.2.1 Commonalities among regional vaccination campaigns

The main commonalities among the analyzed regions are, for sure, symptoms of the fact that the national territory is shared. Moreover, the central government set some key elements of the campaigns, which cannot be modified.

To decide who should be vaccinated first, the national plan uses the criterion by age group, from the oldest to the youngest. Anyway, some corrections are applied. The vaccination of health personnel, over 80, school staff, military, and

law enforcement must be completed in the first phase. The priority is given also to the “extremely fragile” who suffer severely from a series of pathologies plus the disabled, those recognized by law 104. In parallel, each region should follow the criterion of age groups in descending order, starting with people over 70 years old.

To cope with the high number of vaccinations to be done, each region must set up some massive vaccination centers. These can be of multiple typologies: stations, car parks of the shopping centers, congress centers, sport, facilities or stadium.

About the operative model, more degree of freedom was given to regional governments. The first common factor is the distribution of the vaccination centers throughout the territory: all the analyzed regions decided for a distributive model, hence a location of centers following the population density; when it increases, also the number of centers is multiplicated and vice versa: since the vaccine centers are closer to the population, this certainly contributes increasing the administration of the vaccines. The second point of equality is the centrality of the local companies in the distribution of vaccines to the vaccination points. The result is the adoption of the ASL-centric model for all of the regions analyzed.

Last but not least commonality, is the possibility to speed up the overall vaccination process by means of pre-anamnesis: the patients can download the document during the booking procedure, fill it in with the personal medical information and deliver it to the doctor at the vaccine center.

7.2.2 Distinctive features of regional vaccination campaigns

Now that the communal characteristics of the regional campaigns have been defined, it is necessary to shed light on what differentiates them.

For what regards the presented campaign elements, small differences emerge between the regions. For example, talking about the enlistment modalities, Piedmont is the only one that adopted the adhesion-call approach instead of the most common adhesion-booking. Another distinction comes from Liguria; the region decided to involve the pharmacies in the campaign since its earliest phases. This condition could result in a fundamental advantage for the next

development of the vaccination. In the first position, it offers a privileged assessment; it allows an easily accessible administration capacity, which derives from pre-existent structures. This implies that it is not necessary to create new ad-hoc vaccination points in order to meet the same capacity and productivity. The choice of involving pharmacies could also be an advantage for different regions comparing their distribution with the population density across the regional territory. In fact, considering the Liguria case, the number of pharmacies is high with respect to the inhabitants, and moreover, they are displaced homogeneously across the region. The result is easy and fast access for all the population to the vaccination points. Last but not least, the pharmacies as Covid-19 vaccine administration points are receiving more and more attention. With the proceeding of the campaign, the demand to be managed is decreasing, therefore, a tangible hypothesis could be to shoot down the biggest massive centers and continue the administrations in structures of reduced dimensions. Having been involved since the earliest stages, the pharmacies could allow Liguria to score a winning point against the other regions. Indeed, the vaccine administration in the pharmacies is by now well established. Instead, many regions still have to pass through their organization.

However, the main diversities can be assessed through the reasoning that incorporates and compares the main performance drivers of the Covid-19 vaccination campaign.

First of all, an analysis can be carried out on the percentage of the population that received at least the first dose in the reference period (27/12/2020 - 30/07/2021). This is relevant information because it reflects the rapidity of the regions during the observed campaign duration, which is equal to 216 days. The table below represents the ranking (*table 9*).

Region	First Doses/Tot. Population
1. Lombardy	66,1%
2. Lazio	64,6%
3. Liguria	63,5%
4. Piedmont	60,3%

Table 9 - Percentage of first doses achieved

Lombardy, although it is the most populated region, obtained the best performances. The last classified, Piedmont, did not keep up with others.

Another element of interest is to observe the peak productivity of the four cases and particularly to define when it occurred: the regions with a better organization should have reached the peak earlier. In this case, the amount of administered doses must be normalized in order to consider the different population densities of the regions. The outcome is quite linear, 1.115 Piedmont, 1.160 Lombardy, 1.222 Lazio, 1.234 Liguria doses every 100.000 inhabitants. Piedmont and Lombardy achieved their peaks in two consecutive days, respectively, the 29 and the 30 of April 2021. For the others, it needs to pass about one month and a half. Indeed, Liguria obtained its maximum on the 9th of June and finally Lazio on the of 10th June. These data allow to distinguish the cases in two, nevertheless of the capacity installed Lombardy, and Piedmont developed a plan which enables them to reach the maximum productivity ahead of Liguria and Lazio. The figures are associable with the concept of agility. The literature encompasses many definitions of this term; to the regards of this analysis it can be exploited the one by Rigby et al. (2000), determining agility as “the ability of an organization to thrive in a constantly changing, unpredictable business environment”.[10] Given this reference, it can be stated the impact of such analysis on the operational agility of the regions. Piedmont and Lombardy promptly reacted to the pandemic by delineating and activating two effective vaccination plans. The result is high agility that allowed them to reach their peaks earlier than the others. Concerning the other two regions, it can be emphasized that the adapting capability to the

[10] S. Bernarders, E. and Hanna, A theoretical review of flexibility, agility and responsiveness in the operations management literature: Toward a conceptual definition of customer responsiveness", *International Journal of Operations & Production Management,* 2009, Vol. 29 (1), pp. 30-53

emergency is definitely lower. From the analysis of the peaks, it is visible that Lazio and Liguria struggled with organizational issues. Concluding, the four regions settle down to two completely different levels of agility.

To understand the speed and the effectiveness of the vaccination campaign is also possible to look at the effects on the spread of the new infections; the vaccine is supposed to slow it down. This kind of investigation can be conducted by analyzing the Rt figures, in particular, they have been traced weekly during the study time window.

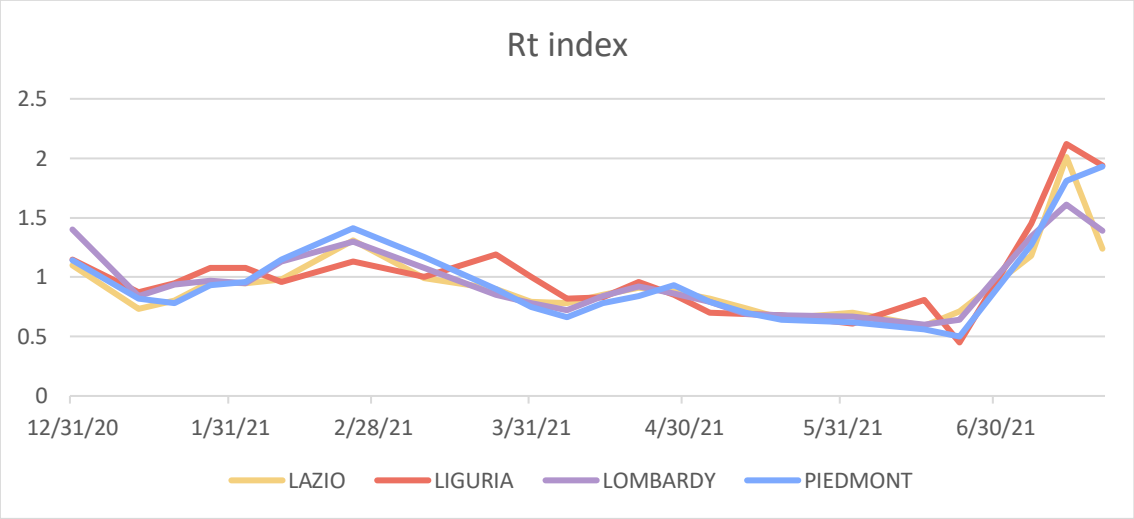


Figure 38 - Rt weekly indexes

As *figure 38* shows, all four regions exhibit similar curves in the first phase of the campaign, at least until the end of February and the beginning of March. Then, Liguria seems to take a different direction. Lazio, Lombardy, and Piedmont reached the highest Rt value on 25/02/21 and, from there, a linear decrease started; Liguria on the other side arrived at the peak five weeks later. The interpretation of these events is that: while at the earlier stages, the vaccination campaign proceeded cohesively across the four regions, during the time frame between March and April, Liguria remained at lower productivity compared to the others. During July, all the four regions manifested a rapid increase of the index, this is mainly due to the presence of the “Delta” variance, which was very contagious and increased the infected people.

Going on, a further consideration arises from the merge of two elements: the level of services offered by the booking platforms of the regions and the grade of compliance to the vaccination campaign, distinct by age group. The second piece

of information is not easily retrievable; therefore, the data may not be completed for all the regions, and the reference dates are different.

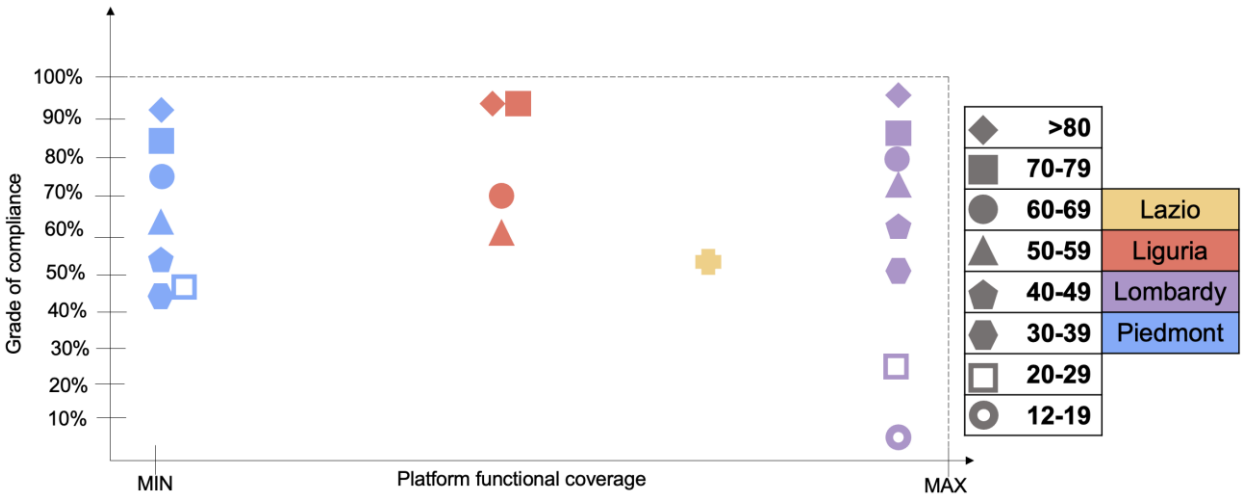


Figure 39 – Matrix platform services vs adhesions

The richest regions in terms of data are Piedmont and Lombardy which are positioned exactly at the two extremities of the platform functionalities scale. In addition, they are a proper comparison since all the grades, except for the 20-29 and 30-39 grades of Piedmont, are measured on 28/05/2021. The results look really similar, Lombardy is slightly ahead in all age groups, and this could be the evidence of a small correlation between the number of platform services offered and the grade of compliance. A relevant exception is visible in the Piedmont 20-29 range, at the 5thJuly is equal to 48,45%[11], more of the double of the Lombardian one (21%[12]) but it needs to be considered the time difference. Anyway, it outranks the following age sector (30-39) which is measured at the same date, while in Lombardy the adhesions follow a linearly decreasing curve. About Lazio, it occupies a middle-high position regarding the platform offer but the only indication regards the total population and registers an overall grade of 52,92% at the 31/07/2021.

[11] https://ricerca.repubblica.it/repubblica/archivio/repubblica/2021/07/05/cinquecento-ricorsi-al-tar-di-sanitari-che-non-si-vaccinanoTorino05.html?ref=search

[12] https://www.ilcittadinomb.it/stories/Cronaca/vaccinazioni-in-lombardia-verso-6-milioni-di-dosi-ladesione-per-tutte-le-fasc_1397441_11/

Finally, Liguria has only partial information dated 25 of May therefore it is quite approachable to the first comparison. In fact, the grades are similar except for the one regarding people in their 70s. In this case, it is perfectly equal to the grade of the immediately older group (93,10%[13]) while in the other cases is always lower. Concluding this analysis, it could be said that there are no indications of a strong correlation between the grade of compliance to the vaccine and the dimension of the functional services range.

A final juxtaposition can be constructed on the ratio between administered doses and delivered doses. The situation in the four regions is here illustrated (*figure 40*).

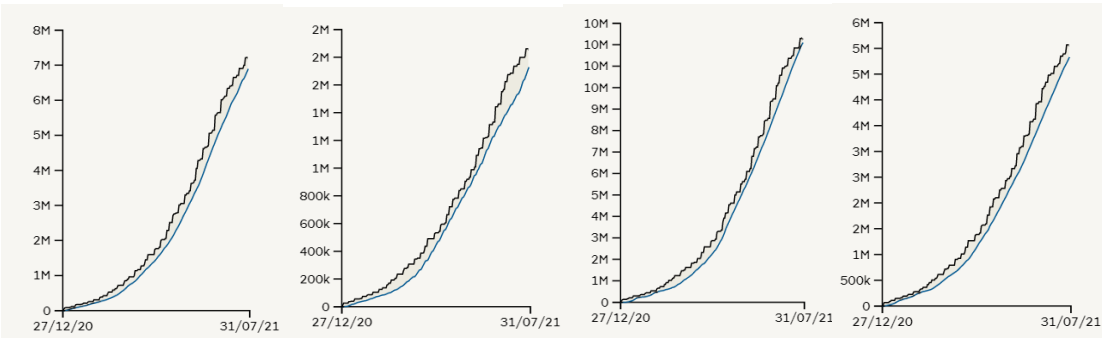


Figure 40 - Doses administered on delivered for Lazio, Liguria, Lombardy, and Piedmont

The broken line represents the administered doses, day by day, while the continuous blue line reflects the total available vaccine stocks.

All the regions have an overall ratio quite good, all of them overcome the threshold of 90%. However, looking at the comprehensive curve and not only the point figure some deviations arise. Lombardy has always kept the ratio at a high level since the very beginning of the campaign, visible by the closeness of the two curves. On the other side, the other three regions seem to have a slowdown in the last part of the monitored period. In fact, the two curves do not match, especially for Liguria which shows the highest discordance between the administered and delivered doses.

This kind of data provides hints for further investigation in terms of logistics performance. Indeed, from the previous figures, it can be derived the useful index

[13] https://www.ansa.it/liguria/notizie/2021/05/25/vaccini-totiin-liguria-quasi-100-sanitari-li-ha-accettati_380ac70d-5503-406c-b12a-752cf9c28191.html

Inventory Turnover. It represents “the number of times a business sells and replaces its stock of goods during a given period.”[14]. This ratio is a helpful tool when it comes to evaluating the effectiveness of stock management. Generally, the goal is to keep an IT high, meaning that the business manages to keep renewing its stocks without risk of obsolescence. However, not always the higher the Inventory Turnover, the better; if the stock rotation is too big, it may lead to shortages due to inadequate inventory levels.

The Covid-19 vaccine doses belong to a particular type of good. The supplies, indeed, are managed by the government rather than the regions directly. Anyway, the different administration rhythms of the regions affect the ratio, which can be adopted as a performance indicator.

In this case, the total regional stocks are computed as the difference between delivered and administered doses. All the data refer to 31/07/2021, the last day of the period of analysis. Finally, the IT ratio is the number of total administered doses on the total regional stocks.

Here is the example computed with the Lombardy data.

TOT. stock Lombardy = doses delivered-administered= 193547 doses in the period of analysis

IT Lombardy = tot doses administered/tot stock Lombardy= 11903155/193547= 61 rotations in 216 days

These figures mean that the stock is renewed 61 times in the period of analysis. The consequence is that the vaccine doses remain in the warehouses for 3,5 days, which indicates a rapid administration.

By performing the same calculation, the total stock and IT values of the other regions are obtained (*table 10*).

Region	TOT. stock (doses)	IT (rotations)
Lazio	239698	28,99
Liguria	115772	14,99
Piedmont	157456	31,03

Table 10- Regional Inventory Turnover

[14] https://corporatefinanceinstitute.com/resources/knowledge/finance/inventory-turnover/

As it is visible, Piedmont and Lazio obtained similar IT ratios. Both the regions completely rotate their stocks in about one week. From the ranking point of view, this locates them still behind Lombardy with Inventory Turnover twice bigger.
Liguria takes the last position. Its ratio indicates a stock renewal only every two weeks that is by far the worst performance.

These data act as a confirmation for the previous analysis. However, it is also supposable that the stock management of Liguria should be revised. With the current administration speed, the level of stock is overestimated.

7.2.3 Key performance drivers

At this point, it is fundamental to derive conclusions about the region which performed better between the ones compared.
For the definition of the ranking, the AHP procedure could be adopted, by comparing the most relevant parameters. In particular, the main variables used are the regional speed to vaccinate all the population, the predisposition of the region in opening pharmacies, MMG and PLS as vaccination centers, the number of over 80 people vaccinated, the vaccination coverage (first doses) on the total population. The scale used to assign the points to each region goes from a maximum of 4 (best performance) to a minimum of 1 (worst performance).
To determine the vaccination speed has been adopted different proxies: the percentage of administered on the delivered doses, the date of the peak productivity, the average capacity normalized, and the peak capacity; by doing a weighted average of the obtained performances is possible to assign 4 points to Lombardy, 3 to Lazio, 2 to Liguria and 1 to Piedmont. Secondly, the predisposition of the region to use alternative vaccination points. It is indicated by the number of people that each pharmacy/PLS/MMG should cope with in case of closing of massive centers, and the most talented region, in this case, is Liguria, followed by Piedmont, Lazio, and Lombardy. The last three variables used are indicators analyzed in the previous paragraphs, for which a rank has been defined based on their values. A summary of the points given to the regions for each variable, is visible in *table 11*.

	Lombardy	Lazio	Liguria	Piedmont
Vaccination speed	4	3	2	1
Pharmacies capacity predisposition	1	2	4	3
Num. vaccinations over 80	4	3	1	2
Services of the booking platform	4	3	2	1
Vaccination coverage (first doses/total pers.)	4	3	2	1

Table 11- Variables definition for each region

After derived the aforementioned table, it is possible to compare each region against the others by performing an AHP matrix. The value of diagonal is equal to 1 for construction, while the remaining cells must be filled by answering the following question. "How many times the $region_i$ is better than the $region_j$?", where i is referring to the regions present in rows, while j to the ones in columns. For example, Lombardy is 4 times better than Lazio, since Lombardy beat Lazio for 4 out of 5 variables, so the number 4 should be put in cell C_{12}.

