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A Cost-Effectiveness Analysis of Remdesivir for the Treatment of Hospitalized Patients With COVID-19 in England and Wales

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ABSTRACT

Objectives: COVID-19 is associated with significant morbidity and mortality. This study aims to synthesize evidence to assess the cost-effectiveness of remdesivir (RDV) for the treatment of hospitalized patients with COVID-19 in England and Wales.

Methods: A probabilistic cost-effectiveness analysis was conducted informed by 2 large trials and uses a partitioned survival approach to assess short- and long-term clinical consequences and costs associated with COVID-19 in a hypothetical cohort of hospitalized patients requiring supplemental oxygen at the start of treatment. Given that it is uncertain whether RDV reduces death, 2 analyses are presented, assuming RDV either reduces death or does not. Published sources were used for long-term clinical, quality of life, and cost parameters.

Results: Under the assumption that RDV reduces death, the incremental cost-effectiveness ratio for RDV is estimated at £11,881 per quality-adjusted life-year gained compared with standard of care (SoC) (probabilistic incremental cost-effectiveness ratio £12,400). The probability for RDV to be cost-effective is 74% at a willingness-to-pay threshold of £20,000 per quality-adjusted life-year gained. RDV was no longer cost-effective when the hazard ratio for overall survival compared with SoC was >0.915.

Conclusions: Results from this study suggest that using RDV for the treatment of hospitalized patients with COVID-19 is likely to represent a cost-effective use of National Health Service resources at current willingness-to-pay threshold in England and Wales, only if it prevents death. Results need to be interpreted cautiously as vaccination was introduced and the SoC and evidence available have also evolved considerably since the analysis is conducted.

Keywords: coronavirus, cost-effectiveness, COVID-19, economic evaluation, health technology assessment, remdesivir, United Kingdom.

VALUE HEALTH. 2022; 25(5):761–769

Introduction

COVID-19 is caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 and causes atypical pneumonia. The disease is transmitted by inhalation or contact with infected droplets, and the incubation period is estimated to range from 2 to 14 days. The symptoms are usually fever, cough, breathlessness, and fatigue, among others. All populations are susceptible to severe acute respiratory syndrome coronavirus 2, with the elderly and people with underlying diseases or low immune function being more likely to become severe cases.

In response to the public health emergency, the National Health Service (NHS) England issued an interim commissioning policy (first published on the July 7, 2020, and updated on the November 12, 2020) for the use of remdesivir (RDV) in England and Wales, for the treatment of hospitalized patients with COVID-19 requiring supplemental oxygen at the start of treatment (as per its European Medicines Agency marketing authorisation), typically defined as those on low-flow oxygen (LFO), high-flow oxygen (HFO), or other noninvasive ventilation (NIV).

The efficacy of RDV in hospitalized patients with COVID-19 on supplemental oxygen is described in a number of studies that are heterogeneous in terms of the included populations, study design, and outcomes. The Adaptive Covid-19 Treatment Trial 1 (ACTT-1) is a double-blind randomized controlled trial (RCT) comparing RDV with placebo in the United States and reported a treatment effect on mortality (hazard ratio [HR]) of 0.85 (95% confidence interval [CI] 0.66–1.09) in hospitalized patients with LFO and 1.02 (95% CI 0.94–1.10) in patients with HFO or NIV at baseline. SOLIDARITY was conducted after ACTT-1 and is an unblinded, multicenter RCT across 30 countries in patients who were hospitalized with COVID-19. ACTT-1 compared RDV with local standard of care (SoC) and reported a rate ratio of death of 0.85 (95% CI 0.66–1.09) for the subgroup of patients requiring any supplemental oxygen (but not mechanically ventilated). Wang et al (2020) was conducted in China and compared RDV with placebo.
in a double-blind RCT and reported a death rate ratio of 0.81 (95% CI 0.21-3.07) in hospitalized patients with LFO and 1.40 (95% CI 0.20-9.52) in patients with HFO or NIV at baseline. Therefore, there is considerable uncertainty in the effectiveness of RDV in preventing death in the overall supplemental oxygen population. These RCTs were also conducted at different phases during the pandemic making any direct comparison challenging.

