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Constrained Optimal Control Problem Applied to Vaccination for COVID-19 Epidemic

Hani Abidi ¹, Rim Amami ², Chiraz Trabelsi ³

December 13, 2021

Abstract

The model describes the epidemic dynamics of Covid-19 in a population after vaccination. Using the maximum principle, our goal is to prove the existence of an optimal strategy such that it minimize the number of infected people after vaccination. Finally, some numerical results are provided.

Keywords: Covid-19 Epidemic, Optimal control, Vaccination, Ordinary differential equations, Maximum Principle.

MSC Classification: 34H05, 49J15.

1 Introduction

Appeared in December 2019 in Wuhan, mainland China, COVID-19 very quickly turned out to be a serious health problem around the world, with catastrophic consequences for the evolution of humankind. Our modern world has never been confronted with a disease of such magnitude. All statistics data about coronavirus COVID-19 comes from World Health Organization, Johns Hopkins CSSE and worldometers. Charts include number of infected, deaths and recovered. Until December 2021, estimate around 270 million people have been infected, of which there are more than 5.32 million deaths.

There is now no medicine or specific treatment for the COVID-19, most countries had been relying on non-pharmaceutical interventions, such as wearing of face masks, washing hands and take care of personal hygiene, physical distancing and even more partial or total lockdown in order to curtail the spread of the disease. However, these measures have been not an effective protection to mitigate the pandemic globally. To bring this pandemic to an end, a large share of the world needs to be immune to the virus. The safest way to achieve this is with a vaccine. Within less than 12 months after the beginning of the COVID-19 pandemic, several research teams rose to the challenge and developed vaccines that protect from SARS-CoV-2. Until December 2021, 8.45 billion doses have been administered globally, and 56% of the world population has received at least one dose of a COVID-19 vaccine.

The study of the novel coronavirus has relatively attracted some importance in mathematical epidemiology due to its seriousness and the way it spreads worldwide. For instance, several models have been proposed to provide insight into the effect that inoculation of a certain portion of the population will have on the dynamics of the COVID-19 pandemic. The motivation of this study is derived from the work [2], who adopt a more modelling approach based on optimal control theory to determine the best strategy to implement until vaccine deployment. Therefore,

¹abidiheni@gmail.com, Faculty of Sciences of Tunis, University of Tunis El Manar, Tunisia.

²rabamami@iau.edu.sa, Department of Basic Sciences, Deanship of Preparatory Year and Supporting Studies, Imam Abdulrahman Bin Faisal University, P.O. Box 1982, Dammam 34212, Saudi Arabia.

³chiraz.trabelsi@univ-mayotte.fr, Centre Universitaire de Mayotte, 8 rue de l'université BP53, 97660 Dembeni, Mayotte, IMAG Montpellier, France.

in the present study, we incorporate the vaccination component to the model in [2], to derive an extended SEAIR model to examine the effectiveness of the COVID-19 jabs which are currently being deployed to many countries to help combat the raging pandemic situation. We first present in Section 2, the structure of our epidemiological model, precisely we present the equations and assumptions of the extended SEAIR model with vaccination. In Section 3 we introduce the objective function we optimise and derive the optimality condition. We use the penalty method to approximate this constrained optimization problem and derive an optimality system that characterizes the optimal control. In Section 5, we carry out numerical simulations using reported data on COVID-19 infections and vaccination in France and in Tunisia, compare these two countries in the face of the pandemic, and conclude with a summary.

2 The Model

The model describes the epidemic dynamics of Covid-19 in a population after vaccination. The model classifies individuals into principale key compartments of:

- Susceptible (S).
- Latent (E): infected but asymptomatic and not infectious.
- Asymptomatic infectious (A).
- Symptomatic infectious (I).
- Immune (R) or Death (D).
- Temporary protection vaccine (VP) which has two issues: Vaccine susceptible (VS) or vaccine immune (VR).

Figure 1 illustrates the different compartments for the model SEAIR with vaccination.

