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Vaccination and prevention: disease diffusion, mandatory vaccination and prevention success in comparative perspective.

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INTRODUCTION

"Overwhelming evidence demonstrates the benefits of immunization as one of the most successful and cost-effective health interventions known. Over the past several decades, immunization has achieved many things, including the eradication of smallpox, an accomplishment that has been called one of humanity's greatest triumphs. Vaccines have saved countless lives, lowered the global incidence of polio by 99 percent and reduced illness, disability and death from diphtheria, tetanus, whooping cough, measles, *Haemophilus influenza* type b disease, and epidemic meningococcal A meningitis." (WHO 2013)

Vaccines are pharmaceutical preparations administered to produce or artificially increase immunity to a particular disease. They can be live attenuated, result of the modification of a wild virus or bacterium, or inactivated, composed of whole inactivated viruses and bacteria or of some of their fractions or products. Their infectious properties are eliminated, whereas their antigenic properties are preserved. Their administration prevents about 2.5 million deaths worldwide every year. By protecting children from vaccine preventable diseases (VPDs) they provide them the best chance to develop their full potential (WHO 2013). Immunizations are a mean to prevent the infection by VPDs, and they have been shown to be responsible for lower morbidity and mortality. Thanks to vaccines, and their development, smallpox was the first disease to be eradicated worldwide, which was officially recognized by the WHO in 1980.

Before the introduction of vaccines, pandemics affected all aspects that characterized a population (Atkinson 2009). Social, economic and geographical aspects of life were all affected, as people could not prevent nor cure VPDs. The first contributions to the development of vaccines were provided by Edward Jenner, who in 1796 discovered the vaccine against smallpox, as he infected a child with pus containing the virus of bovine smallpox. Later on it was demonstrated that the child exposed to the virus had become immune to the virus of human smallpox. Ninety years later, in 1885, Louis Pasteur managed to create the first attenuated vaccine against rabies, through the treatment of rabid rabbit's brain. The contributions that allowed to defeat diphtheria, also known as "the strangling angel" that killed 60% of the infected, were mainly two. In 1891 Emil Adolf von Behring managed to create a serum that decreased the mortality to 20%. Later, in 1924, Gaston Ramon, through the use of formaldehyde, produced a vaccine with the toxoid of diphtheria, allowing for the following production of other vaccines against other VPDs. Polio was a disease that in the aftermath of World War II killed, or paralyzed half a million people in Europe each year. Then in 1955 Jonas Salk created the first vaccine against polio, without claiming property rights in order not to affect availability, which was shortly after replaced by Albert Sabin's. Since 1967 this vaccine was used worldwide in the fight against polio, and prevented 500,000 casualties and 200,000 cases of paralysis. As far as measles, mumps, and rubella are concerned, all the different vaccines were developed by Maurice Hilleman, who later also combined them in the MMR vaccine. Measles, before the availability of vaccinations in 1963 killed more than 2.6 million people a year. The outstanding successes of vaccination allow for the launch of plans aiming

at eradicating other disease such as polio, since 1988, along with measles and rubella, since 2002. The European Region has been officially declared to be polio free since June 21st 2002 (Magurano et al. 2018).

Lately a resurgence of vaccine preventable diseases has been source of preoccupation. Thirty states of the EU/EEA reported 14, 732 cases of measles between February 1st 2017 and January 31st 2018 (ECDC 2018) . Of all these cases the 35% was reported in Romania (5,224), mostly among Roma minorities; the 34% was reported in Italy (4,987), which is almost four times the amount reported in 2016; the 9% was then reported by Greece (1,398) and the 6% by Germany (906). In addition, according to the ECDC Surveillance atlas of Infectious Diseases, in 2015 there were 40,195 cases of whooping cough, 13,519 cases of mumps, and 3,180 cases of haemophilus influenza disease. What is also worrying is that in some European countries the vaccination coverage does not meet the threshold that ensures population immunity. In 2016 the coverage for the second dose of MMR vaccine was below 84% in European countries such as Romania, Italy, France, and Greece (ECDC 2018). Sub-optimal levels of immunization are common to many VPDs, exposing the whole population to possible outbreaks.

In the European region, these outcomes are often linked to an increasingly common phenomena known as vaccine hesitancy. Vaccine hesitant individuals are ambivalent and uncertain about vaccination decisions, due to fears about vaccination risks, effectiveness and side effects (ECDC 2013). This group of people are easily influenced by the media, social networks, but also by health practitioners. In case of adverse rumors or media reports, such individuals can decide to refuse immunizations, as they are skeptic of their benefits. In Europe there are five of the least confident countries worldwide concerning vaccination (Larson et al. 2016, 299), making hesitancy an issue to address.

At the European level the WHO approved the European Vaccine Action Plan (EVAP), as a suitable framework to empower immunization plans through new and ambitious strategies (WHO 2014). The main goals are to:

- Sustain the polio-free status.
- Eliminate measles and rubella.
- Control hepatitis b infection.
- Meet vaccination regional coverage targets at all administrative levels.
- Ground decision making on the introduction of new vaccines on evidence-based data.
- Making immunization programmes financially sustainable.

Since the approval of the EVAP it was clear that the only key to success would have been a significant level of commitment by all Member States.

Some States in the EU responded to the issues described above by making mandatory an increasingly high number of immunizations.

In this thesis the background, in which a the policy change became necessary, will be examined. The environment in which this process has taken, and currently takes place will be described. The bases for mandatory immunizations will be reported, and the phenomena of vaccine hesitancy will be analyzed. The situation at the European level along with the tools that the Union has to ensure public health will be mentioned. In a second part, the phenomena of policymaking concerning immunization policies, that eventually resulted in the choice of mandates over the recommendation principle, is going to be thoroughly examined along with the international influences in the process. The efficiency and applicability of the immunization mandates is going to be studied in the European context. The contingencies that made mandates necessary in some states are going to be analyzed, and situations in which they were not adopted will be taken into account. Case studies will also be taken into consideration to corroborate a literary approach with context-specific data, that will make ultimately possible a comparative study of the phenomena. Ultimately the necessity and applicability of mandatory immunizations will be finally evaluated.

CHAPTER 1 – Disease Prevention and Vaccination

In this first chapter, the context in which the process of policymaking takes place will be taken into account. After a first European example, the bases for immunization mandates will be discussed.

In Europe, vaccines are available to the vast majority of the population, and it has been estimated that nine out of ten children complete at least a basic cycle of vaccination (WHO 2014). This fact allows them to conduct productive and healthy lives, without having to die or carry the burden of vaccine preventable diseases. It was estimated that in Europe alone, the introduction of vaccines has allowed for the elimination of polio from the region, and contributed to the control of other vaccine preventable diseases as well.

Though, it can be said that immunizations in Europe are the victims of their own success (Carrillo-Santisteve and Lopalco 2012, 52). As the "Vaccine Paradox" exemplifies, the immunizations' success, thanks to high coverage, decreases the perceived risk of VPDs and of their complications. Given that the disease is no longer perceived as dangerous, then the main concerns become adverse events following immunization.

As a consequence, some parents fail to grasp the importance of vaccines, and either delay or refuse them. This phenomena has allowed the resurgence of diseases such as measles, diphtheria, rubella, and other diseases that could have been averted with high levels of vaccine coverage. The consequence of such choices do not only endanger the unvaccinated individual, but society as a whole, and so it triggered a response by policymakers in many countries. Vaccine hesitancy, due to its vital role in vaccine delay and refusal, will be thoroughly described.

Policymakers resorted to the introduction of mandates, that oblige parents to comply with the vaccination plan. Still, compulsory immunizations are not a solution to every problem, and they can be an effective response to some societal issues. In some cases other responses, such as tailored interventions, could be more effective.

Last, the European context will be taken into consideration. The distribution of VPDs at the Union level, the regulations regarding immunizations and the policy tools are necessary to be able to assess the situation in the region, which is in turn necessary to understand vaccine policy making. The goal of this chapter is to focus on the contexts where the process of policymaking happens, showing what obstacles it is supposed to overcome.

1.1 French case

France, despite being the motherland of Louis Pasteur, pioneer in the matter of vaccines, is these days a good example on policy change on VPDs. The French case is extremely significant due to the alternations of

waves of mandatory immunizations, followed by skepticism about mandates as the infectious diseases targeted disappear.

In 1902 smallpox vaccination was the first to be made mandatory, and was followed by the vote in favor of the obligatory immunization against diphtheria, tetanus, tuberculosis and poliomyelitis (Nicolay et al. 2008, 5484). In the historical context such measures were first of all necessary to face infectious plagues that caused a significant amount of fatalities. Another objective of mandatory immunization was achieving a high level of protection among the population that would have allowed the elimination of the targeted diseases.

As such measures showed their effectiveness, and the main infectious diseases disappeared, then also the policy changed. Immunization against poliomyelitis was the last one to be made mandatory in 1964, and since then the recommendation principle played a central role in policy making (Nicolay et al. 2008, 5484). Even further, in 1984 the vaccine against smallpox was ruled non-mandatory anymore. Later on, a debate about the necessity of mandatory vaccination against tuberculosis begun, which led to its suspension shortly after in 2007.

As soon as the main infectious diseases disappeared, the perceived relevance of the mandatory vaccine policy sunk. The perception of low risk derived by the lower incidence of vaccine preventable illnesses led to a change of behavior. Perceiving a disease as rare leads to debates about the necessity of the mandatory immunization, which is then shortly followed by doubts on the importance of vaccination as a preventive measure.

Nowadays, parents are more worried about side effects of vaccinations than of the diseases preventable by vaccination, and there is a widespread misconception of the real risk, paired with a lack of trust in science and medicine. This, more and more often, has a huge impact on changes in policies and strategies at the national level on vaccines and immunization.

Moreover, if on one side the importance of mandatory immunization policy is undervalued, on the other, unfounded claims fuel skepticism against vaccines. France, according to Larson et al. (2016, 297), is one of the most skeptic countries worldwide, as 45.2% of the population has doubts on vaccines' effectiveness. in France as well as in the rest of Europe, mass media has long echoed claims and conspiracy theories. Free access to information, and the lack of control when it comes to the reliability of the material consulted, have helped the spread of researches based on fake data, and the spread of allegations not at all supported by proof. Even if some claims are later proved wrong, they still strongly influence a significant portion of the population, and their decisions.

The combination of the misperception of the risks linked to lower disease incidence, and the skepticism resulting from unproven or fraudulent claims echoed through the media, caused debates that led to the

decrease of the amount of the mandatory immunizations and, on the long term, to the decrease in vaccine uptake.

The new preferred method became vaccination adoption through recommendation principle, and only three vaccines, diphtheria-tetanus and polio, remained compulsory in France (ECDC 2015). This change meant that healthcare practitioners had then the duty to inform the population, describing the balance between benefits and side effects and highlighting the role of immunizations in the prevention of VPD outbreaks. The population in turn was empowered, exercising its judgment and its freedom on the matter of vaccines. This on the other hand allowed skeptics to have the choice of not vaccinating their children, causing VPD outbreaks.

The results of the new approach were disappointing to say the least. To prove such statement the data about measles, a vaccine preventable disease, are going to be taken as an example to assess the situation. Between 2008 and 2016, as it can be noted that more than 24,000 cases of measles happened in France of which 10 resulted in the patient's deaths (FIG. 1) (Yang and Rubinstein Reiss 2018, 1323). This critical situation was not only observed in France, but later on all over Europe. In fact, between January 2016 and June 2017 more than 14,000 measles cases were reported in Europe of which 34 resulted in deaths. Yet France has been identified as one of the countries that lags behind in measles immunization, as the herd immunity threshold of 95% with two doses was not met. The data reported makes it possible to infer that a public health goal has been jeopardized by lower vaccine uptake.

As a response, France drastically changed its law on immunizations, and raised the number of compulsory vaccines from 2 to 11 in January 2018 (Yang and Rubinstein Reiss 2018, 1323). Since that date, children will not be able to enroll in school unless they have proof of mandatory vaccination, except those that have medical contraindications. Moreover, even if they are not enforced yet, sanctions will be possible in case of vaccine refusal, but it is already possible to start legal proceedings against parents that endanger their children's health, or that expose other children to VPDs.

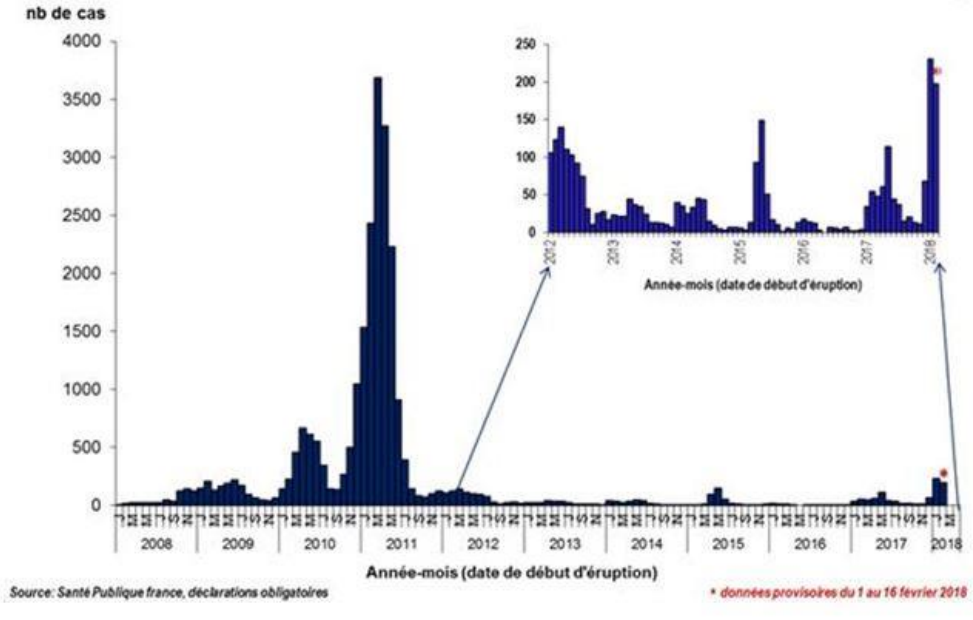

FIG.1:Number of Measles cases per month. Mandatory notification, France.

(Santé Publique France 2017)

France is not the only country to have adopted this kind of policy, yet other European countries have done the same, or are in the process of doing that.

1.2 What are the bases for policies on obligatory vaccination?

Since their first development in 1796, and their widespread usage during the 20th century, vaccination has proven to be among the most successful public health preventive tools. Thanks to their success they have often been compared to the introduction of family planning and drinking water (ECDC 2015). High vaccine uptake does not only allow for the protection of the individual that receives the vaccination, but also for the protection of the entire community, including whomever cannot be vaccinated (herd immunity) (Kim et al. 2011, 683). On the contrary low levels of vaccination uptakes is a threat for community immunity, as they increase exponentially the probability that groups of unvaccinated people come into contact with infected ones, and spread the disease in the population. This means that high vaccination coverage allows for the protection of the whole population, including people who cannot be vaccinated.

In most developed countries the levels of vaccination coverage are still very high, yet clusters of un-vaccinated individuals do exist, and they have been linked to many outbreaks (Dubé et al. 2013, 1763). Vaccine refusal is a threat to herd immunity, and has to be addressed by policymakers. So far, the recommendation principle, was a response to the increased demand for freedom of choice regarding healthcare (Lévy-Bruhl et al. 2018). Still, it has been observed in some contexts with high levels of vaccine hesitancy that policymakers response was to introduce vaccination mandates. Vaccination mandates are most often adopted in contexts where there are issues with the achievement of suitable coverage levels (Lee and Robinson 2016, 661). The objective of mandatory vaccination is to lower vaccine incidence, through policies that oblige parents to vaccinate so that immunization uptake levels are kept high. Nonetheless sanctions in case of deviance are not the only objective, but mandates also aim to restore confidence, and demonstrate the government's commitment in favor of vaccination (Lévy-Bruhl et al. 2018). According to such measures, the parents will need to vaccinate their children, in order to enroll them in any kind of collective services, and in order to avoid financial or legal repercussions in case of deviance (Yang and Rubinstein Reiss 2018, 1323). Mandates, and their effective enforcement, in the short run are linked with higher rates of immunization uptake, and in the long run they are associated with higher levels of up-to-date immunization statuses (Lee and Robinson 2016, 661). Moreover, qualitative surveys carried on in France, showed that the mandatory status of vaccination increased the perceived necessity and urgency among parents, whereas the recommended immunizations were the most questioned (Lévy-Bruhl et al. 2018). This response to low levels of vaccine uptake was feared to become a new fuel to vaccine refusal, as vaccine hesitant individuals can resent the intrusion of their freedoms (Lee and Robinson 2016, 663). As a consequence, to avoid vaccinations the use of exemptions could be abused, and it will then be necessary to strictly control their amount and nature, as they can allow for sub-optimal vaccination levels. The effectiveness of mandatory

immunizations is variable. The greatest effects could be observed among populations with lower immunization levels, whereas populations that had high confidence and uptake levels, where not affected as much (Lee and Robinson 2016, 664). In many contexts mandatory vaccinations are seen as a solution when high levels of hesitancy significantly affected uptake among the whole population. This policy response shows the public commitment of the governmental institutions, that limit the population freedoms to safeguard public health and eventually influence the perception of vaccinations. In case specific pockets of sub-optimal vaccination are to be targeted, then the WHO also proposes alternative practices based on behavioral and social sciences (Dubé et al. 2017, 1509-1510). These actions, also known as Tailored Immunization Programmes (TIP), aim at diagnosing barriers to vaccinations. In all cases policies interventions aim at the highest possible immunization coverage, as immunizations have been proven to be the cause of the reduction of child mortality in the European region (WHO 2014). Despite the fears and claims of vaccine hesitant groups, immunizations have been scientifically proven not to be linked to risks for the health (WHO 2013). The phenomena of hesitancy it will be discussed in the following paragraphs.

1.3 Vaccine hesitancy and uptake

Vaccine confidence in Europe is extremely low, compared to the rest of the world. The European region is characterized by skepticism about vaccine importance, safety, and effectiveness. In fact five of the ten least confident countries are members of the European Union, such as France, Bosnia Herzegovina, Ukraine, Greece, and Slovenia (Larson et al. 2016, 299). The greatest obstacles to vaccine uptake in Europe are reservations about vaccine safety and side effects, that are not significantly mitigated by the perception of vaccines' importance (Larson et al. 2016, 299-300).

"Vaccine hesitancy refers to delay in acceptance or refusal of vaccinations despite availability of vaccination services. Vaccine hesitancy is complex and context specific, varying across time, place, and vaccines. It is influenced by factors such as complacency, convenience and confidence." (MacDonald and SAGE Working Group on Vaccine Hesitancy 2015, 4163)

Vaccine hesitant groups are extremely heterogeneous as far as the levels of confidence and the causes of their skepticism are concerned (Dubé et al. 2017, 1510). The main factors that can influence confidence and hesitancy are cultural, historical and political. So, even if all over Europe widespread access to immunizations is guaranteed, yet the fears that people have about vaccines (safety and side effects) are the reason behind vaccine refusal (Larson et al. 2016, 298).