The final AHP table, filled with the just described logic, is visible in the following *table 12*.

	Lombardy	Lazio	Liguria	Piedmont
Lombardy	1	4	4	4
Lazio	1	1	4	4
Liguria	1	1	1	4
Piedmont	1	1	1	1

Table 12-AHP table

By looking at the AHP table, it is possible to define the final ranking. In particular, in the first place, there is Lombardy, followed by Lazio, Liguria and at the end, Piedmont.

Chapter 8- CONCLUSIONS

Now that the study is completed, a synesis of the results is presented, focusing on the key elements that characterize the two sub-analysis, the related advantages, and future improvements.

8.1 Synthesis of key results

The outcomes provided by the study have the goal of improving the performances of the two fundamental tools used to fight against the Covid-19 pandemic: the RT-PCR tests and the vaccine delivery plans.

For the diagnostic tool, it has been created a FMECA toolkit, composed of two Excel files called FMECA tool and FMECA sources. The first one has the visualization of a classic FMECA. A table, where the rows represent the adverse events for which causes, consequences, effects, and mitigation actions should be found. In the case of analysis, 134 events are presented and cover the phases of demand generation, pre-analytical, analytical, and post-analytical. Other information, like RPN and organizational issues, are present, but not filled already because they should be completed by the risk managers when applying the tool. The information already filled is about the consequences, causes, effects on the patient, and mitigation actions, and they are presented in the tool by means of some codes. The codes are translated in the file FMECA sources, which is a collection of all the information obtained by the literature, experts, and incident reporting provided by Lombardy structures.

The toolkit will be sent to all the Lombardy risk managers, who will exploit the tool to prevent errors and improve their processes. They will be provided also with two FMECA cases, the application of the toolkit on two laboratories located in Brescia and Mantova to have a practical view on how to use the toolkit.

The suggested usage is to start from the FMECA tool, look at what are the possible events that may happen and understand them through causes, consequences, and effects thanks to the codes. At this point compute the RPN to identify the area of highest priority, leveraging on the pre-defined scales; if for

these items there are no preventive actions already in place adjust the mitigation strategy in order to understand which intervention could be useful.

The coverage obtained for the FMECA tool is not homogeneous. In particular, the causes have a final coverage index of 96%, mainly provided by literature and experts information; the consequences and the effects respectively of about 15% and 16%; finally, the mitigation actions have coverage of 43% thanks to the literature and incident reporting sources. The initial level of coverage is a good starting point for the structures that will use it. Of course, it is expected to increase with the future upgrades suggested in the last paragraph.

In conclusion, what has been developed through the toolkit is a base of knowledge upon which all the institutions can integrate information from their personal experience. The more their involvement is the more powerful the toolkit will become.

The second outcome provided by the thesis is the definition of a framework of analysis that can be applied to compare different vaccination campaigns. The framework consists of three main parts: the contextual elements, the key elements and finally, the operational and health performances. The key elements adopted to obtain an overall picture of the region are the demand management, the operative model, the governance, the IT infrastructure, and the communication campaign. Those elements must be defined for the set of regions of interest by compiling the template, which has been created to increase the standardization of the comparison.

In this case, four Italian regions have been analyzed and compared: Lazio, Liguria, Lombardy, and Piedmont. The result is the creation of four Excel tables to trace the key elements describing the plans. The coverage indexes for the four templates are about 45% for Lazio, 44% for Liguria, 55% for Lombardy and 49% for Piedmont. Those values are considered enough to complete the evaluation of the campaigns.

The operational and health performances are the second issue to be defined. The real-time databases on the vaccinations need to be checked constantly till the end of the evaluation period, 31 July. The main variables of interest are reported on an Excel file and used to get comparisons with the key elements.

The main points of analysis regard the vaccination speed, the vaccination mix inside the massive centers, evaluations about possible future closing of massive

centers, the booking platforms adopted in the region and the related services, the communication channels and how these last two features affected the adhesions. Finally, a final ranking has been drafted by taking into account the aforementioned variables of analysis and by performing an analytic hierarchy process (AHP). Lombardy resulted as the most talented region, followed by Lazio, Liguria, and finally Piedmont.

What distinguished Lombardy from the other regions is for sure the high vaccination speed, guaranteed by a high capacity of the vaccine centers, distributed on the territory following a distributed logic. Also, the strong communication campaign and the platform used for the demand management (the Poste Italiane system) gave a push to the number of adhesions for all the age segments.

By looking at the results from the clinical governance perspective the two proposed problems are definitely addressed. In fact, the main objective of the analysis was to look at the lack of resources for health care facilities during pandemics, specifically the Covid-19 pandemic, and how it impacts the protection and prevention strategies.

As it has been highlighted, many issues and difficulties could arise both from the RT-PCR diagnostic procedure and the creation of vaccination campaigns. However, thanks to the conducted study and its outcomes it is now possible to have in your hand simple tools which could be applied to better face these situations. In conclusion, this thesis demonstrated that clinical governance is deeply attacked by the effects of unknown and uncertain events that may cause serious effects. Anyway, it is important to develop research and studies to analyze the conditions and derive possible ways out; in this case standardization is the key to success. The instruments born from the analysis can be used, modified, or further implemented to investigate the current pandemic and not only.

8.2 Contribution to research

The entire study contributes to research for many reasons. The common feature of the two studies is for sure the degree of innovation since no previous works about the RT-PCR test process and evaluation of vaccine campaigns had been

done recently in such a detailed manner. It is an important breakthrough for researchers who want to tackle and deep dive into these two analyses.

Many articles have been written about the real-time PCR tests to discover the presence of viruses; fewer about the articulation of the different phases of the process from the client request to the evaluation of results; rare about the decomposition of the process in adverse events for which causes, consequences and corrective actions should be discovered. What has been done in the thesis is to enrich this last issue, not treated at all by the literature.

The originality of the study arises from the sources used; the pieces of found literature, the incident reporting provided by hospitals, and the expert knowledge on the process. By doing this, researchers can count on a 134-events database combined with as many sources of information. Also, by reading the analysis done, they should be able to repeat the FMECA and apply it to optimize all the tools against covid-19 or to other health fields not dealing with the pandemic.

When the pandemic broke out in Italy, the “pandemic preparedness and response plan” was stuck in 2006.[15] Many, especially within the government, confirmed that this plan was inadequate for two different reasons: first, it was not updated, and second it was referred to the flu, so it could not be applied to the new virus. For that reason, Italy had to work hard to create effective guidelines for the management of the pandemic.

The researcher who approaches the analysis done on the comparison of vaccine campaigns will be offered a more recent point of view on how to manage a pandemic. What is more, he will be able to model, basing on the template created, analyze, and evaluate different pandemic plans. The freshness of the framework of analysis consists of the breadth of the contents, ranging from the demand management to the operative, the governance, the IT services, and the communication.

8.3 Relevance for practitioners and policymakers

Thanks to the two analyses developed in the thesis, the hospitals, and regional healthcare can rely on a set of intuitive and easy to apply tools.

[15] https://www.ilfattoquotidiano.it/2020/12/21/piano-pandemico-litalia-lo-aveva-anche-se-vecchio-dove-e-stato-applicato-ospedale-di-schiavonia-ha-evitato-il-disastro/6043810/

On the one hand, the FMECA toolkit aims at helping the laboratorial structures in Lombardy in the risk assessment of the RT-PCR test process and its optimization. In this way, the structures will have in their hands a powerful tool, the FMECA toolkit. It, not only will help them in achieving better individual results in the PCR testing process but will also enhance a kind of standardization throughout the region.

On the other hand, the vaccine campaigns comparison provides regional healthcare infrastructures a new way to model, evaluate, and describe a plan. What regions should do is: shape their campaign, monitor their performances, and refine the weak points in order to create a strong plan for future campaigns. By continuing to perform the refinement process, the regions should optimize their campaigns and develop an updated regional pandemic plan to be more ready to face future necessities.

8.4 Limitations

The studies were carried out smoothly and without severe difficulties. Obviously, there were obstacles that mostly concerned the relationship with the external parties involved in the study and the limited information on the web. These problems never stopped the work but have slowed it down in several points.

For what concerns the first part, the main criticality is about the translation of the sources of information at our disposal in causes, consequences, and corrective actions needed to enrich the FMECA template. The incident reporting provided by the Lombardy hospitals were arduous to decode since some of them presented near misses and not useful information, few were not inherent to the tampon process, and others had been written superficially and, approximately this last complication made the comprehension longer and complicated to such an extent that the intervention of two experts became necessary and essential.

Finally, the FMECA method had been time-consuming, and it will be a limitation also for the hospitals when they should start using the toolkit provided them.

The second part had been more problematic for the lack and the variability of information available on the web. Indeed, the official websites and articles deal more often about demand management and how to enlist for vaccines rather than the governance, communication campaign, and IT systems. Since the pandemic

is ongoing, the regions are regularly updating decrees and restrictions, therefore it is relevant to stay updated with the changes and keep track of them in the analysis.

Finally, the increase of cases in the last period has meant the lack of regional referents who should have completed the missing template data

8.5 Future research

The future upgrades for the FMECA analysis are synthetized as follow:

- Every year the toolkit should be renewed with new incident reporting coming from the laboratory structures of Lombardy to increase the coverage index for the causes, consequences, effects and especially, the corrective actions to put in place.
- Extend the FMECA analysis throughout all Italian territory to increase the standardization procedure at a national level and the amount of information for the filling procedure.
- Create a panel of experts to increase the population of the FMECA sources.

In the short term, the study should be published on the Agenas portal. Its scope is to support the national health system to manage situations of clinical and organizational complexity.

For what regards the evaluation of the vaccine campaigns, the future research could be:

- Extend the analysis to all the Italian regions to understand the most talented ones and take useful hints to improve the regional plans.
- Evaluate the national campaign and perform a benchmarking with other nations.

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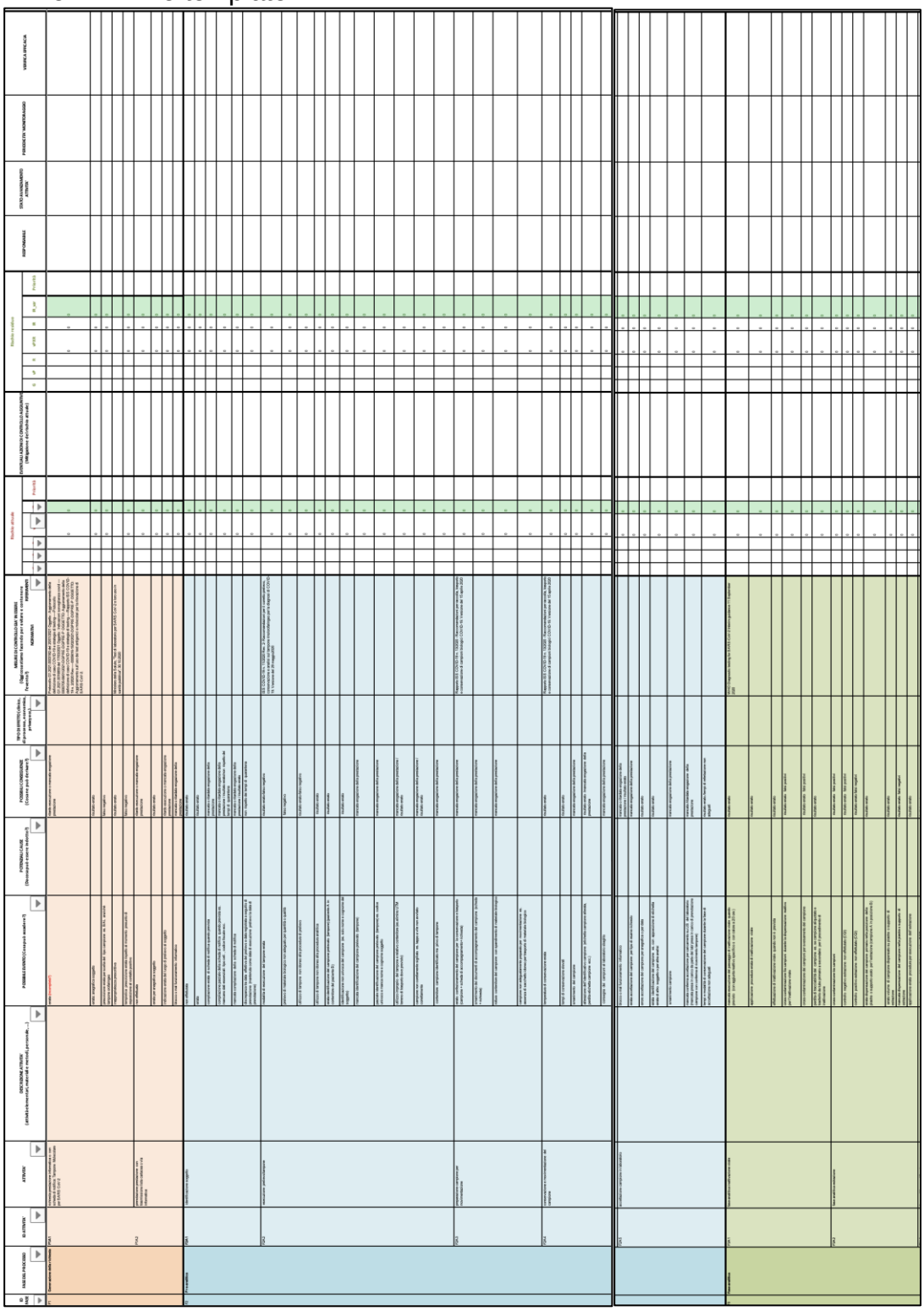
ANNEXES

Annex A - The template.