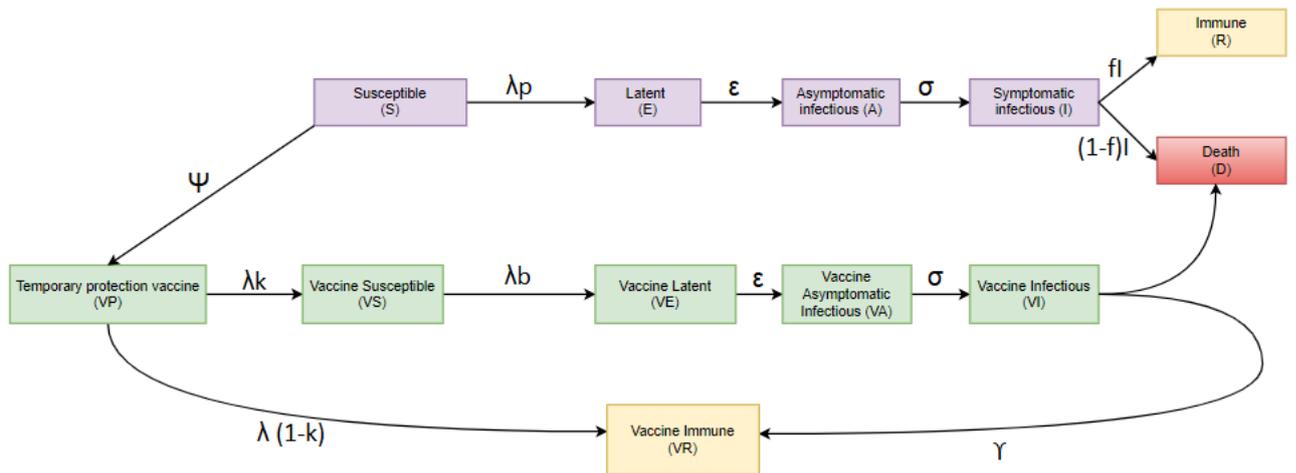


Figure 1: flow diagram for the SEAIR model with vaccination

The main objective of the paper is to minimize the number of people who become infected after vaccination.

The total population size at a given time t is given by

$$N(t) = S(t) + E(t) + A(t) + I(t) + R(t) + V(t).$$

The principale parameters used throughout this paper are:

- I^* : The total number of infected hosts the health care system.
- μ : Natural hospotality rate with hospital saturation.
- Mortality rate for all population $\mu[I] = \begin{cases} 0 & \text{if } I < I^* \\ \mu & \text{if } I \geq I^* \end{cases}$
- α : bound disease induced mortality rate.
- Mortality rate $\alpha[I] = \begin{cases} \alpha_{min} & \text{if } I < I^* \\ \alpha_{max} & \text{if } I \geq I^* \end{cases}$
- $c \in (0, 1)$: control effort. The time dependent control function $c(t)$ measures the rate at which susceptible individuals are vaccinated.
- Force infection: $\lambda = (1 - c)(\beta_A A + \beta_I I)$ where $\begin{cases} \beta_I = & \text{symptotic transmission rate} \\ \beta_A = & \text{asymptotic transmission rate} \end{cases}$
- p : proportion of infections.
- ϵ : waiting rate to viral shedding.
- σ : waiting rate to symptom onset.
- γ : recovery rate from infections.
- ψ : susceptible individuals are vaccinated with vaccine efficacy ψ .
- f : recovery rate from infections.
- k : loss of vaccine protection.
- b : infection rate among vaccines.

The nonlinear system of ODEs desribing the covid-19 dynamic is given by:

(assume $x'(t) = \frac{dx(t)}{dt}$)

$$\begin{aligned}
(1) \quad S'(t) &= -\lambda p S(t) - \psi c(t) S(t) - \mu[I] S(t) \\
(2) \quad E'(t) &= p \lambda S(t) - (\epsilon + \mu[I]) E(t) \\
(3) \quad A'(t) &= \epsilon E(t) - \sigma A(t) - \mu[I] A(t) \\
(4) \quad I'(t) &= \sigma A(t) - (f + \mu[I]) I(t) \\
(5) \quad R'(t) &= f I(t) - \mu[I] R(t) + \psi c(t) S(t) \\
(6) \quad VP'(t) &= \psi S(t) - k \lambda \mu[I] VP(t) \\
(7) \quad VS'(t) &= \psi S(t) + k \lambda VP(t) - (b \lambda + \mu[I]) VS(t) \\
(8) \quad VE'(t) &= b \lambda VS(t) - (\epsilon + \mu[I]) VE(t) \\
(9) \quad VA'(t) &= \epsilon VE(t) - (\sigma + \mu[I]) VA(t) \\
(10) \quad VI'(t) &= \sigma VA(t) - (\gamma + \mu[I]) VI(t) \\
(11) \quad VR'(t) &= \gamma VI(t) - \mu[I] VR(t) + (1 - k) \lambda VP(t) \\
(12) \quad D'(t) &= \alpha[I] I(t) + \mu[I] N - \gamma VR(t) + (1 - \gamma) VI(t)
\end{aligned}$$

with the following initial conditions

$$\begin{aligned} S(0) &= S_0 = N_0 - I_0 \\ E(0) &= A(0) = R(0) = VS(0) = VE(0) = VA(0) = VI(0) = VP(0) = VR(0) = 0 \\ D(0) &= 0. \end{aligned}$$

