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SEIMR/R-S/OPT. Epidemic Management Optimization Model, Control Policies, Vital Health Resources and Vaccination. Theory

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Abstract

Make decision during an epidemic process implies enter in the dialectic of duality of goals: lives saved in the short term versus loss of quality of life of the population in the long term. The optimization models may be used to support epidemic management without entering the duality of goals do not try to compare economic impact with avoided deaths, concentrating the mathematical effort into avoid additional deaths over the minimum natural death due to the biological aspects of the epidemics, considering the real restrictions about economic budgets and logistics constraints. The pandemic is a natural process that follows known mathematical rules, which involve great uncertainty for being unknown, but humanity has developed great scientific (analytical) capacity to face complex natural processes, managing a pandemic like COVID-19 is perhaps the biggest challenge it must overcome. Tackling the pandemic by ignoring humanity's ability to model processes and find the "best" decision means that, despite acting with goodwill, policies that do not produce the greatest social well-being and that possibly generate more dead than the minimum possible and cause an economic impact that negatively affects quality of life by returning to levels 20 or more years ago, it affects strongly to countries in development way. SEIMR/R-S simulation epidemic

model is the core of SEIMR/R-S/OPT, it considers the impact of modeling the population divided into sociodemographic segments based on age and economic stratum (other dimensions, for example: ethnics, gender, …). The added value by mathematical programming approach is to convert simulation models into optimization models enabling decision makers to determine optimal policies for public health management. SEIMR/R-S/OPT may determine optimal policies considering the socio-spatial distribution of the population. SEIMR/R-S/OPT was implemented in GAMS using OPTEX Expert Optimization System.

Keywords: Pandemic Management, Epidemic Mathematics, Optimization, Health Decision Support Systems

1. Epidemic Management Optimization

1.1. General Framework

SEIMR/R-S/OPT is an optimization model of a Health Decision Support System (H-DSS) composed of a suite of advanced analytics mathematical programming models (predictive, prescriptive, and cognitive); to address epidemics, and more specifically the COVID 19 epidemic. The aim is to support public health authorities in decision-making in high complex environments like a pandemic.

The concept of the system is based on the goal of the planning/management process should be:

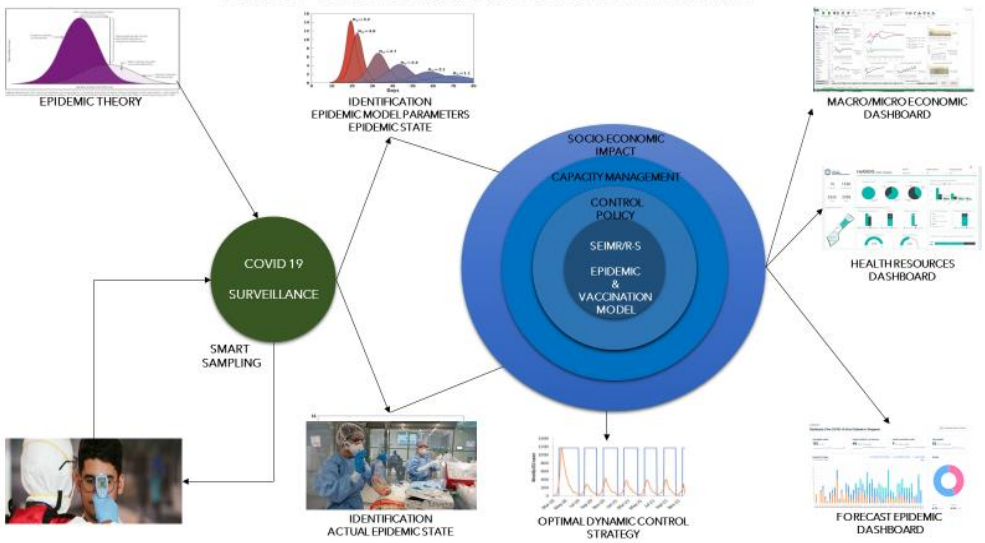
i. Short term: minimize the number of deaths during the epidemic; and
ii. Long term: maximize a quality-of-life index of the society.

The following basic analytic models have been designed and implemented to integrate H-DSS

i) SEIMR/R-S (Velasquez-Bermúdez, 2021a) corresponds to a generalized underlying mathematical model of pandemics that enhances traditional, aggregated simulation models, considering inter-regional impacts in a macro region (conurbed area); SEIMR/R-S also subdivides the population into sociodemographic segments based on age and economic stratum (it is possible to include other dimensions, for example: ethnics, gender, …). It includes inter-region mobility balancing equations, so that it can also evaluate the effects of controlling inter-region communication channels.
ii) SEIMR/R-S/OPT management optimization model that determines optimal policies (mitigation and confinement) considering the spatial distribution of the population, sociodemographic segments, and multiple type of vaccines. SEIMR/R-S is the core of the SEIMR/R-S/OPT, that is described in this paper.

iii) COVID-19 SURVEILLANCE state estimation model based on Dual Multi-State Kalman Filter (Velasquez-Bermúdez, 2021b), oriented to:
- Define the structure of the differential equations model that governs the behavior of the pandemic
- Estimate the parameters that define a specific model among the different possible models that may describe the dynamic process.
- Determine the true state of the pandemic, which is defined by the number of people (or the fraction of the population) which is in each epidemiological state

FIGURE 1. HEALTH DECISION SUPPORT SYSTEM STRUCTURE



Furthermore, these high complex mathematical models can be used in several ways:

1. Coordinated but independent models in which the results of one model are converted into input data for another model,
2. Integrated into a single mathematical model, in a completely holistic approach to the problem. This is the best solution for a static ideal real-world,
3. Integrated as an autonomous Artificial Hypothalamus (Velasquez-Bermúdez, 2021d), so that all models, while acting autonomously, in real-time, communicate with each other when events occur that justify the redefinition of public health control policies. This may be the best solution for a real dynamic real-world.

The added value by mathematical programming approach is to convert simulation models into optimization models to be able to combine them with other mathematical programming models, following the principles of

structured mathematical modeling that allows join multiple problems of mathematical programming in a single holistic model. Velasquez-Bermúdez, Leone and Pick (2021) present a resume of the decision support system.

1.2. Making Decision During A Pandemic Proces

The modeling of epidemics is a solidly developed area of scientific knowledge, widely studied based on simulation models. The table shows some of the best-known model

Table 1. Traditional Epidemic Models

Model	Description	Reference
SIR	Susceptibility (S), Infection (I) and Recovery (R)	Kermack & Mc Kendrick (1927) Jing (2018)
SEIR	Susceptibility (S), Exposure (E), Infection (I) and Recovery (R)	Hethcote (2000)
SEI3RD	Susceptibility (S), Exposure (E), 3+1 Infection States (I3), Recovery (R) and Death (D)	Mejía Becerra et. al. (2020)
SEIQR	Susceptibility (S), Exposure (E), Infection (I), Quarantine (Q) and Recovery (R)	Huang (2016)
SIRS	Susceptibility (S), Infection (I), Recovery (R) and Susceptibility (S)	Cai (2015)

An epidemiological model is defined based on nonlinear differential equations that explain the evolution of the process without human intervention. These differential equations can be established based on the population who are in a certain "epidemic" state or based on the fraction of the population that is in that state. These models have direct connection with biological parameters but ignore the connection with spatial distribution of the sociodemographic segments that live in the territory.

Traditionally the equations system is solved using simulation and are used in an aggregated manner to test the decisions supported in the mental models of the decision makers. Unfortunately for humanity, nature has shown that the processes that develop in it can be understood, explain, and "predict", but that this requires specialized scientific knowledge, and not just experience and good practices.

Make decision during an epidemic process implies enter in the dialectic of duality of goals: lives saved in the short term versus loss of quality of life of the population in the long term. The optimization models may be used to support epidemic management without entering the duality of goals do not try to compare economic impact with avoided deaths, concentrating the mathematical effort into avoid additional deaths over the minimum natural death due to the biological aspects of the epidemics, considering the real restrictions about economic budgets and logistics constraints.

To determine the management criteria (objective function), the pandemic process must be synthesized in terms of its impact that must be

measured in multiple dimensions. In the case of eliminating competition economic impact of public health, at least the following considerations should be considered:

i. The pandemic is a natural process that cannot be avoided, it can only be managed.
ii. The epidemic with the least economic impact is the shortest, this has no discussion.
iii. Public health policies cannot prevent infected people who do not have the capacity to survive the virus from living
iv. Additional dead to those who have no capacity to survive can be generated by scarcity of vital resources. This is the real problem to face.

The pandemic is a natural process that follows known mathematical rules (differential equations) which involve great uncertainty for being unknown, but humanity has developed great scientific (analytical) capacity to face complex natural processes, managing a pandemic like COVID-19 is perhaps the biggest challenge it must overcome. Tackling the pandemic by ignoring humanity's ability to model processes and find the "best" decision means that, despite acting with goodwill, policies that do not produce the greatest social well-being and that possibly generate more dead than the minimum possible and cause an economic impact that negatively affects quality of life by returning to levels of several years ago.

1.3. SEIMR/R-S/OPT. Epidemic Management Optimization Model

The epidemic model is the key element of the optimization model because it simulates the spread of the epidemic combined with the mix of control policies, and produces the optimal dynamic policy to management the epidemic, it is composed of following problems:

- Epidemic: it simulates the spread of the epidemic based on a model of Epidemic states in which the region's population may be distributed. The model used in this case if the SEIMR/R-S (Velasquez, 2021a)
- Vaccination: this model should be integrated into the epidemic model in such a way as to simulate the effect of a vaccination process that by its characteristics must extend for a long period, due to the massive nature of the pandemic and the limitation in i) the availability of vaccines, ii) the logistical capacity to deal with the process and iii) the individual decision of the population about vaccination.
- Capacity: Simulates the impact of the health resources capacity in the spread of the epidemic and optimize the expansion of vital health resources capacity according to an available budget.

- Control: Simulates the spread of the epidemic using control policies based on the traditional premise that social estrangement is the primary way of regulating the pandemic.

The union of these models is called SEIMR/R-S/OPT, it produces the "optimal" dynamic policy to deal with the epidemic. It is formulated following next concepts.

- The time unit of the differential equations is one day.
- The states contain the fraction of the population in each state.
- The time of the optimization model may be divided in periods of multiple days (i.e., weeks, …). In this case, the integration of the differential equations must be made using pre-calculated parameters.

One of the main limitations of the traditional approach is to assume that the entire population is homogeneous with respect to its epidemiological behavior. It is well known that the epidemic manifests differently in each sociodemographic stratum and that the composition of sociodemographic segments depends on each region.

In order to enhance the model and to be useful in real cases, SEIMR/R-S assumes that there is a different pandemic (because it has different parameters) for each pair <rg-region, ss-sociodemographic-segment>. Under the hypothesis of a non-homogeneous population in a region, then the epidemic is assumed to be particular to each duple <rg,ss> and the equations are formulated depending on <rg,ss>. The advantage of this approach will be visualized when the epidemic model is coupled with the management of health resources and control policies, which can be individualized for each duple <rg,ss>.

The model parameters can be grouped by the original source of variation, these sources are:

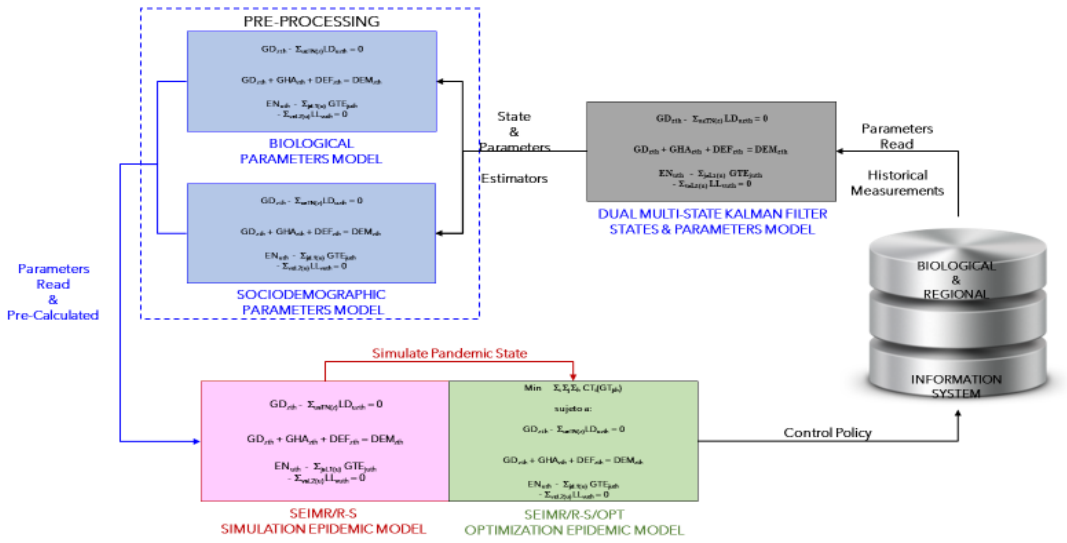
- Pathogen: characteristics of the epidemic due to the pathogen
- Age: It is typical for recovery/worsening times (rates) and probability of recovery to be a function of age.
- Economic stratum: influences the epidemic by means of the intensity of contact, product of the number of contacts, the duration of contacts and the closeness, these variables may also be a combined function of age and economic.