ID FASE	FASE DEL PROCESSO	ID ATTIVITA'	ATTIVITA'	DESCRIZIONE ATTIVITA' (attività elementari, materiali e metodi, personale, ...)	POSSIBILE EVENTO (Cosa può accadere?)	POTENZIALI CAUSE (Perchè può accadere (evento?)	POSSIBILI CONSEGUENZE (Cosa può derivare?)	TIPO DI EFFETTO (clinico, di processo, economico, privacy,.....)	MISURE DI CONTROLLO GIA' IN ESSERE (Oggi cosa stiamo facendo per evitare o contenere l'evento?) RIFERIMENTI NORMATIVI	Rischio attuale						Priorità	EVENTUALI AZIONI DI CONTROLLO AGGIUNTIVE (Mitigazione del rischio attuale)	Rischio residuo						Priorità	RESPONSABILE	STATO AVANZAMENTO ATTIVITA'	PERIODICITA' MONITORAGGIO	VERIFICA EFFICACIA
																		G	vF	S	vFdS	R	R_ver					
		FSA3	fase analitica amplificazione		errata preparazione dei reattivi per real time PCR		risultato errato						0	0							0	0	0					
					applicazione errata procedura per esecuzione amplificazione real time PCR		risultato errato						0	0							0	0	0					
					errato trasferimento del campione estratto in piastra o altro supporto necessario per amplificazione genica in real time PCR (campione A in posizione del campione B)		risultato errato						0	0							0	0	0					
					errato volume di campione estratto utilizzato per real time PCR		risultato errato						0	0							0	0	0					
					mancato trasferimento del campione estratto su piastra o supporto per real time PCR		risultato errato falso negativo						0	0							0	0	0					
					cross-contaminazione tra campioni (al momento del trasferimento del campione da supporto che contiene campione estratto a supporto utilizzato per amplificazione)		risultato errato falso positivo						0	0							0	0	0					
					errato trasferimento di Data base o strumento per amplificazione Real time PCR (LIS no software o mancata di gestione dello strumentazione o inserimento manuale di programmazioni) anagrafica paziente, ID Campione e tipo di prestazione (es. Ricerca SARS COV-2 rispetto ad altri virus o batteri)		risultato errato						0	0							0	0	0					
					errata programmazione dello strumento per real time PCR		risultato errato						0	0							0	0	0					
					errato caricamento campioni su strumento real time PCR che induce errata associazione tra anagrafica, ID Campione e campione stesso, ad esempio verso piastra di amplificazione o sequenza carburos		risultato errato						0	0							0	0	0					
					controllo negativo non inserito nella seduta analitica (CQI)		risultato errato			DDG Sentito n. 32899 19/12/2008 "Linee guida su "Controllo di Qualità Interno nel Servizio di Medicina di Laboratorio"			0	0							0	0	0					
					numero di controlli negativi non idonei alla numerosità di campioni analizzati nella seduta analitica (CQI)		risultato errato						0	0							0	0	0					
					controllo positivo non inserito (CQI)		risultato errato						0	0							0	0	0					
					numero di controlli positivi non adeguati per numerosità seduta analitica (CQI)		risultato errato						0	0							0	0	0					
					ritenuta rilevazione di un gene target a causa di variante molto rara		risultato errato			"TECHNICAL REPORT Methods for the detection and identification of SARS-CoV-2 varianto E CDC marzo 2021 "Methods for the detection and identification of SARS-CoV-2 variants"- WHO Diagnostic testing for SARS-CoV-2 Interim guidance 11 September 2020			0	0							0	0	0					
					ritenuta amplificazione rilevazione di un gene target a causa di variante vista non nota		risultato errato			"TECHNICAL REPORT Methods for the detection and identification of SARS-CoV-2 varianto E CDC marzo 2021 "Methods for the detection and identification of SARS-CoV-2 variants"			0	0							0	0	0					
					necessità di intervento manuale di operatore su sistema automatizzato (es. di dispensazione campione o altro errore di tracciabilità)								0	0							0	0	0					
		FSA4	fase analitica: scelta del sistema analitico/strumentazione di installazione/ controllo sistema analitico/ pre-lavoro		scelta del sistema analitico non adeguato al fabbisogni		tempi di erogazione delle prestazioni non adeguati all'organizzazione utile al processo decisionale clinico (sistema manuale troppo lento) o spreco per insufficiente utilizzo			WHO reference number: WHO/COVID-19/laboratory/2020.5 — WHO reference number: WHO/2019-nCoV-/laboratory/2020.6 WHO Diagnostic testing for SARS-CoV-2 Interim guidance 11 September 2020 — https://www.ecdc.europa.eu/en/novel-coronavirus/laboratory-support — https://www.ecdc.europa.eu/en/all-topics-a-z/coronavirus/threats-and-outbreaks/covid-19/laboratory-support#questions — https://www.linkbio.org/covid			0	0							0	0	0					
					mancata esecuzione dei test a causa dell'indisponibilità del materiale per erogazione della prestazione (plastiche, reagenti di estrazione e di amplificazione)		tempi di erogazione della prestazione non adeguati all'organizzazione utile al processo decisionale clinico																					
					scelta sistema analitico non adeguato al contesto del laboratorio		mancata o ritardata erogazione della prestazione / risultato errato			WHO reference number: WHO/COVID-19/ /laboratory/2020.5 — WHO reference number: WHO/2019-nCoV-/laboratory/2020.6			0	0							0	0	0					
					verifica prestazionale del sistema analitico scelto non eseguita (verifica concordanza diagnostica vetso metodo di riferimento, percorso di verifica dello preformance analitiche sensibilità, riproducibilità, ripetibilità ecc..)		risultato errato			Nota protocollo Ministero della Salute 0009774-20/05/2020-DGPRE-DGPRE-P- Nota Protocollo Regione Lombardia G1.2020.0029969 del 19/05/2020 — Nota Protocollo Regione Lombardia G1.2020.0027848 del 21/07/2020 — WHO reference number: WHO/COVID-19/laboratory/2020.5 — "TECHNICAL REPORT Methods for the detection and identification of SARS-CoV-2			0	0							0	0	0					
					limiti di sensibilità analitica (LoQ) non adeguati al processo decisionale clinico		risultato errato			Rapporto ISS COVID-19 n.26/2020 «Dispositivi diagnostici in vitro per COVID-19. Parte 1: normativa e tipologia» Versione del 19 maggio 2020 — Rapporto ISS COVID-19 del n. 46/2020 - Dispositivi diagnostici in vitro per COVID-19. Parte 2: indicazioni per metodi a riferimento per gli sviluppatori			0	0							0	0	0					
					mancata esecuzione VEQ		risultato errato			Nota protocollo Centro Riferimento Regionale 36/2020 del 20 giugno 2020			0	0							0	0	0					
					esiti performance VEQ non ottimali non considerati		risultato errato			Nota protocollo Centro Riferimento Regionale 36/2020 del 20 giugno 2020 — Protocollo Regionale Sensitivity of SARS-CoV-2 molecular detection in clinical samples" Laboratories external quality assessment, June and July 2020 — J Clin Microbiol 58:e00676-20			0	0							0	0	0					
					mancata manutenzione programmata della strumentazione		risultato errato						0	0							0	0	0					
					mancata pulizia ed sanificazione della strumentazione		risultato errato			Laboratory biosafety guidance related to coronavirus disease (COVID-19) Interim guidance, 29 January 2021			0	0							0	0	0					
					errata manutenzione ordinaria o straordinaria		risultato errato						0	0							0	0	0					
					errata pulizia ed sanificazione della strumentazione		risultato errato						0	0							0	0	0					
					malfunzionamenti informatici LIS/piattaforma analitica non adeguati		risultato errato						0	0							0	0	0					
					pulizia e rispetto degli ambienti di lavoro che per la biologia molecolare prevedono tre distinti locali.		risultato errato						0	0							0	0	0					
					erogazione prestazione con "service" (outsourcing) non prevista		ritardo erogazione prestazione						0	0							0	0	0					
		FSA5	gestione erogazione prestazioni con "service"		smarrimento dei campioni inviati in "service"		mancata o ritardata erogazione della prestazione / risultato errato			DDG Sentito n. 43811 09/10/1998 Direttive in ordine all'attività del Laboratorio di Analisi Medicine a scopo diagnostico			0	0							0	0	0					
					errata conservazione e movimentazione dei campioni inviati in "service"		risultato errato						0	0							0	0	0					
					errata identificazione dei campioni inviati in "service"		risultato errato						0	0							0	0	0					
					errore di trascrizione esiti della prestazioni erogate con "service"		risultato errato						0	0							0	0	0					
					ritardo rivezione risultati prestazioni erogate in "service"		risultato errato						0	0							0	0	0					
	Fase Postanalitica	FAA1	validazione dell'esito real time PCR		errata validazione della curva di amplificazione del campione		risultato errato						0	0							0	0	0					
					errata validazione della curva di amplificazione del controllo interno di reazione quando disponibile (es. housekeeping gene)		risultato errato						0	0							0	0	0					
					errata applicazione dei cut-off decisionali per i CI per ciascun gene target		risultato errato						0	0							0	0	0					
					utilizzo dei cut off decisionali per i CI errati		risultato errato						0	0							0	0	0					
					errata interpretazione dei CI di amplificazione dei gene target		risultato errato						0	0							0	0	0					
					errata validazione del controllo qualità positivo o negativo per seduta analitica		risultato errato						0	0							0	0	0					
					mancata valutazione del controllo qualità positivo o negativo per seduta analitica		risultato errato						0	0							0	0	0					
					Inaccurata funzionamento piattaforma analitica		mancata o ritardata erogazione della prestazione / risultato errato						0	0							0	0	0					
					errore o mal funzionamento informatico in qualsiasi step della fase analitica		mancata o ritardata erogazione della prestazione / risultato errato						0	0							0	0	0					
		FAA2	refertazione		errata trasferimento/trascrizione esiti test da piattaforma analitica a referto		risultato errato						0	0							0	0	0					
					errata riproduzione del referto (non chiara definizione di positivo e negativo es. gene o genoma non rilevato)		risultato errato						0	0							0	0	0					
					Consegna di test eseguito non riportato nel referto ad esempio rilevazione antigene o genoma virale		errata valutazione del paziente						0	0							0	0	0					
					lingua di redazione referto non adeguata alla richiesta		mancata comprensione del risultato						0	0							0	0	0					
					errata anagrafica referto (risultato paziente A in referto del paziente B)		risultato errato						0	0							0	0	0					
					tempi di refertazione non idonei al processo gestionale/decisionale clinico		difficoltà nella gestione logistica e assistenziale						0	0							0	0	0					
		FAA3	Invio, lettura referto e follow up		errata lettura referto (positivo anziché negativo e viceversa)		risultato errato						0	0							0	0	0					
					errore di associazione referto paziente		risultato errato						0	0							0	0	0					
					errata o mancata valutazione di congruenza del/i test di laboratorio con la clinica		risultato errato						0	0							0	0	0					
					errata compilazione flussi		errata interpretazione epidemiologica dei dati						0	0							0	0	0					
					errato tracciamento dei contatti		mancata rivelazione di casi positivi sul territorio						0	0							0	0	0					
					incompleto tracciamento dei contatti		mancata rivelazione di casi positivi sul territorio						0	0							0	0	0					
					Disomogenea disponibilità di piattaforma analitiche		Disomogeneità interpretativa dei risultati						0	0							0	0	0					

Annex B – Experts' information.

FASE DEL PROCESSO	POTENZIALI CAUSE	CODICE
GENERAZIONE RICHIESTA	medico sbaglia l'inserimento anagrafica paziente	esp.01
	medico sbaglia a inserire il tipo di prescrizione	esp.02
	problemi informatici nell'inserimento dei dati (più rari)	esp.03
SCHEDA DI NOTIFICA	può essere cartacea o fatta su MyInfo. Per accedere a MyInfo servono dei prerequisiti (tempo, un pc performante e una scheda fissa)	esp.04
	scheda a volte viene compilata parzialmente (mancano dati anagrafici o clinici del paziente)	esp.05
	causa mancanza dati: carenza di strumenti amministrativi/informatici per poterla compilare	esp.06
	causa mancanza dati: per la mole di lavoro alcuni passaggi sono stati evitati	esp.07
	possibile conseguenza = inappropriatezza dell'approfondimento. Delle varianti mi possono sfuggire. Questo può avere impatto sui vaccini (se ho un paziente positivo e vaccinato potrebbe essere una variante ma se non ho informazioni sul paziente non la colgo (es se ha fatto o meno il vaccino)	esp.08
ANALITICA	contaminazione). Ma operatore non sempre si accorge	esp.09
	se le tutte le curve hanno lo stesso andamento, l'operatore deve sospettare una contaminazione del campione. Ma operatore non sospetta nulla a volte	esp.10
	curva va confrontata con il profilo clinico del paziente. Ma non sempre viene fatto, specialmente se operatore non è esperto	esp.11
	ci sono sistemi analitici che danno il risultato automatico e altri manuali (in quelli manuali la probabilità di avere errori di interpretazione è alta)	esp.12
	mancata manutenzione causata da non rispetto del piano da parte del laboratorio	esp.13
CQI	operatore si dimentica di fare controllo qualità	esp.14
	operatore si dimentica di fare tutti gli step	esp.15
	è costoso inserire il controllo positivo	esp.16
	non ci solo delle linee guida inguardo la CQI	esp.17
SCELTA SISTEMA ANALITICO	output del sistema analitico non ha abbastanza capacità per far fronte ai picchi di domanda	esp.18
	carenza dei reattivi	esp.19
	locali dove si trova il sistema analitico non adeguati: non ci sono abbastanza spazi per permettere una divisione delle fasi	esp.20
Loq	Loq= limite di sensibilità. Se non adeguato perché dipende dal sistema analitico scelto/ricevuto tramite gara	esp.21
	Loq. La sensibilità dipenda da cosa dichiara il costruttore del sistema analitico. Sul foglietto illustrativo può essere dichiarata una sensibilità diversa da quella effettiva	esp.22
VEQ	mancanza di tempo per fare la veq o dimenticanza	esp.23
	errore umano: non vengono inseriti i dati	esp.24
	errore umano: operatore si dimentica un passaggio	esp.25
	operatore non si interessa dell'esito (non apre la non conformità se veq ha risultato negativo)	esp.26
Collegamenti informatici LIS	non adeguati causa elevati costi	esp.27
	non adeguati causa poco tempo	esp.28
OUTSOURCING	laboratorio fa outsourcing perché la capacità del laboratorio è bassa	esp.29
	formazione personale non idonea	esp.30
	problema di tracciabilità dei campioni	esp.31
	operatore formato ma non conosce il laboratorio	esp.32
	servirebbe identificazione univoca del paziente	esp.33
POST-ANALITICA	laboratorista non scrive referto in un linguaggio chiaro	esp.34
	problemi di interpretazione da parte del medico e del paziente	esp.35

Annex C - References of the scientific literature.

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Elena Surkova, Vladyslav Nikolayevskyy and Francis Drobniewski, "False-positive COVID-19 results: hidden problems and costs"; *The Lancet;* vol. 8(12); 2020 September 29; pp. 1167-116
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Healy B, Khan A, Metezai H, Blyth I, Asad H., "The impact of false positive COVID-19 results in an area of low prevalence"; *Clin Med (Lond*); vol. 21(1); 2021; e54-e56.
Ika Trisnawati, Riat El Khair, Dyah Ayu Puspitarani, Aditya Rifqi Fauzi, Gunadi, "Prolonged nucleic acid conversion and false-negative RT-PCR results in patients with COVID-19: A case series"; *Annals of Medicine and Surgery*; vol. 59; 2020; pp. 224-228
İşlek, Akif, and Mustafa Koray Balcı, “Analysis of Factors Causing False-Negative Real-Time Polymerase Chain Reaction Results in Oropharyngeal and Nasopharyngeal Swabs of Patients With COVID-19”; *Ear, Nose & Throat Journal;* 2021 February

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Jim F Huggett, Vladimir Benes, Stephen A Bustin,Jeremy A Garson, "Contamination causing false +ve SARS-CoV-2 results"; *Americal association for clinical Chemistry*
Kanji, J.N., Zelyas, N., MacDonald, C. et al., "False negative rate of COVID-19 PCR testing: a discordant testing analysis"; *Virol Jurnal;* vol.18, article 13; 2021
Leo Lin, John Carlquist, Will Sinclair, Tara Hall, Bert K. Lopansri, Sterling T. Bennett, "Experience With False-Positive Test Results on the TaqPath Real-Time Reverse Transcription-Polymerase Chain Reaction Coronavirus Disease 2019 (COVID-19) Testing Platform"; *Arch Pathol Lab Med;* vol. 145
Lippi Giuseppe and Plebani Mario, "Asymptomatic COVID-19 transmission: the importance of avoiding official miscommunication"; *Diagnosis*, vol. 7(4); 2020; pp. 347-348
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Olson APJ, Linzer M, Schiff GD, "Measuring and Improving Diagnostic Safety in Primary Care: Addressing the "Twin" Pandemics of Diagnostic Error and Clinician Burnout"; *J Gen Intern Med;* vol. 36(5); 2021 May; pp. 1404-1406

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Rezgar Rahbari, Nariman Moradi and Mohammad Abdi, "PCR for SARS-CoV-2: Analytical considerations"; *Clinica Chimica Acta*; vol. 516; 2021; pp.1-7
Roberta Maggiulli, Adriano Giancani, Gemma Fabozzi, Lisa Dovere, Luisa Tacconi, Maria Giulia Amendola, Danilo Cimadomo, Filippo Maria Ubaldi and Laura Rienzi, "Assessment and management of the risk of SARS-CoV-2 infection in an IVF laboratory"; *Reproductive Healthcare Ltd;* vol. 41 (3); 2020 June 27; pp. 385-394
Siacovelli, Laura, Panteghini, Mauro, Lippi, Giuseppe, Sumarac, Zorica, Cadamuro, Janne, Galoro, César Alex De Olivera, Pino Castro, Isabel Garcia Del, Shcolnik, Wilson and Plebani, Mario, "Defining a roadmap for harmonizing quality indicators in Laboratory Medicine: a consensus statement on behalf of the IFCC Working Group “Laboratory Error and Patient Safety” and EFLM Task and Finish Group “Performance specifications for the extra-analytical phases”"; *Clinical Chemistry and Laboratory Medicine (CCLM);* vol. 55(10);2017; pp. 1478-1488
Tu, Yuan-Po DVM, MD; O’Leary, Timothy J. MD, PhD," Testing for Severe Acute Respiratory Syndrome–Coronavirus 2: Challenges in Getting Good Specimens, Choosing the Right Test, and Interpreting the Results"; *Critical Care Medicine;* vol. 48(11); 2020 November; pp. 1680-1689
West CP, Montori VM, Sampathkumar P., "COVID-19 Testing: The Threat of False-Negative Results"; *Mayo Clin Proc;* vol. 95(6); 2020 June; pp. 1127-1129

Wikramaratna Paul S, Paton Robert S, Ghafari Mahan, Lourenço José," Estimating the false-negative test probability of SARS-CoV-2 by RT-PCR"; *Euro Surveill*; vol.25(50); 2020

Annex D - Information extracted from the bibliography.

RIFERIMENTO BIBLIOGRAFICO	LINK URL	CAUSE		AZIONI PREVENTIVE	
		Codice	Descrizione	Codice	Descrizione
Clément Escrier, Géraldine Anthoine and Abdérafi Charki; "Reliability of RT-PCR tests to detect SARS-CoV-2: risk analysis"; *Int. J. Metrol. Qual. Eng.*; vol.11; 2020; pp. 15	https://doi.org/10.1051/ijmqe/2020009	B00.01	PCR è molto sensibile alla qualità del campione analizzato	B00.35	fornire un maggior numero di training agli operatori per la prelevazione del tampone
		B00.02	pre-analitica: la preparazione del campione per il trasporto è fatta manualmente	B00.36	mettere degli scanner per evitare che operatore in fase analitica debba mettere i dati del paziente manualmente
		B00.03	pre-analitica: contaminazione dal campione avviene a causa dell'operatore sanitario che esegue il tampone e non mette in atto tutte le precauzioni necessarie	B00.37	aumentare i turni lavorativi dei tecnici se manca tempo e risorse
		B00.04	analitica: contaminazione campione da altri virioni di altri campioni	B00.38	se etichettatura campione è sbagliata, creare un reminder contenente con quali informazioni ddel paziente dovrebbero sempre essere riportate su etichetta (poka yoke)
		B00.05	analitica: contaminazione campioni dovuti a ambiente non adeguatamente sanificato	B00.39	creare dei registri con numero univoco paziente e tesata posizione che deve avere il campione corrispondente sul piatto di estrazione, che sarà identificato con il numero di
		B00.06	pre-analitica: bassa organizzazione della stazione di lavoro	B00.40	definire un livello di scorte di sicurezza di materiale tecnico per organizzare gli acquisti
		B00.07	pre-analitica: campione non viene etichettato, mancano informazioni del paziente	B00.41	implementare un monitoraggio regolare della temperature dei congelatori, in modo da rendere più facile la identificazione di errori
		B00.08	analitica (estrazione): contaminazione campione causa di operatore	B00.42	creare una lista da controllare e spuntatare prima di mettere il campione nel macchinario per per evitare un errore di programmazione nella fase di amplificazione
		B00.09	analitica (estrazione): freezer guasto/non calibra temperatura correttamente	B00.43	creare uno scanner che legge i barcodes dei pazienti per non eseguire inserimento dei dati manualmente
		B00.10	analitica (estrazione): mancata manutenzione dei freezers		
		B00.11	analitica (estrazione): bassa organizzazione nella stazione di lavoro		
		B00.12	analitica (estrazione): il campione è troppo viscoso, quindi il pipettamento è difficoltoso		
		B00.13	analitica (estrazione): reagenti non sono conservati correttamente (C+; C- poco preservati)		
		B00.14	analitica (estrazione): blocco o malfunzionamento della		
		B00.15	analitica (estrazione): contaminazione della macchina da RNA		
		B00.16	analitica (estrazione): bassa qualità campione		
		B00.17	analitica (preparazione del mix): campione contaminato dalle fasi precedenti del processo		
		B00.18	analitica (preparazione del mix): quantità di RNA estratta non è sufficiente per quantità		
		B00.19	analitica (preparazione del mix): tecnici poco organizzati e poco qualificati		
		B00.25	analitica (preparazione del mix): reagenti del mix non conservati correttamente (temperatura sbagliata)		
Reagai Rabbani, Nariman Moradi and Mohammad Abdi; "PCR for SARS-CoV-2: Analytical considerations"; *Chimica Chimica Acta*; vol. 516; 2021; pp.1-7		B00.26	analitica (preparazione del mix): mix non viene reso omogeneo da operatore		
		B00.27	analitica (preparazione del mix): durante preparazione del mix l' operatore si dimentica un reagente o lo mette in quantità errata		
		B00.28	analitica (preparazione del mix): mancanza di tracciabilità del campione (mancano informazioni sui pazienti)		
		B00.29	analitica: errore operatore che deve inserire i dati del paziente manualmente		
		B00.30	analitica (amplificazione): macchina bloccata		
		B00.31	analitica (amplificazione): errore nella programmazione della PCR (es. disabilitata la funzione lettura della fluorescenza)		
		B00.32	analitica (amplificazione): basso controllo della temperatura durante i cicli		
		B00.33	post-analitica: errore nel leggere le curve di amplificazione e i numeri di ciclo		
		B00.34	post-analitica: i risultati vengono inseriti in software manualmente da operatore, quindi sono soggetti a errori		
		B01.1	pre-analitica: incorretta zona di applicazione del tampone		
		B01.2	pre-analitica: metodo scorretto, il tampone non viene eseguito correttamente dell'operatore		

