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ORIGINAL RESEARCH ARTICLE

Estimation Model for Healthcare Costs and Intensive Care Units Access for Covid-19 Patients and Evaluation of the Effects of Remdesivir in the Portuguese Context: Hypothetical Study

Matteo Ruggeri[1,2] · Alessandro Signorini[3] · Silvia Caravaggio[2] · João Rua[4] · Nuno Luís[5] · Sandra Braz[6] · Filipa Aragão[7,8]

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Abstract

Background and Objectives In March 2020, the World Health Organization announced a state of emergency due to the appearance of a pandemic caused by the Coronavirus 2 (SARS-CoV-2), a severe acute respiratory syndrome, known as Covid-19. Most governments chose to implement precautionary measures, e.g., physical distancing and use of protective devices, which can in part limit the transmission of the virus. However, the healthcare system experienced numerous structural problems in managing the Covid-19 patients given the limited human and technical resources in critical areas, such as the intensive care units (ICUs). Different therapeutic solutions should therefore be assessed, which can potentially minimize the negative impact of the disease on patients, favoring their recovery and optimizing healthcare resources. The objective of this study is to simulate the impact of remdesivir treatment on the pandemic course in the long term.

Methods A forecasting model is designed to estimate how remdesivir would impact the ICU capacity and the healthcare costs from the hospital perspective when managing COVID-19 patients. This model is applied in the Portuguese context with a 20-week projection starting on May 1st and concluding on September 18th, 2021. The data inputs were carefully collected by consulting different sources, such as published global literature, official governmental reports, and available infectious diseases databases, i.e., Our World in Data, Portuguese Ministry of Health, and experts' opinions.

Results The model showed that the introduction of remdesivir-based treatment in patients with Covid-19 pneumonia requiring supplemental oxygen therapy generates a significant reduction in both the number of ICU admissions and deaths, which would produce more than €23 million in cost savings and avoid more than 261 ICUs admissions and 166 deaths.

Conclusion It is demonstrated that alternative treatments such as remdesivir can reduce both the health burden for healthcare facilities, optimize their management, and improve patients' clinical conditions. However, the model is centered on Rt values, which cannot be generalized to the entire country; hence, the results of this research should be considered as a "hypothetical study".

Key Points

Remdesivir is a broad-spectrum antiviral nucleotide pro-drug that showed strong antiviral activity against Covid-19. The administration of remdesivir resulted in higher cost effectiveness.

1 Introduction

Coronavirus disease (Covid-19) is an infectious disease caused by the recently discovered SARS-CoV-2, which primarily results in mild to severe respiratory symptoms. Since the beginning of 2020, Covid-19 has spread at high rates infecting a significant segment of the worldwide population. Many countries suffered serious consequences on both their socio-economic and their medical systems.

Like other severe acute respiratory diseases, patients affected by Covid-19 are often in need of invasive mechanical ventilation (IMV) and intensive care unit (ICU) admission when their medical condition becomes critical. ICUs are limited in capacity and involve expensive and complex

✉ Matteo Ruggeri
matteo.ruggeri@iss.it; matteo.ruggeri@unicamillus.org

Extended author information available on the last page of the article

treatment strategies. Thus, many countries were forced to find alternative solutions to maximize ICU capacity during the pandemic, such as converting clinical wards into ICUs, creating field hospitals, transferring patients to other facilities equipped with available beds, or establishing a partnership with private clinics [1]. The critical levels that countries encountered and are still encountering urges a search for alternative treatments, to reduce the number of ICU admissions.

In Portugal, the first Covid-19 diagnosed patient dates to March 2nd, 2020 [2]. By May 2020, more than 30,000 total cases and 1000 deaths were reported [3]. Starting from mid-March 2020, the Portuguese government implemented many restrictions, in particular, social distancing and closure of public places, following the European Union Guidelines [4]. The spread of SARS-CoV-2 rapidly increased between January 2021 and December 2021 with a total of more than 400,000 cases and 7000 deaths in January 2021 and 1,166,787 cases and 18,537 deaths in December 2021 [5], again, forcing the country to impose restrictions.

The Portuguese healthcare system faced important difficulties due to the limited number of ICU units, especially during the 2021 second pandemic wave. In January 2021, hospitals hit a record of 843 occupied ICU beds of the 850 available [6]. In addition, the Portuguese economy relies heavily on tourism and retail activities [7], and the Covid-19 restrictive measures limited travel, social contact, and store opening hours, which caused a significant economic downturn. According to the Eurostat database (2020) [8], in Portugal, the GDP contracted by 8.4% in 2020, despite the government's support to the economy for approximately +3.9% GDP [9].

