Effectiveness of Remdesivir Treatment for Covid-19:

A Critical Literature Review

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Abstract

The purpose of this paper was to answer a question about the effectiveness of Remdesivir in the treatment of COVID-19 disease. To accomplish this task, 10 research articles were utilized in the attempt to arrive at a credible conclusion about the question at hand. With each article, an analysis was made to determine the limitations of the study, the appropriateness of the sample size, the statistical significance of the results, and whether the study was adequately powered and valid to yield meaningful results. A large number of the clinical studies analyzed showed a positive correlation between treatment with Remdesivir and improved clinical outcomes, whereas a small number of the clinical studies showed no difference in outcome.

Effectiveness of Remdesivir for Covid-19: A Critical Literature Review

Every couple of hundred years there comes a pandemic that changes healthcare and the everyday lives of everyone, not just those residing in the United States. The year 2019 introduced the world to a new severe acute respiratory syndrome (SARS) human coronavirus, colloquially known as Covid-19. The coronavirus is known to cause many different symptoms such as PNA, fever, and breathing difficulty or failure. All these symptoms and more were seen as the waves of the pandemic took over each country, causing millions of deaths and injuries in its wake.

To better understand the treatments that are still used for Covid-19, a literature review was used to identify the effectiveness of practitioners, specifically advanced practice registered nurses (APRN), prescribing Remdesivir (RDV) had on the treatment and prevention of severe respiratory disease. For reference, RDV is prescribed only intravenously and normally as a loading dose of 200 mg on the first day, and subsequent daily doses of 100 mg afterwards (Gottlieb et al., 2022).

Throughout the literature review, the effectiveness, and possible implications/complications of using RDV to treat Covid-19. A conceptual analysis approach will be used throughout this literature review process, with a specific focus on linguistic/pragmatic and ordinary approaches. The Ordinary use approach uses the method of analyzing cases to identify criteria, antecedents, and consequences found within a study (Bomer-Norton, 2021). The linguistic/pragmatic approach consists of the analysis of explicit and implicit concepts found in the literature to identify different criteria, antecedents, and consequences for use in both practice and research (Bomer-Norton, 2021).

Also, the relational approach will be used in determining if there is a positive, negative, or unknown relationship between the use of RDV therapy and positive outcomes of Covid-19. This relational approach could show a positive linear relationship whereas the use of RDV increases, the positive outcome for the patient also increases (Bomer-Norton, 2021). A negative linear relationship would show that as the use of RDV increases, the positive outcomes of for the patient would decrease (Bomer-Norton, 2021).

Multiple search engines for scholarly articles were used to find evidence to either support or negate the idea that the use of RDV was effective in treating patients with Covid-19 when prescribed by practitioners, such as the APRN. Sources such as the cumulative index to nursing and allied health literature (CINAHL), the Cochrane library, Elton B. Stephens Company (EBSCO) and additional medical research websites were used to identify current and relevant research articles on the topic. Using the framework identified previously, the articles were found to be relevant to the topic, or rejected and further research was performed.

An Introduction to Covid-19

Near the end of 2019, a series of pneumonia (PNA) cases of emerged out of Wuhan, China and leading to concern throughout the world (Surati et al., 2020). Only a short while later, a new virus was identified as being the cause of the multiple cases of PNA and deaths that were spreading throughout China; shortly afterwards it began heading towards other countries and continents (Surati et al., 2020). Since then, Covid-19 has affected more than seven hundred million individuals and resulted in more than six million deaths worldwide (Georgakopoulou et al., 2023). The data that has been collected so far has indicated that the viral infection caused by Covid-19 can produce an excessive immune reaction in the host patient, thus leading to severe disease (Surati et al., 2020). In some patients, this immune reaction led to what is known as a

"cytokine storm" that leads to excessive tissue damage, especially in the lungs (Surati et al., 2020).

The symptoms of Covid-19 tend to appear after an incubation period of anywhere between five and seven days, with a period from onset to death ranging anywhere between six and forty-one days (Surati et al., 2020). However, this period is dependent on many variables, such as the age of the patient their immune system; a shorter duration of time was seen in patients that were older than seventy years old (Surati et al., 2020). Clinical features that were identified to be specific to Covid-19 were acute respiratory distress syndrome, acute cardiac injury, and incidence of ground-glass opacities (Surati et al., 2020). Additional features that were seen in Covid-19 include the targeting of the lower airway as seen by rhinorrhea, sneezing, and sore throat, dyspnea and hypoxemia (Surati et al., 2020). Clinical studies began to suggest that RDV, an inhibitor of RNA polymerase with in vitro activity against RNA viruses, was effective as a treatment for Covid-19 (Surati et al., 2020). This drug therapy had been previously tested and found effective in treating a previous human coronavirus, also known as Middle East respiratory syndrome (MERS) (Surati et al., 2020).

Research Process and Inclusion Criteria

Multiple search engines were used to identify different research studies that involved the treatment method of RDV for Covid-19 infection. CINAHL and the Cochrane library were found to be the most effective in finding desired articles, however searching directly through different journal websites was also found to be effective. Specifically, the New England Journal of Medicine, Journal of Clinical Medicine, and Public Library of Science (PLOS) One. Each article was examined to identify if the article clearly identified whether RDV was effective as a treatment or not.

Using the concept analysis frameworks mentioned earlier, research articles could be selected by meeting the following criteria: The antecedents for the articles needed to include patients that were clinically diagnosed with Covid-19; The attributes that were acceptable for the research studies included patients with mild, moderate, severe, and vital cases of Covid-19 and treatment method using RDV in at least one clinical group of the study. The consequences of the research articles were not exclusion criteria, as they were used to determine if the hypothesis that RDV was effective in the treatment of Covid-19 was true or not. A total of eighteen articles were found to meet the criteria listed from the initial framework, however eight were excluded for not having clearly identifiable relationships between RDV therapy and Covid-19 outcomes.