	https://doi.org/10.1016/j.cca.2021.01.011	B01.3	pre-analitica: materiale non appropriato (il tampone non deve essere di cotone, ma di materiale sintetico)		
		B01.4	pre-analitica: non viene estratta una quantità sufficiente di		
		B01.5	pre-analitica: rischio di contaminazione del tampone con materiale esterno (es.guanti)		
		B01.6	pre-analitica: inadeguato carico virale perché paziente è nella fase iniziale della malattia		
		B01.7	pre-analitica: errore del tempo di prelevamento, poiché nello stadio iniziale del infezione il virus è più tracciabile dal naso, mentre genera falsi negativi se tampone è prelevato dalla gola		
		B01.08	analitica: conservazione di primer e sonde errata (ambiente contaminato, esposizione alla luce e temperatura non corretta) alta fonte di errori		
		B01.09	analitica: primer non applicato correttamente		
		B01.10	analitica: sbagliata calibrazione degli strumenti		
		B01.11	analitica: sbagliata concentrazione dei reagenti perché operatori non hanno sufficenti skills e perché le pipette con i reagenti non sono ben calibrate		
		B01.12	post-analitica (refertazione): sbagliata interpretazione dei dati da parte del medico e del paziente. Il linguaggio di comunicazione dei risultati è troppo specifico e tecnico e può provocare problemi di comprensione		
Sciacovelli, Laura, Panteghini, Mauro, Lippi, Giuseppe, Sumarac, Zorica, Cadamuro, Janne, Galoro, César Alex De Oliveira, Pino Castro, Isabel Garcia Del, Shcolnik, Wilson and Plebani, Mario, "Defining a roadmap for harmonizing quality indicators in Laboratory Medicine: a consensus statement on behalf of the IFCC Working Group "Laboratory Error and Patient Safety" and EFLM Task and Finish Group "Performance specifications for the extra-analytical phases"", *Clinical Chemistry and*	https://doi.org/10.1515/cclm-2017-0412	B02.01	CQI: non fatta per mancanza di tempo o perché mancano risorse umane		
		B02.02	CQI: se non viene fatta aumenta il rischio di non determinare correttamente la qualità e il livello di sicurezza dei laboratori		
Giuseppe Lippi, ana-Maria Simundic and Mario Plebani, "Vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19)", *Clin Chem Lab Med;* vol. 58(7); 2017; pp.170-176		B03.01	pre-analitica: quantità di campione non appropriata per quantità	B03.05	fornire istruzioni approfondite su come fare tampone, gestirlo e conservarlo
		B03.02	pre-analitica: mancata procedura di collezione del campione(errori pipettamento..)		
		B03.03	pre-analitica: trasporto inadeguato (tempi lunghi, si possono danneggiare durante il trasporto, temperatura errata)		
		B03.04	analitica: strumenti che non funzionano o danneggiati		
Basso, Daniela, Aita, Ada, Navaglia, Filippo, Franchin, Elisa, Fioretto, Paola, Moz, Stefania, Bozzato, Dania, Zambon, Carlo-Federico, Martin, Barbara, Dal Prà, Chiara, Crisanti, Andrea and Plebani, Mario, "SARS-CoV-2 RNA identification in nasopharyngeal swabs: issues in pre-analytics", *Clinical Chemistry and Laboratory Medicine (CCLM)*; vol. 58(3); 2020; pp. 1579-1586	https://doi.org/10.1515/cclm-2020-0749	B04.01	pre-analitica: la disponibilità dei reagenti è limitata		
		B04.02	pre-analitica: bassa carica virale del capione può provocare falsi negativi		
		B04.03	pre-analitica: temperatura sbagliata durante conservazione e tempi di attesa troppo lunghi provocano errori		
		B04.04	OUTSOURCING: fare outsourcing del campione è pericoloso perché aumenta i tempi e i campioni possono essere esposti a temperature sbagliate durante i due trasporti		
		B04.05	analitica: laboratori possono avere picchi di domanda e quindi campione può dover attendere prima di essere analizzato		
Buchta, Christoph, Görzer, Irene, Chiba, Peter, Camp, Jeremy V., Holzmann, Heidemarie, Puchhammer-Stöckl, Elizabeth, Mayerhofer, Maximilian, Müller, Mathias M. and Aberle, Stephan W., "Variability of cycle threshold values in an external quality assessment scheme for detection of the SARS-CoV-2 virus genome by RT-PCR", *Clinical*	https://doi.org/10.1515/cclm-2020-1602	B05.01	analitica: valuatazione risultati quantitativi dipende da variabilità protocollare,valori Ct gene target (dipendenza moderata)		
Schiff, Gordon and Mirica, Maria, "COVID-19: making the right diagnosis", *Diagnosis;* vol. 7(4); 2020; pp. 377-380	https://doi.org/10.1515/dx-2020-0063	B06.01	post-analitica: risultati forniti ai medici e pazienti in modo non affidabile e tempestivo		
		B06.02	post-analitica: operatore poco affidabile		
Lippi Giuseppe and Plebani Mario, "Asymptomatic COVID-19 transmission: the importance of avoiding official miscommunication", *Diagnosis,* vol. 7(4); 2020; pp. 347-348	https://doi.org/10.1515/dx-2020-0085	B07.01	mancata comunicazione dei risultati al medico		
		B07.02	mancata comunicazione dei risultati al paziente		
		B07.03	i risultati vengono fraintesi		
Benoit, Justin, Benoit, Stefanie W., Lippi, Giuseppe and Henry, Brandon Michael, "False negative RT-PCR or false positive serological testing in SARS-CoV-2 diagnostics? Navigating between Scylla and Charybdis to prevent misclassification bias in COVID-19 clinical investigations", *Diagnosis;* vol. 7(4); 2020; pp. 405-407	https://doi.org/10.1515/dx-2020-0091	B08.01	post-analitica (valutazione esito PCR): valori limiti dettati da produttori potrebbero non fornire corretta interpretazione in una data popolazione		
		B08.02	pre-analitica/analitica: cause falsi positivi--> bassa carica virale, tecnica di campionamento, metodo di conservazione e movimento, errori manuali, contaminazione dei		

Olson APJ, Linzer M, Schiff GD, "Measuring and Improving Diagnostic Safety in Primary Care: Addressing the "Twin" Pandemics of Diagnostic	ps://pubmed.ncbi.nlm.nih.gov/33575	**B09.01**	errori umani: causati da vincoli di tempo e ambiente confusionale		
Christopher R. Carpenter, Philip A. Mudd, Colin P. West, Erin Wilber, and Scott T. Wilber,"CME Information: Diagnosing COVID-19 in the Emergency Department: A Scoping Review of Clinical Examinations, Laboratory Tests, Imaging Accuracy, and Biases"; *Society for Academic Emergency Medicine;* vol. 27; 2020; pp. 654-670	https://onlinelibrary.wiley.com/doi/abs/10.1111/acem.14048	**B10.01**	analitica(PCR): varietà di reagenti e sequenze di RNA target senza un formato di analisi standard accettato.		
		B10.02	analitica(PCR): forniture non adeguate di reagenti--> riduzione capacità di testing e tempo		
		B10.03	analitica (PCR):riduzione tempo (forniture non adegaute)--> test simulatanei di più campioni (poi singoli per campioni risultati positivi)		
		B10.04	analitica: sul mercato esistono molte varianti di test disponibili con diverse affidabilità		
		B10.05	sbagliata tempistica del campionamento in relazione al corso della malattia		
		B10.06	pre-analitica: ottenere campione nasofaringei richiede training appropriato		
Işlek, Akif, and Mustafa Koray Balcı, "Analysis of Factors Causing False-Negative Real-Time Polymerase Chain Reaction Results in Oropharyngeal and Nasopharyngeal Swabs of Patients With COVID-19"; *Ear, Nose &*	https://journals.sagepub.com/doi/10.1177/0145561321996621	**B11.01**	analitica (PCR): se la quantità di campione è stata prevelata scorrettamente nella fase pre analitica	**B11.02**	training e formazione per i clinici che eseguono il tampone
Daniel C Edson, MS, MT(ASCP), Danielle L Casey, Susan E Harmer, Frances P Downes, DrPH, MPH," Identification of SARS-CoV-2 in a Proficiency Testing Program"; *American Journal of Clinical Pathology;* vol. 154 (4); 2020 October ; pp. 475-478	https://academic.oup.com/ajcp/article/154/4/475/5873802?login=true	**B12.01**	VEQ: in media 302 laboratori con risultati positivi (97.4%), 8 laboratori con risultati discordanti (2.6%)		
		B12.02	VEQ: la probabilità di errore nel riportare il risultato di un test è 1%		
Tu, Yuan-Po DVM, MD; O'Leary, Timothy J. MD, PhD," Testing for Severe Acute Respiratory Syndrome-Coronavirus 2: Challenges in Getting Good Specimens, Choosing the Right Test, and Interpreting the Results"; *Critical Care Medicine;* vol. 48(11);2020 November; pp. 1680-1689	https://journals.lww.com/ccmjournal/Fulltext/2020/11000/Testing_for_Severe_Acute_Respiratory.16.aspx	**B13.01**	pre-analitica: mancata fornitura di test nei centri di prelevamento	**B13.09**	laboratori e clinici devono lavorare insieme per validare alternative con i loro sistemi di test in mancanza di materiale per eseguire i tamponi
		B13.02	pre-analitica: mancata/scarsa conoscenza parte anatomica per raccogliere campione		
		B13.03	post-analitica: difficoltà di valutazione causata da varietà protocolli		
		B13.04	post-analitica: valutazaione influenzata da tempistica prelevamento campione; parte anatomica campione; carica virale stimata dal laboratorio		
		B13.05	pre-analitica: bassa qualità del campione può cacusare fasi positivi		
		B13.06	pre-analitica(conservazione e movimentazione): durante pandemia scarsità di tamponi--> richerca di alternative		
		B13.07	pre-analitica(conservazione e movimentazione): non tutti tipi di tampone sono compatibili con le tipologie di		
		B13.08	pre-analitica(conservazione e movimentazione): medici dovrebbero usare tamponi e movimentazione definiti dai laboratori, se non disponibili usare alternative		
Healy B, Khan A, Metezai H, Blyth I, Asad H., "The impact of false positive COVID-19 results in an area of low prevalence"; *Clin Med (Lond);* vol. 21(1); 2021; e54-e56.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7850182/	**B14.01**	errata identificazione campione durante il processo: errata etichettatura		
		B14.02	analitica: contaminazione causata da errori umani, mancanza controllo qualità, procedure non ben definite.		
		B14.03	post-analitica (valutazione): personale non formato		
Premraj A, Aleyas AG, Nautiyal B, Rasool TJ., "Nucleic Acid and Immunological Diagnostics for SARS-CoV-2: Processes, Platforms and Pitfalls"; *Diagnostics;* vol.10(11); 2020; pp. 866	https://www.mdpi.com/2075-4418/10/11/866	**B15.01**	analitica (service): conservazione errata causata da mancata osservanza protocolli		
		B15.02	analitica: mancanza kit PCR dovuta da domanda elevata		
		B15.03	analitica (PCR): sonde e primer non adatti causano errori		
		B15.04	analitica (amplificazione): errori causati da condizioni errate della reazione		
		B15.05	analitica: mancanza di curve di amplificazione ben definite dovuta a fallimento di un primer/ reagente o sonda		
Wikramaratna Paul S, Paton Robert S, Ghafari Mahan, Lourenço José," Estimating the false-negative test probability of SARS-CoV-2 by RT-	https://doi.org/10.2807/1560-7917.ES.2020.25.50.2000568			**B. 16.01**	effettuare test ripetuti per campioni sospetti
Di Maio, P, Iocca, O, Cavallero, A, Giudice, M., "Performing the nasopharyngeal and oropharyngeal swab for 2019-novel coronavirus (SARS-CoV-2) safely: How to dress, undress, and technical notes"; *Head & Neck;* vol. 42; 2020; pp. 1548- 1551	https://doi.org/10.1002/hed.26230	**B17.01**	pre-analitica: processo di prelevamento del campione ha una procedura standard che non viene seguita precisamente (abbassare mascherina paziente,inserire tampone fino a che non si sente ostacolo, poi girare in senso orario e antiorario per alcuni secondi..)		