In this paper, the sociodemographic segments are a combination of age with an economic stratum. The biological parameters depend on age. Additionally, may be considered people coming for the exogenous systems (out of the region) to the region.

SEIMR/R-S/OPT can be visualized as the coordinated integration of multiple modeling layers: i) simulation epidemic model, represents the dynamic process of the evolution of epidemic, ii) control of public health policies, allows the user to coordinate the policies of spread control of the epidemic having an epidemic simulation model as reference, and iii) vital resource capacity model, allows to integrate the epidemic management to determine the optimal management of the resources according to the decision makers criteria. In addition, it is possible to include a fourth layer oriented to evaluate the detailed economic impact of the pandemic. This document presents the modelling of the first three layers.

The integrated model consists of two main models: i) the optimization of epidemic management, and ii) calculation of the parameters required by the optimization model. The calculation of the model parameters corresponds to an information pre-processing model that is made prior to the optimization process, its complexity can be very large to the extent that the decision-maker want to represent reality in the greatest degree of detail. The preprocessing model consists of two sub-models: i) biological parameters and ii) sociodemographic parameters. The diagram shows the process of the three models, including the state estimation model.

FIGURE 2. HEALTH DECISION SUPPORT SYSTEM STRUCTURE – MODEL CONNECTIVITY



The construction of the data must follow a "bottom-up" methodology, that is, the most detailed data is located and added, the calculations must be performed at the lowest level, so as not to lose the detail. This approach makes the difference with aggregated parameters (trending to average values) that are disaggregated with logical rules and that lose the detail of what happens at the level of each atom (in this case each sociodemographic segment in a region).

2. SEIMR/R-S General Epidemic Model

2.1. General Framework

Below is presented a resume of the SEIMR/R-S model of epidemic that is the result of integrating the SIR, SEIR and SEI3RD epidemic models. SEIMR/R-S extends the modeling to a multi-segment-sociodemographic multi-region system, the description of the model is presented by Velasquez-Bermúdez (2021a). This document covers only what is relevant to the formulation of the model in terms of mathematical programming.

SEIMR/R-S describes the epidemic with following states:

S Susceptible: initially covers all population that potentially can be infected (SU)

E Exposed: Population that has been infected and are in an incubation (latency) period (EX). The model SIR does not include this state.

IM Multi-Infected: Population that has been infected and has active the pathogen in different states of development (I0, I1, I2, …, IN). The active infected states are ordered according to the severity of the infection. The modeled SIR and SEIR consider only one infected state. For convenience, the last state is called "IN"

R Recovered: Recovering population (RE)

R-S is related with the Region-Segment model that considers multiples regions where live people classified in multiples sociodemographic segments. The epidemic states considered are showed in the next table. The table includes the symbol used in the traditional models and the code used in the information system to reference the state.

Table 2. SEIMR/R-S/OPT - Epidemic States

Model Symbol	Epidemic State Code	Description	Comments
STANDARD STATES MBC-SEI3RD MODEL			
S	SU	Susceptible Population	Those individuals who have not been exposed to the pathogen and are susceptible to being infected by it.
E	EX	Exposed Population	Those individuals who are in the latency state; that is, they have been inoculated by the pathogen but are not yet infectious
I	IN	Infected Population	In SIR and SEIR models is infected population. It must be the most critical state for infected people; this is important for models that have more than one epidemic state to describe the infection process.
I_0	I0	Asymptomatic Infectious	Those individuals in the population who have been inoculated by the virus are infectious but have not developed symptoms. Those infected in this state rarely learn that they have been infected.

I_1	I1	Moderate Symptoms Infectious	Those individuals in the population who are infectious and have mild or moderate symptoms. They are those who can be given management of the disease at home.
I_2	I2	Severe Symptoms Infectious	Those individuals in the population who are infectious and have severe but not critical symptoms. Individuals present in this state require hospitalization.
I_3	IN	Critical Symptoms Infectious	It must be the most critical state for infected people; this is important for models that have more than one epidemic states to describe the infection process. In SIR and SEIR models is infected population
R	RE	Recovered Population	Those individuals recover from infection, having developed antibodies. In most of the models they cannot be re-infected.
	ED	Epidemic Dead	Individuals who fail the infection and die.
	ND	Natural Dead	Individuals who die by other reason different to the epidemic
	NP	New Population	Individuals coming from an exogenous macro-region.
ADDITIONAL CAPACITY STATES			
	IU_2 IU_3	Infected Population Unattended	Individuals that require hospital attention and do not received hospital ty attention in state I_2, I_3, …
	CD	Collateral Dead	Individuals who die by during the epidemic by reasons different to the epidemic.

The measurements used are:

Table 3. Measurement Unit

Measurement Unit	Description
1/peo-day	1/ persons-day
fpo/day	Fraction of population per day
peo-day	Persons-day

2.2. Algebraic Notation

The index/entity used in the models is presented below; Master Set indicates the name of the SET for all element associated to the index in the model.

Table 4. SEIMR/R-S/OPT Model - Indexes

Index	Code Entity	Description	Master Set
ag	AGE	Age	AGE
cp	CPO	Epidemic Control Policy	CPO
es	SEC	Economic Stratum	SEC
hr	HRS	Health Resource	HRS
mr	MRE	Macro-Region (Territory)	MRE
rd	UBT	Destination Region	UBT

rg	UBT	Region (Basic Territory Unit)	UBT
ro	UBT	Origin Region	UBT
ss	SDS	Sociodemographic Segment	SDS
st, s1	STA	Epidemic State	STA, STA1
t, q		Time (periods)	
tm	MTR	Transport Mode	MTR
fv,fx	FVA	Vaccination Phase	FVA, FVAA
va	VAC	Vaccine	VAC
gr	GRE	Vaccination Regional Group	GRE

It should be noted, due to the number of sets, parameters, variables, and constraints (which far exceed the number of Greek letters), the algebraic formulation the model is presented following the standard notation used in OPTEX Expert Optimization System (OPTEX, Velasquez-Bermúdez, 2019) which is based on codes (ID, names) assigned to each algebraic element. This notation, while not traditionally followed by small models, with few algebraic elements, is equally valid, and it is used in the implementation of SEIMR/R-S/OPT.

Including regional and sociodemographic segment modeling (age and economic stratum) involves associating the biological parameters with these aspects. Therefore, biological parameters may be related to indices: rg (region), ss (sociodemographic segment), ag (age) and/or ec (economic stratum). The biological parameters are described below, it includes the "standard" original formulation (Mejía Becerra, J. D. et. al., 2020) and the SEIMR/R-S/OPT formulation.

Table 5. SEIMR/R-S - Basic Biological Parameters

Parameter	**SEIMR/R-S Parameter**	**Source**	**Description**	
m^N	MIUN	Info-System	Natural mortality rate	fpo/day
k	KAPP	Info-System	The latency period of the virus before developing	day
m_{ag}	$MIUU_{ag}$	P-Model	Epidemic mortality rate dependent of age	fpo/day
$w_{rg,ss}$	PTRA	P-Model	Probability of that a person may be contagion	prob
$d_{ag,st}$	$DELX_{ag,st}$	P-Model	Probability of I_0, I_1, I_2, I_3, … of recovering	prob
$p_{ag,st}$	$PHIX_{ag,st}$	P-Model	Time a patient in I_0, I_1, I_2, I_3, … recovers	day
$h_{ag,st}$	$ETAX_{ag,st}$	P-Model	Time a patient in I_0, I_1, I_2, I_3, … to next infected state	day
b		P-Model	Transmissibility rate of an individual in state st	
z		P-Model	Total contact free rate in I_1, I_2, I_3, …	1/day

l_E	$LAME_{rg,ss}$	Info-System	Exposed rate coming from the exogenous system	fpo/day
l_S	$LAMS_{rg,ss}$	Info-System	Susceptible rate coming from the exogenous system	fpo/day
l_I	$LAMI_{rg,ss}$	Info-System	Infectious rate coming from the exogenous system	fpo/day
l_R	$LAMR_{rg,ss}$	Info-System	Recovered rate coming from the exogenous system	fpo/day
$j_{ro,rg,ss}$	$FPRR_{ro,rg,ss}$	Info-System	Population fraction traveling to other regions	
$f_{ro,rg,ss}$	$FTRR_{ro,rg,ss}$	Info-System	Time fraction traveling to other regions	

The source Parameters Model (P-Model) indicates that parameters should be the result of the mathematical model of parameters to be constructed from the regional distribution of sociodemographic segments and their characterization from specific studies developed for the macro-region. This topic will be discussed in detail in the implementation of SEIMR/R-S to the City of Bogotá (Velásquez-Bermudez, 2020). The calculated biological parameters used in SEIMR/R-S model is presented below; they are divided in basic and auxiliary parameters that are included to make easier the implementation process.

Table 6. SEIMR/R-S - Calculated Biological Parameters

Parameter	**Equation**	**SEIMR/R-S**		**Description**	**Measure Unit**
		Parameter	**Equation**		
y	1/k	FHII	1/KAPP	Inverse virus latency period	1/day
b	dd × w	BETA	DEI1 × PTRA	Inverse contact intensity × infectivity	1/fpo-day
	d^{-1}	DEI1	1/DELT	Inverse contact intensity	
$g_{ag,st}$	$1/p_{ag,st}$	$GAMX_{ag,st}$	$1/PHIX_{ag,st}$	Fraction of people who recover in one day	fpo/day
$s_{ag,st}$	$1/h_{ag,st}$	$RHOX_{ag,st}$	$1/ETAX_{ag,st}$	Fraction of people who develops symptoms	fpo/day
$br_{rg,ss}$		$PCON_{rg,ss}$	Model	Contagion probability function of regional and sociodemographic characteristics	prob
$bb_{rg,ss}$	$S_{ag\in AGS(ss)}\ dd_{ag,st} \times br_{rg,ss}$	$BESS_{rg,ss}$	$S_{ag\in AGS(ss)}\ DEDE_{ag,st} + PCON_{rg,ss}$	Inverse contact intensity × infectivity	1/fpo-day
$dd_{ag,st}$	$dg_{ag,st} + ds_{ag,st}$	$DEDE_{ag,st}$	$DEGX_{ag,st} + DERX_{ag,st}$	$dg_{ag,st} + ds_{ag,st}$	

$dg_{st,ag}$	$d_{ag,st}$ ´ $g_{ag,st}$	$DEGX_{ag,st}$	$DELX_{ag,st}$ × $GAMX_{ag,st}$		
$sd_{ag,st}$	$d_{ag,st}$ ´ $s_{ag,st}$	$RODX_{ag,st}$	$DELX_{ag,st}$ × $RHOX_{ag,st}$	$d_{ag,st}$ ´ $s_{ag,st}$	
$ds_{ag,st}$	(1 - $d_{ag,st}$) ´ $s_{ag,st}$	$DERX_{ag,st}$	$RHOX_{ag,st}$ - $RODX_{ag,st}$	(1 - $d_{ag,st}$) ´ $s_{ag,st}$	
$dg_{ag,st}$	$d_{ag,st}$ ´ $g_{ag,st}$	$DEGX_{ag,st}$	$DELX_{ag,st}$ × $GAMX_{ag,st}$	$d_{ag,st}$ ´ $g_{ag,st}$	
$da_{st,ss}$	$S_{ag\in AGS(ss)}$ $dd_{ag,st}$	$DSAL_{st,ss}$	$S_{ag\in AGS(ss)}$ $DEDE_{ag,st}$	Total exit rate	
$dz_{st,ss}$	$S_{ag\in AGS(ss)}$ $ds_{ag,st}$	$DSZE_{st,ss}$	$S_{ag\in AGS(ss)}$ $DERX_{ag,st}$	Worsening exit rate	
$db_{st,ss}$	$S_{ag\in AGS(ss)}$ $dg_{st,ag}$	$DSBE_{st,ss}$	$S_{ag\in AGS(ss)}$ $DEGX_{ag,st}$	Recovering exit rate	
ms_{ss}	$S_{ag\in AGS(ss)}$ m_{ag}	$MISS_{ss}$	$S_{ag\in AGS(ss)}$ $MIUU_{ag}$	Mortality rate depending on segment	
$jf_{rg,rd,ss}$	$j_{rg,rd,ss}$ ´ $f_{rg,rd,ss}$	$PTRR_{rg,rd,ss}$	$FPRR_{rg,rd,ss}$ × $FTRR_{rg,rd,ss}$	Fraction Population x Fraction Time in other regions	

