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Re-engineering of COVID-19 vaccination processes: ASL TO3 analysis and procedural automation

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Introduction

The thesis is about explaining the enormous effort put towards the vaccination campaign taken place in Italy during the entire year 2021 with a focus on region Piedmont. As part of the planning office in ASL TO3, I have personally taken part of the organizing process trying to improve the quality of the system, analyzing it and speeding up technical procedures.

A macro-analysis is made to understand the whole vaccination campaign in order to give shape to the entire supply chain, emphasizing the main actors and stakeholders, so a clear picture of the dynamics occurring between national authorities and local ones will be depicted.

In the central part, a deep study of the informational flow of vaccination process is made in order to focus on the possible failures due to a poor system robustness.

In the effort to optimize the vaccination supply chain a mixed linear programming model is presented highlighting the main features and results to understand where it's preferable to improve.

In the final section, Pandas library is analyzed explaining how a possible implementation can save time and automatize informational processes leading to a better service.

Chapter 1

Plan

The first document written by the Ministry of Health was presented in the Parliament on the 2nd of December reporting the strategic plan[1]. Firstly, it is needed to clarify that Italy was part of the seven negotiators (France, Germany, Italy, Poland, Spain, Sweden, The Netherlands) that reached an agreement with the main pharmaceutical companies that were going to produce the tested vaccines. During the negotiations, there were signed deals (APA- Advanced Purchase Agreement, under the supervision of Steering Committee) accounting for a total of 1.3 billions of doses to be redistributed around the entire EU taking into account the population of the countries. An example of an APA (in this case the contract signed by the European Commission and Astrazeneca) it's reported at the end of the page[2].

In the following table it is reported the raw estimation of the number of doses arriving in Italy starting from Q1 2021 and it's clear that it was not enough to cover indiscriminately the entire population, thus a roadmap was tracked.

[1] https://www.trovanorme.salute.gov.it/norme/renderPdf.spring?seriegu=SG&datagu=24/03/2021&redaz=21A01802&artp=1&art=1&subart=1&subart1=10&vers=1&prog=001

[2] https://ec.europa.eu/info/sites/default/files/eu_apa_-_executed_-_az_redactions.pdf

***Tabella 1** - Stima della potenziale quantità di dosi di vaccino disponibili (in milioni) In Italia nel 2021, per trimestre (Q) e per azienda produttrice, in base ad accordi preliminari d'acquisto (APA) sottoscritti dalla Commissione europea e previa AIC*

Vaccini (azienda)	Q1 2021	Q2 2021	Q3 2021	Q4 2021	Q1 2022	Q2 2022	TOTALI
Astra Zeneca	16,155	24,225	-	-	-	-	40,38
PF/BT	8,749	8,076	10,095	-	-	-	26,92
J&J *	-	14,806	32,304	6,73	-	-	53,84
Sanofi/GSK**	-	-	-	-	20,19	20,19	40,38
Curevac	2,019	5,384	6,73	8,076	8,076	-	30,285
Moderna	1,346	4,711	4,711	-	-	-	10,768
TOTALE	**28,269**	**57,202**	**53,84**	**14,806**	**28,266**	**20,19**	**202,573**
media x mese	9,421	19,065	17,947	4,935	9,422	6,73	

(milioni di dosi)
** Se due dosi per regime vaccinale per J&J (altrimenti ½)*
***Come da comunicazione Sanofi, si modificano i tempi di consegna conseguenti allo sviluppo e produzione del vaccino.*

Figure 1.1: Estimation of vaccine supplies

In the phase One, the categories selected were three:

- Frontline health and social care workers (doctors,nurses,..)
- Older adults and staff workers in care homes
- All those 80 years of age and over

As it is known the categories that suffered more from Covid-19 disease are those that were more exposed to the virus and those that were older and/or had other chronic disease. The sum of all three accounted for 6.4 millions (10%). The second step was the immunization of other two categories:

- All those 60-79 years of age
- All those considered extremely vulnerable

With the arrival of new doses the vaccination was opened to a wider part of the population in order to reach the target of 90% of population. A brief consideration is needed before going on: the entire scheme is linked to the expected quantities of vaccines and it was just a forecast and as such liable to risks linked to the contracts signed. Another issue concerned the strong bargaining power that Pfizer had in the negotiation phase thanks to the fast development and great capability of production, thus leading the EU to be subjected to delays or to lower doses than estimated (with basically zero damage for Pfizer). As a result the strategy implemented was a reactive one, trying to minimize and reduce the potential threats relative to a lack of vaccines. It's clear that the negotiations were too hasty but it's because of the extraordinary situation in which we are living now that pushed the need to start the vaccination process as fast as possible (just thinking about the possibility to save people's life).

***Figura 1** - Volumi di potenziali dosi disponibili e % di copertura della popolazione. Le fasi indicate (T) dipendono dai tempi delle autorizzazioni delle agenzie regolatorie.*

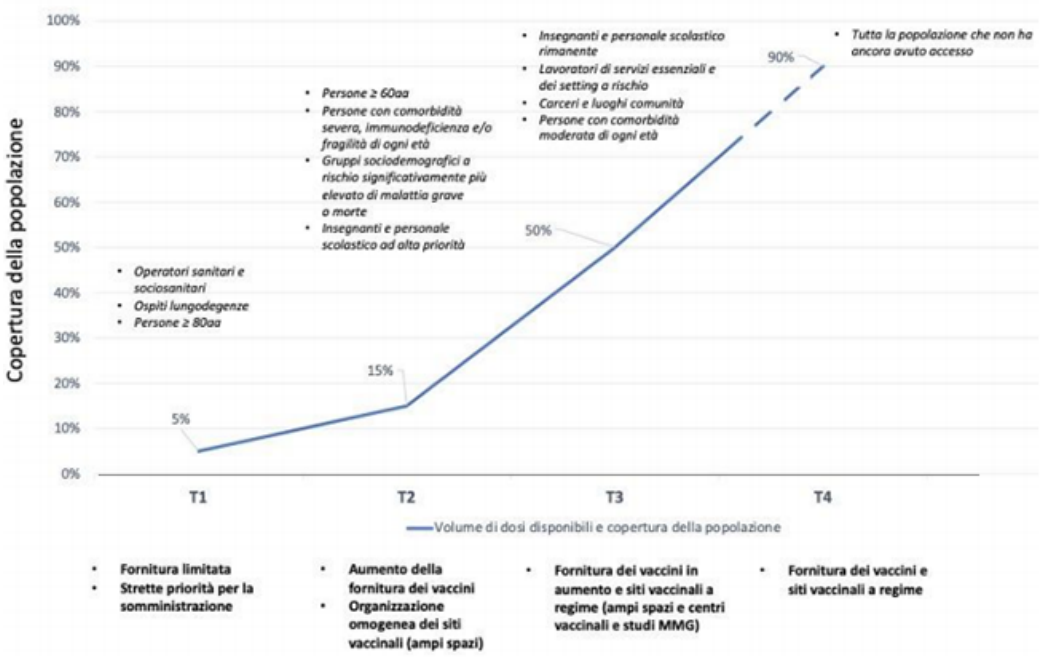


Figure 1.2: Estimation of progress of % vaccinated people

After the immunization of vulnerable people it was decided to vaccinate categories crucial to the state functions (teachers, police workers, school staff) in a phase 3. In the end in the final phase 4 vaccination was opened to everyone.

1.0.1 Logistic

From a logistic point of view the responsible of the management of supply chain is special commissioner (Figliuolo) that is in charge since 1st March replacing Arcuri[3]. With the help of Protezione Civile, he is responsible for the supplying and distribution of vaccines. The whole process starts from the manufacturing companies Moderna, Astrazeneca, Johnson&Johnson that send the vaccines in containers with cargo aircrafts (with the support of delivery companies such as DHL) to the central hub of Pratica di Mare near Rome. Here the containers are sorted based on the demand from the regions and they are redistributed in other intermediate hubs by SDA express courier escorted by the army or Police corp. Then the next step is represented by splitting out the trays to be sent to the local public health companies (ASL), that have an internal storage with freezers, in proportion to the population and the requests. Now the last-mile distribution to the vaccination centers is carried out by ASLs.

However because of the unfavorable conservation condition (requiring an ultra low temperature supply chain), this strategy was not implemented for the Pfizer vaccine, instead it was used a more decentralized distribution from the airports or other arrival points to the inoculation/storage centers. Pfizer built a solid network in collaboration with their supplier partners having temporary hubs all around Europe (freezer farms), where the vaccine can be stored up to 10 days before the delivery to the final destination.[4]

[3] https://www.governo.it/sites/governo.it/files/210313_Piano_Vaccinale_marzo_2021_1.pdf

[4] https://www.theguardian.com/business/2020/nov/10/pfizer-and-biontechs-vaccine-poses-global-logistics-challenge

1.0.2 Cold Chain

The cold chain is the set of transport and storage equipment, trained personnel and efficient management processes adopted in order to maintain the vaccine in a suitable environment preventing it from heat exposure.

Keeping the adequate temperature is the goal of the entire supply chain because an incorrect conservation leads to an irreversible damage. To guarantee the stability of biological parts of vaccines it is essential to preserve the cold chain causing an higher complexity for the system. For example, the lack of a robust cold chain in low-middle income countries could result in a decreasing vaccination rate, slowing down the negative effects of COVID-19 (from both a medical and economic point of view). Lack of temperature controlled storage, inefficient cooling equipment, inadequate maintenance are the main sources of this possible inefficiency. In addition to this it's necessary to state that the electricity requirement can be a problem for developing countries, which don't have a robust grid. Last mile distribution is the main critical phase because it's carried out by local authorities, while from the beginning to the shipment to the airport the supply chain can be managed by a collaboration between the manufacturer and a courier service that has the adequate equipment.[5]

To transport Pfizer vaccine which has the most tighten conservation requirements the company developed an innovative shipper, where there is the need to use dry ice, that is the solid form of carbon dioxide. Manipulating dry ice could be dangerous (main health risks are: asphyxia, possible burns), so the procedure for opening the packages containing the trays is sensitive. The package contains: a box with dry ice, the trays with vials, polystyrene lid for keeping constant the internal temperature and GPS-enabled thermal sensors that detect the temperature in order to avoid unknown temperature deviations. If there is no ULT (ultra low temperature) freezer available for the conservation, then it's possible to use the transportation package as a temporary deposit but with the exception that the dry ice must be replaced.[6]

[5] Webinar IMechE `https://youtu.be/T19JTl7OTCE`

[6] `https://www.aifa.gov.it/documents/20142/1279946/01_Linee_guida_per_la_spedizione_e_la_manipolazione_Brochure_IT.pdf`

1.0.3 Organization

The main stakeholders are: Ministry of Health, Special Commissioner, AIFA, ISS, AGENAS, regions, local public health companies (ASL), citizens, army and police corps. From an organizational point of view at a central level there are established: the procedures, the operational standards, guidelines, the ideal lay-out, while the territory decides the physical location, the allocation of resources and the control phase. The departments of Prevenzione (prevention) are responsible for implementing the strategy at a local level designing the adequate operations in order to respect the regional targets. The main duties are: scheduling the appointments, allocating the required resources (personnel and equipment), monitoring and reporting the vaccination administered to the national authorities.

As we can see in the ministerial act[7], there were designed three kind of inoculation centers:

- Punto Vaccinale Ospedaliero (PVO) - hospital vaccination centre
- Punto Vaccinale Territoriale (PVT) - extra-hospital vaccination centre
- Punto Vaccinale in Struttura Residenziale (PVSR) - extended care vaccination centre

The first centres were opened inside or close to the hospitals to guarantee that the medical staff, that was one of the first categories to be vaccinated, could receive the dose in a very rapid way because there is basically no need to displace kits (syringes, plasters) and the necessary equipment. At the same time, due to the high difficulties to move the patients hosted in Extended care units (RSA), it was developed a plan where basically the main goal was to create internal inoculation areas. Then because of the increase of administrations there was the urgency to open new centers close to specific key areas. Essentially two models were developed: model A and B.

[7] https://www.ansa.it/documents/1608806126328_CircolareVaccino.pdf

Before proceeding on, I need to briefly describe the vaccination process (that will be analyzed mathematically in chapter 3), that consists of seven steps:

- Acceptance
- Counselling
- Anamnesis
- Vaccine dilution
- Injection
- Registration
- Patient monitoring

In the first step, the personnel tries to take care of the incoming flow of people asking them personal data, directing them to a specific line according to the appointment, where for example there is administered only a type of vaccine, checking the body temperature and managing the queues. Secondly the patient signs an agreement where he deliberately gives consent to be vaccinated with the vaccine administered in that day. After that, the patient describes his medical history to a doctor, who does or does not allow him to receive the dose. Consequently a nurse is responsible for the injection of the vaccine. The process ends with the registration of the occurred administration and the supervision of the vaccinated people (for a minimum of 15 mins).

Analyzing the process, the anamnesis phase represents the bottleneck because the majority of the time the doctor spends at least 3 minutes asking questions before allowing the patient to get the dose. Sometimes this phase can take up to 10 mins if the person is old and has other chronic diseases forcing the incoming people to stop in the pre-anamnesis room and blocking the system. Thus a crucial way to speed up the process is opening new vaccination lines where

From the lay-out we can identify three areas:

- Acceptance
- Clinic Area with Preparation Room
- Check-room

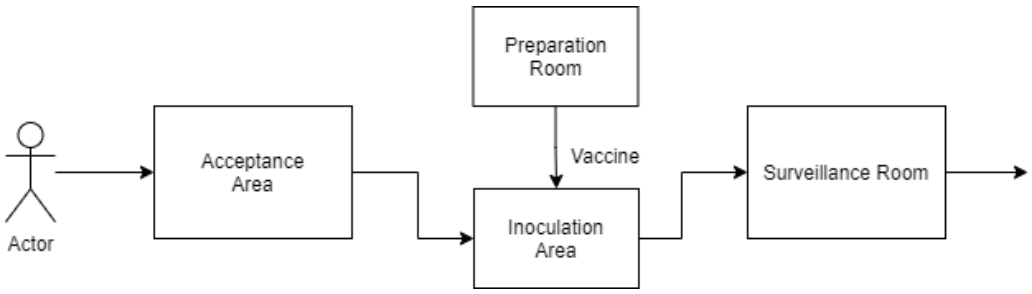


Figure 1.3: Vaccination Center - Lay-Out

The following scheme synthesizes the whole process. The procedures completed in each area depend on the model adopted by the vaccination center. Basically there are two models: model A and B.

The main difference between the two models is that in the former one in the clinic area the only activity done is the administration of vaccine, while in the latter one there are concentrated more activities: anamnesis, administration and registration. Thus in the second model it is required at least two people (nurses or assistants) for each administration point, while in model A just one person is enough. Theoretically the minimum number of doctors is: one to five (model A), one to four (model B) administration points, but practically there is a one to one ratio. The administrative staff needed for carrying out the registration into the system and for verifying the correct procedure is in proportion one to two.

