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A Multi-age Group Cost-effectiveness Analysis of Lockdown to Mitigate the Spread of Covid-19

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Master in Economics

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Department of Economics

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Resumo

Existe um reconhecimento crescente dos danos que o confinamento tem causado à vida económica e social. A motivação original para o confinamento foi o receio de que o sistema de saúde entrasse em colapso se a doença ficasse fora de controlo. O confinamento de longa data pode ser explicado pelos valores atribuídos à vida (VOL) de potenciais vítimas do COVID-19. Um modelo de Markov incorpora a população suscetível (S) à infecção, população infectada (I) e infecciosa e população removida (R). O último grupo inclui pessoas que morreram da doença. O modelo SIR de propagação da doença, informado pelo curso clínico retrospectivo dos casos positivos da COVID-19 em Portugal, foi desenvolvido para avaliar a relação custo-eficácia do confinamento. Os dados são retirados da plataforma de suporte à tecnologia de informação do Sistema Nacional de Vigilância Epidemiológica (BI SINAVE). Os dados sobre os casos confirmados de infecção por SARS-CoV-2 / COVID-19 dizem respeito ao período de 3 de março de 2020 a 12 de julho de 2022. Os dados sobre probabilidades de transição, custos e utilidades foram recuperados tanto dos dados retrospectivos como da literatura publicada. Este manuscrito também explora que o custo da prevenção da actividade económica através de confinamentos é heterogéneo dentro da população. O risco de mortalidade das pessoas com mais de 65 anos de idade por infecção é substancialmente mais elevado do que o das pessoas com 20-49 anos. As diferenças de mortalidade dentro da população merecem examinar o custo-benefício do confinamento para diferentes grupos etários. Simulamos o modelo Markov para três grupos, jovens (20-49), de meia-idade (50-64) e idosos (65+). O nosso principal resultado neste artigo é que as medidas de distanciamento podem ser significativamente melhoradas com políticas específicas que aplicam bloqueios diferenciais nos vários grupos de risco. No sistema de saúde português e sob hipóteses específicas, de uma perspectiva social, o confinamento proporciona mais QALYs a um custo menor para os idosos do que para a população de meia-idade e jovem.

Palavras-chave: COVID-19, custo-benefício, custo-eficácia, confinamento

JEL Codes: C61, H12, J17

Abstract

There is a growing recognition of the damage the lockdown has caused to economic and social life. A Markov model incorporates population susceptible (S) to infection, population infected (I) and contagious, and population removed (R). The removed group includes people who have died from the disease. The SIR model of disease propagation, informed by the retrospective clinical course of COVID-19 positive cases in Portugal was developed to assess the cost effectiveness of the lockdown. The data are taken from the Business Intelligence of the information technology support platform for the National Epidemiological Surveillance System (BI SINAVE). The confirmed cases of SARS-CoV-2 / COVID-19 infection data are between March 3, 2020 until July 12, 2022. The data on transitional probabilities, costs and utilities were retrieved from both the retrospective data and published literature. This manuscript also explores that the cost of preventing economic activity through lockdowns is heterogeneous within the population. The mortality risk for those over 65 years old from infection is substantially higher than those aged 20-49. The differences in mortality within the population merit examining the cost-benefits of lockdown for different age groups. We simulate the Markov model for three groups, young (20- 49), middle-aged (50-64) and old (65+). Our main result in this paper is that distancing measures can be significantly improved with targeted policies that apply differential lockdowns on the various risk groups. In the Portuguese public healthcare system and under specific hypotheses, from a societal perspective, lockdown provides more QALYs at lower cost for old than for both middle-aged and young population.

Keywords: COVID-19, cost–benefit, cost–effectiveness, lockdown

JEL Codes: C61, H12, J17

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List of Abbreviations

COVID-19- Coronavirus Disease 2019

CBA – Cost-Benefit Analysis

QALY – Quality Adjusted Life Year

VOL – Value of Lives

PSA – Probabilistic Sensitivity Analysis

WTP – Willingness to Pay

SINAVE – Sistema Nacional de Vigilância Epidemiológica

WHO – World Health Organization

VBA – Visual Basic for Applications

GDP – Gross Domestic Product

NPIS – Nonpharmaceutical Interventions

NHS – National Health Service (United Kingdom)

CTMC– Continuous-Time Markov Chain

IFR – Infection Fatality Rate

PCR test – Polymerase Chain Reaction test

ICU – Intensive Care Unit

ICER – Incremental Cost-Effectiveness Ratio

Contents

CHAPTER 1

1. Introduction

In December 2019, an outbreak of a new respiratory infection was identified in Wuhan, China. This disease was found to be caused by a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which is related to Middle East respiratory syndrome (MERS-CoV) and the original severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) (Wang, et al., 2020). The World Health Organization (WHO) has designated it a new type of coronavirus, COVID-19 (WHO, 2020).

To manage the COVID-19 pandemic, several forms of epidemiological surveillance have been developed and used. The mitigation measures encouraged hygiene and social distancing, e.g. careful hand-washing, face masking, use of disinfectants, ban of large public gatherings, the closing of schools, restaurants and shops, quarantine, and restrictions on national and international travel. The most extreme mitigation measure is lockdown in which people are required to stay in their homes and refrain from activities outside the home.

Since the outbreak of the epidemic there has been research on economic aspects of COVID-19. Mainly the impact of restrictive government measures to contain COVID-19 outbreaks has been critically analyzed. The benefits of lockdowns on controlling the infection may outweigh the negative impacts on the economy, social structure, education, and mental health (Meyerowitz-Katz, Bhatt, Ratmann, Brauner, & et al., 2021; Favero, Ichino, & Rustichi, 2020). Lockdown was implemented in order to smooth the spread of the disease, but it continued to be implemented after that aim was accomplished (Rowthorn & Maciejowski, 2020).

This thesis aims to analyse if the lockdown policy to control COVID-19 is more cost-effective than a laissez-faire policy. We examine targeted lockdowns in different age groups: the young, the middle-aged, and the old. Several studies concluded that targeted policies can minimize both economic losses and deaths (Acemoglu, Chernozhukov, Werning, & Whinston, 2020; Baqaee, Farhi, Mina, & Stock, 2020; Ellison, 2020).

We developed a Markov model, based on the Susceptible, Infected, and Recovered (SIR) model, to incorporate probabilities and risks of the two mitigation strategies to determine the costs and quality-adjusted life-years (QALYs) obtained by each strategy. The data are taken from the Business Intelligence of the information technology support platform for the National Epidemiological Surveillance System (BI SINAVE). The confirmed cases of SARS-CoV-2 / COVID-19 infection data are between March 3, 2020 until July 12, 2021. The data on transitional probabilities, costs and utilities were retrieved from both the retrospective data and published literature. We used a deterministic and a probabilistic model. The probabilistic model uses Monte Carlo simulation using Macro Visual Basic Applications (VBA) in Excel.

This dissertation is organized as follows: Chapter 2 examine the studies on how cost-effective it is to assess a lockdown during COVID-19 pandemic; Chapter 3 is dedicated to describing the data and procedures we used to estimate our model and conduct a Cost-Benefit analysis.; in Chapter 4 we will describe and discuss our results of both deterministic and probabilistic analysis, obtained using Normal, Gamma and Beta distributions.; lastly Chapter 5 concludes.

CHAPTER 2

2. Literature Review

This chapter is directed to review studies that relate to the cost-effectiveness of lockdown during on COVID-19 pandemic. The review starts with research about the main aspects of this new coronavirus outbreak. Followed by the research review related to the costs and benefits of COVID-19 control measures: we identify and compare the most relevant (economic and health) outcomes for a lockdown scenario and for no control measures. Afterwards follows a review of QALYs technique to access both the quality and the quantity of life lived. Finally, the investigation encompassing heterogeneity in their COVID-19 related research.

2.1. COVID-19

Even though early research indicates that COVID-19 may have an animal origin, probably from bats, the origin of the disease has not yet been established (Lin, et al., 2020). The new virus is mostly spread from human to human by the air contaminated by the virus, just as SARS-CoV[1]and MERS-CoV[2] (Allen, 2022). The intensity of symptoms is influenced by a variety of variables, including race, sex, pregnancy, certain medical problems and drug use, overcrowding and poverty, and specific professions (Mendes, Baptista, Oliveira, Jardim, & de Castro Neto, 2022). COVID-19 symptoms include cough, shortness of breath, fever, and muscle pains. Less common symptoms are sore throat, headache, diarrhea, and chest pain. A significant minority have noticed that their sense of smell has diminished or is lost entirely (Pascarella, et al., 2020).

Since "patient zero", identified in China, on 31 December 2019, the illness has spread globally, and has the time of writing, approximately a total of 562,000,000 infected cases and 6,370,000 deaths had already been confirmed worldwide (Johns Hopkins Coronavirus Resource Center, 2022). Patients with pre-existing medical conditions are more likely to have

[1] SARS-CoV or SARS-CoV-1 was first identified in Asia in the end of 2002 and the first of the seven known coronaviruses that can infect people (Zhu, et al., 2020). From 2002 to 2004 this virus infected over 8,000 people and caused over 800 deaths worldwide (Tesini, 2020).

[2] MERS-CoV (Middle East respiratory syndrome coronavirus) just like SARS-CoVis a zoonotic virus which meaning that it can be transmitted from animals to people. This virus was first identified in Saudi Arabia in 2012 (Wong, Li, Lau, & Woo, 2019).

the severe COVID-19 outcomes, which are defined as hospitalization, admission to the intensive care unit (ICU), intubation or mechanical ventilation, or death (Mendes, Baptista, Oliveira, Jardim, & de Castro Neto, 2022).