2.3. Differential Equation Formulation

The differential equations of the regional-segmented model are (Velasquez-Bermúdez, 2021a):

$$\partial S_{rg,ss}(t)/\partial t = - S2I_{rg,ss}(t) - \mu^{N} \times S_{rg,ss}(t) + \lambda^{S}{}_{rg,ss} \times NPX(t) \quad (1)$$

$$\partial E_{rg,ss}(t)/\partial t = S2I_{rg,ss}(t) - \psi \times E_{rg,ss}(t) + \lambda^{E}{}_{rg,ss} \times NPX(t) \quad (2)$$

st=I0

$$\partial I_{st,rg,ss}(t)/\partial t = \psi \times E_{rg,ss}(t) - \delta\alpha_{st,ss} \times I_{st,rg,ss}(t) + \lambda^{I}{}_{rg,ss} \times NPX(t) \quad (3)$$

st∈I1F = { I1, I2, I3 }

$$\partial I_{st,rg,ss}(t)/\partial t = \delta\zeta_{st-1,ss} \times I_{st-1,rg,ss}(t) - \delta\alpha_{st,ss} \times I_{st,rg,ss}(t) \quad (4)$$

$$\partial R_{rg,ss}(t)/\partial t = \Sigma_{st\in I1F}\, \delta\sigma_{st-1,ss} \times I_{st,rg,ss}(t) - \mu^{N} \times R_{rg,ss}(t) + \Sigma_{ss\in SSR(rg)}\, \lambda^{R}{}_{rg,ss} \times NPX(t) \quad (5)$$

$$\partial D_{rg,ss}(t)/\partial t = \Sigma_{st\in I1F}\, \mu\sigma_{ss} \times I_{st,rg,ss}(t) \quad (6)$$

$$\partial NR_{rg}(t)/\partial t = \mu^{N} \times SR_{rg,ss}(t) + \mu^{N} \times RR_{rg}(t) \quad (7)$$

The following table shows the differential equations dividing the increment and the decrement on each state, it must be considered in the implementation of the mathematical models. The table includes the sets that defined the existence of the equations manly for the infected states.

Table 7. SEIMR/R-S - Differential Equations

Set	State	State Increment	State Decrement	Natural Dead	Exogenous Increment
SU	$\partial S_{rg,ss}(t)/\partial t$		$S2I_{rg,ss}(t)$	$\mu^N \times S_{rg,ss}(t)$	$\lambda^S{}_{rg,ss} \times NPX(t)$
EX	$\partial E_{rg,ss}(t)/\partial t$	$S2I_{rg,ss}(t)$	$\psi \times E_{rg,ss}(t)$		$\lambda^E{}_{rg,ss} \times NPX(t)$
I0	$\partial I_{st,rg,ss}(t)/\partial t$	$\psi \times E_{rg,ss}(t)$	$\delta\alpha_{st,ss} \times I_{st,rg,ss}(t)$		$\lambda^I{}_{rg,ss} \times NPX(t)$
I1F	$\partial I_{st,rg,ss}(t)/\partial t$	$\delta\zeta_{st-1,ss} \times I_{st-1,rg,ss}(t)$			
RE	$\partial R_{rg,ss}(t)/\partial t$	$\Sigma_{st\in I1F}$ $\delta\sigma_{st,ss} \times I_{st,rg,ss}(t)$		$\mu^N \times R_{rg,ss}(t)$	$\lambda^R{}_{rg,ss} \times NPX(t)$
ED	$\partial D_{rg,ss}(t)/\partial t$	$\Sigma_{st\in I1F}$ $\mu\sigma_{ss} \times I_{st,rg,ss}(t)$			
ND	$\partial NR_{rg}(t)/\partial t$	$\mu^N \times (SR_{rg}(t) + RR_{rg}(t))$			

These equations require the following algebraic definition:

$$IS_{rg,ss}(t) = \Sigma_{st\in INF}\, I_{st,rg,ss}(t) \quad (8)$$

$$IX_{rg}(t) = \Sigma_{ss\in SSR(rg)}\, IS_{rg,ss}(t) \quad (9)$$

$$II_{rg}(t) = \Sigma_{ss\in SSR(rg)}\, \Sigma_{ro\in ROR(rg)}\, \varphi\phi_{ro,rg,ss} \times IS_{ro,ss}(t) \quad (10)$$

$$IE_{rg}(t) = \Sigma_{ss\in SSR(rg)}\, \Sigma_{rd\in RDE(rg)}\, \varphi\phi_{rg,rd,ss} \times IS_{rg,ss}(t) \quad (11)$$

$$IR_{rg}(t) = IX_{rg}(t) + II_{rg}(t) - IE_{rg}(t) \quad (12)$$

$$SR_{rg}(t) = \Sigma_{ss\in SSR(rg)}\, S_{rg,ss}(t) \quad (13)$$

$$SI_{ro,rg,ss}(t) = \varphi\phi_{ro,rg,ss} \times S_{ro,ss}(t) \quad (14)$$

$$SE_{rg,rd,ss}(t) = \varphi\phi_{rg,rd,ss} \times S_{rd,ss}(t) \quad (15)$$

$$SN_{rg,ss}(t) = S_{rg,ss}(t) - \Sigma_{rd\in RDE(rg)}\, SE_{rg,rd,ss}(t) \quad (16)$$

$$SIN_{rg}(t) = \beta\beta_{rg,ss} \times IR_{rg}(t) \times SN_{rg,ss}(t) \quad (17)$$

$$SIE_{rg,ss}(t) = \Sigma_{rd\in RDE(rg)}\ \beta\beta_{rd,ss}\, IR_{rd}(t) \times SE_{rg,rd,ss}(t) \quad (18)$$

$$S2I_{rg,ss}(t) = SIN_{rg}(t) + SIE_{rg}(t) \quad (19)$$

$$RR_{rg}(t) = \Sigma_{ss\in SSR(rg)}\, R_{rg,ss}(t) \quad (20)$$

$$DR_{rg}(t) = \Sigma_{ss\in SSR(rg)}\, D_{rg,ss}(t) \quad (21)$$

From now on, the above mathematical definitions (constraints) will be summarized as

$$\{ S, E, I_{st}, D, N \} \in Q$$

2.4. Finite Differences Formulation

To introduce the previous equation in a standard mathematical programming model, the differential equations must be redefined in equivalent discrete equations:

$$[S_{rg,ss}(t+\Delta t) - S_{rg,ss}(t)]/\Delta t = - S2I_{rg,ss}(t) - \mu^{N} \times S_{rg,ss}(t) + \lambda^{S}_{rg,ss} \times NPX(t) \quad (22)$$

$$[E_{rg,ss}(t+\Delta t) - E_{rg,ss}(t)]/\Delta t = S2I_{rg,ss}(t) - \psi \times E_{rg,ss}(t) + \lambda^{E}_{rg,ss} \times NPX(t) \quad (23)$$

$st \in I0$

$$[I_{st,rg,ss}(t+\Delta t) - I_{st,rg,ss}(t)]/\Delta t = \psi \times E_{rg,ss}(t) - \delta\alpha_{st,ss} \times I_{st,rg,ss}(t) + \lambda^{I}_{rg,ss} \times NPX(t) \quad (24)$$

$st \in I1F = \{ I1, I2, I3 \}$

$$[I_{st,rg,ss}(t+\Delta t) - I_{st,rg,ss}(t)]/\Delta t = \delta\zeta_{st-1,ss} \times I_{st-1,rg,ss}(t) - \delta\alpha_{st,ss} \times I_{st,rg,ss}(t) + \lambda^{I}_{rg,ss} \times NPX(t) \quad (25)$$

$$[R_{rg,ss}(t+\Delta t) - R_{rg,ss}(t)]/\Delta t =$$
$$\Sigma_{st \in I1F}\, \delta\beta_{st-1,ss} \times I_{st,rg,ss}(t) - \mu^{N} \times R_{rg,ss}(t) + \Sigma_{ss \in SSR(rg)}\, \lambda^{R}_{rg,ss} \times NPX(t) \quad (26)$$

$$[D_{rg,ss}(t+\Delta t) - D_{rg,ss}(t)]/\Delta t = \Sigma_{st \in I1F}\, \mu\sigma_{ss=AGS(ss)} \times I_{st,rg,ss}(t) \quad (27)$$

$$[NR_{rg}(t+\Delta t) - NR_{rg,ss}(t)]/\Delta t = \mu^{N} \times SR_{rg,ss}(t) + \mu^{N} \times RR_{rg}(t) \quad (28)$$

If $\Delta t = 1$, one day, the above equations may be included directly in the optimization model.

3. SEIMR/R-S/OPT Mathematical Programming Epidemic Model

The following is the SEIMR/R-S/OPT epidemic optimization model algebraic formulation.

3.1. SEIMR/R-S Algebraic Epidemic Model

The equations used to regional-segmented model are presented in the following groups:

i. Discrete version of differential equations for each epidemic state in all region-segment. The equations are divides in increments and decrements. They are function of the rates (or transition probabilities) in the previous t-period that depends on each epidemic model.
ii. Balance regional modeling to estimate the total population in each state for all region-segments. The balance equations allow to calculate the population fraction in rg-region ss-segment at the end of each period of the planning horizon.

For algebraic implementation of SEIMR/R-S, the variable $POP_{t,st,rg,ss}$ represents the fraction of the population of the rg-region, ss-sociodemographic-segment, at the end of t-period and $PSR_{t,st,rg,ss}$ the total susceptible population of the rg-region and $PRP_{t,st,rg}$ the total regional population. The following sets contains: $ss \in SSR(rg)$ the ss-segments that live in rg-region, $ro \in ROR(rg)$ the ro-origins regions where it is possible to travel to rg-region, and $rd \in RDE(rg)$ the rd-destination regions where it is possible to travel from rg-region.

The balance equation defines that the number of people in a state at the end of t-period ($POP_{t,st,rg,ss}$) is equal to the number of people at the end of the previous period ($POP_{t-1,st,rg,ss}$), plus people who enter that state ($IPO_{t,st,rg,ss}$) minus people leaving that state ($DPO_{t,st,rg,ss}$). Some additional auxiliary variables are used in the modeling: $SIR_{t,rg,}$ $DPS_{t,st,rg,ss}$ and $DPN_{t,st,rg,ss}$

The next table resumes the definition equations included in the SIEMR/R-S epidemic model.

Table 8. SIEMR/R-S Model – OPTEX Algebraic Definitions

State Existence	OPTEX Equation	Algebraic Formulation
Population Balance Equations		
st∈STA	$BPOP_{t,st,rg,ss}$	$POP_{t,st,rg,ss} = POP_{t-1,st,rg,ss} + IPO_{t,st,rg,ss} - DPO_{t,st,rg,ss}$
st∈STA	$BPRP_{t,st,rg}$	$PRP_{t,st,rg} = S_{ss∈SSR(rg)}\ POP_{t,st,rg,ss}$
Natural Deaths		
st∈SURE	$DPPND_{t,st,rg,ss}$	$DPN_{t,st,rg,ss} = MIUN \times POP_{t-1,st,rg,ss}$
Susceptible State Equations		
st∈SU	$DSUSR_{t,st,rg}$	$PSR_{t,rg} = S_{ssÎSSR(rg)}\ POP_{t,st,rg,ss}$
st∈SU	$DSUSI_{t,st,ro,rg,ss}$	$PSI_{t,ro,rg,ss} = PTRR_{ro,rg,ss}\ ´\ POP_{t,st,rg,ss}$
st∈SU	$DSUSE_{t,st,rg,rd,ss}$	$PSE_{t,st,rg,rd,ss} = PTRRA_{rg,rd,ss}\ ´\ POP_{t,st,rg,ss}$
st∈SU	$DSUSN_{t,st,rg,ss}$	$PSN_{t,rg,ss} = POP_{t,st,rg,ss} - S_{rdÎRDE(rg)}\ PSE_{t,st,rg,rd,ss}$
	$DSUSIN_{t,rg,ss}$	$SIN_{t,rg,ss} = BESS_{rg,ss} \times PIN_{t,rg}\ ´\ PSN_{t,rg,ss}$
	$DSUSIE_{t,rg,ss}$	$SIE_{t,rg,ss} = S_{rdÎRDE(rg)}\ BESS_{rg,ss}\ ´\ PIN_{t,rd}\ ´\ PSE_{t,st,rg,rd,ss}$
	$DSUS2I_{t,rg,ss}$	$S2I_{t,rg,ss} = SIN_{t,rg,ss} + SIE_{t,rg,ss}$
Infected State Equations		
	$DINIS_{t,rg,ss}$	$PIS_{t,rg,ss} = S_{stÎINF}\ POP_{t,st,rg,ss}$
	$DINIX_{t,rg}$	$PIX_{t,rg} = S_{ssÎSSR(rg)}\ PIS_{t,rg,ss}$
	$DINII_{t,rg}$	$PII_{t,rg} = S_{ssÎSSR(rg)}\ S_{roÎROR(rg)}\ PTRR_{ro,rg,ss}\ ´\ PIS_{t,rg,ss}$
	$DINIE_{t,rg}$	$PIE_{t,rg} = S_{ssÎSSR(rg)}\ S_{rdÎRDE(rg)}\ PTRR_{rg,rd,ss}\ ´\ PIS_{t,rg,ss}$
	$DINPR_{t,rg}$	$PIN_{t,rg} = PIX_{t,rg} + PII_{t,rg} - PIE_{t,rg}$

The next table present the resume of SEIMR/R-S discrete approximation equations.

