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Retrospective modelling of hospital bed capacities associated with the administration of remdesivir during the first wave of COVID-19 in a German metropolitan city

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Objectives: Internationally, healthcare systems are confronted by an ever-increasing scarcity of medical resources due to the ongoing novel coronavirus disease 2019 (COVID-19) pandemic. The aim of this study was to investigate the impact of remdesivir on the demand of hospital bed capacities for hospitalized COVID-19 patients and to evaluate the potentially created capacities for treating additional COVID-19 patients or elective treatments at the hospital.

Methods: An epidemiological model was developed that utilized the population of Cologne (Germany) during the first COVID-19 wave (first hospitalized patient—30 September 2020) to compare two scenarios: no administration of remdesivir (A) and the administration of remdesivir according to the EMA label (B). The results of the Adaptive COVID-19 Treatment Trial were used to evaluate the potential impact of remdesivir on hospital capacity.

Results: With the first recorded patient on 2 March 2020, a total of 576 COVID-19 hospitalized patients were detected during the first wave in Cologne. Comparing both scenarios (A versus B) of the model, the administration of remdesivir increased the number of discharges from 259 to 293 (+5.8%) and fewer patients needed ICU admission [214 versus 178 (−6.3%)]. In addition, the model estimated 20 fewer deaths (scenario B). Based on a reduced length of stay, 31.4 hospital beds (57.0 versus 25.6) could have been freed by administering remdesivir to eligible patients. This would have allowed either the treatment of an additional 730 COVID-19 patients or 660 elective treatments.

Conclusions: In our model, remdesivir administration profoundly contributed to free hospital capacities in the metropolitan city Cologne in Germany.

Introduction

The novel coronavirus disease 2019 (COVID-19) first appeared at the end of 2019 and quickly reached global pandemic status, with millions affected worldwide.[1–3] COVID-19 has heterogeneous symptom manifestation, ranging from no symptoms to pneumonia, acute respiratory distress syndrome (ARDS) and multiple organ failure.[4–6] Besides its clinical effects, COVID-19 strains healthcare systems by demanding massive medical resources.

The federal government of Germany took several measures to lessen the impact on the healthcare system and to offer appropriate treatment to all hospitalized COVID-19 patients. For instance, hospital beds with ventilation equipment on an ICU were

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financially incentivized and care providers were called upon to cancel elective treatments.[7] The latter, however, was only a short-term solution, as elective treatments are not necessarily less severe or urgent. Delays can cause negative outcomes, which may result in an additional burden for patients and the healthcare system.[8] While increasing overall capacity to treat COVID-19 patients was a reasonable measure, it is also important to look at the potential contribution of treatments to reducing the burden of illness for patients and the healthcare system.

Remdesivir, originally developed to treat Ebola, alleviated progression of COVID-19 and reduced the median time to recovery, shown in the Adaptive COVID-19 Treatment Trial (ACTT-1; NCT Nr: 04280705).[9,10] Based on this evidence, remdesivir was conditionally approved by the EMA for the treatment of patients with pneumonia requiring supplemental low- or high-flow oxygen or other non-invasive ventilation.[11]

This study applied the efficacy data from ACTT-1 to a retrospective epidemiological model to elucidate the impact remdesivir would have had on the first COVID-19 wave in Cologne, Germany.

Patients and methods

Ethics

Ethical approval was not necessary due to the retrospective study design and the use of pseudonymized, publicly available sources. Moreover, according to the Health Data Protection Act of North-Rhine Westphalia (GDSG NW), no patient informed consent was needed for this study.[12]

Methodological approach

To retrospectively evaluate the effect of remdesivir on hospitalized patients (in the following referred to as patients) with COVID-19, an epidemiological model estimating the number of hospital beds that would have been needed to treat COVID-19 patients was developed.

Two scenarios were compared: no administration of remdesivir (scenario A) and administration of remdesivir in patients corresponding to the current EMA-approved label (scenario B), in the following referred to as eligible patients. By applying the model on the population of Cologne (a city with about 1 million inhabitants) in Germany during the first pandemic wave, it was intended to reflect the medical care situation of a high-income country. Focusing on Cologne as a whole, the analysis was conducted irrespectively of actual number of hospitals.