Figure 1 shows a flow diagram for model (1) and points out the different parameters used.

Remark 2.1 Equations (6), (7), (8), (9), (10), and (11) can be replaced by the following global equation:

$$(13) \quad V'(t) = \psi S(t) - k\lambda V(t) - (1-f)I(t) + \gamma V(t).$$

3 Objective function

The strategy consists to minimize the number of people infected after vaccination. The control scheme is optimal if it minimizes the following objective function

$$(14) \quad J(c) = \int_0^T [PI(t) + Bc^2(t)]dt.$$

The first integral corresponds to the total number of infected individuals by the Covid-19 Epidemic. The second one represents the total cost associated with the implementation of the control measure. It's a quadratic expression to find a known solution (for more details see [5]).

B is a coefficient allowing to weight the "cost" associated to the control implementation c .

The goal of this paper is to find a function c^* such that

$$J(c^*) = \min J(c).$$

To find the optimal control $c^*(t)$, that minimizes $J(c)$, we follow standard results from optimal control theory applied to systems of ordinary differential equations. The main tool that can be used is the Pontryagin's Maximum Principle which is helpful to prove the existence of an optimal solution of the constrained minimization problem.

Realistic restrictions associated with vaccination are incorporated using state variable inequality constraints. This can be stated as following:

$$(15) \quad \begin{cases} 0 & \leq c(t) \leq 1 \\ c(t)S(t) & \leq c_{max} \\ \int_0^T c(t)S(t)dt & \leq c_{total} \end{cases}$$

where c_{max} is the maximum daily vaccination and c_{total} is the vaccine coverage.

Our goal is to minimize the number of infected individuals using a limited total vaccination which implies to minimize $J(c)$.

Let us introduce the following auxiliary state variable

$$z(t) = \int_0^t c(s)S(s)ds.$$

Then, we get

$$(16) \quad \begin{cases} z'(t) &= c(t)S(t) \\ z(0) &= 0 \\ z(T) &\leq c_{total} \end{cases}$$

So the constrained minimization problem associated to (15) and (16) becoms:

$$(17) \quad \begin{cases} z'(t) & = c(t)S(t) \\ z(0) & = 0 \\ z(T) & \leq c_{total} \\ 0 & \leq c(t) \leq 1 \\ c(t)S(t) & \leq c_{max} \end{cases}$$

Using the monotonically increasing propriety of $z(t)$, we get

$$z(T) \leq c_{total} \quad \text{is equivalent to} \quad z(t) \leq c_{total}.$$

Theorem 3.1 *There exists an optimal solution to the problem (17).*

The existence of an optimal solution of the constrained minimization problem (17) is proved using the following Filippov-Cesari existence theorem ([1, 6]):

Theorem 3.2 [1] *Let $x(t) = (x_1(t), \dots, x_n(t)) \in \mathbb{R}^n$ be a state vector and $u(t) = (u_1(t), \dots, u_r(t)) \in \mathbb{R}^r$ be a control vector associated to the following optimal control problem*

$$(18) \quad \min \int_{t_0}^{t_1} F(x(t), u(t), t) dt.$$

with

$$(19) \quad \dot{x} = f(x(t), u(t), t), \quad x(t_0) = x^0,$$

with the terminal conditions

$$(20) \quad \begin{aligned} x_i(t_1) &\geq x_i^1, & i = 1, \dots, m \\ x_i(t_1) &\text{free}, & i = m, \dots, n. \end{aligned}$$

and for $u(t) \in U$, with U is a fixed set in \mathbb{R}^r we have the following constraints

$$(21) \quad g(x(t), u(t), t) \geq 0.$$

Assume that there exists an admissible pair $(x(t), u(t))$ and

1. U is closed.
2. $N(x, t) = \{y = (y, y_{n+1}) : y = f(x, u, t), y_{n+1} \geq F(x, u, t), g(x, u, t) \geq 0, u \in U\}$ is convex for all $(x, t) \in \mathbb{R}^n \times [t_0, t_1]$.
3. There exists a number $\theta > 0$ such that $\|x(t)\| < \theta$ for all admissible pairs $(x(t), u(t))$, and all $t \in [t_0, t_1]$.
4. There exists an open ball $B(0, \gamma) \subset \mathbb{R}^r$ which contains the set $\Omega(x, t) = \{u \in U : g(x, u, t) \geq 0\}$ for all $x \in B(0, \theta)$.