Jim F Huggett , Vladimir Bones, Stephen A Bustin,Jeremy A Garson, "Contamination causing false +ve SARS-CoV-2 results"),Americal association for clinical Chemistry	http://creativecommons.org/licenses/by/4.0/			**B18.01**	pulire a fondo i laboratori con detergenti che sconfiggono gli acidi nucleici (es. candeggina e UV)
				B18.02	elminare i reagenti collegati alla contaminazione. Si consiglia comunque di sostituire tutti i reagenti presenti in laboratorio e ripartire da zero
				B18.03	dividire in ambienti diversi le varie fasi del processo (manipolazione campione,..) in modo da evitare contaminazioni
Leo Lin, John Carlquist, Will Sinclair, Tara Hall, Bert K. Lopansri, Sterling T. Bennett, "Experience With False-Positive Test Results on the TaqPath Real-Time Reverse Transcription-Polymerase Chain Reaction Coronavirus		**B19.01**	analitica: il tecnico ha pipettato il campione nella parte sbagliata del piattino		
Alireza Tahamtan & Abdollah Ardebili,"Real-time RT-PCR in COVID-19 detection: issues affecting the results, Expert Review of Molecular Diagnostics"; *Taylor & Francis;* vol. 5 *(5);* 2020; pp. 453-454	https://doi.org/10.1080/14737159.2020.1757437	**B20.01**	post-analitica (valutazione PCR): non vengono considerati i dati clinici paziente nel stabilire la diagnosi	**B20.06**	Migliorare la valutazione dei risultati PCR combinandoli con immagini CT
		B20.02	analitica: primer e sonde non adatte data alta variabilità e rapida evouzione virus	**B20.07**	utilizzare tecniche di estrazioni e kit di qualità
		B20.03	pre-analitica (conservazione e movimentazione): il campione non raggiunge immediatamente il laboratorio		
		B20.04	analitica (amplificazione): inibitori di amplificazione nel		
		B20.05	analitica (amplificazione): quantità organismi insufficienti (errori raccolta/transporto/manipolazione)		
Bustin S, Mueller R, Shipley G, Nolan T., "COVID-19 and Diagnostic Testing for SARS-CoV-2 by RT-qPCR—Facts and Fallacies"; *International Journal of Molecular Sciences;* vol. 22(5); 2021; pp. 2459	https://doi.org/10.3390/ijms22052459	**B21.01**	pre-analitica/analitica: controllo e sanificazione del materiale non fatta in modo appropriato	**B21.04**	Per migliorare valutazione compiere analisi incrociata tra dati clinici del paziente e i risultati del test
		B21.02	pre-analitica: operatore non abile a estrarre campione		
		B21.03	pre-analitica: paziente non sopporta la procedura		
Mitchell SL, St George K, Rhoads DD, Butler-Wu SM, Dharmarha V, McNult P, Miller MB., " Understanding, Verifying, and Implementing Emergency Use Authorization Molecular Diagnostics for the Detection of SARS-CoV-2 RNA"; *J Clin Microbiol;* vol.58(8); 2020 July 23	https://pubmed.ncbi.nlm.nih.gov/32381642/	**B22.01**	CQI: mancanze di materiali per controllo positivo, di fondi e ti personale/tempo, mancanza di personale qualificato e di training, mancanza di materiale	**B22.05**	CQI: se manca materiale si usano residui dei campioni dei pazienti
		B22.02	analitica: mancanza dl reagenti, materiali e strumenti	**B22.06**	CQI: se risultati sono discordanti provare a rifare il test o contattare produttore macchinario
		B22.03	pre-analitica:mancanza tamponi e mezzi per trasportarli		
		B22.04	analitica/pre-analitica: mancanza di personale qualificato		
Braunstein GD, Schwartz L, Hymel P, Fielding J., "False Positive Results With SARS-CoV-2 RT-PCR Tests and How to Evaluate a RT-PCR-Positive Test for the Possibility of a False Positive Result"; *J Occup Environ Med* vol. 63(3):e159-e162, 2021 March 1	https://pubmed.ncbi.nlm.nih.gov/33405498/	**B23.01**	post-analitica: problemi con il software		
		B23.02	post-analitica: mancata comunicazione dei risultati o inserimento di dati sbagliati		
Matthew J. Binnicker,"Challenges and Controversies to Testing for COVID-19"; *Journal of Clinical Microbiology* ; vol.58(11), e01695-20; 2020 October	https://jcm.asm.org/content/58/11/e01695-20	**B24.01**	analitica (PCR): sensibilità PCR =60-70%		
		B24.01	analitica (PCR): risultati altamente legati a tempistica di collezione del campione, tipologia e qualità del campione		
Pham HP, Staley EM, Raju D, Marin MJ, Kim CH., "Laboratory Assay Evaluation Demystified: A Review of Key Factors Influencing Interpretation of Test Results Using Different Assays for SARS-CoV-2	ps://pubmed.ncbi.nlm.nih.gov/32634234	**B25.01**	analitica: i macchinari di analisi sono difficili da utilizzare e interpretare		
Jelili Olaide Mustapha, Idris Nasir Abdullahi, Odunayo O.R. Ajagbe, Anthony Uchenna Emeribe, Samuel Ayobami Fasogbon, Solomon Oloche Onoja, Charles Egede Ugwu, Chikodi Modesta Umeaguru, Folake Olubunmi Ajayi, Wudi Natasha Tanko, Pius Omoruyi Omoigho, Abdulmumuni Samuel Aliyu, Halima Ali Shuwa, Justin Onyebuchi Nwofe, Amos Dangana, Oyye Alaba, Peter Elisha Ghamba, Yakubu Ibrahim, Dorcas Aliyu, Olawale Sunday Animasaun, Nkechi Blessing Ugboaja, Mala	https://doi.org/10.1016/j.heliyon.2021.e05951	**B26.01**	analitica (varianti): varianti non rilevate a causa di errori di sequenziamento		
		B26.02	analitica (varianti): varianti non rilevate a causa di non ottimizzazione oligonucleotidi usati nei test		
		B26.03	analitica (varianti): varianti non rilevate a causa di cambiamenti dei siti di primer binding e probe binding		
Ika Trisnawati, Rist El Khair, Dyah Ayu Puspitarani, Aditya Rifqi Fauzi, Gunadi, "Prolonged nucleic acid conversion and false-negative RT-PCR results in patients with COVID-19: A case series"; *Annals of Medicine and Surgery;* v ol. 53; 2020; pp. 224-228	https://doi.org/10.1016/j.amsu.2020.03.040	**B27.01**	pre-analitica: quantità di materiale virale insufficiente per quantità		
		B27.02	pre-analitica: Incuranza delle procedure per il trasporto dei campioni		
Roberta Maggiulli, Adriano Giancani, Gemma Fabozzi, Lisa Dovere, Luisa Tacconi, Maria Giulia Amendola, Danilo Cimadomo, Filippo Maria Ubaldi and Laura Rienzi, "Assessment and management of the risk of SARS-CoV-2 infection in a IVF laboratory"; *Reproductive Healthcare (Md);* vol. 41	https://doi.org/10.1016/j.rbmo.2020.06.017			**B27.03**	Revisione dei protocolli dei laboratori per diminuire contaminazione dei campioni
P. D. Kirkland and M. J. Frost, "The impact of viral transport media on PCR assay results for the detection of nucleic acid from SARS-CoV-2"; *Pathology;* vol.5(7); 2020 December; pp. 811-814	https://doi.org/10.1016/j.pathol.2020.09.013	**B28.01**	analitica (movimentazione): mancanza di kit dovuta ad alta domanda		
Elena Surkova, Vladyslav Nikolayevskyy and Francis Drobniewski, "False-positive COVID-19 results: hidden problems and costs"; *The Lancet;* vol. 8(12); 2020 September 23; pp. 1167-116	https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30453-7/fulltext	**B29.01**	analitica: alta probabilità di contaminazioni dei reagenti (US)	**B29.02**	Imporre standard più stringenti per esecuzione test per evitare falsi negativi
				B29.03	Fornire linee guida per l'interpretazione dei dati
				B29.04	Revisione dei protocolli sulla prevenzione trasmissione virus tra i lavoratori
Guinea-Molinos S, Andrade JM, Medina Negrete A, Espinoza Vidal S, Rios E, "Interoperable Platform to Report Polymerase Chain Reaction SARS-CoV-2 Tests From Laboratories to the Chilean Government: Development and Implementation Study"; *JMIR Med Inform;* vol. 9(1), e25143; 2021	https://medinform.jmir.org/2021/1/e25149/	**B30.01**	analitica: causa collegamenti informatici LIS/piattaforme analitiche non adeguati perchè non c'è interoperabilità tra sistemi informativi sanitari e il collegamentoviene fatto manualmente (quindi ci son possibili errori)		
West CP, Montori VM, Sampathkumar P., "COVID-19 Testing: The Threat of False-Negative Results"; *Mayo Clin Proc;* vol. 95(6); 2020 June; pp. 1127-1129	https://pubmed.ncbi.nlm.nih.gov/32376102/			**B31.01**	Diminuire possibili contaminazioni seguendo misure di prevenzione (distanziamento, igenizzare le mani, disinfettare ambiente e mascherine adeguate)
Kanji, J.N., Zelyas, N., MacDonald, C. et al., "False negative rate of COVID-19 PCR testing: a discordant testing analysis"; *Virol J* vol.18, article 13; 2021	https://doi.org/10.1186/s12985-021-01489-0	**B32.01**	pre-analitica: campionamento fatto troppo presto rispetto al livello dell'infezione		
		B32.02	pre-analitica: carica virale è variabile (bassa-alta-bassa) percui farla nel periodo in cui è bassa può creare dei fasi negativi		

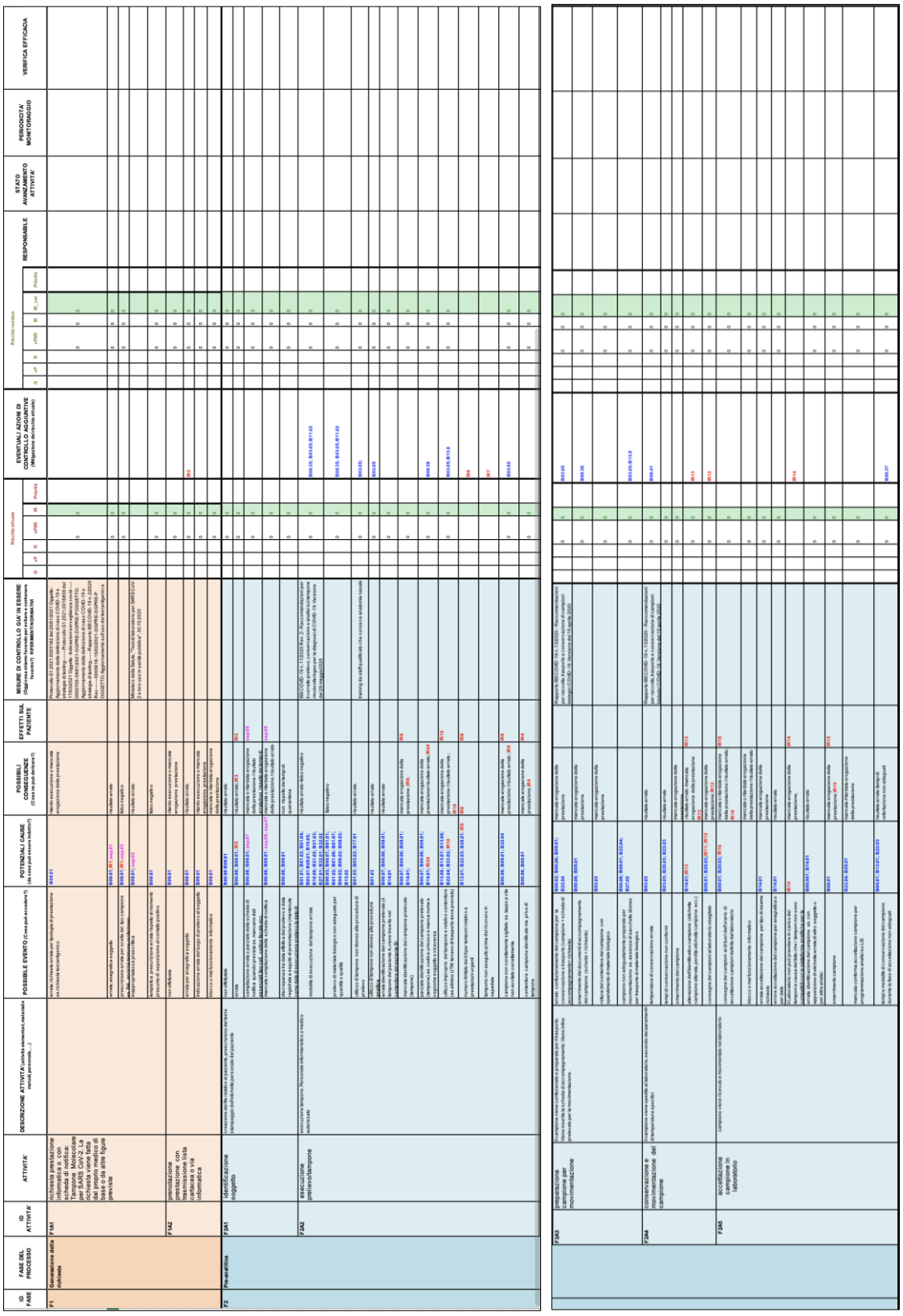
Annex E - incident reporting.

ID FASE	FASE DEL PROCESSO	ID ATTIVITA'	ATTIVITA'	DESCRIZIONE ATTIVITA'(attività elementari, materiali e metodi, personale...)	EVENTO	CAUSA	CONSEGUENZE	FETTO SUL PAZIEN	AZIONI CORRETTIVE	CODICE
F1	**Generazione della richiesta**	**F1A1**	richiesta prestazione informatica o con scheda di notifica: Tampone Molecolare per SARS CoV-2.		Dati accettazione errati	Inserimento errato da parte operatore				IR1
		F1A2	prenotazione prestazione con trasmissione lista cartacea o via informatica		inserimento errato della anagrafica del paziente in fase di accettazione				sollecito al personale amministrativo dedicato all'attività di accettazione di controllare a posteriori i dati inseriti sul sistema gestionale del laboratorio in fase di accettazione	IR2
F2	**Pre-analitica**	**F2A1**	identificazione soggetto	creazione del file relativo al paziente, collezione informazioni pratiche e del background medico, prescrizione del test e stampaggio dell'etichetta, personale: segretari di laboratorio/ personale amministrativo	Errori di identificazione del paziente		Contattata Struttura di provenienza del tampone e prolugamento dei tempi di refertazione	richiesta la ripetizione esame		IR3
					assenza di tampone all'interno della provette inviate in Microbiologia		Contattata Struttura di provenienza del tampone e prolugamento dei tempi di refertazione	richiesta la ripetizione esame		IR4
					errore di identificazione paziente (esempio mancano dati durante la fase di accettazione)	compilazione errata da parte dell'accettazione				IR5
		F2A2	esecuzione prelievo/tampone	esecuzione tampone. personale: tecnici, infermieri, laboratori	(carenza di materiale) numero limitato dei kit per tamponi urgenti	scarsità della fornitura di kit	problemi organizzativi per gestire accesso alla diagnostica urgente (si deve decidere a chi riservare il tampone).	molti pazienti non hanno accesso al tampone	individuazione delle priorità di urgenza con i clinici	IR6
					tampone non eseguito prima del ricovero in ospedale				Direzione medica manda mail a tutti i dipendenti per sollecitare la corretta applicazione della procedura aziendale di riferimento	IR7
					tamponi non idonei (esempio manca lo scovolino)		impossibilità di stabilire esito per il paziente	ripetizione esame		IR8
					tamponi non identificati		impossibilità di stabilire esito per il paziente	ripetizione esame		IR9
					i campioni non vengono messi nell'adeguato contenitore per il trasporto verso il laboratorio.	assenza dei contenitori idonei	ritardo nella presa in carico del campione	ritardo dell'esito		IR10
		F2A4	conservazione e movimentazione del campione	il campioe viene spedito al laboratorio, secondo dei paramentri di temperatura specifici (i campionipossono essere trasportati fino a 72 ore alla temperatura di 2-8 gradi)	campioni vengono inmandati al centro prelievi e messi nel area dei "vuoti"	autista e personale del laboratorio non controllano il contenitore dei campioni prima di restituirlo al punto di prelievo.			individuazione e attuazione di criteri di gestione e controllo contenitori (es. fascette sigillate colorate)	IR11
					consegna campioni in laboratorio sbagliato	autista lascia il contenitore con i tamponi nel laboratorio sbagliato	non è garantito il rispetto dei tempi di consegna dei campioni		interventi sul gestionale di check-in al fine di velocizzare le operazioni di verifica e presa in carico dei campioni	IR12
					Invio di un campione non identificato	non conoscenza dei documentidistruzioni operative	ricerca del soggetto coinvolto incrociando dati campioni e soggetti che hanno eseguito il test	ripetizione tampone	Sensibilizzazione sul rispetto delle procedure aziendali	IR13
		F2A5	accettazione campione in laboratorio	campione viene ricevuto e immagazzinato nel laboratorio	Laboratorio non può prendere in carico dei tamponi	I tamponi non sono compatibili con strumentazione per la processazione dei		aumento tempi di refertazione	richiesta di forniture compatibili con i sistemi analitici a disposizione	IR14
					smarrimento campione		il campione non è stato ricevuto dal laboratorio e il nuovo campione è stato processato con procedura urgenza	ripetizione tampone		IR15
					problemi nella consegna dei campioni	orario di arrivo non compatibile con gli orari dei fattorinaggi previsti per la	ritardi nella ricezione dei campioni	ritardi nella refertazione	sollecito alle unità cliniche ttramite mail sugli orari di accettazione di laboratorio	IR16

F3	**Fase-analitica**	**F3A1**	fase-analitica inattivazione virale	campione viene inattivato tramite reattivi specifici	contaminazione dei campioni	gli strumenti utilizzati in fase analitica sono contaminati	curve di amplificazione non attendibili	risultati errati	1. richiesta alla dita fornitrice delle strumentazioni di fare degli interventi tecnici per eliminare qualunque fonte di contaminazione. 2.implementare una formazione del personale sul corretto utilizzo della strumentazione e sul corretto utilizzo dei DPI durante la manipolazione dei campioni	IR17
		F3A2	fase analitica estrazione	si estrae RNA puro dal campione di partenza. RNA viene trascritto in cDNA	contaminazione campioni in fase di estrazione	attrezzature insufficienti per il fabbisogno;fatica e stress degli operatori.	falsi positivi	diagnosi errata su più pazienti	spostare attrezzatura estrazione in locale con cappa aspirante;definire azioni per evitare contaminazione; traspostare piastre in contenitore chiuso ermeticamente.	IR18
					fenomeno di carry-over di materale biologico/reagenti di amplificazione presenti su strumentazione	sovraccarico attrezzature;elevato turnover del personale con necessità di formazione specifica;passaggio da pronta disponibilità a guardia attiva per il personale con conseguente difficoltà a recuperare turni di riposo compensativo; saturazione spazi disponibili;criticità nella consegna/smistamento dei campioni che	Riprocessamento	Refertazione di risultati falsi positivi e falsi negativi	attenzione in fase di dispensazione dei campioni sugli strumenti per evitare fenomeno di carry-over;manutenzione straordinaria sulla strumentazione implicata;revisione protocolli laboratorio.	IR19
					contaminazione del campione		ripetizione analisi; referti errati	più soggetti ricevono errata dia	inserire controllo negativo di estrazione	IR20
					errore di pipettatura		Riprocessamento su un'altra piattaforma strumentale	più soggetti ricevono errata diagnosi		IR21
		F3A3	fase analitica amplificazione	il DNA viene sottoposto ad alte temperature, in modo tale che si sdoppia. Un enzima ricostruisce il filamento di DNA. Il DNA sintetico che si è andato a creare ha dei nucleotidi fluorescenti: ad ogni ciclo di amplificazione lo strumento	impossibilità di utilizzo dello strumento	malfunzionamento dello strumento	problemi organizzativi e gestionali per la mancanza del macchinario	tempi di refertazione aumentati	intervento tecnico e manutenzione dei guasti	IR22
		F3A4	fase analitica: scelta del sistema analitico/manutenzioni /installazione/ controllo sistemi analitici una tantum		errato inserimento dei dati relativi ai campioni inviati in "service" sul LIS	i dati vengono inseriti manualmente			1. inserimento manuale dei risultati sul LIS con controllo in doppio da parte del personale tecnico. 2.consegna al clinico del referto con allegato anche il referto prodotto dal laboratorio "service".	IR23
					parziale identificazione dei campioni	ambulatorio non è dotato di idonei strumenti di etichettatura dei campioni	etichettatuta manuale			IR24
					scarsità di reagenti		rallentamento analisi			IR25
					mancanza di reattivi per la gestione dei pazienti urgenti del PS	scarsa fornitura dei reattivi		Tempi di refertazione aumentano	invio con urgenza dei tamponi presso altri laboratori per la processazione veloce dei tamponi	IR26
		F3A5	gestione erogazione prestazioni con "service"	Il laboratorio, in momenti di picco di domanda elevati, può decidere di effettuare l'analisi dei campioni in modalità "outsourcing", inviando i campioni presso	i tamponi vengono mandati ad analizzare in laboratori al di fuori della propria ASST	quantità di campioni da analizzare è troppo elevata		Tempi di refertazione aumentano	acquisire propri strumenti per la processazione	IR27
					errore elaborazione dei dati del laboratorio "in service"	mancato allineamento tra id richiesta e id referto		tempi di refertazione allungati	richiesto intervento del SIA per riallineare correttamente i referti	IR28