Originally based on the Hill–Burton Act in 1946,[13] the equation of average hospital occupancy was applied (i) to determine and compare the number of hospital beds that would have been needed for the treatment of COVID-19 patients in both scenarios (A and B) and (ii) to quantify potentially freed capacities, measured in COVID-19 patients or elective treatments.[14]

$$\textit{Average hospital occupancy} = \frac{\textit{patients} \times \textit{length of stay}}{\textit{time period} \times \textit{hospital beds}}$$

The time period (first COVID-19 patient until 30 September 2020) and the average hospital occupancy for large hospitals (more than 600 hospital beds) in Germany (71.2%) were assumed to be the same for all calculations.[15]

The number of confirmed COVID-19 cases retrieved from the Independent Regional Centre for Health in North Rhine-Westphalia[16] was multiplied by the weekly hospitalization rates reported by the Robert Koch Institute (RKI), a Federal Institute under the administration of the German Federal Ministry of Health,[17] to determine the number of patients. The target population was distributed in categories based on the eight-category ordinal scale applied in ACTT-1. Categories describe the disease severity at the day of hospitalization (baseline) and by day 15 after hospitalization (outcome).[10] According to label, the administration of remdesivir is only approved for patients with baseline categories 5 and 6 (Table 1).[11] Although patients in outcome category 3 are formally hospitalized, in this model they were considered as discharged as they do not require ongoing medical care. To avoid bias, the category was handled similarly in both scenarios (A and B). Thus, categories 1–3 and 8 were exclusively considered as outcome, as this analysis focused on the hospital setting. Patients who fulfilled the criteria of the outcome categories 6–8 were assumed to be treated on an ICU.[18]

Table 1. Categories according to the eight-category ordinal scale applied in ACTT-1[10]

Categories/ category	Description
1–3	not hospitalized or hospitalized not requiring supplemental oxygen and no longer requiring ongoing medical care
4	hospitalized, not requiring supplemental oxygen but requiring ongoing medical care (related to COVID-19 or to other medical conditions)
5	hospitalized, requiring any supplemental oxygen
6	hospitalized, requiring non-invasive ventilation or use of high-flow oxygen devices
7	hospitalized, receiving invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO)
8	death

The distribution of cases across baseline categories was compared with the distribution across outcome categories to quantify disease progression.

In scenario A, a length of stay (LOS) of 15 days was applied, based on the overall intention-to-treat placebo control population, across all baseline categories of ACTT-1.[10] Scenario B comprised two groups of patients: patients in baseline categories 5 and 6 who would have been eligible for the administration of remdesivir according to label (B1) and the remaining patients not eligible for the administration of remdesivir represented in baseline categories 4 and 7 (B2). To detect the weighted LOS per baseline category, baseline category LOS in days was weighted with the patient percentage distribution per baseline category (scenario B).

To identify the additional number of treatable patients (COVID-19 and elective treatments), the number of freed hospital beds was inserted into the above-described equation. LOS for COVID-19 patients depended on the respective baseline category, retrieved from ACTT-1.[10] The average LOS for elective treatments was thereby based on an average hospital stay of 7.2 days in hospitals, as reported by the German Federal Statistical Office.[19]

The epidemiological model in the study at hand was deterministic in nature as it applied fixed values reported by ACTT-1.[10] A discrete time interval was considered, i.e. the first wave of COVID-19. A homogeneous patient sample of hospitalized COVID-19 patients in Cologne, Germany, was investigated to model the impact of COVID-19 on the infection dynamic, measured in hospital beds.[20]

Results

There was a total of 5100 confirmed COVID-19 cases in Cologne during the 213 day time period, with the first recorded hospitalized patient on 2 March 2020 (Table S1, available as Supplementary data at *JAC* Online). The weekly hospitalization rate ranged