1.0.4 Implementation of the plan - First Phase

During the first phase of the vaccination campaign, the responsible of the management of the supply chain was Arcuri, Italian officer, nominated by the Prime Minister. One of the key parts to understand the strategical plan presented by Arcuri in the Parliament at the end of December is the construction of ad hoc structures, called "primule" for the administration of vaccines. The name stands for a flower and it should have represented the rebirth of the nation after the COVID-19 crisis. The number of buildings should have been up to 3000 units with a unit cost of 400k€. The excessive costs in addition to the time needed to erect them stopped the regions from implementing this solution, instead opting for a reconversion of old buildings, industrial sheds, gyms or public structures.

However it was the harsh criticism regarding the management of the expenses (not even clearly reported) related to the vaccinations (contracts about supply of needles) and COVID-19 crisis (masks, gel, exc...) that forced the government to change the responsible of the campaign.

1.0.5 Implementation of the plan - Second Phase

When Figliuolo was selected to replace Arcuri, he immediately set the target of 500k administrations/day and it was reached at the end of April thanks to a considerable increase of supply of vaccines. The first point of discontinuity was the interruption of contracts signed by his predecessor regarding the construction of primule, that according to Figliuolo saved at least 345M€. The second step taken was to liquidate old contracts in order to decrease the payable account and pay the effort of the suppliers. Thirdly some contracts were reformulated or deleted.

From an organizational point of view, it's needed to clarify that the system taken in charge by Figliuolo was earlier designed by Arcuri (except for primule never realized), so he just needed to make small adjustments such as using more frequently open days (also as a way to incentivize people to get their fist dose) and the implementation of drive-in points, where you could receive the vaccine without getting off the car.

Difference in numbers

Analyzing the data provided by Lab24, the key parameter to understand the difference between the two phases is the percentage of used stock. While in the first phase there was put the limit to preserve at least 30% of the stock, then this limit was canceled trying to go instead for the 100% (theoretically). This strategy was based on the fact that the priority was to guarantee the second dose and conclude the vaccination cycle. Then, emulating the example from England, it was chosen to extend the time lapse for the booster dose and administer first doses as much as possible giving a first coverage to more people. This shift is reflected also in the overlapping graphs of first and second doses where it is evident that in the first phase there was obviously a first dose massive administration during the first month and then a time window for second doses and then again a prevalence of first and second. This scheme was interrupted in favour of an increase of first administrations per day.

1.0.6 Vaccination Speed

Analyzing the data, that exclude the under 12 years old people, we can clearly see that the most intensive days were in June when it was reached the maximum of 623k administrations in a singe day, contributing to vaccinate more than 1% of the entire population. Obviously once that the category 18-30 years old was eligible to be vaccinated and thanks to the increase of supply of vaccines, the objective of reaching the 70% of population could be pursued, despite the part of people not willing to receive the dose. When the young pro vaccine part of population was finished, the boost of June and July ended. This is one of the reason why the green pass was introduced in order to achieve the goal of the vaccination campaign by the end of September (before the arrival of autumn). This effect can be seen in the end of August where it is evident the small jump in administrations (especially first doses).

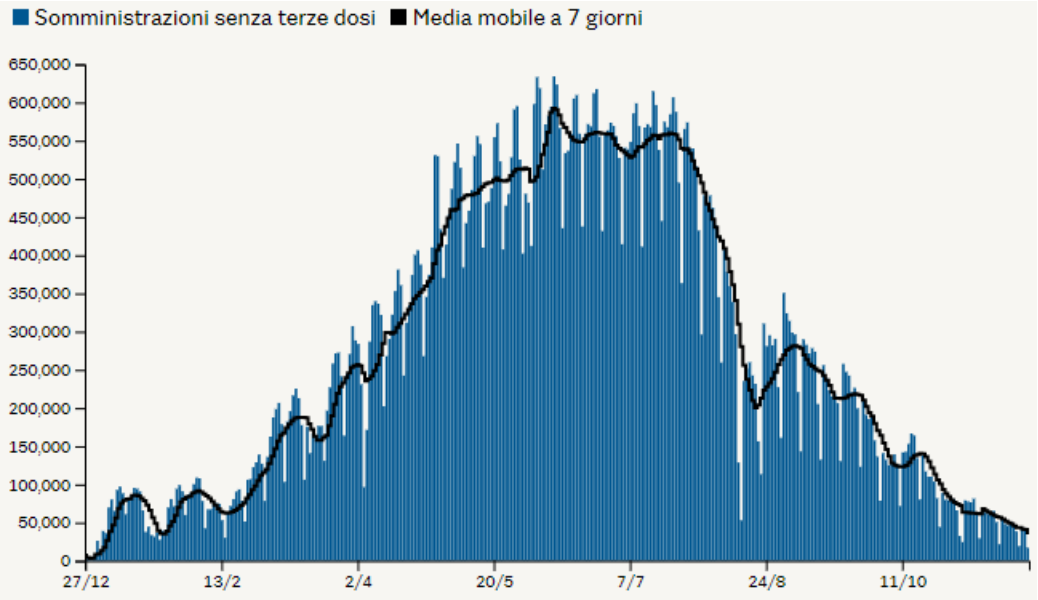


Figure 1.4: Administrations per day

1.0.7 Vaccinations Cumulative

By looking at the cumulative curve it's possible to monitor and compare the trend respect to the initial plan. The target of 80% was reached in the beginning of October (it was missed by just a few days) consolidating the success of the vaccination campaign. Despite the initial cut of supplies, difficulties regarding the vaccination structures, the resources spent were enough to pursue the goal. Data can be found at the following link.[8]

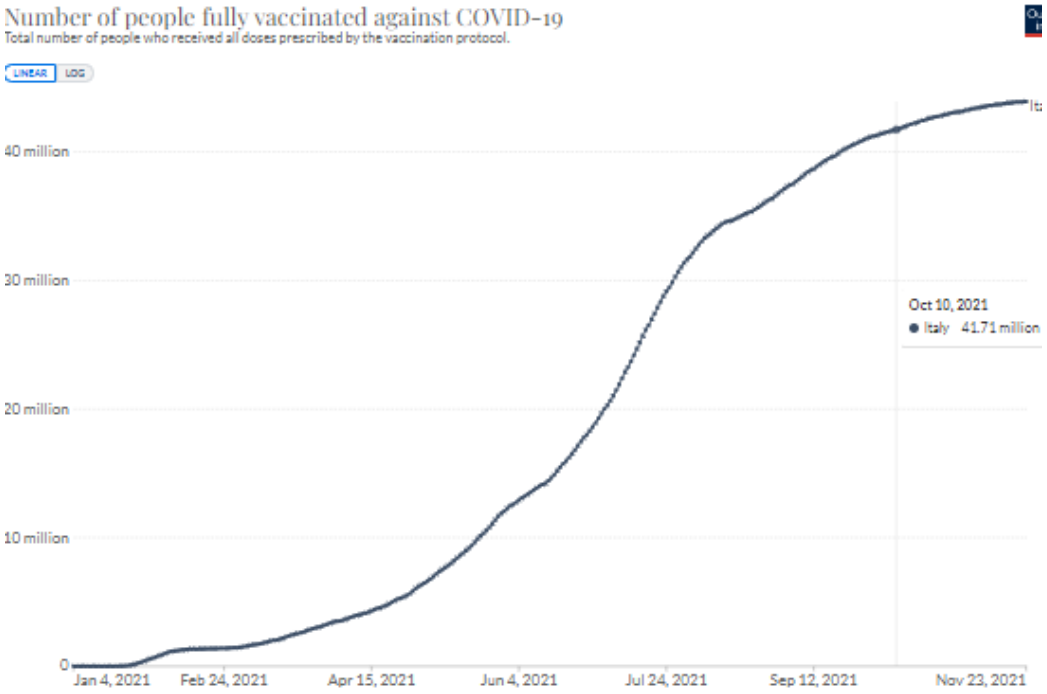


Figure 1.5: Fully vaccinated people cumulative

[8] https://github.com/italia/covid19-opendata-vaccini

1.1 Vaccines

1.2 Vaccine efficacy

In this paragraph it will be briefly explained how the efficacy of a vaccine is calculated[5]. Basically in the last step of clinical trials two groups of same population are divided and in the first group the COVID-19 vaccine is administered while in the second one (control group or placebo group) a "fake" vaccine is inoculated. Now the patients of the two groups are followed-up for at least two weeks after receiving the booster dose in case of two dose vaccines, during this time they are tested and monitored. Then they are compared and the efficacy is calculated as:

$$1 - relativerisk$$

Where the relative risk is computed as:

$$\frac{\%ofvaccinatedpeoplegettingCOVID-19}{\%ofunvaccinatedpeoplegettingCOVID-19}$$

While the efficacy of vaccines is calculated in clinical trials where there are certain conditions such as age, sex, no patients with chronic diseases and no mistakes in handling the vaccine, the effectiveness is determined in the real world environment and differences can occur. Other aspects to take into account for the calculation of efficacy are: during the phase 3 trials of vaccines there were more restrictions (no gatherings, wearing masks outside was mandatory) and the most crucial one is that virus hadn't mutated as much. As the virus mutated, new studies were made trying to figure it out if efficacy was dramatically decreased by Alpha or Delta variants.

1.2.1 Complexity in development, manufacturing and supply of vaccines

Starting from the manufacturing plant, the main challenge of producing a vaccine is its molecular composition much complex than a simple non-biological drug because of the various core components. Due to this biological complexity it can happen that various parts of a vaccine are effectively produced in different plants with the need to ship resources to the main plant where they are assembled. In addition to that, external requirements are strict to ensure safety and efficiency and this results in accurate quality control tests. A delay can occur in each phase: poor source materials, machine failures, external quality control not compliant with the internal one, non-compliant batches, ex... The duration of the time to market of a vaccine typically takes from 10 to 30 years. At least 70% of the time is spent on quality testing. A manufacturing journey considering raw material reception till the end (a retailer that receives the vaccine) can take more than one year considering the following time: raw material reception (2 weeks), bulk manufacturing and maturation (10-12 months), coupling, filling, formulation and quality control (6-10 months), lot release, packaging and shipment (6-18 weeks).

1.2.2 Vaxzevria

The Vaxzevria vaccine, developed by Astrazeneca in collaboration with Oxford University, is a viral vector type-one having an efficiency of 81.3%[6], increasing up to 90, new studies are testing the vaccine against new variants (Alpha, Delta). Furthermore a deeper analysis shows that the efficacy of vaccine is extremely influenced by the administration of the booster dose.

As it's reported in the study conducted by a pool of experts published in The Lancet[12], the efficacy is linked to the interval that occurs between the two doses: the number of symptomatic cases in case of an administration prior to 6 weeks was 111 out of a group of 7746 people (35/3905 in the vaccinated arm, 76/3871 in placebo group) leading to an efficacy of 55.1%, while waiting at least 12 weeks for a booster dose raises the efficacy up to 81.3%. It's crucial to highlight that only two people of the vaccinated pool were hospitalized due to COVID-19 (one receiving first dose on day zero, the other on day ten) and nobody was admitted to hospitals after 14 days having received the booster dose. However the vaccine is not efficient in preventing asymptomatic infections (only 22.2%).

Vaxzevria was approved by EMA on 29th of January followed by AIFA on 30th boosting the vaccination campaign in Europe.[9] Since the beginning of February the Astrazeneca vaccine was preferably administered to the 18-55 years old category as suggested by CTS (Comitato tecnico scientifico)[10](but it was then stated as well the validity of use in the over 65 years old population)[11], raising up the number of vaccinations per day up to 200k before the block imposed by AIFA on 15th of March because of the death of a teacher occurred after the administration.[12][13]

[9] https://www.aifa.gov.it/documents/20142/1289678/Comunicato_AIFA_626.pdf

[10] https://www.aifa.gov.it/documents/20142/1289678/Vaccino-AstraZeneca_parere-CTS_30.01-01.02.2021.pdf

[11] https://www.aifa.gov.it/documents/20142/1314153/Circolare_Min_Sal_08.03.2021.pdf

[12] https://www.ansa.it/piemonte/notizie/2021/03/14/morto-docente-a-biella-piemonte-sospende-astrazeneca_ab9682f0-ff3a-4f7b-8de6-0e799fab4024.html

[13] https://www.aifa.gov.it/documents/20142/1289678/Comunicato_AIFA_637.pdf

After further investigations by a committee of health and legal experts and an accurate autopsy there was found no evidence of correlation between the death and the administration of the Astrazeneca vaccine. [14] This stop slowed down the speed of the campaign not only because of the lack of Astrazeneca administrations for 3 days but also because of bad advertisement (that during the first months was highlighting thrombosis cases and only negative risks making the counter-effects bigger than how actually the reality was), that decreased the trust of people on the benefits of Vaxzevria vaccine.

Inoculations restarted on 19th of March after the day when EMA stated the reliability of the vaccine. However subsequently the analysis of thrombosis cases that happened more frequently but still very rarely in the 18-55 years old category[15], AIFA started suggesting the use of Astrazeneca in the over 60 years old group due to an higher benefit/risk ratio[16].

Despite the controversial history, Astrazeneca was administered 12 million times contributing to around 12.5% of the totality of injections.

[14] https://www.lastampa.it/biella/2021/07/06/news/docente-di-musica-morto-dopo-il-vaccino-nessuna-causalita-fra-il-decesso-e-la-dose-di-astrazeneca-somministrata-1.40468399

[15] https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood

[16] https://www.aifa.gov.it/documents/20142/0/79629_1.pdf

Product Information

The product is sold in pack containing 10 multidose vials (8 or 10 doses of 0.5ml per vial). The shelf life is 6 months for unopened vials when stored in a refrigerator (2°C-8°C), with a possible unexpected excursion for: maximum 12 hours up to 30°C and 72 hours down to -3°C. Obviously after the exposure the vials must be returned to refrigerated storage. In case of opened vials, the chemical and physical stability is unaltered for 6 hours when they are outside at a temperature up to 30°C, conversely when they are immediately put back into the refrigerator after the puncture they can be stored for a maximum of 48 hours.[17]

Because of the favorable storage condition (a normal refrigerator is needed and not an extra-cold one), Astrazeneca vaccine could be the solution for last mile distribution when talking about low-middle income countries that do not have a robust cold chain.

Product Manufacturing

Biomanufacturing Astrazeneca vaccine implies four steps. It all starts from modifying the genetic code of a common virus, which causes cold, in order to carry the information of the surface protein of SARS-CoV-2 (spike protein).Then the modified adenoviral vector is transferred into cells, which help the vector to replicate and grow. This second step takes time to achieve the required amount of replication (cell division can take about 30 hours to occur). This process takes place in large bioreactors where parameters such as temperature and ph concentration are strictly monitored. Once the adequate concentration is reached the cells are burst opened using a lysine chemical to release the vaccine, then it is cleaned through a series of filtration steps to remove cell debris and finally purified using chromatography. Fourth and final step is filling the multi-dose vials, labeling and packaging them. It takes 3-4 months to have the final product ready. The quantity of vaccine realized through this process depends on the size of the bioreactor. Scaling the manufacturing phase means having different sites that can share know-how to optimize the whole process.[18]

[17] https://www.ema.europa.eu/en/documents/product-information/vaxzevria-previously-covid-19-vaccine-astrazeneca-epar-product-information_en.pdf

[18] https://covid19.astrazeneca.com/en/manufacturing.html

1.2.3 Janssen

Janssen is the name used for the vaccine developed by Janssen Vaccines and Janssen Pharmaceutics, a subsidiary of American company Johnson and Johnson. It is based on the viral vector technology depending on the adenovirus type 26 (Ad26) modified with the gene for making the spike protein that causes COVID-19. It is until the moment I am writing the only monodose vaccine approved and it has an efficacy of 66% increasing up to 85% in preventing severe COVID-19[10]. As it is reported in the phase 3 trials results, the efficiency evaluated 14 days and 28 days since the first and only one injection it's similar, drawing conclusions that 14 days is enough time for the immune system to develop antibodies.