Article Review and Analysis

A total of ten articles were reviewed after performing the initial literature search. Of these, six articles found a significant positive relationship with use of RDV therapy in treatment of Covid-19. The other four articles showed that there was no apparent relationship between the use RDV and recovery time/positive outcomes in patients diagnosed with Covid-19. Further appraisal of each article will be explained after reviewing the study of the articles chosen for this literature review.

Table 1 provides information on the first article to show a positive relationship between RDV and Covid-19 outcomes with the critical analysis demonstrated after.

Table 1

Article one: Marginal positive response to RDV

Clinical antiviral efficacy of Remdesivir in Coronavirus disease 2019: An open-label, randomized controlled adaptive platform trial	
Purpose/Problem	To clarify the therapeutic benefit of intravenous RDV in the treatment of Covid-19.

Sample	Consisted of previously healthy adults aged between 18 and 50 that had early symptomatic Covid-19 (Jittamala et al., 2023). A total of 439 patients were enrolled in this study.
Concepts	The treatment effect was determined by the presence of a difference in the viral clearance rate relative to the control (Jittamala et al., 2023). A 50 percent increase in clearance rate would be equivalent to a 33 percent reduction in clearance half-life (Jittamala et al., 2023).
Design	An open label, controlled, adaptive, pharmacometrics platform trial (Jittamala et al., 2023). Interventional
Instruments	After randomization, oropharyngeal swabs were taken from both tonsillar regions daily from days 0 to 7 and on day 14 (Jittamala et al., 2023). The levels of viral density were calculated through the polymerase chain reaction (PCR) and quantified and graphed.
Results	Parenteral RDV was found to accelerate the viral clearance in early symptomatic Covid-19 (Jittamala et al., 2023).
Implications for Advanced Practice Nursing	Prescribing RDV therapy in patients early on in their Covid-19 illness will help to reduce the likelihood of severe disease. Reduction of severe disease reduces the burden on healthcare by preventing patients from needing excessive medical interventions.
Comments	This study has one major limitation and no concerns about validity.

The article title gives a clear identification of the purpose of the research study as well as the research methodology that was used. The authors are clearly listed with their affiliated hospitals and healthcare associations; however, their specific titles are not listed to be able to determine their qualifications as authors of this study. The research was performed to identify the efficacy and safety of RDV in the treatment of early Covid-19 to prevent severe respiratory disease. Severe respiratory illness has been a problem since the onslaught of Covid-19, with a high morbidity and mortality rate occurring because of lung injury (Surati et al., 2020). The study was intentionally performed on low-risk adults presenting with high viral burdens to assess the comparative effect of RDV versus no interventions (Jittamala et al., 2023).

Throughout the discussion of the article, several different case studies regarding the use of RDV in treatment for Covid-19 are discussed. Many of these studies showed that there was a

decrease in mortality rates, as well as a reduction in the average duration of hospitalization in response to RDV (Jittamala et al., 2023). All these trials in favor of RDV explained in this article were conducted early in the pandemic before vaccine availability (Jittamala et al., 2023). However, there was an additional study mentioned in the discussion of the article lead by WHO that had nearly the same rate of deaths in the experimental group receiving RDV and those in the control group (Jittamala et al., 2023).

The introduction to the article explains the recent utilization of RDV in the treatment of Covid-19 and how it has been found to beneficial in certain populations where oral medications are not ideal, such as molnupiravir and ritonavir-boosted nirmatrelvir commonly known as Paxlovid (Jittamala et al., 2023). The article clearly states that a linear model with intercept and slope adjusted main model is used as the framework for this study (Jittamala et al., 2023).

Oropharyngeal PCR swabs were performed at differing stages throughout the study process to identify the viral loads as treatment progressed (Jittamala et al., 2023). In this research study, the viral clearance rate was expressed as the half-life; while the treatment effect was defined as the percentage of change in the viral clearance relative to the control group in the study (Jittamala et al., 2023). A fifty percent increase in clearance rate would then equal a thirty-three percent reduction in the clearance half-life (Jittamala et al., 2023). All analytical models of oropharyngeal virus clearance agreed (Jittamala et al., 2023). Compared to the control group, clearance of the virus, as identified by PCR tests, in patients receiving RDV was forty-two percent faster (Jittamala et al., 2023).

Overall, the research does have good evidence to show that there is a positive relationship between the use of RDV and improved clinical outcomes in patients diagnosed with Covid-19. However, the number of individuals that are treated with RDV and that were placed in the

control group are relatively small in comparison to the additional treatment methods group of the study.

Table 2 provides information on the second article to show a positive relationship between RDV and Covid-19 outcomes with the critical analysis demonstrated after.

Table 2

Article two: Marginal positive response to RDV

Remdesivir for the treatment of patients in hospital with Covid-19 in Canada: A randomized controlled trial	
Purpose/Problem	To determine the efficacy and safety of RDV in the treatment of Covid-19.
Sample	52 hospitals were selected to participate in the research study, a total of 1282 patients were selected overall. 634 patients were selected to receive RDV, 648 were selected to receive standard of care treatment (Ali et al., 2022).
Concepts	The efficacy of RDV treatment was based of in-hospital mortality rates, new need for mechanical ventilation (MV) and the hospital length of stay for the patient (Ali et al., 2022).
Design	This was an open-label pragmatic randomized controlled trial; patients were to receive either 10 days of RDV or only standard of care (Ali et al., 2022). Interventional.
Instruments	A Wilcoxon rank-sum test was used to compare the groups, and a Fine-Grey model was used to compare the time to discharge to alive accounting for competing risk of death (Ali et al., 2022).
Results	RDV was found to be marginally effective in treating Covid-19.
Implications for Advanced Practice Nursing	Prescribing RDV to patients when they were first hospitalized with Covid-19 can reduce the risk for the patient needing to be placed on MV and will reduce the risk of death in patients significantly.
Comments	Has some limitations and no concern about validity.