Table 9. SIEMR/R-S – OPTEX Algebraic Discrete Equations

Epidemic State	State Increment Variable: $IPO_{t,st,rg,ss}$	State Decrement Variable: $DPO_{t,st,rg,ss}$
st∈SU	$LAMS_{rg,ss} \times NPX_t$	$S2I_{t-1,rg,ss} + DPN_{t,st,rg,ss}$
st∈EX	$S2I_{t-1,rg,ss}$	$FHII \times POP_{t-1,st,rg,ss}$
st∈I0	$S_{s1∈EX}\ DPO_{t,s1,rg,ss} + LAMI_{rg,ss} \times NPX_t$	$DSAL_{st,ss} \times POP_{t-1,st,rg,ss}$
st∈I1F	$DPO_{t,st-1,rg,ss}$	
st∈RE	$S_{s1∈INF1}\ DSBE_{st,ss} \times POP_{t-1,st,rg,ss} + LAMR_{rg,ss} \times NPX_t$	$DPN_{t,st,rg,ss}$
st∈ED	$S_{s1∈INF}\ MISS_{ss} \times POP_{t-1,st,rg,ss}$	
st∈ND	$S_{s1∈SURE}\ DPN_{t,st,rg,ss}$	

NPX_t represents the exogenous population coming from exogenous regions, it may be equal to i) a parameter (border condition), ii) a result of the control policy (open or close de frontiers).

3.1.1. Population Balance Equations

The balance equation defines that the people fraction in a state at the end of t-period ($POP_{t,st,rg,ss}$) is equal to the people fraction at the end of the previous period ($POP_{t-1,st,rg,ss}$), plus people who enter that state ($IPO_{t,st,rg,ss}$) minus people leaving that state ($DPO_{t,st,rg,ss}$). They are:

1. $BPOP_{t,st,rg,ss}$: population balance in each epidemic state, each region, and each segment.

$$POP_{t,st,rg,ss} = POP_{t-1,st,rg,ss} + IPO_{t,st,rg,ss} - DPO_{t,st,rg,ss}$$
$$\forall t \ \forall st \in STA \ \forall rg \in REG \ \forall ss \in SSR(rg) \quad (29)$$

2. $BPRP_{t,st,rg}$: fraction of population in each epidemic state and each region.

$$PRP_{t,st,rg} = \Sigma_{ss \in SSR(rg)} POP_{t,st,rg,ss}$$
$$\forall t \ \forall st \in STA \ \forall rg \in REG \quad (30)$$

3. $GNPX_t$: Defines the people incoming from the foreign system as a variable; it may be useful to simulate open and/or close frontiers.

$$NPX_t = NPFS_t$$
$$\forall t \quad (31)$$

3.1.2. Definition Equations

The following numerals present the equations for the epidemiological model; they are calculated considering the equivalent population after modeling quarantine decisions, i.e., considering the $POF_{t,st,rg,ss}$ variable not the $POP_{t,st,rg,ss}$ variable. $POF_{t,st,rg,ss}$ will be explained in a posterior section.

3.1.2.1. Susceptible State Definitions

The definition equations for susceptible state are:

1. $DSUSR_{t,st,rg}$: Definition – Total susceptible population in rg-region

$$PSR_{t,rg} = \Sigma_{ss \in SSR(rg)} POF_{t,st,rg,ss}$$
$$\forall t \ \forall st \in SU \ \forall rg \in REG \quad (32)$$

2. $DSUSI_{t,st,ro,rg,ss}$: Definition – Susceptible population traveling to rg-region from ro-region ($PSI_{t,st,ro,rg,ss}$)

$$PSI_{t,st,ro,rg,ss} = PTRR_{ro,rg,ss} \times POF_{t,st,rg,ss}$$
$$\forall t \ \forall st \in SU \ \forall rg \in REG \ \forall ro \in ROR(rg) \ \forall ss \in SSR(rg) \quad (33)$$

where

$$PTRR_{ro,rg,ss} = FPRR_{ro,rg,ss} \times FTRR_{ro,rg,ss}$$

3. $DSUSE_{t,st,rg,rd,ss}$: Definition – Susceptible population traveling from rg-region to rd-region ($PSE_{t,st,rg,rd,ss}$)

$$PSE_{t,st,rg,rd,ss} = PTRRA_{rg,rd,ss} \times POF_{t,st,rg,ss}$$
$$\forall t \ \forall st \in SU \ \forall rg \in REG \ \forall rd \in RDE(rg) \ \forall ss \in SSR(rg) \quad (34)$$

where

$$PTRRA_{rg,rd,ss} = \Sigma_{ro \in RORG(rg)} PTRRD_{ro,rd,ss} \quad (35)$$
$$PTRRD_{ro,rd,ss} = \Sigma_{rg \in RGRD(rd)} PTRR_{ro,rg,ss} \quad (36)$$

4. $DSUSN_{t,st,rg,ss}$: Definition – Net susceptible population staying in rg-region

$$PSN_{t,rg,ss} = POF_{t,st,rg,ss} - \Sigma_{rd \in RDE(rg)} PSE_{t,st,rg,rd,ss} + \Sigma_{ro \in ROR(rg)} PSI_{t,st,ro,rg,ss}$$
$$\forall t \ \forall st \in SU \ \forall rg \in REG \ \forall ss \in SSR(rg) \quad (37)$$

5. $DSUSIN_{t,rg,ss}$: Definition – Net susceptible population living in rg-region infected in rg-region

$$SIN_{t,rg,ss} = BESS_{rg,ss} \times PIN_{t,rg} \times PSN_{t,rg,ss}$$
$$\forall t \ \forall rg \in REG \ \forall ss \in SSR(rg) \quad (38)$$

6. $DSUSIE_{t,rg,ss}$: Definition – Net susceptible population living in rg-region infected in other regions

$$SIE_{t,rg,ss} = \Sigma_{st \in SU} \Sigma_{rd \in RDE(rg)} BESD_{rg,ss} \times PIN_{t,rd} \times PSE_{t,st,rg,rd,ss}$$
$$\forall t \ \forall rg \in REG \ \forall ss \in SSR(rg) \quad (39)$$

where

$$BESD_{rd,ss} = \Sigma_{rg \in RDRG(rd)} BESS_{rg,ss} \quad (40)$$

7. $DSUS2I_{t,rg,ss}$: Definition – Net susceptible population to infected living in rg-region

$$S2I_{t,rg,ss} = SIN_{t,rg,ss} + SIE_{t,rg,ss}$$
$$\forall t \ \forall rg \in REG \ \forall ss \in SSR(rg) \quad (41)$$

3.1.2.2. Infected State Definitions

The definition equations for infected states are:

1. $DINIS_{t,rg,ss}$: Definition – Net infected population infected living in rg-region in ss-segment

$$PIS_{t,rg,ss} = \Sigma_{st \in INF} POF_{t.st,rg,ss}$$
$$\forall t \ \forall rg \in REG \ \forall ss \in SSR(rg) \quad (42)$$

2. $DINIX_{t,rg}$: Definition – Net infected population infected living in rg-region

$$PIX_{t,rg} = \Sigma_{ss \in SSR(rg)} PIS_{t,rg,ss}$$
$$\forall t \ \forall rg \in REG \quad (43)$$

3. $DINII_{t,rg}$: Definition – Net infected population traveling to rg-region from other regions

$$PII_{t,rg} = \Sigma_{ss \in SSR(rg)} \Sigma_{ro \in ROR(rg)} PTRR_{ro,rg,ss} \times PIS_{t,rg,ss}$$
$$\forall t \ \forall rg \in REG \quad (44)$$

4. $DINIE_{t,rg}$: Definition – Net infected population traveling from rg-region to other regions

$$PIE_{t,rg} = \Sigma_{ss \in SSR(rg)} \Sigma_{rd \in RDE(rg)} PTRRA_{rg,rd,ss} \times PIS_{t,rg,ss}$$
$$\forall t \ \forall rg \in REG \quad (45)$$

5. $DINPR_{t,rg}$: Definition – Net infected population in touch with susceptible population in rg-region

$$PIN_{t,rg} = PIX_{t,rg} + PII_{t,rg} - PIE_{t,rg}$$
$$\forall t \ \forall rg \in REG \quad (46)$$

3.1.3. Discrete Dynamic Equations

This section shows the algebraic formulation of the SEMIR/R-S regional-segment epidemic model.

1. $IPOSU_{t,st,rg,ss}$: State: SU – Increment

$$IPO_{t,st,rg,ss} = LAMS_{rg,ss} \times NPX_t$$
$$\forall t\ \forall st \in SU\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (47)$$

2. $IPOSUR_{t,st,rg,ss}$: State: SU – Increment – Recovered Reinfected
In the event that recovered ones become susceptible again over time, a term should be included that increases those susceptible by keeping in mind the FRES fraction of people who recovered LAGR days ago. This equation substitutes the equation $IPOSU_{t,st,rg,ss}$, it is formulated as

$$IPO_{t,st,rg,ss} = FRES \times IPO_{t-LAGR,s1,rg,ss} + LAMS_{rg,ss} \times NPX_t$$
$$\forall t\ \forall st \in SU\ \ \forall s1 \in RE\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (48)$$

3. $DPPND_{t,st,rg,ss}$: State: SURE – Natural Dead Decrement

$$DPN_{t,st,rg,ss} = MIUN \times POP_{t-1,st,rg,ss}$$
$$\forall t\ \forall st \in SURE\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (49)$$

4. $DPOSU_{t,st,rg,ss}$: State: SU - Decrement

$$DPO_{t,st,rg,ss} = S2I_{t-1,rg,ss} + DPN_{t,st,rg,ss}$$
$$\forall t\ \forall st \in SU\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (50)$$

5. $IPOEX_{t,st,rg,ss}$: State: EX - Increment

$$IPO_{t,st,rg,ss} = S2I_{t-1,rg,ss}$$
$$\forall t\ \forall st \in EX\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (51)$$

6. $DPOEX_{t,st,rg,ss}$: State: EX - Decrement

$$DPO_{t,st,rg,ss} = FHII \times POP_{t-1,st,rg,ss}$$
$$\forall t\ \forall st \in EX\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (52)$$

7. $IPOI0_{t,st,rg,ss}$: State: I0 – Increment

$$IPO_{t,st,rg,ss} = \Sigma_{s1 \in EX1}\ DPO_{t,s1,rg,ss} + LAMI_{rg,ss} \times NPX_t$$
$$\forall t\ \forall st \in I0\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (53)$$

8. $DPOI0_{t,st,rg,ss}$: State: I0F – Decrement

$$DPO_{t,st,rg,ss} = DSAL_{st,ss} \times POP_{t-1,st,g,ss}$$
$$\forall t\ \forall st \in I0F\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (54)$$

where set $st \in I0F$ is equal to: $st \in I0 \cup st \in I1F$. The set $st \in I1F$ is equal to: $st \in \{I_1, I_2, I_3 \ldots\}$

9. $IPOIF_{t,st,rg,ss}$: State: I1F – Increment

$$IPO_{t,st,rg,ss} = \Sigma_{s1 \in ANT(st)}\ DPO_{t,s1,rg,ss}$$
$$\forall t\ \forall st \in I1F\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (55)$$

where the set $s1 \in ANT(st)$ is the set that contains the epidemic state s1 previous to the state st,

10. $IPORE_{t,st,rg,ss}$: State: RE - Increment

$$IPO_{t,st,rg,ss} = \Sigma_{s1 \in I0F1}\ DSBE1_{s1,ss} \times POP_{t-1,s1,rg,ss} + LAMR_{rg,ss} \times NPX_t$$

$$\forall t\ \forall st \in RE\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (56)$$

where the set $s1 \in I0F1$ is the set that contains all active infected epidemic states s1

11. $DPORE_{t,st,rg,ss}$: State: RE – Decrement

$$DPO_{t,st,rg,ss} = DPN_{t,st,rg,ss}$$
$$\forall t\ \forall st \in RE\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (57)$$

12. $DPORER_{t,st,rg,ss}$: State: RE – Decrement – Recovered Reinfected
If recovered ones become susceptible again over time, a term that decreases those recovered should be included, this equation substitutes the equation $DPORE_{t,st,rg,ss}$, it is formulated as

$$DPO_{t,st,rg,ss} = FRES \times IPO_{t\text{-}LAGR,st,rg,ss} + DPN_{t,st,rg,ss}$$
$$\forall t\ \forall st \in RE\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (58)$$

13. $IPOED_{t,st,rg,ss}$: State: ED - Increment

$$IPO_{t,st,rg,ss} = \Sigma_{s1 \in IF1F}\ MISS_{ss} \times POP_{t,s1,rg,ss}$$
$$\forall t\ \forall st \in ED\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (59)$$

where the set $s1 \in IF1F$ is the set that contains all active infected epidemic states s1 lees the last infected state

14. $IPOND_{t,st,rg,ss}$: State: ND - Increment

$$IPO_{t,st,rg,ss} = \Sigma_{s1 \in SURE1}\ DPN_{t,s1,rg,ss}$$
$$\forall t\ \forall st \in ND\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (60)$$

where the set $s1 \in SURE1$ is the set that contains the susceptible or recovered state s1

These equations imply that the optimization problem corresponds to one with quadratic constraints. There is the possibility of linearizing these constraints based on a piecewise linear approximation in two dimensions, converting the problem in a Mixed Integer Problem (MIP).