The wide and intense complications of the outbreak in many countries have prompted the World Health Organization to decreed a pandemic on March 11,2020 (WHO, WHO Director-General’s opening remarks at the media briefing on COVID-19-11 March 2020, 2020). In Portugal the first “wave” of infections started at the beginning of March 2020. On March 18, 2020, followed by the case of most of the European countries, the Portugal President decreed a state of emergency, which lasted until May 2, 2020 (Cádima & Ferreira, 2021).

This period included several measures to control the pandemic. The objectives of the mitigation measures ranged from preventing to get infected, save lives, and ensure essential supply chains for essential goods and services. These measures consist of restrictions on the movement of citizens, suspension of various establishments and activities, excluding those that provide essential goods and services. It was also implemented measures to prevent the propagation of the virus, namely social distancing (at least 6 feet from others), face masks, washing hands frequently (for at least 20 seconds) and ventilation of indoor spaces (Cirrincione, et al., 2020).

2.2. Cost-Benefit Analysis

The government's strategies to control the disease involved an implicit balancing of the costs and benefits of action, as with any decision, and was driven by a desire to lower the number of direct and indirect deaths from Covid-19 (Dolan & Jenkins, 2020).

Cost-benefit analysis is a systematic, analytical process for weighing the costs and benefits of a project or program and to assess its appropriateness, often of a social character. It tries to address questions including whether a project proposal is beneficial, what the appropriate proposal size should be, and the relevant restrictions (Mishan & Quah, 2020). This concept of cost-benefit analysis and compartmental models have gained, over time, more and more relevance. Currently, cost-benefit analysis is frequently used by governments and other organizations to provide a basis for comparing the expected benefits and costs of a set of alternatives.

"The argument for lockdown benefits is intuitive. If a new virus enters an unknowing population with no immunity and spreads exponentially, causing an overwhelming of hospitals and subsequent large numbers of deaths, then a physical, government mandated, intervention that isolates people and slows down the transmission of the virus" (Allen, 2022). The measures necessary to stop the spread of disease have additional advantages, such as relieve the pression in hospitals and in intensive care units and give time for developing new treatment approaches (Yaesoubi, et al., 2021), as well as numerous negative effects on the economy and society, such as depression and other "diseases of despair" among the millions of people who lose their jobs, lives lost and ruined by the inability to access services, unemployment, divorce, and suicide (Rowthorn & Maciejowski, 2020).

McKibbin & Fernando (2021) found that the economic disturbances of not imposing lockdown are originated by the substantial number of additional fatalities, lost productivity related to sick days, and excessive demand on the healthcare system during the epidemic. Their projections of the COVID-19 pandemic's impact range from a 1.5 to 8.4 percent drop in GDP when social distance is not included. (Flaxman, et al., 2020) studies the effects of major NPIS (non-pharmaceutical interventions) across 11 European countries. The author estimates that in Europe COVID-19 lockdown saved 3 million lives.

Thunström, et al. (The benefits and costs of using social distancing to flatten the curve for COVID-19, 2020) measure benefits by the number of lives saved from reducing the spread of COVID-19 through social distancing. The results using a 3 percent discount rate and a 30-year planning horizon show that in a lockdown scenario the economic benefits of lives saved exceed the value of the expected losses of GDP by nearly 5.2 trillion dollars. For United States Broughel & Kotrous (The benefits of coronavirus suppression: A cost-benefit analysis of the response to the first wave of COVID-19 in the United States, 2021) estimate that the cumulative benefits of suppression strategies on economic output range between 632.5 billion dollars and 765.0 billion dollars.

Płomecka, et al. (Mental Health Impact of COVID-19: A global study of risk and resilience factors, 2020) explored the mental health impact related to coronavirus disease 2019 (COVID-19) pandemic from March 29th to April 14h, 2020. This study considered a total of 12,817 responses from 12 featured countries and five WHO regions. The results show an incidence of posttraumatic stress, depression, and symptoms of general psychological disorders, with 16.2% of patients expressing suicidal ideas. Laranjeira, et al. (COVID-19 pandemic and its psychological impact among healthy Portuguese and Spanish nursing students, 2021) analyse the presence of psychological and mental health outcomes of the COVID-19 pandemic, and the author demonstrates the existence of a substantial prevalence of psychological and mental health issues, including anxiety, stress, depression, sleeplessness, among others. She also verifies that is a tendency for this effect is anticipated to be more pronounced in certain and/or susceptible groups such women, young people, health professionals, and those who have had mental illness in the past. Parallel with the previous study, Dos Santos, et al. (COVID-19 and mental health—what do we know so far?, 2020) concludes that these health impact of the pandemic on general population and vulnerable groups are particularly associated with the imposed confinement measures.

2.3. Quality-Adjust life years

The National Health Service (NHS) used the Quality-Adjust life years (QALYSs) statistic for around 20 years. Using this technique, a life-quality year's is assessed on a scale from 0 to 1 (0 meaning not worth living; 1 meaning full health). One QALY equals one year of healthy life, but if one person suffers from depression gets only 0.8 QALYs. Many aspects of health policy are advised by QALYs (O'Donnell & Begg, 2020).

To calculate the "Life Years" saved by an intervention, health economists often multiply the projected lives saved by the average residual life expectancy of the victims without the intervention. If the quality of these life years saved would be worse than that of a typical healthy person, a discount is then applied. The outcome is known as the Quality Adjusted Life Year (QALYs) saved by the intervention (Lally, 2022).

Poteet & Craig (QALYs for COVID-19: a comparison of US EQ-5D-5L value sets, 2021) compares the distribution of QALYs values utilizing a national survey and the two published value sets to assess the correlation between COVID-19 results and QALY losses. From the results of this study is concluded that to each year a person lives as “healthy” is attributed 0.90 QALYs; as “symptomatic” 0.81 QALYs; as “asymptomatic” 0.86 QALYs; “very ill” (ICU patient) 0.30 QALYs.

In the meantime, were developed many theories, and the researchers also gave monetary values to these metrics. For instance, $125,000 is assigned to 1 QALY in the research by Schonberger, et al. (Cost benefit analysis of limited reopening relative to a herd immunity strategy or shelter in place for SARS-CoV-2 in the United States, 2020) and £30,000 is utilized in the study by Miles, et al. (Living with COVID-19: balancing costs against benefits in the face of the virus, 2020).

Robinson, et al. (2021) estimate the 'The Value of a Statistical Life' (VSL) for different age-groups based on each group life expectancy. They estimate that on average the VSL for a new-born is 14 million dollars, 12 million dollars for 25-34 years, 8 million dollars for 55-64 years and 2 million dollars for a person with 85 years old.

2.4. Compartmental Models in Epidemiology

Predictive mathematical models are essential for successful epidemic control planning and understanding of the epidemic's trajectory. One usually applied model is the Susceptible, Infected, and Recovered (SIR) model for direct transmission between humans and describes the dynamics of the disease. In this model the population can be divided into three distinct compartments: Susceptible, Infectives and Removed.

In the Susceptible state is the group of the population who could potentially catch the disease, in the Infectives state there is the group of the population who currently have the disease and can infect others and in the Removed state there is the group of the population who have already caught the disease and have recovered and the people who have died (Teles, 2020).

Many economists rapidly were interested in using their expertise to enhance knowledge of the COVID-19 epidemic given the significance of the problem and the influence that these early models made. Several of this works include economic trade-offs and carry out optimum policy analysis inside the SIR Model Atkeson, et al. (2020). Avery,et al. (2021) go over the predictions of cases and fatalities that have been based in a SIR framework, what went wrong with the early predictions, and how they have changed to account for the current COVID-19 epidemic.

Rowthorn & Maciejowski (2020) present a simple cost–benefit analysis inspired by optimal control theory and incorporating the SIR model of disease propagation. They demonstrated that under a baseline cost structure a lockdown with 5 weeks duration is only optimal if the considered value of life is around 2 million pounds and a lockdown with 10 weeks duration is only optimal if the considered value of life exceeds 10 million pounds. Lin, et al. (2020) used an extended on the basic SIR model: the 'Susceptible-Exposed-Infectious-Removed' (SEIR) framework considering a latency period, associated with compartment E, when people have been infected but are not yet infectious. Al-Zoughool, et al. (2022) proposed a stochastic continuous-time Markov chain (CTMC) model with eight states including the environment. The model was then used to forecast the outcomes of lockdown in Mexico, China, Canada, and Niger.

Dashtbali & Mirzaie (2021) analyze the effect of COVID-19 control policies on Egypt, Belgium, Japan, Nigeria, Italy, and Germany. The authors used two compartmental models: the susceptible, exposed, infected, hospitalized, recovered, and death (SEIHRD) model. The second model included the health state: Semi-susceptible (M) (SMEIHRD). This model is similar to the one used by Biala & Khalid (2021) which considers the following stages of infection: susceptible, exposed, infected (asymptomatic and symptomatic), hospitalized, recovered and dead. The findings in this paper show that “stricter measures such as the use of face-masks, social distancing, contact tracing, and even longer stay-at-home orders” need to be required.

2.5. Multi-Age Models

Heterogeneous tastes and preferences are now often used in various fields of economics. Given this standard, it is not unexpected that economists are using heterogeneity in their COVID-19 related research. According to research by Britton, et al. (2020) the herd immunity threshold decreases from 66.7 percent to 62.5 percent, when age-specific contact patterns are taken into consideration (for instance, those over 80 have much less contacts than people in the age group 20-40). If we further assume that the volume of interactions between persons in the same age group varies substantially herd immunity may be reached with just 50% population immunity.