NHS England’s interim commissioning for RDV was produced in response to the public health emergency and the rapid need for effective treatments to help reduce morbidity and mortality posed by COVID-19. This decision was not based on economic consideration. Therefore, it is unclear whether RDV represents a cost-effective use of NHS resources in England and Wales for the treatment of hospitalized patients with COVID-19 on supplemental oxygen at entry.

The objective of this study is to assess the cost-effectiveness of RDV in England and Wales within its current marketing authorisation and interim NHS commissioning policy, from a health services perspective.

**Strategies Compared and Population Entering the Model**

A decision-analytical model was constructed in Microsoft Excel to assess the short-term (during the hospitalization episode) and long-term (after hospital discharge) clinical consequences and costs associated with COVID-19 in a hypothetical cohort of hospitalized patients requiring supplemental oxygen at the start of treatment (defined as patients on LFO or HFO or NIV) in England and Wales.

The intervention assessed is RDV (Veklury®) 200 mg on day 1, followed by RDV 100 mg maintenance up to 5 days, in line with current NHS England interim commissioning for RDV. The comparator is established clinical management (previous routine use of tocilizumab [TCZ] and sarilumab [SAR]) with or without corticosteroids. RDV is assessed as an adjunct to SoC.

**Model Structure**

The structure of the decision-analytical model is depicted in Figure 1, and uses what is commonly referred to as a partitioned survival/area under the curve (AUC) approach, composed of 3 main mutually exclusive health states; (1) discharged from hospital and alive, (2) hospitalized with or without COVID-19, and (3) death from any cause (COVID-19 or because of other causes).

Patients enter the model when hospitalized with COVID-19 and requiring supplemental oxygen (LFO, HFO or NIV) at the start of treatment. During their hospital stay (defined as the AUC between the time to death and discharge curves), patients are further separated into 5 hospitalization subhealth states based on their hospitalization/oxygen requirement according to the clinical status ordinal scale as defined in the ACTT-1 trial (ie, no care because of COVID-19, no oxygen, LFO, HFO or NIV, and invasive ventilation), each associated with different cost and utility impact. Movements between hospitalization health states are not explicitly modeled. Instead, the partitioned model deals with health state occupancy within each time intervals.

Due to their short duration, not everyone in trials for COVID-19 treatments will have been discharged or died at the time of outcome assessment. Therefore, time to death is extrapolated parametrically beyond the trial duration using a daily cycle length up to 70 days (35 days in the base-case), followed (weekly cycle length) by an elevated risk of death compared with background mortality up to week 52 (varied between 6 months and 2 years in sensitivity analysis), and unadjusted background mortality used thereafter. Time to discharge is extrapolated parametrically until everyone either dies or is discharged.

Discharged patients are assumed to have a reduced quality of life (QOL) 52 weeks from model entry in the base-case) to reflect emerging evidence on the effect of COVID-19 after hospital discharge. Emerging evidence also suggests that some patients are at an elevated risk of multiorgan dysfunctions (such as respiratory diseases, diabetes, cardiovascular, liver and kidney...
diseases) and may require long-term management/monitoring.12 These potential impacts are included in this economic model as an average one-off cost and quality-adjusted life-year (QALY) loss per patient discharged.

Model Parameters

Baseline characteristics
The mean age and sex distribution at entry (Table 18,9,13-20) are taken from a UK study among 47 780 hospitalized patients with COVID-19 and discharged alive.8

Time to death in patients initiated on SoC (previous use of RDV)
The time to death in patients for the SoC arm is taken from a large UK trial; the first RECOVERY trial that compared usual care versus corticosteroids (dexamethasone).21 Since this trial was conducted, clinical practice has changed with corticosteroids widely used. Therefore, a weighted spline model (3 knots) was constructed from the pseudo-individual patient data (IPD; reconstructed based on a published algorithm22) that assumes that 90% of patients are on corticosteroids (dexamethasone arm from RECOVERY21), with the remaining not on dexamethasone.