4. Control Policy Modeling

For implementation in the NPI (Non-Pharmaceutical Interventions) mathematical model, the following fundamental aspects should be considered:

- The relationship of how epidemic spread rates affect policies
- How control policy is applied in different <regions, segments>.

The objective of the control policy is to regulate the epidemic in such a way as to minimize the number of deaths due to factors other than the epidemic.

According to social estrangement, control policies are classified as

- Confinement: Fully isolates the sociodemographic segments that are the subject of confinement policy. It is characterized by:
- Two confinement policies, or more, cannot be applied to the same segment in a region.

- If confinement measures are applied, mitigation policies are not applicable.

This policy is disjunctive, it is applied or is not applied; then, it corresponds to a binary variable.

- Mitigation: Decreases social contact, limiting social activities involving agglomeration (e.g., attendance at schools, universities, bars, restaurants). This policy may be:
  - Continuous, it applies to a fraction of the population, varies between 0 and 1. The effect on the spread of the epidemic is linear, as the intensity of mitigation increases the decrease in the rate of spread of the epidemic increases.
  - Discrete, it applies to the entire population, is represented with a binary variable that is 1 if policy is activated.

This type of policy is not considered in this document.

- Circulation: Decreases social contact, limiting the people mobility between regions. This type of policy is considered superficially in this document.

4.1. Simple Confinement Policies

These confinement policies are based on determining the fraction of the population to be confined to each region-segment during each period of the planning horizon. The impact on the epidemic is measured by altering the epidemiological parameters that are calculated based on an analysis that refers to the work of Mejia Becerra et. al (2020), who established two scenarios:

i. The population has no restrictions (population can move freely), and
ii. The quarantined population (population stay in their homes), to achieve this is modeled the dynamic changes in the rate of transmissibility $bd_{t,st}$ that is function of the quarantine policy.

4.1.1. Simulation Model

In a simulation model $bd_{t,st}$ is a parameter, $BETEF_{t,st}$, implicitly defined by the user because the fraction of the people under quarantine, $a_{t,st}$, is predefined. It is defined as

$$BETEF_{t,st} = ALFA_{t,st} \times BETAQ_{st} + BETAB_{st} \times (1 - ALFA_{t,st}) \quad (61)$$

where

$BETEF_{t,st}$	Effective transmissibility rate in st-state during t-period
ALFAt,st	Fraction of population in quarantine during t-period ($a_{t,st}$)
$BETAB_{st}$	Free transmissibility rate in st-state
$BETAQ_{st}$	Quarantine transmissibility in st-state

$BETAB_{st}$ (b_{st}) and $BETAQ_{st}$ (b^{Q}_{st}) are transmissibility rates (parameters) for an asymptomatic or moderate individual who circulates freely within the population and an individual who stays in their home, respectively. They can be expressed as the total contact rate (the total number of susceptible contacts by an effective or non-effective infective individual, per unit of time), multiplied by the probability of infection, given the contact between an infectious and susceptible individual.

When the control policy is user-defined the equation that defines the number of net infected population in touch with susceptible population in rg-reg is define by the equation

1. $DSUINS_{t,rg,ss}$: Net infected population interacting with susceptible population in rg-region (simulation model)

$$SIN_{t,rg,ss} - \Sigma_{st \in INF} BESAB_{t,st,rg,ss} \times PNN_{t,rg,ss} = 0$$
$$\forall t \ \forall rg \in REG \ \forall ss \in SSR(rg) \quad (62)$$

where

$$BESAB_{t,st,rg,ss} = BETEF_{t,st} \times BESS_{rg,ss}$$

$BESS_{rg,ss}$ represents the inverse contact intensity function in rg-region ss-segment. This equation substitutes the equation $DSUSIN_{t,rg,ss}$

2. $PINPSN_{t,rg,ss}$: Definition of the variable $PNN_{t,rg,ss}$

$$PNN_{t,rg,ss} = PIN_{t,rg} \times PSN_{t,rg,ss}$$
$$\forall t \ \forall rg \in REG \ \forall ss \in SSR(rg) \quad (63)$$

3. $DSUSIES_{t,rg,ss}$: Definition – Net susceptible population living in rg-region infected in other regions. This equation substitutes the equation $DSUSIE_{t,rg,ss}$

$$SIE_{t,rg,ss} = \Sigma_{st \in SU} \Sigma_{rd \in RDE(rg)} BESDD_{t,rg,ss} \times PIN_{t,rd} \times PSE_{t,st,rg,rd,ss}$$
$$\forall t \ \forall rg \in REG \ \forall ss \in SSR(rg) \quad (64)$$

where

$$BESDD_{t,st,rg,ss} = BETEF_{t,st} \times BESD_{rg,ss} \quad (65)$$
$$BESD_{rd,ss} = \Sigma_{rg \in RDRG(rd)} BESS_{rg,ss} \quad (66)$$

4.1.2. Optimization Model

For the optimization model the fraction of the fraction of the population in quarantine ($FQU_{t,st}$, $a_{t,st}$) is the key variable of the control policy. $FQU_{t,s}$ is the epidemic control variable that represents the population fraction of the st-state that cannot circulates freely ($0 \leq FQU_{t,s} \leq 1$). Then $bd_{t,st}$ is a variable, $BDE_{t,st}$, that is calculated by the model. It is defined as

$$BDE_{t,st} = BETAB_{st} \times (1 - FQU_{t,st}) + \times BETAQ_{st} \times FQU_{t,st}$$
$$\forall t \ \forall st \in INF \quad (67)$$

In the previous formulation the parameters $BETAB_{st}$ and $BETAQ_{st}$ are a function of the state of the epidemic, this formulation can be extended so that these parameters are a function of the region and/or the sociodemographic segment. This deployment will only consider dependency on state. However, the decision variable will be dependent to rg-region and ss-segment, this is $FQU_{t,st,rg,ss}$.

When the control policy is model-defined the equation that establishes the number of net infected population in touch with susceptible population in rg-region is define by the equations

1. $DSUDTR_{t,st,rg,ss}$: Dynamic optimized transmissibility rate

$$BDE_{t,st,rg,ss} = BETAB_{st} \times (1 - FQU_{t,st,rg,ss}) + BETAQ_{st} \times FQU_{t,st,rg,ss}$$
$$\forall t\ \forall st \in INF\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (68)$$

The above expression can be formulated as

$$BDE_{t,st,rg,ss} + BETADI_{st} \times FQU_{t,st,rg,ss} = BETAB_{st}$$
$$\forall t\ \forall st \in INF\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (69)$$

where

$$BETADI_{st} = BETAQ_{st} - BETAB_{st}$$

2. $DSUINO_{t,rg,ss}$: Net infected population interacting with susceptible population in rg-region (optimization model)

$$SIN_{t,rg,ss} - \Sigma_{st \in INF}\ BESS_{rg,ss} \times BDE_{t,st,rg,ss} \times PNN_{t,rg,ss} = 0$$
$$\forall t\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (70)$$

This equation substitutes the equation $DSUSIN_{t,rg,ss}$

$DSUSIEO_{t,rg,ss}$: Definition – Net susceptible population living in rg-region infected in other regions. This equation substitutes the equation $DSUSIE_{t,rg,ss}$

$$SIE_{t,rg,ss} = \Sigma_{st \in SU}\ \Sigma_{rd \in RDE(rg)}\ BESDD_{t,rg,ss} \times PIN_{t,rd} \times PSE_{t,st,rg,rd,ss}$$
$$\forall t\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (71)$$

4.2. Complex Confinement Policies

The complexity is because in the model is introduced the possibility of mixing different control policies, focusing them at the level of the <region, segment> and not as in the previous case, based on a general policy for the whole population. The cost of complexity is a model with more variables, some of them binary, which requires for real cases large greater computational capacity and powerful optimization algorithms to solve the problem.

4.2.1. Variables And Restrictions

Below are the complex confinement policies included in the model and the variables and equations used.

Table 10. CONFINEMENT CONTROL POLICIES VARIABLES		
Variable	Description	Existence Conditions
QGL_t	Binary variable equal to 1 when a total quarantine control-policy is applied over all macro-regions.	$\forall t$
$QRE_{t,rg}$	Binary variable equal to 1 when a quarantine control-policy is applied over rg-region	$\forall t$ $\forall rg \in REGQ$
$QSS_{t,ss}$	Binary variable equal to 1 when a quarantine control-policy is applied over ss-sociodemographic segment in all regions	$\forall ss \in SSRQ$
$QST_{t,st}$	Binary variable equal to 1 when a quarantine control-policy is applied over st-epidemic-state in all regions. It has sense for epidemic susceptible and infected states ($st \in SUIN$), but in economics aspects when the susceptible are confined, the recovered people of the same rg-region ss-segment if confined.	$\forall t$ $\forall st \in SUIN$
$QRS_{t,rg,ss}$	Binary variable equal to 1 when a quarantine control-policy is applied over ss-sociodemographic segment in rg-region	$\forall t$ $\forall rg \in REGQ$ $\forall ss \in SSR(rg)$
$QRT_{t,st,rg}$	Binary variable equal to 1 when a quarantine control-policy is applied over st-epidemic-state in rg-region	$\forall t$ $\forall st \in SUIN$ $\forall rg \in REGQ$
$QDE_{t,st,rg,ss}$	Binary variable equal to 1 when a quarantine control-policy is applied over st-epidemic-state and ss-sociodemographic segment in rg-region	$\forall t$ $\forall st \in SUIN$ $\forall rg \in REGQ$ $\forall ss \in SSR(rg)$
$CPQ_{t,st,rg,ss}$	Binary variable that is equal to 1 when the any quarantine control-policy is applied in rg-region for the ss-sociodemographic-segment during t-period.	$\forall t$ $\forall st \in SUIN$ $\forall rg \in REGQ$ $\forall ss \in SSR(rg)$
$CPM_{t,st,rg,ss}$	Binary variable that is equal to 1 when the any mitigation control-policy is applied in rg-region for the ss-sociodemographic-segment during t-period.	$\forall t$ $\forall st \in SUIN$ $\forall rg \in REGQ$ $\forall ss \in SSR(rg)$
$CPN_{t,st,rg,ss}$	Binary variable that is equal to 1 when no control policy is applied in rg-region for the ss-sociodemographic-segment during t-period.	$\forall t$ $\forall st \in SUIN$ $\forall rg \in REGQ$ $\forall ss \in SSR(rg)$

The following equation is required for the simulation of the confinement control policies:

1. $CCPQ_{t,st,rg,ss}$ defines that a confinement control policy is activated in the st-epidemic-state in the ss-segment in rg-region

$$CPQ_{t,st,rg,ss} = QGL_t + QRE_{t,rg} + QSS_{t,ss} + QST_{t,st} + QRS_{t,rg,ss} + QRT_{t,st,rg} + QDE_{t,st,rg,ss}$$
$$\forall t \ \forall st \in STA \ \forall rg \in REGQ \ \forall ss \in SSR(rg) \quad (72)$$

2. $CPSI_{t,st,rg,ss}$ controls the concurrency of control policies, only a mitigation control policy or a confinement control policy may affect the st-epidemic-state, the ss-segment in rg-region

$$CPQ_{t,st,rg,ss} + CPM_{t,st,rg,ss} + CPN_{t,st,rg,ss} = 1$$
$$\forall t \ \forall st \in STA \ \forall rg \in REGQ \ \forall ss \in SSR(rg) \quad (73)$$

4.2.2. Impact of Quarantine Policy

The transfer rate resulting from the confinement control policy must be different of the transfer rate without control policy. Considering the definition of the parameter $bb_{rg,ss}$ ($BESS_{rg,ss}$), the inverse of contact intensity multiplied by the transmission probability, as function of the confinement policy, it is called $bq_{rg,ss}$ ($BEQU_{rg,ss}$). The definitions of these parameters are

$$bb_{rg,ss} = dd \times br_{rg,ss} \quad (74)$$

$$bq_{rg,ss} = dd \times bq_{rg,ss} \quad (75)$$

The probability of contagion $br_{rg,ss}$ and $bq_{rg,ss}$ (in OPTEX, $PCON_{rg,ss}$ and $PQUA_{rg,ss}$) are the result of the parameter calculation model. To determine the change in the probability of contagion as a result of quarantine. The efficacity between free movement and quarantine is calculated as

$$EFQC_{rg,ss} = PQUA_{rg,ss}/PCON_{rg,ss} \quad (76)$$

If $PQEF_{rg,ss}$ is less than 1 the quarantine decreases the effect of the epidemic, otherwise quarantine will be counterproductive; this case can occur when people living in a spray condition are quarantined, which can end up increasing the intensity of contacts and thus the contagion probability.