The Portuguese government endeavors to raise awareness and implement restrictive measures to prevent/limit the transmission of the virus as the country's vaccination campaign moves at a satisfactory rate. In May 2021, Portugal was the 12th country in the European Union to administer vaccines, while in July 2021 it became 23rd in the world ranking with the most vaccines administered per percentage of population [10]. At the time of the publication, approximately 49% of the Portuguese population had received one dose of vaccine and approximately 28% had received two doses. Portugal is now vaccinating the population of over 35-years-olds by self-appointment and those aged > 50 years who are not yet vaccinated with no appointment needed. However, virus variants emerge along with uncertainty about the efficacy of the vaccine against those variants, hence, Portugal needs alternative solutions to reduce the pressure in the ICUs and prevent the long-term consequences of the pandemic.

In this regard, remdesivir (GS-5734) was identified at the end of 2020, as one of the most promising candidates for the treatment of patients affected by Covid-19. Remdesivir is a broad-spectrum antiviral nucleotide pro-drug that showed strong antiviral activity against SARS-CoV-1, MERS-CoV, and SARS-CoV-2 in vitro [11] and was developed by the US drug company Gilead Sciences, Inc. The U.S. Food and Drug Administration (FDA) and European Commission (EC) approved the use of remdesivir for COVID-19 adult and pediatric patients, aged from 12 years and weighing at least 40 kilograms, with pneumonia and requiring supplemental oxygen (low flow, high flow, or other non-invasive ventilation at the start of treatment), as per label the last update on December 2020 [12, 13]. This medical drug is available in Europe under a Joint Procurement Agreement [12]. Duration of treatment must be at least 5 days and no more than 10 days. Remdesivir obtained conditional market authorization approval in July 2020, which was renewed in May 2021.

A clinical study conducted by Beigel et al. (2020) [11] summarizes the results of an independent, placebo-controlled, double-blind, randomized trial on 1062 hospitalized patients with Covid-19 disease. The patients were divided into two groups, one treated with remdesivir while the other was treated with placebo. This study demonstrated, in the overall population of the study, a shorter time to recovery from 15 days to 10 days, and an increased recovery rate of 29% of patients treated with remdesivir compared to placebo. In severe patients, those requiring supplemental oxygen, who represent 89% of the total population recruited, the time to recovery was shortened from 18 days to 11 days in patients treated with remdesivir versus placebo [11]. Also, the authors concluded that non-mechanically ventilated patients treated with remdesivir had less progression to ventilation or death compared to placebo patients, the progression rate for patients treated without remdesivir is 18% with a 30% reduction when administering remdesivir. Remdesivir was associated with a 70% significant reduction in mortality among patients requiring low-flow oxygen in a post hoc analysis of ACTT-1 [11]. The benefits for remdesivir are remarkable for the National Health System (NHS) and the entire society. Remdesivir allows an improvement in both ICU management and patient recovery, generating remarkable cost savings for the health system.

A forecasting model is designed to estimate the cost effectiveness of a therapeutic solution, such as remdesivir, on ICU patients, direct healthcare costs, and mortality costs in the Portuguese context during the Covid-19 pandemic.

2 The Experts' Opinion

During the data-selection process, three experts were asked to give their contribution to the research. The experts were selected based on their experience with the Portuguese health system in general and with the management and

treatment of COVID-19 disease in their respective institutions. Their role was relevant during the process of data validation. The experts helped in the selection of the most appropriate sources for the data used to populate the model. In addition, the experts verified the data consistency with the study's objectives and suggested values for the missing parameters according to their professional experience. The three experts invited for this model adaptation were Dr. João Rua, Internal Medicine Specialist, Executive Coordinator of COVID-19 Intermediate Care Unit, Hospital Assistant in Centro Hospitalar Universitário de Coimbra, Coimbra, Dr. Nuno Luís, Infectious Diseases Specialist, Hospital Assistant in Centro Hospitalar de Setúbal, Setúbal, and Dra. Sandra Braz, Internal Medicine Specialist, Co-Coordinator of Emerging Viral Infection Contingency Inpatient Unit, Hospital Assistant in Centro Hospitalar Lisboa Norte, Hospital Santa Maria, Lisbon. The data selection process was supported by Maple Health Group, a consulting firm specializing in strategic market access and health economics insights, with a special contribution from Dr. Filipa Aragao, Maple Health Group, New York, USA, and NOVA National School of Public Health, Public Health Research Centre, Universidade NOVA de Lisboa, Portugal.