Table 1. Model input parameters.

| Parameter                                      | Expected value | Range for sensitivity analysis | Measure of uncertainty | Source |
|------------------------------------------------|----------------|-------------------------------|------------------------|--------|
| Baseline characteristics                       |                |                               |                        |        |
| Age                                            | 64·5           | 56·2                          | 66·5*                  | Normal (SD 19·2) 8 |
| Sex distribution (female %)                    | 40·1%          | 40%*                          | 55%*                   | Beta   8 |
| Treatment effect                               |                |                               |                        |        |
| HR OS                                          | 0·85           | 0·66                          | 1·09                   | Lognormal (95% CI) 6 |
| HR time to discharge                           | HR1 (day 0-4): 0·56 | HR2 (day 5-9): 1·00          | HR3 (day 10-14): 1·07  | HR4 (day 15-19): 1·35 | HR5 (day 20+): 1·24 | Multivariate normal 6 |
| Health-related QOL—utility value               |                |                               |                        |        |
| Invasive ventilation                           | 0             |                               |                        | Assumed |
| Health-related QOL—applied as decrement        |                |                               |                        |        |
| Increased comorbidities at entry               | −0.116         | 0*                            | 0·15*                  | Normal1 13 |
| Discharged (first 52 weeks)                    | −0.097         | 0·077                         | 0·116                  | Normal1 9 |
| Hospitalized, not on oxygen                   | −0.36          | 0·288                         | 0·432                  | Normal1 14 |
| Hospitalized, on LFO, or HFO or NIV           | −0.58          | 0·464                         | 0·696                  | Normal (95% CI) 15 |
| Costs                                          |                |                               |                        |        |
| RDV—price per vial                            | £340           |                               |                        | Not varied 16 |
| SoC—cost per day                              | £0·53          |                               |                        | Not varied 17 |
| Hospitalization cost per day                   |                |                               |                        |        |
| Hospitalized, not on oxygen and no ongoing care because of COVID | £337           | £270                         | £405                   | Gamma1 18 |
| Hospitalized, not on oxygen and require care because of COVID | £347           | £278                         | £416                   | Gamma1 18 |
| Hospitalized, on LFO                          | £616           | £493                         | £739                   | Gamma1 18 |
| Hospitalized on HFO or NIV                    | £933           | £747                         | £1120                  | Gamma1 18 |
| Hospitalized, on invasive ventilation         | £1518          | £1215                        | £1822                  | Gamma1 18 |
| Medium- to long-term after discharge           |                |                               |                        |        |
| Elevated risk of death                         | 7·7            | 7·2                           | 8·3                    | Lognormal (95% CI) 8 |
| MOD QALY loss                                  | −0·023         | −0·011                       | −0·069                 | Beta1 Appendix Table1 |
| MOD cost                                       | £1362          | £681                         | £4085                  | Gamma1 Appendix Table1 |
| Monitoring one-off cost                        | £364·6         | 182·3                        | 1093·8                 | Gamma1 Assumed 19,20 |

CI indicates confidence interval; HFO, high-flow oxygen; HR, hazard ratio; LFO, low-flow oxygen; MOD, multiorgan dysfunction; NIV, noninvasive ventilation; OS, overall survival; QALY, quality-adjusted life-year; QOL, quality of life; RDV, remdesivir; SE, standard error; SoC, standard of care.

*Range assumed.
^SE assumed to be 10%.
^Range assumed to be ±20%.
^Range assumed to be halved or tripled.

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THEMED SECTION: COVID-19
763
A spline model with 3 knots was selected after visual inspection and statistical tests; with the addition or removal of knots not materially changing the fit within the observed or short-term extrapolation in this study. Scenario analyses are conducted using the control arm from SOLIDARITY6 or the control arm from the RECOVERY TCZ trial23 in people with progressive COVID-19.