In terms of equivalent population, the reduction, or increase, in the population participating in the contagion process (susceptible and infected) is calculated based on the effectiveness of population circulation reduction during quarantine in the rg-region ss-segment ($ef_{rg,ss,}$ $EFQP_{rg,ss}$), the full effectivity reduction is equal to 1; it combined with the effectiveness of quarantine allows to calculate the net effectiveness ($EFQN_{rg,ss}$) of quarantine.

$$EFQN_{rg,ss} = EFQC_{rg,ss} \times (1 - EFQP_{rg,ss}) \quad (77)$$

For mathematical modeling, the concept of equivalent people with free movement, $POF_{t,st,rg,ss}$, can be defined as the population in a state minus the variation in equivalent population if quarantine is imposed, $POR_{t,st,rg,ss}$. Implementing this requires the following two equations:

1. $PPOR_{t,st,rg,ss}$: variation in the circulation of people in equivalent population due to quarantine

$$POR_{t,st,rg,ss} = EFQN_{rg,ss} \times CPQ_{t,st,rg,ss} \times POP_{t,st,rg,ss}$$
$$\forall t \ \forall st \in SUIN \ \forall rg \in REQ \ \forall ss \in SSRQ \quad (78)$$

   where $rg \in REQ$ corresponds to the set of regions and $ss \in SSRQ$ to the set segments where quarantine policies can be applied.
2. $PPOD_{t,st,rg,ss}$: The previous equation may be modeled using the concepts of Disjunctive Programming (DP) that is based on setting constraints that depend on a logical (binary) variable if it is equal to 1 triggers the associated constraint. $CPQ_{t,st,rg,ss}$ Defining $CPQ_{t,st,rg,ss}$ as a logical variable,

the previous equation in disjunctive form is formulated as (where ∨ corresponds to the or operator).

$$POR_{t,st,rg,ss} =$$
$$[\ EFQN_{rg,ss} \times POP_{t,st,rg,ss};\ \text{if}\ \ CPQ_{t,st,rg,ss} = 1\ ]$$
$$\forall t\ \forall st \in SU\ \forall s1 \in INDE$$
$$\vee$$
$$[\ 0\ ;\ \text{if}\ \ CPQ_{t,st,rg,ss} = 0\ ]$$
$$\forall t\ \forall st \in SUIN\ \forall rg \in REQ\ \forall ss \in SSRQ \quad (79)$$

When the algebraic language or the solver handles DP, it is easy to implement. it is the GAMS case.

3. $PPOF_{t,st,rg,ss}$: equivalent population with free movement

$$POF_{t,st,rg,ss} = POP_{t,st,rg,ss} - POR_{t,st,rg,ss}$$
$$\forall t\ \forall st \in SUIN\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (80)$$

4.2.3. Mitigation Policies

Implementing mitigation policies requires differentiating the activities that each segment performs and how long those activities last. This case is not considered in this document.

4.2.4. Mobility Policies

Mobility control policies aim to reduce the rate of contagion in regions that attract large numbers of people by increasing proximity leading to an increase in the rate of contagion in the region. The reasons for these restrictions are to prevent people from:

i. Moving to regions at high risk of contagion, for example, isolation of a region in such a way that people are not allowed in and out.
ii. Using transport modes where closeness between travelers increases the likelihood of contagion (since it is normal that by public transport the proximity between people shops to zero); for example, restricting the factor of use of modes of transport. The ideal is to include the travel times because it is determinant of contagion during the travel.

The following discusses a policy based on the total isolation of a rg-region; this implies that the following equation must be satisfied

$$0 = S_{st \hat{I} SU}\ S_{ss \hat{I} SSR(rg)}\ (S_{rd \hat{I} RDE(rg)}\ PSE_{t,st,rg,rd,ss} + S_{ro \hat{I} ROR(rg)}\ PSI_{t,st,ro,rg,ss}) \quad (81)$$

For modeling the binary variable $MRE_{t,rg}$ must be included, it will be equal to 1 if mobility to/from the rg-region is allowed, this involves including two new equations.

1. $DSUSIM_{t,st,ro,rg,ss}$: Definition – Control of susceptible population traveling to rg-region from ro-region ($PSI_{t,st,ro,rg,ss}$). This equation substitutes the equation $DSUSI_{t,st,ro,rg,ss}$

$$PSI_{t,st,ro,rg,ss} = PTRR_{ro,rg,ss} \times MRE_{t,rg} \times POF_{t,st,rg,ss}$$
$$\forall t\ \forall st \in SU\ \forall rg \in REG\ \forall ro \in ROR(rg)\ \forall ss \in SSR(rg) \quad (82)$$

2. $DSUSEM_{t,st,rg,rd,ss}$: Definition – Control of susceptible population traveling from rg-region to rd-region ($PSE_{t,st,rg,rd,ss}$). This equation substitutes the equation $DSUSE_{t,st,rg,rd,ss}$

$$PSE_{t,st,rg,rd,ss} = PTRRA_{rg,rd,ss} \times MRE_{t,rg} \times POF_{t,st,rg,ss}$$
$$\forall t\ \forall st \in SU\ \forall rg \in REG\ \forall rd \in RDE(rg)\ \forall ss \in SSR(rg) \quad (83)$$

The above equations are mixed quadratic, which could be handled by disjunctive equations. It is also possible to relax the binary character of $MRE_{t,rg}$ to allow partial isolations.

4.3. Multi-Period Decisions

For practical purposes it seems unreasonable to take changing health policies every day; however, the observed practice indicates that this possibility has been used in many regions that continually change their control policy daily. This validates the decision-making periods of a day for short-term planning horizons, on the agenda of the weeks.

Therefore, to facilitate long-term planning, the concept of decision periods is introduced which correspond to a group of contiguous days (several days, one week, one month) in which the variables that define the control policy are equals. These periods can be user-defined. This is done by entering the pp subscript associated with a new entity called the decision t-period that groups multiple days. The equation to be included is

$$XXX_{t,st,rg,ss} = UXXX_{pp,st,rg,ss}$$
$$\forall t\ \forall pp \in PDP(t)\ \forall st \in STA\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (84)$$

where

pp	Decision period
PDT(t)	Decision t-period which the t-period belongs
$XXX_{t,st,rg,ss}$	Decision variable associated with the t-period
$UXXX_{t,st,rg,ss}$	Decision variable associated with the decision period pp

$XXX_{t,st,rg,ss}$ is a wildcard that represents all decisions related to pandemic control in the t domain, and the same variable in the pp domain.

For example, for simple control policy modeling, this equation limited $FQU_{t,st,rg,ss}$ to

1. $UFQU_{t,st,rg,ss}$: Unification of decisions by period. Variable $UFQU_{pp,st,rg,ss}$

$$FQU_{t,st,rg,ss} = UFQU_{pp,st,rg,ss}$$
$$\forall t\ \forall pp \in PDP(t)\ \forall st \in STA\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (85)$$

5. Vital Resources Capacity Modeling

This modeling is aimed at coordinating pandemic management with the physical vital resources required to minimize the impacts due to the

pandemic. It must be clear that managing the epidemic is managing the resources, then the availability of resources must be considered regarding the epidemic peaks are consequence of the NPI policies selected by public health authorities. Coordination of the two aspects is essential to minimize the deaths from due to the epidemic.

Health resources are divided into two types:

- Vitals (hr∈HRV): a subset of resources whose scarcity is reflected in the change in epidemic status of affected patients, increasing the number of deaths for reasons other than the epidemic.
- Complementary (hr∈HRC): resources whose scarcity creates management problems but do not affect the development of the pandemic.

The management policy of the pandemic should consider the expansion of capacity of vital resources (the scarcity of which generates additional deaths) and the adequacy of complementary resources to such expansion, in accordance with the development of the pandemic.

5.1. Vital Resources Availability

The basic epidemic model cannot represent an epidemic process considering how the installed capacities of vital health resources affect the natural process. When the capacity of a vital resource is exceeded, for example the number of beds for care for severe patients requiring intensive care and/or intermediate care (ICU), the probability of transition between states changes, this can be modeled directly, building capacity-dependent rates simulating the process that occurs.

The concept of alternative state is introduced, to which, with probability 1, is directed the population that cannot be served by capacity deficit. This state must be a new state that receives the population of the state chain itself plus the forced transfer due to the capacity deficit. Then two additional states must be included in the epidemic model:

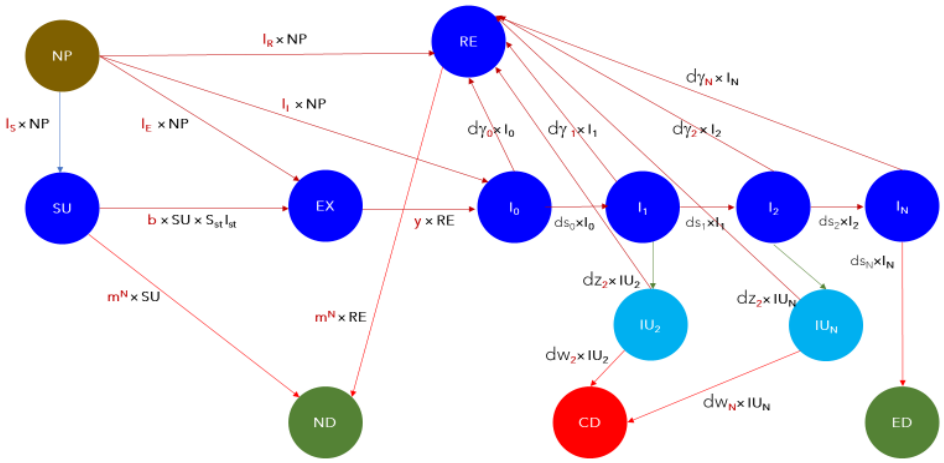
IU Unused Infected: Infected population not attended

CD Epidemic Collateral Deaths: caused by reasons other than the epidemic (mainly due to capacity or by management policies).

It should be noted that deaths directly generated by the epidemic (ED state) corresponds to a constant value (this is due to the differential equations model) independent of the management of the epidemic; therefore, trying to minimize this number of total deaths cannot be the goal of optimization. If nothing is done and the number of resources remains constant, the ED value will also correspond to a constant value. However, managing installed

capacity over the planning period can decrease the number of deaths occurring in the CD state.

FIGURE 3. STATE TRANSITION DIAGRAM – SEIMR/R-S EPIDEMIC MODEL LIMITED CAPACITY



1. $CARE_{t,rg,hr}$: Determines the available capacity at the beginning of t-period in a rg-region for a hr-resource(set hr∈HRV). This equation is analyzed in a posterior section.

$$CHS_{t,rg,hr} = CARE_{rg,hr} + \Sigma_{q=1,t} CEX_{q,rg,hr}$$
$$\forall t \ \forall rg \in REG \ \forall hr \in HRV \quad (86)$$

2. $RIPO_{t,rg,hr}$: Controls that does not exceed capacity for the "vital" resources. This equation considers that $CHS_{t,rg,hr}$ the capacity of the resource is regional and that all segments share that resource.

$$\Sigma_{st \in INF} \Sigma_{ss \in SSR(rg)} CIRG_{st,rg,hr} \times IPO_{t,st,rg,ss} \leq CHS_{t,rg,hr}$$
$$\forall t \ \forall rg \in REG \ \forall hr \in HRV \quad (87)$$

where

$$CIRG_{st,rg,hr} = RECO_{st,hr} \times RPOB_{rg} \quad (88)$$

where $RPOB_{rg}$ represents the population in the rg-region at the beginning of the planning horizon (it converts fraction of population into population) and $RECO_{st,hr}$ the unitary consumption per person of hr-health-resource in st-state.