Janssen vaccine was authorized by EMA followed by AIFA on 11th March 2021 being the fourth one[19]. At the beginning of June[20], after a manufacturing error as reported in the article by Financial Time[21], F.D.A (Food and Drug Administration) obliged Janssen to destroy 60 millions doses of vaccines because these vials were contaminated. These vials were manufactured in a plant in Baltimora managed by Emergent BioSolutions, a key economic partner of Johnson & Johnson and Astrazeneca. In the plant an human error occurred: the ingredients of Janssen were mixed up with that ones of Astrazeneca, leading to wrong formulation of final product. This obviously caused not only an enormous economic loss for BioSolutions but a social wealth loss because of the delay of the product arrival in the United States.

[19] https://www.aifa.gov.it/documents/20142/1289678/Comunicato_AIFA_634.pdf

[20] https://www.nytimes.com/2021/06/11/us/politics/johnson-covid-vaccine-emergent.html

[21] https://www.ft.com/content/bc05beba-ef13-4db6-8bb0-ffc4ed94df29

On 21st of April, AIFA gave the same indication of use as Vaxzevria: preferential administration to people 60 years older because of the higher risk/benefit ratio[22]. This guideline, that arrived when the majority of over 60 years old people received the first dose of another vaccine in addition to the lower efficiency made Johnson being the less used in Italy (1.5 millions that is approximately 2.5% of the total vaccinated population).

At a certain point, Janssen started being administrated to homeless[23], incarcerated or refugee people because of the complication to inject the 2nd dose of other vaccines to this slice of population that is difficult to be contacted. Thanks to this aspect combined with relative relaxed storage condition, the potentiality of reaching low income countries is higher than the other candidates.

Product Information

The vaccine is distributed in packs of 10 or 20 vials, having 5 doses of 0.5 mL. It's not necessary to dilute or shake the product before the injection. The shelf life of Janssen is 2 years when stored at -25°C to -15°C for unopened vials and once refrigerated at 2°C/8°C it is of 4.5 months. When frozen, the carton of vials can be thawed in the refrigerator and it will take approx. 13 hours or at a room temperature (max 25°C) taking 4 hours in this case. There is the possibility to transport the product at 2°C to 8°C but it will be stored in a refrigerator and not refrozen.[24]

This guarantees the opportunity to have normal cold supply chains that do not include extra-cold equipment, thus delivering this kind of vaccine to low-middle income countries it will be easier.

[22] https://www.aifa.gov.it/documents/20142/1446021/79916_1.pdf

[23] https://www.wsj.com/articles/johnson-johnsons-covid-19-vaccine-emerges-as-preferred-shot-for-homeless-11617530400

[24] https://www.ema.europa.eu/en/documents/product-information/covid-19-vaccine-janssen-epar-product-information_en.pdf

1.2.4 Comirnaty

Comirnaty is a m-RNA vaccine developed by the synergy between Pfizer and BioNTech, launched in the end of 2020, having an efficiency of 95% in preventing symptomatic infections, as shown by the study published after the third trial[7]. 37706 people were recruited and followed up to 2 months after the second dose and the results showed that 8 patients out of 18198 that received the vaccine developed at least one symptom, while just one patient got hospitalized. The efficacy of vaccine is linked to the time passed between the two administrations, showing basically no significant increase after passing 21 days. New studies[11] are trying to assess the duration of the protection after the booster dose, showing a decrease in the efficacy after 3-4 months since the booster dose. In the study there was not analyzed if vaccinated people developed asymptomatic COVID-19 infection and the vaccine initially was not tested on certain categories (children, pregnant women and immunocompromised people). Further studies[8], coming from the results of a clinical trial carried out on 2260 people in the beginning of 2021, indicated that the vaccine is 100% effective on 12 to 15-years old teenagers extending the EUA (Emergency Use Authorization) to this category.

On the 21 of December, the vaccine was approved for Emergency use by Ema followed by AIFA[25] leading the start of the vaccination campaign, while on the 23rd of August FDA fully approved the vaccine after a complete verification of the BLA (Biologics Licence Application)[26]. In this document provided by Pfizer and BioNTech along with the information coming from the clinical trials, there are contained: manufacturing process details, quality tests and inspections made on the plants where the vaccine is produced.

Since the start of the vaccination campaign, Pfizer vaccine was the most used in Italy, contributing to 70% of the totality of administrations.

[25] https://www.aifa.gov.it/-/autorizzato-il-vaccino-biontech-pfizer

[26] https://www.fda.gov/news-events/press-announcements/fda-approves-first-covid-19-vaccine

Product Information

The product is distributed in packs of 195 vials (6 doses of 0.3 mL). The liquid contained inside the vials must be diluted before the administration in that way: first of all frozen vials should be thawed at a temperature between 2°C/8°C and then diluted with 1.8 mL sodium chloride 9 mg/mL solution in its original vial. Once the procedure is completed, the vial should be stored at 2°C to 30°C and used within 6 hours. The shelf life for a frozen vial is 9 months in a freezer that keeps the temperature in the range -60°C/-90°C while for a thawed and not diluted vial is 1 month at 2°C to 8°C. Within the 9-month shelf life unopened vials can be distributed at -25°C to -15°C for a single time (maximum of 2 weeks in this condition) and then must return at extra-cold temperature.[27] Notice that this possibility facilitates the transportation process allowing some flexibility. For Pfizer vaccine, DHL played an important role being one of the first logistics companies to invest in freezer farms and extra-cold equipment to guarantee the stability of the vaccine.[28]

Product Manufacturing

Given the mRNA technology Pfizer vaccine has an advantage regarding the manufacturing process because the way mRna vaccines operate is different than traditional viral vector ones. In fact, there is no need to grow the virus, on the other side the mRNA sequentially modified is inserted into a plasmid, put in a reactor where an enzymathic reaction triggers the synthesis of the mRNA. Now the synthetized mRNA is encapsulated in a lipid nanoparticle and is ready to be delivered inside the human cells bringing the information to produce the antibodies against a future possible COVID-19 infection. [9]

[27] https://www.ema.europa.eu/en/documents/product-information/comirnaty-epar-product-information_en.pdf

[28] https://www.dhl.com/global-en/spotlight/globalization/vaccine-distribution.html

1.2.5 Spikevax

Spikevax is the commercial name used for the vaccine developed by the collaboration of American company Moderna, NIAID (National Institute of Allergy and Infectious Diseases), BARDA (Biomedical Advanced Research and Development Authority). It is a m-RNA vaccine having an efficiency of 94.1% as emerged from the phase 3 trial test, where 11 cases of symptomatic COVID-19 were reported in the vaccine group (15181 people) versus 185 in the placebo group (15170 people). Full immunization is reached after two weeks since the administration of the booster dose.[1]

Moderna vaccine was approved by EMA on 6th of January 2021 and by AIFA the next day[29] being the second one after Pfizer raising the number of vaccination per day with peaks of 100k during the more intensive months (June and July). Spikevax was not recommended for under aged people until 28th of July when AIFA authorized the administration[30]. This aspect limited the planning possibility for people under aged who needed to be vaccinated with Pfizer. With the arrival of considerable doses during the summer months Moderna approached Astrazeneca being used 12.5% of the times and filling up a reduction in supply of Pfizer vaccine.[31]

[29] https://www.aifa.gov.it/documents/20142/1289678/Comunicato_AIFA_623.pdf

[30] https://www.aifa.gov.it/documents/20142/1289678/Comunicato_AIFA_656.pdf

[31] https://torino.repubblica.it/cronaca/2021/06/22/news/vaccini_piano_da_rifare_in_piemonte_figliuolo_taglia_le_dosi-307084194/

Product Information

The product is sold in packs consisting of 10 multidose vials, each containing 10 doses of 0.5 mL. There is no need to dilute or shake the vial, but it's ready to be administered once the vial is thawed. The vials should be stored in a freezer with temperature within the range -25°C/-15°C and then thawed in refrigerator (2°C-8°C) taking 2 hours or 1 hour at a room temperature. The shelf life of an unopened and frozen vials is 7 months while for unopened but refrigerated ones is 1 month. Conversely a thawed and unpunctured vial can stay in a refrigerator for maximum 30 days or in a room for 24 hours while an used vial should be finished within 19 hours.[32]

Regarding the transportation, if it's not feasible to keep under control (-25°C/-15°C) the cold chain there is the possibility to ship the thawed vials in liquid state at a normal cold chain temperature (2°C/8°C) for up to 12 hours, but once arrived the vials should be kept in a refrigerator and used within the 30 days of shelf life.

On 22 April 2021, an accident happened in Pharmacy Department of Hospital del Mar where Moderna vaccine was stored: a temperature variation of 5 hours (reaching a maximum of -2°C, way out of the range of product specifications) was detected by the control system. Afterwards the vials were analyzed to test the stability of mRNA if it was still not degraded, showing that mRNA vaccines can manage possible thermal shocks.[4]

[32] https://www.ema.europa.eu/en/documents/product-information/spikevax-previously-covid-19-vaccine-moderna-epar-product-information_en.pdf

1.2.6 Curevac

The Curevac Covid-19 vaccine is a mRna type one developed by CureVac N.V and CEPI (Coalition for Epidemic Preparedness Innovations) and it was one of the candidates emerging out of phase I/II clinical trials with promising results. This was translated into a stipulation of deals that authorized EU to receive 225 millions of doses (30 millions planned to be used in Italy) plus an option of an additional 180 millions in case of a successful phase III clinical trial in the 2021 year.[33].

Despite the optimism, the results of the study were disappointing: Curevac vaccine showed only 47% of efficiency[2]. Possible explanations of this failure can be: Lambda variant (that was dominant in Perù where part of the 40000 people in the trial was living), issues regarding the dosage of mRNA in the final formulation of the vaccine.

Curevac vaccine showed better data than the rivals regarding conservation (supposed to last longer and in more favorable condition around 5°C) and manufacturing costs because of the use of unmodified mRNA. Unfortunately due to poor efficiency EMA rejected the submission for emergency use and thus prevented the company from starting manufacturing.

[33] `https://ec.europa.eu/commission/presscorner/detail/en/ip_20_2136`

Chapter 2

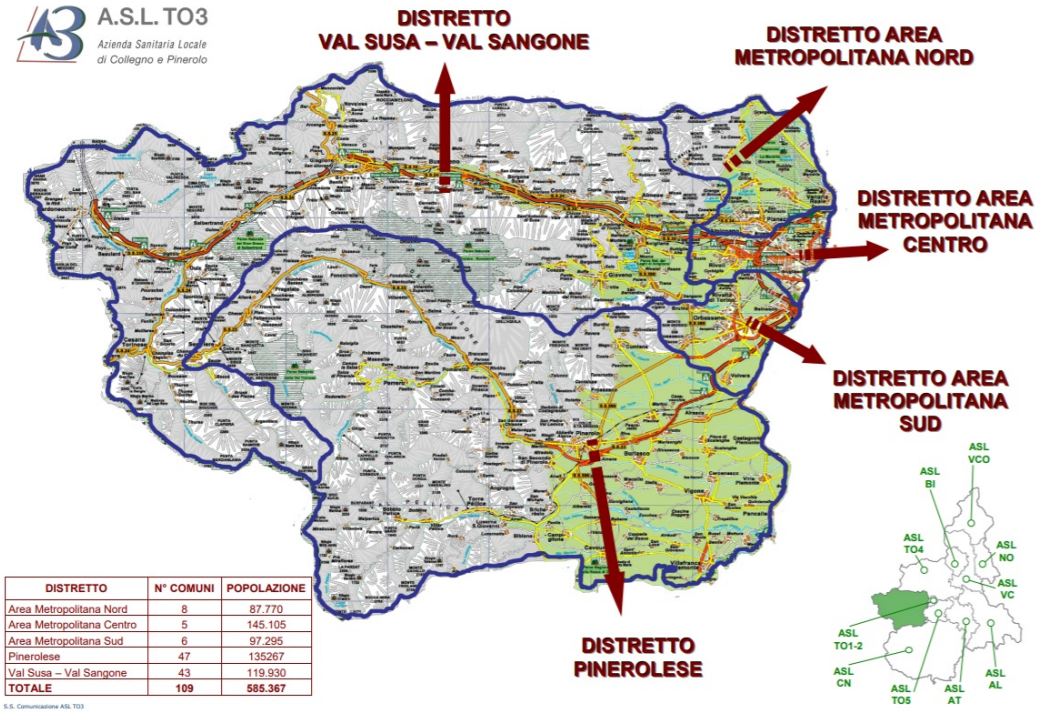
ASL TO3 - Organization

2.0.1 ASL TO3

ASL TO3[1] (Azienda sanitaria locale) is a public healthcare company with the duty to provide health services to people living in the East part of the district of Turin. The area is subdivided logically in five pieces: Area M.Centro, Area M.Sud, Area Nord, Valsusa Valsangone, Pinerolese. In the following image it will be clearer[2]. The total number of inhabitants is around 590k covering 109 municipalities with a total extension of 2950Kmq. A deeper analysis of the population subdivided in categories is necessary in developing a sustainable and fair vaccination plan. As far as we can see from the tables, the majority of inhabitants is concentrated in the districts that are close to Turin while Pinerolese and Valsusa despite of low numbers they clearly have a wider area.

[1] https://www.aslto3.piemonte.it/

[2] https://www.aslto3.piemonte.it/azienda/territorio-e-popolazione/territorio-2/



DISTRETTO	N° COMUNI	POPOLAZIONE
Area Metropolitana Nord	8	87.770
Area Metropolitana Centro	5	145.105
Area Metropolitana Sud	6	97.295
Pinerolese	47	135267
Val Susa – Val Sangone	43	119.930
TOTALE	**109**	**585.367**

S.S. Comunicazione ASL TO3

Figure 2.1: Caption

The organization chart is one of an hierarchical type. At the top level there is the DG (Direttore generale) dott.ssa Franca Dall'Occo, who has the duty to fulfill the national regulations and represents the entire company from a legal point of view. She can: designate Direttore amministrativo (amministrative director) and Direttore sanitario (health director), designate the head of the districts, make the organizational and strategic plan, validate the balance sheet. While running the company, she is helped by two key figures: the amministrative director (Dott.ssa Ada Chiadò) and the health director (Dott.Davide Minniti). Under the lead of DG there are the following offices: Strategic Planning office that collaborates with Management of Waiting lists and management control, management of clinic risk supported by research and innovation office. The communication office and the service "Medico Competente" complete the framework.