Contretas, et al. (2020) illustrate the transmission of COVID-19 throughout the population, using the multi-group SEIRA (Suscepitble, Exposed, Infected, Recovered, Asymptomatic) model. They conclude that the way people interact vary with geographical, behavioral, or economic factors. Using a multi-group SEIR model, Dolbeault & Turinici (2021) emphasized the significance of mitigating policies for people with a high degree of social interactions. In fact, their research shown that, even a small number of people as a group of 2% of the total population, with a high transmission rate may start an outbreak.

Many of the COVID-19 related research using heterogeneity demonstrate how fatality rates vary with age. For instance, Ferguson, et al. (2020) reports that the infection fatality rate (IFR) is 9.3% for people with age above 80, 2.2% for people 60-69, 0.15% for people 40-49, and 0.03% for people 20-29. In Levin, et al. (2020) the infection fatality rate (IFR) was calculated using several smaller studies from around the globe. The COVID-19 IFR was shown to be very age-specific. Children and younger individuals have relatively low IFRs, which climb with age and peak at age 70. They concluded that the IFR ranges from 0.4% at age 55 to 14% at age 85. As a result, older generations received most of the benefits of lockdown while younger people paid a higher price in terms of reduced labor and education.

Based on the literature reviews we conclude that to choose between imposing a lockdown or not to control for the COVID-19 pandemic, we must balance the costs and benefits of the mitigation measure considering the heterogeneity of the population. In the next chapter, it is described the methodology to analyse the cost effectiveness analysis of the lockdown for three groups, young (20- 49), middle-aged (50-64) and old (65+).

CHAPTER 3

3. Methodology

This chapter describes the data and procedures we used to estimate our model and conduct a Cost-effectiveness analysis. First, we will present the data. Second, we describe the Markov model based on a SIR-type model. In our model we will not consider births and deaths resulting from COVID-19 non related causes, the population will eventually split into six groups of people: Susceptible, Infected revealing symptoms (Symptomatic), Infected not revealing symptoms (Asymptomatic), Hospitalized[3], Recovered and Dead.

This research focuses on the Portuguese case during the COVID-19 pandemic. Our objective is to evaluate if the government option to confine the population is better in terms of costs and QALYs than the option to leave the confinement unexercised.

3.1. Data

Our data on confirmed cases are taken from the Business Intelligence of the information technology support platform for the National Epidemiological Surveillance System (BI SINAVE). SINAVE received the confirmed cases of COVID-19 infection according to type of test that confirmed the case – Nucleic Acid Amplification Reaction in Real Time for SARS-CoV-2 (PCR) and Rapid Antigen Test for SARS-CoV-2 (ANTIGEN).

We obtained data from 3 March 2020 until 12 July 2021 for the following variables: the unique patient identifier, the date when the person was identified as a confirmed case of infection by COVID-19 on the SINAVE computer support platform, patient's age when the case was confirmed (i.e., the date of notification), and information on symptoms and signs collected at the time of notification: Asymptomatic or Symptomatic. Regarding the health level of the confirmed cases, the data also indicated if the patient had comorbidities and died. Table 1 presents the summary statistics.

[3] This group of population face a critical diagnosis of infection by covid-19 which need treatment in intensive care units (ICU).

Table 1-Dataset Summary

Age	Avg. Age	SE	Distribution	Formula	Health Level	Avg. Age	Nr. Infected Cases (%)		Nr. Deaths (%)	
						Sym/Asym	Sym/Asym	Total	Sym/Asym	Total
20-49	34.96	6.21	Normal	24.30	Symptomatic	35,11	121,788 (32.7)	384,442 (54.3)	70 (0.018)	161 (0.042)
					Asymptomatic	34,88	262,654 (77.3)		91 (0.024)	
50-64	56.43	7.59	Normal	65.48	Symptomatic	56,48	52,375 (31.1)	168,337 (23.8)	404 (0.24)	882 (0.52)
					Asymptomatic	56,41	115,962 (68.9)		478 (0.28)	
>65	77.88	9.73	Normal	84.37	Symptomatic	76,54	44,552 (28.7)	155,016 (21.9)	5,464 (3,52)	14,189 (9.14)
					Asymptomatic	78,33	110,464 (71.3)		8,725 (5,62)	

We shown in Table 1, we analyzed 707,795.0 positive cases between March 2020 and July 2021. The total number of asymptomatic cases is 489,080.0 and the total number of asymptomatic cases is 218,715.0, i.e. 69.1% and 30.9% of the total number of infected cases, respectively. The number of infected individuals with age between 20 and 49 years old is approximately 2.3 times the value for individuals in the '50-64' age group and the value for the '50-64' is nearly the same as the value for individuals in the '>65' age group.

Analyzing the number of deaths, we can observe that it increases significantly with age. During the period of research 161 people died with age between 20 and 49 years; 881 people died with age between 50 and 64 years old, which is almost 6 times the last value; 14,189 people died older than 65 years old, which is more than 16 times the last value. Table 1 shows that, not surprisingly, the elderly population reach a much higher mortality rate, which is, even more significant if we look at the ratio between confirmed cases and death cases: from the 20-49 cases, 50-64 cases and >65 cases respectively 0.042%, 0.052% and 9.14% died. As these numbers suggest elderly population is drastically more vulnerable to die from the disease.

The average age was calculated weighted by the number of positive tests in each age. Table 1 shows that average age is similar for symptomatic and asymptomatic cases, in the three age groups. Since we collected data for individuals between 20 and 100 years old, the weighted average age for the sample, 56 years old, is very close to the median value, 60 years old. The weighted average for the '20-49' group is 34.96 years old, for the '50-65' group is 56.43 years old and for the '>65' group is 77.87 years old.

Some important assumptions were made in order to get to the cost-benefit analysis. We assume that when patients recover, they become immune and out of risk to develop the disease again, If citizens test positive, they do not work, and citizens older than 70 years old have no productivity loss since they are retired. During confinement, we assume that everyone work-at-home or telework.

Data on costs[4] are presented in Table 2 and Table 3. Data on annual productivity loss per COVID-19 case was obtained from (Gabinete de Estratégia e Planeamento do Ministério do Trabalho, 2022) and (Office for Budget Responsibility, 2020) and Cirrincione, et al. (2020). The annual productivity loss was proxied by the Portuguese average wage per hour in Euros

[4] The data we obtained on costs are correspondent to a healthcare payer perspective.

obtained from INE. The cost of lockdown is approximately 35 per cent of GDP per capita at factor cost (Office for Budget Responsibility, 2020). If infected by COVID-19, there are also the cost of illness (medication, doctor visits, tests) and when necessary, the cost of hospitalization, i.e. intensive care unit (ICU) (Cirrincione, et al., 2020). Finally, there is the cost of death which is usually proxied by the value of life (VOL) (Office for Budget Responsibility, 2020). For the deterministic model it is used the Mean Values. For the probabilistic model Gamma distributions were assign for costs Briggs, et al. (2006) based on standard errors derived from our dataset and literature.

Table 2-Annual Productivity Loss per Positive Case

Start Age	Average Hourly Wage (euros)	Source	Annual Productivity Loss Per Patient (euros)
18-24	4.8	(Gabinete de Estratégia e Planeamento do Ministério do Trabalho, 2022)	9,984.0
25-49	7.34	(Gabinete de Estratégia e Planeamento do Ministério do Trabalho, 2022)	1,5627.0
50-59	8.9	(Gabinete de Estratégia e Planeamento do Ministério do Trabalho, 2022)	18,512.0
60-69	9.5	(Gabinete de Estratégia e Planeamento do Ministério do Trabalho, 2022)	19,760.0
70-79	0.0	(Gabinete de Estratégia e Planeamento do Ministério do Trabalho, 2022)	0
>80	0.0	(Gabinete de Estratégia e Planeamento do Ministério do Trabalho, 2022)	0

Table 2 shows that the annual productivity loss per patient with age between 18 and 24 years old is 9,984.0 euros, with age between 25 and 49 years old is 1,5627.0 euros, with age between 50 and 59 years old is 18,512.0 euros, with age between 60 and 69 years old is 19,760.0 euros. These values represent the missed income of the group of population incapable of working due to COVID-19 disease. We assume that the group of population older than 70 years old have no productivity loss since they are retired.

Table 3-Annual Costs

Annual Cost Per Patient	Mean Value (euros)	Stand. Dev. (euros)	Alpha	Beta	Distribution	Source
Cost of Confinement	7,294.32	1,197.50	37.10	196.59	gamma	(Gabinete de Estratégia e Planeamento do Ministério do Trabalho, 2022); (Office for Budget Responsibility, 2020)
Cost of Illness	2,759.00	132.00	436.87	6.32	gamma	(Cirrincione, et al., 2020)
Cost of ICU	8,431.00	1,197.50	49.57	170.09	gamma	(Cirrincione, et al., 2020)
VOL	2,000,000.00	1,217,072.99	2.70	740,633.33	gamma	(Office for Budget Responsibility, 2020)

Table 3 shows the annual cost of lockdown is 7,294.0 euros. For the computation of the lockdown costs, firstly we looked at the data given by (Office for Budget Responsibility, 2020) which estimated that the weekly cost of a full lockdown in UK is £200 which is approximately 35 per cent of GDP per capita, then using the same calculations and considering the Portugal GDP obtained from (Gabinete de Estratégia e Planeamento do Ministério do Trabalho, 2022) we obtained a value for the weekly cost of lockdown in Portugal and finally we multiplied this same value for the number of weeks in a year. The cost of illness is approximately 2,759.0 euros and the cost of intensive care unit (ICU) is approximately 8,431.0 euros considering the values presented by the Portuguese health department Cirrincione, et al. (2020). Finally, the VOL is 2,000,000 euros (Office for Budget Responsibility, 2020).