3. $RIPOD_{t,rg,hr}$: Control focused on important dates. It allows the planner to determine the policy that "guarantees" that on certain dates (e.g., easter, christmas, national holidays, ...) the consumption levels of critical hospital resources (e.g., ICUs) ensure availability greater than or equal to a predefined value. This is necessary due to the model is deterministic. This is to define periods of controlled reliability, in which the use of critical vital resources is controlled to be below a certain availability level. The process involves adjusting the $RIPO_{t,rg,hr}$ equation by

introducing a slack factor ($FCHS_{t,rg,hr}$) in terms of the minimum fraction of installed capacity that should be available. The new formulation of $RIPO_{t,rg,hr}$ introduces a maximum use factor ($UCHS_{pc,rg,hr}$).

$$UCHS_{t,rg,hr} \times CHS_{t,rg,hr} \geq \Sigma_{st \in INF} \Sigma_{ss \in SSR(rg)} CIRG_{st,rg,hr} \times IPO_{t,st,rg,ss} \quad \forall t \ \forall rg \in REG \ \forall hr \in HRV \tag{89}$$

where

$$UCHS_{t,rg,hr} = 1 - FCHS_{t,rg,hr} \tag{90}$$

Depending on the patient's mobility and/or vital resources in the macro-region, the above equation can be reformulated in such a way that an infected patient can be treated in any region (applies for territories associated with cities or metropolitan areas).

4. $GIPO_{t,hr}$: Controls that does not exceed the global capacity for the "vital" resources. This equation considers that the capacity of the resource is global (macro-regional) and that all segments share that resource.

$$\Sigma_{rg \in REG} \Sigma_{st \in INF} \Sigma_{ss \in SSR(rg)} CIRG_{st,rg,hr} \times IPO_{t,st,rg,ss} \leq \Sigma_{rg \in REG} CHS_{t,rg,hr} \quad \forall t \ \forall hr \in HRV \tag{91}$$

To satisfy the above equations it is necessary to incorporate a slack variable that allows to redirect the unattended population to an "alternative" state in which the probability (rate) of death is greater than if it had been served. This term affects the differential equations that describe the epidemic; therefore, an additional term, that takes nonzero value when the capacity constraints of a vital resource are activated, is introduced in algebraic equations.

Then, the increment population that exceeds the capacity is redirected to one of the s1 alternative state, $s1 \in SUN(st)$. This implies that in the infected states equations it is necessary to calculate the increment of people in the alternative state as shows the following algebraic expression where the second term represents the population that is unattended due to capacity.

$$IPO_{t,st,rg,ss} + \Sigma_{s1 \in SUN(st)} IPO_{t,s1,rg,ss} \tag{92}$$

Considering that $IPO_{t,st,rg,ss}$ always satisfies the capacity constraints to calculate the deficit are considered the following two equations.

5. $DIPX_{t,st,rg,ss}$: Unattended infected patients in st-state

$$IPX_{t,st,rg,ss} = \Sigma_{s1 \in SUN(st)} IPO_{t,s1,rg,ss} \quad \forall t \ \forall st \in INF \ \forall rg \in REG \ \forall ss \in SSR(rg) \tag{93}$$

The variable $IPX_{t,st,rg,ss}$ must be used in the incremental equation for infected states in all epidemic models.

6. $DEHR_{t,rg,hr}$: Deficit of vital health resources in rg-region

$$DHR_{t,rg,hr} = \Sigma_{st \in INF} \Sigma_{s1 \in SUN(st)} \Sigma_{ss \in SSR(rg)} RECO_{st,hr} \times RPOB_{rg} \times IPX_{t,s1,rg,ss} \quad \forall t \ \forall rg \in REG \ \forall hr \in HRV \tag{94}$$

5.2. Health Resource Expansion

The capacity expansion of vital resources should consider two aspects:

- The cost structure of the expansion, and
- The time (period) at which the expansion is made.
- The budget available for capacity expansions

For the expansion cost it assumes a structure composed of a fixed cost ($CRFX_{rg,hr}$) plus a variable cost ($CRVX_{rg,hr}$) that is caused by each expanded resource unit. It is caused at the time of deciding the expansion. Simulating the expansion process requires the following variables:

$EXC_{t,rg,hr}$ Binary variable that represents the decision to expand the capacity of an hr-resource in the rg-region at the beginning of t-period , and

$CEX_{t,rg,hr}$ Continuous variable that represents the magnitude of the expansion.

The basic restrictions required are:

1. $CARE_{t,rg,hr}$: Determines the available capacity at the beginning of t-period in a rg-region for a hr-resource. It was defined

$$CHS_{t,rg,hr} = CARE_{rg,hr} + \Sigma_{q=1,t}\, CEX_{q,rg,hr}$$
$$\forall t\ \forall rg \in REG\ \forall hr \in HRV \qquad (95)$$

2. $REXP_{t,rg,hr}$: Control that the available capacity at the beginning of t-period in a region for a vital resource

$$REC_{t,rg,hr} \leq CHS_{t,rg,hr}$$
$$\forall t\ \forall rg \in REG\ \forall hr \in HRV \qquad (96)$$

3. $RCEX_{t,rg,hr}$: Controls that a capacity expansion is not performed in a period if the construction decision has not been made; and therefore, the fixed cost is assumed.

$$CEX_{t,rg,hr} \leq \infty \times EXP_{t,rg,hr}$$
$$\forall t\ \forall rg \in REG\ \forall hr \in HRV \qquad (97)$$

4. $RCOX_{t,rg,hr}$: Determines the cost of expansions in a period in a rg-region for a hr-resource.

$$COX_{t,rg,hr} = CRFX_{rg,hr} \times EXP_{t,rg,hr} + CRVX_{rg,hr} \times CEX_{t,rg,hr}$$
$$\forall t\ \forall rg \in REG\ \forall hr \in HRV \qquad (98)$$

In addition to them there may be multiple variations that should be considered for particular real-life cases (for example lead-times); equations that represent these variations should be added to the model. The following is an example of territory budget constraint.

5. BREG: Controls that investment made over the entire planning horizon over all regions.

$$\Sigma_t\, \Sigma_{rg \in REG}\, \Sigma_{hr \in HRX(rg)}\, COX_{t,rg,hr} \leq BREG \qquad (99)$$

6. Vaccination Process Management

The vaccination process management must analyze the vaccination process in terms of the different types of vaccine that exist, which have different characteristics that affect the time of control of the epidemic due to the time they are available, the effectiveness of their protection and the logistical process involved in their application. The indexes va (for the brand of the vaccine) and fv (for the vaccination phase) should be included in mathematical modeling.

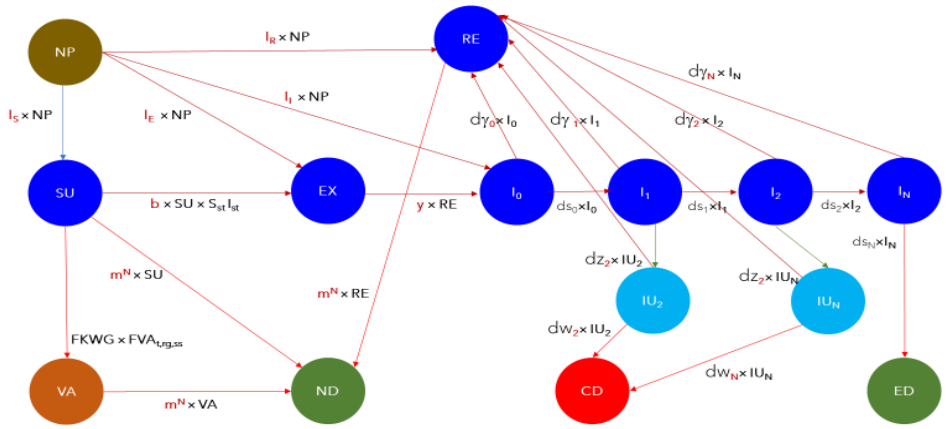
The hypotheses made about the functioning of vaccines are (for real cases, these hypotheses must be validated with an expert in the vaccination process):

1. Two types of vaccines are considered: one-phase (e.g., Johnson & Johnson) and two-phase (e.g., Pzifer, ...). All vaccines may be considered of multiple phases and this characteristic will be parametrized with the set $fv \in PVA(va)$ that define the phases of a vaccine.
2. The vaccine effectiveness is defined by two parameters
   - $FRVA_{va}$ defined as the fraction of vaccinated people who will not develop the disease despite being infected, and who will not infect susceptible people.
   - $FRIN_{va}$ defined as the fraction of people who being vaccinated develop the disease at critical levels. This caseis not considered in this document.
3. Infected people (exposed and active) who are vaccinated do not alter their epidemiological process and the same goes for recovered ones.
4. With the exception of the first phase, fv-phase should be administered $TFVA_{va,fv}$ periods (days) after applying the previous phase (fv-1).
5. At each phase of the vaccination process the effectiveness factor is increased, it depends on the type of vaccine and is represented by the parameter $FEVA_{va,fv}$.
6. A percentage of confidence in the vaccine is assumed for a phase such as the fraction of people vaccinated in phase fv-1 who are revaccinated in phase fv ($FPVA_{fv}$).
7. It is considered a percentage of effectiveness in understanding the state of the epidemic by means of a factor (FKWG) that indicates the fraction of vaccinated people who are susceptible. This factor is because (under the hypothesis 2) if the sampling process was perfect and the epidemic state of entire population had been identified, only susceptible people to be infected should be vaccinated, for this case FKWG is equal to 1. When the measurement process is deficient FKWG decreases to a limit established by the relationship between susceptible persons and the total population. It is important that this is true if the hypothesis of that the recovered people cannot be infected twice or more time during the pandemic planification period.

6.1. Vaccination Process

For mathematical modeling purposes it should be noted that the vaccination process alters the process of evolution of epidemic states which involves new differential equations or adjustment of those already formulated.

FIGURE 4. STATE TRANSITION DIAGRAM – SEIMR/R-S EPIDEMIC MODEL LIMITED CAPACITY + VACCINATION



The diagram shows the connection between all the epidemic states including the VA state that represents the equivalent fraction of population that has been vaccinated.

The modeling process will be analyzed in three stages.

To model multiple vaccines and multiple phases each additional phase is equivalent to decreasing the susceptible population considering:

i) Increment of va-vaccine effectiveness in fv-phase ($VAEF_{va,fv}$), and

ii) Fraction of the population that is revaccinated in fv-phase ($FRVA_{va,fv}$)

iii) Time elapsed from the previous phase ($TPVA_{va,fv}$). For ease of algebraic formulation, the accumulated time parameter ($TAVA_{va,fv}$) is set from the first phase to the va,fv-phase, it is calculated as:

$$TAVA_{va,fv} = S_{fx \in FVA(fv)} TPVA_{va,fx} \quad (100)$$

where $fx \in FVA(fv)$ represents the set of phases fx previous or equal to the phase fv.

The equation required to simulate the vaccination process are:

1. $UVA1_{t,rg,ss,va,fv}$: Number of vaccines applied in the first phase
The gross vaccination fraction, $FVA_{t,rg,ss,va,fv}$, multiplied by the susceptible population and by the population of the region, determines the number of vaccines in the first phase to be applied during a day, $UVA_{t,rg,ss,va,fv}$). Algebraically this is

$$UVA_{t,rg,ss,va,fv} = \Sigma_{st \in SU} RPOB_{rg} \times FVA_{t,rg,ss,va,fv} \times POP_{t,st,rg,ss}$$
$$\forall t \ \forall rg \in REG \ \forall ss \in SSR(rg) \ \forall va \in VAC \ \forall fv \in PH1 \quad (101)$$

where the set $va \in VAC$ defines the vaccines included in the model and $fv \in PH1$ defines the first phase of the vaccination process.