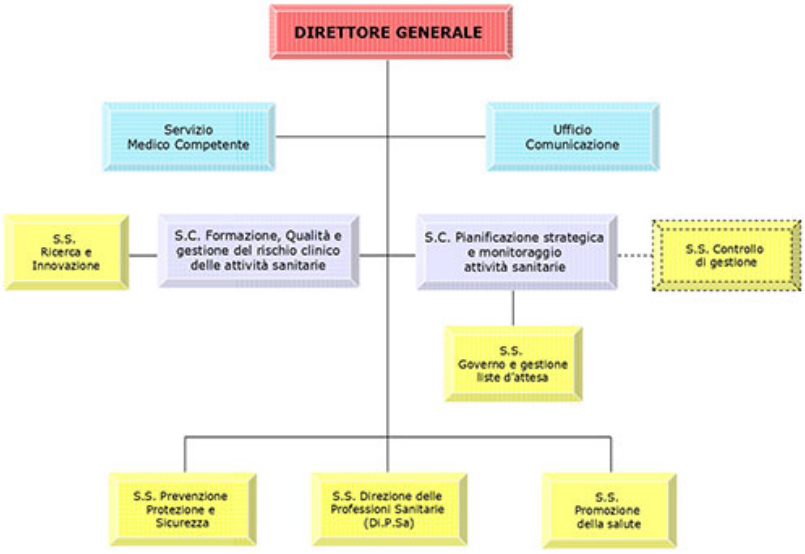


Figure 2.2: Caption

I will now focus my attention on the Strategic Planning Office, where I have worked as an intern. During the times prior to the spread of Coronavirus, the main tasks assigned to the office were:

1. Analysis of the health needs (in terms of materials and staff) of the population of ASL in collaboration with the head of districts in order to guarantee the health service
2. Implementation of the regional acts through planning activities (Piano di attività annuale, Piano di riqualificazione dell'assistenza e riequilibrio economico)
3. Development of the framework Health Technology Assessment
4. Analysis of the efficacy of new health technology to be introduced
5. Analysis of suitability of use regarding new technologies
6. Elaboration of KPIs
7. Formulation of report about the Performance over the year
8. Analysis of waiting time and creation of new procedures
9. Budgeting process
10. Support to DG in order to set new strategic goals, verifying the achievement of them
11. Support to Supervisory Commission to verify the congruity between the service granted and the mission of private health service companies
12. Stipulation of contracts, specifying budget and duties, with private entities to support the Districts

2.0.2 S.S and S.C

Generally speaking, the term structure or operational unit stands for an internal part of a department in a company, that has the duty and responsibility to manage human and financial resources. The main differences between Struttura Semplice and Struttura Complessa are:

- Complexity of the activities carried out: for a simple structure the activities are more specific to their existence
- Management of human and financial resources is limited for a simple structure
- Responsibilities, which are greater for complex structures

Usually Strutture Semplici are created as sons relative to Strutture Complesse with a specific limited role and duties in order to help Struttura Complessa(the core area, that can have more than one unit) to fulfill its assignments.

2.0.3 During COVID-19 third wave and vaccination campaign

From an organizational point of view, I need to divide the entire period in two phases: the first one that goes from the beginning of January to the end of April and the latter one that is still going on. The main difference between the two phases regards the tasks to be done by the planning office. At the beginning of the campaign there was a clear centralized organization with the planning office having a key role in scheduling all the vaccinations in each center, but with the increase of the workload this kind of structure revealed several problems. First of all, the lack of knowledge about the structure of the center (how many vaccination lines can be implemented, how to manage queues,...) represented an issue that could have lead to discrepancies. Secondly the effort to manage exceptions (eg:rescheduling) was time-consuming and excessive to handle everything correctly. So in order to better planning the vaccination day it was decided to decentralize the task and assign it to the leaders of five districts, having planning office that backs up and sets the targets for each district/center.

Management and planning of USCA activities

One of the main tasks done by the strategic planning office during the COVID-19 second and third waves was to support and collect data from the USCA (Unità speciali di continuità assistenziale), that is a special unit formed by doctors and nurses, that covered a fundamental role during the toughest times of COVID-19 crisis. The main task assigned to the USCA is to follow the patients infected by Sars-CoV-2 virus and checking their health state. They need to support them through periodic inspection (physically or remotely depending on the critical status of the patient). They have the responsibility and duty to call the ambulance and admit infected people to hospitals in case of severe symptoms, trying to keep them at home as much as possible in order to avoid filling the COVID-19 department and intensive care beds. As requested by the Direction and in tight collaboration with the strategic planning office, they needed to compile an excel file

Management of Green Pass issues

The green pass is a tool used by the government in order to allow only vaccinated or COVID-19 tested negative people to access closed spaces (restaurants, museums, cinemas, etc...) to lower down the probability for the diffusion of the virus. It is seen by many also as an instrument to convince people to get vaccinated and target the slice of dubious population. As soon as it became legally official on the 6th of August, the management of issues regarding the emission of the document was assigned to the office. To be precise, the release of the certification is an automatic process that happens thanks to the informational connection between the central authority (Ministry of Health) and the regional vaccination platforms (connection that is based on the number of the health insurance card). In this flow of information or human error can occur (typing the wrong number, name, telephone number, e-mail during the registration of the happened administration) and thus the certification is not emitted automatically

Collaboration with other entities

During the whole vaccination campaign the collaboration with DIRMEI (Dipartimento interaziendale malattie ed emergenze infettive) and the regional entities was constant in order to give continuous feedback to evaluate the progress of vaccinations. Another point of contact was the communication office, that sometimes was asking the office to elaborate reports in order to provide data to the community.

2.0.4 Hub and vaccination centers

In this chapter it's described where the vaccination centers were opened in order to understand how the entire territory was covered. It all starts from the main and only hub that is physically located in the Rivoli hospital which redistributes the vaccines to the vaccination centers every morning according to the plan. Analyzing the districts and during the time I was contributing to the plan, it's possible to subdivide the centers according to the district of reference:

1. AM Nord (Venaria)
2. AM Centro (La nave, Collegno, Castello, le Gru, Ospedale di Rivoli)
3. AM Sud (Poli Orbassano, Drive Orbassano, San luigi)
4. ValSusa (Avigliana, Giaveno, Susa, Drive Susa, Oulx)
5. Pinerolese (Madonnine, Pomaretto, Torre Pellice, Ospedale Pinerolo)

As it's predictable, bigger areas such as Pinerolese and Val Susa need more vaccination centers with lower volumes in order to offer a better service to the population that is more distributed. This is why in the Val Susa area five vaccination centers stayed opened during the most intensive days, while after the peak of vaccinations it was decided that extra-hospital centers that are smaller and which required extra-resources, should stay closed. It's interesting to notice that only one huge and well-organized structure, that could implement a maximum of 10 vaccination lines, was responsible for the vaccination of the Venaria area.

Following the national plan, extra-hospital structures were opened to increase the administrations and a drive-through strategy was adopted to speed up the process. A drive-through is a convenient solution for people that were arriving at the point by car.

2.0.5 As-is Analysis

Taking a snapshot of the situation of the vaccination centers during the most intensive days, it was decided to set the targets of the number of administrations according to the percentage of population covered by the districts in such a way:

1. Totality (at 95% of stock usage): 33835 vaccines/week
2. AM Nord (15% of population): 5075/week
3. AM Centro (25% of population): 8459/week
4. AM Sud (17% of population): 5752/week
5. ValSusa (20% of population): 6767/week
6. Pinerolese (23% of population): 7782/week

According to the target of districts it was then calculated the capacity of the centers based on physical space (in relation to implementable lines) and number of days opened (weekly) in such a way to evaluate possible increases of the capacity (opening a new line or opening an extra-day per week) if needed and then the target was converted into appointments.

AM Nord (total: 5390/week)

1. Venaria: 5390/week

Am Centro (total: 9110/week)

1. La Nave: 5250/week
2. Collegno: 480/week
3. Castello: 360/week
4. Le Gru: 220/week
5. Osp. Rivoli: 2800/week

AM Sud (total: 4980/week)

1. Poli Orbassano: 750/week + 380/week
2. Drive Orbassano: 2100/week
3. San Luigi: 1750/week

Val Susa (total: 7190/week)

1. Avigliana: 3080/week
2. Giaveno: 1750/week
3. Susa: 960/week
4. Drive Susa: 800/week
5. Oulx: 600/week

Pinerolo (total:8240/week)

1. Madonnine: 3920/week
2. Pomaretto: 1050/week
3. Torre Pellice: 1050/week
4. Ospedale Pinerolo: 1500/week + 720/week

Considerations

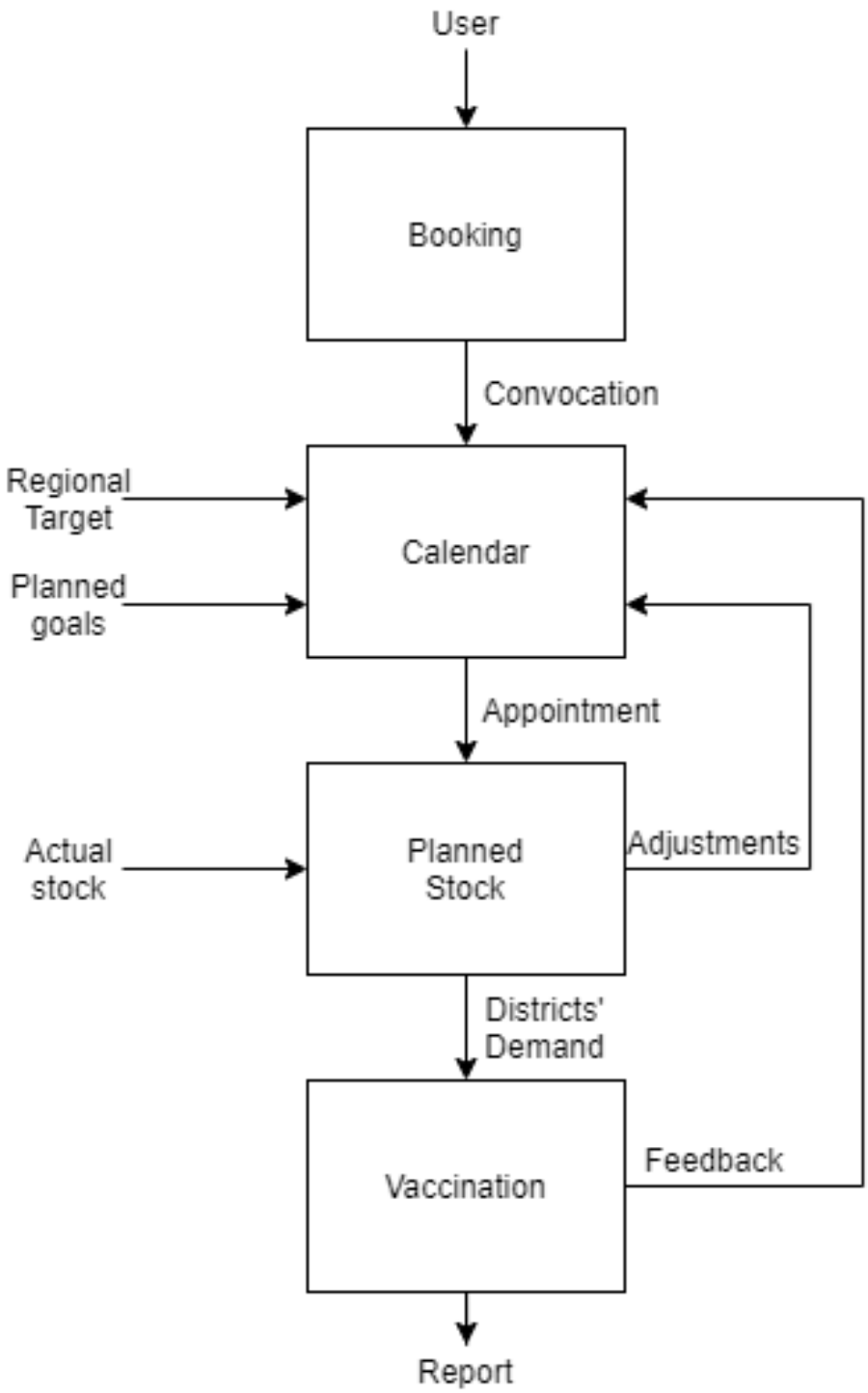
Analyzing the capacity of the centers and comparing them to the target, it's clear that the AM Sud was drastically unable to stay on line with the benchmark value. A clear motivation of the failure was the design of the vaccination centers: too small for the unexpected increase of vaccination rate in addition to the impossibility to open new lines into the structures because of lack of physical space. In a prior phase the number of vaccinations were increased by simply keeping the vaccination centers opened for an extra-day but as they reached a full schedule with 7 days capacity, there was no more space in such direction. Making up for this incapacity, it was considered to open a new center, but no adequate structure was found, thus part of the vaccines and was redirected to other districts nearby (AM centro usually) and appointments rescheduled to closest vaccination centers available in the period.

Another strategy implemented to boost the administrations per day was to extend the opening hours for a few days of the week (ex: Ospedale Pinerolo). This possibility was tried to be avoided because of the risks linked to fatigue of operators that could easily be turned into mistakes.

Chapter 3

Information System process

In this chapter, I will analyze the whole process from a computer system point of view trying to identify the main blocks that characterize the vaccination. As we can see in the next page it's a feedback system containing two loops. This is because obtaining data from the vaccination block that is made of registering the occurred administration and monitoring the amount of vaccinations is crucial for setting new realistic targets resulting in variations of the calendar. After the analysis of future stock, adjustments to the calendar are needed when dealing with uncertain supply in order to avoid possible lack of vaccines and an interruption of service. External inputs are represented on the left highlighting that regional target (based on number of vaccines sent to ASL TO3) drives the office to create a detailed plan for each district and center in order to give shape to an efficient calendar.


User
Booking
Convocation
Regional Target
Planned goals
Calendar
Appointment
Actual stock
Planned Stock
Adjustments
Districts' Demand
Vaccination
Feedback
Report

3.0.1 Booking

The entire procedure starts with the booking process. The user accesses the website and fills in the form providing the information required: health insurance card, fiscal code card and so on. Now the adhesion is registered into a DB managed by CSI (Consorzio per Il Sistema Informativo) that links it to the the system SIRVA (Sistema Informativo Regionale per la gestione delle Vaccinazioni), platform that is used by Piedmont to handle all kind of vaccinations. Afterwards a reminder is created and the person is taken in charge by SIRVA and can be selected by who handles the calendar. Eventually the responsible picks up automatically from the list (with a FIFO approach - First Input First Output) the amount of people needed to complete the day. This results in converting the adhesion into an appointment composed by vaccination center, day and hour and the system sends an SMS to the user. From here on out, the user could not modify the date.