The research team conducted a group interview with this experts' panel, two Gilead representatives and two Maple Health Group representatives, on April 23rd, 2021. The group interview was structured as follows: an introduction, including a presentation of the participants and the issues to be discussed, a presentation from the UniCamillus University team with a full explanation of the forecasting model, and a question-and-answer section with the experts. During the interviews, different arrangements were accomplished to improve the model and adapt it to the Portuguese framework.

3 Model Structure

The Rt variation—the contagion index—is the core parameter around which the model is designed. The model's objectives are:

- Simulate the course of the pandemic in order to estimate the number of infected among the Portuguese population.
- Simulate and estimate direct costs related to hospitalization and ICUs for Covid-19 patients, considering the two therapeutic solutions, SoC (standard of care) or SoC plus remdesivir, in patients on supplemental oxygen.

Two stages compose the model (Fig. 1). In the first stage, the model estimates the course of the pandemic over a 20-week time horizon, starting on May 1st, 2021. The estimated parameters are the number of positive cases for Covid-19, ICUs admissions—with and without invasive mechanical ventilation (IMV)—and deaths, according to the weekly Rt. In the second stage, a cohort Markov model was populated with patients collected among the number of positive patients, estimating the probability of those in need of ward or ICU (with and without IMV) and death. Direct costs are estimated considering the length of stay (days) and hospital care standards. The model includes 20 cycles, each cycle lasting one week, to follow the settings of the first simulation. A 20-week time period was chosen due to the unpredictable nature of the virus in the longer term.

In order to adapt the model to the Portuguese context, it was assumed that the characteristics of the pandemic are similar to the Italian scenario as the epidemic in the two countries appears to evolve homogeneously [14].

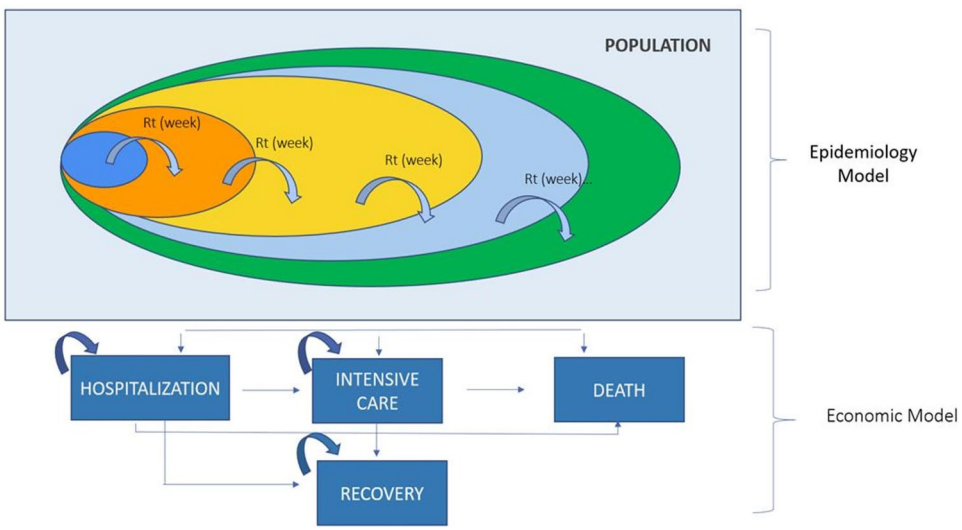

Fig. 1 Epidemiology model and economic model

3.1 Population of the Model

Data used to populate the model were carefully selected from national and global online sources and published peer-reviewed clinical studies on Covid-19 in both the global and the Portuguese contexts. The data collected were presented in front of three Portuguese medical experts to support and evaluate the quality of the data sources and their adaptability to the Portuguese context.

Despite the collecting efforts, some data were missing as certain parameters were non-existing or unavailable by the Portuguese Central Administration of the Health System (in Portuguese, ACSS). In detail, the missing data were the ICU admissions, the mortality rate, ICU length of stay (LoS) and LoS for deceased patients. For modeling purposes, the experts provided the data for ICU admissions in the Portuguese model by employing the linear epidemic trend in the base-case scenario in France, while the mortality rate was extrapolated from Macedo et al. (2021) [15]. For the same reason, data on ward and ICU LoS were extrapolated by Gomes and Gomes (2020) [16] and confirmed by the experts. Experts were asked to give an estimation based purely on their opinion for LoS for deceased patients as no alternative reference was available.

The model is based on historical data from the second and third waves of the pandemic and sets out to forecast the end epidemic scenario and what benefits can be achieved with the administration of remdesivir. As previously mentioned, the effects of remdesivir were determined by referring to the clinical trial by Beigel et al. (2020) [11].