Then there exists an optimal pair $(x^*(t), u^*(t))$ to the problem (19),(20),(21) with $u^*(t)$ measurable.

Proof of Theorem 3.1. Fist remember the nonlinear system of ODEs describing the covid-19 dynamic:

$$(22) \quad \begin{cases} S'(t) & = -\lambda p S(t) - \psi c(t) S(t) - \mu [I] S(t) \\ E'(t) & = p \lambda S(t) - (\epsilon + \mu [I]) E(t) \\ A'(t) & = \epsilon E(t) - \sigma A(t) - \mu [I] A(t) \\ I'(t) & = \sigma A(t) - (f + \mu [I]) I(t) \\ R'(t) & = f I(t) - \mu [I] R(t) + \psi c(t) S(t) \\ V'(t) & = \psi S(t) - k \lambda V(t) - (1 - f) I(t) + \gamma V(t). \end{cases}$$

We assume that $x(t) = (S(t), E(t), A(t), I(t), R(t), V(t), z(t))^T$, $u(t) = c(t)$ and $F(x(t), u(t), t) = Px_3(t) + Bu^2(t)$. Then, we get

$$(23) \quad f(x(t), u(t), t) = \begin{bmatrix} -\lambda pS(t) - \psi c(t)S(t) - \mu[I]S(t) \\ p\lambda S(t) - (\epsilon + \mu[I])E(t) \\ \epsilon E(t) - \sigma A(t) - \mu[I]A(t) \\ \sigma A(t) - (f + \mu[I])I(t) \\ fI(t) - \mu[I]R(t) + \psi c(t)S(t) \\ \psi S(t) - k\lambda V(t) - (1-f)I(t) + \gamma V(t) \\ c(t)S(t) \end{bmatrix}$$

and $g(x(t), u(t), t) = c_{max} - u(t)x_1(t)$. Note that F, f and g are of classe C^1 and f is bounded. Then, there exists a solution for the system (22) which garantees an admissible pair $(x(t), u(t))$. By using that the control function c is verifying $0 < c(t) < 1$, and for that the control set $U = [0, 1]$ is compact, conditions of Filippov-Cesari existence theorem are verified.

The control set U is convex, so $f(x, u, t) = \alpha(x, t) + \beta(x, t)u$, $F(x, ., t)$ and $g(x(t), ., t)$ are convex on U .

The function f is expressed as a linear function of the control variable with coefficients dependent on the state variables and time in (23), and F and g are convex on U . Then $N(x, t)$ is convex, which is Condition 2 of Theorem 3.2.

Condition 3 follows from the boundedness of solutions to the system (22) for the finite time interval. ■

3.1 Penalty Method

A penalty function of the constrained minimization problem is

$$J_p(c) = \int_0^T \left[PI(t) + Bc^2(t) + \mu_1(c(t)S(t) - c_{max})^2 H_1(c(t)S(t) - c_{max}) + \mu_2(z(t) - c_{total})^2 H_2(z(t) - c_{total}) \right] dt$$

where P, Q are constants, μ_1, μ_2 are penalty parameters, $H_1(c(t)S(t) - c_{max}) = \begin{cases} 0 & \text{if } c(t)S(t) \leq c_{max} \\ 1 & \text{if } c(t)S(t) > c_{max} \end{cases}$

and $H_2(z(t) - c_{total}) = \begin{cases} 0 & \text{if } c(t)S(t) \leq c_{total} \\ 1 & \text{if } c(t)S(t) > c_{total} \end{cases}$

Then, to minimize the solution of constrained optimization problem (17), we should minimize $J_p(c)$.

4 Numerical simulations

4.1 Stastical results

In this section we will simulate the solutions of the SEAIR model (1) to estimate the impact of the vaccination program in Tunisia that started in March 2021 to combat the COVID-19 pandemic. Tunisia has only acquired two-dose vaccines. It recently granted a Marketing Authorization to Johnson and Johnson vaccine, which requires only one dose. The latter has not yet been distributed in the country.