This research study was a randomized trial that had patients either receiving a ten-day course of RDV or standard care treatment to determine the effectiveness of RDV on treating Covid-19 (Ali et al., 2022). This research study utilized a control group of patients that were diagnosed with Covid-19 and that were to receive no additional anti-viral treatment methods. The research group received a dose of 200mg RDV on day one and 100mg on days two through

nine to determine the effectiveness of RDV therapy (Ali et al., 2022). The standard outcome that was studied was the patient's morbidity and mortality rate while in the hospital setting, with secondary outcomes consisting of changes in the patient's clinical severity, need for oxygen/ventilation support, as well as duration of hospital stay (Ali et al., 2022). A total of 1282 patients were chosen, however 15 were excluded for either not meeting criteria or from withdrawing themselves from the research study (Ali et al., 2022).

Ali et al. (2022) found in their research that the in-hospital mortality rate of patients that received RDV was lower at 18.7% versus those that received standard of care treatment that had a mortality rate of 22.6%. The confidence interval for these identified results, per Ali et al. (2022) was 95%. The 60-day mortality rate for patients that received RDV was 24.8% and those that received standard of care was 28.2% (Ali et al., 2022). There was a higher incidence of patients requiring ventilation support in those patients that were given the standard care versus those that received RDV treatment (Ali et al., 2022). After looking at these results, it can be shown that RDV did have a "modest, but significant effect" on the treatment of Covid-19 in compared with standard of care treatment therapy (Ali et al., 2022).

The first threat is that the research may not have a high enough statistical power, or participants, to minimize the risk of a type two error where the null hypothesis should have been rejected (Gray, 2021). This study did have a relatively small population, in comparison with other research studies that were performed on the same topic and therefor has a limited power to show statistical significance on the mortality rate on the patients receiving RDV versus standard of care (Ali et al., 2022). The second threat is that the research may violate assumptions of statistical tests, where the characteristics of the data were not adequate to use parametric tests and inaccurate results may have been produced (Gray, 2021). With this study, parametric tests

were able to be used to determine effectiveness, especially when reviewing the effectiveness of RDV in preventing the patients from having to be placed on supplemental oxygen or ventilator (Ali et al., 2022).

The third threat is the occurrence of multiple analyses and error rates where there is an increased likelihood that a result will be significant by chance (Gray, 2021). To avoid this error, a stringent and appropriate p value should be used, as well as limiting the statistical analyses to only those that are needed to address the research question (Gray, 2021). For this study, a p value of 0.006 and 0.007 were used in researching the effectiveness of RDV versus standard of care in patients diagnosed with Covid-19 (Ali et al., 2022). However, this may still be a concern regarding the fact that the population sizes used in this study were small. In total, 634 patients received RDV and 647 received standard of care.

The fourth threat is the possibility of unreliable measures, where the analyses of the data is more likely to produce results that include errors (Gray, 2021). To prevent this threat from being a problem, the researcher should select measures that have had evidence of reliability in past studies (Gray, 2021). Ali et al., (2022) used measures of morbidity and mortality that were used in other research studies performed in Canada at the time to determine the effectiveness of different antiviral medications or treatment methods. The fifth threat is unreliable implementation of the treatment where the analyses is more likely to produce results that include errors (Gray, 2021). The research that was performed by Ali et al. (2022) had strict guidelines of the dosage and administration protocol for patients in the experimental group, as well as what constituted as standard of care for the control group.

The sixth threat is the possibility of environmental extraneous variables where the analyses may produce results that include the effects of these variables, resulting in errors (Gray,

2021). The patients that were included in this research study were already hospitalized and had tested positive for Covid-19. The patients were in differing degrees of severity of the illness, however the outcomes were determined upon examining the reduction of need for increasing supportive care, such as the need to intubate a patient that was previously only on oxygen via nasal canula (Ali et al., 2022).

The last threat is of random heterogeneity of participants where the analyses may produce results that include the effects of characteristics of the participants, resulting in errors (Gray, 2021). This was a concern that was voiced by Ali et al. (2022), in that they stated that each patient's specific viral variant they were infected with was not able to be determined during the study, so the effect of RDV on the different variants of Covid-19 cannot be determined. However, on the other aspect, patients were assigned randomly to their group of either received RDV treatment versus standard of care (Ali et al., 2022). There were clearly identified exclusion criteria mentioned in the study, such as allergy to the research agent, anticipated discharge or transfer to site outside of research study, patient was not expected to survive past 24 hours, or were already receiving RDV treatment at the enrollment period of the study (Ali et al., 2022).

Table 3 provides information on the third article to show a positive relationship between RDV and Covid-19 outcomes with the critical analysis demonstrated after.

Table 3

Article three: Significant response to RDV in Covid-19

Inhaled Remdesivir reduces viral burden in a nonhuman primate model of SARS-CoV-2 infection	
Purpose/Problem	To determine the effectiveness of inhaled RDV as opposed to parenteral RDV as a method of treatment for patients diagnosed with Covid-19 (Vermillion et al., 2022).
Sample	30 African green monkeys were used for this study, 12 male and 18 female (Vermillion et al., 2022).

Concepts	Researchers wanted 22 to make RDV more convenient for non-hospitalized patients earlier in the disease process, as currently RDV is only being offered via intravenous route (Vermillion et al., 2020). The efficacy, safety, and pharmacokinetics of the drug via inhalation was being tested (Vermillion et al., 2022).
Design	Interventional.
Instruments	Peak plasma concentration of RDV and their corresponding viral burdens of Covid-19 were assessed at days 1-, 2-, 4- and 6-days post inoculation (Vermillion et al., 2022).
Results	Inhaled RDV resulted in lower systemic exposures to RDV (Vermillion et al., 2022). Positive response to RDV in treatment of Covid-19.
Implications for Advanced Practice Nursing	This method of treatment would offer a lower systemic dosage to patients, reducing the risk for possible adverse reactions and allowing for better treatment of Covid-19 with inhaled RDV treatment. Also, these patients could be treated with RDV outpatient instead of needing to be inpatient, or in a clinic to receive the intravenous RDV treatment.
Comments	Not performed on humans, however validity is not concerning.