Rt values were heterogeneous among the various Portuguese regions, therefore, the base-case model relies on national data extrapolated from the Portuguese Ministry of Health [17]. In addition to the base-case and treatment scenarios, an analysis during the peak of the pandemic was performed.

3.2 Model Data

3.2.1 Clinical Data

Table 1 summarizes the values of the corresponding parameters that were employed to populate the model for the simulation of the epidemiological course of the pandemic. The Rt values for the 20-week interval were determined by referring to the last Rt value officially recorded in order to simulate the trend of the last curve in the pandemic wave. The data on hospitalization rate in ward originate from the open online database Our World in Data (2021) [3], while the ICU admission rate was extrapolated from the European Centre for Disease Prevention and Control (ECDC) [18]. Mortality rates among hospitalized and ICU patients were based on experts' opinions. Finally, the relative risk reduction of patients' progression to ICU under remdesivir-based treatment stems from the study of Beigel et al. (2020) [11].

Table 1 Summary of clinical and epidemiological data used to populate the model

Parameters	Value	Source	Distribution	SD
Rt week 1–2	0.98	Estimate	Beta	±0.1
Rt week 3	0.98	Estimate	Beta	±0.1
Rt week 4	0.97	Estimate	Beta	±0.1
Rt week 5	0.94	Estimate	Beta	±0.1
Rt week 6	0.9	Estimate	Beta	±0.1
Rt week 7–8	0.8	Estimate	Beta	±0.08
Rt week 9–14	0.75	Estimate	Beta	±0.08
Rt week 15	0.74	Estimate	Beta	±0.08
Rt week 16	0.73	Estimate	Beta	±0.08
Rt week 17	0.72	Estimate	Beta	±0.08
Rt week 18	0.71	Estimate	Beta	±0.08
Rt week 19	0.70	Estimate	Beta	±0.08
Rt week 20	0.69	Estimate	Beta	±0.08
Hospitalization rate—ward	11.60%	Ritchie et al. [3]	Beta	±0.04
Hospitalization rate—ICU	18%	ECDC [18]	Beta	±0.06
Mortality rate—among hospitalized	10%	Macedo et al. [15]	Beta	±0.03
Mortality in ICU	35%	Experts' opinion	Beta	±0.11
Relative reduction in risk of progression to ICU with remdesivir	30%	Beigel et al. [11]	Beta	±0.09

ICU intensive care unit, *SD* standard deviation

3.2.2 Economic Data

The analysis is accomplished with the healthcare system's perspective, the hospitalization LoS is assessed as the main agent for the direct costs' estimation. The evaluation of the average reduction in hospital LoS, which results from the administration of remdesivir, was computed by considering the time to recovery in Beigel et al. (2020) [11]. The data on the daily costs of ward and ICU originated from the governmental official reports [17]. The data on ward and ICU lengths of stay stem from Gomes and Gomes (2020) [16], while experts were consulted for the average number of hospitalization days for the deceased.

The cost of the remdesivir treatment was set at €345, in line with most European countries. As per the treatment guidelines, a total of 6 ampoules (5 days) was assumed in order to simulate the length of the treatment and estimate the total costs of the therapy. A summary of the values corresponding to the economic parameters used is reported in Table 2.

4 Sensitivity Analysis

In both the first and the second simulation stages, a probabilistic sensitivity analysis was performed on all the parameters in the model to test its sensitivity to a change of the parameters. Beta and gamma type distributions were used on the different parameters, divided as follows:

- Beta: Rt, ICU admission rate, ward admission rate, reduction of the probability of being admitted to ICU, and reduction in death rate;
- Gamma: LoS ward, LoS ICU (with and without IMV), LoS state of death (duration of hospitalization of patients who died).

For the beta distribution parameters, the standard deviation (SD) was selected to be consistent with the published data. Details on the scale and slope of the two distributions are reported in Table S1.

5 Scenario Analysis

A scenario analysis was performed on a 20-week time frame during the peak of the pandemic, from January 1st, 2021, to May 20th, 2021, to have an extended comprehension of the potential for the remdesivir-based treatment. The procedure for the scenario analysis was identical to that for the baseline scenario. Adjustments on Rt and slope of the model were accomplished to fit with the distribution and show a realistic scenario, i.e., the number of infected patients on January 1st, 2021.