2. $FPVA_{t,rg,ss,va,fv}$: Equivalent fraction of vaccination in the susceptible population ($FVA_{t,rg,ss,va,fv}$, the effective fraction of vaccination) in the susceptible population is equal to

$$PVA_{t,rg,ss,va,fv} = \Sigma_{st \in SU}\ FKWG \times FVA_{t,rg,ss,va,fv} \times POP_{t,st,rg,ss}$$
$$\forall t\ \forall rg \in REG\ \forall ss \in SSR(rg)\ \forall va \in VAC\ \forall fv \in PH1 \quad (102)$$

3. $UVA2_{t,rg,ss,va,fv}$: Number of vaccines applied in the fv-phase different than first phase, for the next phases, the number of vaccines used depends on the date of the first vaccination

$$UVA_{t,rg,ss,va,fv} = RPFP_{rg,va,fv} \times PVA_{t\text{-}TAVA_{va,fv},rg,ss,va,fv}$$
$$\forall t\ \forall rg \in REG\ \forall ss \in SSR(rg)\ \forall va \in VAC\ \forall fv \in PH2(va) \quad (103)$$

where $fv \in PH2(va)$ represents the set that defines the phases of the vaccination process for the va-vaccine excluding the first and

$$RPFP_{rg,va,fv} = RPOB_{rg} \times FPVA_{va,fv} \quad (104)$$

4. $IPOVA_{t,st,rg,ss}$: State: VA – Increment. Considering all phases, the increase in equivalent fraction of people vaccinated is equal to

$$IPO_{t,st,rg,ss} = \Sigma_{va \in VAC}\ \Sigma_{fv \in PH1}\ VAEF_{va,fv} \times PVA_{t,rg,ss,va,fv}$$
$$+ \Sigma_{va \in VAC}\ \Sigma_{fv \in PH2(va)}\ VAFR_{va,fv} \times PVA_{t\text{-}TAVA_{va,fv},rg,ss,va,fv}$$
$$\forall t\ \forall st \in VA\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (105)$$

where the set $fv \in PH1(va)$ define the first phase of the vaccination process and

$$VAFR_{va,fv} = VAEF_{va,fv} \times FRVA_{va,fv} \quad (106)$$

5. $DPOSUV_{t,st,rg,ss}$: State: SU – Decrement – Vaccination Process. The decrement of the susceptible population for vaccination reasons is

$$DPO_{t,st,rg,ss} = S2I_{t-1,rg,ss} + IPO_{t,s1,rg,ss} + DPN_{t,st,rg,ss}$$
$$\forall t\ \forall st \in SU\ \forall s1 \in VA1\ \forall rg \in REG\ \forall ss \in SSR(rg) \quad (107)$$

As vaccines that do not apply to the susceptible population are distributed, it is not important for the development of the pandemic as they do not decrease the infection rate.

6.2. Vaccines Inventory

The number of vaccines applied ($UVA_{t,rg,ss,va,fv}$) must be subject to various logistical and budget restrictions. Below are some of the restrictions to consider, depending on each specific case additional restrictions may be included.

1. $IVAC_{t,va,fv}$: Vaccine Inventory. Total vaccine availability is assumed differentiated by phases in the macro-region, so the following inventory balance restriction must be met

$$IVA_{t,va,fv} = IVA_{t-1,va,fv} - \Sigma_{rg\in REG} \Sigma_{ss\in SSR(rg)} UVA_{t,rg,ss,va,fv} + EVA_{t,va,fv} + EVAC_{t,va,fv}$$
$$\forall t \ \forall va\in VAC \ \forall fv\in PHA(va) \quad (108)$$

Where the parameter $EVAC_{t,va,fv}$ represents the amount of va-vaccine fv-phase that arrive to the macroregion during the t-period and $EVA_{t,va,fv}$ the vaccines buy by the model (a decision variable that must be controlled by the user through set va∈VBY).

2. $VCAR_{t,rg}$: Regional Group Vaccination Capacity. It is assumed that vaccination capacity ($CVA_{t,rg}$) is differentiated by group of regions (index gr), and that it is dynamic and therefore a variable of the optimization problem. Like vital hospital resources, it can be assumed that there is a cost to the development of vaccination capacity, this for purposes of estimating the budget associated with vaccination. All regions of a vaccination regional group share the availability of vaccination resources.

$$\Sigma_{rg\in RGR(gr)} \Sigma_{va\in VAC} \Sigma_{va,fv\in PHV(va)} \Sigma_{ss\in SSR(rg)} UVA_{t,rg,ss,va,fv} \leq CVA_{t,gr}$$
$$\forall t \ \forall gr\in GRE \quad (109)$$

where the set fv∈PHV(va) defines all the phases of the vaccination process for va-vaccine and rg∈RGR(gr) the regions that are included in the gr regional group.

3. $VRES_{t,gr}$: Regional Group Vaccination Resources Availability. Dynamic behavior is assumed for vaccination capacity (CVA_t) through an equation that determines the number of resources required to prepare to deal with the campaign throughout the vaccination period. For each vaccination regional group, the dynamic equation can be written as

$$CVA_{t,gr} = CVA_{t-1,gr} + DVA_{t,gr}$$
$$\forall t \ \forall gr\in GRE \quad (110)$$

where DVA_t represents the increase in vaccination capacity during the t-period in the macroregion.

4. $VCST_t$: Total Vaccination Cost.
Equation aimed at determining the cost of the vaccination process. It must be defined by the user and for now it is considered an equation to estimate vaccination costs plus the cost of the vaccine.
The total cost of vaccination (CTV_t) is calculated as the cost of the vaccine ($CVAC_{va,fv}$) plus the cost of applying the vaccine in the rg-region ($CVRG_{rg}$) plus the unitary cost of increasing vaccination capacity (CDVA), the equation will be:

$$CTV_t = \Sigma_{va\in VAC} \Sigma_{fv\in PHA} CVAC_{va,fv} \times EVA_{t,va,fv} + \Sigma_{rg\in REG} \Sigma_{ss\in SSR(rg)} \Sigma_{va\in VAC} \Sigma_{fv\in PHA} CVRG_{rg} \times UVA_{t,rg,ss,va,fv} + \Sigma_{gr\in GRE} CDVA \times DVA_{t,gr}$$
$$\forall t \quad (111)$$

7. Objective Function

First, it is impossible to avoid the pandemic process, optimization model can be used to support epidemic management without entering the dialectic of duality of goals: lives saved versus loss of quality of life of the population.

The differential equations model establishes that the number of deaths due to the epidemics if fixed (it depends on the biological parameters of the population and is independent of the public health policies) the most economical pandemic minimizes the longest epidemic time, i.e., the one that is caused without public health policies aimed at slowing down the natural speed of the pandemic process. Then, minimizing the number of susceptible persons at the last day of the planning horizon is a measure of pandemic control that tries to make the process as short as possible because when the susceptible are zero, the pandemic will be over; this indirectly minimizes the negative economic impact. This is

Min z = SSU

where

$$SSU = S_{t=T}\, S_{st \in SU}\, S_{rg \in REG}\, S_{ss \in SSR(rg)}\, POP_{t,st,rg,ss} \qquad (112)$$

The definition of SSU must be include in the model as a constraint, SSUR.

There may be other approaches to setting the objective function that represents the criteria decision-making, but they are not considered in this document.

8. Problems & Models

The information defined in this section is intended to define problems and mathematical models in accordance with the methodologies chosen for its solution. OPTEX orientation towards handling large size problems, it is important to consider the definitions that are typical of OPTEX. In the setup process, the user must define:

- Problems: are associated to a set of constraints, and possibly a set of variables over which they have control.
- Models: are associated with a set of problems that make up the model.
- Decisions Support Systems: are associated with a set of models that integrate decision support system.

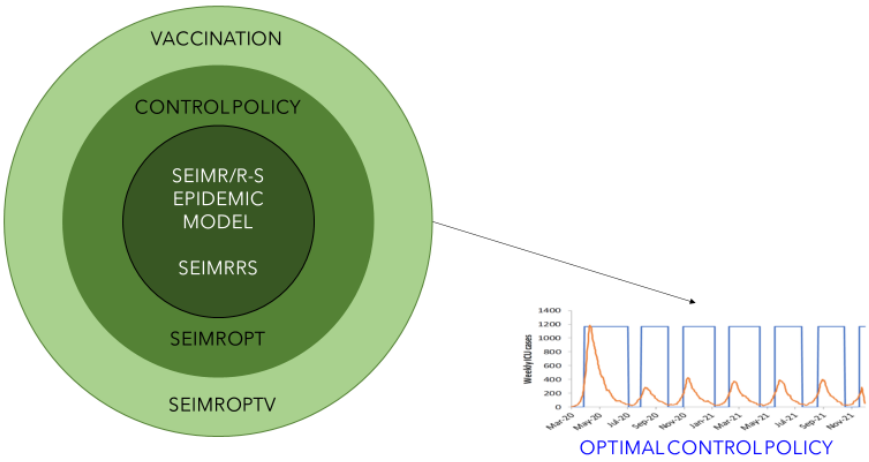
Problems or models can be simple problems, in a direct relationship problem-model, or may be associated with cycles of solution depending on the methodology chosen by the modeler to address the solution. An optimization problem is associated to a set of constraints that define it and a set of variables over which the problem has control.

SEIMR/R-S/OPT consists of three layers each associated with a given capacity to the mathematical modeling, they are presented in the following table.

Table 11. SEIMR/R-S/OPT - Epidemic Decision Support System Models	
Model	**Description Model**
SEIMRRS	SEIMR/R-S Epidemic Model
SEIMROPT	SEIMR/R-S/OPT Optimization Epidemic Model
SEIMROPTV	SEIMR/R-S/OPT Optimization Epidemic Model + Vaccination

The diagram shows the structure.

FIGURE 5. MATHEMATICAL PROBLEMS OF A PANDEMIC OPTIMIZATION MODEL



In turn each layer may be subdivided into several problems. The problems and topics considered are presented in the following table, they are organized in the three layers presented previously. A problem integrates constrains and other problems.

Table 12. H-DSS Optimization Problems				
Model / Problem			**Problem (Topics)**	**Description Problem**
SEIMROPTV	SEIMROPT	SEIMRRS	EPIDEF	Definitions
			EPIDDY	Discrete Dynamic Equations
			EPIPBA	Population Balance
			EPIRSC	Resources Availability
			EPICON	Control Policies
			EPIVAC	Vaccination Process

The restrictions associated with each problem are presented below.

Table 13. SEIMROPTV - Regional-Segment Optimization Epidemic Model + Vaccination

SEIMROPT - Regional-Segment Optimization Epidemic Model					**Vaccination Process (EPIVAC)**
SEIMRRS - Regional-Segment Epidemic Model			**Resources Capacity (EPIRSC)**	**Control Complex Policies (EPICON)**	
Definitions (EPIDEF)	**Discrete Dynamic (EPIDDY)**	**Population Balance (EPIPBA)**			
DSUSR	IPOSU IPOSUR	BPOP	RIPO	CCPQ	DPOSUV
DSUSI	DPOSU	BPRP	GIPO	CPSI	FPVA
DSUSE	DPPND	GNPX	RREC	PPOR	IPOVA
DSUSN	IPOEX		CREC	PPOD	IVAC
DSUSIN	DPOEX		DEDR	PPOF	UVA1
DSUINS	IPOI0		CARE	Simple Control Policies	UVA2
DSUINO	DPOI0		REXP		VCAR
DSUSIE	IPOIF		RCEX	DSUDTR	VCST
DSUSIES	IPORE		RCOX	UFQU	VRES
DSUSIEO	DPORE		BREG	PINPSN	
DSUS2I	DPORER				
DINIS	IPOED				
DINIX	IPOND				
DINII					
DINIE					
DINPR					

9. Optex Implementation

SEIMR/R-S/OPT was implemented in GAMS by RCADT using OPTEX Expert Optimization System (Velásquez-Bermudez, 2019)

FIGURE 6. LOGIN SCREEN TO SEIMR/R-S/OPT

The interested reader can review the implementation process in Velasquez-Bermúdez (2021e, 2021f). SEIMR/R-S/OPT is available under GNU licensee in GAMS algebraic language. The instructions for download the source code are in:
http://www.doanalytics.net/Documents/SEIMR-R-S-OPT-GNU-license.pdf

Conclusion

One of the main limitations of the traditional approach is to assume that the entire population is homogeneous with respect to its epidemiological behavior. It is well known that the epidemic manifests differently in each sociodemographic stratum and that the composition of sociodemographic segments depends on each region.

The added value by mathematical programming approach is to convert simulation models into optimization models to be able to combine them with other mathematical programming models, following the principles of structured mathematical modeling that allows join multiple mathematical programming problems in a single holistic model. Based on the above, the formulation of the models is done by means of algebraic equations that represent how the epidemiological process evolves during the planning horizon.

While models like SEIMR/R-S/OPT can be difficult to use for the COVID-19 pandemic (mainly because of the non-existence of the model and the scarcity of appropriate databases at the beginning of the pandemic), their greatest benefit is laying the groundwork for high complexity analytical tools to help manage a low-speed disaster such as the present pandemic.

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