The food and drug administration (FDA) approved Remdesivir as the first line treatment in hospitalized patients with Covid-19 in 2020 (Vermillion et al., 2022). RDV is a "nucleotide analog prodrug" that has demonstrated beneficial outcomes in patients with COVID-19 (Vermillion et al., 2022). To make this medication more readily available, this study was made to determine if alternative routes for RDV in non-hospitalized patients (Vermillion et al., 2022). Vermillion et al. (2022) investigated the pharmacokinetics and efficacy of RDV administered via inhalation in African green monkeys. The dose administered was significantly lower and produced comparable concentrations of the "pharmacologically active triphosphate in [the] lower respiratory tract issues (Vermillion et al., 2022). Inhalation of RDV resulted in lower systemic effects as compared with the intravenous RDV (Vermillion et al., 2022). This form of RDV demonstrated reductions in viral replication compared to the placebo (Vermillion et al., 2022). The administration method for the inhaled RDV was a head dome that worked similarly to a

nebulizer machine (Vermillion et al., 2022). The efficacy was found to be like that of the intravenous version of RDV (Vermillion et al., 2022).

The authors of the research study were investigated. All authors stem from one of two different clinical investigation research centers, Lovelace Biomedical and Gilead Sciences. Lovelace is a center that focuses primarily on respiratory research studies and infectious disease with designated physicians that research different treatment methods for various illnesses (Vermillion et al., 2022). Gilead Sciences is a research facility that focuses primarily on virology, oncology, and inflammatory illnesses with designated physicians that research possible treatment methods for treatment in known diseases (Vermillion et al., 2022). Given the background of the authors, they seem more than effective and appropriate to be testing the effectiveness of RVD inhalation solution versus RDV intravenous preparation.

The research article was published by Science Transitional Medicine, which is backed and supported by the American Association for the Advancement of science. The articles that are posted within this journal consist of original research papers that represent significant advances in research (Science Translational Medicine [STM], 2023). Also, STM's articles are peer-reviewed and science-based research articles that report successful advances in patient care (STM, 2023). The title of the research paper clearly covers the topic of the research study, as well as having all the necessary components of a research article: abstract, introduction, results, methods, discussion, statistical analyses, and references. The abstract in the research article is precise and clearly explains the purpose of the research study, as well as including major findings and methodological approaches used in the research. The body of the research article is broken down in an understandable manner, with each section of the results explained with various graphs and tables that support the evidence provided in the results section. The

references are organized in an appropriate manner for the type of research article, with notes added at the end of the references and supplemental materials provided for additional information on the research that was performed.

Ever since the onslaught of Covid-19 shutting down nearly every country, everyone became frantic to find a solution to treat the illness. When considering this, the research study addresses a significant problem and helps to address possible solutions. It is important that APRNs have the most up-to-date research studies on different treatment methods, that way they can treat their patients appropriately. Specifically, with the addition of RDV inhalation therapy, there may be a large reduction in the number of patients that are hospitalized with Covid-19.

The main weakness that was identified in this research study was that the research was performed on primates, instead of human subjects. As a result, there is not accurate research data to identify whether inhaled RDV would be just as effective at treating Covid-19 in human patients. Although this is a significant issue, this is the general practice for testing the effectiveness of new drug therapies. Per Batool et al. (2019), the drug researching process consists of the discovery phase, developmental phase, clinical trial phase and registry phase. During the drug discovery phase, it is common for conceptual medications to be tested on animals to determine if there is a therapeutic effect (Batool et al., 2019).

As Covid-19 continues to evolve and mutate, it would be beneficial to continue the research that was started in this article. For practitioners, such as the APRN, having an additional treatment method for Covid patients that have significant symptoms, however, do not require admission, would be ideal.

Table 4 provides the information for an article that shows substantial success with RDV in Covid-19 patients with a critical analysis following.

Table 4

Article 4: Substantial response to RDV treatment

Early Remdesivir to prevent progression to severe Covid-19 in outpatients	
Purpose/Problem	To determine the efficacy/safety of RDV treatment in patients diagnosed with Covid-19 and not hospitalized.
Sample	A total of 562 patients were selected and randomized into two groups: 279 patients received RDV and 283 received the placebo (Gottlieb et al., 2022). Eligible patients were 12 and older and had one pre-existing condition that placed them at higher risk for severe Covid-19 (Gottlieb et al., 2022).
Concepts	Non-hospitalized patients that are at high risk for severe disease can obtain RDV outpatient to prevent them from needing to be hospitalized.
Design	This was a randomized, double-blind, placebo-controlled trial (Gottlieb et al., 2022). Interventional.
Instruments	Viral loads via PCR testing, symptom tracking, need for hospitalization were units of measure for determining effectiveness of treatment in patients involved in the research study (Gottlieb et al., 2022).
Results	Acceptable safety, decreased Covid-19 progression. Positive response to RDV in treatment of Covid-19.
Implications for Advanced Practice Nursing	The administration of RDV outpatient to those at high risk can help prevent the need for hospitalization, or for excessive outpatient visits with urgent cares or primary care providers. This would decrease the healthcare burden and increase the desired outcomes in the patients at high risk for severe disease.
Comments	No concerns about validity.

The article title gives a very good representation of the purpose of the research study, as it was created to determine the effectiveness of RDV in preventing severe Covid-19 in outpatients with high-risk for complications. After researching a couple of the names listed as authors of this article, they are found to be medical investigators that work for the Pinetree company, however their specific titles and roles are not listed in the authors sections to be able to determine their qualifications as authors and founders of this research study. The primary efficacy end point of this research study was a composite of Covid-19 related hospitalizations, or deaths from any cause, by day 28 (Gottleb et al., 2022). This test was performed on high-risk

patients, however there was an underrepresentation of those with chronic liver disease, chronic kidney disease, immunocompromised patients, and those with cancer (Gottlieb et al., 2022).