**Time to discharge in patients initiated on SoC (previous use of RDV)**

The time to discharge for the SoC arm is approximated by adjusting a spline model (3 knots) estimated from pseudo-IPD from the control arm from SOLIDARITY6 using an HR we calculated so that the proportion of patients predicted to be discharged and alive at day 28 matches the proportion reported in the RECOVERY trial21 (70.86% for the weighted analysis [base-case: 90% assumed to receive corticosteroids], 67.40% [n = 1755 of 2604] for usual care without dexamethasone, 72.01% [n = 921 of 1279] for the dexamethasone arm).

**Treatment effects for RDV**

The effectiveness of RDV at reducing death in patients on supplemental oxygen at entry is very uncertain and therefore 2 analyses are conducted. The base-case uses the point estimate from the on-oxygen population subgroup from SOLIDARITY6 (ratio of death rate 0.85; 95% CI 0.66-1.09). A secondary analysis is presented assuming an HR of 1 (eg, RDV does not have an impact on survival) as the treatment effect is not statistically significant despite the large sample size for this subgroup in SOLIDARITY (n = 3639). Similar findings were observed in Wang et al7 (2020). A significant treatment effect was also reported in patients with LFO in ACTT-1, but not in HFO.5

The treatment effects for time to discharge are estimated from the published data (IPD reconstructed using a published algorithm22) from SOLIDARITY6 using piecewise HRs (day 0-4, 5-9, 10-14, 15-19, 20+) calculated simultaneously in a model that is stratified by time group.

**Distribution of patients by intensity of hospital care required**

The distribution of hospital care type in patients initiated on RDV is shown in Figure 2. The distribution at baseline and at day 14 are informed by the distribution (derived from the ordinal scale of clinical status) from the ACTT-1 trial5 and Goldman et al24 (RDV for 5 and 10 days). We then assumed that the proportion of patients on invasive ventilation, NIV and no longer on oxygen increased linearly from day 0 to 14 and was carried forward beyond day 14 informed by the trend observed in ACTT-1 for RDV.5

The treatment effect for the probability of ventilation in patients initiated on SoC (compared with RDV) is taken from an unpublished UK study25 for the base-case, and assumed to be same as RDV for the secondary analysis assuming no survival difference.

**Mortality rate beyond parametric extrapolation**

The unadjusted rate of mortality for the general population is taken from the England and Wales life table 2017 to 2019.26 Between the end of extrapolation (day 35 in the base-case) and week 52, patients hospitalized with COVID-19 are assumed to be, on average, at an elevated risk of death of 7.7 (95% CI 7.2-8.3) compared with the general population based on the rate ratio reported by Ayoubkhani et al8 (2021) in the UK.

**Costs**

We adopt a health service perspective. Unit costs are summarized in Table 1.6,8,9,13-20 The unit costs per hospital bed day, according to the intensity of care required as measured by the ordinal scale of severity, are taken from NHS reference costs.18

Figure 2. Hospital health state occupancy in patients initiated on RDV.
list price for RDV is taken from the BNF. The number of RDV doses is taken from an unpublished UK study.

Only drug costs for corticosteroids are included for SoC and calculated from the electronic market information tool based on the weighted average of relevant formulations.

As the population entering the model is hospitalized, additional administration costs are likely to be minimal and are therefore not included in this economic evaluation.

**Health Utilities**

Health utility values are summarized in Table 1. Utility values are age-adjusted as patients get older based on Ara and Brazier, with the baseline utility value pre-COVID-19 estimated from the mean age at entry, adjusted by a decrement in utility taken from Ara and Brazier to reflect increased comorbidities for patients with COVID-19 compared with the general population. During the hospitalization episode, decrements in utility values are applied (subtracted) to the baseline, taken from the published literature. As with the assignment of costs, these utility decrements align with the degree of care required while in the hospital as indicated by the ordinal scale. Following hospital discharge patients with COVID-19 have a reduced QOL with QOL returning to pre-COVID-19 baseline after 52 weeks.

**Increased risks of multiorgan dysfunction and monitoring—one-off cost and QALY decrement at the point of discharge**

A one-off cost and QALY loss per patient discharged (Table 1) is applied in the economic model to reflect the elevated risk of multiorgan dysfunction after COVID hospitalization (assumed to last a year). These are calculated from the rates reported by Ayoubkhani et al. (2021) in the UK in patients hospitalized with COVID-19 compared with matched-controls and assumptions on costs and QALY loss (Appendix Table 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.12.015).