6 Results

The results of the first simulation stage are detailed in Table 3. Over the 20-week time period, 23,579 active cases were observed, and more than 692 ICU admissions and 251

Table 2 Summary of economic data used to populate the model

Parameter	Value (€)	Source	Distribution	SD
Ward cost per day	832.54	Ministério da Saúde [17]	Deterministic	NA
ICU cost per day	3751.24	Ministério da Saúde [17]	Deterministic	NA
Hospitalization length—ward	19 days	Gomes and Gomes [16]	Gamma	±4
Hospitalization length—ICU	10 days	Gomes and Gomes [16]	Gamma	±2
Hospitalization length (deceased)	6 days	Experts' opinion	Gamma	±1.5
Therapy days with remdesivir	5 days	Beigel et al. [11]	Gamma	±2
Cost of treatment remdesivir	345	Gilead	Deterministic	NA

ICU intensive care unit, *NA* not applicable, *SD* standard deviation

Table 3 Results first simulation stage

	Standard treatment	With remdesivir	Difference	SD	Max-Min
Infected	23,579	23,579			
ICUs	692.16	430.56	−261.60	101.2	825 to −65
Deaths	251.38	85.47	−165.91	52.8	340 to 24

ICU intensive care unit, *SD* standard deviation

deaths were estimated. If the remdesivir treatment in patients with Covid-19 and supplemental oxygen therapy were introduced, the number of ICU accesses and deaths would lower by 261 ICUs and 165 deaths.

Figure 2 summarizes the distribution of weekly ICU admissions over 20 weeks and the number of ICUs decreasing with remdesivir compared with the standard treatment, showing the efficacy of remdesivir on patient recovery and ICU management. The yellow bars stand for the scenario without remdesivir, the orange bars stand for the scenario with remdesivir.

The analysis reported in Table 4 highlights the difference between the two treatment approaches, in detail SoC or SoC plus remdesivir in terms of healthcare costs and possible savings. The remdesivir treatment would generate a total of €23,531,001 cost savings, which can be mainly explained by the reduction in the number of admissions and length of stay in ICUs.

6.1 Multivariate Sensitivity Analysis

Figures 3 and 4 describe the results obtained from the multivariate sensitivity analysis, which are represented on the cost effectiveness (CE) plane. Figure 3 shows that the greater the decrease in ICU admissions, the higher the cost savings. Figure 4 shows that the lower the death rate, the higher the cost savings generated. The analysis implies that in most simulations the highest cost savings are achieved by reducing the number of ICU admissions and the number of deaths. The multivariate sensitivity analysis confirms the significance of the remdesivir administration.

The cost saving maximum value was €104,164,724 while the minimum value was −€151,876,264, with a SD of €38,224,101.

6.2 Univariate Sensitivity Analysis

The results of the univariate sensitivity analysis are shown in Figs. S1–S3. Three tornado diagrams are presented because reporting the results in a single tornado diagram would not be feasible as the outcome shows a situation of dominance and a negative incremental cost-effectiveness ratio cannot be interpreted. Therefore, the sensitivity outcomes were divided into three parts.

Each tornado diagram highlights the results of the observed variation on the three fundamental elements of the study, direct cost savings, avoided deaths, and ICUs, following the administration of the remdesivir. Each bar stands for

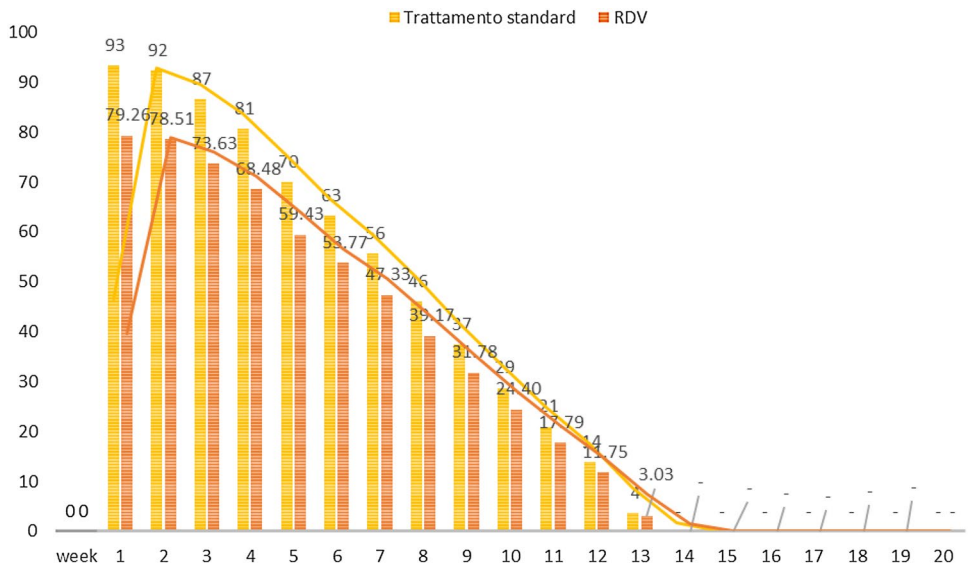

Fig. 2 Distribution of ICU admissions over the 20-week time period: the yellow bars represent the scenario without remdesivir, and the orange bars represent the scenario with remdesivir. *ICU* intensive care unit