The table (1) below represent the cumulative number of administered and received doses for each vaccines until the end of July.

Vaccines used	administered doses	received doses	Efficiency rate
Pfizer	1555606	1718514	95%
AstraZeneca/Oxford	240193	580760	70%
Sputnik V	44753	119986	91.60%
CoronaVac	332219	699994	50.38%
Johnson and Johnson	0	0	66%

Table 1: DISTRIBUTION OF VACCINES IN TUNISIA

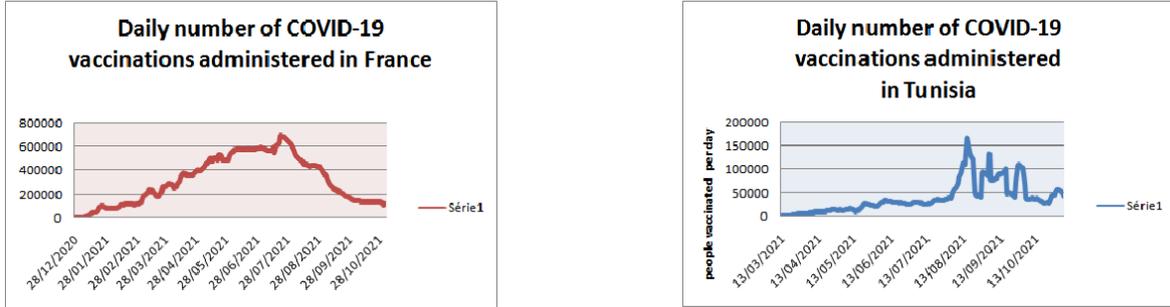


Figure 2: Daily number of Covid-19 vaccinations administered in France and Tunisia

First, we consider the model (1) before the vaccine deployment, that is $\psi = 0$, during the period from December 2020 through October 2021. We assume that the vaccinated subpopulations VP , VS , VE and VI are equal to zero. The set of differential equations was solved using Matlab.

4.2 SEAIR with vaccination model

In this part, we will be interested to implement some numerical results for the SEAIR model with vaccination in both France and Tunisia.

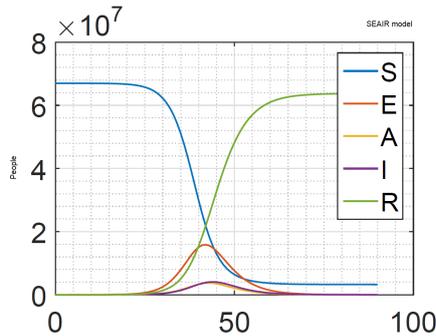


Figure 3: the model solutions before the vaccination program in France began

The allure of the SEAIR is the same like the France case but in two different periods. By the vaccine effect, we can see that the Tunisian case is translated.

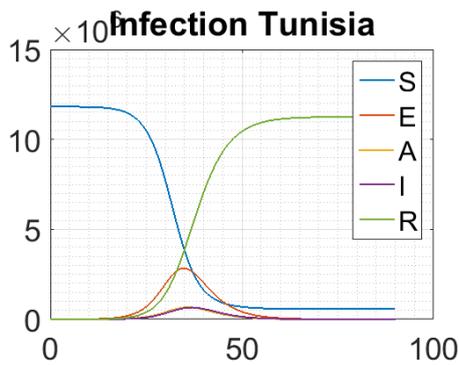


Figure 4: SEAIR model for Tunisia case

4.3 Simulations of the model in France and vaccination effect

This results is given for the period from 15-february 2021 to 50-April 2021 when the number of case go past 5000 infected cases (Figure 2.1). (Figure 2.2) proves by the increasing of the person vaccinated the amplitude of the infected person goes to 500. The deareasing of the number of infected people influence to the number of death in the same period (Figure 3.1) and (Figure 3.2)