Table 2. Overview of disease severity across outcome categories at day 15

	No administration of remdesivir (scenario A)		Administration of remdesivir[a] (scenario B)		Difference	
	number of inpatients	proportional distribution	number of inpatients	proportional distribution	number of inpatients	proportional distribution
Outcome categories 1–3	259	45.0%	293	50.8%	+34	+5.8%
Outcome category 4	37	6.4%	48	8.4%	+11	+2%
Outcome category 5	66	11.4%	57	9.9%	−9	−1.5%
Outcome category 6[b]	26	4.5%	25	4.3%	−1	−0.2%
Outcome category 7[b]	125	21.7%	110	19.1%	−15	−2.6%
Outcome category 8[b]	63	11.0%	43	7.5%	−20	−3.5%
	576	100%	576	100%		

[a]Administration of remdesivir in baseline categories 5 and 6 according to EMA label (B2).
[b]ICU treatment.

from 5% to 22%, resulting in a total of 576 hospitalized patients (Table S1).

At baseline, these patients were allocated to category 4 ($n = 76$), 5 ($n = 238$), 6 ($n = 106$) and 7 ($n = 156$). Table 2 presents the results of the ordinal scale distributions at day 15. The results indicated that patients in scenario B were consistently more likely to improve clinically towards day 15 than patients in scenario A. The model estimated that more patients would have been discharged (outcome categories 1–3; $n = 34$; +5.8%), fewer patients would have needed ICU admission (outcome categories 6–8; $n = 36$; −6.3%) and fewer patients would have died (outcome category 8; $n = 20$; −3.5%).

Furthermore, the model estimated that 57.0 hospital beds were needed to treat all identified COVID-19 patients (scenario A) compared with 25.6 hospital beds (scenario B). Of these, 12.8 hospital beds would have been needed to treat COVID-19 patients ineligible for remdesivir (scenario B1) and another 12.8 to treat eligible remdesivir patients (scenario B2). This model resulted in additional capacities of 31.4 hospital beds gained by administration of remdesivir. If these additional capacities would have been available during the first wave, they could have been used for either the treatment of an additional 730 COVID-19 patients or 660 elective treatments. The model of hospital beds and the quantification of freed capacities through the administration of remdesivir are summarized in Figure 1.

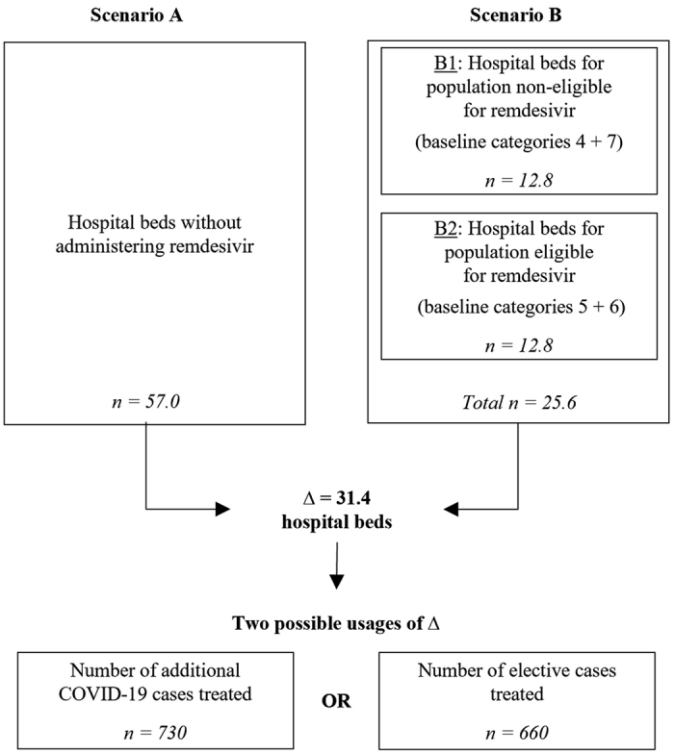

Figure 1. Summary of remdesivir effect on capacity of hospital beds in Cologne during the first wave of COVID-19.