Table 4 Results second simulation stage

	Standard treatment	With remdesivir	Difference
Costs for hospitalized patients	€87,386,094.58	€77,418,370.58	−€9,967,724.01
Costs for hospitalized patients in ICU	€25,980,376.42	€16,151,392.38	−€9,828,984.04
Costs for deaths	€5,658,019.37	€1,923,726.59	−€3,734,292.79
Total costs	€119,024,490.38	€95,493,489.55	−€23,531,000.83

ICU intensive care unit, *SD* standard deviation

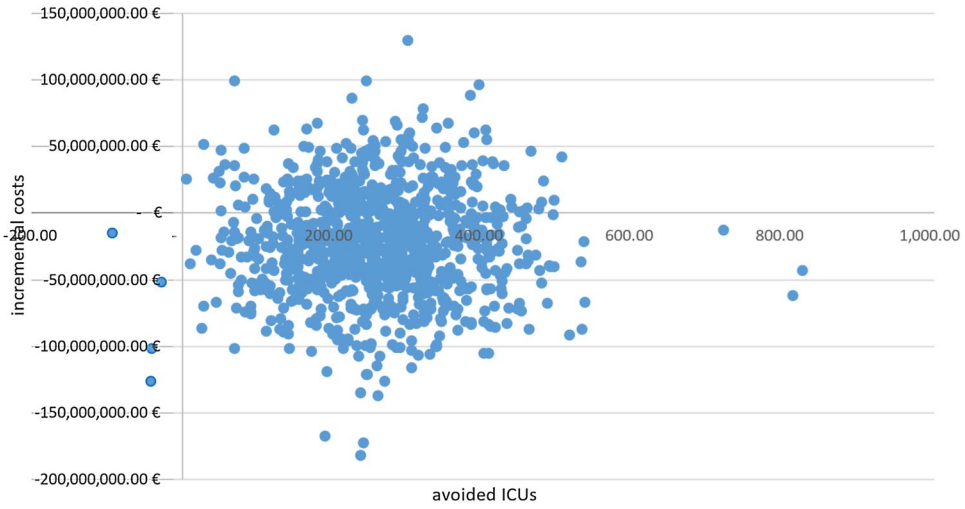

Fig. 3 Correlation between incremental costs and avoided ICU admissions. *ICU* intensive care unit

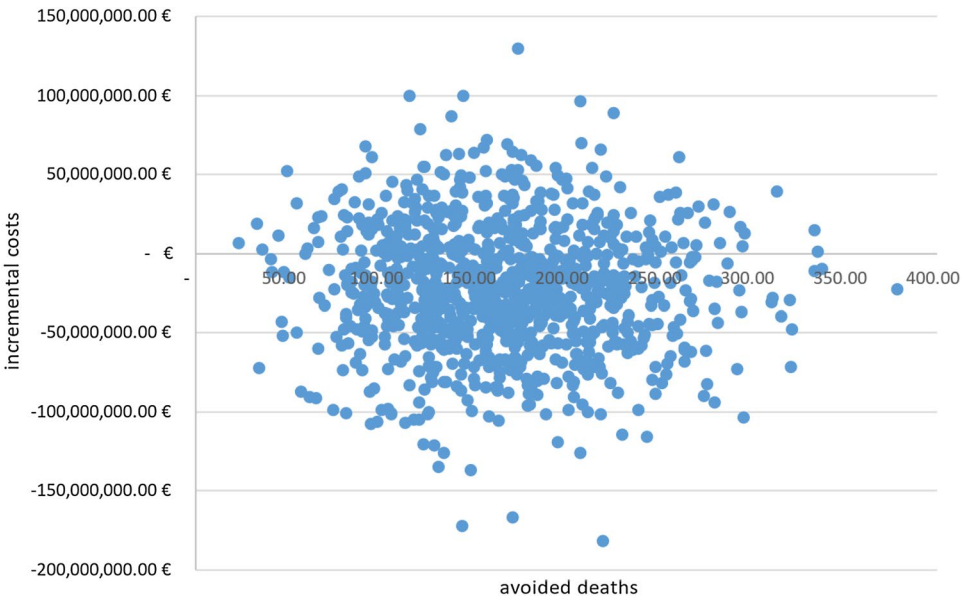

Fig. 4 Correlation between incremental costs and avoided deaths

the variation of the observed variable when combined with the parameter's lowest and highest values.