Hesitancy is characterized by reluctance, delay, lack of confidence and indecisiveness, when faced with the issue of immunization uptake (Valetto 2017, 34). It is possible to make a distinction between different segments of the population that do not have positive attitudes towards vaccines.

First of all a group of hesitant parents has been identified (Valetto 2017, 34). They are mainly concerned with the safety of vaccines, and have reservations on the protocol in place. Hesitancy is not common only among the unvaccinated population, but also among the vaccinated one (ECDC 2015). Specific concerns that vary among vaccine hesitant individuals.

Second, a group of parents has been defined as unconcerned (Valetto 2017, 34). These parent does not see immunizations as a priority, due to the fact that they fail to understand risks associated to VPDs. The reason behind their beliefs is that infectious diseases targeted are thought to be already eradicated, or at least they are not perceived as severe, lowering the perceived importance of immunizations. Moreover, in case of contagion, excessive confidence in the cures is also not uncommon.

A third group identified is the one of the poorly reached (Valetto 2017, 34). This part of the population has to face significant social, economic or cultural barriers that do not allow them to have a fair access to immunizations.

Last, some segments of the population strongly refuse vaccination due to personal, cultural and religious beliefs (Valetto 2017, 34). They do not only lack trust towards vaccination, but they actively try to avoid it. As opposed to vaccine hesitancy, vaccine refusal is harder to overcome.

To control behaviors that can harm vaccine coverage, institutional action at all levels is required. It is necessary to inform the groups that misunderstand or mistrust the importance of immunizations, and it is fundamental to include all the stakeholder in the decision-making process. Both of the actions described above are essential because, with the appropriate campaigns, there is margin for change. As a matter of fact, in Italy a study has shown that 63% of the parents, who so far avoided vaccinations are prone to change their minds (Valetto 2017, 35).

To further understand vaccine hesitancy, and all the other positions that can contribute to a lower vaccine coverage, the different factors that come into play are going to be analyzed. First, it is necessary to address the role of healthcare professionals, and what contributions they can provide in vaccine hesitancy and acceptance.

The intervention of healthcare professionals, according to different studies, is central (Dubé et al. 2013, 1767). They are the ones in charge of providing reliable information to their patients, and they are the ones that most often are in charge of recommending immunizations. Yet, healthcare workers do not always manage to successfully incentivize vaccination uptake (ECDC 2015). This phenomena is due to the interaction of different dynamics.

First, healthcare professionals can be vaccine hesitant. They can be aware of the benefits vaccines have, but they can still share the fears and reservations of the rest of the population. The concerns can vary according

to the different countries. In fact, the fear of side effects and risks, shared in many European regions, can be expressed differently. In Greece, for example, the most commonly expressed fear is the high number of vaccines administered to children, and their low level of efficacy. Though, in Romania, the feeling of guilt perceived by doctors was central when side effects are concerned, (ECDC 2015). Reservations about immunizations influence health practitioners' actions, and their ability to persuade their patients of the importance of vaccines. If the most reliable source of information to the public is not able to provide an unequivocally favorable opinion on the matter, then the patients themselves are going to fear the procedure.

Second, health professionals might not be able to overcome the skepticism that mass media, or the cultural environment in general, has instilled in their patients about immunizations (ECDC 2015). The cultural environment that surrounds patients daily might undermine the credibility of the main institutions associated with vaccination. Then, the population will translate the mistrust towards the targeted institutions to vaccination itself, and the uptake will further drop. In this environment the process of building trust can go beyond the doctors' abilities, despite their efforts. Additionally, in some cases popular beliefs, and not mass media, are the cause of mistrust. In France, for example, healthcare professionals have reported that one of the main obstacles to higher MMR (measles, mumps and rubella) vaccine uptake is due to the misconception that measles is not a severe illness. As a matter of fact, it is possible that healthcare professionals themselves might be influenced by these misconceptions, which would hurt further the success of trust-building practices. In fact, doctors alone will not be able with their intervention to undermine the mistrust built by the cultural and political environment over decades.

Third, lately there has been a rise in the number of doctors that publicly condemn vaccination, reinforcing hesitancy (ECDC 2015). One of the most well-known studies, published on "The Lancet" in 1998, is the one by Wakefield. His claims were that the MMR (measles, mumps and rubella) vaccine was linked to autism. His opinions, only corroborated by fraudulent data, are still circulating. Yet, he was not the only one to criticize vaccination. The doctor Jean-Jacques Crèvecoeur publically criticized influenza A (H1N1) vaccines. His criticisms were based on the fact that there was not a pandemic episode in place, as the number of casualties caused by influenza A (H1N1) (4,500), was significantly less than the ones caused by common influenza (250,000). He argued against the vaccine's safety and efficacy, and also alleged possible unduly influences by pharmaceutical manufacturers on the WHO, concerning the launch of the H1N1 flu vaccine. His claims were proved invalid and dismissed by the scientific community, but not by the public. Other doctors even started petitions or symposiums to spread their criticism. The French doctor Henri Joyeux even started a petition against vaccines and obtained around 700,000 signatures. These interventions are significant because their professional training increases their credibility among masses, despite the proofs of their misconduct. The repercussions such doctors had to face do not have the effect of lowering their credibility. On the contrary, they become martyrs, victims of a corrupted society, in the point of view of some groups. Their position harms the institutional efforts to increase vaccine coverage, and the authority of

said institutions. And if what they yet achieved was not enough, the literature they created, and their newly constructed image, is used as the basis of public discourse against vaccination.

Healthcare professionals have a great authority, both on the personal level, as far as their relationships with patients is concerned, and in the public eye, when they share their opinion through researches and interventions in the media (Dubé et al. 2013, 1767). Health professionals are the most trusted source of information concerning vaccines, and then providers rely on their help to address vaccine hesitancy. Accordingly they have a central role in the debate about hesitancy and immunizations' refusal, giving them the power to shape the public's outlook on the topic.

As explained, actions of healthcare professionals do have an impact, but they are not the only aspect that comes into play when addressing the issue of hesitancy. Another set of factors, that influence both trust, and mistrust towards immunizations, are rooted in social, and especially cultural characteristics of the population.

Nowadays free access to information is easier than ever, thanks to the increased accessibility provided by the Internet, as online media platforms give unprecedented access to geographical areas inaccessible before. Parents are often affected by what they can read on the Internet, and have access to material not supported by scientific evidence (Meleo-Erwin et al. 2017, 1895-1896). Blogs, and social media are seen as a reliable source of information, as opposed to health organization websites, and as a platform for parents to encourage each other and promote anti-vaccination content. Studies, such as the one conducted by Davies (2002, 22), show that the results on 7 search engines, following the search for the word "vaccination", yield a significant amount of vaccine hesitant websites (43%). This phenomena allows the spread of misinformation based on untrustworthy sources and affects behaviors related to vaccinations (Meleo-Erwin et al. 2017, 1899-1900). There are multiple allegations that have a great resonance on the Internet. For example, the fear of exposing children to an excessive amounts of antigens through vaccination is unfounded, as it has scientifically proven that immunization expose to hundreds of antigens, as opposed to the thousands reached with infectious diseases (Valetto 2017, 36). Moreover, contrary to the common beliefs, VPDs are serious diseases that can be fatal, and not always effectively treatable. In fact, even the diseases that are considered under control, can, unexpectedly, affect unvaccinated groups in sporadic outbreaks. Some may use also the new platforms available to spread unproven claims (Meleo-Erwin et al. 2017, 1895). Two of the most relevant examples are the allegation that healthcare professionals and their families, aware of the side effects, avoid vaccination, and that immunizations and their additives are the cause of the spread of disease (Valetto 2017, 37). Regarding the first claim, the data available suggests that actually rates of vaccinations are higher among healthcare professionals (Valetto 2017, 36). Then, as far as the second is concerned, the incidence of infectious diseases has been proven in the centuries before vaccination even existed, and is not as a consequence a result of vaccinations. In addition the French Official Medicine Control Laboratory (OMCL) has recently proven that additives, including mercury (Grandjean et al. 1997), aluminum and squalene (Lippi

2010), in such insignificant doses are completely safe (Valetto 2017, 37). Yet unproven claims and allegations, once they spread through the media, can become valid arguments for groups that do not research or trust official data (Carrillo-Santisteve and Lopalco 2012, 52). The outcome of this sequence of events is, most likely, greater skepticism against vaccines and the institutions related to them, and greater rates of hesitancy and refusal.

Besides common beliefs, other factors can have a role in the loss of confidence and the avoidance of vaccines. One factor that correlates to vaccine refusal is religious belief. Some problems of refusal rose, for example, in some Christian communities for different reasons. In the Netherlands, an outbreak of mumps in a small orthodox community that lives in the so-called Bible belt (Pelčić et al. 2016, 516). The Protestant community is divided on the topic, as some pastors decide not to address the issue of vaccinations due to its widespread acceptance, others prefer to allow parents to choose freely, and some object it, or give it a negative connotation. What is most criticized about vaccination, is its alleged interference with the divine providence. So, if there are side effects, they are interpreted as a divine sign, whose purpose is to punish a wrongful act. On the other hand protestant pro-vaccines parents see the development of vaccination as a Godly sign (Pelčić et al. 2016, 518). In Catholicism, the main concern is about the use of voluntarily aborted fetuses cell lines, yet no directed criticisms are directed to vaccination itself (Pelčić et al. 2016, 516-517). The Catholic Church's Magisterium identifies some substances that shall not be used in vaccines, and the procedures involving them should be opposed by "objection of conscience", but it still allows their use in case of extrema ratio (Pelčić et al. 2016, 517-18). Regarding the Orthodox view, religious leaders have made public their beliefs in 2008, as the result of a Synod. According to the Orthodox leaders, immunizations are a necessary tool to avoid infectious diseases, yet they still express caution on the possible side effects. As far as the Jewish community is concerned, immunizations are seen as a tool to obey God's commandment to "be fruitful and multiply", so they are proactively adopted and recommended, yet some ultra-orthodox communities disagree about that (Pelčić et al. 2016, 518). In Islam, on the other hand, issues might arise if the products employed are not halal, but this issue can be overcome thanks to the "law of necessity" to the purpose of protecting life (Pelčić et al. 2016, 518). Anyways it has to be noted that strong faith related objections are more common among religious fundamentalists, and that objections based on religion are sporadic in Europe (Larson et al. 2016, 300).

Other factors beyond religion, that have a role in the perception of immunizations, are education and employment. Researches have shown that countries with higher mean years of schooling most likely host a greater number of skeptics about immunizations (Larson et al. 2016, 298). Within such countries those with a middle level of education are most likely to have a positive outlook on vaccinations. Yet, despite what could be expected, most highly educated élites (such as the Dutch one), as well as the citizens with the lowest level of education, are the most likely to be vaccine hesitant. Among the workforce the ones who are found to be the least trusting of vaccines are the unemployed and the ones with lowest salaries.

Different levels of trust towards vaccines can also be found based on age (Larson et al. 2016, 298). Different age groups, even if very close, have different views on vaccination. As a matter of fact 18-24 years olds have a greater trust in immunizations than people in the age range 25-34, who, on the other hand, are found to be one of the most skeptical age group. On the other hand, the oldest age group, over 65, is the one that most trusts vaccine effectiveness, but also the one that could have the greatest reservations on the basis of religion. These stark differences might be based on social dynamics, and on the different generational involvement in the debate on vaccines' safety and effectiveness.

Moreover it is necessary to examine the economic dynamics that can have a role in the social perception of vaccinations. Access to vaccines is particularly widespread in Europe, through the private and public sectors. The main bases of hesitancy, are shown not to be rooted in access, but on low levels of trust in the benefits of immunizations as opposed to the risks (Larson et al. 2016, 299-300).

Nonetheless it shall be noted that Member States of the EU are facing shortages. Stocks are limited or not available, both because of the high costs and also because the quantities are limited. The unpredictable demand, and as a consequence the unsure profit, is one of the reasons why industries are less prone to invest in vaccines in Europe. The variety of vaccination schedules, the absence of forecast planning are not suitable for investments that require long lead times, such as vaccine production. In case of VPD outbreak the situation could be complicated, not only by the lack of the necessary products, but also by legal complications, that do not allow States to easily share vaccines across borders (COM(2018) 245/2). If access to vaccines is complicated by minimal availability issues, the least trusting recipients could either abandon their attempt to comply with vaccine recommendations, or they could refuse to comply the following time to avoid complications.

Currently, in most of the European countries, vaccination only represent the 0.5% of the prevention funding. This minimal amount of financial support does not allow for the expensive investment necessary to develop new innovative vaccines or to adapt and improve the existing ones. When this is perceived by the population, either through propaganda by vaccine skeptics or else, the level of confidence in vaccine effectiveness and safety will undoubtedly decrease.

1.4 Risks for public health due to vaccine hesitancy

Vaccine hesitancy, and the possible refusal, entail a great risk, both for the individual and for the community. The fact that growing segments of the population might fear, and then avoid immunizations, means that herd immunity is threatened. Community immunity happens when over a certain proportion of the population is vaccinated. In these circumstances, most of the population is immune to a particular infectious disease, and the disease cannot spread. If, on the contrary, vaccine uptake decreases (due to a lack of confidence in vaccines for example), then less people will be immune to such disease and outbreaks become more likely,

and even whoever cannot be vaccinated could be infected. Given that, as stated above, most VPDs are serious conditions that can also provoke casualties, their spread in the population is a hazard. Furthermore the risks linked to VPDs are not only linked to the possible outcomes of contagion. What even increases risks is that now such conditions are almost non-existent in Europe, so doctors are less likely to recognize and diagnose them, and the treatments might not be in stock due to their unlikely usage. Cases of diphtheria like the one happened in Spain (2015) proved to be a real challenge (ECDC 2015). Given that diphtheria has been almost eradicated from the European region, and measures for mass vaccination are in place all over Europe, several countries stopped manufacturing diphtheria antitoxin (DAT). Spain then had to import DAT, due to its unavailability in the country, from France and Russia, that had kept stockpiles. With lower vaccine uptakes similar situations are bound to happen more often. Institutions then need to intervene to protect public health. To do so it is vital that the amount of vaccinated individuals is maintained above the threshold through institutional action, and that in the meantime treatment in case of outbreaks is stocked.

1.5 Situations and regulations in Europe

The EU is characterized by the coexistence of countries that have different levels of VPDs incidence, different regulations and different levels of vaccine hesitancy. In this section an overview at European level is provided.

1.5.1 Vaccine-preventable diseases in Europe

All over the European region, in 2017 the amount of measles cases tripled if compared to 2016, as 14,000 people were infected (COM(2018) 245/2). Furthermore, the amount of children susceptible to measles in a decade (2006-2016) is close to four millions (COM (2018) 244/2) (see FIG.2). Cases of diphtheria, made possible by the uptake level being below 95%, are still a threat, even if the disease is rarely seen. The number of victims reached the amount of 52, only taking into account measles (50) and diphtheria (2) (COM(2018) 245/2). Only in 2017, in the EU there were more than 696 rubella cases. Moreover, some National Surveillance agencies fail to report all suspected VPD cases, making case investigations incomplete (Datta et al. 2017). The WHO targets are apparently not being met in the European region, in particular

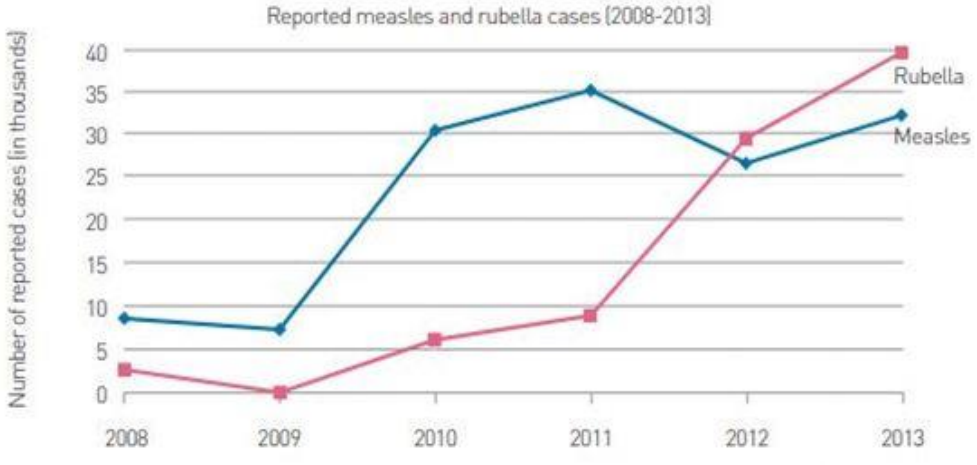

FIG. 2: Reported cases of measles and rubella cases (2008-2013)

(WHO 2014)

measles eradication by 2020 is far from being achieved (COM(2018) 245/2). Lower vaccine rates, paired with possible contacts with populations where polio is endemic, poses a remote risk for reintroducing poliovirus. This would potentially mean the loss of the polio-free status at a European level.

In the EU, both sporadic and widespread cases of VPDs have been reported. Outbreaks often have origin from unvaccinated groups, also known as pockets of sub-optimal vaccination (Datta et al. 2017). Contagion is easier in such circumstances as, given that the amount of vaccinated people is low and possibly non-existent, as soon as one of the members is exposed to VPDs, then the whole group is most likely to be infected. Then the members of the group come in contact with the rest of the population and infect the individuals that were previously protected by herd immunity. The individuals that happen to be part of these pockets might have some characteristics in common. Groups having in common the same cultural background, if they refuse vaccination in mass, could be an example. Outbreaks are common in the Roma community in Bulgaria, as well as among the Anthroposophic community in Germany, the ultra-orthodox protestant community in the Netherlands, and the ultra-orthodox Jewish community in Belgium (Datta et al. 2017). Age groups could also be subject to outbreaks, if a significant portion of the age cohort has not been vaccinated, as it happened in Germany (2015), and in the UK (2014) with measles. Outbreaks can also be caused by unvaccinated healthcare workers (HCW). Due to their profession, HCW are more likely to come in contact with VPDs, get infected and transmit it in the hospital setting.

1.5.2 Different regulations about vaccines

All over Europe, the tradition of vaccine implementation is deeply rooted, yet its characteristics vary based on the country. In the European region, according to Haverkate's study (2012), there is a high rate of dis-homogeneity regarding the approach to vaccination. In fact of the 27 European countries taken into account, plus Iceland and Norway, 15 do not have any mandatory immunization, whereas 14 do at least have one. Mandatory vaccinations, as opposed to recommended vaccinations, must be administered by law to every child, and, no matter if there could or could not be legal or economic repercussions, the parents or guardians cannot oppose it. Recommended vaccinations are included in the immunization programme, yet they could both be funded or not, and they could also be prescribed only to specific groups of the population. Anyways, some vaccines are mandatory in most of the EU, such as the one against polio (mandatory in 12 countries), the one against diphtheria and tetanus (mandatory in 11 countries), and the one against hepatitis B (mandatory in 11 countries). Moreover, for the majority of vaccines mixed strategies are employed.