I want to make a brief digression about this strategic decision adopted by Piedmont because it's crucial to understand the entire strategy. Not allowing the user to be flexible of deciding the day, the type of vaccine and the center guarantees a strong centralized decision power. For example, the biggest centers can handle more vaccines and in case of a shortage of Pfizer they can easily switch to Moderna. Another strong advantage was hiding the vaccine used (in the booking phase) during the critical days after the bad advertisement due to the death of a person consequent to an inoculation of Astrazeneca. Thus the person scheduled arriving at the center was somehow convinced to take his dose of Astrazeneca.

Surely there are issues concerning the possibility that the person cannot be present the booked day creating problems in terms of missing the daily target of vaccines. These issues were smaller when the number of administrations were few and filling the gap calling someone else was easy, but with the increase in numbers and with holidays coming a measure was taken. Around the beginning of June it was possible to call to reschedule the appointment and since July this was feasible by the user accessing ilPiemontetivaccina. This stopped possible customer related inefficiencies, but complicated the entire procedure. For contrasting possible absences, the solution adopted were: overbooking and the creation of reserve lists for the people that gave availability to reach the center whenever called before the end of the shifts.

3.0.2 Calendar

The next step is filling in the agenda. From an organizational point of view, as described before in chapter 4, this task was done by the planning office until the end of April and then it was assigned to the administrative staff of districts. This operation can be completed in two ways: automatically and manually.

The administrative staff in charge of this task opens the software SIRVA and fills in the list of the center considering that it's not possible to book two people at the same time (forcing to divide and create new fictional surgeries where you can reserve additional people). For example if in the center x there is the target of 800 vaccines (considering an average of 3 minutes per each administration and considering 8 hours as the operative time of the center), there is the need to keep opened 5 lines, dividing them in two surgeries A and B, where in A you book every minute a person, while in B every minute and a half. This system bug created a lot of issues because it resulted in making a lot of copies of a single center leading to general chaos. Anyway once the calendar is completed, there is the possibility to change manually someone , but if the amount of people is unmanageable there is an other procedure. There is the possibility to upload an excel file with the fiscal code and a reference hour and then automatically the system will delete the schedule of the day replacing it with the new one. This scheme was repeated at the beginning of July when, after having scheduled a lot of young people at the end of August, there was the urgency to anticipate them to stay in line with the increased target.

Checking the calendar can be done by querying SIRVA or by using PADDI (Piattaforma per l'Analisi Dati Decisionali Integrati della Sanità) that cumulates the data in a more manageable way. You can download the two excel files: first doses appointments and second doses appointments. Now it's possible to merge both files to give shape to the calendar. However an additional precaution is needed: the appointments for first doses are without the typology of vaccine because as previously explained the entirely policy was based on not allowing people to choose the vaccine. As the strategy of the office was to concentrate the inoculation of Moderna in selected centers, allowing flexibility.

As long as the planning office was in control of setting up the agenda, the districts were respecting the guidelines of the office. However, when everything changed the districts were independently deciding which kind

of vaccine to administer. Basically this was done by checking the booster doses and then picking it out for first dose administrations in order to avoid possible mix that could lead to mistakes. So with the aim to lowering risks related to wrong matching (ex: 1st dose Pfizer 2nd Moderna), in a first phase it was decided to administer only a type of vaccine per day. In doing that, there was paid attention to schedule Moderna (having booster dose on the 28th day) and Pfizer (having booster dose on the 21th day) in such a way that if in the day x 1st doses of Moderna were used in day x+6 it was not possible to schedule Pfizer in order to avoid that booster doses will coincide (x+27=x+6+21).

Poor flexibility of the system created a lot of problems, that resulted in an imperfect system efficiency. One of the main issue regarded the creation of appointments for booster dose: cases of missed appointments because of an human error (generating an appointment in a closed vaccination center) or a server error (incorrect generation of the SMS) were relevant. This resulted in having people that received their second dose out of the time lapse and this can noticeably alter the efficiency of the vaccine.

3.0.3 Stock

From a logistic point of view, the management of supply of doses is in the hands of Carabinieri corps (physical displacements) collaborating with D.I.R.M.E.I (Dipartimento Interaziendale Malattie ed Emergenze Infettive) that establishes the numbers of doses to be sent to all ASLs in proportion of amount of inhabitants. The central hub in ASL TO3 is the hospital of Rivoli that has the equipment and personnel to preserve the vaccines.

The internal office responsible for managing the arrival of trays of vaccines is S.C Farmacia Ospedaliera (Grazia Ceravolo being the head). Everyday each center sends a request with the doses needed for the next day so that we proceed with thawing them. After this procedure, Grazia sends to the planning office a communication with the number of vaccines being present in the deposit less the thawed vaccines for the next day. In this way, we update the excel file with the correct stocks and we forecast the consumption of the doses according to the calendar. Another additional info needed before the calculation of the stock is the future planned arrivals of vaccines that were communicated week by week in collaboration with DIRMEI. To be precise there was just only one supply of each vaccine almost every week with regular cadence, having basically no problem for Moderna, Astrazeneca, Johnson, while for Pfizer differences arised between planned and actual quantities.

Typically there were two situations: underuse of the stock, and in this first case it was needed to reschedule the farthest appointments earlier in order to use the vaccines and reach the target imposed by region; overuse of stock that was generating negative future stock (usually for Pfizer), in this second case two solutions could be used: asking for an extra tray of Pfizer or delaying the appointments as much as possible but respecting the time window (up to 5 days could be gained).

Another issue occurred during July that limited the planning possibility was the introduction of the direct access: unregistered people not having an appointment that could receive their first dose. As it was not possible to predict the number of adherents, especially when this solution was adopted to make underage people receive their first dose, it was fixed a limit on the administrations of this type in order to maintain the stock under control.

3.0.4 Vaccinations administered

The vaccination process consists of three phases:

- Anamnesis
- Injection
- Registration

The exam of the past case history of patients is essential before proceeding on with the vaccination. In fact, the doctor has the responsibility to allow the patient to be vaccinated and to register the anamnesis form. Basically this part represents the bottleneck of the entire line because it can take from approx. 4-5mins to 10mins. The clinical history is examined carefully trying to find out if events of anaphylactic shock or adverse reaction to past vaccinations happened in the past. Other cases of rejections can be: COVID-19 symptoms in the last 30 days, another vaccination in the last 30 days, extremely vulnerable subjects.

In the case of a positive response from the doctor the patient can go to the inoculation point where a nurse will inject the dose. The last step is represented by registering the vaccination into the system SIRVA and printing a certification that testifies the inoculation keeping track of it. If it's the first dose a new appointment for the second one (in case of mRNA and Astrazeneca) will be generated by the administrative staff in the same center considering the data sheet (after 21 days in the first months then shifted to 35 days for mRNA vaccines).

During the surveillance phase if adverse reactions were noticed the doctor had the duty to report it into the system for evaluating if the patient could receive the booster dose or not. Keeping track of this cases it's necessary so a statistical report analyzing the consequences of the vaccine could be created in addition to an estimate of the amount of exempted people from the second administration.

3.1 Monitoring

The monitoring part is essential in a system with a feedback loop. As the planning office has the task to guide the districts imposing them a target in terms of vaccinations per day/per week, monitoring is an active action in a way that it's possible to reach the target established by Piedmont.

3.1.1 KPIs

The key performance indicator used by the region was the percentage of doses used, calculated as it follows:

$$\frac{Numberofvaccinesadministered}{Numberofdosessent}$$

I want to express my personal view about this index. As there is a cycle time between the two doses and the supply of vaccines is extremely uncertain, in case of a future shortage there is a concrete risk that the second inoculation could not be guaranteed. In the first stages the limit was set to 80% then it was increased reaching 95% at the beginning of July. Thus reaching 95% means the possibility of not having stock for booster doses. In our case we had issues during the end of July because we were using Pfizer for first inoculations in the final days of June generating second appointments for July. We planned the first doses according to scheduled future arrivals of Pfizer, but we realized that the actual numbers of vaccines were lower than the expected ones. This realization forced us to shift the planned first doses of Pfizer to Moderna trying to guarantee the booster dose of Pfizer as much as possible without delaying it. Hence a qualitative index is needed for better describing the whole situation. This is why I want to focus on the utilization of other indexes such as:

$$\frac{Numberofvaccinedosesreceivedbypatients}{Numberofvaccinedosesneededbypatients}$$

To evaluate the efficiency of the supply chain this parameter could be more precise because the denominator is linked to people registered into the system, while the vaccine doses received by our center is related to people living under our restriction. So basically this value is calculated on the number of adherents (considering also second doses).

Another parameter that could express the efficiency of the supply chain is by evaluating the number of vaccine wasted because of opened vials or because the shelf-life is ended, but it's very difficult to track it.

Last but not least, another key parameter to understand the progress is time: how much time was needed to achieve 80% of vaccinated people and if we look at the data provided by Lab24[1](that is a complete and reliable source of information about the status and progress of the administrations.) the administrations followed the national plan that set the target at the end of September and it was reached a few days after that day.

Concluding there is a very efficient guide written by World Health Organization (WHO), that presents a set of additional techniques regarding the monitoring of vaccination penetration.[2]

[1]https://lab24.ilsole24ore.com/numeri-vaccini-italia-mondo/
[2]https://apps.who.int/iris/rest/bitstreams/1334960/retrieve

3.2 Report

3.2.1 Daily Report

A report containing information about the number of vaccines administered the previous day was sent to the direction everyday since the beginning of January until the end of July. The file was done using excel manipulating data downloading the information from PADDI and creating a pivot table where for each center it's detailed the division between first and second doses.

The daily report was needed to understand if the vaccination target was reached and if not why (comparing with the number of appointments of the day) and in which direction it could be possible to increase. Possible failures were: unexpected absences that could drastically reduce the administrations and/or resource related issues (personnel delay or lack of enough workers to guarantee the fixed target).

Another issue was the communication between the two platforms: PADDI and SIRVA. As long as the first one takes data and elaborates them from SIRVA, there is a time gap that can create misalignment and thus lowering the actual data. In fact, the system should work in parallel one with each other to provide the same result, but this is not the case.

Last but not least, an operator having the duty to register the administrations can do it whenever he wants and thus falsifying on time data.

3.2.2 Weekly Report

Covid-19 analysis

In addition to the daily report, each Monday a more detailed document where the analysis starts from the evolution of COVID-19 cases comparing Italy with Piedmont. Then the focus passes on the number of hospitalized people, that now has more importance than in the past, considering that it became a crucial parameter to define the colour of a region. The limit before changing colour is represented by crossing three parameters:

- Percentage of COVID-19 patients hospitalized (15%)
- Percentage of COVID-19 patients in intensive care (10%)
- Weekly COVID-19 cases of 50 per 100000 inhabitants

Sistema per la determinazione dei colori delle Regioni ai sensi del DL 105/2021

Incidenza settimanale: <50 casi per 100.000 abitanti
Bianca Rispetto dei parametri per 3 settimane consecutive

Incidenza settimanale: 50-149 casi per 100.000 abitanti				
	TI ≤10%	**TI 11-20%**	**TI 21-30%**	**TI >30%**
AM ≤15%	Bianca	Bianca	Bianca	Bianca
AM 16-30%	Bianca	Gialla	Gialla	Gialla
AM 31-40%	Bianca	Gialla	Gialla	Gialla
AM >40%	Bianca	Gialla	Gialla	Gialla

Incidenza settimanale: ≥150 casi per 100.000 abitanti				
	TI ≤10%	**TI 11-20%**	**TI 21-30%**	**TI >30%**
AM ≤15%	Bianca	Bianca	Bianca	Bianca
AM 16-30%	Bianca	Gialla	Gialla	Gialla
AM 31-40%	Bianca	Gialla	Arancione	Arancione
AM >40%	Bianca	Gialla	Arancione	Rossa

GIMBE EVIDENCE FOR HEALTH

Figure 3.1: Caption

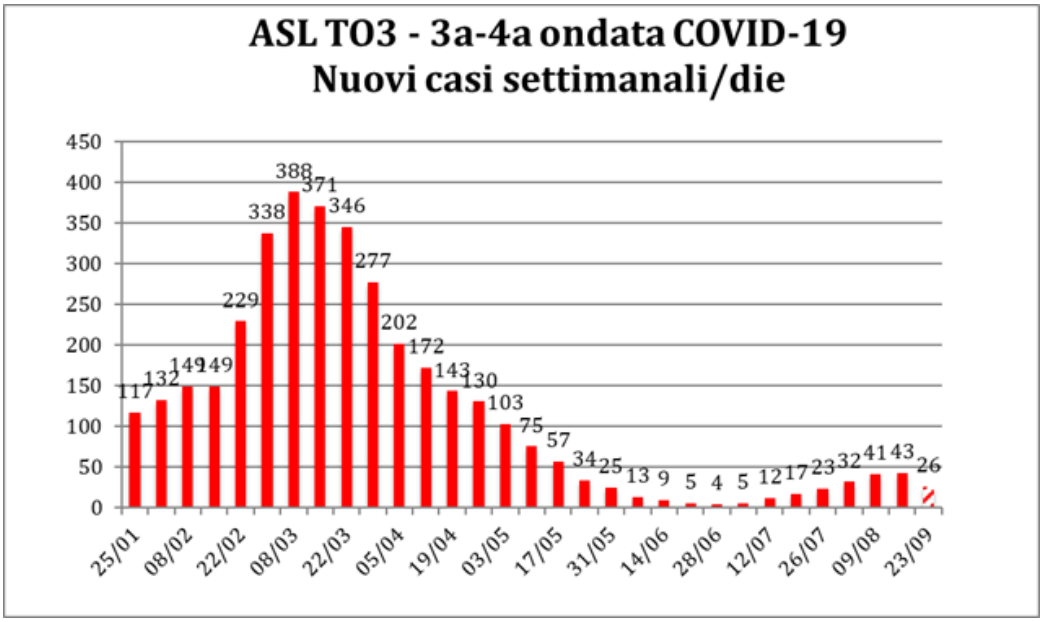


Figure 3.2: Caption

Covid-19 tests

The report continues with a graph about ASL TO3 situation analyzing the cases and number of COVID-19 tests. The data are collected and sent to planning office by SISP (Servizi di Igiene e Sanità Pubblica), that is responsible for controlling critical issues and protecting the public health by preventing the diffusion of infectious diseases (SARS-CoV-2). As we can see from the images below during the time I am writing the fourth wave of COVID-19 diffusion is slowed down by the effect of vaccines. It's clear that the increase of cases is not so high as in March where it was reached a peak of 388 cases/day during the second week, despite a similar RT index (1.82 relative to last days of July).