F4	**Fase Post-analitica**	**F4A1**	valutazione dell'esito real time PCR	Analisi delle curve di amplificazione da parte dell'operatore. Le curve di						
		F4A2	refertazione	Analisi dei risultati e eventuale comuincazione ai pazienti positivi	Ritardo comunicazione positività tampone				sensibilizzazione del rispetto della procedura aziendale di riferimento	IR29
					Scambio di referti tra pazienti	il laboratorio che eroga la prestazione in service, identifica i campioni con numeri di serie facilmente confondibili e non con i	Più soggetti hanno ricevuto una doppia chiamata			IR30
					mancata comunicazione esito positivo al paziente	pazienti irreperibili (non rispondono al telefono o i numeri telefonici sono errati)				IR31
					ritardata comunicazione del referto (ATS-all'utente)	aumento del numero di richieste esami al la	ripetizione analisi	ripetizione esame; ritardo		IR32
					referto errato	errore umano	Ricontattare paziente	Paziente riceve esito errato		IR33
					errore di refertazione	guasto temporaneo all'apparecchiatura di analisi	test viene rifatto dal laboratorio a seguito del guasto	paziente negativo collocato in reparto covid		IR34
		F4A3	Invio, lettura referto e follow up	Invio dell'esito del test ai pazienti tramite mail,fax,posta o chiamata	errato inserimento dei dati relativi ai tamponi nel file di invio per la segnalazione ad ATS dei casi da segnalare per il contact tracing	l'inserimento dei dati viene fatto manualmer	errori nella gestione dei pazienti nell'ambito dell'attività di contact tracing	errori di refertazione	creato programma informatico che consente l'estrapolazione dei risultati positivi direttamente dal LIS di laboratorio sottoforma di tabella disponibile per l'invio dei dati ad ATS	IR35
					mancato esito	Campioni inviati per la processazione a strutture esterne vengono persi		Più pazienti non hanno ricevuto risultato		IR36
					assenza referto tampone	il campione non è stato ricevuto dal laboratorio, che quindi non ha potuto analizzarlo e produrre il referto		Ritardo ricovero	programma di accettazione informatica (check in) delle provette dei tamponi da eseguire contestualmente all'esecuzione del check in, confronto tra tamponi richiesti ed eseguiti e confronto tra tamponi eseguiti e accettati dal laboratorio.	IR37
					esito tampone non presente nella documentazione al momento del ricovero	il tampone è stato smarrito		Ritardo ricovero	effettuare la tracciatura del tampone tramite barcode scanner	IR38

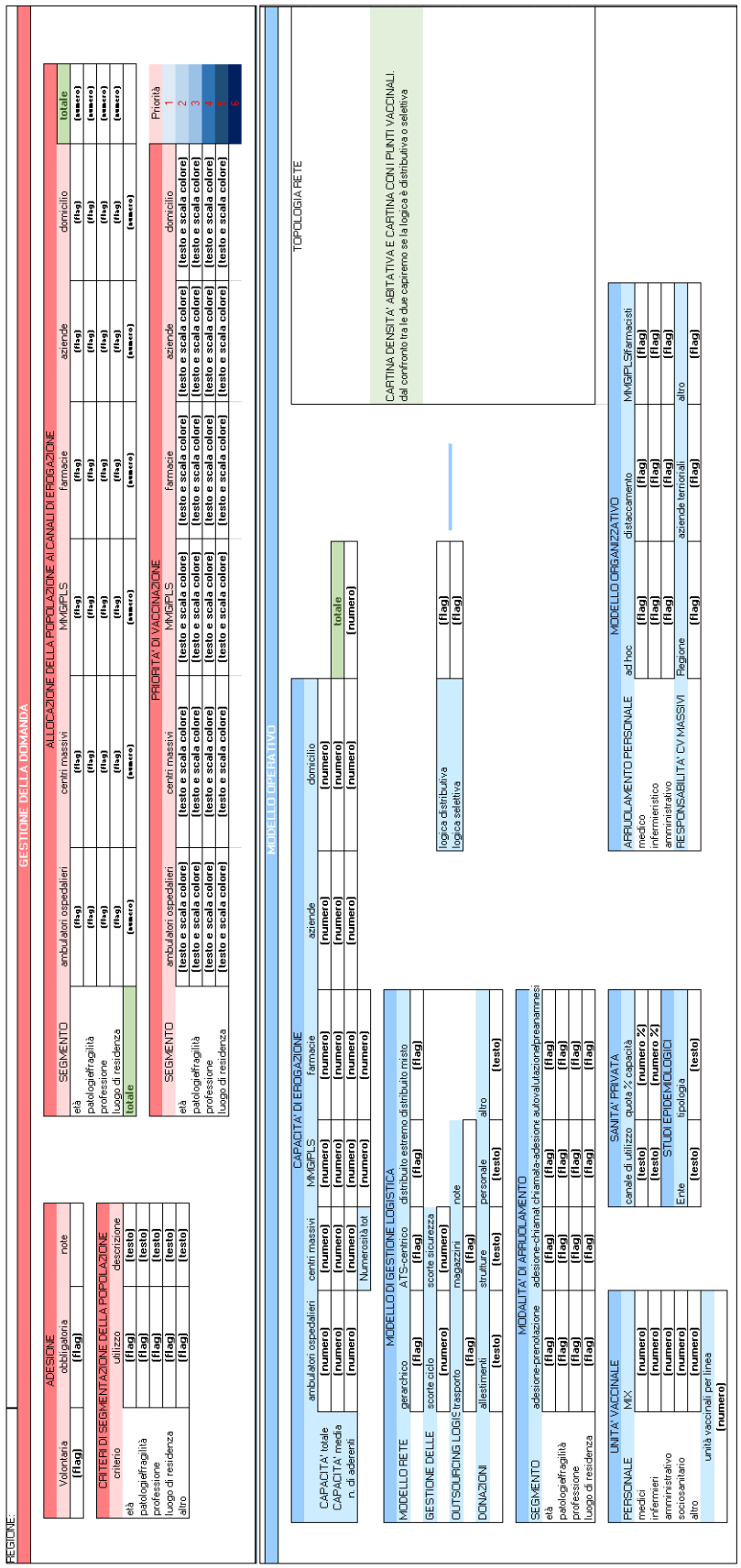
Annex F - Final FMECA tool.



ID FASE	FASE DEL PROCESSO	ID ATTIVITA'	ATTIVITA'	DESCRIZIONE ATTIVITA'(attività elementari,materiale metodi,personale,...)	POSSIBILE EVENTO (Cosa può accadere?)	POTENZIALI CAUSE (da cosa può essere indotto?)	POSSIBILI CONSEGUENZE (Cosa ne può derivare?)	EFFETTI SUL PAZIENTE	MISURE DI CONTROLLO GIA' IN ESSERE (Oggi cosa stiamo facendo per evitare e contenere l'evento?) RIFERIMENTI/MODALITA'	Rischio attuale G	vP	R	vPRR	IR	Priorità	EVENTUALI AZIONI DI CONTROLLO AGGIUNTIVE (Mitigazione del rischio attuale)	Rischio residuo G	vP	R	vPRR	IR	IR_var	Priorità	RESPONSABILE	STATO AVANZAMENTO ATTIVITA'	PERIODICITA' MONITORAGGIO	VERIFICA EFFICACIA
	Fase-analitica	F3A1	fase-analitica inattivazione virale	campione viene inattivato tramite reattivi specifici	mancata esecuzione del passaggio di inattivazione virale quando previsto (con aggiunta reattivo specifico e con incubazione del campione a temperatura e tempi ecc.)	B03.04; B09.01; B22.04	risultato errato		WHO Diagnostic testing for SARS-CoV-2 Interim guidance 11 September 2020			0								0						
					applicazione procedura errata di inattivazione virale	B03.04; B09.01; B22.04	risultato errato					0								0						
					diffusazione di inattivazione virale quando non è previsto	B09.01	risultato errato					0								0						
					cross-contaminazione tra campioni durante la dispensazione reattivo per l'inattivazione virale	B03.04; B14.02; R17	risultato errato falsi positivi; R17	R17				0						B10.02;B27.03;B29.04;B31.01;R17						
					cross-contaminazione dei campioni per scambio del contenitore	B03.05; B14.02	risultato errato falsi positivi					0						B10.03;B27.03;B29.04;B31.01						
					perdita di tracciabilità del campione ex. se campione aliquotato e trasferito da tubo primario a secondario per l'procedimento di inattivazione	B09.01	risultato errato					0								0						
		F3A2	fase analitica estrazione	viene estratto RNA puro dal campione di partenza.	cross-contaminazione tra campioni	B03.06; B09.11;R10;R13	risultato errato falsi positivi; R20;R10;R13	R20;R10;R13				0						B10.03;R20;R10;R13						
					controllo negativo estrazione non effettuato (CQI)	B09.11	risultato errato falsi positivi					0								0						
					controllo positivo estrazione non effettuato (CQI)	B09.11; B22.01	risultato errato falsi negativi					0								0						
					errata dispensazione del campione primario nella posizione della piastra o supporto usato per l'estrazione (campione A in posizione B)	B09.11; B19.01; B22.04	risultato errato					0						B09.39						
					errato volume di campione dispensato su piastra o supporto di estrazione	B09.12; B09.11; B20.05; R21	risultato errato;R21	R21				0												
					mancata dispensazione del campione su piastra o supporto di estrazione	B09.12; B09.11	risultato errato falsi negativi					0						B09.39						
					applicazione errata procedura per esecuzione dell'estrazione	B09.09; B09.10; B09.11; B09.13; B09.14; B09.15;R21;R20;R27	risultato errato					0						B20.07						
		F3A3	fase analitica amplificazione	retroscrizione del RNA virale in cDNA e reazione di amplificazione a catena del DNA.	errata preparazione dei reattivi per realtime PCR	B09.27; B09.28; B09.29; B01.06; B01.11; B15.02; B15.03; B15.04; B15.02; B20.02; B22.02	risultato errato					0								0						
					applicazione errata procedura per esecuzione amplificazione realtime PCR	B09.32; B09.28; B09.19;B01.06; B01.09; B15.02; B15.03	risultato errato					0						B09.42						
					errato trasferimento del campione estratto in piastra o altro supporto necessario per amplificazione genica in realtime PCR (campione A in posizione del campione B)	B09.19; B22.04	risultato errato					0						B09.42						
					errato volume di campione estratto utilizzato per real time PCR	B09.02; B09.19; B09.18; B11.01; B13.05; B20.05	risultato errato					0						B09.42						
					mancato trasferimento del campione estratto su piastra o supporto per realtime PCR	B09.19; B19.01	risultato errato falsi negativi					0						B09.42						
					cross-contaminazione tra campioni (al momento del trasferimento del campione dal supporto che contiene il campione estratto al supporto utilizzato per realtime PCR)	B09.04; B09.17; B14.02	risultato errato falsi positivi					0						B27.03;B29.04;B31.01						
					errato trasferimento di liste lavoro a strumento per amplificazione realtime PCR (LIS vs software o inserimento manuale di programmazione): anagrafica paziente, ID Campione e tipo di processazione (es. ricerca SARS-COV-2 rispetto ad altri)	B09.24; B09.23; B23.01	risultato errato					0						B09.43						
					errata programmazione dello strumento per real time PCR	B09.19; B01.10; B23.01	risultato errato					0								0						
					errato caricamento campioni su strumento realtime PCR che induce errore associazione tra anagrafica, ID Campione e campione reale, ad esempio verso piastra di amplificazione o sequenza carteggio	B09.24; B09.23; B23.01	risultato errato					0						B09.39						
					controllo negativo non inserito nella seduta analitica (CQI)	B03.01; cap.14	risultato errato		DGG Sanità n. 32656 19/12/2000 "Linee guida su "Controllo di Qualità Interno nel Servizio di Medicina di Laboratorio".			0						B22.06						
					numero di controlli positivi non adeguato alle numerosità di campioni analizzati nella seduta analitica(CQI)	cap.17	risultato errato					0						B22.05						
					controllo positivo non inserito (CQI)	B02.01; cap.14; cap.15	risultato errato					0								0						
					numero di controlli positivi non adeguati per numerosità sedute analitica (CQI)	cap.17	risultato errato					0						B22.05						
					impossibilità di utilizzo di uno strumento	B22	B22	B22										R22						
					allerata rilevazione di un gene bersaglio causa di variante virale nota	B26.02; B26.01; B26.02; B26.03	risultato errato		TECHNICAL REPORT Methods for the detection and identification of SARS-CoV-2 variants ECDC marzo 2021 "Methods for the detection and identification of SARS-CoV-2 variants" – WHO Diagnostic testing for SARS-CoV-2 Interim guidance 11 September 2020				0								0						
					allerata rilevazione di un gene bersaglio causa di variante virale non nota	B26.02; B26.01; B26.02; B26.03	risultato errato		TECHNICAL REPORT Methods for the detection and identification of SARS-CoV-2 variants ECDC marzo 2021 "Methods for the detection and identification of SARS-CoV-2 variants"				0								0						
					necessità di intervento manuale di operatore su sistema automatizzato (es. di dispensazione campione o altro errore di tracciabilità)	B09.25; B03.04							0								0						
		F3A4	fase analitica: scelta del sistema analitico/manutenzio ni /installazione/ controllo sistemi analitici		scelta del sistema analitico non adeguato ai fabbisogni	cap.16; R27	tempi di erogazione delle prestazioni non adeguati all'organizzazione ed al processo decisionale clinico (sistema insufficiente) vs ospedali		WHO-reference number: WHO/COVID-19laboratory/2020.5 ——WHO reference number: WHO/2019-nCoV-19laboratory/2020.6 WHO Diagnostic testing for SARS-CoV-2 Interim guidance 11 September 2020 ——				0								0						
					mancata esecuzione dei test a causa dell'indisponibilità del materiale per erogazione della prestazione (es. puntali, piastre, reagenti di estrazione e di amplificazione)	B13.02; B22.02; R26	tempi di erogazione delle prestazioni non adeguati all'organizzazione ed al processo decisionale clinico;R26	R26											B09.40; B13.09;R26						
					scelta sistema analitico non adeguato all'organizzazione del laboratorio	cap.16; cap.09	mancata o ritardata erogazione della prestazione /risultato errato		WHO-reference number: WHO/COVID-19laboratory/2020.5 ——WHO reference number: WHO/2019-nCoV-19laboratory/2020.6				0								0						
					errato inserimento dei dati relativi ai campioni inviati in "service" sul LIS	B13												R13								
					verifica prestazionale del sistema analitico scelto non eseguita (es. verifica della concordanza diagnostica verso metodo di riferimento)	cap.09	risultato errato		Nota protocollo Ministero della Salute 0009774-23/03/2020-DGPRE-DGPRE-P. Nota Protocollo Regione Lombardia G1.2020.0020666 del 19/03/2020 Nota Protocollo Regione Lombardia G1.2020.0027048				0								0						
					limiti di sensibilità analitica (LoQ) non adeguati al processo decisionale clinico	cap.01; cap.22	risultato errato		Rapporto ISS COVID-19 n.2/2020 -Dispositivi diagnostici in vitro per COVID-19. Parte 1: normative e tipologie Versione del 19 maggio 2020 ——— Rapporto ISS COVID-19 date 4/6/2020 - Dispositivi				0								0						
					mancata esecuzione VEQ	cap.23	risultato errato		Nota protocollo Centro Riferimento Regionale 3/2/2020 del 25 giugno 2020				0								0						
					esiti non conformi programmi VEQ	B13.01; B13.02; cap.24; cap.25; cap.26	risultato errato		Nota protocollo Centro Riferimento Regionale 3/2/2020 del 25 giugno 2020 —— Pischer C etal. Variable sensibility of SARS-CoV-2 molecular detection in European expert laboratories: external quality assessment June and July 2020. J Clin Microbiol				0								0						
					mancata manutenzione programmata della strumentazione	B22.02; cap.13	risultato errato						0					B22.01								
					mancata pulizia e/o sanificazione della strumentazione	B09.01; B22.04; B22.02	risultato errato		Laboratory biosafety guidance related to coronavirus disease (COVID-19): Interim guidance, 28 January 202				0								0						
					errata manutenzione ordinaria o straordinaria	B22.02; cap.13	risultato errato						0					B22.01								
					errata pulizia e/o sanificazione della strumentazione	B09.01; B21.01; B22.02	risultato errato						0					B19.01								
					Collegamenti informatici LIS/piattaforme analitiche non adeguati	B30.01; cap.01; cap.20	risultato errato						0								0						
					non idonea pulizia degli ambienti di lavoro	B21.01; B09.01	risultato errato						0					B19.01								
					attivazione del "service" non programmata (malfunzioni)	B13.02	ritardo erogazione prestazione						0								0						
		F3A5	gestione erogazione prestazioni con "service"	Elaborazione, in momenti di picco di domanda elevati, può rendere difficoltoso l'analisi dei campioni in modalità "outsourcing", inviando i campioni presso altri laboratori. Questa modalità implica altre criticità, principalmente legate al trasporto e alla identificazione dei campioni.	inserimento dei campioni inviati in "service"	B09.01; B15.01; cap.09; cap.22	mancata o ritardata erogazione della prestazione /risultato errato		DGG Sanità n. 42811 05/10/1999 Direttive in ordine all'attività dei Laboratori di Analisi Mediche e sciopri derivativi.				0								0						
					errata conservazione e movimentazione dei campioni inviabile "service "	B04.01; B04.04; B15.01; cap.02; cap.03	risultato errato						0								0						
					errata identificazione dei campioni inviabile "service"	B09.01; cap.02; cap.03	risultato errato						0					cap.23								
					errore di trascrizione esiti della prestazioni erogate in "service"	B09.01; cap.09; cap.22; R29	risultato errato						0								0						
					ritardo ricezione risultati prestazioni erogate in "service"	B04.02; B22.02	mancata o ritardata erogazione						0								0						