Increased monitoring/follow-up is assumed to occur in the first year only. An average one-off cost (Table 1) is applied at the point of discharge calculated based on the assumption that discharged patients require on average 2 chest x-ray and 6 GP electronic consultations, and unit costs from Stokes et al. (2016) and Curtis and Burns (2020).

**Analysis**

In accordance with the National Institute of Clinical Excellence reference case, patients are followed over a lifetime horizon, an NHS/personal social services perspective is used and costs and benefits are discounted at 3.5% per annum.

Results are presented both deterministically and probabilistically to take account of the simultaneous effect of uncertainty relating to model parameter values. A total number of 1000 simulations were performed to obtain sufficient precision. Base-case results are also presented as cost-effectiveness planes and cost-effectiveness acceptability curves.

The treatment effect for RDV on overall survival (OS) is a key driver and highly uncertain. Consequently, a threshold analysis is conducted, with results presented in terms of net monetary benefits to determine the point at which RDV is no longer cost-effective at a willingness to pay (WTP) of £20,000 under our base-case assumptions. Threshold analysis to determine the cost-effective price was also conducted. A range of sensitivity and scenario analyses are also conducted to test the robustness of results to key input parameters and assumptions (Appendix Table 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.12.015).

**Results**

**Base-Case Analysis: Assumption That RDV Reduces Death—Using the Point Estimate for the Treatment Effect Observed in On-Oxygen Subgroup of SOLIDARITY**

The determinstic and probabilistic results are presented in Table 1. For the probabilistic analysis, under the assumption that RDV reduces death, the model estimates total discounted costs associated with RDV to be £12,758 compared with £9,393 for established clinical management, an incremental cost of £3,365. The total discounted QALYs for RDV are estimated to be 6.62 compared with 6.35 for patients treated with established clinical management, an incremental QALY gain of 0.27. The probabilistic incremental cost-effectiveness ratio (ICER) is £12,400 per QALY gained.

We found that 89.3% of Monte Carlo simulations comparing RDV with established clinical management were in the northeast quadrant (more costly and more effective) of the cost-effectiveness plane. RDV was more costly but less effective in 10.7% of cases (northwest quadrant [Fig. 3]). Cost-effectiveness acceptability curves demonstrate that RDV has a 74% probability of being a cost-effective treatment option at a £20,000 per QALY gained WTP threshold.

**Secondary Analysis: RDV Does Not Reduce Death**

When it is assumed that RDV does not reduce death (Table 2), RDV is predicted to lead a very small increase in QALYs (0.00002), at an incremental cost of £1,666, leading to a high ICER (£1 million per QALY). Approximately half of Monte Carlo simulations (52.2%) were in the northeast quadrant (more costly and more effective) of the cost-effectiveness plane, with RDV having a 0% probability of being a cost-effective treatment option at an incremental cost of £20,000 per QALY gained WTP threshold.

**Threshold Analyses**

At its current list price, the threshold analysis (Fig. 3) shows that RDV is no longer cost-effective at a WTP of £20,000 per QALY gained when the HR is >0.915.

If no survival difference is assumed between RDV and SoC (Fig. 4), the price per 100 mg vial for RDV needs to be <£18.6 for RDV to be cost-effective under current WTP threshold.

**Scenario Analyses**

In addition to the treatment effect for OS and list price for RDV, ICERs were affected the most by the model time horizon, the baseline curve for SoC (patients with progressive COVID-19 included in the RECOVERY TCZ trial), and inclusion of unrelated costs.

**Discussion**

This is the first study to undertake an economic evaluation of the use of RDV for the treatment of hospitalized patients with COVID-19 in England and Wales. This study found that, although RDV reduces time to recovery, it is likely to be cost-effective only if it also prevents death. Nevertheless, the effectiveness of RDV at reducing death is highly uncertain within the overall supplemental oxygen population. Evidence suggests that patients requiring LFO are more likely to derive benefits from RDV than patients on HFO or IV. Therefore, RDV is likely to represent a cost-effective use of NHS resources in patients with LFO only. The analysis was conducted during the second wave of the pandemic. Since the analysis was conducted, vaccination was introduced in...
the United Kingdom and the SoC and evidence available for RDV have evolved considerably. Therefore, results from this analysis should be interpreted in this context.