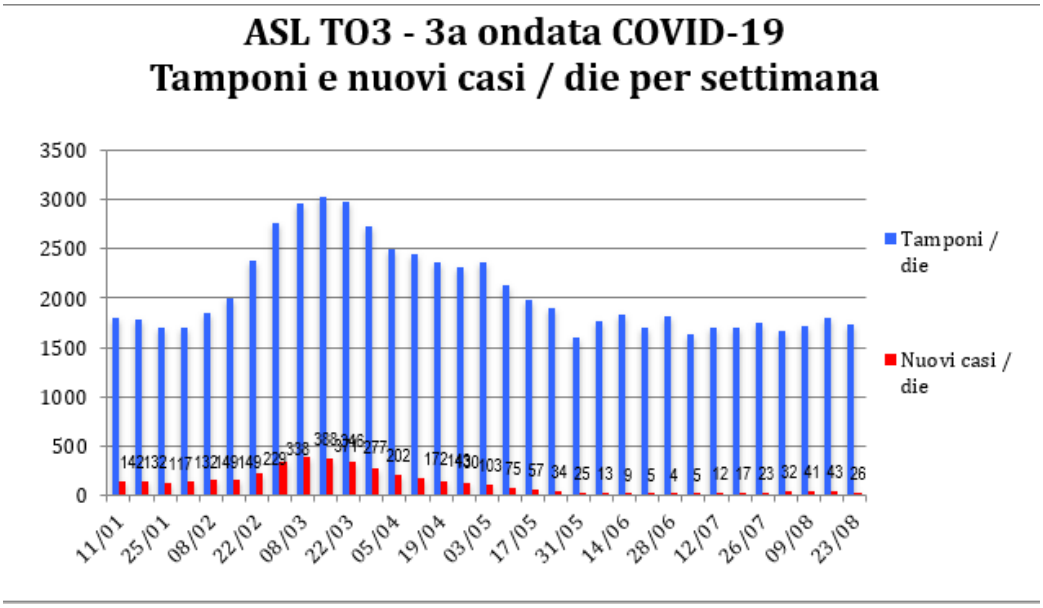


Figure 3.3: Caption

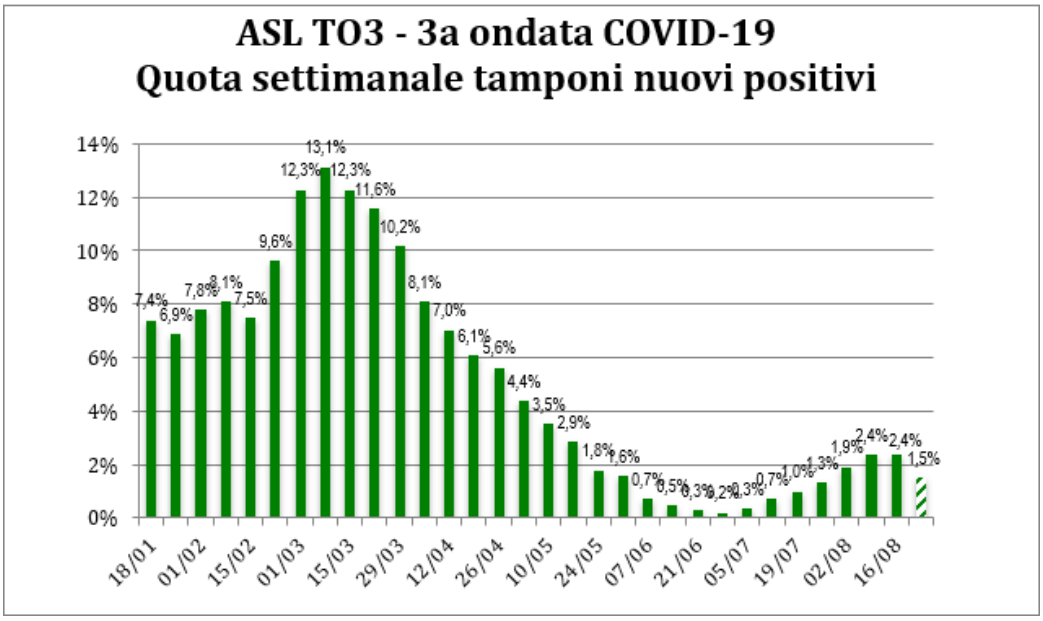


Figure 3.4: Caption

Vaccine Administrations

The next session has the focus on the analysis of administrations of vaccines trying to estimate the number of vaccinated people living under the territory covered by ASL TO3. As it's deductible from the graphs the number of vaccines is on line with the national data, regarding the proportion of vaccines used and the percentage of vaccinated people.

A bar chart is used to follow the trend of administrations distinguishing first from second dose injections. As it emerges clearly, during the first phase of the campaign before starting vaccinating new people with first doses it was preferred to save some stock of the vaccines in order to guarantee the booster administration.

This strategy was stopped when it was evident that the vaccine was efficient since the first dose, thus it was chosen to use as much as possible the vaccines stocked considering that the future arrival of vaccines was higher than the past. This assumption was necessary because if the supply of vaccine was to be considered constant, this strategy could lead to possible excessive delays of second doses, resulting in a disastrous scenario. Hopefully this fact didn't happen, although Pfizer cut part of the planned supply in July, but fortunately Moderna supplied more than the planned quantities.

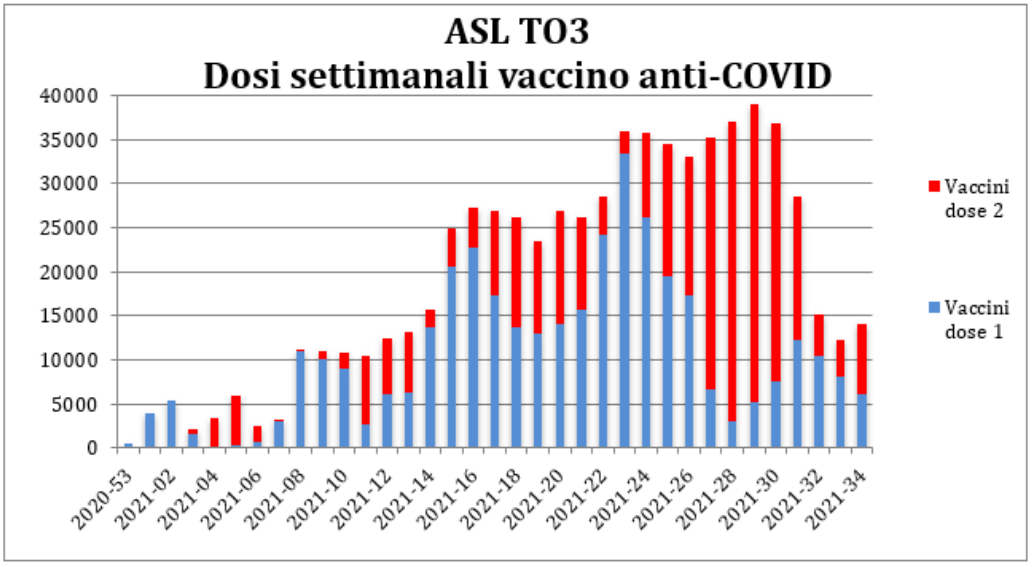


Figure 3.5: Caption

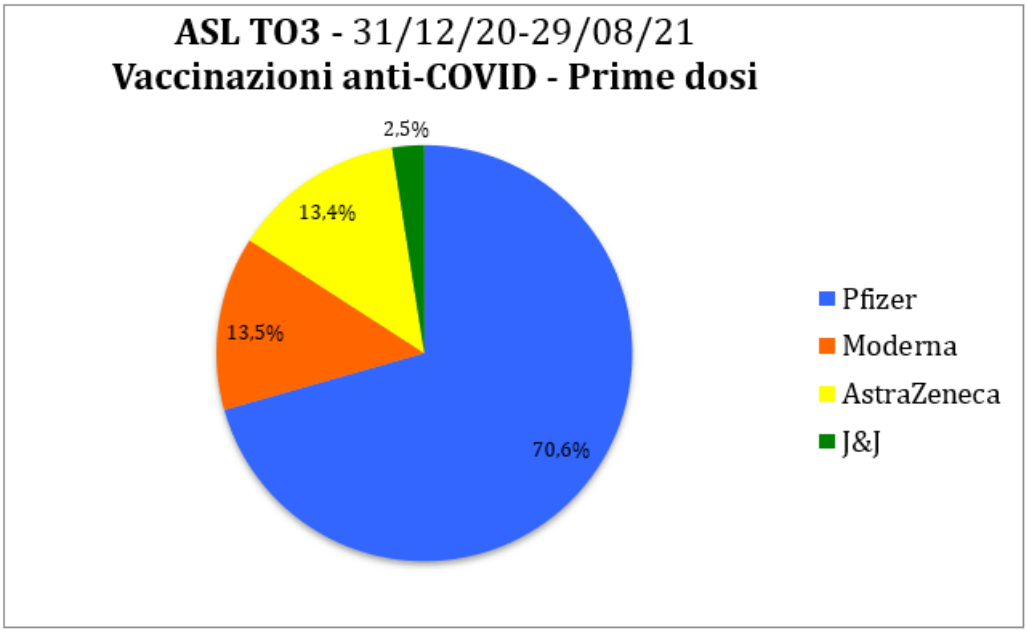


Figure 3.6: Caption

Chapter 4

Linear Programming Model

4.0.1 Linear Programming

Linear Optimization or Linear Programming is a mathematical tool used by engineers trying to find the optimal solution to a problem written in a certain way. We have to define the problem as it follows:

$$findavector: \ X$$

$$\max C^t X$$

$$subjectto: \ AX \leq b$$

$$and: \ X \geq 0$$

Where X is a vector and A a matrix. The relationships between the variables are expressed in a linear way and the objective function is linear. There are a lot of algorithms implemented in programs such as Excel (that uses the Solver add-in) and Python, which has a library PuLP that implements solvers like: GUROBI, CPLEX, SCIP, exc... that can find the solution in a relatively short time depending on the complexity of the problem.

4.0.2 Case study: Optimal planning of the COVID-19 vaccine supply chain

In the following subsection a mixed integer linear programming model (MILP) for the optimization of the COVID-19 supply chain is presented thanks to the contribution of professor Georgiadis that published the study in the journal Vaccine[3].

The target of the model is to minimize total costs: storage and transportation costs but also costs linked to staff requirements and doses wasted. The scale that is undergone by this study is large, thus there is the need to subdivide the problem in two horizons: one that is short-term planning and the second one that consists of a longer time horizon. A simulation of a small case that considers one hub and five vaccination centers is analyzed with the goal to understand which costs are more impacting.

The supply chain is composed by three parts: manufacturing plants, hubs, vaccination centers. The flows are considered to have sense in just one direction (vaccine returns to the hubs are not allowed), the capacity of vaccination centers varies according to the employed staff and the active vaccination lines. Within the time horizon (that is 14 days discretized in a daily base) a number of appointments should be satisfied and a list with the daily appointments at each center is find and this generates the storage necessities at each hub and vaccination centers and the amount of extra-personnel needed to complete all appointments.

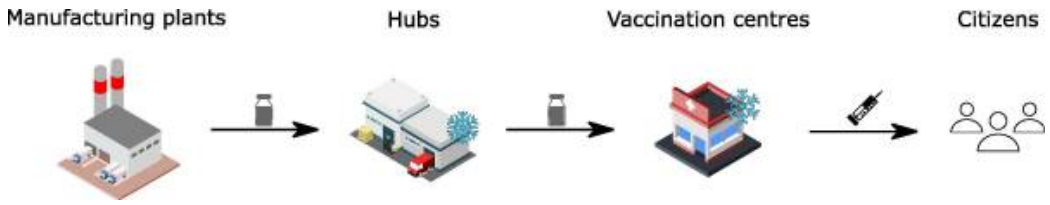


Figure 4.1: Vaccine Supply Chain

Indices

i, j: Locations
v: Vaccine
c: Cold storage technology
t: Time periods
w: Weeks

Sets

f_i: Manufacturing Plants
h_i: Hubs
vc_i: Vaccination centers
cl_i: Clusters
FV: Vaccine v produced in manufacturing plant f
IJ: Connectivity between the locations of supply chain
HVC: Connectivity between hubs h and vaccination centers vc
CV: Cold storage technology c necessary for storage of vaccine v
SL_v: Subset of vaccines that have a shelf-life smaller than the horizon

Parameters

$\pi_{h,v}^{max}$: Maximum supply of vaccine v to hub h (vials)
$\alpha_{i,v}$: Initial stored amount of vaccine v in location i (vials)
β_i: Ratio of vaccine wasted in location i
$\gamma_{h,c}$: Storage capacity of technology c in hub h (vials)
θ_{vc}: Storage capacity in vaccination centre vc (vials)
$\epsilon_{i,v}$: Safety stock of vaccine v in location i (vials)
$\rho_{i,j}^{min}$: Minimum flow allowed between locations i and j
$\rho_{i,j}^{max}$: Maximum flow allowed between locations i and j
δ_v: Doses per vial of vaccine v
λ_v: Shelf-life of vaccine v in refrigeration (days)
ζ_{vc}: Vaccination appointments goal for each vc
η: Operating cost of cold storage technology c (€ per daily storage of a single vial)
ι_{vc}: Base number of healthcare workers in vaccination centre vc
ψ_c: Operating cost of cold storage technology c (€ per daily storage of a single vial)

k: Average fuel consumption of truck transporting vaccines (litres/100 km)

ϕ: Fuel price (€/litre)

$\mu_{i,j}$: Distance between locations i and j (km)

τ: Average speed of vehicles transferring the vaccines

o: Cost of employing a driver (€/hour)

ξ_v: Cost of vaccine v (€/dose)

σ: Cost for utilizing extra healthcare workers (daily)

ν: Cost of renting a truck (Two weeks)

Variables

$X_{i,j,v,t}$: Amount of vaccine v transferred from location i to j in period t (vials)

$S_{i,v,t}$: Amount of vaccine v stored in location i in period t (vials)

$P_{f,v,t}$: Amount of vaccine v supplied by manufacturing plant f in t (vials)

$LS_{i,v,t}$: Wasted vials of vaccine v in location i in time period t

$VU_{vc,v,t}$: Vials of vaccine v used in vc in period t

$L_{vc,v,t,t'}$: Amount of vaccine v transferred in vc in t and used in t' (vials)

$WD_{vc,v,t}$: Wasted doses of vaccine v in vaccination centre vc in period t

$DU_{vc,v,t}$: Doses of vaccine v used in vc in period t

$DA_{vc,t}$: Vaccination appointments in location i in time period t

$VA_{i,v,t}$: Appointments using vaccine v in location i in time period t

$WE_{i,t}$: Vials wasted due to expiration in location i in time period t

WE_i^I: Vials from initial storage wasted due to expiration in location i in time period t

$HW_{i,t}$: Vials from initial storage wasted due to expiration in location i in time period t

$AH_{i,t}$: Additional healthcare workers (more than base) required in location i in time period t

NT: Number of trucks required for transportation

$SU_{vc,slv,t}$: Vials of initially stored vaccine slv used in vaccination centre vc in period t

$VU_{vc,v,t}^I$: Integer number of vials of vaccine v used in period t

$Y_{i,j,t}$: Binary variable that equals 1 if vaccines are transferred between locations i and j in period t

The goal of the entire model is to minimize the total costs taking into account storage conservation costs of the vaccines in each hub and in each vaccination center.

$$\min \sum_{h} \sum_{v} \sum_{c \in csv_{c,v}} \sum_{t} S_{h,v,t} * \psi_c + \sum_{vc} \sum_{v} \sum_{t} S_{vc,v,t} * k_r$$

The first addend regards the sum of operating costs of cold storage technology for each vaccine (variable) conserved in all hubs while the second one is about the sum of costs holding the amount of vaccines (variable) in all vaccination centers depending on the k of refrigerators (energy conversion factor).

$$\sum_{h} \sum_{vc \in HVC} \sum_{t} 2 * \mu_{h,vc} * \frac{k * \phi}{100} * Y_{h,vc,t} + \sum_{h} \sum_{vc \in HVC} \sum_{t} 2 * \frac{\mu_{h,vc}}{\tau} * o * Y_{h,vc,t} + \nu * NT$$

The second part refers to the transportation costs: fuel costs about the transport of vaccines from the hubs to the vaccination centers and sum of all driver's wage employed plus costs of renting the required number of trucks.

$$\sum_{vc} \sum_{v} \sum_{t} WD_{vc,v,t} * \xi_v + \sum_{vc} WE^{I}_{sl} * \delta_{sl} * \xi_{sl} + \sum_{vc} \sum_{t} WE_{sl,t} * \delta_{sl} * \xi_{sl}$$

Third part of the costs is related to the waste of vaccines in terms of: wasted doses of vaccine in each vaccination centers, vials from initial storage wasted in all vaccination centers due to expiration in the subset of vaccines that have a shelf-life smaller than the considered horizon, vials for the considered time horizon wasted due to expiration.

$$\sigma * \sum_{vc} \sum_{t} AH_{vc,t}$$

Last addend expresses the costs of additional healthcare workers needed to complete all appointments scheduled.