Table 4-Utilities

Utilities	Mean Value	Se	Alpha	Beta	Distribution	Source
Healthy	0.90	0.20	1.13	0.13	Beta	(Poteet & Craig, 2021)
Symptomatic	0.81	0.02	310.84	72.91	Beta	(Poteet & Craig, 2021)
Asymptomatic	0.85	0.01	1,082.90	191.10	Beta	(Poteet & Craig, 2021)
ICU (very ill)	0.30	0.10	6.00	14.00	Beta	(Poteet & Craig, 2021)
Confinement	0.86	0.18	2.34	0.38	Beta	(Poteet & Craig, 2021)

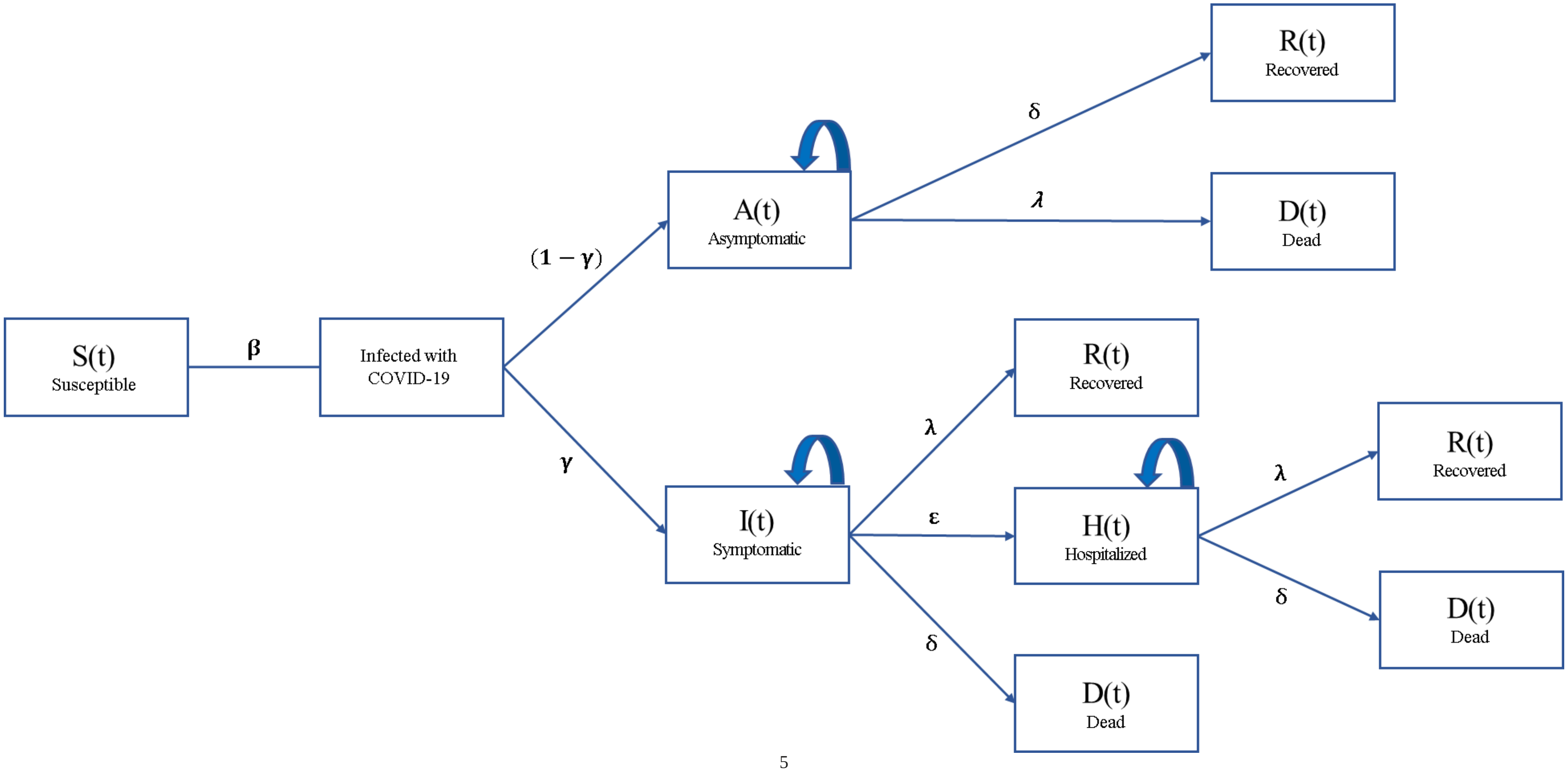
Data on utilities values were obtained from Poteet & Craig (2021) and are shown in Table 4. Poteet & Craig (2021) studied how the health state of the infected group of population is related to QALY losses using a national survey and the two published value sets. In the probabilistic model the utilities values follow a beta distribution. For the deterministic model it is used the Mean Values. For the probabilistic model Beta distributions were assign for costs Briggs, et al. (2006) based on standard errors derived from our dataset and literature.

3.2. Methodology

The analysis in this research uses a Markov Model inspired by the standard SIR compartment model of disease propagation. The Markov model accounted for the dynamics of the positive COVID-19 cases in a cohort of 1000 individuals susceptible to be infected. We have 3 base cases, for the young adult group is approximately 35 year old individual; for the adult group is around 57 year old; and for the elderly group is around 78 year old individual susceptible to be infected by the virus that was applied to all cohort individuals. These mean average individuals were assigned to one of the two mitigation strategies: confinement or laissez-faire. These individuals progressed through the Markov model (see Fig. 1) informed by utilities (Table 4) and costs (Tables 2 and 3), on the basis of transition probabilities (Table 5).

In the Markov model, as shown in the flow diagram in Figure 1, the state susceptible, S(t), denotes the susceptible group of the population that may be infected; when infected, A(t) state, represents the asymptomatic group of the population; I(t) state, the symptomatic group of the population; H(t) state, the hospitalized group of the population; R(t) state, the recovered group of population; and D(t) state, the individuals who died. When patients recover, they become immune and out of risk to develop the disease again. The healthy population at the beginning of this disease is normalized to 1, so these various quantities will be explained as fractions. The main difference to the traditional SIR model is that the infectious group of population is divided in two groups: the symptomatic and asymptomatic. Also, if symptomatic, there is a risk of hospitalization.

Figure 1-Markov Model (based on the extended SIR Model)



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[5] The <u>blue curved arrows</u> indicate that people may remain for more than one year in the health states: Asymptomatic, Symptomatic and Hospitalized.

The transition probabilities shown in figure 1 are defined as follows: β is the transmission rate of infection; γ is given by portion of infected individuals with symptoms; ε is the percentage of infected cases that are hospitalized; δ is the rate at which infectious recover from the disease; λ is the share of mortality. Concluding, the dynamics of the disease transmission are determined by the following differential equations:

$$\frac{\mathbf{dS(t)}}{\mathbf{dt}} = \mathrm{S(t)} - (\beta(\mathrm{t})\gamma + \beta(\mathrm{t})(1-\gamma)) \tag{1}$$

$$\frac{\mathbf{dA(t)}}{\mathbf{dt}} = \beta(\mathrm{t})(1-\gamma)\mathrm{S(t)} - \delta(\mathrm{t})\mathrm{A(t)} - \lambda(\mathrm{t})\mathrm{A(t)} \tag{2}$$

$$\frac{\mathbf{dI(t)}}{\mathbf{dt}} = \beta(\mathrm{t})\mathrm{S(t)}\gamma - \varepsilon(\mathrm{t})\mathrm{I(t)}\delta(\mathrm{t})\mathrm{I(t)} - \lambda\mathrm{I(t)} \tag{3}$$

$$\frac{\mathbf{dH(t)}}{\mathbf{dt}} = \varepsilon(\mathrm{t})\mathrm{I(t)} - \delta(\mathrm{t})\mathrm{H(t)} - \lambda(\mathrm{t})\mathrm{H(t)} \tag{4}$$

$$\frac{\mathbf{dD(t)}}{\mathbf{dt}} = \lambda(\mathrm{t})\mathrm{A(t)} + \lambda(\mathrm{t})\mathrm{I(t)} + \lambda(\mathrm{t})\mathrm{H(t)} \tag{5}$$

$$\frac{\mathbf{dR(t)}}{\mathbf{dt}} = \delta(\mathrm{t})\mathrm{A(t)} + \delta(\mathrm{t})\mathrm{I(t)} + \delta(\mathrm{t})\mathrm{H(t)} \tag{6}$$

$$\mathrm{S(t)} \geq 0 \tag{7}$$

$$\mathrm{A(t)} \geq 0 \tag{8}$$

$$\mathrm{I(t)} \geq 0 \tag{9}$$

$$\mathrm{H(t)} \geq 0 \tag{10}$$

$$\mathrm{D(t)} \geq 0 \tag{11}$$

$$\mathrm{R(t)} \geq 0 \tag{12}$$

$$\mathrm{S(t)} + \mathrm{A(t)} + \mathrm{I(t)} + \mathrm{H(t)} + \mathrm{D(t)} + \mathrm{R(t)} = 1 \tag{13}$$

Equations (2) and (3) indicate that after the susceptible individuals develop the disease, they may change to the Asymptomatic or Symptomatic health states, respectively. Then patients will remain infected until they recover or die. The symptomatic group of population has a risk to get very ill and move to the hospitalized health state (see Equation (4)). Equations (5) and (6) indicate, respectively, the recovered state rate of change and death state rate of change.

The patients progress in the model according to transition rates described in Table 5. Since these parameters are age-dependent we show, as reference, the mean value from our dataset, for each parameter and each age group.