Eligible patients for this study were those twelve years of age and older, having at least one preexisting condition that increased their risk for progression to severe Covid-19 disease (Gottlieb et al., 2022) If they could not meet those criteria, then they had to be meet the criteria of being over the age of sixty years; with this age, it did not make a difference if the patient had any additional preexisting conditions that placed them at higher risk for severe disease (Gottlieb et al., 2022). Patients were considered ineligible for this research study if they were currently receiving, or were expected to receive soon, supplemental oxygen or the need for hospitalization at the time of the initial research study screening (Gotlieb et al., 2022). They were also ineligible if they had previously been hospitalized for Covid-19 or had received the vaccine (Gottlieb et al., 2022).

Among the patients in the research study, those that were placed in the RDV group received a three-day course of RDV and were found to have substantially lower risk of hospitalization or death, as compared with the placebo group (Gottlieb et al., 2022). Covid-19 deaths or hospitalizations occurred in two patients in the RDV group and fifteen patients in the placebo group (Gottlieb et al., 2022). Nearly thirty-five percent of patients in the RDV group and twenty-five percent in the placebo group reported alleviation of their symptoms by the second week of treatment (Gottlieb et al., 2022). Despite the clearly identified beneficial clinical effects of RDV, the upper airway viral load was not found to be lower in patients who received the drug therapy, as opposed to those that received that received only the placebo; these results support the hypothesis that the nasopharyngeal viral loads of Covid-19 cannot be a reliable prediction of the treatment outcomes of RDV or other therapy methods (Gottlieb et al., 2022).

Regarding the first threat of possible low statistical power, the research study on a rather small group of patients, with not a lot of representation for countries outside of the U.S., where only 8 patients were not residing in the U.S. at the time of the study (Gottlieb et al., 2022). This small population leads to a possible limited power to independently show statistically significant on the true benefit of RDV in preventing severe disease with early intervention in Covid-19 patients. Parametric tests were performed in this research study, which prevents the threat that the data was not adequate and may lead to inaccurate results.

For this study, a p value of 0.008 was used when determining the effectiveness of RDV in early Covid-19 to prevent severe disease, however this may still lead to a threat of multiple analyses and error rate due to the small population. This study used measures of patients' outcomes and mortality rates to determine the effectiveness of RDV, which have used in previous studies to determine the effectiveness of other antiviral methods. As a result, this helps to prevent the possibility of the fourth threat that states unreliable measures, where the data is more likely to produce results that include errors (Gray, 2021).

This research study had strict guidelines on the dosage and administration of the RDV to the experimental group, which prevented the possibility of the fifth threat to validity. With regards to the possibility of environmental extraneous variables, the patients within the group were screened for the risk to be hospitalized, whether they had already had a prior history of severe Covid-19 disease, as well as if they had been vaccinated (Gottlieb et al., 2022) Lastly, with regards to the possibility of random heterogeneity of the participants within the study; Gottlieb et al., (2022) voiced the concern that the lack of representation may lead to this risk of validity. However, there were strict exclusion criteria mentioned in the study, which helped to prevent this threat from being a problem.

Table 5 provides information on the fifth articles to show that although RDV is safe and tolerable, it doesn't have much of an effect in treating Covid-19 patients.

Table 5

Article 5: Little to not effect in treating Covid-19

Remdesivir treatment for patients with moderate to severe Covid-19	
Purpose/Problem	To determine if RDV is effective in treating patients with moderate to severe Covid-19.
Sample	494 patients were included in this study; 392 patients had moderate Covid-19 and 102 patients had Severe illness (Hasanoglu et al., 2022)
Concepts	RDV was first approved for the treatment of Ebola, however it was found to not meet the expectations (Hasanoglu et al., 2022). It was found effective in treating other viruses and was then tested for efficacy in treating Covid-19.
Design	This was a multicenter prospective observational study (Hasanoglu et al., 2022). Non-interventional, observational.
Instruments	A Hosmer-Lemeshow test was used to determine the accuracy of the results (Hasanoglu et al., 2022).
Results	RDV is found to be safe and well-tolerated for treatment of moderate/severe Covid-19 (Hasanoglu et al., 2022). Did not provide positive effects in treating Covid-19 with RDV.
Implications for Advanced Practice Nursing	With understanding that even though the drug is safe and well-tolerated, it has little to no effect in reducing the severity of Covid-19 in patients, it helps the APRNs know that there is no clinical reasoning to prescribe the medication to patients.
Comments	Some limitations are found within the research, however the validity is not concerning.

The title of the paper clearly identified the topic of the study; however, it didn't clarify initially that it was an observational, not experimental study. This study was performed to determine the efficacy of RDV for the treatment of severe and moderate Covid-19. This research was performed via a multicenter prospective noninterventional observational study in 14 different centers throughout Turkey (Hasanoglu et al., 2022). 500 patients were initially selected for this study, however 6 were excluded because they did not complete the full therapy of RDV as prescribed/planned by the physician/research study (Hasanoglu et al., 2022). Patients had to meet several specific criteria to be qualified for this study: diagnosis of Covid-19 via PCR test,

respiratory rate greater than 30 or severe respiratory distress, and patients greater than 18 years of age (Hasanoglu et al., 2022). Patients were then administered RDV as a loading on day one and followed by maintenance dosing for the next consecutive 4 days (Hasanoglu et al., 2022). The clinical presentations of the patients were recorded of days 0, 3, 5, 7 and 14 if they were still hospitalized (Hasanoglu et al., 2022). Overall, the 28-day mortality rate of the patients receiving RDV was 10.1% in total (Hasanoglu et al., 2022).

This research study was found to have several limitations, the first being that this study does not have a control group, or an alternative treatment method, for RDV to be compared to. As a result, this creates the possibility that the effect of other forms of treatment leading to improvement in patients with Covid-19 and not receiving RDV could not be evaluated (Hasanoglu et al., 2022). Secondly, the study only included severe and moderate cases of Covid-19 patients, which means the results cannot be generalized for all patients' groups that have contracted Covid-19. Next, the trend of the Covid-19 viral load under RDV treatment was not evaluated throughout the study. Fourthly, the study was conducted in fourteen different locations throughout Turkey, where each center had different laboratory parameters that could possibly skew the results and change the outcome predictors (Hasanoglu et al., 2022).