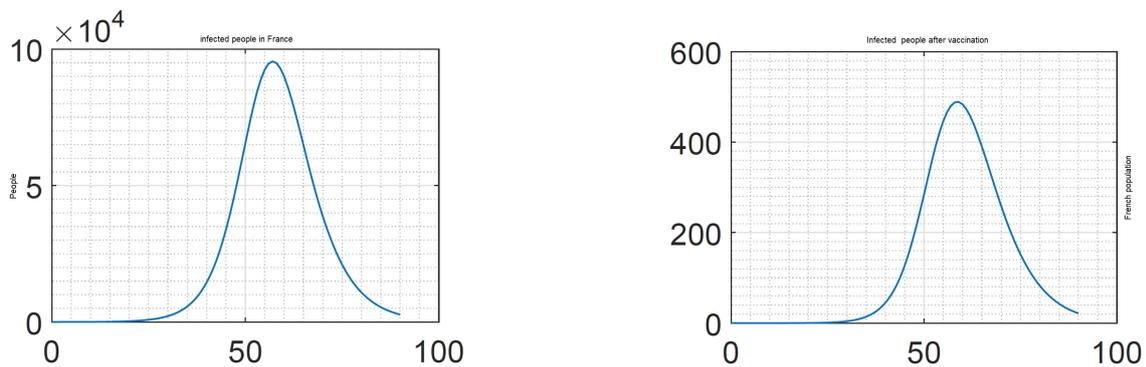


Figure 5: Comparison infected people in France before and after vaccination

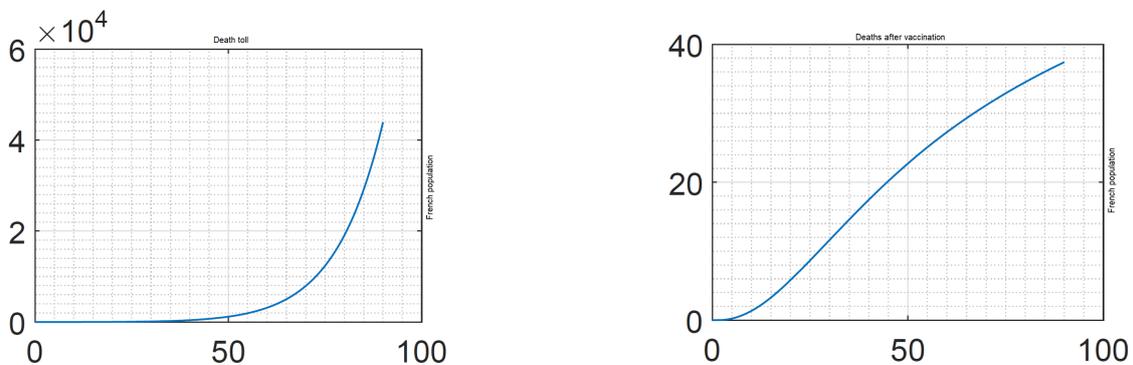


Figure 6: Comparison infected people in France before and after vaccination

4.4 Simulations of the model in Tunisia and vaccination effect

4.5 Simulations of the model SEAIR with vaccination

For the case of Tunisia, the strongest wave is in the period between 15 Mai 2021 and 15 juillet 2021 which returns to the "delta various" of Covid 19. The influence of that is the big number of death 20000. the strategy of vaccination in Tunisia is so late if we compare with case of France (We can see in the previous section)

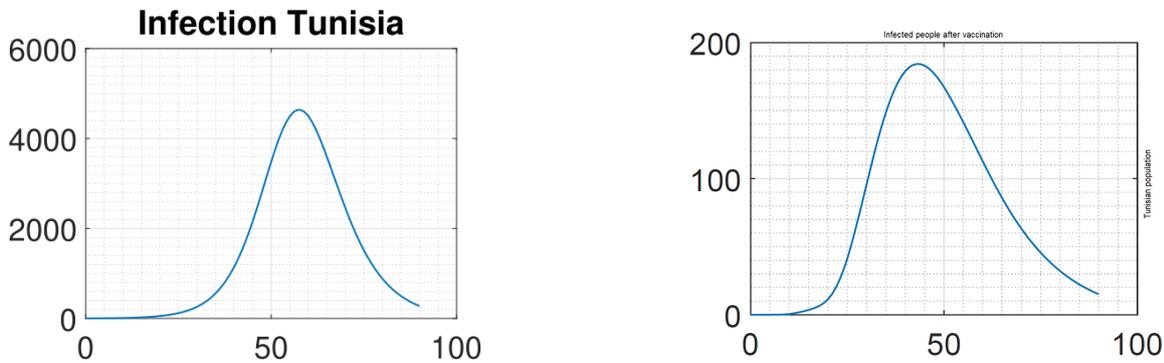


Figure 7: Comparaision infected people in Tunisia before and after vaccination

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