Table 5-Parameters of the model described in Fig. 1

		Reference Values per Age Group								
		20-49			50-64			>65		
		Min	Max	**Average**	Min	Max	**Average**	Min	Max	**Average**
	β	0.47%	1.34%	**0.91%**	1.37%	1.79%	**1.58%**	1.82%	2.87%	**2.77%**
β- contact rate; γ- clinical outbreak rate	**γ**	28.68%	32.92%	**32.70%**	30.40%	32.15%	**31.10%**	33.77%	16.41%	**28.70%**
	(1-γ)	67.08%	71.32%	**77.30%**	69.60%	67.85%	**68.90%**	66.23%	83.59%	**71.30%**
ε- hospitalization rate	**εI**	0.36%	1.52%	**0.90%**	1.52%	4.32%	**2.90%**	5.81%	8.61%	**7.20%**
	δI	8.80%	5.90%	**7.40%**	5.80%	4.40%	**5.10%**	4.30%	0.80%	**2.50%**
δ- recovery rate	**δA**	8.80%	8.51%	**8.70%**	8.50%	8.36%	**8.40%**	0.84%	0.80%	**8.20%**
	δH	0.00%	75.00%	**26.00%**	41.00%	98.00%	**71.00%**	9.00%	100.00%	**90.00%**
	λI	0.02%	0.10%	**0.06%**	0.08%	1.48%	**0.78%**	1.48%	3.23%	**2.36%**
λ- death rate	**λA**	0.03%	0.14%	**0.09%**	0.16%	1.25%	**0.69%**	2.19%	5.69%	**2.40%**
	λH	0.36%	1.52%	**0.10%**	1.52%	4.32%	**0.90%**	5.81%	8.61%	**5.70%**

In summary, the population start in the Susceptible group, but with time will progress in the model according to the differential equations (2) to (6) and values of the transition parameters presented in Table 5. The time of change between compartments is one day. So, we assume that in the first-day individuals may get the disease and only after there is the probability to be hospitalized, die or recover.

The analysis in this research uses data from SINAVE of the variables: patient's age, symptoms, and signs: asymptomatic or symptomatic; data on costs from (Gabinete de Estratégia e Planeamento do Ministério do Trabalho, 2022) and (Office for Budget Responsibility, 2020) of the variables: productivity loss, cost of confinement, cost of illness; the VOL used follows (Office for Budget Responsibility, 2020); data on utilities are from Poteet & Craig (2021) of the variables: healthy, symptomatic, asymptomatic, ICU, confinement. The model will include probabilistic sensitivity analysis with Monte Carlo simulation programmed using Visual Basic for Applications in Excel is available in Appendix A.

CHAPTER 4

4. Results and Discussion

In the previous chapter we presented the data used in this study and described the methodology used for the cost-effectiveness analysis to evaluate if, during the COVID-19 pandemic, the option to confine the population is better in terms of costs and QALYs than the laissez-faire policy. In this chapter, we describe our results of both deterministic and probabilistic analysis, obtained using Normal, Gamma and Beta distributions.

In both analysis we considered three age groups, young-adult group, individuals with age between 20 and 49 years old (20-49), adult group (50-64) and elderly group (>65). For each age group we summed the costs and summed the QALYs of every age belonging to the respective group. With those values we could obtain the incremental cost effectiveness ratio (ICER) that gives how much the confinement strategy is more or less expensive than the laissez faire policy per QALY gained.

In the deterministic model, we have 3 base cases, for the young-adult group is a 35-year-old individual; for the adult group is a 57-year-old; and for the elderly group is a 78-year-old individual susceptible to be infected. These mean average individuals were assigned to one of the two mitigation strategies, confinement, and laissez-faire. The probabilistic sensitivity analysis was performed by varying all variables simultaneously over their plausible ranges. This process involved assigning distributions to 12 variables (3 mean age, 4 costs, and 5 utilities) used in the model. For the Monte Carlo simulation, 1000 iterations were run for both mitigation strategies using unique combinations of the 12 distributions, with values for each variable selected randomly. The differences of the strategies for each run were recorded to determine how often each was considered more cost-effective.

4.1. Cost-Benefit Deterministic Analysis

Table 6 shows the costs and QALYs for both mitigation strategies: confinement or no confinement. The costs of the laissez-faire policy (no confinement) for the group of individuals with age between 20 and 49 is 22,682.0 million euros, for the group of individuals with age between 50 and 64 is 9,114.0 million euros and for the group of individuals with age between 65 and 100 is 52,342.0 million euros. Concerning the costs of imposing confinement, the cost for the age group 20-49 is 5,818.0 million euros, for the age group 50-64 is 2,796.0

million euros, and for the age group >65 is 20,773.0 million euros. The costs for the laissez-faire strategy are considerable higher than the confinement policy in any group.

Table 6-Cost-Benefit Deterministic Analysis

				Incremental		ICER
		Costs (m €)	QALYs	Costs (m €)	QALYs	Eur/QALY
20-49	**Confinement**	5.818	24.57	-16.864	1.51	-11.138
	No Confinement	22.682	23.06			
50-64	**Confinement**	2.796	12.50	-6.318	0.35	-17.866
	No Confinement	9.114	12.15			
>65	**Confinement**	20.773	25.12	-31.570	6.73	-4.691
	No Confinement	52.342	18.39			

As shown in Table 6, for no confinement the QALYs level of the age group 20-49 is 23.06, of the age group 50-64 is 12.15 and of the age group >65 is 18.39. For individuals subject to confinement the QALYs level of the age group 20-49 is 24.57, for the age group 50-64 is 12.50 and for the age group >65 is 25.12. The QALYs loss increases substantially in the elderly age group (>65) when not using the confinement strategy.

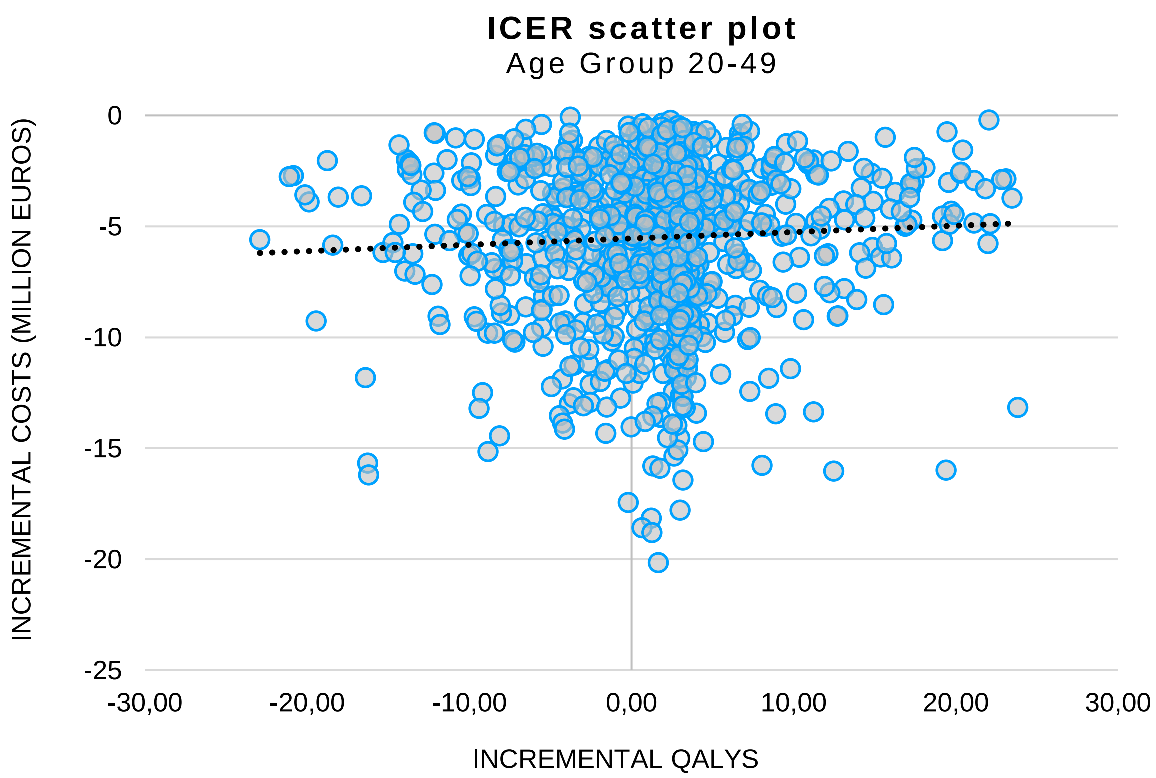
To compare the COVID-19 confinement strategy to the no confinement strategy, we use the Incremental Cost-Effectiveness Ratio. First, we compute the incremental cost by subtracting the no confinement cost to confinement cost. Then the incremental QALYs are calculated by subtracting the no confinement QALYs to confinement QALYs. Finally, the ratio of the incremental cost to the incremental QALYs gives the Incremental Cost-Effectiveness Ratio.

Analyzing Table 6, the ICER for the three age groups are negative, ranging between 6.3 and 31.6 million euros, i.e. the confinement strategy is less expensive and more efficacious than no confinement policy. The young-adult group saves approximately 16 million dollars per QALY gained with the confinement, the adult group saves around 6.3 million euros, and the old group saves 31.6 million euros per QALY gained.