ID FASE	FASE DEL PROCESSO	ID ATTIVITA'	ATTIVITA'	DESCRIZIONE ATTIVITA'(attività elementari,materiali e metodi,personale,...)	POSSIBILE EVENTO (Cosa può accadere?)	POTENZIALI CAUSE (da cosa può essere indotto?)	POSSIBILI CONSEGUENZE (Cosa ne può derivare?)	EFFETTI SUL PAZIENTE	MISURE DI CONTROLLO GIA' IN ESSERE (Oggi cosa stiamo facendo per evitare e contenere l'evento?) RIFERIMENTI INFORMATM	Rischio attuale						EVENTUALI AZIONI DI CONTROLLO AGGIUNTIVE (Mitigazione del rischio attuale)	Rischio residuo							RESPONSABILE	STATO AVANZAMENTO ATTIVITA'	PERIODICITA' MONITORAGGIO	VERIFICA EFFICACIA
										G	vP	R	vPXR	IR	Priorità		G	vP	R	vPXR	IR	IR_var	Priorità				
F4	Fase Post-analitica	F4A1	valutazione dell'esito real time PCR	Analisi delle curve di amplificazione da parte dell'operatore. Le curve di amplificazione vengono valutate per ogni gene targets per ogni campione. Una curva di amplificazione è visualizzata in funzione del ciclo della fluorescenza. Un campione è positivo se, in corrispondenza di cicli bassi la fluorescenza è elevata.	errata valutazione delle curve di amplificazione del campione	B00.28; B00.29; B01.13; B05.01; B09.01; B13.03; B14.03; B15.05; esp.09; esp.10; esp.11; esp.12	risultato errato						0	0		B20.06; B21.04; B29.03				0	0	0					
					errata valutazione delle curva di amplificazione del controllo interno di reazione quando disponibile (es. housekeeping genes)	B00.28; B01.13; B09.01; B13.03; B14.03; B15.05	risultato errato						0	0		B20.06; B21.04; B29.03				0	0	0					
					errata applicazione dei cut-off decisionali per i Ct per ciascun gene target	B08.01; B09.01; B14.03; esp.12	risultato errato						0	0		B29.02				0	0	0					
					utilizzo dei cut-off decisionali per i Ct errati	B08.01; B09.01; B14.03	risultato errato						0	0		B29.02				0	0	0					
					errata interpretazione dei Ct di amplificazione del gene target	B00.28; B08.01; B09.01; B13.03; B14.03	risultato errato						0	0		B20.06; B22.4; B29.03				0	0	0					
					errata valutazione del controllo qualità positivo o negativo per seduta analitica	B09.01; B14.03	risultato errato						0	0						0	0	0					
					mancata valutazione del controllo qualità positivo o negativo per seduta analitica	B09.01	risultato errato						0	0						0	0	0					
					blocco/mal funzionamento piattaforma analitica	B23.01; R34	mancata o ritardata erogazione della prestazione /risultato errato						0	0						0	0	0					
					blocco o mal funzionamento informatico in qualsiasi step della fase analitica	B23.01	mancata o ritardata erogazione della prestazione /risultato errato						0	0						0	0	0					
		F4A2	Refertazione, invio, lettura referto e follow up	Analisi dei risultati e eventuale comunicazione ai pazienti positivi; invio dell'esito dei test ai pazienti tramite mail, fax, posta, fascicolo sanitario o chiamata	errato trasferimento/trascrizione esiti test da piattaforma analitica a referto	B00.29; B09.01	risultato errato						0	0						0	0	0					
					errata impostazione del referto (non chiara definizione di positivo e negativo es: gene e	B00.29; B09.01; esp.06	risultato errato						0	0						0	0	0					
					ritardata comunicazione del referto (dalla ATS all'utente)	R32	R32	R32																			
					mancata/ritardata comunicazione esito positivo al paziente	R31										R29											
					tipologia di test eseguito non riportato nel referto ad esempio rilevazione anticorpi o persona vista	B00.29; B09.01	errata valutazione del paziente						0	0						0	0	0					
					lingua di redazione referto non adeguata alla richiesta	B00.29; B09.01; esp.06	mancata comprensione del risultato						0	0						0	0	0					
					errata anagrafica referto (risultato paziente A in referto del paziente B)	B00.29; B09.01; R30	risultato errato; R30						0	0						0	0	0					
					tempi di refertazione non idonei al processo decisionale clinico	B24.02; B23.02	difficoltà nella gestione logistica e assistenziale						0	0		R29				0	0	0					
					errata lettura referto (positivo anziché negativo e viceversa)	B01.12; B09.01; esp.06	risultato errato						0	0						0	0	0					
					errore di associazione referto paziente	B09.01; B23.01	risultato errato						0	0						0	0	0					
					errato inserimento dei dati relativi ai tamponi nel file di invio per la segnalazione ad ATS dei casi da sorvegliare per 4 contatti/caso	R35	R35	R35								R35											
					errata o mancata valutazione di congruenza dell'esito dei test di laboratorio con la clinica	B09.01; B20.01	risultato errato						0	0						0	0	0					
					mancata visualizzazione dei referti sul fascicolo sanitario elettronico																						
					assenza referto tampone	R37		R37								R37											
					errata compilazione flussi	B09.01	errata interpretazione epidemiologica dei dati						0	0						0	0	0					
					esito tampone non presente nella documentazione al momento del ricovero	R38;R36		R38;R36								R38											
					errato tracciamento dei contatti	B09.01; B23.01	mancata rilevazione di casi positivi sul territorio						0	0						0	0	0					
					incompleto tracciamento dei contatti	B09.01; B23.01	mancata rilevazione di casi positivi sul territorio						0	0						0	0	0					
					disomogenea disponibilità di piattaforme analitiche	B10.04	disomogeneità interpretativa dei risultati						0	0						0	0	0					

Annex G - Model template.



MODELLO DI GOVERNANCE

MODELLO GERARCHICO DECISIONALE				
funzionale	task force	commissariale	misto	altro
(flag)	(flag)	(flag)	(flag)	

PERIMETRO FUNZIONALE						
ATTORI COINVOLTI	gestione medica	farmacovigilanza/rischio	gestione operativa/logistic	studi epidemiologici	gestione domanc	gestione sist
attore 1	(flag)	(flag)	(flag)	(flag)	(flag)	(flag)
attore 2	(flag)	(flag)	(flag)	(flag)	(flag)	(flag)
....	(flag)	(flag)	(flag)	(flag)	(flag)	(flag)
attore n	(flag)	(flag)	(flag)	(flag)	(flag)	(flag)

INFRASTRUTTURA E SERVIZI IT

GESTIONE DELLA DOMANDA		
CANALI	piattaforma di prenotazion	d
ambulatorio ospedaliero	(flag)	(testo)
centri massivi	(flag)	(testo)
MMG/PLS	(flag)	(testo)
farmacie	(flag)	(testo)
aziende	(flag)	(testo)
domicilio	(flag)	(testo)

GESTIONE DELL'EROGAZIONE	
Strumenti di pianificazione/gestione cv	strumenti gestione logistica
(testo)	(testo)

INFRASTRUTTURA E GOVERNANCE IT	
Architettura	modello gestione
(testo)	(testo)

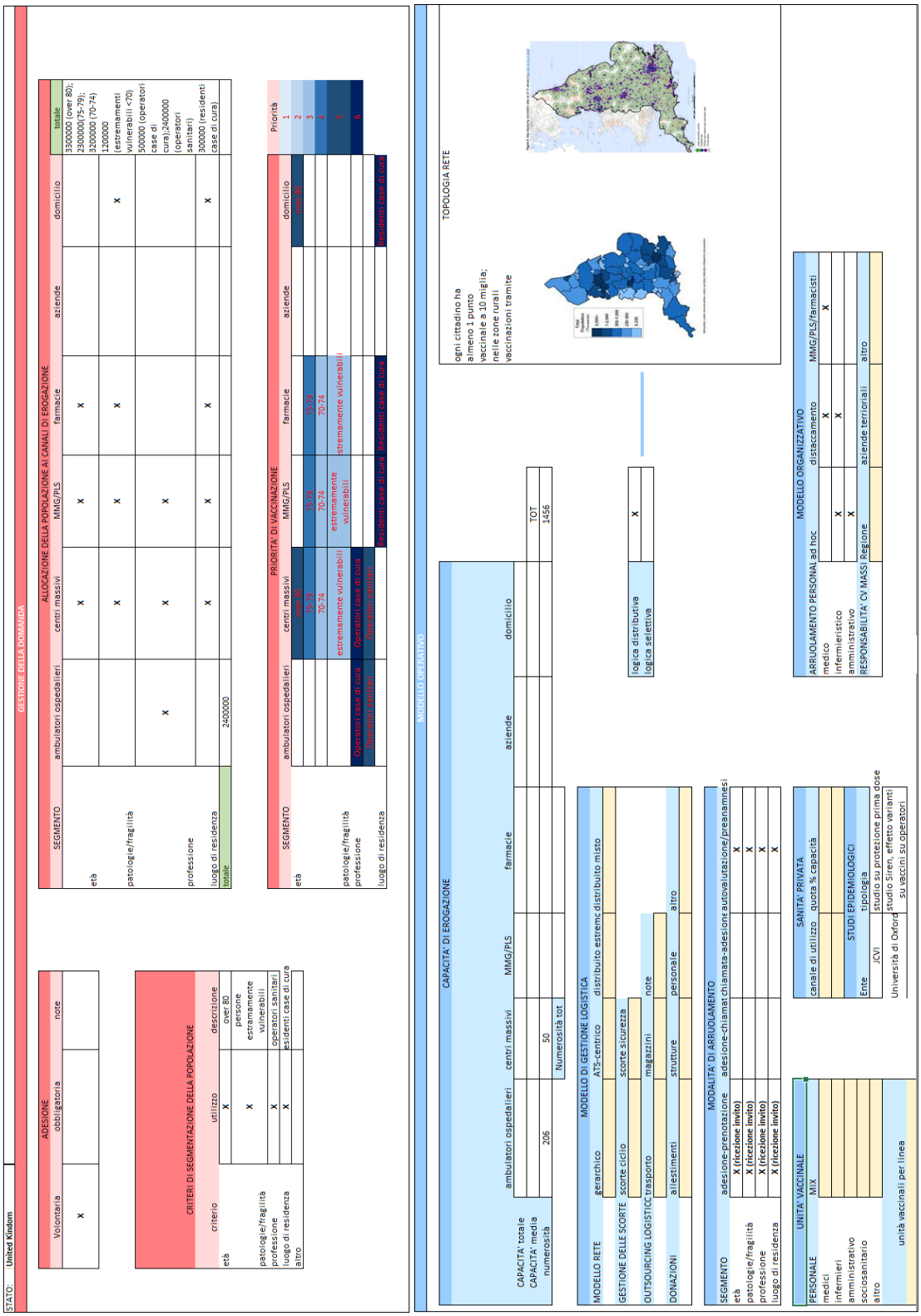
CAMPAGNA DI COMUNICAZIONE

CONTENUTI	
completezza e accessibilità	
numero di faq	(numero)

CANALI				
CRITERIO SEGME	SEGMENTO	canale1	canale2	canale3
età	range1	(flag)	(flag)	(flag)
	....	(flag)	(flag)	(flag)
	range n	(flag)	(flag)	(flag)
patologie/fragilità	patologia 1	(flag)	(flag)	(flag)
	...	(flag)	(flag)	(flag)
	patologia n	(flag)	(flag)	(flag)
professione	professione1	(flag)	(flag)	(flag)
	...	(flag)	(flag)	(flag)
	professione n	(flag)	(flag)	(flag)
luogo di residenza		(flag)	(flag)	(flag)

CHI COMUNICA	
politico	(flag)
dirigente	(flag)
portavoce	(flag)

Annex H – UK case.



MODELLO DI GOVERNANCE

MODELLO GERARCHICO DECISIONALE				
funzionale	task force	commissariale	misto	altro
	X			

PERIMETRO FUNZIONALE						
ATTORI COINVOLTI	gestione medica	farmacovigilanza/rischi	gestione operativa/logist	studi epidemiologici	gestione domand	gestione sistemi
Vaccine Taskforce			X		X	
4 UK Chief Medical Officers			X			
NHS (National Health Service)		X	X			
MHRA		X				
NHSEI						X (commissionato NIMS)
PHE (Public Health England)		X				X
Local and regional governi	X					
Research institutions				X		

INFRASTRUTTURA E SERVIZI IT

GESTIONE DELLA DOMANDA		
CANALI	piattaforma di prenotazior	numero
ambulatorio ospedaliero		tramite autorià locali
centri massivi	X (piattaforma nazionale di prenotazione)	
MMG/PLS		chiamata tramite registri personali
farmacie	X (piattaforma nazionale di prenotazione)	
aziende		
domicilio		

GESTIONE DELL'EROGAZIONE	
Strumenti di pianificazione/gestione cv	strumenti gestione logistica
Registri elettronici per monitorare eventi avversi; ImmForm platform (registri medici di base) per aggiornare copertura vaccino; NIMS (National Information Management	

INFRASTRUTTURA E GOVERNANCE IT	
Architettura	modello gestione

CAMPAGNA DI COMUNICAZIONE

CONTENUTI	
completezza e accessibilità	
numero di faq	69

https://www.essexcovidvaccine.nhs.uk/coronavirus-vaccine/faqs/

CANALI				
CRITERIO SEGMENT(	SEGMENTO	canale1	canale2	canale3
età	range1			
	....			
	range n			
patologie/fragilità	patologia 1			
	...			
	patologia n			
professione	professione1			
	...			
	professione n			
luogo di residenza				

CHI COMUNICA	
politico	
dirigente	
portavoce	

Annex I – References for each Italian region.

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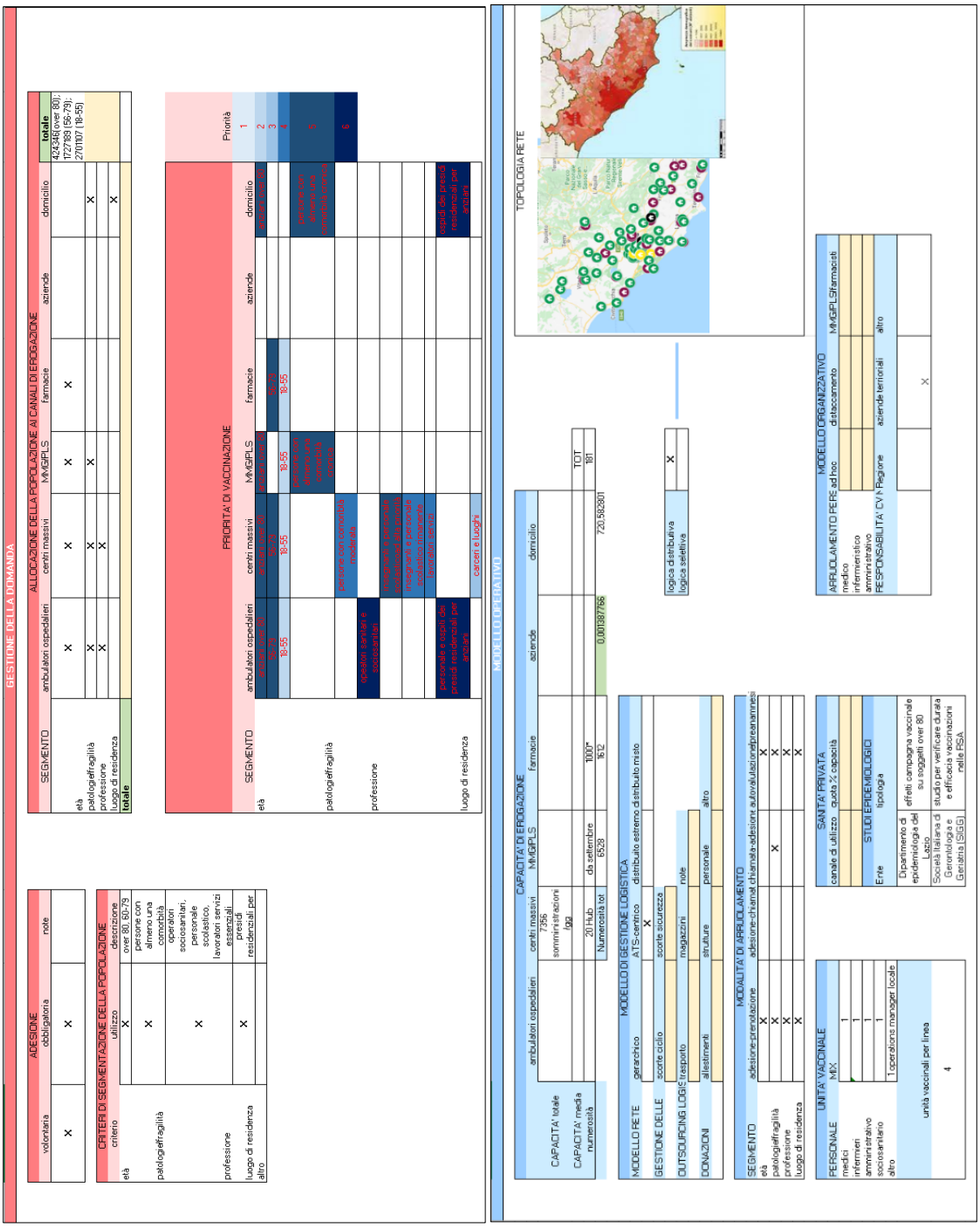
https://www.cliclavoro.gov.it/Normative/DL-1aprile2021-n44.pdf
https://www.iss.it/news/-/asset_publisher/gJ3hFqMQsykM/content/vaccino-anti-covid-e-operatori-su-eurosurveillance-lo-studio-di-efficacia-di-iss-e-ulss-2-treviso
https://www.regione.veneto.it/web/guest/emergenza-coronavirus?articleId=7435075
http://federfarmaveneto.it

Annex J – Lazio template.