In the sensitivity analysis, the parameters that emerged as being more sensitive are:

- Rt values.
- Death rate.
- Ward admission rate.
- ICU admission rate.
- Hospitalization rate.
- Decrease in ICU admission due to remdesivir.
- Decrease in number of deaths due to remdesivir.

In Fig. S1, the first tornado diagram summarizes the variation of each parameter on savings. It shows an Rt rate ranging between − 30 and 30% with associated cost savings fluctuating from €8,000,000 to €59,000,000. The ICU admission rate is between 10 and 33% with associated cost savings between €16,000,000 and €56,000,000. The mortality rate goes from 5 to 15% with associated cost savings between €9,000,000 and €48,000,000. Hospitalization rate ranges between 3 and 14% with associated cost savings from €8,000,000 to €44,000,000. The decrease in the rate of ICU admissions due to remdesivir varies between 20 and 52% with associated cost savings of €11,000,000 and €42,000,000. The decrease in the death rate due to remdesivir ranges between 25 and 75% with associated cost savings of €12,000,000 and €36,000,000.

In Fig. S2, the second tornado diagram details the variation in the number of deaths for each parameter considered. The mortality rate, which varies between 5 and 15%, has a corresponding number of deaths equal to 128 deaths and 218

deaths. The decrease in death rate ranges between 25 and 75% with associated 136 deaths and 204 deaths. The ICU admission rate goes from 10 to 30% and reports a minimum of 144 deaths and a maximum of 200 deaths. The Rt, ranging between − 30% and 30%, has an associated number of deaths equal to 152 deaths and 196 deaths. Hospitalization rates vary between 3 and 14%, corresponding to 154 deaths and 192 deaths. The decrease in ICU rate due to remdesivir ranges between 20 and 52% with associated deaths of approximately 156 deaths and 190 deaths.

In Fig. S3, the third tornado diagram reports the change in the number of ICUs related to each parameter. The rate of ICU admissions varies between 10 and 30%, with a corresponding number of ICUs from 228 units and 300 units. ICUs equal to 232 units and 292 units correspond to the Rt range (− 30% to 30%). The hospitalization rate (3–14%) has associated ICUs equal to 242 units and 286 units. The last parameter, the decrease in ICU rate due to remdesivir, is associated with ICUs equaling to 244 units and 284 units.

6.3 Scenario Analysis

The model outcomes are listed in Table S2 and Fig. S4. Figure S4 emphasizes the effect that the administration of remdesivir would have on the epidemiological course of the pandemic and the cost savings during its highest peak, in detail, January 1st to May 20th, 2021. Table S2 shows that, compared to the base-case scenario, the use of remdesivir would decrease the number of ICU admissions by 2780 units, the number of deaths by 1901 units, and would generate a total direct cost savings of €196,782,935.

7 Discussion

This study supports the conclusions of the previous study in the Italian context [14]. Remdesivir, when administered to patients requiring supplemental oxygen therapy, can have a great positive impact on the healthcare system, especially in terms of cost savings for hospitalization (ward and ICU) and deaths. In Portugal, the cost savings are estimated at €23,531,000 over the forecasted 20-week time interval, which are a direct consequence of the benefits of remdesivir treatment, in particular, the reduction of time to recovery. This index decreases the ward length of stay and ICU admissions, limiting the congestion of hospital capacity and improving healthcare infrastructure management. The congestion of hospital capacity is an important factor to be considered for countries with a similar context to Portugal where ICU capacity is limited and there is a risk of overcrowding. The impact of remdesivir on hospitalization LoS is also confirmed in other academic studies, for example, Kaka et al. [19], and Carta et al. [20]. Both studies conclude that remdesivir reduces time to recovery in hospitalized patients and contributes to reducing the overall costs, although little or no efficacy on mortality was observed.

The authors recognize the limitations of this study. First, the negative effects of remdesivir, in particular bradycardia [21–24], were not considered. The forecasting model is built around estimated data, in detail, the epidemiological framework with its associated Rt values. The model simulates and presents a hypothetical scenario, which takes into consideration historical data, governmental restrictive measures, and other external factors, such as the vaccination campaigns. Consequently, there is the possibility that this simulation will not be accurate in representing the actual epidemiological situation. However, this issue can be readily solved as the model can rapidly be adjusted using the most recent available data.