4.2. Probabilistic Analysis

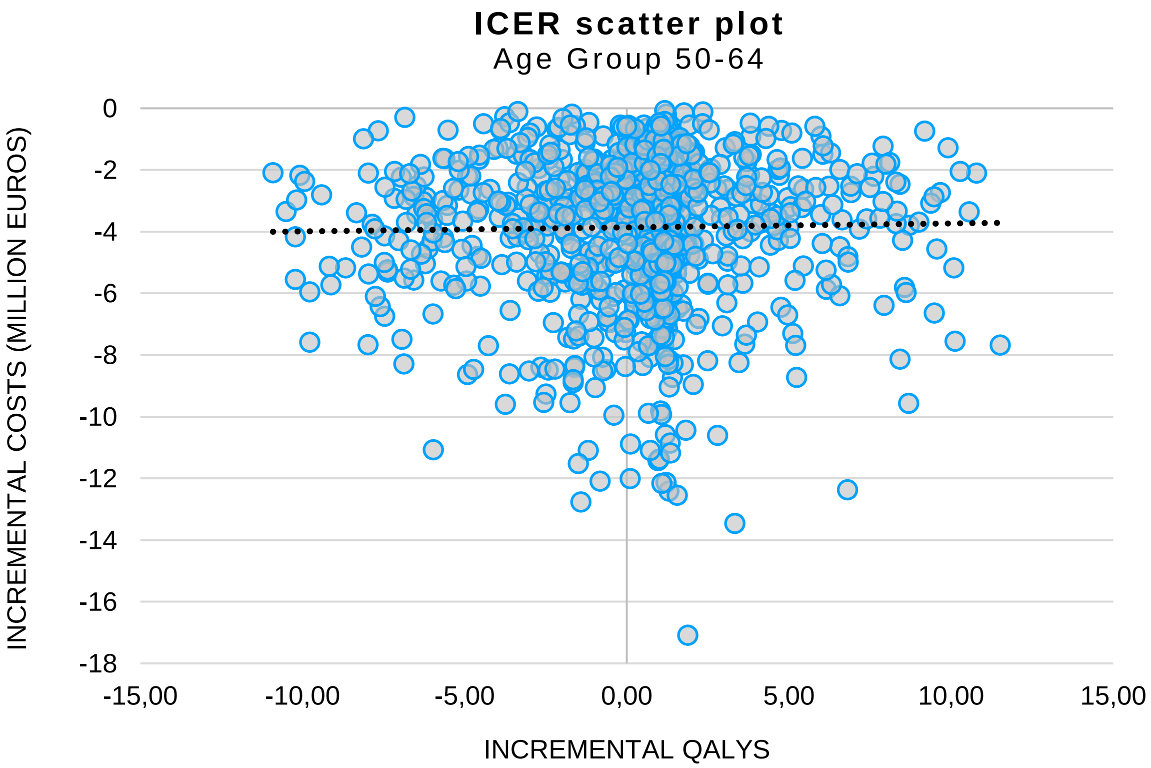
In this section we present the results of the probabilistic sensitivity analysis (PSA). Figures 2, 3 and 4 illustrate respectively the results for the age groups 20-49, 50-65 and >65. The y-axis represents the difference in mean costs, and the x-axis represents the difference in mean quality-adjusted life-years (QALYs). This analysis is based on 1000 Monte Carlo simulations, taking parameters for each input from probability distributions.

Figure 2-Incremental cost-effectiveness bootstrap scatterplot for adult group (20-49).



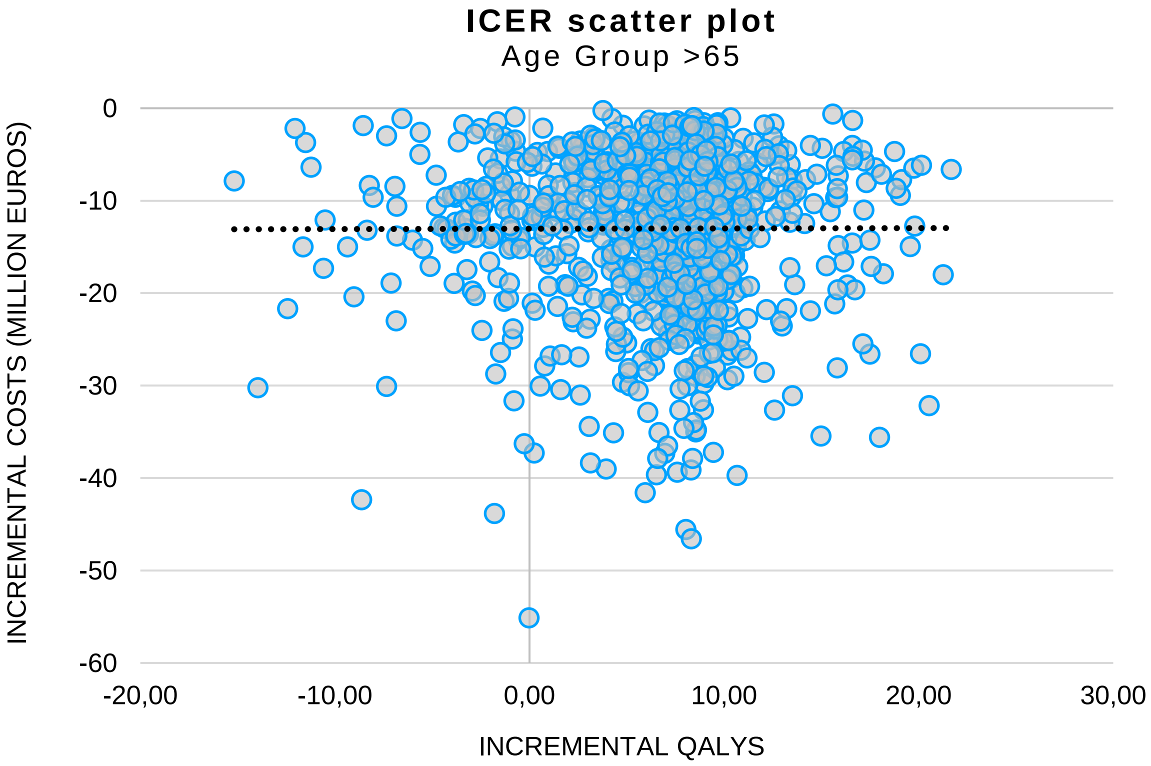
In Figure 2 we present the ICER (additional QALYS cost) for the age group ‘20-49’. In blue points we represent 1000 iterations for the probabilistic analysis. ‘Incremental Costs’ varies between 0 and (-20) million euros, and ‘Incremental QALYS’ varies between (-23) and 24. The trendline of the average cost for each QALY is slightly increasing, i.e. there is a direct relation between incremental cost and QALYs.

Figure 3-Incremental cost-effectiveness bootstrap scatterplot for adult group (50-64).



In Figure 3 the incremental costs vary between -17 and 0 million euros, and the QALYs value vary between -10 and 11.5. Comparing figures 2 and 3 we observe that in both cases the cost of confinement is similar. The trendline of the average cost per QALYs is slightly increasing.

Figure 4-Incremental cost-effectiveness bootstrap scatterplot for elderly group (>65)



In Figure 5 the incremental costs vary between -55 and 0 million euros, and the QALYs value vary between -15 and 21. The trendline is this graph is constant.

The comparison of the results under these three scenarios illustrates clearly that elderly people have much lower costs interval and higher incremental QALYS. In practice this means that for those over 65 the confinement policy give rise to more economic savings and is more important and beneficial for these individuals health.

Table 7-Probabilistic Analysis

				Incremental			Probability of Cost Effective (m€)			
Age Group		**Costs (m€)**	**QALYs**	**Costs (m€)**	**QALYs**	**ICER**	**0.3**	**3.0**	**4.0**	**6.0**
20-49	**Confinement**	3.607	24.569	-5.616	1,514	-3.709	97%	78%	76%	75%
	No Confinement	9.223	23.055							
50-65	**Confinement**	2.337	12.504	-3.983	0,354	-11.261	98%	76%	75%	73%
	No Confinement	6.320	12.150							
>65	**Confinement**	13.008	24.645	-12.823	6,397	-2.005	100%	95%	94%	92%
	No Confinement	25.831	18.248							

After estimating the ICER (EUR/QALY), the probability of paying for additional QALYs given a maximum "willingness to pay" (WTP) is also estimated. To evaluate the probability to pay for additional QALYs, we multiply the number of QALYs of confinement with the WTP and subtract the costs of confinement. Then, we multiply the number of QALYs of no confinement with the WTP and subtract the costs of no confinement. If $QALYs\ conf.* WTP - Costs\ conf. > QALYs\ no\ conf.* WTP - Costs\ no\ conf$, the decision is to pay for additional QALYs. Then, we obtain the response for each iteration and estimate the probability.

At a willingness to pay (WTP) of 300,000 euros the probability is 97% for the age group 20-49, 98% for the age group 50-64 and 100% for the age group >65¸ at a WTP of 3 million euros the probability is 78% for the age group 20-49, 81% for the age group 50-64 and 96% for the age group >65, at a WTP of 4 million euros the probability is 76% for the age group 20-49, 75% for the age group 50-64 and 94% for the age group >65, at a WTP of 6 million euros the probability is 75% for the age group 20-49, 73% for the age group 50-64 and 92% for the age group >65. We may conclude that the probability to invest in additional QALYs increases with age.

Figure 5-Cost-Benefit Probabilistic Analysis for Young group (20-49).