Historically, it was not necessary to impose mandatory immunizations, as the recommendation principle was sufficient to ensure compliance (Haverkate et al. 2012). However, lately achieving satisfactory levels of compliance has become increasingly difficult, due to peaks of vaccine hesitancy and refusal. As a result, many countries are considering to change their legislations in favor of a mandatory approach. To enforce vaccination mandatory policies a great variety of penalties are envisioned. Some examples could be

obstacles during school enrollment procedures, fines, and even prison in case of a lawsuit. Such measures though are not consistently applied; depending on the region, institutions can decide not to take action. Internationally the effectiveness of such measures is strongly questioned, even if at the national level, they can appear as the only viable option.

The differences among immunizations programs go beyond the presence and number of mandatory immunizations, as opposed to the recommended ones (Haverkate et al. 2012). Other significant variations among different countries' in vaccination programmes mainly consist in the vaccines included, the amount of doses required, the type of vaccines used, and the timing of administration. Moreover, the offer may vary, as some states offer them through the National healthcare system, whereas in other countries they have to be paid for upfront by the recipient. Such differences are motivated both by historical, social and economic factors, as well as by the organization at the National level of the healthcare system (COM(2018) 245/2)

1.6 Agencies in charge of surveillance of VPDs to promote European policies

1.6.1 Tools to enforce policy at Union Level

According to the Article 168 of the Treaty on the Functioning of the European Union (TFEU), it is one of the duties of the Union to complement national policies, as far as public health is concerned (Council Conclusions 438/04). The Union shall support the fight against threats to public health, by supporting research, information and education. Monitoring possible cross-border threats is another function that the Union has taken up over time. The Union has still to refrain from interfering with the State's responsibility to shape their health policy and to manage its means to deliver health services. The Union can promote cooperation and in case support State's action.

The European Center for Disease Prevention and Control (ECDC) is one of the EU agencies deputized to the prevention and control of infectious diseases, including vaccine preventable diseases. It was established in 2004 through the Regulation (EC) 851/2004 of the European Parliament and of the Council. Its mission is to "enhance the capacity of the scientific expertise in Member States with regard to the prevention and control of communicable diseases, epidemiological surveillance and training programmes and to foster the exchange of best practices and experience with regards to vaccination programmes" (Regulation (EC) 851/2004 of the European Parliament and of the Council). This agency, thanks to its multidisciplinary approach, allows Member States to strengthen their capacities and improve their public health security (ECDC 2017). The ECDC is not only in charge of passive monitoring, but it also provides independent scientific opinions and advice (Kramarz et al. 2013, 2). Their work is based on standard procedures supported by evidence-based methods. Creating a competent public healthcare workforce, able to control and prevent VPDs, will benefit the whole Union.

The European Medicines Agency (EMA) is a decentralized agency of the European Union, whose mission is to provide scientific evaluations, supervision, and safety monitoring, about medicines distributed in the EU, including vaccines (European Medicines Agency 2018). EMA's scientific committees are made up of thousands of experts that work under the supervision of an independent Management Board. This agency has seven scientific committees whose duties are to facilitate the development and access to vaccines, to provide recommendations based on data evaluations, to continuously monitor the safety of medicines that have been approved in the EU, and to provide impartial information about drugs and their usage (European Medicines Agency 2018). Their recommendations about vaccines mostly concern the pre-marketing phase. This body promotes research and innovation in the pharmaceutical sector. EMA also coordinates inspections in connection with marketing-authorization applications, and monitors medicines', and vaccines', balance between risks and benefits.

Another useful tool, important in surveillance activities is Immunization Information Systems (IIS). IIS are confidential databases in which all the participants residing in a certain location record all immunization doses administered (ECDC 2017). As recognized by the European Council and the WHO, IIS could be a significant improvement in the performance of vaccination campaigns. The aggregate data provided could guide public health policy decisions and increase vaccination uptake. So far, of the 27 countries surveyed by the ECDC, 14 had already a national system in place (52%), whereas 7 used a subnational system (26%), and the rest did not have yet a system in place. Member States are currently relying on the ECDC support to develop their IIS system.

1.6.2 Nations' freedom of action

Even if VPDs are not threats that can be contained within the borders of Member States, vaccination programs, according to the principle of subsidiarity, are part of the State's competencies. The State has the responsibility to organize its healthcare system and to shape its own vaccination plan. In the EU this aspect is crucial, as the free movement of people could facilitate the spread of outbreaks to other States. Nonetheless, in case of serious threats to public health, Member States shall collaborate with the Commission through the Health Security Committee to coordinate their response (European Parliament Decision No 1082/2013/EU). Still, even commitments in acquiring medical countermeasures is on a voluntary basis.

National Technical Advisory Groups (NITAGs) are bodies whose responsibilities change based on the country. These bodies, are independent expert advisory committees, that in most industrialized countries are in charge of providing recommendations regarding the risks and benefits of a certain vaccine through the transparent assessment of all available evidence on a national basis (ECDC 2015). One of the findings of the ECDC survey was that all 26 countries that participated in the study have a NITAG (21) or an expert group that is part of the vaccine recommendation process. NITAG's work allows for the informed evaluation of

immunizations, also taking into account effectiveness and budget concerns. NITAGS employ a great variety of structures, depending on their role within the State. Among them, 65% have an administrative office and 45% have their own website. As far as their research methods are concerned, 20 of them employ a systematic approach, that in 13 cases means that they have to follow a list of key criteria, and that in 15 cases using systematic literature review is required. It is a common belief that collaboration in the framework of NITAGs could be of great use, and despite the obstacles currently in place, most of them would be willing to collaborate.

1.7 Conclusions

Vaccination is internationally recognized as one of the most effective tools to reduce morbidity and mortality linked to VPDs. Vaccines are available to the majority of the population, and in the European Region health systems and immunization policies are strong.

Nonetheless, the number of outbreaks, and the rising levels of vaccine hesitancy among multiple countries of the Union make policy change necessary. Policymakers need to involve the population in the immunization process, making it a parent's prerogative. To do so, social, cultural, and economic factors that diminish trust in vaccines need to be understood and addressed through context-specific actions.

The risk of new future outbreaks in the European Region is high, and possibly there is also the threat of the reintroduction of diseases so far eliminated from the Region. This would jeopardize public safety, causing suffering and death.

In the next chapter the possible paths for change are going to be analyzed in the detail. The whole process, from the evaluation of the situation, to the perception of the issue, until the formulation, adoption, and implementation of policies will be studied, and applied to immunization policies.

CHAPTER 2 – Making Vaccination Policy

2.1 Policy and Policy making

Vaccines are part of a complex system, where interactions of different nature happen, including economic, behavioral, sociological, cultural, and political (Lee et al. 2016, A36-A37). Each one of these dimensions affects the success of policies, and neglecting even insignificant aspects of the matter can undermine the decision makers' efforts. In the vaccine framework not all cause-and-effect relationships are apparent, and their flawed assessment can lead to sub-optimal policies, causing waste of time, efforts and resources. As a result, to understand policy making in the matter of vaccines, the system has to be assessed as a whole.

To understand policies regarding vaccine plans and their variation over time, it is first necessary to understand the concept of policy. All government laws, regulations, decision, orders, and overall all statements indicating a course of action, can be considered policy (Knill et al. 2014, 336-337). Nonetheless, often one single action is not enough to be considered policy, but rather it is a set of decisions undertaken by the decision makers to obtain a certain goal. In particular, public policies are all actions with the objective of offering a solution to societal problems, and the introduction and modification of immunization plans is part of their scope. Immunization policies have the purpose of preventing contagion from vaccine preventable infectious diseases, and all their possible consequences, including death. Public authorities, civil servants or political leaders, both at the European and National level are in charge of implementing regulations about vaccinations, to safeguard public health. Most often vaccine policies are aimed at the whole population, but occasionally they could also be targeted to groups of unvaccinated individuals, like pockets of sub-optimal vaccination.

Over time policies have been thoroughly analyzed and classified on different levels, and immunization policies can also fit in such analytical typologies. First, taking into consideration Lowi's policy categories, immunization policies can be both analyzed on the basis of the likelihood, and applicability of coercion (Lowi 1972, 298-310). Accordingly, all policies that regulate vaccine uptake, on mandatory or recommended basis, at the National level, can be defined as regulatory policies. They rule and bind possible ways of conduct, imposing strict sanctions on individual deviant behavior, and they are legitimated by the protection of the common good. Moreover, immunization policies also shift resources from one actor, in this case the public health institutions, to another actor, the population. In case of deviance, the environmental conduct can be object of sanctions. What is at stake is in fact the distribution, by healthcare professionals, to the population, of goods purchased at the National level from pharmaceutical industries. As argued by Wilson (1973, 327-336), these categories can at times overlap, which made necessary to introduce new analytical tools to assess policy. Wilson (1973, 327-336) focuses further on the policies' costs and benefits, identifying four main categories on the basis on their level of distribution. Immunization policies are best represented by

majoritarian policies, as both the costs and benefits are distributed. The costs of vaccines part of the National Immunization Plan (NIP) are usually paid by Social Security, or reimbursed by health insurance.

Policymaking is characterized by multiple dynamics, such as constraints, the co-existence of multiple policy processes, and the cycle of decisions and policies resulting from their evaluation and following modifications. First, the presence of a significant amount of constraints is not uncommon in the process of policymaking (Knill et al. 2014, 338-339). In the framework of vaccinations, a significant amount of examples can support this statement. In fact, policymaking concerning vaccinations has to be developed taking into account both the limited amount of time, and the resources available. Policy needs to change in a limited amount of time in order to achieve the WHO goals by the established deadlines on one hand, as, according to the European Vaccine Action Plan 2015-2020 (WHO 2014), measles should be eliminated from the European region by 2020. Low vaccine uptake could be an obstacle to the achievement of such goal, and as a consequence the Institution's intervention is necessary. Moreover, policy cannot be delayed excessively, as the reintroduction of eradicated diseases, like polio, at the European level is a possible threat (European Commission COM (2018) 244/2). Low vaccine uptake could lead to the reintroduction of the poliovirus, undermining the EU's polio-free status, if no prompt action is taken. Budget constraints are also significant, and NITAGs are in charge of ensuring the best possible balance between vaccine safety and cost effectiveness regarding vaccinations introduced in the National Immunization Programme (NIP) (ECDC 2015). Other constraints and obstacles can derive from the public opinion. Mandatory vaccination has been strongly criticized by vaccine hesitant parents, and by groups that oppose vaccination, as it is perceived as a mean to repress the freedom of thought, and as a possible threat to children's health. Furthermore, when in Milan children were not allowed into school when they were not vaccinated, it was argued that their right to receive an education had been breached, and outrage in certain groups ensued (Corica and Venni 2017). Another dynamic common in policymaking is the coexistence of various policy making processes (Knill et al. 2014, 338-339). This is true also on the matter of vaccinations, as policy is developed on multiple levels. The European Commission issues recommendations, and prompts action at the European and national level, based on the ECDC's advice. National authorities have then the chance to shape policy according to their judgment, thanks to the subsidiarity principle. Last, regional authorities have to further devise action at the local level. Policies at the different levels can either overlap, or contradict one another, but possible conflicts are resolved by the existing institutions. One more feature that characterizes the decision making process, is the creation of an infinite cycle of policies and decisions. It shall not be forgotten that the policies in force today are the result of the evaluation of previous policies, that were over time modified. Current policies are not immune from this same phenomena, and evaluation will lead to future policies. The French case presented at the beginning of the first chapter exemplifies this phenomena. In fact since 1964 no new mandatory immunizations were introduced, and the number of recommended immunizations increased, because enforcing vaccination on a compulsory basis was not perceived necessary (Nicolay N. et al. 2008,

5848). Outbreaks were seemingly under control, and the vaccine uptake was satisfactory, so empowering the population was prioritized. Lately, France because of the increased skepticism towards vaccination has experienced a worrying number of outbreaks, and the levels of vaccine uptake were below satisfactory. As a consequence the new priority was to raise the number of mandatory immunizations (Yang and Rubinstein Reiss 2018, 1323). The process observable is similar to the trial and error, where evaluations of the previous policies shape the current ones.

The characteristics of policymaking, even in the framework of vaccination, allow for its conceptualization as a process or a cycle (Knill 2014, 336-337). Five main stages come one after the other. First, the assessment of previous immunization policies is going to be taken into account. At this stage the public and policymakers will evaluate the outcomes of previous policies, and a balance of their successes as opposed to their failures will be made. This step is usually considered last, but in this case it is going to be analyzed first, because in the design of immunization policies the circumstances at the beginning of the process are fundamental. The failure or success of previous actions, and the subsequent threat to public health, are the primary cause of further action. Being the analysis of previous policies so central, then it is necessary to analyze it first, to have a clear description of the genesis of new policies. The process of agenda setting follows, and the main issues are identified and introduced in the agenda. Then, as a result of negotiations, and expert recommendations, new policies would be formulated and, in some cases adopted. The new policies shall then be implemented at the National level. Then the results of such decisions would be once again assessed, leading once again to the evaluation stage. The cycle described is currently particularly relevant, as many States are in the process of re-evaluating their policies, whereas others do not have the need to do so. As a result each stage will be discussed in greater detail in the following paragraphs.

2.1.1 Evaluation

Vaccination has been identified as one of the main achievements of public health (Dubé 2013, 1763). All over the world, and in particular in the WHO European region, immunizations are the medical procedure that has saved the highest number of infant's lives (COM(2018) 244/2). Vaccine policies have allowed for the decrease of the incidence, the speed of transmission, and the risk of infection of VPDs (Dubé 2013, 1763). Nonetheless, over the European region there has been a resurge of VPDs, due to a lower vaccine uptake (ECDC 2017). In the last 10 years, there have been multiple VPD outbreaks, linked to under-vaccinated or non-vaccinated communities, and to a decreasing level of trust among the population about vaccines (Dubé et al. 2013, 1763). Outbreaks are likely to start in groups with sub-optimal levels of vaccination, where recommendations, for a multitude of reasons were not followed. Once exposed to antigens, such individuals, are infected (Datta 2017). Attitudes about vaccination are hard to categorize, as social, cultural, and political factors come into play, and are not successfully handled in every case (Dubé et al. 2013, 1763). The increase of VPD cases, the increased frequency of outbreaks, and the rising skepticism

about immunizations can be a signal of policy failure. Evaluation of the current policies is then necessary to prevent the reintroduction of eradicated VPDs, to limit the occurrence of outbreaks and possibly avoid future pandemics.

Efficient immunization policies, aimed at improving vaccination coverage and equity, are necessary in a strong and well-functioning health system (WHO 2014). The main objectives of immunization policy are to control the spread of VPDs, and to safeguard public health. Outbreaks shall be controlled and possibly avoided, and vaccine hesitancy should be kept to a minimum. The characteristics of the ideal policy framework are mainly six, and their effective implementation will make the achievement of the initial goals possible. First, both strong political commitment to the cause, and a strong community demand for vaccines are necessary, in order to ensure vaccine uptake. Second, the needs of the population should be catered by tailored immunization programs, as each social group can face circumstances that require a specific response. Third, funding needs to be predictable and sustainable to ensure reliable supply, and support the research. Fourth, immunization information systems' efficiency shall make possible the assessment of the current vaccine uptake among the population. Fifth, NITAGs shall be supported, in order to allow for evidence-based decision-making. Last, healthcare professionals need to be skilled and engaged in the implementation of immunization programs. The situation, that strongly varies based on the geographic location, does not always live up to these ideal standards.

In some regions, community demand for immunizations recently decreased, due to doubts about safety, efficacy, and necessity (Larson et al. 2016, 299-300). Vaccine hesitant views, often echoed by the media, and especially mass media (Meleo-Erwin et al. 2017, 1895), are more common among the population. Doubts about the balance between risks and benefits are frequent, and the information provided by the institutions, according to the rules in force, does not always mitigate them. As the percentage of people that mistrust or avoid vaccines increases, policies in force did not successfully stimulate vaccination uptake. Both policies, based on the recommendation, and the mandatory principle, have proved to have faults. Mandatory immunizations are perceived by the population as more important (Lévy-Bruhl et al. 2018), and harder to deviate from, yet they do not guarantee the wanted level of uptake. Exemptions can be granted on different basis, and their amount can increase, as happened in the U.S. (Omer et al. 2009, 1982-1983). Still, in some contexts, recommended vaccinations are perceived as optional, and easily avoided (Lévy-Bruhl et al. 2018). Informative channels devised by policy were not effective, and often policies were inefficient.

In particular, the inefficiency of the policies in place can be proved by the being of sub-optimal immunization pockets (Datta 2017), as not all social and cultural groups are properly reached. Outbreaks can start in these contexts, and then spread to the rest of the citizens. The pockets' existence could have been prevented if the policies in place had efficiently tailored intervention on all of these communities. Yet, the data shows that the lack of specific consideration of these social groups, and their specific needs, in the

policy framework threatens both herd immunity, and the progress towards disease elimination (Dubé et al. 2018, 1509).

Funding for vaccination is relatively low when seen in the context of healthcare budgets, and a disinvestment in immunizations is noticeable (COM (2018) 244/2). This aspect of policies concerning immunization can be argued to be not optimal, due to the consequences it carries. A limited budget, in contexts where demand is unpredictable, can prompt decisions that can lead to an undervaluation of the actual need for vaccines, and subsequent shortages. Furthermore, a low level of funds hampers research, limiting the range of new and more efficient products produced. Both of these consequences in turn affect vaccine uptake, given that they lower availability, and safety expectations.

Immunization information systems (IIS) are tools that can provide access to immunization data through confidential, and population-based databases (ECDC 2017). IIS can allow for the assessment of the different levels of vaccine uptake, and the subsequent configuration of possible responses. At the moment, a significant amount of countries are still piloting, or do not have such systems in place. The main obstacle in the way of their full implementation, and possible developments, is a lack of sufficient funds. As a consequence, human resources and technological developments cannot be sustained. Their support is vital in the process of surveillance, and when outbreaks need to be faced (Lochlainn et al. 2017, 5832-5833). The challenges that policies have not managed to tackle yet, are most likely a factor that favors future outbreaks.

NITAGs are also possibly affected by sub-optimal policy making. NITAGs are bodies that provide evidence-based guidance to policymakers and national authorities, thanks to their technical resources (Nohynek et al. 2013, 1099-1103). Policymakers can, at times, fail to create policies that allow closer synergies between such bodies. In fact, often literature reviews and evidence assessment, which are not country specific, are done by multiple NITAGs. This requires excessive efforts, that could be differently, and more efficiently addressed.