The strengths of the model are, indeed, noteworthy. Given the availability of data, its application can be extended to more concentrated areas, such as local or regional areas. As a result, the model can be used as a decisional and preventive instrument for decision makers during their managerial activities at any territorial level, especially, when facing a critical situation such as the 2020–2021 pandemic outbreak. Also, the model can be adjusted to assess the impact of the vaccination campaigns and other treatments in addition to remdesivir and can estimate their impact on both the course of the pandemic and the direct costs associated with the different treatments. This increases the relevance of the model for administrators and/or politicians as it can be used should another pandemic wave occur. Indeed, the model can simulate the behavior of other pandemics caused by different viruses with the proper adjustments.

In addition, an alternative simulation was conducted to estimate what to expect in 2022. The model was updated with new estimated Rt values, both increasing and decreasing as the peak of the pandemic had already been reached and the Rt is now falling at the end of January 2022 in Portugal. The results were still in favor of remdesivir, despite the growth in the vaccination rate.

A careful analysis of remdesivir clinical trials was performed, in detail, Goldman et al., Spinner et al., and Wang et al. [25–27]. There were major reasons why these publications were not included in this study: lack of data on low-flow oxygen therapy, discontinuation of the study, missing analysis between treatment and placebo patients. As a consequence, the ACTT-1 independent, double-blind, randomized controlled trial performed by the National Institute of Allergy and Infectious Diseases group (NIAID) of the National Institute of Health (NIH) [11] was exclusively employed to estimate the effects of remdesivir in this study, because its methods guarantee consistency and reliability of the data on the efficacy of the remdesivir therapy on patients affected by Covid-19, and confirms that remdesivir improves

patients' clinical conditions and reduces both their probability of transitioning to ICU and death in patients requiring low flow oxygen on the baseline (result with statistical significance in the post hoc analysis of ACTT-1) [11].

It is useful to mention studies that have a different position on remdesivir. Solidarity [28] and DisCoVeRy [29] agree that there are no clinical benefits observed from remdesivir in hospitalized patients affected by Covid-19. As reported in the correspondence by Núñez et al. [30], although the three studies are similar, ACTT-1 results cannot be applicable to the current SoC because of the different conditions at the time of the study. Last, Congly et al. establish that remdesivir is unlikely to be cost effective; nonetheless, the study did not assess the LoS of hospitalized patients in the cost estimation [31]

8 Conclusion

This study is based on our previous research in an Italian context on the administration of remdesivir in patients on low-flow oxygen therapy. The findings are consistent with that study. The ability of remdesivir to decrease ward LoS and ICU admissions would produce significant cost savings for hospitals, a more manageable hospital capacity in a public health emergency, and a faster recovery for hospitalized patients with pneumonia who require supplemental oxygen in treatment with remdesivir.

This model can offer the decision makers in the health, regulatory, and governmental national authorities potential resources for the management of public health emergencies, such as the SARS-CoV-2 and Covid-19 pandemics. The research findings are useful to local national authorities for analysis and decision making with regards to the management and treatment measures to improve the control of COVID-19 pandemic. These measures impact the national health system in terms of patient recovery, hospital capacity congestion, and subsequent cost savings. The authors' findings encourage the administration of remdesivir according to the product indication [32].

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40261-022-01128-8.

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Declarations

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Conflict of interest The authors declare that there is no conflict of interest.

Availability of data and materials Data are fully available.

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent to publication Not applicable.

Code availability Not applicable.

Author contributions Matteo Ruggeri, study design and analysis; Alessandro Signorini, analysis and writing of the paper; Silvia Caravaggio, analysis and writing of the paper; Filipa Aragão, literature review; João Rua, Nuno Luís, and Sandra Braz, validation of the model.

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Authors and Affiliations

Matteo Ruggeri[1,2] · Alessandro Signorini[3] · Silvia Caravaggio[2] · João Rua[4] · Nuno Luís[5] · Sandra Braz[6] · Filipa Arag ão[7,8]

1 National Center for HTA, Istituto Superiore di Sanità, Viale Regina Elena, 299, 00161 Rome, Italy

2 School of Medicine, St. Camillus International University of Health Sciences (UniCamillus), Via di Sant'Alessandro, 8, 00131 Rome, Italy

3 Department of Business Administration, John Cabot University, Rome, Italy

4 Centro Hospitalar Universitário de Coimbra, Coimbra, Portugal

5 Centro Hospitalar de Setúbal, Setúbal, Portugal

6 Centro Hospitalar Lisboa Norte, Hospital Santa Maria, Lisbon, Portugal

7 Maple Health Group, New York, NY, USA

8 NOVA National School of Public Health, Public Health Research Centre, Universidade NOVA de Lisboa, Lisbon, Portugal