Now that the function to minimize is well defined a set of constraints are needed.

$$\sum_{f \in FV} \sum_{t} P_{f,v,t} \leq \pi_{h,v}^{max} \; \forall h, v$$

$$\sum_{t \in TW} Y_{f,h,t} \leq 1 \; \forall f, h, w$$

The first two constraints reveals that the supply of vaccines are limited by the maximum number produced by the manufacturer and that each producer can supply each hub h only once per week

$$\sum_{h} X_{f,h,v,t} = P_{f,v,t} \; \forall f \in fv, v, t$$

$$S_{h,v,t} = \alpha_{h,v} + \sum_{f} X_{f,h,v,t} - \sum_{vc \in HVC} X_{h,vc,v,t} - LS_{h,v,t} \; \forall h, v, t = 1$$

$$S_{h,v,t} = S_{h,v,t-1} + \sum_{f \in FV} X_{f,h,v,t} - \sum_{vc \in HVC} X_{h,vc,v,t} - LS_{h,v,t} \; \forall h, v, t > 1$$

$$S_{vc,v,t} = \alpha_{vc,v} + \sum_{h \in HVC} X_{h,vc,v,t} - VU_{vc,v,t} - LS_{vc,v,t} \; \forall vc, v, t = 1$$

$$S_{vc,v,t} = S_{vc,v,t-1} + \sum_{h \in HVC} X_{h,vc,v,t} - VU_{vc,v,t} - LS_{vc,v,t} \; \forall vc, v, t > 1$$

A set of constraints check the material balances around the hubs and vaccination centers. The first of the list sets the number of vaccine supplied by manufacturing plants equal to the amount received in all hubs, while the second and third calculate the balance of vaccines at each hub where the amount of vaccines is equal to the initial storage plus the new supplies less the vials sent to the vaccination centers and the wasted vials for the initial week(t=1), conversely for a time span greater than one the initial storage is changed with the inventory computed at time t-1. The same line of reasoning is repeated in the last two ones where instead of the hubs the balances are set at the vaccination center level.

$$LS_{i,v,t} = S_{i,v,t} * \rho_i \ \forall i, v, t$$

$$\sum_v S_{i,v,t} \geq \sum_v \epsilon_{i,v} \ \forall i \in vc_i \cup h_i, t = T$$

$$\sum_{v \in CV} S_{h,v,t} \leq \gamma_{c,h} \ \forall h, c, t$$

$$\sum_v S_{vc,v,t} \leq \theta_{vc} \ \forall vc, t$$

$$\rho^{min}_{f,h} * Y_{h,vc,t} \leq \sum_{v \in FV} X_{f,h,v,t} \leq \rho^{max}_{f,h} * Y_{h,vc,t} \ \forall f, h, t$$

$$\rho^{min}_{h,vc} * Y_{h,vc,t} \leq \sum_v X_{h,vc,v,t} \leq \rho^{max}_{h,vc} * Y_{h,vc,t} \ \forall h \in HVC, v, t$$

Checking one by one the list of constraints: the first one calculates the number of wasted vials of vaccine, while the second sets a safety stock in each hub and center connected for a time span that equals T, third and fourth are related to impose the amount of vaccine stored lower than the maximum capacity while the last two forces the amount of vaccine to be transported to be greater than minimum and lower than the maximum flow allowed. Now to be precise variable decisions are continuous, while it's clear that in reality they are integer: this relaxation is needed in order to avoid adding complexity to the problem and the solutions can be easily rounded.

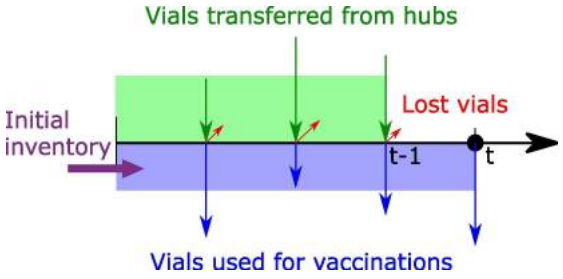


Figure 4.2: Transportation time constraints

$$\sum_{vc}\sum_{t'\leq t} X_{h,vc,v,t'} \leq \alpha_{h,v} + \sum_{f\in FV}\sum_{t''\leq t-1} X_{f,h,v,t''} - \sum_{t''\leq t-1} LS_{h,v,t''} \; \forall h,v,t$$

$$\sum_{t'\leq t} VU_{vc,v,t'} \leq \alpha_{vc,v} + \sum_{h}\sum_{t''\leq t-1} X_{h,vc,v,t''} - \sum_{t''\leq t-1} LS_{vc,v,t''} \; \forall h,v,t$$

These two constraints are set following the reasoning that the vials used in the vaccination centers have to be less than the initial inventory plus the vials arrived in the time t'' lower or equal t-1 (this meaning that it needs a time t+1 for the vials to arrive at the vaccination centers from the hubs) less the wasted vials of vaccine in the time period $t'' \leq t-1$

$$\sum_{t'\geq t+1^{t+\lambda_{sl}}} L_{vc,v,t,t'} + WE_{vc,t} = \sum_{h\in HVC} X_{h,vc,v,t} \; \forall vc, v, \in SL, t \leq (T-\lambda_{sl})$$

$$\sum_{t'\geq t+1} L_{vc,v,t,t'} \leq \sum_{h\in HVC} X_{h,vc,v,t} \; \forall vc, v \in SL, t > (T-\lambda_{sl})$$

$$VU_{vc,sl,t'} = SU_{vc,sl,t'} + \sum_{t\leq t'-1} L_{vc,sl,t,t'} \; \forall vc, sl, t' \leq \lambda_{sl}$$

$$VU_{vc,sl,t'} = \sum_{t\geq t'-\lambda_{sl}}^{t'-1} L_{vc,sl,t,t'} \; \forall vc, sl, t' > \lambda_{sl}$$

$$\sum_{t\leq\lambda_{sl}} SU_{vc,sl,t} + WE^{I}_{vc} = \alpha_{vc,sl} \; \forall vc, sl$$

Shelf-life issues are encapsulated into the first constraint that forces the amount of vaccine transferred in a vaccination center in period t and used in t' $L_{vc,v,t,t'}$ plus the wasted vials to be equal to the total amount of vaccine transferred. The next constraints link the total quantity of vials used in the vaccination plan of time period t to the transferred vaccines. Finally the last constraint computes the number of initial vials that are spoiled.

$$\sum_{v} DU_{vc,v,t} = DA_{vc,t} \ \forall vc, t$$

$$\sum_{t} DA_{vc,t} = \zeta_{vc} \ \forall vc$$

$$VU_{vc,v,t} * \delta_v = DU_{vc,v,t} \ \forall vc, v, t$$

The first constraint equals the number of doses used to the daily appointments for each vaccination center, the second one instead simply matches the vaccine used multiplied by the doses per vial to the doses consumed, while the last one sets the sum of daily appointments equal to the target (ζ_{vc}).

$$DA_{vc,t} \leq \eta * HW_{vc,t} \ \forall vc, t$$

$$AH_{vc,t} \geq HW_{vc,t} - \iota_{vc} \ \forall vc, t$$

$$\sum_{h} \sum_{vc \in HVC} Y_{h,vc,t} \leq NT \ \forall vc, t$$

This set of boundaries defines the personnel needed for the vaccination fixing the number of vaccination lines in the center multiplied by the number of vaccination done daily by a single line composed by two people to be greater than the daily appointments. The second constraint is used to understand if there is the urgency to add additional vaccination lines to increase the doses administered and the third one calculates the fleet size for distributing vaccines.

$$VU^{I}_{vc,v,t} \geq VU_{vc,v,t} \ \forall vc, v, t$$

$$WD_{vc,v,t} = (VU^{I}_{vc,v,t} - VU_{vc,v,t}) * \delta_v \ \forall vc, v, t$$

The last two constraints count the number of vaccines wasted as the difference between the actual number of vials opened (that are obviously more numerous than the planned ones) less the programmed ones.

4.1 MILP - based solution

Because of the high computational complexity of the problem the creation of sub-problems is necessary in a way to facilitate the research of the solution. In this case a decomposition approach based on clustering is used to simulate a possible realistic scenario of two hubs and 20 vaccination centers, that are allocated to the closest hub (it means linking the centers only to one hub). Then the vaccination centers are divided into clusters based on political reasons (let's think about districts for ASL). At this point the problems created are solved at a cluster level (aggregating the data coming from the vaccination centers included in the cluster). Now it's possible to set binary decisions $Y_{h,cl,t}$ according to the clusters, meaning that if the link is active in the time period then the hub will supply all vaccination centers of the cluster.

Because of the static solution that does not take into account possible variation of appointments during the considered time span, a rolling horizon algorithm is considered to stop possible underperfomance. The planned time period T_p is split into two pieces: T_r and T_f, where the first time span corresponds to the first part of the planned horizon having the binary variables and daily number of vaccines used fixed and equal to the previous solution; conversely T_f corresponds to the second more flexible part where the previous solutions are used only as a lower bound. Finally T_c, that is the control time, is needed in order to better replan the vaccinations taking information from the time passed.

A graph is presented in the next page where the distinction between the rigid and flexible times is clear. It's noticeable that the control time is equal to one, while the prediction horizon is equally split into two pieces.

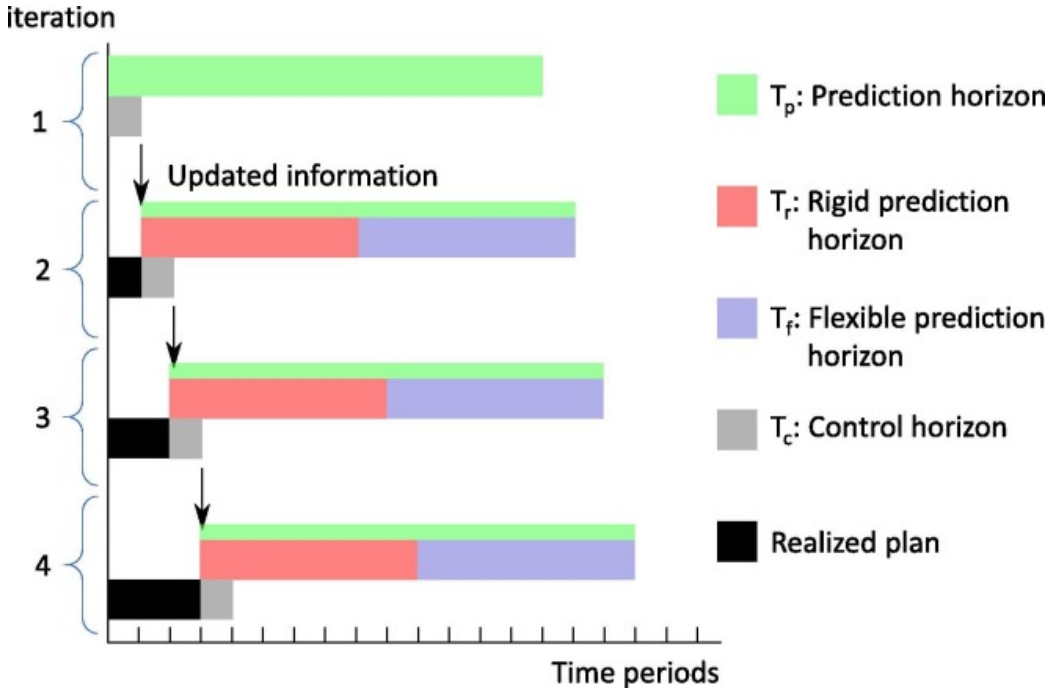


Figure 4.3: Rolling Horizon approach

4.1.1 Simulation and results

The following results are obtained simulating the model considering one hub and five vaccination centers and two vaccines: Pfizer(P) and Moderna(M). Using the initial parameters and capacity limits provided at the following link, it's possible to check the solution and analyze it: 60% of the total costs are attributable to storage costs in hubs and 19% are storage costs in vaccination centers, while the rest is divided more or less equally. This means that for trying to save as much financial resources as possible it's necessary to optimize the storage costs in order to lower down the totality.

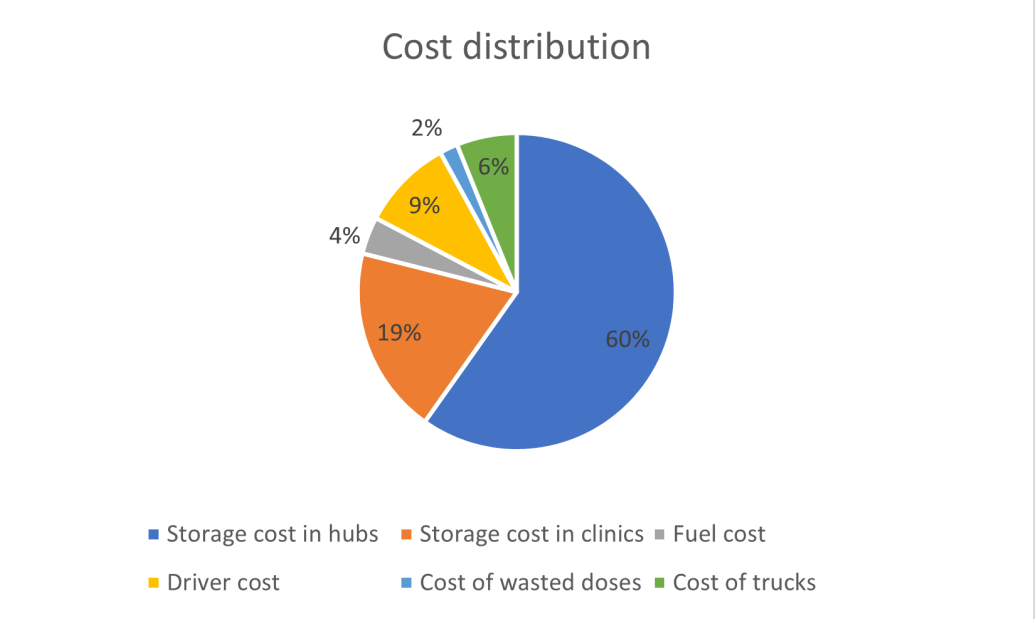


Figure 4.4: Cost Distribution

4.2 Modelling of vaccination lines

It's useful to see the problems starting from the decision variables that can be taken. In this case having a full picture of the system is necessary before choosing the right variables.