Considering that several different facilities were used in this non-interventional observation study, the sample size was small and should have included more patients to provide more accurate data on the subject. As a result, this places the study at a greater risk of having low statistical power to prove validity of the research (Gray, 2021). Also, the test did not have the trends of viral loads on the patients, which is provided in almost every other research study on the effectiveness of RDV therapy for Covid-19 (Hasanoglu et al., 2022). As a result, this places the research study at risk of having unreliable measures (Gray, 2021). Lastly, it does not appear

as if subjects were randomly selected to participate in this research study, which places the internal design at risk of improper selection (Gray, 2021).

Table six provides information about another article that concludes there is no clinical evidence of improvement from the use of RDV therapy.

Table 6

Article 6: No clinical evidence of improvement with RDV

Remdesivir in combination with dexamethasone for patients hospitalized with Covid-19: a retrospective multicenter study	
Purpose/Problem	To determine the effectiveness of RDV therapy alongside dexamethasone (DXM) in treating patients with Covid-19.
Sample	325 total patients were selected, however only 180 patients were included. 90 patients received RDV and DXM together, the other 90 received DXM alone.
Concepts	DXM is considered as the standard treatment of care for patients diagnosed with Covid-19 and requiring oxygen therapy (Gressens et al., 2022). The study is to determine if the addition of RDV creates better clinical outcomes.
Design	This was a retrospective multicenter cohort study (Gressens et al., 2022). Outcomes Research.
Instruments	Wilcoxon and Fischer tests were used to measure the outcomes, generalized linear models were used to come prevalence of adverse events in the patients (Gressens et al., 2022).
Results	The addition of RDV was found to have no correlation between a shorter hospitalization nor lower in-hospital mortality rates (Gressens et al., 2022). No clinical evidence of improvement of Covid-19 related to RDV.
Implications for Advanced Practice Nursing	Seeing that there was not much clinical improvement from the addition of RDV to DXM treatment, it may be found more beneficial to simply prescribe the patient with DXM treatment instead.
Comments	The study had several limitations; however the validity is not concerning.

This study's title clearly identified the purpose of the study, as well as the type of study that was performed. Since the beginning of the Covid-19 pandemic, DXM has been considered as the standard of care for patients needing oxygen therapy due to Covid PNA (PNA). This research study was a retrospective cohort study of patients that were hospitalized and diagnosed

with Covid-19 PNA, requiring low-flow oxygen and already received concurrent DXM therapy performed in Paris, France (Gressens et al., 2022). The first outcome of this study was the duration of hospitalization after oxygen therapy, whereas secondary outcome was in-hospital death or transfer to a higher level of care, such as the ICU (Gressens et al., 2022). To prevent the possibility of any bias that could skew the results, outcome comparison was performed (Gressens et al., 2022).

Initially, 325 patients were selected for the study, however only 180 were used for research after matching propensity scores (Gressens et al., 2022). 90 patients received RDV therapy concurrently with DXM and 90 patients received DXM alone (Gressens et al., 2022). At the time of admission for the patients included in the study, the average time from symptom onset was seven days; average age of 68 years and 38 percent of the patients enrolled in the DXM group were female (Gressens et al., 2022).

Throughout the study, DXM was labeled the standard of care in all patients diagnosed with Covid-19; the experimental group was therefore then the combination of RDV and DXM (Gressens et al., 2022). Exclusion criteria for the study included decreased renal function as defined as a decreased creatinine clearance level or elevated live enzymes greater than five times the normal values (Gressens et al., 2022). Also, patients that were ill enough that they had to be directly admitted a higher level of care, such as the ICU, were not included in the study either, as the effectiveness of RDV and DXM was supposed to be tested on patients that only required low-flow oxygen therapy with Covid-19 PNA (Gressens et al., 2022).

Clinical and laboratory results from the patients were collected from the patients' electronic health record (EHR) by trained physicians (Gressens et al., 2022). When RDV was prematurely discontinued, the patient's EHR was analyzed to identify the reason for

discontinuation to determine if the cause was due to intolerance, adverse reaction, or discharge (Gressens et al., 2022). In-hospital mortality and other outcome measures of interest were measured from the day of oxygen therapy initiation (Gressens et al., 2022). Baseline characteristics were compared between the two groups based on Wilcox rank sum tests or Fisher tests (Gressens et al., 2022). To avoid the likelihood of indication bias because of potential differences between the two treatment groups, a propensity matching analysis was conducted to assess the two outcomes (Gressens et al., 2022).

The estimation of effect the treatment had on patients was based on the matched cohort of 180 patients and measured using the Cox model (Gressens et al., 2022). Overall, the study did not observe any serious adverse events related to the use of the duo therapy of combining DXM and RDV as a single treatment method (Gressens et al., 2022). Importantly, the combination of these two medications did not cause a reduction in the length of hospital stay, as the study had initially hypothesized (Gressens et al., 2022). Of note, secondary outcomes did show a non-statistically significant reduction of the rate of in-hospital deaths seen in the RDV and DXM group (Gressens et al., 2022). Conclusively, the study showed that in mild and more severe cases of patients hospitalized and diagnosed with Covid PNA, requiring oxygen therapy, the combination of RDV and DXM did not produce a reduction in the length of admission, the rate of in-hospital deaths, nor transfer to the ICU (Gressens et al., 2022).

The sample of the patients was diverse, with many patients having greater than one comorbidity (Gressens et al., 2022). Also, they were all requiring low-oxygen therapy and had baseline treatment of DXM therapy on board. As a result, this prevents the threat of homogenous samples (Gray, 2021). The initial selection of patients was much larger than the selected sample size, which does place the study at risk for differential subject attrition (Gray, 2021). In fact, this

is mentioned in the study, stating that other research studies that have been conducted to study the effectiveness of RDV have been with much larger cohort groups (Gressens et al., 2022). This small sample size also places the study at risk for low statistical power (Gray, 2021). There were no patients in the research study that were excluded due to refusal to participate, which prevents the threat of high refusal (Gray, 2021). The Fisher test is parametric; however, the Wilcox test is non-parametric. Seeing as a parametric test was used to determine the effectiveness of RDV in combination with DXM, this prevents the threat of violated assumptions of statistical tests (Gray, 2021).