The interaction between healthcare workers, and their patients, is one of the basis of vaccine confidence (Dubé et al. 2013, 1767). The practitioner's confidence, and attitudes, have a determinant effect on the patients' choices, as shown by multiple studies. So far, in some cases, the healthcare professionals have issues trusting the government, health authorities, their guidelines, pharmaceutical industries and research (ECDC 2017). Moreover, some doctors have doubts on whether it is their responsibility to recommend immunizations. The healthcare workers' concerns described above prove that there have been some policy failures. Policymakers failed to act in order to cast away any fear about lacks of transparency.

The circumstances resulting from sub-optimal policy choices, in part described above, are not equally applicable to all countries. Each region faces its own different challenges that are introduced in the agenda.

2.1.2 Agenda setting

Agenda setting consists in the identification of a social issue that requires institutional intervention and is then introduced in the agenda by decision makers (Knill and Tosun 2014, 339-340). The reasons that are behind the choice of a particular problem can be different in nature. Usually four main actors are responsible of setting the agenda, especially on the matter of immunizations.

First, the elected public officials can set the agenda, which is later defined by the bargaining process and ideological conflict happening between the organs that have executive and legislative functions. The representatives of governmental institutions that can insert issues in the agenda concerning the current vaccine policies, or the levels of vaccine uptake, can both be members of National or International organizations. Public officials can bring the attention to the results of inefficiencies that make necessary a change in vaccine policies, and make proposals to address it.

Second, bureaucracy and bureaucrats can be agents in charge of agenda setting. Through passive legislation they have the power to influence the process of policymaking, yet they do not have enough power to impose their preferred choice. At the national level, healthcare facilities, healthcare professionals, and all other state officials in charge of delivering immunizations have an impact on immunization policies. Health facilities that administer immunizations might not be able, or interested, to internally address issues linked to the delivery of vaccinations, resulting in the creation of pockets of unvaccinated individuals among marginalized groups. The strict enforcement of certain requirements, such as the need for identification papers to access immunizations, or granting the permission for doctors to refuse patients, or the lack of effort to make healthcare culturally appropriate, are all factors that complicate access for marginalized minorities (WHO 2013) or newcomers (Wilson et al. 2018, 1060-1061). The role of healthcare practitioners, that in some countries of the European region are State officials, is central as well. The way in which they see their role influences the outlook that patients have on vaccinations. Some healthcare practitioners might not perceive that it is their duty to recommend immunizations (ECDC 2015), shifting the burden of choice completely to parents, allowing them to gather information where they deem most appropriate. Other healthcare practitioners believe that it is their duty to convince parents of the benefits of immunizations (ECDC 2015). These two different approaches will yield different behaviors among parents, having then an influence on the context in which policymaking takes place. Moreover, these behaviors by doctors can also affect the levels of coverage, and have an effect on the issue, even though they do not have decision-making powers. Similarly, the way in which institutions apply the regulations in place will affect uptake, coverage, and confidence among the population.

Third, mass media have a significant role in agenda setting, through the processes of priming and framing (Knill and Tosun 2014, 339-340). Priming is the influence that media can exercise through news coverage that changes the population's standards of evaluation on a topic. For example, publishing material in support

of the claims of vaccine hesitant doctors, or that supports claims based on insufficient or false data, make greater scopes of mandatory immunization seem like an issue. Similarly, if the media portrays the decreasing levels of vaccine uptake, and the increased possibility of outbreaks, then the public could identify a different problem. The data about immunizations, available to the population, will influence the identification of the societal problems to be addressed. Framing, on the other hand, concerns the connotations attributed to the issue. The portrayal of mandatory immunizations as an abuse in breach with citizen's rights, as opposed to the description of VPDs outbreaks as easily preventable, but life threatening incidents will lead to the introduction of different issues in the agenda.

Fourth, interest groups, groups of scientific experts, and groups that oppose vaccination, have the ability to introduce issues in the public agenda. The ECDC, as a European agency, is an independent source of scientific advice (EC 851/2004). Through its reports, and its data analysis, it has the responsibility to support the States part of the European Union in risk assessment. Its action, and recommendations, have a pivotal role in the identification of societal issues, and can influence the EU and the national agenda-setting. NITAGs, thanks to their reports, can inform the decision-makers at the National level of specific issues, and courses of action (Nohynek et al. 2013, 1097-1098). Their reports address the disease burden and their severity in the country, but also vaccine safety and efficacy, and they identify societal problems on the matter. Other interest groups that influence agenda-setting are communities that condemn vaccination through collective action. Anti-vax can attempt to shape the issues introduced in the agenda through mass media (Meleo-Erwin 2013, 1899-1900), public demonstrations (CorriereTV 2017), petitions (Casciano 2015) and even symposiums (ECDC 2017).

The issues identified nowadays, following the evaluation of current circumstances, are many and different in nature. One first societal problem identified are the frequent measles (ECDC 2018), rubella (ECDC 2018), and other VPD outbreaks. These outbreaks are significant, and need to be taken into consideration, because they endanger the population as a whole. To address this specific issue, more dynamics must be taken into account, and added to the agenda. To control outbreaks it is necessary to control low vaccine uptake, determined both by a high tax of vaccine hesitancy (Larson 2016, 299-300), and by the existence of population pockets (Datta 2017). This means that the factors that generate high rates of vaccine hesitancy shall be targeted. In addition, solutions that can mediate between the needs of specific communities and the necessity to increase vaccination rates within the community itself shall be designed (Dubé 2017, 1509-1510). Furthermore, outbreaks could be controlled through accurate and through surveillance (Lochlainn 2017, 5832-5833). To implement more effective information gathering, the investment in immunization information systems, along with incentives in favor of NITAGs' collaboration, shall be added to the agenda. To solve these issues, different paths of action can be identified, and are later on formulated.

The process of agenda-building described by Cobb et al. (1976, 126-127), as the translation of various demands by the public into items deserving of public officials' attention, can also be applied to immunization policies. In fact, issues with immunizations are integrated both by the formal, and public agenda. In fact, issues with immunizations are introduced in the formal agenda by international governmental bodies, such as the UN, through the WHO (WHO 2014), and the European Union (EC 851/2004), and at the National level thanks to the Ministries of Health. According to Cobb et al. (1976, 126-127), one of the central aspects in agenda building is how the population gains awareness, and later participates in the political conflict. As far as immunization policies are concerned, depending on the circumstances, the agenda setting has originated from political leaders' initiative, as well as from the general public. Over time, all the models of agenda building, as they were described by Cobb et al. (1976, 127-137), could be identified. Policies that diminished the amount of mandatory immunization, following public debates that supported the lack of need of compulsive immunizations (Nicolay 2008, 5484), remind of the outside initiative model. In fact, the issue was first supported by the population, and introduced in the public agenda. Decision makers subsequently decided to introduce the issue, as interpreted by the public, it in the formal agenda. In the case of policymaking in favor of mandatory vaccination a common case scenario is the application of the mobilization model, and of the initiation model. Issues concerning immunization policies, can be introduced in the formal agenda by policymakers. Then, in some cases, the issue needs to be transposed in the public agenda for successful implementation. In other cases groups, like NITAGs, can prompt government action and exclude the public from the stages of agenda building and policy formulation. This sequence of actions is better described by the inside access model (Cobb et al. 1976, 132-133). The two models can also be combined over time. For example, the inside access model can be followed by the mobilization model. Policymaking concerning mandatory immunization can start from the collaboration between expert groups (ECDC and NITAGs), excluding the public. Then, the public is introduced to the issue, to its interpretation and to the modes of action. Public inclusion is fundamental to increase the levels of vaccine uptake. For its successful implementation the public needs to be committed in the issue. The circumstances change deeply based on the country and the historical period, so there is not common pattern that can be identified.

Once the issues are identified, and the agenda has been built, feasible courses of action have to be identified to solve the issue. This phenomena is described in the following stage, policy formulation.

2.1.3 Policy formulation

Policy formulation is the stage that follows agenda setting. This phase involves the elaboration of the possible viable alternatives of action, through negotiation, in order to address the issues identified in the previous stage (Knill and Tosun 2014, 340-341). In case an issue concerning vaccination arises, such as low levels of coverage, recurrence of outbreaks, or widespread public unrest, there is the need to design solutions

that are most likely effective, and applicable in the National context. To do so, the different expert groups, interest groups, legislative committees, and specials commissions need to cooperate.

In the formulation of immunization policies all stakeholders play a role. Stakeholders are a wide variety of actors. First, individuals and communities participate in policy formulation through their participation, both in debates about immunizations, and in their delivery process, as well as through their demands of safe and effective vaccines (WHO 2013). Then, also the Government and providers of immunizations are also considered stakeholders (WHO 2013). They participate in the negotiation process, and development of new policies, through dialogue of manufacturers, other stakeholders, and experts groups. Healthcare professionals also have a role in the design of new vaccination policies (WHO 2013). Their duty is to provide high-quality immunization services. They engage in the assessment of inefficiencies within the immunization services, and they are in charge of engaging in dialogue about vaccination (WHO 2013). The academia has the role pursue multidisciplinary research. By doing so, it provides for evidence-based data, that allows to provide information essential for policymakers. Immunization policy formulation, both at the European and National level, is also influenced by the action the expert groups (ECDC, NITAGs, EMA), interest groups (anti-vax), and of course stakeholders as well, because they often have the skills and time that ministerial departments lack. The ECDC, EMA, and NITAGs are groups made up of experts that through risk assessment, literature review, mathematical models, and economic evaluations, can recommend different courses of action. They engage differently, according to their capabilities, and functions in negotiation, and possibly cooperate with national or supranational authorities. They often cooperate in the assessment of policy formulation with the National Ministry of Health, and with international bodies (Nohynek et al. 2013, 1097-1101). The duties of global agencies, such as the WHO, UNICEF, and the World Bank, are multiple (WHO 2013). First, they shall promote healthy immunization practices by designing guidelines and action plans based on scientific data. Then they also strengthen infrastructures, and mechanisms, at the national and international level. Third, they should also promote the idea of sustainable funding, or innovative funding mechanisms, in favor of immunizations. Vaccine manufacturers are also involved, as they participate in the discourse about sustainable access to immunizations with other stakeholders (WHO 2013). Development partners, such as foundations, and philanthropists, can support the regional entities to improve immunizations. Nonetheless, they do not only provide funding, but they also participate in international advocacy (WHO 2013). Last, civil society, media, and the private sector are three additional stakeholders, that have a profound impact over policy making. These actors advocate in favor or against vaccination, depending on their beliefs. All the stakeholders described participate, and negotiate, according to their functions, and their powers to policymaking. Their synergy is at the basis of the formulation of policies.

Multiple possible solutions can be designed for the societal problems described above. Still, not every course of action is equally applicable to every scenario.

Some experts may see mandatory vaccination as a viable option to address the issues identified in the stage of agenda setting, such as low coverage, possibly due to high rates of hesitancy. Compulsory immunizations are seen as a possible solution to low vaccine coverage, and reluctance, or unwillingness to comply with immunization policies, because they force the whole population to abide to the norms deemed most appropriate to safeguard public health (Haverkarte et al. 2010). In fact, making vaccinations compulsory allows, in case of deviance, to enforce sanctions of varying gravity. These measures give significant powers to the institutions, and the possible repercussions are seen as an effective deterrent. Mandates can be seen as a risky action, as there is the fear that the anti-vaccination movement will increase their resistance (Lévy-Bruhl et al. 2018). Still, mandates can also be intended to be a temporary policy, whose goal is to restore confidence by demonstrating that immunizations are of such high priority that even the State becomes involved (Lévy-Bruhl et al. 2018). This kind of policy is not immune to deviance. In fact, usually exemptions are granted, and parents can exploit them to evade the intrusion of their personal rights (Lee and Robinson 2016, 663), possibly jeopardizing the positive effects of policy. Accordingly, it is necessary to implement other policies that can increase the population willing commitment to mandates (Opel and Marcuse 2013, 2672). Such policies have been deemed feasible, even if they were not always adopted, as possible solutions in multiple States, such as France, Italy and Romania, between 2017 and 2018.

Tailored immunization programmes (TIPs) are a type of action whose objective is to tackle low coverage, and hesitancy, in specific communities. The tailored approaches are based on the identification of the characteristics of the group that is being targeted, in order to diagnose the causes of low uptake (Dubé et al. 2017, 1509-1510). After a first stage in which a diagnostic interpretation of the issue is made, the intervention has the main goal to prompt community engagement. This approach is based on in-depth understanding, trust building, and not on coercion. The focus is on educating the population on the importance of vaccination, by organizing seminars, by providing tools to health practitioners to improve communication, and by providing material dense with evidence-based data (Lindstrand n.d). These programmes are based on the informed cooperation, inclusion and participation of the subjects (Dubé et al. 2017, 1513-1514). The WHO actively endorses and supports such practices, and it has been a key actor necessary for the successful implementation of TIPs. These policies have been deemed feasible in multiple occasions. In Sweden TIPs became necessary to tackle the approaches to immunizations by both Somali, and Anthroposophic communities (Lindstrand n.d). In Bulgaria, this approach was made necessary by the occurrence of measles outbreaks among the Roma population between 2009 and 2011 (Dubé et al. 2017, 1511). In Lithuania, TIPs targeted pregnant women, as influenza vaccine uptake was significantly low (Dubé et al. 2017, 1511). What all these cases have in common is that a single community was targeted, due to its opposition to uptake. This method is usually applicable to communities of limited size, in which conducting qualitative research, that allows to understand the deepest reasons that explain low vaccine uptake is possible.

Also the immunization information systems (IIS) are seen as a useful tool to face low levels of coverage, that could be easily implemented and empowered by policy. IIS are computerized databases that record all immunization doses administered by registered providers in a given area (ECDC 2017). These systems are confidential, and population-based. Their use is central in monitoring and surveillance, and allows to monitor the levels of coverage. Having access to immunization information on a geographic basis allows to improve the performance of immunization programmes, by identifying the areas where coverage is lowest. What makes the implementation of policies that support IIS extremely feasible, is that they make access to data easier, and allow policymakers to effectively address issues concerning low vaccine uptake (ECDC 2017). In Europe, the Netherlands has successfully implemented this method to face measles outbreaks between 2013 and 2014 (Lochlainn 2017, 5829). The information system allowed for a targeted outbreak intervention, targeting 29 of the municipalities with low vaccination coverage.

Another set of policies that can address low coverage is the implementation of NITAG collaboration. Many NITAGs argue in favor of increased cooperation. Sharing studies made at the national levels, about safety, immunization confidence, and effectiveness, can be useful even in other national contexts (ECDC 2015). In the international context the possibility to increase collaboration through policy is seriously taken into consideration, though there are obstacles to be overcome. The three main factors that are an obstacle to the application of this kind of policies are the lack of expertise and resources, the cultural and linguistic differences, and structural incompatibilities (ECDC 2015).

Policy formulation can be limited by technical or political constraints of state action. Technical issues are related to the formulation of the policy, and its compliance with formal and constitutional requirements. In the case of immunizations, political constraints to policy decisions, on the other hand can be both substantive, and procedural. Substantive limits are related to the societal problem in its nature, whereas procedural issues are linked to possible institutional and tactical constraints. For example, mandatory immunization policies have often been opposed on the basis that they limit the individual's freedom of choice, and possibly infringe the right of children to receive an education. In this case the issue is technical as the policy's constitutionality is in question. Tailored programmes could be countered due to their excessive specificity, and lack of cost-effectiveness, that can be classified as procedural obstacles. Concerning both investment in NITAGS, or IIS, that would allow for their further development, objections could be made on the basis of the costs that would need to be faced, which once again could be classified as a procedural barrier.

2.1.4 Policy adoption

In the framework of policy adoption, the bodies that have a predominant role are government institutions (Knill and Tosun 2014, 341). In fact, NITAGs and the ECDC, as well as the other stakeholders, can have a role in the identification of the issue, or in the policy formulation itself, but they do not have the power to adopt policies.

Moreover, not even the European Union can impose policy decisions, due to the subsidiarity principle, according to which it is the State's responsibility to design the National immunization policy (COM (2018) 244/2). Still, International actors, such as the WHO, and the European Union can stimulate action at the national level through recommendations and action plans, to which States can commit. National commitment can be binding, and then make necessary policy change.

The factors that can determine the success of a policy over another are both the necessity for political and public support, and the allocation of competencies (Knill and Tosun 2014, 341). Majorities are necessary for policy approval, so party affiliations, constituency interests and public opinion gain significant relevance. Broad party affiliations make the approval of a policy more likely as it will be endorsed by a greater number of actors. Also, for immunization policies there is the need for widespread of political support, otherwise the policies formulated could be just be rejected.

Considerations about the constituency ideological stand might lead policymakers to prefer solutions that yield a lower amount of benefits for the population, in other words it can result in the approval of sub-optimal policies (Knill and Tosun 2014, 341). Strong anti-vax demonstrations could, as a matter of fact, slow down, or prevent, policies that enforce mandates. Policymakers could fear going against their constituents' values, in fear of having to pay a political price, and possibly lose public support. Still, the laws that have not been adopted because of fear of the public reaction could have been necessary to prevent outbreaks, but were still undermined. For example, in Romania the ProVita movement has caused delays in the approval of mandatory vaccination legislation, and made necessary to re-formulate it multiple times (European Forum for Vaccine Vigilance 2018).

2.1.5 Implementation

This stage of the policy cycle describes how new regulations are translated into practice. Implementation of policies can be described according to three main models, depending on what body controls the policy's implementation (Knill ans Tosun 2014, 341-342). The models are a useful tool to gain a clearer insight on the specific dynamics concerning immunizations. Immunizations policies can be enforced by institutions concerned with policymaking, in different ways. Vaccine policies are established by policymakers, but their implementation can be a responsibility, either of the policymaker, or it can be one of the duties of local functionaries, who do not have decision-making powers. The implementation of vaccine policies does not only possibly include mandates, but it also concerns the management of vaccine stocks and the delivery of vaccines themselves. Implementation is an essential step as it translates the whole process of policymaking in real life.

In top-down models policymakers are the ones that establish policy objectives, and they are also in charge of implementing them. A real life example, is when mandates allow for legal prosecution of the parents on the

basis of child mistreatment, and, or endangerment (Yang and Rubinstein Reiss 2018, 1323). The courts are a locus of policy making, and they can set precedents, that can be binding from that moment on. Their action is also necessary for enforcement, just as much as for policymaking, because their intervention in case of deviance allows to deter parents from refusing vaccination. This is a reality in France, since 2018, when the immunization policy changed, and criminal sanction are a possibility, even if they not yet enforced (Yang and Rubinstein Reiss 2018). In some cases, to enforce mandates, even the Ministry of Health becomes involved. In particular, in States such as Croatia, the pediatricians can report to the Ministry, that after an inspection can impose fines. Moreover, the government is in charge to ensure the efficient logistic management of immunizations, in order to allow for access in all areas. In these cases, in particular, it can be observed that the policymakers' action does not end with the approval as they are involved even in the implementation.