This study also sets out a framework to capture the key drivers of costs and benefits (mortality, duration of stay, and intensity of care required while in the hospital) that can be used to rapidly evaluate other treatments for hospitalized patients with COVID-19. This is important during a public health emergency because COVID-19 is associated with significant morbidity and mortality, and therefore, there is need to inform public policy rapidly and ensure that NHS resources are allocated efficiently and fairly.

A key strength of this study is that it addresses an important public health question for decision makers in the light of uncertain information, synthesizes many sources, and reflects uncertainty. This emphasizes the value of modeling given the difficulty to conduct clinical research in a rapidly changing environment. Key strengths of this study also include that it is based on 2 large open-label trials: the RECOVERY trial\(^2\) and SOLIDARITY.\(^6\) This study also focuses on patients treated with RDV on supplemental oxygen at the start of treatment (defined as LFO, HFO, or NIV) in line with its European marketing authorization and NHS England commissioning policy.\(^3,4\) The duration of hospitalization is calculated from the starting health state and therefore only applicable to the overall ACTT-1 population. Compared with previous economic evaluations, our model further considers that COVID-19 patients are, on average, at an elevated risk of death, reduced QOL, and multiorgan dysfunctions after discharge. None of these effects were included in previous published economic evaluations at the time this analysis was conducted.\(^30-32\)

As with any economic evaluation, there are limitations to be acknowledged. First, any economic evaluation for COVID-19 is challenging to conduct because of the rapidly changing environment. SoC is consistently evolving and has changed since the evidence used in this economic evaluation was published. Corticosteroids are now the SoC in England and Wales, and this has been reflected in the base-case. NHS England recently issued advice for the use of TCZ and SAR. Unlike RDV, TCZ and SAR have different mechanisms of action, and it is unclear to what extent these treatments would be considered in patients who would have been otherwise eligible for RDV in England and Wales (and be appropriate comparators). Albeit limited to the supplemental oxygen subgroup from the respective source of evidence, this economic evaluation combines evidence from different studies that are heterogeneous in population, design,
and outcomes. The level of patients’ oxygen requirement was also not reported.

Evidence is also constantly evolving. For instance, time to discharge had to be approximated because only the proportion of events at the end of trial was reported at the time of conducting study, but new data have now been published. Using the recently published KM was explored (Appendix Table 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.12.015). Therefore, the model needs to develop as more evidence is available on both the impact of treatments on COVID-19 and its long-term effect. Since this analysis was conducted, additional evidence of the effectiveness RDV has been published from a phase III, open-label, adaptive, multicenter RCT conducted in 48 sites in Europe (DisCoVeRy).33 This study found that no clinical benefit was observed from the use of RDV in patients who were admitted to hospital for COVID-19 and requiring oxygen support. The model uses an AUC approach that does not allow us to track individual patients, leading to assumptions being required. A cohort partitioned survival approach was chosen in the absence of individual patient level data from the key relevant trials/studies used in this economic evaluation and necessity to work with aggregate published data. This is a limitation because patients with COVID-19 admitted to the hospital are heterogeneous, with important factors affecting the progression of their disease. It was also not possible to conduct subgroup analysis in the absence of subgroup data reported in patients on supplemental oxygen at

Table 2. Model base-case and secondary scenario results.