Discussion

In this analysis, the impact on hospital capacity of treating eligible patients with remdesivir was evaluated utilizing the population of Cologne. Our epidemiological model estimated that the use of remdesivir in eligible patients resulted in freeing hospital capacity. Thus, treatment with remdesivir could alleviate some disease burden, allowing for additional COVID-19 patients or avoiding delays in elective treatments. Extrapolating these results from Cologne to the population of Germany, while referring to official data of the RKI considering the respective time period and applying equal percentage distributions as the study at hand, a decrease of 2102 ICU treatments of COVID-19 patients may be concluded.[21]

However, the importance of meeting the demand of elective treatments during the COVID-19 pandemic is not exclusively a German challenge but also affects healthcare systems on an international scale. As reported in the study by the COVIDSurg Collaborative, approximately 28 million elective operations were postponed or cancelled within a 12 week peak period in 359 hospitals in 71 countries at the beginning of the first wave in 2020. As the study exemplarily evaluated cancer patients, this led to an increased mortality risk of 4%–8%.[22,23]

This analysis indicated that integrating promising innovative products into the clinical routine, herein using the example of remdesivir, could have a considerable impact on medical resources and thus could positively influence medical care provision and

stressed healthcare systems. Although this analysis was based on incidence data of Cologne, Germany, results may be generalizable to other cities and countries, as the international literature describes similar crisis management approaches between countries.[22,24,25] Nevertheless, results outside of Cologne may deviate, for instance due to differences in healthcare infrastructure, such as population density and hospital availability.

Although the epidemiological model was developed and conducted in all conscience, this analysis has some limitations. Due to the retrospective study design, it was assumed that remdesivir was administered from the beginning of the first pandemic wave onwards (scenario B). However, this model was based on applying clinical trial data retrospectively and does therefore not correspond to the actual treatment recommendation at the time. Nevertheless, the study results demonstrate relevant insights on resource management for healthcare decision makers in a still ongoing pandemic.

Moreover, this retrospective model was solely based on findings of ACTT-1. Therefore, this evaluation did not result in data series or variety in values and was not statistically tested. Yet, findings of ACTT-1 were statistically analysed in the study itself, for example by the conduct of a log-rank test of time to recovery between the remdesivir and placebo groups, explicitly stratifying according to disease severity.[10] In contrast to other studies, which also investigated the impact of remdesivir, only ACTT-1 allowed separate analysis of study subgroups according to label and development of a model based on this information.[26–29] Findings of other studies deviating from ACTT-1 results were therefore not possible to consider in this model. The model at hand intended to represent a first attempt of modelling the resource-saving potential during the COVID-19 pandemic by administering remdesivir in eligible patients (scenario B). Thereby, it may generate a new way to deal with resource scarcity during the COVID-19 pandemic.

Additionally, the underlying analysis considered a constant hospital occupancy rate of large hospitals over the entire time period, although it may have fluctuated. Hospital occupancy rates may further differ across basic-, standard- and maximal-care hospitals. Yet, as this analysis was conducted for the city of Cologne, which is characterized by mostly large and specialized hospitals, hospital occupancy was assumed to remain steady due to hospital sizes and wide catchment areas.

Considering the pandemic, innovative and multifaceted approaches to reduce the burden on patients and health systems were developed. While cancelling or reducing the number of elective treatments can immediately free hospital capacity, it is a short-term solution. Indefinite delays can result in worsening health for patients and an increased burden later for the health system. This research highlights that pharmaceutical intervention can also play a role in freeing up capacity and should be considered as part of a wider set of initiatives to improve health. By the time of executing this analysis, remdesivir was approved for patients who require supplemental oxygen at the start of treatment. However, an extension to patients not requiring supplemental oxygen (baseline category 4) at the start of treatment has been submitted to the EMA by the manufacturer.[30] In the case of label extension, updated investigations would be needed.

Moreover, future research is needed to investigate whether the results of this model can be validated in clinical studies, including rural areas and regions where COVID-19 incidence is above or below that in the present study. Thereby, further research obtaining parameters regarding healthcare infrastructure, such as population density and hospital availability, would then verify the results of this study.

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Transparency declarations

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Supplementary data

Table S1 is available as Supplementary data at *JAC* Online.

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