In other circumstances, the bottom-up model better represents the ongoing dynamics, as the bureaucracy delivers policy through negotiation processes within the institutional network. As a matter of fact the distribution itself of immunizations is not usually implemented by policymakers, but by regional functionaries, and in particular healthcare practitioners and nurses. It can be observed that vaccines, in Europe, can be usually accessed either through hospitals, Local Health Care Centers, Child Health Care Centers, or through the School System. Moreover Educational Facilities are in some cases responsible to collect vaccination certificates, or to report parents who refuse vaccination. In Italy, for example, immunizations are usually available at Local Health Care Centers, or in Vaccination centers (Decree Law 73/2017). Italian children need also to provide the school with proof that they have received vaccinations, and the school itself has to report to the Local Health Care Centers the data gathered (Decree Law 73/2017). In Sweden, children are administered immunizations through nurses of the Child Health Care Centers, or by school nurses (The Public Health Agency of Sweden 2016). In other countries, such as Romania, immunizations are distributed through healthcare facilities, by family doctors (ECDC 2015). In this cases the bottom-up model is extremely fitting, because policy is delivered and implemented almost exclusively by functionaries.

Concerning immunization policies in general, elements of both situations previously described come into play just as described by the hybrid model. Both the bureaucracy and the policymakers can be in charge of the implementation of specific aspects of policy. The courts or the Health ministries can intervene directly in surveillance, and coercion. Still, there is the need for the healthcare practitioners to perform the appropriate procedures. The most effective implementation of policy comes from the synergies resulting from the cooperation of both parties.

2.2 International sources that affect policy making - Role of the European Union

National commitment to improving the implementation of immunization policies is strongly influenced by International actors. In particular, actions by the WHO, and by the European Union prompt action at the local level, through recommendations and action plans. Their goals are to increase immunization coverage, in order to maintain the polio-free status in the European region, topossibly eliminate VPDs such as measles and rubella, and to safeguard public health.

In 2013 the WHO issued the "Global Vaccine Action Plan – 2011-2020", and it was followed in 2014 by the "European Vaccine Action Plan – 2015-2020", which is specifically concerned with issues of the European Region. These strategic frameworks have the objective to reiterate previous objectives, set new ones, and provide a description of the stakeholder's responsibility (WHO 2013). In particular, the European Vaccine Action Plan was crafted on the basis of the States' requests to facilitate the implementation of the Global Vaccine Action Plan (WHO 2014).

The commitment at the European level in favor of the improvement of vaccine coverage is clear. Both the proposals for strengthened cooperation against vaccine preventable diseases, COM(2018) 244/2, and COM(2018) 245/2, not only support the Vaccine Action Plans, but they also prompt State action in order to safeguard the population. The objectives of the Action Plans by the WHO are shared at the European level, and State action is prompted in favor of the implementation of more effective immunization policies.

Influence exercised by these international actors can be described, in part, as international harmonization (Knill and Tosun 2014, 345-347). The Member State's best interest is to cooperate, to yield policies that can effectively raise the rates of coverage, and to counter potential outbreaks. Nations depend on one another for the safeguard of public health, as if another European Nation fails, then there is the risk that outbreaks spread to the rest of the Union. To be able to live up to the commitment made at the international levels, some national freedom could be sacrificed. It has to be noted, though, that the principle of Subsidiarity makes coercion on the part of the European authorities unlawful (COM(2018) 244/2). Another framework, relevant in these circumstances, is the one of transnational communications. As opposed to the first model described, in this case the focus is on lesson-drawing, communication, and problem solving. Different Nations engage in transnational problem-solving, trying to emulate policies that have proven to be successful in other countries. Likewise, concerning immunization policies there are attempts to implement policies that have proven to be successful abroad. Even if the European Institutions support policymaking processes that can lead to the creation of positive externalities, though they do not actually focus on the implementation of similar policies. Immunization policies strongly rely on mediation by domestic policies, but their goal is to achieve the objectives established by the WHO, and the EU. Accordingly, the approach that can be identified on the topic of vaccinations is a middle ground between these two frameworks.

2.3 Conclusions

Policymaking in the matter of immunizations is extremely complicated, and it can be affected by the results of foreseeable and unforeseeable interactions. Nonetheless, it can be studied through the policy cycle model. This framework allows for the simplification of the process, and the focus on the subsequent stages allows to isolate the dynamics that take place, and identify the stakeholders involved. This allows the achievement of a greater insight in the issue.

What has also to be reminded in the assessment of the immunization policies are the influences of international actors. Even when the interventions are not coercive, they still prompt State action. In addition such bodies recommend courses of actions, that are implemented through mediated domestic policies. International institutions set the goals, suggest courses of actions, and prompt national commitments to the achievement of well-defined results. Accordingly, their action shall not be underestimated.

In the following chapter, case studies will be analyzed. Examples of courses of action, and national policies concerning mandatory immunizations in particular will be studied. The contexts, and responses at the domestic levels are described. Taking into account the circumstances, the applicability of mandates is evaluated on a case-by case basis.

CHAPTER 3 – Vaccination and Prevention: Four Case Studies

In this section four cases, and their National policymaking processes, will be analyzed. These cases are chosen because they all provide an interesting insight in the policy process concerning mandatory immunizations. In all cases policymakers had to find a solution, as outbreaks were occurring, or because hesitant communities demanded to change legislations. Yet, not all of the cases considered have proven to be a suitable setting for the introduction of mandates. This fact makes their study more significant, as it will bring to light what are the factors that make the application of mandates sub-optimal, or even not feasible. First, the Italian example will be addressed. In Italy the number of mandatory immunizations was raised from four to ten, after the occurrence of measles outbreaks and a significant drop in immunization coverage. Sweden is a country in which immunizations are all offered free of charge and on voluntary basis. To respond to the outbreaks happened in 2013, it did not resort to mandates, instead it implemented tailored intervention to address the obstacles that the communities with the lowest levels of coverage endured. The third case study is about Romania, that is since 2016 going through significant measles outbreaks (ECDC 2017). The Romanian immunization coverage is significantly below the standards imposed by the WHO, both because of low levels of uptake among the general population, due to widespread hesitancy, and because of the presence of a significant pocket of sub-optimally vaccinated individuals among the Roma population. It has not so far been possible to enforce the existing legal framework, or to approve new policies, in favor of mandates due to strong anti-vax communities. Last, the case of Croatia will be examined. In Croatia mandates have been steadily in force in the last decades, causing the almost complete elimination of most VPDs. Lately anti-vax groups have unsuccessfully demanded the Constitutional review of the legal framework in place, in order to substitute mandatory with recommended immunizations. In all the case studies an there will be a description, and an evaluation of the policy making cycle that took place, and its results, in the national context.

3.1 Italian case

The State, according to the article n. 32 of the Constitution of the Italian Republic, has the duty to safeguard health both as a fundamental right of the individual and as a collective interest, and also guarantees free medical care to the indigent. Specifically the law of December 23rd 1978 n.883 art. 6 rules State competencies regarding infectious diseases, including vaccination. After the Constitutional Law of October 18th 2001, n. 3, on the modification of the title V, second section of the Constitution, allocated to the regions the almost exclusive responsibility of organizing and managing healthcare services (Const L. 18 October 2001, n. 3). The State, on the other hand establishes the fundamental principles and the modes of action, as well as the essential levels of assistance that have to be guaranteed nationwide. Despite the State's action, this change has been the cause of regional heterogeneity (Bonanni and Ferro 2011). The National Health Ministry has four main duties concerning immunizations. First, it has the duty to ensure equitable access to healthcare services. Then, it shall ensure that the services provided are of equal quality. Third, it has to

ensure that the levels of vaccine uptake remain high. Last, it has to avoid outbreaks caused by a lack to central coordination. The National Immunization Plans have to be elaborated at the National level, and should be elaborated using evidence-based data, in respect of both Regional competencies, and European recommendations, that in turn are based on WHO recommendations.

In Italy vaccination was first diffused thanks to the actions of Luigi Sacco, who, in 1799, promoted the widespread usage of immunizations against smallpox in the cities of Milan, Florence, and Bologna. Following the success of his initiative, in 1888, the vaccine against smallpox became the first mandatory vaccination, thanks to the law Crispi-Pagliani (5849/1888). In 1939 also the vaccine against diphtheria became mandatory in the first two years of life (L. 6 June 1939, n.891). Similarly, since then new immunizations were introduced in the immunization plan. In the time period from 2000 and 2012, vaccine coverage remained high and stable. Some immunizations' uptake even increased, such as the one against measles, mumps, and rubella (MMR), or the one against Hepatitis B (Ministero della Salute 2018).

Between 2013 and 2016, on the other hand, vaccine coverage decreased by almost one percent a year, for both recommended and mandatory immunizations (Epicentro 2018). The situation was even more critical for vaccines against measles and rubella, whose coverage decreased even faster, at a pace of 1.1 percent a year (Ministero della Salute 2018). As a consequence VPD cases became increasingly common, but measles outbreaks had the most resonance. In 2017, 5,000 cases of measles were recorded in Italy, of which four resulted in casualties. Italy was the second in Europe right after Romania that counted 5,226 cases in 2018 (ECDC 2018). Among the infected the 88% was not vaccinated. Outbreaks also started in clinical contexts, as 315 cases occurred among healthcare professionals. This outbreak did not only have a significant human cost, but also had significant economic repercussions as 44% of the infected was hospitalized, and in 35% of the cases there were complications that required treatment. The costs of the services provided through welfare, hospitalizations, lost productivity and so on, are extremely high (Ministero della Salute 2017). It has been estimated that each euro spent on vaccination corresponds to four euros saved in case of infection. These outbreaks are worrying, for multiple reasons. First off, they endanger the whole population, including the individuals that need the protection of herd immunity. In fact 6% of the infected were children under the age of one, that were too young to be vaccinated. In addition, not only the national public health would be at risk, but being members of the European Union, and having considerable freedom of movement, also the other member states would be under threat. Their occurrence proves that the vaccination coverage in place is not sufficient, so, possibly, other VPDs', such as polio or diphtheria could occur once again, jeopardizing the efforts of the last decades. Furthermore, if no actions are undertaken, Italy would not be able to meet the goals of the Global Vaccine Action Plan, as the elimination of measles requires further efforts. Last, when preventive measures fail, the expenses weighting on the national budget rise. It was estimated that effective immunization policies, without taking into account vaccinations against polio and meningococcus, can allow the State to save 200 million euros (Ministero della Salute 2017).

One of the main causes that lead to lower levels of uptake is vaccine hesitancy. In 2016 a group of experts of the National Center for Disease Control and Prevention, conducted a study among parents of children 16 to 36 months old, to achieve a better understanding (De Mei, 2018). Concerning immunizations, the parents were classified either as in favor (83.7%), hesitant (15.6%), or against (0.7%) (De Mei, 2018). Safety was a concern in all groups of parents, and was identified as the main cause of refusal (38.1%), or interruption of the vaccination cycle (42.4%) (De Mei, 2018). Italian society has been characterized in the last years by increasing levels of mistrust, and the perceived credibility of the Institutions has also diminished. In a context in which the Internet can easily provide colossal amount of sources, of which not all employ evidence-based data, the Internet can become the preferred provider of information, and spread anti-vax material. During this last wave of hesitancy, it was observed that the level of trust changed with different levels of declared hesitancy. The 96.9% of the parents in favor of vaccination trusted the pediatricians as the most reliable source of information, as opposed to the 83.3% of the hesitant parents and the 45% of the parents against immunizations (Giambi et al. 2018, 779).

After an evaluation of the events that were taking place, policymakers and groups of experts included the following issues in the agenda. The societal problems identified were of course the low immunization coverage, that resulted in outbreaks, but also the high level of hesitancy that grew stronger in the current social context. There are various agents that contributed to the introduction of these societal problems in the agenda. First, the Group of Experts for Investigations on Vaccines, which is the Italian recommending body, even if it does not self-designate as a NITAG (ECDC 2015), along with the National Health Institute provided data and recommended action to the Ministry of Health. Moreover, the National Committee for Bioethics, invited the Government, the Regions, and the other institutions to take action, so that coverage optimal levels are restored, for both compulsory and recommended immunizations. Also the National Board of Physicians, Surgeons and Orthodontists took a strong stance on the matter, signing a document that reported the risks of misinformation and renovated their commitment to the deontological code, that confers them the ethical duty to safeguard individual and public health (Ministero della Salute 2017). Among them, the Professor, and healthcare practitioner, Roberto Burioni, started a fierce social media campaign against misinformation, and anti-vax stances, that often resulted in public discussions with members of the Five Star Movement (Grasso 2018). The model of agenda setting that could be observed, according to Cobb et al. (1976, 127-137), are a combination of inside action model and mobilization model. Expert groups supported the introduction of the societal problem discussed in the formal agenda, without including the public excessively. Still, after the introduction of the issue in the agenda the public was included, as successful immunization policies need public endorsement.

Accordingly, the negotiation that happened between expert groups, the government, interest groups and the different legislative committees, resulted in the formulation of Ministerial Decrees, later converted into Law 119/2017, and in the formulation of the National Immunization Plan 2017-2019. The Ministerial Decree of

January 12th 2017, whose object is to define and update the levels of essential assistance, redefined the healthcare services to which free access has to be granted to the whole population, that include all vaccinations of the immunization plan. Furthermore, the Italian National Immunization Plan 2017-2019 has been formulated and approved. This program is strongly endorsed by health practitioners and other experts, such as the National Health Institute, and the *Agenzia Italiana del Farmaco*, by the Regions, and also by the scientific communities most active in the field of immunization, like the Italian Institute of Hygiene and Preventive Medicine, the Italian Federation of Family Doctors, and the Italian Pediatric Association (Iannazzo and D'Ancona 2018). Its objectives are to lower the diffusion of infectious diseases, both at the community and individual level, as well as to harmonize immunization practices all over the Country, but also to ensure equal access to the safe and high-quality immunizations. The Immunization Plan does not only establish a schedule that targets all age groups, but it also sets the priorities for the immunization strategies that the Regions have to follow. The priorities of the plan, in line with the European Vaccine Action Plan, are the safeguard of the polio free status, the elimination of measles and rubella, and the promotion of free access, targeting action to reduce pockets. The elaboration of efficient communication strategies is also necessary in the fight against hesitancy. The plan regulates the terms of the vaccine offer as designed by the schedule, that shall be proactive and free, but rules in favor of interventions to promote optimal immunization practices. Last, it emphasizes the need for the implementation of stronger immunization information systems (*Anagrafe Vaccinale*), to improve surveillance, monitoring, and control of vaccination practices. Last, the Decree Law 73/2017, converted with some modifications in the Law 119/2017, made the ten immunizations included in the schedule free and mandatory for minors, from birth until sixteen years of age. Policymakers, when this Decree Law, and the following Law were formulated and approved under request of the Regions that wanted to enforce mandatory immunization for access to education facilities. The Law and the National Immunization Plan are not exclusive, in fact their coexistence facilitates the attainment of the objectives and priorities of the plan. An aspect of the Decree Law 73/2017 is that vaccinations are not mandatory only to access education facilities. The school has actually the function of a filter that allows to identify deviant families, as the Law is still binding upon children that do not attend classes. These policies, according to the National Health Institute still need to be complemented by strong communication campaigns that target the community and the individual.

Implementation of the new regulations in Italy can be well represented by a mixed model, which includes characteristics of the top-down and bottom-up model (Knill ans Tosun 2014, 341-342). In the first place schools have the duty to collect the documentation attesting the uptake of the mandatory immunizations as a prerequisite to admittance. In the meantime Local Healthcare Facilities (ASLs), and healthcare professionals are in charge of providing relevant information to the parents, administering immunizations, and monitoring the population's coverage. In order to prevent sub-optimal coverage pockets among newcomers, Italy administers vaccinations included in the National Plan to both adults and minors, no matter of the

immunization status, at holding and community level (Giambi et al. 2018). In case no immunization card, reporting previous vaccinations is available during the verification process, blood tests can be administered. ASLs are, in particular, in charge of having a dialogue with patients, informing them of the benefits of vaccination, and the risks linked to its avoidance. Furthermore, the data gathered at the local level is transmitted to the Region, with a maximum delay of 12 months, that in turn will transmit it to the Ministry of Health on an yearly basis. All these actions have characteristics of the bottom-up model, as the duty to deliver policy is assigned to the bureaucracy (Knill ans Tosun 2014, 341-342). Still, the policymakers, and the Ministry of Health in particular, are in charge of producing the informative material necessary for the awareness campaigns, designed by policies, to fight hesitancy. Their action has specifically been defined as essential for the success of mandatory vaccinations (Iannazzo and D'Ancona 2018). Moreover they have the role to coordinate the different bodies that are in charge of the implementation of the policy. Accordingly, it can be observed that elements of the top-down model are present as well, as a consequence the system can be defined as hybrid.

Implementing vaccination on a mandatory basis in Italy was necessary as there was the need for prompt action, given that epidemics were already taking place, targeting behaviors that were widespread to the whole population, and not limited to specific communities. Hesitancy in Italy coexists with a strong distrust of institutions. Tailored action on specific communities was not possible, but a quick response, that could have raised vaccine coverag was necessary. Vaccination mandates were a suitable measure as they limited the freedom of choice in order to contain the emergency. Nonetheless, they were not the only result of the policymaking process, as also increased communication with the patients was identified as a priority, and as the only mean to solve the problem on the long term. Formative material, about vaccines and communication strategies, was provided to healthcare practitioners. So far, the combination of these two factors has proven to be successful, as data for all cohorts for all vaccinations improved in 2017 (Ministero della Salute 2017). Coverage for the first measles vaccine dose increased by 4.42%, allowing the national average to reach 91,68% coverage. Also the anti-polio vaccine coverage improved, among children born in 2015 it rose by 1.2% since 2016 and the WHO threshold was almost reached. The final goal has not been reached, and further actions need to be taken, but so far the results should not be underestimated.

3.2 Swedish case

According to the Health and Medical Services Act of 1982, County Councils have the duty to promote the health of their residents and to ensure equal access to health care. In Sweden, according to the Communicable Disease Act (SFS 2004:168) infectious diseases need be covered by the National Vaccination Programme if the immunization against the disease respects three conditions. The vaccine shall effectively prevent the disease from spreading, it shall be socioeconomically cost-effective, and finally it shall be ethically and humanitarianly sustainable (The Public Health Agency of Sweden 2016). Four main stakeholders were recognized in the matter of immunization plans (The Public Health Agency of Sweden

2016). The government has the decisional power to choose which immunizations to include in the plan. The public Health Agency of Sweden is in charge of providing recommendations to the government about possible changes to complement the immunization programme, with supporting documentation. This body shall identify target groups, and formulate immunization schedules. The agency is also in charge of having clear communication with the public about the vaccination programmes. Another duty of this body is surveillance, by implementing vaccination registries, by monitoring coverage, and by recording the effects of vaccinations. The Medical Products Agency is a body in charge of both monitoring vaccine safety, as well as reviewing adverse reaction reports. Finally, County Councils and Municipalities have the responsibility to ensure access to immunizations, duty also taken over by school health services from the age of six. The delivery system consists of the nurses of the Child Health Centers, and later by school health nurses. All the nine immunizations of the National Immunization Plan are free and assumed on a voluntary basis. In case selective programmes to respond to specific needs are recommended, counties have the choice to follow the recommendation or not, and on whether to do it free of charge (The Public Health Agency of Sweden 2016). In case children are not up-to date with the immunization schedule, and did not start a vaccine cycle or not all the doses were administered, they are entitled to catch up vaccination programmes (The Public Health Agency of Sweden 2016). All information about immunizations are subsequently introduced in the National Vaccination Registry, that allows for surveillance and monitoring. Before the introduction of this informative system statistics were collected yearly.