MODELLO DI GOVERNANCE

MODELLO GERARCHICO DECISIONALE				
funzionale	task force	commissariale	misto	altro
	x			

PERIMETRO FUNZIONALE						
ATTORI COINVOLTI	gestione medic	farmacovigilanza/risch	gestione operativa/logisti	studi epidemiolog	gestione domanc	gestione sistemi IT
Dipartimento di epidemiologia del Lazio				x		
attore 2						
...						
attore n						

INFRASTRUTTURA E SERVIZI IT

GESTIONE DELLA DOMANDA		
CANALI	piattaforma di prenotazione	numero
ambulatorio ospedaliero	x	https://prenotavaccino-covid.regione.lazio.it/main/home
centri massivi	x	https://prenotavaccino-covid.regione.lazio.it/main/home
MMG/PLS		
farmacie		
aziende		
domicilio		

GESTIONE DELL'EROGAZIONE		
	Strumenti di pianificazione/gestione cv	strumenti gestione logistica

INFRASTRUTTURA E GOVERNANCE I	
Architettura	modello gestione

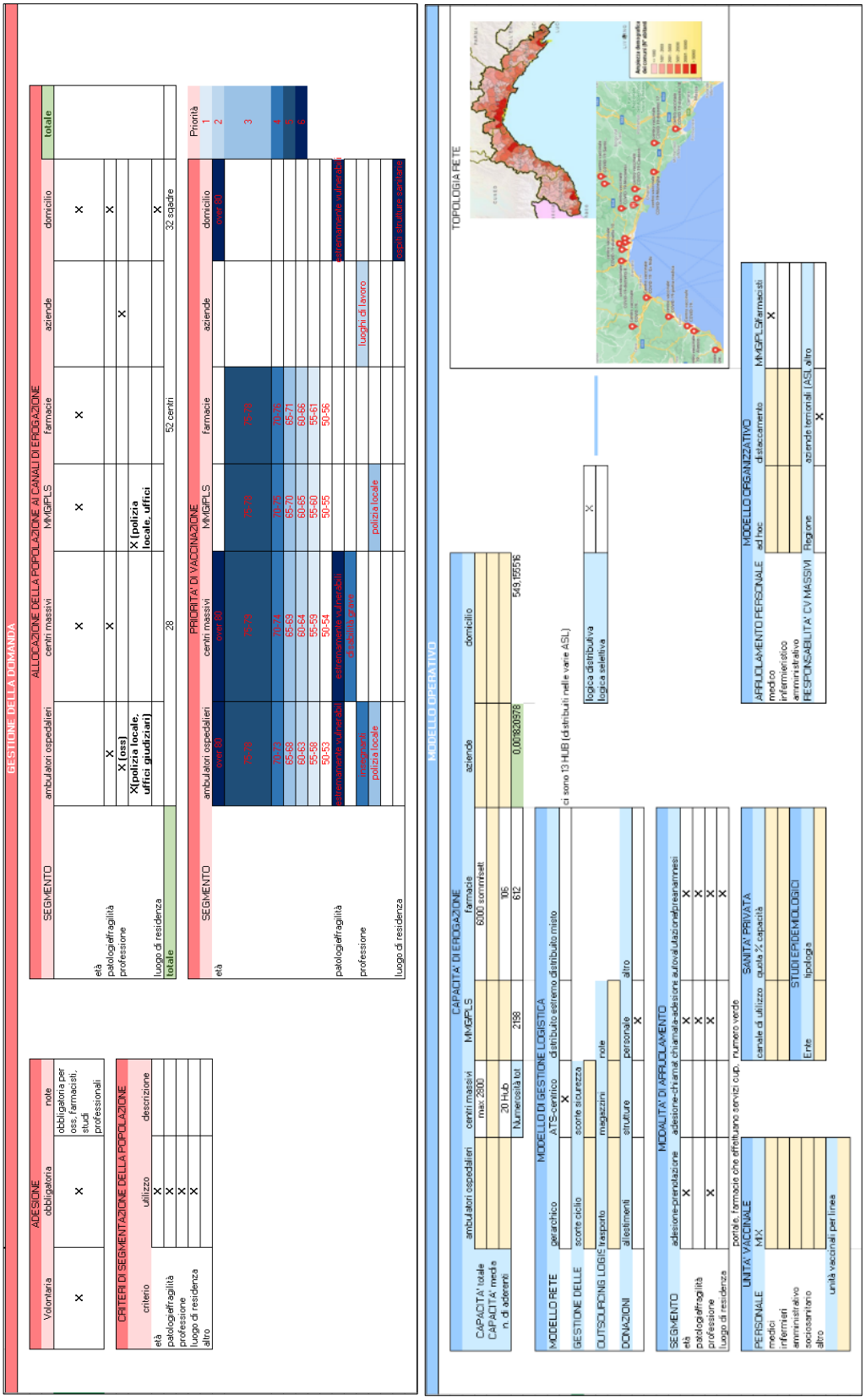
CAMPAGNA DI COMUNICAZIONE

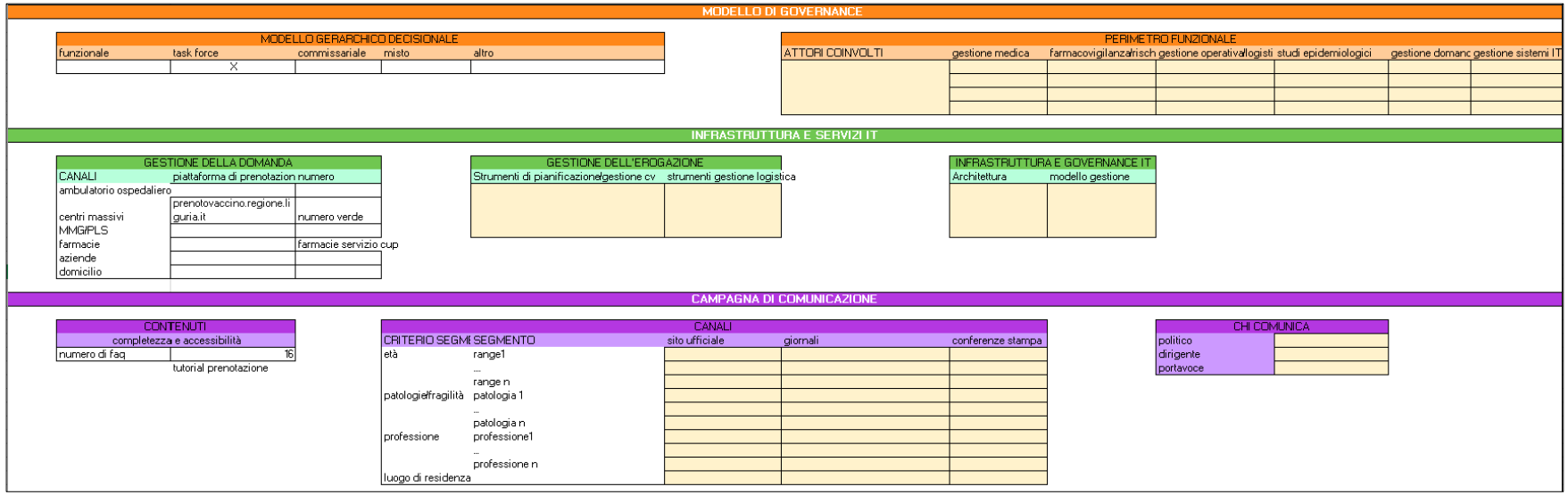
CONTENUTI	
completezza e accessibilità	
numero di faq	42

CANALI				
CRITERIO SEGMI	SEGMENTO	canale1	canale2	canale3
età	range1			
	...			
	range n			
patologie/fragilità	patologia 1			
	...			
	patologia n			
professione	professione1			
	...			
	professione n			
luogo di residenza				

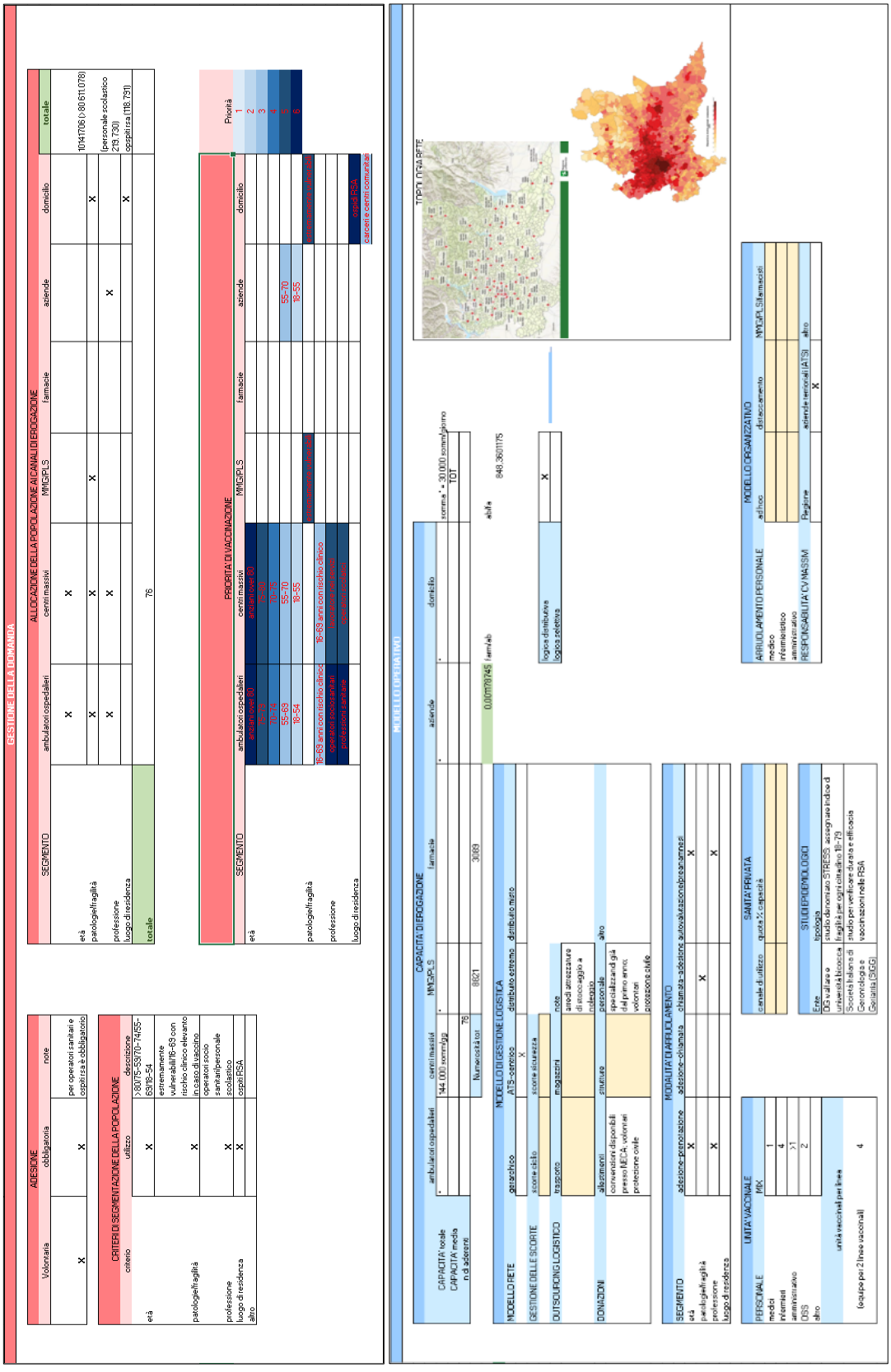
CHI COMUNICA	
politico	
dirigente	
portavoce	

Annex K - Liguria template.




MODELLO DI GOVERNANCE
MODELLO GERARCHICO DECISIONALE
funzionale
task force
commissariale
misto
altro
X
PERIMETRO FUNZIONALE
ATTORI COINVOLTI
gestione medica
farmacovigilanza/risch
gestione operativa/logisti
studi epidemiologici
gestione domanc
gestione sistemi IT
INFRASTRUTTURA E SERVIZI IT
GESTIONE DELLA DOMANDA
CANALI
piattaforma di prenotazion
numero
ambulatorio ospedaliero
centri massivi
prenotovaccino.regione.liguria.it
numero verde
MMG/PLS
farmacie
farmacie servizio cup
aziende
domicilio
GESTIONE DELL'EROGAZIONE
Strumenti di pianificazione/gestione cv
strumenti gestione logistica
INFRASTRUTTURA E GOVERNANCE IT
Architettura
modello gestione
CAMPAGNA DI COMUNICAZIONE
CONTENUTI
completezza e accessibilità
numero di faq
16
tutorial prenotazione
CANALI
CRITERIO SEGMI
SEGMENTO
sito ufficiale
giornali
conferenze stampa
età
range1
range n
patologie/fragilità
patologia 1
patologia n
professione
professione1
professione n
luogo di residenza
CHI COMUNICA
politico
dirigente
portavoce

Annex L - Lombardy template.



MODELLO DI GOVERNANCE

MODELLO GERARCHICO DECISIONALE				
funzionale	task force	commissariale	misto	altro
		X		

PERIMETRO FUNZIONALE						
ATTORI COINVOLTI	gestione medica	farmacovigilanza/rischio	gestione operativa/logistica	studi epidemiologici	gestione domanda	gestione sistemi IT
comitato guida vaccinazioni anti covid						
comitato esecutivo vaccinazioni anti co	X		X		X	X
Centro regionale di Farmacovigilanza		X				
direzione generale welfare				X		

INFRASTRUTTURA E SERVIZI IT

GESTIONE DELLA DOMANDA		
CANALI	piattaforma di prenotazione	numero
ambulatorio ospedaliero		
centri massivi	Sistema poste italiane	
MMG/PLS		
farmacie		
aziende	Sistema poste italiane	
domicilio		

GESTIONE DELL'EROGAZIONE	
Strumenti di pianificazione/gestione cv	strumenti gestione logistica
SIAVR = sistema informativo anagrafe vaccinazione regionale. Per gestione delle vaccinazioni; APP SALUTE FSE; sistema MIP per	siavr

INFRASTRUTTURA E GOVERNANCE IT	
Architettura	modello gestione

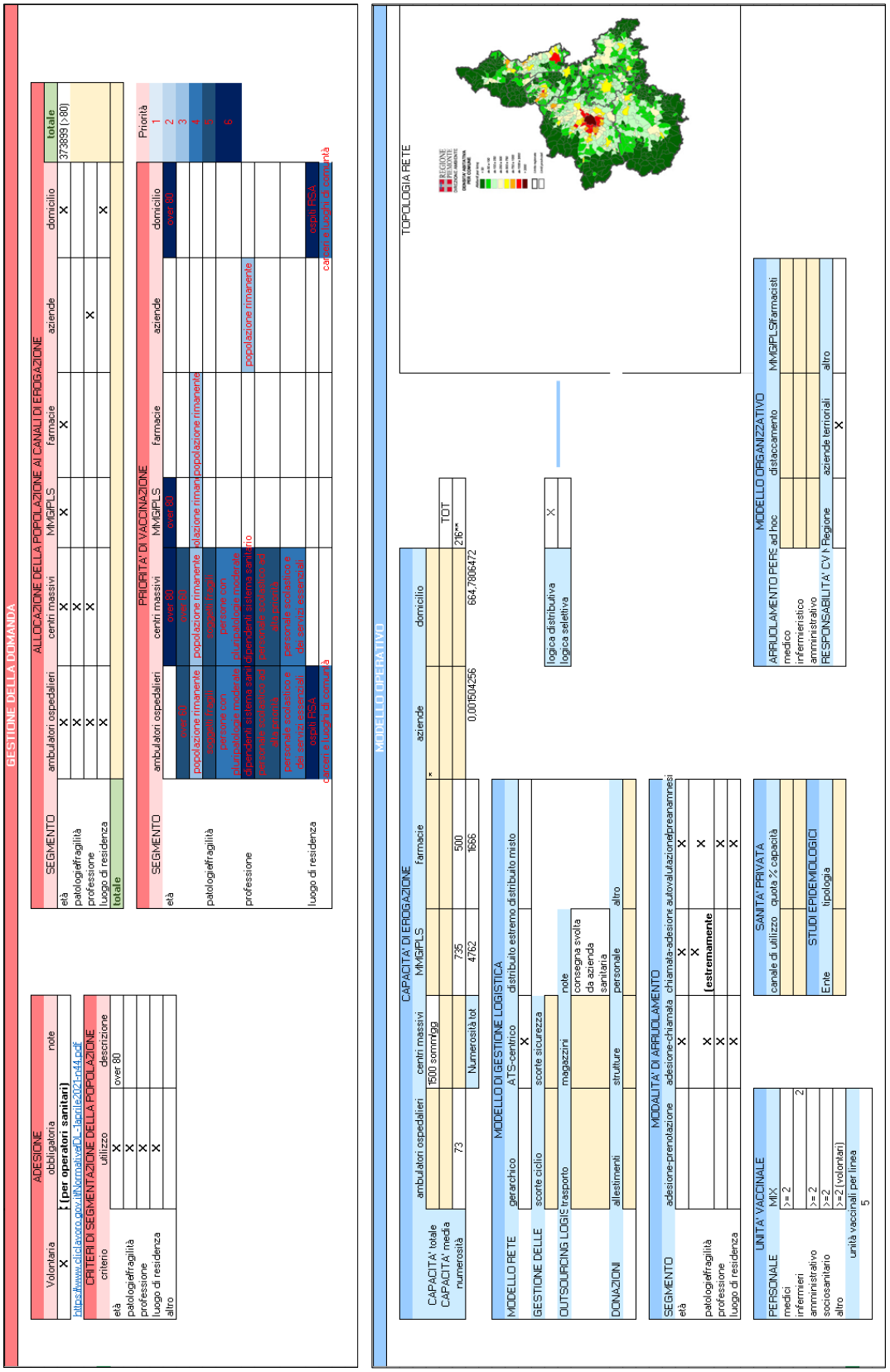
CAMPAGNA DI COMUNICAZIONE

CONTENUTI	
completezza e accessibilità	
numero di faq	17
attivazione numero verde informativo	X

CHI COMUNICA	
politico	X
dirigente	
portavoce	X

CANALI								
CRITERIO SEGMEN	SEGMENTO	portale web	social media	call center	stampa	radio	tv locali	OOH
età	range1							
	...							
	range n							
patologie/fragilità	patologia 1							
	..							
	patologia n							
professione	professione1							
	..							
	professione n							
luogo di residenza								

Annex M - Piedmont template.



MODELLO DI GOVERNANCE

MODELLO GERARCHICO DECISIONALE				
funzionale	task force	commissariale	misto	altro
	X			

PERIMETRO FUNZIONALE						
ATTORI COINVOLTI	gestione medic	farmacovigilanza/risch	gestione operativa/logisti	studi epidemiologici	gestione domanc	gestione sistemi
attore 1						
attore 2						
....						
attore n						

INFRASTRUTTURA E SERVIZI IT

GESTIONE DELLA DOMANDA		
CANALI	piattaforma di prenotazion	numero
ambulatorio ospedaliero		
centri massivi	X	il piemonte ti vaccina.it
MMG/PLS		
farmacie		prenotazione in farmacia
aziende		
domicilio		

GESTIONE DELL'EROGAZIONE		
Strumenti di pianificazione	gestione cv	strumenti gestione logistica

INFRASTRUTTURA E GOVERNANCE I	
Architettura	modello gestione

CAMPAGNA DI COMUNICAZIONE

CONTENUTI	
completezza e accessibilità	
numero di faq	42
	video tutorial su funzionamento sito prenotazione

CANALI				
CRITERIO SEGMI	SEGMENTO	social	TV	giornali
-	popolazione generale	X	X	X
	....			
	range n			
patologie/fragilità	patologia 1			
	...			
	patologia n			
professione	professione1			
	...			
	professione n			
luogo di residenza				

CHI COMUNICA	
politico	X
dirigente	
portavoce	(personaggi famosi)