As a matter of fact the duty of the planning office was to set a target to the districts/vaccination centers, trying to comply with the regional KPIs (95% of the stocks to be used during the peak). This procedure can be done randomly or following a path. As far as the campaign was going on increasing the volume of vaccines, the deployment of staff was poor leading to chaotic situations where there were too much vaccination lines opened. This issue could be solved collecting data from the districts finding out the capacity constraints (in terms of maximum number of lines to be implemented), the cost of keeping one opened, the productivity in terms of vaccines per day (in average). The analysis is made on a single daily base. So we define the problem as it follows:

$$\min \sum_{i=0}^{n} c_i * y_i$$

$$\sum_{i=0}^{n} p_i * y_i \geq k$$

$$\forall i \; i = 0, ...n \; y_i \leq l_i$$

$$\forall j \; j = 1, ...5 \; \sum_{i \in j} p_i * y_i \leq q_j + 0.1$$

$$\forall j \; j = 1, ...5 \; \sum_{i \in j} p_i * y_i \geq q_j - 0.1$$

$$y_i \in \mathbb{Z}$$

Here the minimization function regards only the costs relative to keeping the vaccination lines opened having a set of constraints that guarantees an adequate level of service. This is why the first constraint forces to respect a number of total vaccines k. Then it's not possible to open in a vaccination center more than a fixed number of vaccination lines due to physical space issues, while the last two constraints imposes to the districts a redistribution (staying around an interval of +-10%) of vaccinations respect to the population.

4.3 Considerations

In this simple model, formulated by myself, the main core is related to decide how many vaccination lines are needed in order to fulfill all requests at the minimum cost and where to implement them.

By simulating the scenario according to the plan made by the office, this tool could be useful to identify if it was necessary or not to keep opened the structure more costly (that was using external personnel) to complete all scheduled appointments. By tracking the history of the past administrations it is possible to understand and estimate a parameter linked to the efficiency of the vaccination centers (that could considerable vary because of the coordination exc...). The more performing structures were hospital vaccination points where thanks to the possibility to open more areas (and in such a way to parallelize the system increasing the rate of the bottleneck, that it is represented by the anamnesis) there were administered more doses.

So that it is clear then that the solution of the problem would assign more lines to the vaccination centers in the districts more capable and less expensive, while keeping small vaccination centers opened would be essential only when the combined effort of the hospitals would be not enough to cover all appointments.

Possible failures of the model concern the precision of collecting input data. If the estimation and the analysis of vaccination centers (regarding the space, the personnel, efficiency) is done properly then the model will return a solid result, while a poor understanding of the structures would be disastrous for the model.

Chapter 5

Automation of processes

5.0.1 Pandas library

Pandas[1] is a library implementable in Python language for data analysis and data manipulation. Pandas is based on NumpPy[2], an open-source library, which handles multi-dimensional arrays and matrices.

The basic element of Pandas is called DataFrame(df) and maps index and column labels to values. The simplest item is composed by an array with row labels and a name (Series, s). It's possible to import data using the method $pd.read_*$, where * stands for the file type that can be csv, xls, html, txt, sql and so on. Once that the manipulation of data is completed it is feasible to export the dataframe applying the $pd.to_*$ method.

For indexing the loc[] and iloc[] methods are used, where the first one refers only to the index label, while the second one refers to the integer location.

Manipulating data implies creating masks for slicing the databases, applying mathematical operations to the data, applying functions (such as .pipe), deleting rows and checking for missing values.

Combining DataFrame is easy through .merge or .join functions that have an SQL-type logic.

[1] `https://pandas.pydata.org/`
[2] https://numpy.org/

5.0.2 Comparison with Excel

Comparing Pandas with Excel [3], it's clear that using Pandas has pros and cons.

Firstly because Pandas is a library used in Python, it's extremely fast and efficient and it's linked to the computational power of the CPU, while Excel after exceeding 10000 rows starts to slow down. So basically while adding data to the DataFrame is not heavy and it does not impact negatively the performance, adding rows to Excel can drastically reduce the quickness of the calculations causing in some cases the system to crash. Moving on, Pandas can be used to automatically clean up the damaged data and fill in blank spaces while using Excel with formulas can be tedious.

Conversely a requirement for adopting Pandas is the basic knowledge of coding and this can be an obstacle to normal users, while the friendly Excel interface widens the user base. Concluding with the comparison, automation of procedures is easier in Python rather than implementing macros in Excel or coding in VBA (Visual Basic for Applications), that is the programming language serviceable to replace user click-on actions by running the code. This is why I have chosen to start using Pandas.[4]

In conclusion working with both tools and exporting the output of the Python code as an excel file is the best solution in order to automatize processes and having a simple .xls file, which can be read by everyone, as the output is preferable for the visualization of the computations.

[3] https://www.cbtnuggets.com/blog/certifications/microsoft/why-pandas-is-a-better-data-analysis-tool-than-excel

[4] https://pandas.pydata.org/docs/dev/getting_started/comparison/comparison_with_spreadsheets.html

5.0.3 Monitoring

I have started trying to minimize the time needed for preparing the daily report. In this case, the steps are: downloading from PADDI the data from the previous day in a csv format, then copying it in the spyder, that is the IDE (Integrated development environment), folder named data and finally running the following code:

```
import pandas as pd
import numpy as np
vaccinazioni = pd.read_csv("data/vaccini1420.csv")

vaccinazioni.head(10)
vaccinazioni.columns
new_vaccinazioni = vaccinazioni.assign(PrimaoSeconda="S")
new_vaccinazioni.rename(columns={'Ves Data Effettuazione2':'
    Data2'},inplace=True)
new_vaccinazioni.fillna('',inplace=True)
for i in range(len(new_vaccinazioni)) :
    if new_vaccinazioni.loc[i,'Data2'] == '':
        new_vaccinazioni.loc[i,'PrimaoSeconda']='P'

table = pd.pivot_table(new_vaccinazioni,values='Nr. Dosi',
    index=['Cns Descrizione'],columns=['PrimaoSeconda'],
    aggfunc=np.sum,margins=True)
table.fillna(0,inplace=True)
print(table)
table.to_excel(r'export/vaccinipivot1420.xlsx',index=True)
```

Listing 5.1: Python example

A few comment are mandatory before explaining the output. Firstly the data are structured in a way that each row represents a vaccinated person and it has the following information: Fiscal Code, Age, E-mail, Patient Category, 1st inoculation date, 1st inoculation center, 1st vaccine administered, 2nd inoculation date, 2nd inoculation center, 2nd vaccine administered and so on. This is why before making any computation I need to distinguish each row creating a new column and assigning a value (P that stands for first dose, S for second dose) in a way that it clarifies everything. This is done by using a loop where if the date of 2nd inoculation is empty it's obviously the 1st one and it returns P, otherwise it gives back S. Now the next step is rearranging the table creating a new pivot table where the index is the name of the vaccination center and the columns are composed by first and second dose and the values are calculated counting for each center the numbers of P's and S's.

This code produces automatically as an output an excel file in the folder export in Spyder main folder (an example is shown in the next page).

A further solution that can improve the quality of the system is allowing the download of the data to be automatic, but this step requires to collaborate directly with PADDI, that is a SAP-based system, and asking an authorization for accessing directly the data from the server. Thus it's useless and it saves just few seconds (time needed for downloading the csv file and putting in the right folder). Anyway a real time counter could be desirable but the complexity of developing it was too high and the effort to be spent was not worthy.

Finally comparing the time needed to do the same operation using just Excel features, that takes at least 15 mins, with respect to running the code (lower than one minute of time wasted), it's considerably a good performance.

	A	B	C	D
12	CVASLTO3 AOU SAN LUIGI GONZAGA	0	15	15
13	FARMACIE COVID19 COLLEGNO	41	72	113
14	HUB NUVOLA LAVAZZA TORINO	0	1	1
15	LA NAVE GRUGLIASCO COVID	162	525	687
16	MMG VACCINO COVID19 COLLEGNO	1	0	1
17	OSPEDALE AGNELLI PINEROLO	58	123	181
18	OSPEDALE DEGLI INFERMI RIVOLI	83	330	413
19	OSPEDALE DI SUSA	40	160	200
20	POLIAMBULATORIO DI COLLEGNO	0	3	3
21	POLIAMBULATORIO ORBASSANO	55	106	161
22	POLIAMBULATORIO OULX	0	1	1
23	POLIAMBULATORIO PINEROLO	0	77	77
24	POLIAMBULATORIO TORRE PELLICE	0	12	12
25	POLIAMBULATORIO VENARIA REALE	119	133	252
26	POLO SANITARIO AVIGLIANA	63	197	260
27	POLO SANITARIO GIAVENO	23	146	169
28	RESIDENZA BERGOGLIO GIAVENO	0	1	1
29	VAC COVID PINEROLO V MADONNINE	117	245	362
30	All	829	2223	3052
31				
32				
33				

Sheet1

Figure 5.1: Vaccines per vaccination centers

5.0.4 Stock

Now I have tried to minimize the effort needed to proceed to the calculation of planned demand of vaccines. As before, the process starts with downloading two csv files from PADDI: 1st dose appointments and 2nd dose appointments, after copying them to the data folder it is needed to run the following code:

```
import pandas as pd
import numpy as np
prenotazioni1 = pd.read_csv("data/prenotazioniprima.csv")
prenotazioni2 = pd.read_csv("data/prenotazioniseconda.csv")
prenotazioni1new = prenotazioni1.replace(to_replace={'COVID 19 ASTRAZENECA','COVID 19 PFIZER','COVID 19 MODERNA'}, value={'AZ1','PF1','MO1'},regex=True)
prenotazioni2new = prenotazioni2.replace(to_replace={'COMIRNATY':'PF2','VAXZEVRIA (EX COVID 19 VACCINE ASTRAZENECA) 10 DOSI':'AZ2','COVID 19 VACCINE MODERNA':'MO2'})
prenotazioni1new.rename(columns={'Associazione':'Vaccino'}, inplace=True)
prenotazioni2new.rename(columns={'Noc Descrizione':'Vaccino'},inplace=True)
frames = [prenotazioni1new, prenotazioni2new]
prenotazionitot = pd.concat(frames)
prenotazionitot.insert(6,'Nr.Dosi',1)
tablep = pd.pivot_table(prenotazionitot,values='Nr.Dosi', index=['Descrizione Centro','Data Appuntamento'],columns=['Vaccino'],aggfunc=np.sum, margins=True)
tablep.to_excel(r'export/prenotazionitot1.xlsx',sheet_name='Foglio1',index=True)
tablep2 = pd.pivot_table(prenotazionitot, values='Nr.Dosi', index=['Data Appuntamento'],columns=['Descrizione Centro'],aggfunc=np.sum, margins=True)
tablep2.to_excel(r'export/prenotazionitot.xlsx',sheet_name='Foglio2',index=True)
tablep3 = pd.pivot_table(prenotazionitot, values = 'Nr.Dosi', index=['Data Appuntamento'],columns=['Vaccino'], aggfunc=np.sum, margins=True)
tablep3.to_excel(r'export/prenotazionidata.xlsx',sheet_name='Foglio1',index=True)
```

Listing 5.2: Python example

Basically, in this code Python merges the two files after renaming the vaccines in a more readable way (replacing the commercial names with an abbreviation -PF1, PF2 ect...). Once merged, the outputs are three different kind of tables: the most important one is a pivot table where for each center and for each day it's shown the demand of vaccines, the second one where for each day in the columns there are the total booked appointments for each center, the last one where for each day there is the aggregated demand in terms of vaccines. At this moment, these files support the final operation of filling out an excel file where for each day, knowing the actual stock communicated by email everyday at 5pm by Grazia Ceravolo, there is a cell with a simple formula that calculates the future planned stock.

	A	B	C	D	E	F	G	H	I	J	K
1	Descrizione Centro	Data Appuntamento	PF1	AZ1	AZ2	COVID	VACCII	MO1	MO2	PF2	All
2	CV DRIVE THROUGH ORBASSANO	2021/06/22 00:00:00	2			78		1			81
3		2021/06/23 00:00:00	1			104		5	204	1	315
4		2021/06/24 00:00:00				300					300
5		2021/06/25 00:00:00		1		237		3	30		271
6		2021/06/26 00:00:00	2			274		1			277
7		2021/06/27 00:00:00	1			269	1	1	2		274
8		2021/06/28 00:00:00				273		1			274
9		2021/06/29 00:00:00	1			249					250
10		2021/06/30 00:00:00				112					112
11		2021/07/01 00:00:00					1				1
12		2021/07/03 00:00:00	1		104	2			55		162
13		2021/07/04 00:00:00			176				32		208
14		2021/07/05 00:00:00			166						166
15		2021/07/06 00:00:00	1		193						194
16		2021/07/07 00:00:00			216						216
17		2021/07/08 00:00:00			214	2					216
18		2021/07/09 00:00:00	2		217						219

Figure 5.2: Demand of vaccines for each center

	A	B	C	D	E	F	G	H	I	J
1	Data Appuntamento	PF1	AZ1	AZ2	COVID 19	19 VACCINE JA	MO1	MO2	PF2	All
2	2021/06/22 00:00:00	9	12		2246		1			2268
3	2021/06/23 00:00:00	4	11	894	1307	1	6	211	2049	4483
4	2021/06/24 00:00:00	1	56	342	2536			87	1710	4732
5	2021/06/25 00:00:00	6	34	148	2337		3	32	2242	4802
6	2021/06/26 00:00:00	22	27	181	3468	1	1		1237	4937
7	2021/06/27 00:00:00	9	40	1	3456	1	1	32	888	4428
8	2021/06/28 00:00:00	17	38	206	3052		1	45	1039	4398
9	2021/06/29 00:00:00	7	15	4	3123				826	3975
10	2021/06/30 00:00:00	23	35	190	2140				1587	3975
11	2021/07/01 00:00:00	53	17	16	1568	1		2	2062	3719
12	2021/07/02 00:00:00	26	9	1	1334			2	2167	3539
13	2021/07/03 00:00:00	1	6	474	1059			123	2025	3688
14	2021/07/04 00:00:00	1	12	695	1395		1	32	1767	3903
15	2021/07/05 00:00:00	28	4	943	932				1782	3689
16	2021/07/06 00:00:00	1	3	1260	566			3	2329	4162
17	2021/07/07 00:00:00	4	1	1229	680			2	2300	4216
18	2021/07/08 00:00:00	17	2	1645	632			9	2185	4490

Figure 5.3: Daily requirements of vaccines

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