In Sweden infectious diseases that in the past caused a great amount of deaths now are almost extinct. In 2013 the immunization coverage for diphtheria, tetanus, pertussis, polio and Haemophilus influenzae type b vaccines was over 98% (The Public Health Agency of Sweden 2016). The measles, mumps and rubella vaccine reached 97.5% of coverage and the pertussis vaccine reached 97% (The Public Health Agency of Sweden 2016). Over the last few years the percentages have remained stable. Nonetheless, some measles and rubella outbreaks occurred after the contact with people infected abroad. These phenomena brought to the surface the fact that in some areas vaccination coverage was lower, and that sub-optimal vaccination pockets were created. To have an insight about the issue, the Public Health Agency of Sweden piloted a Tailored Immunization Programme (TIP), and was supported by the WHO, the ECDC, the Karolinska Institute, the Department of Communicable Disease Control, the Stockholm County Council, and the Regional child preventive services, (The Public Health Agency of Sweden 2016). This qualitative study aimed at identifying barriers and facilitating factors for MMR vaccination. Parents, healthcare professionals and informants of previously identified communities, with low vaccination coverage were all included. The three populations under scrutiny were the Anthroposophic community in Järna, southern Stockholm, the Somali community in Rinkeby and Tensta, northern Stockholm, and the community of undocumented migrants.

The Anthroposophic community living in Järna, counts 7,000 individuals, of whom 150 were born in 2015. In 2012 there were a measles outbreak, that resulted in the infection of 16 individuals, and a rubella outbreak, that resulted in 50 cases (Lindstrand n.d). Among the Anthroposophic population the levels of vaccine coverage in 2013 were extremely low, mostly for mumps pertussis and rubella (MPR) vaccine, that at two years of age reached 40.3% of coverage. In this community context, natural immunity against measles is seen as a positive factor in the development of the child. Many members of the community are vaccinated before their adolescence, or before international travels.

The Somali community, established in the northern part of Stockholm, counts 35,000 inhabitants, of which 3,311 are children under five years of age (Lindstrand n.d). Overall the community is young, as the majority of its members are younger than 45 years old. The 90% of this population is of foreign origin, and the 30% has a Somali background. The low MPR coverage, that since the late 1990s is around the 70%, is caused by a strong fear of autism, also known as the "Swedish disease". Parents seek greater information on the balance between risks and benefits, that could be transmitted through existing and trustworthy networks, preferably in Somali language.

Outbreaks, even in a society where immunization sign up rates are extremely high, have to be introduced in the agenda. Being the issue mainly common among specific communities, it was necessary to target hesitancy and refusal in its original context. To do so, not only is necessary to identify the context in which vaccination uptake is the lowest, but there is the need to identify barriers and enablers to immunization. Then, evidence-informed responses to hesitancy have to be designed (Butler 2015, 4176-4177). It was not needed to insert in the agenda interventions targeting the whole population, as the overall available data about vaccinations was positive, and the current approach had been effective for the greatest majority of the population. This model of agenda building, as devised by Cobb et al. (1976, 132-135), mostly reminds of the mobilization model. The issue as soon as it was incorporated by the government in the formal agenda was transferred in the public agenda. The community affected needed to be made aware of the risks. The individual's understanding that their behaviors had to be changed for the public good was also central. The issue had to be identified by the public as well in order to efficiently promote the voluntary uptake of immunizations among the community.

The viable course of action that was designed, and approved by the government, was the application of TIPs. At the National level the policy approved promoted the facilitated professional dialogue between healthcare professionals and the public (Lindstrand n.d). Informative material on how to relate with the parents, on vaccine hesitancy, and translated ECDC material was provided. In addition, informative pages about VPDs, vaccine, and vaccine safety were updated. Another measure envisioned was to implement communication strategies about vaccines at the National level (Lindstrand n.d). Tailored messages to new young parents were implemented. Measures to identify pockets and attitudes towards vaccination were designed. Some

specific in-loco intervention were also carried on. Lectures, Motivational Dialogue Educational Programmes, Workshops on vaccines with nurses were held. Written, and reference heavy material, under the form of education packages, were provided. The information about vaccines was disseminated also through media, local NGOs, and even on a peer-to-peer basis, empowering the people that previously took part in the seminars (Lindstrand n.d). The implementation of these new policies happened at the community level. The TIP measures described have the goal to build trust and in-depth understanding, and mainly focused on individual behavior change (Lindstrand n.d). This approach can be most easily linked to the bottom-up model (Knill ans Tosun 2014, 341-342), as community level intervention, both for the administration of immunizations and for the educational campaigns, took place through the action of local officials and nurses.

Mandatory immunizations have not lately been considered as a necessity in Sweden. The most obvious reason for this choice is that the levels of coverage exceed significantly the thresholds established by the WHO. As a consequence, most of the diseases targeted by vaccines are not significantly in circulation (The Public Health Agency of Sweden 2016). The capillary access to vaccines, and the relationship with the nurses, makes them a commonly accepted measure among parents. Even in case of outbreaks mandatory immunizations are not a feasible solution. First, the outbreaks that have taken place in 2013 are not as widespread, and have not caused as many casualties as others that took place in other parts of Europe. In addition, the communities that have most difficulties to accept vaccines are easily identified, and can be targeted with interventions that specifically take into account their needs (Lindstrand n.d). By doing so, future outbreaks, taking place within such segments of the population, can be prevented by undertaking actions that increase the community's understanding about vaccines and about its benefits. For these reasons enforcing vaccinations through mandates, and so limiting the citizens' freedom, is not the optimal solution. First, vaccine accessibility and widespread acceptance make it unnecessary. Second, contexts in which pockets are formed can be most efficiently addressed through tailored actions at the community level.

3.3 Romanian case

In Romania the immunization program is under the responsibility of the Ministry of Public Health, that operates through the collaboration with the Centre for Prevention and Control of Communicable Disease, and the Regional Institutes for Public Health (Chichin 2006). Its duty is to set up the immunization schedule, and regulations, as well as to manage their organization and implementation. The immunization schedule is set at the national level, and applies to the whole country (Chichin 2006). In case of outbreaks, circumstances that would require a local response, it is the Ministry that takes the decisions, in collaboration with regional authorities. The 42 County Authorities of Public Health are in fact in charge of promoting immunizations. The four Regional Institutes for Public Health can conduct studies, about attitudes and practices concerning vaccination, among healthcare practitioners, or in the general population (Chichin 2006). Studies on the Epidemiological surveillance, and the evaluation of both coverage and the

introduction of new immunizations, is instead one of the responsibilities of the Centre for Prevention and Control of Communicable Disease. The National Medicine Agency is responsible of the marketing authorization and of the vigilance after having been marketed (Chichin 2006).

Measles outbreaks have been going on since 2016. Since January 1st 2016 until June 30th 2017 there were 7,491 cases, including 31 deaths (ECDC 2017). In 2017 alone 5,224 cases occurred (ECDC 2018), and in 2018 2,712 people were infected (ECDC 2018). The amount of the infected by measles in Romania constitutes the 43% of the cases all over the Union (Pop 2017). These outbreaks were made possible because of the low rates of coverage. In 2016 the coverage for the first measles vaccine dose was of about 86%, and of 76% for the second dose, when the WHO recommends a minimum coverage of 95% to prevent outbreaks (WHO 2018). The rates of coverage for other immunizations are lower too, as the coverage of diphtheria, tetanus and pertussis (DTP) vaccine reaches only 51% (Pop 2017). An overall trend of decreasing vaccine coverage is observable. The vaccination coverage of the DTP vaccine had a 21% fall from 2013 to 2015, when from 96% it reached 75% coverage (Pop 2017). Then it fell further by 2017, and it reached 51% coverage. Similarly, the first dose of immunizations against measles and rubella fell from 94% in 2010 to 86% in 2015 (Pop 2017). The coverage for the second dose of the MMR vaccine fell from 93% to 67% (Pop 2017). The levels of confidence and the modes of access to immunizations have worsened in the last years, making public authorities unable to stop or prevent outbreaks. These facts are extremely worrying, and can possibly endanger the Romanian people, as well as the whole people of the Union. There are three main contexts that jeopardize either access to vaccines, and suitable levels of uptake, that are going to be discussed.

First, the anti-vax propaganda, and the action of anti-vax groups, as well as religious organizations, all contribute to an environment of skepticism on the topic of vaccinations (Pop 2017). Anti-vax stands gained relevance since the introduction of the HPV vaccine (ECDC 2015). One of the main anti-vaccine supporters is Olivia Steer, a TV presenter and Romanian public figure, who also gained the support of the ProVita association and religious organizations (Iordache 2017). She opposes vaccines, as she alleges that they are useless and that their components can be threatening. Olivia Steer along with the whole anti-vax movement, fights for the parent's rights regarding the health of their children, and their freedom not to vaccinate (Iordache 2017). Healthcare practitioners perceive that the information about immunizations should be improved to inform the parents of the benefits of vaccination (ECDC 2017). Meetings focused on sharing knowledge about immunizations are held by healthcare practitioners (ECDC 2017). Still, even if the meetings were object of praise by the WHO, healthcare practitioners doubt that their actions can be sufficient, in the first place because the natural lifestyle is seen as fashionable, but also because the patients have more trust in what they read on the internet, rather than in what the doctors have to say (ECDC 2017). In the ECDC study (2017) that focused on hesitancy among healthcare workers, some of the subjects

declare that doctors lack the communication skills, and so far they are not achieving their objective to contain hesitancy.

Second, there is a serious issue concerning the Roma community, whose levels of coverage are extremely low. The Roma community accounts for the 3.2% of the country's total population (619,000 individuals), and it is the third largest ethnic group after Romanians (88.6%), and Hungarians (6.5%) (WHO Regional Office for Europe 2013). Even if the estimate of the Roma population present in the State is the highest of the last decades, it is still believed to be an underestimation. The European Commission acknowledged in 2003 the presence of a range of 1,800,000– 2,500,000 individuals, instead of the lower figures reported (WHO Regional Office for Europe 2013). This people is geographically dispersed, as they represent in all counties from 1% to 9% of the local population, but they are also culturally diverse. Still, on an economic side their situation is critical, as twice of the Roma, compared to the non-Roma do not have an income, and the majority of them rely on social benefits, inactive sources, and informal lucrative activities (WHO Regional Office for Europe 2013). Also, their access to education is not optimal, as 80% of the unschooled youth is Roma. This is significant in the matter of immunization for various reasons, as the 45.7% of Roma children do not complete the compulsory immunization scheme, and among them half have not received any vaccine (WHO Regional Office for Europe 2013). The limited access of this population to medical service is rooted in multiple causes. First, significant portions of the population do not have access to immunizations due to the absence of identity documents (WHO Regional Office for Europe 2013). Moreover, in the community lack of medical insurance can be an obstacle access to immunizations not funded by the National Health system, such as in the case of HPV vaccine. Prejudices also have an important role because family doctors' have the leeway to accept or deny patient enrolment, allowing for discriminatory practices in the medical system against a marginalized community (WHO Regional Office for Europe 2013). These dynamics are central when it comes to immunizations, as they increase mistrust towards healthcare practitioners, and they limit Roma's access to vaccinations. Low levels of coverage among the Roma community make them a pocket of sub-optimal immunization, and their marginalization makes the issue even harder to address.

Third at the national level access to immunizations can be a complicated issue. An ECDC study in 2017 showed that healthcare practitioners themselves have shown dissatisfaction with the Health Authorities practices. Vaccines were not supplied in time, or in sufficient amounts (ECDC 2017). In fact in Romania there are currently anomalies with the parallel vaccine exports (Pop 2017). In fact vaccines produced in Romania have low costs compared to the ones in the rest of the Union. As a consequence there could be high demand for them abroad, undermining the access within Romania. The lack of availability of vaccines can put healthcare practitioners in the position of having to send patients looking for immunization back. Then, the patient could possibly, having lost trust in Health Authorities, not come back at all. In addition,

according to the healthcare professionals interviewed by the ECDC, frequent changes to the immunization calendar negatively affect the public opinion, and institutions are not perceived as trustworthy, nor coherent.

The Romanian situation is critical these days, as they are perceived as a possible threat for neighboring countries and for the Union as a whole. The number of VPD cases and fatalities that occurred so far is the highest in the Union, and it needs to be taken into consideration for the public good. The issues of low coverage, vaccine pockets, and the unavailability of immunizations, shall be addressed in the agenda. To address widespread vaccine hesitancy among Romanian Nationals, vaccines should be portrayed as a mean to live a natural and healthy life (ECDC 2017). There is the need to fight against misinformation, and to spread studies full of evidence-based data, that can convince the population of the benefits of vaccination, and inform of the risks of VPDs. To address pockets, and improve the coverage levels, the Roma community should be granted easier access to vaccines. This is possible only if an effort to facilitate the integration of the community as a whole is made. To address the issue of availability, schedules should be kept stable, in order to stabilize productivity, and control parallel exports of vaccines.

So far, there are no mandatory immunizations, and the existing legal frameworks are not enforced (Pop 2017). In order to avoid vaccination only a signed form, stating the reasons behind such choice, is required (ECDC 2017). To solve the issues present in the agenda, mandatory immunizations have been considered before 2015. The formulation of this last policy greatly changed over time due to the pressures of groups that oppose vaccination. At the beginning, policymakers wanted to impose significant sanctions on parents, though the groups of anti-vax parents made the approval of such policy impossible (European Forum for Vaccine Vigilance 2018). Then, as a part of the policy, serious repercussions on the doctors that refuse to follow the immunization schedule were envisioned, yet several protests and the intervention of anti vax NGOs made it necessary to devise different solutions (European Forum for Vaccine Vigilance 2018). No final draft of legislation was formulated, nor accepted, so far in 2018. Other commitments undertaken by the Romanian government are aimed to solve the management system of immunization. The goals are to amend the existing legislation, so that the purchase of vaccines becomes transparent and predictable, and to build vaccine stocks for emergency situations (Jakab 2017).

Implementation of new policies that can address the issues reported in the agenda is not yet possible. Policies on mandatory immunizations, are still being formulated, and the existing legal frameworks that could be enforced are so far ignored.

The lack of a strong response in Romania has allowed the outbreaks to go on since 2016, causing several deaths. The decline of immunization coverage was not countered either, which also allowed for the spread of VPDs. Actions should be taken, and as Pop specifies in her report (2017). Mandatory immunization could have positive effects on the current trend, if sufficient attention is given to the details. Nonetheless a strenuous fight has to be carried on in this social context, as the anti-vax communities are strong, and they

hold significant negotiating powers. Their contribution to negotiations can mitigate the response to the VPDs outbreaks. Policies that enforce mandatory immunizations could also in a way help communities such as the Roma, by reducing the obstacles they have to face to access healthcare. Tailored interventions, that take into account the specific circumstances, would also be a suitable response. Romania is an example of a country where mandates are necessary to compel hesitant parents to vaccinate their kids. On the other hand, the power given to anti-vax communities makes the solution to the critical circumstances more complicated to achieve.

3.4 Croatian case

In Croatia a centralized system of vaccination is implemented, that clearly defines both the objectives and plans (Raguž 2015). A monitoring system of implementation, a surveillance system that keeps possible side effects under control, and an alarm system in case of delay or refusal that alerts the population, are in place. The Ministry of Health is the body in charge of designing the program of mandatory immunizations on a three years basis, and announcing the special implementation act concerning the immunization program yearly, following the recommendations of the Croatian National Institute of Public Health (Raguž 2015). In Croatia 10 vaccinations are compulsory, and they are purchased by the State free of charge (Tešović 2012, 152). Immunizations are funded by the Croatian Insurance fund (Raguž 2015). Vaccines, to be legally used, need a licensure by the Agency of Medicinal Products and Medical Devices, that certifies their safety, efficacy, and cost-effectiveness (Kaić 2007, 117). In the Croatian system, pediatricians have the duty to inform and recommend vaccination to their patients. In case of persistent rejection of vaccinations, after further counselling, parents are reported to the Sanitary Inspection Unit of the Ministry of Health, and fined (ECDC 2015).

The introduction of the first vaccines dates back to 1948, when immunizations against tuberculosis and diphtheria were introduced. The vaccine against tuberculosis has allowed a regressive trend since 1955, when the highest number of diagnoses was made since the end of World War II, and was only interrupted between 1991 and 1995 because of the Croatian War of Independence. In the time span from the early 1990s, until 2009 tuberculosis incidence decreased by three fold (Tešović 2012, 152). Since the introduction of diphtheria immunizations, there has been a positive trend in the uptake, that allowed for the elimination of the disease, as the last case happened in 1974 (Tešović 2012, 154). Despite this fact, it is necessary to maintain the levels of coverage high as the causative agent is still present among certain population, and a halt to diphtheria immunizations could possibly lead to its reemergence. Since 1955, until the beginning of the 1960s, tetanus (1955), pertussis (1959) and polio (1961) vaccines were introduced (Tešović 2012, 154-157). Nowadays the toxoids for diphtheria, tetanus and pertussis are administered in combinations, also known as the DTP vaccine. In the following decade immunizations against measles (1968), mumps (1976), and rubella (1975), were made mandatory, and are usually administered as a

combination, the MMR vaccine (Tešović 2012, 158-160). The fight against measles was particularly successful, as since the 21st century less than ten cases were annually reported, with no cases at all in 2007. Moreover, the level of 95% coverage for the measles vaccine, demanded by laws passed in the 1980s, was consistently exceeded in the early 2000s (Tešović 2012, 158). The last two immunizations that became compulsory were the ones against hepatitis b (1999), and the one against haemphilus influenza type b, that prevents bacterial meningitis. More immunizations are provided to at-risk groups to complement the action of mandatory vaccinations.

In December 2014 a measles outbreak begun (Raguž 2015). At the start the majority of the infected had come in contact with the disease abroad. As measles spread, the majority of patients did not have direct or indirect contact with foreign countries. The majority among them were unvaccinated or sub-optimally vaccinated. By the end of 2015 a total of 200 people were infected (Raguž 2015). Nonetheless, in the last few years a strong anti-vaccine movements rose. Their objectives are to abolish the obligation to vaccinate, and the fines following the failure to abide to the immunization schedule, for both parents and healthcare professionals (Raguž 2015). They also advocate in favor of equal access to nurseries and kindergartens for the unvaccinated, and the creation of a national forum for vaccination policy (Raguž 2015). The roots of this movement are to be found in the media influence, the publication of works based on inaccurate, incomplete or false data, and a failure on the part of the institutions and the practitioners to effectively communicate with the patient. The public, as a result, is afraid of the possible effects of immunizations, and distrust the Health institutions at varying degrees.