| Intervention | Base-case: RDV reduces death | Secondary scenario: RDV does not reduces death* |
|--------------|------------------------------|-----------------------------------------------|
|              | Total costs (£) | Total LYG (und) | Total QALYs | Incr. costs (£) | Incr. LYG (und) | Incr. QALYs | ICER (£/QALY) | Total costs (£) | Total LYG (und) | Total QALYs | Incr. costs (£) | Incr. LYG (und) | Incr. QALYs | ICER (£/QALY) |
| SoC          | £9386 | 14-34 | 6-35 | - | - | - | - | £10 311 | 14-34 | 6-35 | - | - | - | - |
| RDV          | £12 718 | 14-97 | 6-63 | £3332 | 0-64 | 0-28 | £11 881 | £11 970 | 14-34 | 6-35 | £1659 | - | 0-00 | >£1M |
| SoC          | £9393 | 14-34 | 6-35 | - | - | - | - | £10 316 | 14-33 | 6-35 | - | - | - | - |
| RDV          | £12 758 | 14-95 | 6-62 | £3365 | 0-62 | 0-27 | £12 400 | £11 982 | 14-33 | 6-35 | £1666 | - | 0-0002 | >£1M |
| Probability CE | 74% | 0% |

Probability CE indicates cost-effective; ICER, incremental cost-effectiveness ratio; Incr., incremental; K, thousand; LYG, life-year gained; und, undiscounted; QALY, quality-adjusted life-year; RDV, remdesivir; SoC, standard of care; >£1M, more than £1 million.

*In this scenario, RDV the treatment effect for the probability of ventilation in patients initiated on SoC (compared with RDV) is assumed to be same as RDV.

Figure 4. Threshold analysis for the treatment effect for overall survival—NMB at a WTP threshold of £20 000 and £30 000 per QALY gained.

K indicates thousand; NMB, net monetary benefit; QALY, quality-adjusted life-year; WTP, willingness to pay.
entry. Treatment effects from studies evaluating RDV for 10 days as a proxy for RDV for 5 days. The assumption of equivalence for survival is likely and is supported by Goldman et al.33 (2020) and Spinner et al.34 (2020), albeit in a broader population. The trend for time to discharge is taken from SOLIDARITY where patients were treated up for to 10 days, which could have affected the decision to discharge patients. It is possible that patients on RDV in SOLIDARITY were kept longer at the hospital to finish the 10-day course.

Analyses are conducted at list prices. Any confidential discount offered to the NHS is not considered in this analysis. It is also unclear whether RDV reduces or increases ventilation/oxygen support because of mixed evidence.

Since this economic evaluation was conducted, 2 UK studies—the PHOSP-COVID collaborative group10 and ISARIC11—reported estimates on QOL before COVID-19 and for lower mean age. Therefore, it is unclear whether the additional decrement in utility associated with comorbidities included in this analysis was required and led to double counting. This was explored in a scenario analysis and led to an improvement in the ICER (Appendix Table 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.12.015).

Assumptions were required to capture the effect of COVID-19 in the medium to long term. It is unclear how long discharged COVID-19 patients are at an elevated risk of death or reduced QOL. It is also unclear whether multiorgan dysfunctions reported in the literature are acute (temporary) or chronic. The approach to capture costs and impact on QOL associated with multiorgan dysfunction is simplistic because of the heterogeneity in patients experience and does not take into account patients with post-COVID-19 syndrome and the recommendation for them to have rehabilitation. It also does not take account of other reported long-term effects on mental health that have been reported such as posttraumatic stress disorder. The duration and frequency of monitoring after discharge of patients with COVID-19 are also unknown and challenging to capture because of the heterogeneity in patient experience. The mortality, costs, and morbidity impact associated with readmission because of COVID-19 is not included separately to avoid double counting because evidence suggests that readmission because of COVID-19 occurs shortly after the initial hospitalization episode, typically within 5 to 10 days.5,35

The model conservatively assumes that patients initiated on RDV or SoC experience the same long-term outcomes, in the absence of evidence. Consequently, any short-term difference in survival will translate into commensurate gain in the long-term. It is possible that outcomes for patients initiated on RDV may be worse if more patients require ventilation because of the reduced death rate.

Conclusions

RDV is likely to represent a cost-effective use of NHS resources if it reduces death and does not increase ventilation requirement. RDV is likely to be more cost-effective in patients requiring LFO at entry only than those requiring more intensive HFO or NIV.

Supplemental Materials

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2021.12.015.

Article and Author Information

Accepted for Publication: December 25, 2021

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