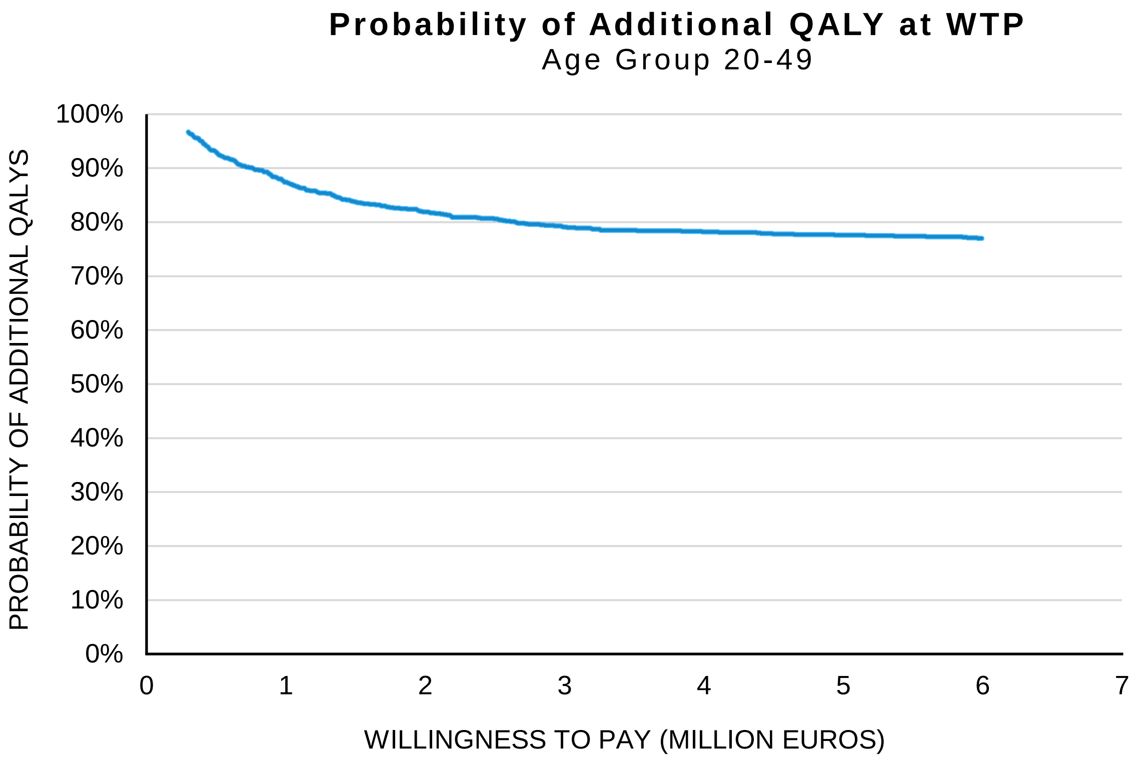


Figure 6-Cost-Benefit Probabilistic Analysis for Adult group (50-65).

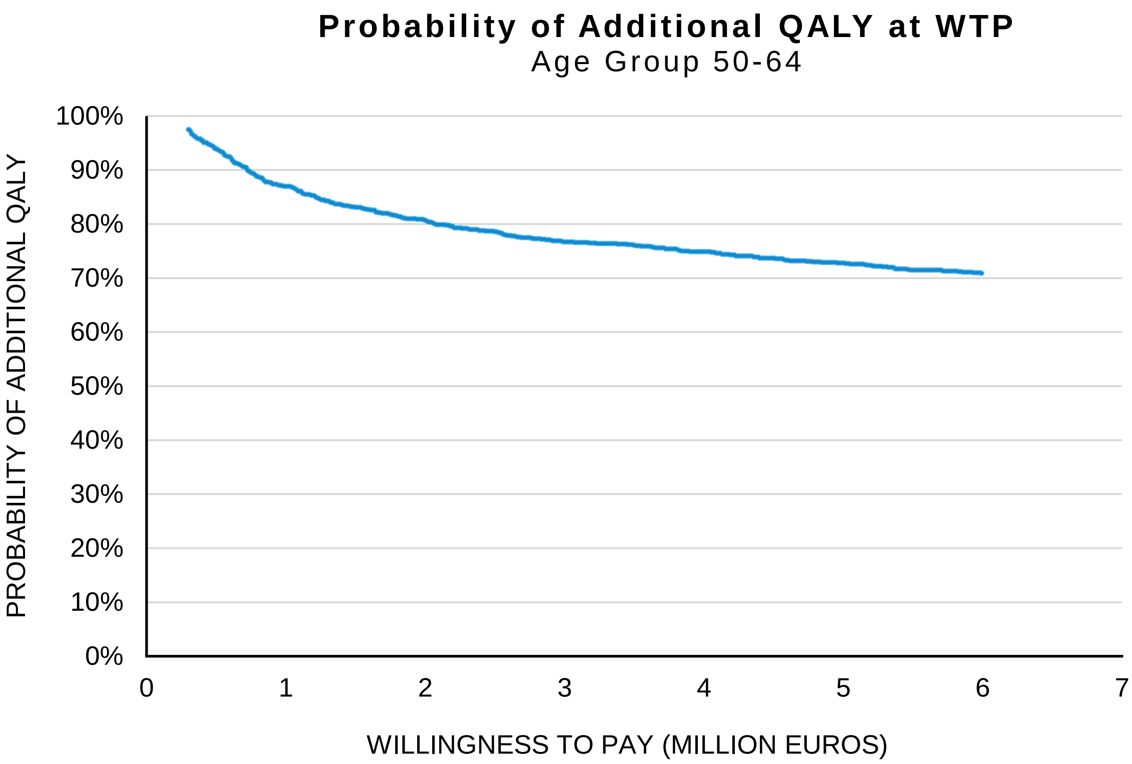
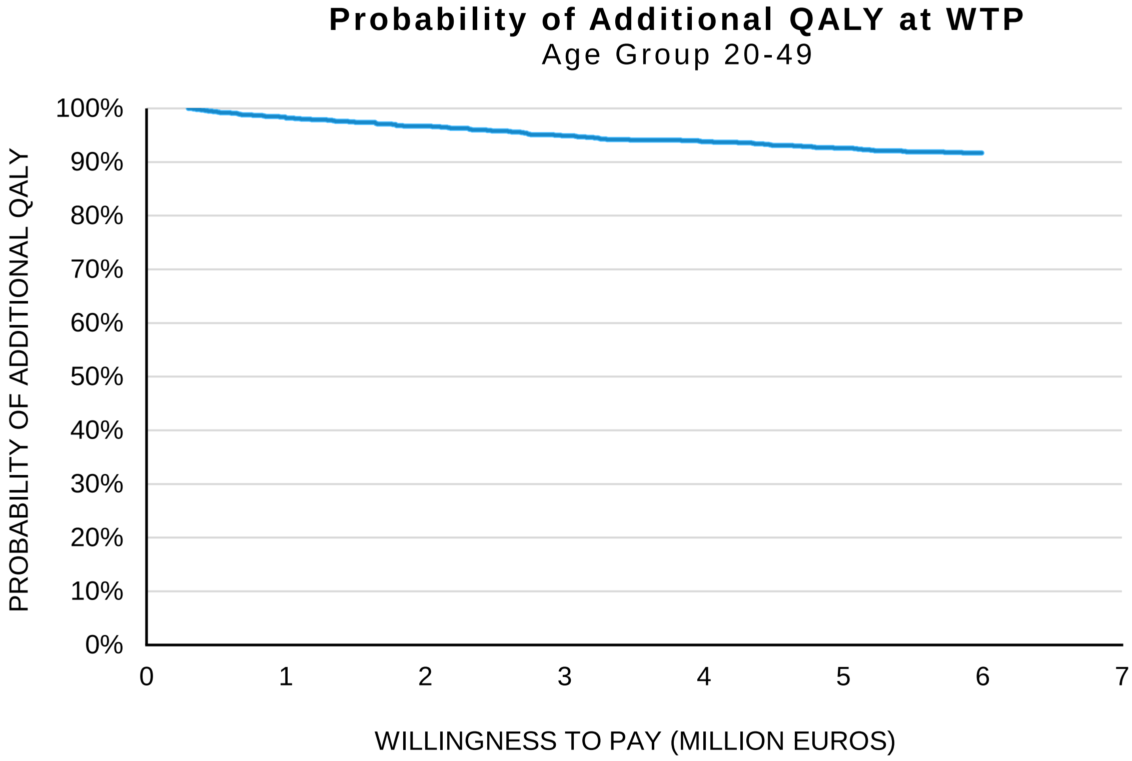


Figure 7-Cost-Benefit Probabilistic Analysis for Old group (>65).



Figures 5, 6 and 7 show the cost-effectiveness acceptability curves representing the probability that the confinement strategy is cost-effective for a given maximum willingness-to-pay threshold per QALY gained. The cost-effectiveness acceptability curves are representing the probability that each strategy is cost-effective for a given maximum willingness-to-pay threshold per quality-adjusted life-year gained. The graphs are based on 1000 Monte Carlo simulations, drawing parameters for each input from probability distributions. All cost-effectiveness acceptability curves demonstrated that confinement was consistently cost-effective strategy across a broad plausible range of willingness-to-pay thresholds (from 300,000.0 euros to 6,000,000 euros).

All cost-benefit acceptability curves, shown in Figures 10 to 12, are consistent, decreasing. For the 20-49 age group at a willingness to pay threshold of 300,000 euros, over 53,6% of simulation will add QALYs above average. This probability decreases as WTP increases, reaching 48,4% and 41,9% for a WTP of 2 million euros and 6 million euros, respectively. For the 50-64 age group at a willingness to Pay threshold of 300,000 euros, over 53,6% of simulation will add QALYs above average. This probability increases as WTP increases, for a WTP of 2 million euros and 6 million euros, respectively. For the >65 age group at a willingness to Pay threshold of 300,000 euros, over 53,6% of simulation will add QALYs above average. This probability increases as WTP increases, reaching 48,4% and 41,9% for a WTP of 2 million euros and 6 million euros, respectively.