As a result, the issue of eliminating mandates entered into the public agenda. Given the fact that the issue was introduced in the formal agenda as a result of the people's mobilization, it can be argued that these dynamics resemble the outside-initiative model, as described by Cobb et al. (1976, 128-132). The fear of immunizations, and the decreasing levels of trust, allowed for the creation of civil initiatives that strongly oppose mandates. According to this segment of the population the policies in place limit the freedom of the parents, and of the people in general, to manage one's own bodies, and possibly cause harm (Raguž 2015). Given that mandates were perceived as a breach of the people's rights and as the imposition of practices that endanger the youngest, so they had to be addressed as a societal problem.

In order to achieve the goal of eliminating mandates, and introducing vaccination on the recommendation principle, the Constitutional Court of Croatia was demanded to review the constitutionality of compulsory immunizations. Such demands were based on the fact that there were conflicting regulations on the topic. On one side, both the Healthcare Act (1993) and the Patient Protection Act (2004), allow the patients to accept or refuse examinations, diagnostics, or other medical procedures. The Healthcare act guarantees the patients a wide set of rights (Babić-Bosanac 2007, 38-42). As far as information is concerned patients have the right to access accurate information and ask questions about their health and the procedures they should

undergo. Patients have the right to choose between treatments, and they have the right to refuse observation, or any other kind of procedure, and they have the right to change doctors as they deem necessary (Babić-Bosanac 2007, 38-39). In addition patients have the right to seek protection when they perceive that they have been violated, and the institution's officers have the duty to respond, and eventually they can seek help from relevant professional chambers or courts (Babić-Bosanac 2007, 38-39). The Patient Protection Act is adopted by Croatia in 2003, and incorporated in the national health legislation, following the Council of Europe Convention for the Protection of Human Rights and Dignity of the Human Being concerning the Application of Biology and Medicine of 1997 (Babić-Bosanac 2007, 40). This Act also allows the application of the provisions of the World Health Organization's Declaration on the Promotion of Patients' Rights in Europe of 1994. The promulgation of the Patient Protection Act was also due to recurrent media reports that emphasized the breach of patient's rights. According to Anti-Vax these two laws strongly clash with the Law on Protection of Population from Infectious Diseases (2007) and the Preschool Education Act (2013). This Law indicates what diseases are subject to prevention and control, and it bounds both healthcare professionals working in private or public institutions (Art. 4), and the whole population (Art. 7-8) to adopt all measures possible to protect people from infectious diseases. All individuals have the duty to allow healthcare practitioners to supervise the situation and adopt the measures necessary (Art. 7-8). The Preschool Education Act does not allow access to kindergarten unless children are vaccinated (Raguž 2015). Keeping into account the legal framework in force, anti-vax groups believed that a ruling of the Constitutional Court would have caused a change in policies that would have eliminated mandates. Such groups thought that the freedom to accept or refuse treatment for one's own child would have prevailed over both the Law on Protection of Population from Infectious Diseases and on the Preschool Education Act (Raguž 2015). On the other hand, the Ministry of Health argued in favor of the child's right to health, protected by Law on Protection of Population from Infectious Diseases and the Preschool Education Act, over the right of parents to freely chose, supported by the Healthcare Act and the Patient Protection Act (Raguž 2015). The Constitutional Court rejected to rule mandatory immunizations as unconstitutional (Patryn 2016, 2204). The Court argued that the parents' ideological stands about immunizations, and their freedom of choice is secondary, as opposed to their children's health that is of primary interest (Raguž 2015). The result of the policymaking process was the opposite of what was first envisioned by vaccine sceptic communities, still the process is going further. The Ministry of Health, and other institutions, are planning actions to support the pediatricians and fight against hesitancy (Raguž 2015). Despite the ruling of the Constitutional Court, hesitant parents could still find ways to avoid vaccinations, or they could still switch pediatrician if the first one was pressuring them to vaccinate their children (Raguž 2015). So, the Ministry of Health is preparing checklists to facilitate pediatricians to report refusals and report parents. In addition the Croatian Epidemiological Society has translated in 2015 guides to vaccination, written by the European Centre for Disease Prevention and Control (ECDC), in order to spread awareness (Raguž 2015). Additional support is provided by the Croatian Medical Chamber, which supports expert-based

recommendations to immunization programs, and provides assistance to colleagues exposed to criticism, due to the implementation of their duties (Raguž 2015).

The implementation of mandatory immunization policies in Croatia are similar to the hybrid model (Knill ans Tosun 2014, 341-342). Doctors, are in fact in charge of administering the vaccines and informing the parents, and dealing with the institutions, in case of parental deviance. This would remind of a bottom-up model, as the bureaucracy delivers policy within the institutional framework. Still, the policy makers become directly involved in case of deviance. The Department of Epidemiology at Public Health Institute is the first institution that comes into play in the first instance of refusal. Moreover the Ministry of Health intervenes in case of refusal through inspections, and imposes fines when necessary.

Mandatory immunization policies have been in force in Croatia for several decades with remarkable success. In the last few years there have been attempts to start policy cycles to dismantle the compulsory nature of the National Immunization programmes, yet they were unsuccessful. The reasons behind their failure are mainly three. First, the long tradition of mandates in Croatia have ensured the safety of the population for many decades, and among their evident successes there is the almost complete elimination of many VPDs (Tešović 2012, 150). If the results were not sufficiently convincing, part of the merit can be attributed to path dependence dynamics. The second reason is that the proposals to introduce vaccination based on the recommendation principle were badly timed. The proposals were carried on almost at the same time as one of the few measles outbreaks of the 2000s. This factor, and the presence of increasingly numerous sub-optimally vaccinated groups, most likely had an influence on decision makers. Third, policymakers, supporting mandates, had a strong support by institutions, and healthcare professionals. Widespread support is crucial in policymaking, and weakened the position of the anti-vax. It has to be noted that maintaining mandates have so far brought positive results. Croatia was one of the few European countries that in 2016 and 2017 has had no significant outbreaks of measles nor rubella (ECDC Atlas n.d). In particular, in 2018 in Croatia there have been zero cases of measles and rubella (ECDC Atlas n.d). It can be then inferred that, despite a period of widespread hesitancy, the policies in place are successfully safeguarding public health.

3.5 Discussion and Conclusions

All the cases have been chosen due to the peculiarity of their relationship with mandates. All States considered face different circumstances, that affect the applicability of mandatory immunizations. The comparative study of all cases allows for the understanding of what are the optimal circumstances in which mandates can be implemented.

In Italy, since 2016, there have been VPD outbreaks. In particular, in the peninsula the cases of measles were the second most numerous in Europe. The reasons behind these outbreaks were the insufficient levels of coverage, that in turn were caused by low levels of confidence in vaccinations, and in the institutions. To control the epidemic, and minimize the damages, a swift raise in immunizations uptake was necessary. Mandates were the most suitable solution, as persuading the population of the benefits of vaccines through informative material, without coercion, would have required undetermined lengths of time. Making immunizations mandatory would have obliged parents to vaccinate, despite their beliefs on the topic. The results available show that mandates have so far been successful (Ministero della Salute 2018).

Sweden in 2012 has experienced VPDs outbreaks, but in this case mandates would have been a sub-optimal solution. The levels of coverage exceeded the WHO thresholds among most part of the population. The outbreaks started from individuals that had been abroad, and then spread through pockets of sub-optimally vaccinated individuals. In this case, targeting such communities with tailored interventions would have been more effective then mandates. Limiting personal freedoms in a context where average coverage is so high is useless, and could be counterproductive.

In Romania in the last few years there has been the highest number of measles cases, and subsequent fatalities, in Europe. The levels of immunization coverage in the State are low, and there are as well pockets of sub-optimal levels of immunization. Hesitancy is a very widespread phenomena, and refusal is supported by multiple associations, and by public figures. Following the outbreaks, there have been efforts to introduce mandates, or to enforce the existing legislation. Still, all attempts have so far been unsuccessful, also thanks to the strong negotiating power of anti-vax communities. In this social context mandates are not applicable, because the policymakers in favor of such actions do not have the support necessary to proceed. Another obstacle is the marginalization of the Roma community. The presence of such pockets, even if mandates are implemented, would still allow for the diffusion of VPDs. Mandatory immunizations would then bound to fail.

In Croatia, shortly after a measles outbreak in 2014, the constitutionality of mandates was questioned, and the matter was brought before the Croatian Constitutional Court. Since the 1990s a strong immunization policy that strongly relied on mandates was in force. In the early 2000s these policies were overall successful. Though, anti-vax communities, when the ruling of the Constitutional Court was requested, had the objective to eliminate mandatory immunization. Still, the Court ruled in favor of mandates, as they safeguard the children's right to health. The support to mandatory immunizations can be traced back, both to dynamics of path-dependence, and to the occurrence of the 2014 outbreak.

The cases examined, and the existing literature, allow for the identification of the possible advantages and disadvantages of immunizations, depending on the context. First, the circumstances in which mandates can lead to positive outcomes are addressed.

Mandates are a coercive method, based on expertise concluding on an overall risk-benefit balance (Nicolay et al. 2008, 5492). They strip parents of their freedom of choice, and introduce possible sanctions, that can be a deterrent for hesitant parents who do not want to face the possible consequences of refusal. In Italy, the introduction of the requirement of vaccine certificates for school admissions has made it necessary for parents to vaccinate their children, in order to assure their access to school. Similarly, in Croatia, mandates do not allow access to unvaccinated children in education facilities, and they even impose fines to parents that refuse vaccination after counselling, which similarly forces parents to vaccinate.

Lévy-Bruhl et al. (2018) argues that mandatory immunizations are perceived differently. In fact, the government's commitment in enforcing mandatory vaccines persuades the population of their importance, whereas recommended immunizations are perceived as optional. Whoever is indecisive can be convinced to get vaccinated. The fact that the government comes to the point of coercing uptake raises the perception or risk linked to the disease, and it reassures the population of the safety and efficacy of vaccines (Lévy-Bruhl et al. 2018). This logic can also be observed in real life. Polio, which is usually mandatory, is perceived as dangerous and severe. On the other hand measles, which is usually recommended, is perceived as neither dangerous nor severe. Nonetheless, they can both be debilitating, and in some cases deadly.

Accordingly, mandates through coercion (Nicolay et al. 2008, 5492), and persuasion (Lévy-Bruhl et al. 2018), have positive effects, such as a decrease of refusal of vaccinations included in immunization programs, and as a consequence an increase in coverage. This was corroborated by the results obtained both in Croatia, and Italy. In Croatia, VPDs were kept under control for decades. Diphtheria was eliminated, the incidence of tuberculosis was decreased by threefold, and measles cases remained below ten a year, until 2007, when there were none (Tešović 2012, 158-159). Even the Italian case seems to prove further this statement, as after the introduction of mandates there has been a positive trend in vaccine uptake (Ministero della Salute 2018). Lee and Robinson (2016, 664) argued that mandates have different effects depending on the levels of uptake at the moment of their introduction. The trend they have observed is that, in populations where coverage is low at the moment of introduction will enjoy more significant effects, than populations where coverage is already high. Introducing mandates in Sweden, would not have the same effects as introducing mandates in Italy, as only a very low percentage of Swedish refuse immunizations.

Then, also the possible negative outcomes of mandatory immunizations shall be analyzed.

Limitations of freedom can be deeply resented by the people, that do not feel empowered to make their own choices. Anti-vax might even increase their levels of resistance once faced with coercion. Hesitant individuals, can be more motivated than before to opt out of mandatory immunizations through exemptions (Lee and Robinson 2016, 663). In fact, the abuse of exemption can be critical, as it allows for the creation of pockets, that will then undermine the efforts so far made. An example of increased resistance can be found in Romania. Parents are allowed to avoid vaccination only by signing a form explaining the reasons of

refusal. Moreover, the attempts to introduce policies about mandates are met with even stronger resistance, that does not allow for their approval.

Another fault that can be attributed to mandates is that they do not provide the necessary information to convince the population of the benefits of immunization, if not paired with other measures. Barbara De Mei et al. (2018) stress the importance of engaging with the patients to help them overcome the obstacles that make them refuse vaccination. De Mei argues that underestimating the communicative aspects does not allow the effective enforcement of mandatory immunizations. Following this stream of reasoning, the Swedish government preferred tailored interventions to mandatory immunizations. In fact, the average Swedish citizen recognizes, as shown by the levels of coverage, the benefits of vaccination. The issue of refusal was only relevant among certain communities, that with the advent of mandates could have taken advantage of exemptions in order not to change their behavior. Still, by providing scientific material, rich of evidence-based data addressing their fears, the members of these groups could actually be informed, and persuaded to change their conduct.

Another aspect that has a great impact on mandates is the presence of communities that cannot be reached, as there is no record of their presence, or as they are not registered as citizens. The existence of such societal groups allows for the existence of pockets, that undermine the mandates' achievements. Illegal immigrants, or individuals of the Roma community often do not have the identification papers necessary to access vaccination services. Factors as stigma, discrimination, or the fears of being reported to the authorities also diminish the likelihood that parents will actually persist in the search for immunizations. When these situations are not addressed then sub-optimally vaccinated groups do not only exist, but they cannot even be reached.

Mandatory vaccinations, are not applicable to all circumstances. In some cases, due to the socio-political context, they can be a solution, and in others they would be inapplicable or harmful. Their efficacy is context-dependent, and in order to take advantage of their features it is necessary to know in what situations they can be exploited at full potential. By knowing the circumstances that can be source of inefficiencies in the application of mandates, it will then be possible to choose the circumstances where their benefits outbalance their faults. Mandatory immunizations cannot be are not good or bad, but they can be an optimal policy when applied to the right circumstances, as well as a sub-optimal policy when applied in the wrong environment.

CONCLUSIONS

Immunizations, as already stated multiple times in this thesis, are recognized as one of the most effective tools to safeguard public health. Overwhelming evidence-based data, and the WHO itself, support the claim that immunizations have been one of the most cost-effective and successful medical inventions (WHO 2013). They have contributed, through the control of VPDs, to the reduction of child mortality, illnesses and disability (WHO 2013). Nonetheless, in the last few years, there have been recurrent outbreaks, that caused thousands of cases of VPDs, and even fatalities, all over the European region. The spread of VPDs was due to the decrease of coverage in the region, and to the creation of sub-optimal vaccination pockets. This phenomena was linked to rising levels of hesitancy, and the subsequent delay or refusal. This fact has the potential to jeopardize the efforts made so far at the European level, and at the global level. The goals of maintaining the European region polio-free, and the elimination of measles and rubella, could be compromised in the long run, if no efforts are made to maintain coverage at suitable levels. To solve the issue, action was undertaken both at the European, and the WHO level. The WHO designed both the Global Vaccine Action Plan (2013), and the European Vaccine Action Plan (2014) to prompt action by defining priority action areas, and set a course. The European Union also issued several recommendations to solve this societal problem, and stimulate member States to find solutions domestically. States, to live up to the commitments, have attempted to solve the issue through policymaking. One course of action, that has enflamed public debate, is the introduction, or further enforcement and support of mandatory immunizations.

When mandatory immunizations are in force, parents have the duty to vaccinate their children according to the vaccination schedules. Depending on the country, mandatory immunization policies require children to be vaccinated in order to be enrolled in school or childcare services. In case of refusal, sanctions, ranging from fines, up to criminal proceedings, can be enforced. Mandates are a coercive method; they limit free choice, based on what the risk-benefit balance is considered to be. This method strips parents of their freedom of choice, causing positive as well as negative, outcomes. Possible sanctions are a deterrent for hesitant parents who do not want to face the possible consequences of refusal, leading to higher levels of coverage. Moreover, mandatory immunizations are perceived as more important and safe than the recommended ones. The government's commitment persuades the population of their importance. In addition, mandates' effects are different based on what the levels of uptake were when introduced. When coverage is low at the moment of introduction, the results of mandates are more easily observable. Who might be indecisive about immunization can be convinced to get vaccinated, as the fact that the government comes to the point of coercing uptake, raises the perception or risk linked to the disease. Citizens are also reassured of the safety and efficacy of the vaccines. Still, mandatory immunizations are unpopular among the population, that is not allowed to make its own choices. Resistance among anti-vax can even grow stronger, to respond to what is perceived as an abuse. Another fault that can be attributed to mandates is that their aim is not to inform about the benefits of immunization, but force a raise in uptake. Nonetheless, the

engagement with the patients is necessary to let them overcome the perceived obstacles to vaccine acceptance. Underestimating the communicative aspects jeopardizes effective enforcement of mandatory immunizations, as the citizens will find ways to opt out. The presence of communities that cannot be reached, as there is not record of their presence, increases the threat of pockets, that undermine the mandates' achievements. Mandatory vaccinations are not applicable to all circumstances, but thanks to the comparative study conducted it is possible to observe when they can be effective, and when they cannot.

In Italy, France, and Croatia, mandates have been deemed necessary. In both France and Italy, the number of mandatory immunization has been raised. Also significance of sanctions in case of refusal has increased. In both countries, immunization policies relying on the recommendation principle did not prevent a decrease of coverage below the thresholds recommended, which led to significant outbreaks. Due to a multitude of socio-cultural factors, the levels of mistrust of immunizations had risen. These circumstances required swift intervention in order to stop the outbreaks, and reduce the risks for the population. Yet, convincing such great portions of the population of the benefits linked to vaccination, would have required a long process of uncertain lengths, and would not have ensured the safeguard of public health within reasonable, and certain timeframes. Then, mandates were necessary to achieve the desired coverage. Still, in order to successfully implement this kind of policies, political support was necessary. Otherwise the approval of such measures would not have happened. Furthermore, the intervention and commitment of interest groups, such as the scientific community, was necessary for the policymaking process in favor of mandates, but also to reach the population itself. In the case of Croatia, mandates had been an effective tool for decades, allowing to almost completely eliminate some VPDs from the area. Then, because of the significant results obtained so far, it would not have been wise to switch policies, in a moment of rising hesitancy and decreasing vaccine uptake. What all these cases have in common is the necessity for a solution, that sets public health as a priority, and allows to raise coverage. Mandates give policymakers the time to persuade the population of the benefits of immunizations, while at the same time protecting the population through coercion. These policies are especially important when policymakers, and institutions fail to convince the people to vaccinate based on their own free will. Mandates are adopted when it is believed that the short and long term risks for the public good outweigh the benefits of free choice. Nonetheless, the adoption of mandates requires political support and in a second stage also public support.