Table seven provides information about a research study that shows RDV was effective in preventing the need for mechanical interventional.

Table 7

Article 7: Positive treatment effect of RDV therapy.

Early administration of Remdesivir to Covid-19 patients is associated with higher recovery rate and lower need for ICU admission: a retrospective cohort study.	
Purpose/Problem	To determine the effects of the timing of administration of RDV initiation on clinical outcomes of Covid-19 patients (Hussian Alsayed et al., 2021).
Sample	Consisted of a total of 323 patients, separated into three different experimental groups. 107 received no RDV therapy, 107 received RDV earlier within seven days within the onset of symptoms, and 109 received RDV more than a week after symptom onset (Hussian Alsayed et al., 2021).
Concepts	That the earlier RDV is given within Covid-19 diagnosis, the better the clinical outcomes for the patient.
Design	This was a retrospective cohort study (Hussian Alsayed et al., 2021). Interventional.
Instruments	Fisher exact tests and/or Chi-square tests were used for categorical, and Mann-Whitney U or t-test for continuous variables (Hussian Alsayed et al., 2021).
Results	RDV treatment resulted in improved clinical status and better outcomes in patients diagnosed with Covid-19 PNA (Hussian Alsayed et al., 2021). Positive response to RDV in Covid-19 treatment.

Implications for Advanced Practice Nursing	If administering RDV early in treatment can help prevent the progression of mild to more severe cases of Covid-19, it should be utilized to prevent the need for prolonged hospitalization, MV, or ICU transfer.
Comments	This research study has a few limitations that were concerning. The study's validity was not a concern.

The title of the article clearly states the purpose and concept behind this research study; it also describes the type of research process that was used. Even though the use of RDV has been known and further studied since the beginning of the pandemic, the specific timing, and benefits of such had yet to be researched. This article's purpose was to study the importance of early RDV initiation on clinical outcomes in Covid-19 patients (Hussian Alsayed et al., 2021). Important to note that the allocation of patients to either group was not influenced by patients, physicians, or researchers (Hussian Alsayed et al., 2021). This research study was performed as a retrospective cohort study to examine patients that were diagnosed with Covid-19 and treated with either RDV or standard of care treatment; the primary outcomes of the study was the patients' recovery rate, which was defined as "clinical improvement and patient's discharge by day 14 of symptom onset" (Hussian Alsayed et al., 2021). Secondary outcomes of the study were considered as the need for ICU admission, MV, and/or death within twenty-eight days of the first onset of patient's symptoms of Covid-19 (Hussian Alsayed et al., 2021).

Since RDV has been authorized for the treatment of Covid-19 in infected patients, there have been many randomized trials conducted on the use of RDV in such patients. RDV has since been reported by many different research articles to reduce the time between beginning of illness and recovery in patients who received the first dose of RDV within ten days of symptomatic onset; RDV was also associated with benefits, such as decreased mortality rates, when given early in treatment those identified with mild/moderate disease, but who require low-flow oxygen (Hussian Alsayed et al., 2021). In this study, adults with confirmed Covid-19 infection via

positive PCR and were hospitalized between September 2020 and January 2021 were chosen to be placed in this research study (Hussian Alsayed et al., 2021). There were three categories included in this research group: patients who received no RDV due to elevated live enzymes or decreased kidney functioning, early RDV cohort where patients received RDV within one week (seven days) of symptom onset, and the late treatment cohort where patients got their RDV therapy at eight days or more after the initial symptom onset occurred (Hussian Alsayed et al., 2021).

For this study, RDV was administered via intravenous route with a loading dose on the first day, subsequently followed by a standard maintenance dose daily for up to an approximate average of six days, or until hospital discharge or passing of the patient occurred (Hussian Alsayed et al., 2021). To determine the effectiveness of such treatment, Fisher exact tests or Chi-square tests were used for categorial variables, and the Mann-Whitney or t-tests were used for continuous variables to compare baseline clinical characteristics between the two RDV cohorts (Hussian Alsayed et al., 2021). To adequately estimate the odds ratio for patients who recovered after fourteen days, a logistic regression analysis was used after being adjusted for several different patient characteristics that may have skewed the results (Hussian Alsayed et al., 2021).

For ICU admission, the requirement of MV, or death within twenty-eight days of symptom onset, a Cox proportional hazard model and Kaplan-Meir survival curves were then constructed to show cumulative survival over said period (Hussian Alsayed et al., 2021). All the tests that were performed were conducted as a two-tailed analysis with a P-value of less than 0.05 and therefore considered the gold standard of statistical significance (Hussian Alsayed et al., 2021).

Of the 323 patients enrolled in the study, 107 were placed in the group to receive no RDV, 107 placed to receive RDV early within the first seven days of symptom onset, and 109 patients placed to receive RDV later at eight days or more after following their symptom onset (Hussian Alsayed et al., 2021). Four weeks, or twenty-eights days, was the standard period to follow the patients throughout the study; throughout the study, there was no difference identified in related laboratory markers between all three patient categories (Hussian Alsayed et al., 2021). Also, there was no difference between the two RDV groups regarding disease severity status (Hussian Alsayed et al., 2021).

Supportive medications, such as tocilizumab, were used more in the no standard of care group as compared to the RDV groups (Hussian Alsayed et al., 2021). Surprisingly, the number of recovered patients on day fourteen after symptom onset were higher in the early RDV as compared to the other groups within the study (Hussian Alsayed et al., 2021). Additionally, the early RDV group was associated with lower ICU admission (15.9%), late RDV (22%) and no RDV (51.4%) groups (Hussian Alsayed et al., 2021). Overall, the findings suggest that early treatment with RDV had a greater impact on positive clinical outcomes as opposed to the other groups of patients with Covid-19 PNA; early RDV was also found to have prevented the progression to more severe respiratory disease (Hussian Alsayed et al., 2021).