4.3. Discussion

The deterministic model provides information based on mean values for three base cases: the 35-year-old individual representing the young-adult group; 57-year-old individual representing the adult group; the elderly group is represented by 78-year-old individual. Table 5 shows that costs of the no confinement strategy, depending on the age of the groups are from 2.5 and 4 times higher than costs for confinement. These costs differences suggest the lockdown strategy to save millions of euros when compared to the laissez-faire strategy. Thus, confinement is a cost-effective strategy.

From the deterministic results, we may also observe that lockdown reduces the QALYs loss in every age group, achieving positive incremental QALYs. Consequently, we obtain negative ICER values for the young, adult, and elderly groups. These results corroborate the conclusion that costs of improvement in quantity and quality of life lived (O'Donnell & Begg, 2020) have negative costs.

The probabilistic sensitive analysis (PSA) uses a sample including 1000 pairs of differences in costs and QALYs. These results are described in the Incremental cost-effectiveness scatter in Figures 2, 3 and 4. The trendline (blackline) is almost flat in the three graphs showing that costs do not increase with the incremental QALYs.

Comparing the results presented in table 6 (deterministic model) with the results presented in table 7 (probabilistic model) we can see that the changes are relatively small for all the three age groups. Because all ICER values are negative under the probabilistic analysis, it corroborates the deterministic results that a confinement strategy is less expensive and more efficacious than a non-confinement strategy. The cost-effectiveness acceptability curves (Figures 5, 6 and 7) demonstrated that confinement was consistently cost-effective across a broad plausible range of willingness-to-pay thresholds.

Like previous studies, this study suggests targeted lockdowns in different groups is the best strategy. Our results found that an elderly person (with poorly health) is more willing to pay for the benefits of lockdown than the other two age groups. Acemoglu et al. (Optimal Targeted Lockdowns in a Multi-Group SIR Model, 2020) examine targeted lockdowns in different groups: the young, the middle-aged, and the old and concluded that targeted policies can minimize both economic losses and deaths.

Thus, our results suggest that mitigation measures can be significantly improved with targeted policies that apply differential lockdowns on the various age groups. A corollary of this result is to increasing the “social distance” between the old group and the rest of the population, e.g. temporarily reduce visits to older relatives; regulations that better protect nursing homes, shorten visits to elderly families, establish a timetable for the demographic groups to go to grocery stores and pharmacies.

After the outcomes of the confinement people started to wonder if the economic and social 'sacrifice' was worthy (Miles et. al., 2020). Governments started looking for economical measures that would allow them to end the lockdown. The simulations described here, and their underlying theory provides an important insight on government policy.

CHAPTER 5

5. Conclusion

In this study, we took a further step in studying multiple risk groups into an epidemic compartmental model. In the case of the COVID-19 pandemic, this generalization is crucial since the research currently available shows that there are significant disparities in hospitalization and death rates between age groups. After presenting a fundamental analysis of the dynamics of infections in this multi-group situation, we moved on to a quantitative investigation of the best course of action, particularly analysing the impact of restrictive government measures to contain COVID-19 outbreaks.

The main objective in this study is to analyse the cost effectiveness analysis of the lockdown for three groups, young (20-49), middle-aged (50-64) and old (65+). The Markov model accounted for the dynamics of the positive COVID-19 cases in a cohort of 1000 individuals susceptible to be infected. For each iteration we summed the costs and summed the QALYs and obtained the incremental cost effectiveness ratio (ICER) that gives how much the confinement strategy is more or less expensive than the laissez faire policy per QALY gained.

Our major finding is that tailored interventions can lead to better outcomes. In the Portuguese public healthcare system and under specific hypotheses, from a societal perspective, lockdown provides more QALYs at lower cost for controlling the surge of COVID-19 than a non confinement strategy. We also find that the bulk of these improvements may be made with a straightforward targeted strategy that treats the rest of the population equally while applying a differential lockdown to the elderly group.

This study has several limitations, the most important of which concerns overlooking endogeneity of parameters. It is assumed that social distancing is determined by government. However, as the disease spreads, people voluntary start social distancing (Farboodi, Jarosch, & Shimer, 2021). Ignoring endogeneity may misinterpret the effects on disease dynamics of government policies (Goolsbee & Syverson, 2021). Future research aims to take into account the endogeneity of the parameters in the cost effectiveness of the lockdown.

Given the urgency of the epidemic, research on the economic and social impact of mitigation policies is being pushed to its limits. Despite the limitations of this study, we think that the methodology used in this research offers a helpful framework for evaluating COVID-19 control policies and their timing.

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Appendix A

Appendix A – Visual Basic Applications Macro to estimate the model

```
Sub PSA()

'declare variabels
Dim total_cost_confinement(1000) As Double
Dim total_qalys_confinement(1000) As Double
Dim total_cost_no_confinement(1000) As Double
Dim total_qalys_no_confinement(1000) As Double
Dim incremental_cost(1000) As Double
Dim incremental_qalys(1000) As Double

'delete old results'
Application.ScreenUpdating = False
    Sheets("Simulation").Select
        Range("D6:I1005").Select
            Selection.ClearContents
    Range("Q6:Q1006").Select
            Selection.ClearContents
    Sheets("Start Page").Select


Application.ScreenUpdating = True


'probabilistic model
Range("model_type") = 2

'random sampling
For i = 1 To 1000

    Calculate

    'copy and paste results to sheet simlation
    total_cost_confinement(i) = Range("total_cost_confinement")
    total_qalys_confinement(i) = Range("total_qalys_confinement")
    total_cost_no_confinement(i) = Range("total_cost_no_confinement")
    total_qalys_no_confinement(i) = Range("total_qalys_no_confinement")
    incremental_cost(i) = total_cost_confinement(i) - total_cost_no_confinement(i)
    incremental_qalys(i) = total_qalys_confinement(i) - total_qalys_no_confinement(i)

Next i 'loop 1000 times

'print the results
For i = 1 To 1000

    Sheets("Start Page").Select
    Application.ScreenUpdating = True
```

```
    Application.ScreenUpdating = False
    Sheets("Simulation").Select
    Cells(5 + i, 4).Value = total_cost_confinement(i)
    Cells(5 + i, 5).Value = total_qalys_confinement(i)
    Cells(5 + i, 6).Value = total_cost_no_confinement(i)
    Cells(5 + i, 7).Value = total_qalys_no_confinement(i)
    Cells(5 + i, 8).Value = incremental_cost(i)
    Cells(5 + i, 9).Value = incremental_qalys(i)


Next i

'CEAC
Sheets("Simulation").Select
Dim wtp As Double
Dim prob_ce As Double

For i = 1 To 1000
    wtp = Cells(5 + i, 16)
        Range("wtp").Value = wtp

    prob_ce = Range("prob_ce")
        Cells(5 + i, 17).Value = prob_ce

Next i

'reset to deterministic model
Range("model_type") = 1
Sheets("Start Page").Select
Range("A1").Select


End Sub



Sub automatic_results_table()

Dim ref_row As Integer

'scenario 1 30y'

    'make the settings'
        Range("control_time") = 2
    'define reference row'
        ref_row = 7
    'call macro'
        Call run_time_categories(ref_row)
    'restore settings'
```

```
'scenario 2 15y'

    'make the settings'
        Range("control_time") = 1
    'define reference row'
        ref_row = 10
    'call macro'
        Call run_time_categories(ref_row)
    'restore settings'


'scenario 3 36'

    'make the settings'
        Range("control_time") = 3
    'define reference row'
        ref_row = 13
    'call macro'
        Call run_time_categories(ref_row)
    'restore settings'
        Range("control_time") = 1

End Sub



Function run_time_categories(ref_row) As Integer



'declare variables'
Dim cost_confinement As Double
Dim qalys_confinement As Double
Dim cost_no_confinement As Double
Dim qalys_no_confinement As Double
Dim incremental_cost As Double
Dim incremental_qalys As Double
Dim ICER As Double

Dim CEAC_245 As Double
Dim CEAC_505 As Double
Dim CEAC_725 As Double
Dim CEAC_1005 As Double

Dim i As Integer

i = 1

'set age category'
```

```
    If Range("control_time") = 2 Then Range("age_control") = 1
    If Range("control_time") = 1 Then Range("age_control") = 2
    If Range("control_time") = 3 Then Range("age_control") = 3


    'store the deterministic results'
    cost_confinement = Range("total_cost_confinement")
    cost_no_confinement = Range("total_cost_no_confinement")
    qalys_confinement = Range("total_qalys_confinement")
    qalys_no_confinement = Range("total_qalys_no_confinement")
        incremental_cost = cost_confinement - cost_no_confinement
        incremental_qalys = qalys_confinement - qalys_no_confinement
            ICER = incremental_cost / incremental_qalys

    'run the PSA
        PSA
    'store prob from CEAC
        CEAC_245 = Range("CEAC_245")
        CEAC_505 = Range("CEAC_505")
        CEAC_725 = Range("CEAC_725")
        CEAC_1005 = Range("CEAC_1005")
    'print results
        Sheets("Result Table").Select
            Cells(ref_row + i, 5).Value = cost_confinement
            Cells(ref_row + i + 1, 5).Value = cost_no_confinement
            Cells(ref_row + i, 6).Value = qalys_confinement
            Cells(ref_row + i + 1, 6).Value = qalys_no_confinement
                Cells(ref_row + i, 7).Value = incremental_cost
                Cells(ref_row + i, 8).Value = incremental_qalys
                    Cells(ref_row + i, 9).Value = ICER

                        Cells(ref_row + i, 10).Value = CEAC_245
                        Cells(ref_row + i, 11).Value = CEAC_505
                        Cells(ref_row + i, 12).Value = CEAC_725
                        Cells(ref_row + i, 13).Value = CEAC_1005

    'go to the next category


End Function

    '
```