Political and public support are the keys for the success of mandates. Risks for public health, or recommendations by international actors, do not automatically lead to the adoption, or implementation of mandatory vaccinations. Threats and societal problems need to be identified as such in order to be addressed. Moreover, before that the identified societal issue is translated into policy, the stakeholders at the national level have to negotiate on how to address it. The difficulties that have come up in the institution of mandates in Romania are a clear example of such dynamics. Low vaccination coverage is the reason why Romania has had the highest number of measles cases and related fatalities. The low levels of confidence, and the

misconception about immunizations supported by the anti-vax community, have significantly slowed down the process of policymaking in this direction. Furthermore, the size of the anti-vax community is so significant, that it has to be considered in the negotiation process. In these circumstances, despite the rising number of the infected, the societal problem identified is not insufficient coverage, but the possible threats that are linked to adverse events linked to vaccination. As a consequence, when the policies in favor of mandates lack the support necessary, their approval, and effective implementation, are less likely to happen. Another aspect that would make mandates ineffective in Romania is the unaddressed existence of marginalized minorities, such as the Roma, that do not have access to immunizations due to their lack of identity papers. The application of mandates would then be inefficient, also because part of the Roma community do not have access to immunizations, and their status cannot be monitored. Sub-optimal vaccination pockets, of size similar to the ones found in the Roma community, would jeopardize the effectiveness of coverage, no matter if mandates were in place.

Even if mandates have proven in multiple occasions to be useful, and effective, they are not always necessary. In situations where confidence in immunization is high on average, outbreaks could still start in pockets of sub-optimal immunization, and then spread to other vulnerable individuals of society. Similar circumstances occurred in Sweden, when outbreaks among the Anthroposophic and the Somali community occurred. Among the rest of the population the levels of coverage exceed the WHO recommendation, and the delivery of immunizations is capillary at the community and school level. The bond that is built with the nurses, in charge of delivering vaccines, allows parents to ask questions when in doubt, and raises confidence in vaccinations. The only circumstances that led to the outbreaks were the creation sub-optimal immunization pockets among said minority groups. Still, given that the hesitant communities could be easily identified, it would have been more effective to understand what were the obstacles that compelled them to refuse immunizations. Imposing mandates on the whole population would have not been necessary, because the recommendation principle had proved to be enough to ensure optimal levels of coverage. Policies that strip citizens of their freedom to choose, when there are other possible solutions, and no serious threats are sub-optimal. In cases similar to the Swedish one, the empiric evidence shows that mandates are not necessary, as the immunization plan is already effectively implemented through the recommendation principle.

The policies that rule into force mandates cannot be defined as absolutely effective, or as absolutely unnecessary. These policies attempt to provide a solution to societal issues that rise in the different contexts. Based on the circumstances, mandates could be the ideal policy, as well as inapplicable, or sub-optimal. In order to establish whether mandates are a viable solution it is necessary to examine the domestic situation. Mandates are necessary when the levels of coverage are so low to endanger public health, and at the same time there are no feasible means to convince the population of the benefits of immunizations. Mandatory immunizations take advantage of coercive methods to safeguard the common good. It has to be remembered

that in some States the recommendation principle is sufficient to achieve the necessary levels of coverage. In such contexts, the population is already aware of the importance of vaccination, as shown by the uptake levels. In situations in which the population is already aware of the importance of immunizations mandates are unnecessary, and possibly harmful. In contexts where specific concerns, that have proven to be an obstacle to the achievement of the necessary coverage, have been identified coercion is not as effective as tailored interventions. Furthermore, mandatory immunization policies, in order to be feasible, need political, and community support for their correct and efficient implementation. Then, they shall also be applicable to the whole population to avoid the formation of unreachable pockets. Mandates are not a one fits all solution, but they can provide a solution to specific problems. Accordingly, an evaluation of mandates is only possible in its social, political, and cultural context.

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RIASSUNTO

In questi ultimi anni l'utilità e l'efficacia dell'introduzione, o del rafforzamento, delle politiche di obbligo vaccinale sono state oggetto di accesi dibattiti in molti Paesi Europei. Alcuni percepiscono l'inasprimento delle politiche vaccinali come un abuso nei confronti della popolazione i cui diritti non sono presi in considerazione. Altri descrivono l'obbligo vaccinale come una necessità al fine di tutelare la salute pubblica. L'obiettivo di questa tesi è descrivere le caratteristiche delle politiche di obbligo vaccinale, per poi cercare di analizzare su quali basi l'obbligo vaccinale viene introdotto e quali livelli di efficacia e applicabilità possono essere previsti. In primo luogo, viene fornita una descrizione delle circostanze che a livello Europeo hanno creato la necessità di rafforzare le politiche vaccinali e dei dibattiti in merito. Successivamente viene analizzato il processo decisionale che permette l'approvazione e l'implementazione di tali politiche. Per completare l'analisi, quattro "casi studio" sono presi in considerazione al fine di rendere possibile l'identificazione dei contesti in cui tali politiche hanno maggiore, o minore, successo.

I vaccini sono stati riconosciuti dall'Organizzazione Mondiale della Sanità (OMS) come una delle innovazioni più importanti nella storia della medicina. I vaccini sono preparati biologici composti da microrganismi uccisi, o attenuati, oppure da alcuni loro antigeni o derivati. Tali preparati possono inoltre contenere adiuvanti e conservanti; essi migliorano la risposta del sistema immunitario e preservano le proprietà del vaccino nei periodi di stoccaggio. I vaccini hanno permesso di proteggere la popolazione da malattie, disabilità e morte, permettendo ai giovani di condurre vite produttive e libere da malattie vaccino-prevenibili. L'incidenza di malattie vaccino-prevenibili è stata mantenuta sotto controllo e ne è stata ridotta la mortalità; i vaccini hanno permesso l'eradicazione del vaiolo e la pressoché completa eliminazione della poliomielite dalla regione europea (oltre che da altri Paesi). La somministrazione del vaccino permette di sviluppare una risposta immunologica simile a quella creata dall'infezione naturale; il sistema immunitario potrà quindi contrastare tempestivamente l'infezione. I vaccini non proteggono solo il singolo individuo; se la loro assunzione è pari o superiore a determinate soglie (specifiche per singole malattie) stabilite dall'OMS si può ottenere un fenomeno noto come immunità di gregge. Se la maggior parte della popolazione è correttamente protetta da una determinata malattia allora la malattia non viene trasmessa/non circola nella popolazione, e anche individui che non possono essere vaccinati non vengono infettati.

Negli ultimi anni ci sono stati molteplici focolai di malattie vaccino-prevenibili in tutta Europa. La diffusione di morbillo e di rosolia (e di altre ancora tra le quali, addirittura, di difterite) è dovuta all'insufficiente copertura vaccinale comune alla maggior parte d'Europa. L'insufficiente numero di persone immunizzate permette la trasmissione dell'agente infettante da un individuo all'altro e compromette l'immunità di gregge. In alcuni casi si formano dei gruppi in cui il livello di vaccinazione è assolutamente basso. Il risultato di questo fenomeno è la diffusione di malattie precedentemente tenute sotto controllo, potenzialmente mortali, che possono mettere a rischio la salute pubblica. La diminuzione nell'assunzione dei

vaccini, date le possibili conseguenze, deve essere indagata. Una delle maggiori cause della mancata vaccinazione in Europa è l'esitazione vaccinale.

L'esitazione vaccinale è alla base di molteplici fenomeni, quali l'indecisione, l'incertezza, il ritardo nell'adesione, fino alla riluttanza e al rifiuto nell'adesione. Causa dell'esitazione è la mancanza di fiducia nella sicurezza e nell'efficacia di determinati vaccini, o in chi li somministra, un'incorretta percezione della necessità ed ostacoli culturali o socioeconomici sono alla base dei comportamenti esitanti. La moltitudine di cause di esitanza rende la definizione di questo fenomeno complicata. Comunque, ci sono degli attori e delle dinamiche che hanno una rilevanza particolare. In primo luogo, il personale medico ha l'autorevolezza necessaria a influenzare le scelte del pubblico, in favore o contro le vaccinazioni. La loro formazione professionale li rende figure di riferimento in materia, ergo quando il personale medico ha a sua volta dubbi, i pazienti saranno ancora meno motivati a vaccinarsi. Come se ciò non bastasse, medici come Andrew Wakefield hanno ulteriormente contribuito a diminuire la fiducia nei vaccini, anche se in un secondo momento i dati dello studio in questione sono stati dichiarati fraudolenti. Nonostante ciò, gli Autori di simili studi hanno persuaso una grande porzione della popolazione e convinto molti individui a rifiutare le vaccinazioni; ogni attacco alle loro tesi viene visto (da comunità contrarie ai vaccini) come tentativi di insabbiamento. Altri fattori che hanno contribuito alla diffusione di comportamenti esitanti sono fattori culturali. In primo luogo, la diffusione di Internet ha permesso la diffusione di materiali non basati su dati scientifici e che possono alimentare il rifiuto delle vaccinazioni. Inoltre, la minore incidenza di malattie prevenibili e il fatto che in molti casi possano essere curate ha ridotto la percezione del rischio, portando a sottovalutare gli effetti delle complicanze di tali patologie. Un altro fattore culturale che ha un significativo impatto sui comportamenti relativi alle vaccinazioni è il fondamentalismo religioso. Comunità protestanti ortodosse, ebree ortodosse e antroposofiche presenti in Europa hanno tutte posto problemi a livello nazionale a causa delle loro convinzioni e la loro opposizione alle vaccinazione è ferma. La loro "prossimità" permetteva il rapido contagio agli altri membri della comunità. L'esitanza vaccinale è inoltre correlata al livello di istruzione degli individui e alla loro età. Altre cause di esitazione possono essere di natura economica. Il basso livello di fondi specifici contribuisce alla mancanza di rapidi sviluppi tecnologici nell'ambito dei vaccini e al miglioramento di quelli esistenti alimentando l'insicurezza della popolazione. Inoltre, l'instabilità della domanda di vaccini e i lunghi tempi di attesa per l'approvvigionamento possono creare ulteriori ostacoli al raggiungimento di una soddisfacente copertura vaccinale.

Istituzioni come l'OMS e l'Unione Europea hanno attivamente preso posizione in questa situazione di crescente esitazione e quindi di livelli inappropriati di copertura vaccinale e di protezione di fronte a specifici agenti). Nel 2013 e nel 2014 l'OMS ha pubblicato il *Global Vaccine Action Plan* e lo *European Vaccine Action Plan*, documenti che rinnovano l'impegno a favore degli obbiettivi relativi al controllo delle malattie prevenibili attraverso la vaccinazione. In particolare, a livello europeo si vuole mantenere lo status *polio-free* e possibilmente eliminare sia il morbillo che la rosolia. L'Unione Europea, tenendo in

considerazione i dati forniti dal Centro Europeo per il Controllo delle Malattie Infettive, e l'Agenzia Europea del Farmaco hanno redatto varie raccomandazioni al fine di raggiungere gli obbiettivi stabiliti dall'OMS ed evitare la diffusione di malattie infettive prevenibili attraverso la vaccinazione. Tali raccomandazioni non vincolano gli stati ad intraprendere determinate azioni visto che le politiche vaccinali, secondo il principio di sussidiarietà, è responsabilità degli Stati Membri. A livello nazionale i dati necessari allo sviluppo di politiche e le relative raccomandazioni vengono forniti da Gruppi Tecnici Consultivi Nazionali sulle Vaccinazioni che collaborano con gli organi decisionali, ed in particolare il Ministero della Salute. Stimoli, valutazioni, e raccomandazioni a livello nazionale ed internazionale, hanno un peso significativo nella formulazione di politiche vaccinali.

Alla base delle politiche vaccinali c'è un articolato processo decisionale che può essere analizzato nelle cinque fasi del ciclo delle politiche pubbliche. Il primo stadio da me preso in considerazione è quello della valutazione delle politiche precedenti. Questo è estremamente importante in quanto i risultati ottenuti fino ad un certo momento, positivi, o negativi, sono alla base delle fasi successive del processo decisionale. Le politiche vaccinali hanno lo scopo di porre rimedio a problematiche sociali che possono essere alla base di una copertura vaccinale insufficiente o della creazione di focolai epidemici e quindi rischiosi per l'incolumità della popolazione. Successivamente gli organi decisionali identificano le problematiche legate ai vaccini che vanno affrontate. Questa identificazione può essere il risultato di pressioni da parte della popolazione, gruppi di esperti, o altre comunità specifiche o, in altri casi, può essere stimolata dagli attori direttamente coinvolti nel ciclo delle politiche pubbliche. Dopo aver selezionato la problematica sociale sulla quale concentrare gli sforzi, attori di diversa natura collaborano alla formulazione di politiche che possono fornire una soluzione o sotto forma di riforme o di nuove politiche. In questo stadio è caratteristica la partecipazione di diversi attori che includono membri di diverse aree politiche, gruppi di esperti, personale medico e la popolazione stessa. I risultati di questo processo di negoziazione devono poi essere approvati dalle istituzioni governative, visto che altri attori coinvolti precedentemente non hanno potere decisionale. Va inoltre notato che non tutto ciò che viene formulato nella fase precedente verrà poi approvato. Successivamente le politiche approvate devono essere implementate attraverso l'intervento diretto dei *policymakers* o dalla burocrazia. Le nuove politiche vengono nuovamente valutate ed esse saranno la base di futuri cicli politici.

Ultimamente in vari Paesi Europei il risultato di questi cicli politici, per la diminuzione della copertura vaccinale e quindi per la comparsa di epidemie di malattie vaccino-prevenibili, è stato l'aumento del numero di vaccinazioni obbligatorie e, in alcuni casi, l'introduzione dell'obbligo vaccinale. Per testare l'efficacia di tali politiche, quattro casi studio sono presi in considerazione. Il primo caso preso in considerazione è quello italiano. Tra il 2013 ed il 2016 una significativa diminuzione nella copertura vaccinale su base annua ha permesso la ricorrenza di focolai epidemici e nel 2017 l'Italia è stata la seconda nazione Europea per numero di casi di morbillo. I livelli di esitazione vaccinale sono stati particolarmente alti negli ultimi anni e la

diffusione di malattie prevenibili ha richiesto una pronta ed efficace reazione. In risposta il numero di vaccini obbligatori è stato aumentato a 10 ed il "Piano Nazionale Prevenzione Vaccinale 2017-2019" è stato redatto. In questo caso l'introduzione dell'obbligo, fortemente supportata dalla comunità medica, era ritenuta "necessaria" per porre un veloce rimedio ad una situazione critica. L'Istituto Superiore di Sanità e il Ministero della Salute hanno riconosciuto la necessità anche di altri interventi volti a migliorare la comunicazione tra medici e pazienti riguardo le vaccinazioni. I dati disponibili, al momento, sembrano corroborare il successo di queste misure. Il secondo caso analizzato è quello della Svezia dove non è istituito l'obbligo vaccinale per nessun vaccino. In Svezia i livelli di copertura vaccinali sono tra i più alti in Europa sfiorando il 100% per il morbillo e l'incidenza di malattie vaccino-prevenibili è minima. La somministrazione avviene in *Child Health Centers* e nelle scuole in modo capillare. Gli unici focolai sono avvenuti in comunità antroposofiche e somale. Data la facilità di identificare le comunità esitanti e la possibilità di affrontare le loro remore con approcci qualitativi prendendo in considerazione le preoccupazioni specifiche dei singoli membri, non è stato ritenuto necessario adottare metodi "coercitivi" in una nazione dove i livelli di fiducia nei vaccini sono alti e dove i livelli di copertura sono significativi. Il terzo caso preso in considerazione è quello della Romania. Nel 2017 la Romania ha avuto il numero più alto di casi di morbillo in Europa a causa dei livelli di copertura vaccinale sotto i limiti consigliati. Le problematiche principali affrontate in Romania sono un livello molto elevato di esitanza vaccinale e la presenza di minoranze Rom per le quali l'accesso alle vaccinazioni è costellato di ostacoli. Posizioni esitanti sono molto pubblicizzate dai media e sono supportate da organizzazioni religiose e celebrità. Questa mancanza di supporto popolare ha ostacolato in maniera significativa l'introduzione di vaccinazioni obbligatorie al fine di limitare la ricorrenza di focolai. Inoltre, la mancata registrazione di individui di etnia Rom all'anagrafe non permette alla comunità di usufruire dei servizi vaccinale e non permette allo Stato di monitorare i loro livelli di vaccinazione. Questo fenomeno non permette l'efficiente applicazione dell'obbligo vaccinale in quanto ulteriori gruppi, difficili da raggiungere e di dimensione e identità non definita, potrebbero causare ulteriori focolai. L'ultimo caso è quello della Croazia. L'obbligo vaccinale è stato in vigore dalla fine degli anni novanta e ha permesso la diminuzione nella frequenza di varie malattie vaccino-prevenibili. Negli ultimi anni, gruppi di antivaccinisti hanno tentato di eliminare l'obbligo, in quanto incostituzionale a loro parere, ma senza successo. La Corte Costituzionale ha difeso la costituzionalità delle leggi che determinano l'obbligo vaccinale. Le politiche di obbligo vaccinale hanno funzionato per una decade e sarebbe stato rischioso abolirle in un momento di crescente esitazione.

Le politiche di obbligo vaccinale possono essere più o meno efficaci sulla base del contesto socio-politico. La natura di queste politiche è controversa e ha scatenato in molteplici occasioni un acceso dibattito, visto che riducono la libera scelta dell'individuo. La loro finalità è di salvaguardare la salute pubblica a costo di imporre determinate scelte. L'obbligo vaccinale è solitamente introdotto, o esteso, quando il principio di raccomandazione dei vaccini non è sufficiente e altri strumenti non sono stati efficaci nella prevenzione della

diffusione di malattie vaccino-prevenibili. La protezione della salute a livello nazionale non è necessaria solo per la salvaguardia dei cittadini residenti ma anche dei cittadini dell'Unione Europea in generale, messi a rischio dal libero movimento delle persone. I genitori sono obbligati a vaccinare i loro figli per iscriverli a scuola, al fine di evitare sanzioni quali multe ed in alcuni casi procedure legali. Le sanzioni, funzionando da deterrente, sono spesso efficaci nel convincere la comunità a rispettare gli obblighi legati al piano vaccinale. Inoltre l'impegno da parte delle istituzioni dello Stato nella lotta contro il rifiuto vaccinale aumenta la percezione del rischio legato alle malattie che si cerca di prevenire. Entrambi questi elementi permettono di aumentare la copertura vaccinale e quindi di prevenire l'occorrenza di focolai. Comunque è necessario un appoggio politico e sociale affinché tali politiche siano approvate ed implementate. L'obbligo deve essere accompagnato da un impegno continuo nell'informazione della popolazione sui benefici dei vaccini. Individui che sono contrari ai vaccini continueranno a rifiutarli, attraverso le esenzioni, se non convinti del contrario. Inoltre, l'obbligo non è applicabile in situazioni in cui parte della popolazione è marginalizzata. L'obbligo vaccinale non è una soluzione ad ogni problematica relativa alla vaccinazione, ma ha il potenziale comunque di porre rimedio ad alcune di esse, e pertanto va analizzato per essere sfruttato al meglio.