It is important to note that this study had some limitations: this study was not a randomized controlled trial but the effect of possible unwanted variables that would skew the results (Hussian Alsayed et al., 2021). However, there could have been unobserved confounders that could only be prevented with a randomized controlled trial (Hussian Alsayed et al., 2021). Moreover, this study was only limited to a single hospital in the United Arab Emirates (UAE), which may have also limited the generalized of the results (Hussian Alsayed et al., 2021).

This study had a significant number of patients within each group to have prevented the possibility of low statistical power (Gray, 2021). The characteristics of the data were adequate enough to be able to use parametric tests, preventing the possibility of violated assumptions of statistical tests (Gray, 2021). There were multiple analyses that were permed within this test, which could have led to a threat to its' validity (Gray, 2021). Reliable instruments were used to obtain data, preventing the threat of unreliable measures (Gray, 2021). The study had strict protocols for the initiation and use of RDV, which prevented the threat of unreliable implementation of the treatment (Gray, 2021). Overall, the study did not have multiple threats and shows high validity.

Article eight resulted in evidence that showed high efficacy of RDV treatment in the elderly population of patients. Table eight will provide additional information with an analysis following.

Table 8

Article 8: High efficacy of RDV in elderly patients

Early 3-day course of Remdesivir for the prevention of the progression to severe Covid-19 in the elderly: A single-centre, real-life cohort study.	
Purpose/Problem	To determine the effectiveness of RDV in the treatment of Covid-19 and the prevention of progression of mild/moderate to severe disease (Georgakopoulou et al., 2023).
Sample	143 patients in total that were non-hospitalized, diagnosed with Covid-19 and greater than or equal to 65 years of age who attended the emergency department of Laiko General Hospital and symptoms appearing within the prior 7 days (Georgakopoulou et al., 2023).
Concepts	Elderly patients are known to be at higher risk of severe disease with Covid-19, especially when they have comorbidities (Georgakopoulou et al., 2023). No research study has specifically studied the effect of RDV in different age groups (Georgakopoulou et al., 2023).
Design	This study was a single-centre prospective cohort (Georgakopoulou et al., 2023). Interventional.

Instruments	The Kolmogorov-Smirnov test and Cox proportional hazards univariate regression analysis were used in this research study (Georgakopoulou et al., 2023).
Results	High efficacy and positive results from treatment with RDV in Covid-19 patients.
Implications for Advanced Practice Nursing	The elderly are one of the highest at-risk patient groups regarding Covid-19. If the prophylactic administration of RDV when first diagnosed with Covid-19 can help prevent mortality, the prescribing of this medication would be extremely beneficial.
Comments	The study has limitations that were concerning. The study's validity was found to be concerning.

Although the article's title did have a good representation of what the research study article was about, it did not give the impression that it was an observational research study. Since RDV was approved for the treatment of Covid-19, it has been found, in most cases, to lead to an increase in positive clinical outcomes in patients with moderate to severe Covid-19 (Georgakopoulou et al., 2023). This research study was labeled as a prospective real-life cohort study that involved 143 elderly non-hospitalized patients that were diagnosed with Covid-19 and had attended the emergency department of Laiko General between the period of January and October of 2022 (Georgakopoulou et al., 2023). Eligible patients were those 65 years of age, or older, who had mild to moderate Covid-19 infection (Georgakopoulou et al., 2023).

The different sets of information that were recorded during this study include the following: age and sex of the patient, Covid-19 vaccination status, time since onset of symptoms, PCR and antigen test results, laboratory parameters, details of RDV treatment and the clinical outcomes of the patient throughout the 28 days of the study post RDV (Georgakopoulou et al., 2023). The participants were administered a loading dose of RDV intravenously on the first day and maintenance doses for two additional days afterwards (Georgakopoulou et al., 2023). The primary endpoint was the progression to severe Covid-19 and the subsequent need for

hospitalization; secondary outcome was any possible cause of mortality during the study period (Georgakopoulou et al., 2023).

Continuous variables were reported as the median with minimum-maximum ranges, categorical variables were displayed as absolute numbers and percentages in the statistical analysis that was performed (Georgakopoulou et al., 2023). The Kolmogorov-Smirnov test was used for determined the normality of the data and to identify predictors of events statistically significant factors were examined using Cox proportional hazards univariate regression analysis (Georgakopoulou et al., 2023). A two-sided P-value less than 0.05 was considered to indicate a statistically significant difference (Georgakopoulou et al., 2023). In total, 143 patients received RDV, and no notable side-effects were observed from the prophylactic administration of the medication administration (Georgakopoulou et al., 2023). In total, 6 patients were admitted to the hospital due to the progression of severe disease following the completion of RDV, and 5 of these patients succumbed to the disease process within the study period (Georgakopoulou et al., 2023).

The results obtained from this study were notable, considering that during the predominance of the omicron variant, the majority of sever cases and in-hospital deaths occurred among patients that were greater than 65 years of age (Georgakopoulou et al., 2023). No disease progression or mortality was observed among the elderly solid organ transplant recipients, suggesting that immunosuppressive drugs used in solid organ transplantation may also have a beneficial anti-inflammatory role in treating and preventing progression of Covid-19 (Georgakopoulou et al., 2023). Just as all studies do, this study has limitations: the largest being the lack of a control group, which prevents a baseline for the data to be compared against (Georgakopoulou et al., 2023). Additionally, this was only a single-centre study, which causes

there to be no information from additional locations to be compared to (Georgakopoulou et al., 2023). Lastly, during the follow-up period, only a few events occurred that did not permit the performance of multivariable analysis in order to determine how different independent variables affected and were associated with poor outcomes (Georgakopoulou et al., 2023).

This research study focused primarily on the elderly as a high-risk population in contracting severe Covid-19 and was also conducted in only a single hospital location. As a result, this places the study at risk for the threat of homogenous sample as it was not as inclusive as it possibly could have been (Gray, 2021). Another threat that having the study in only one location leads to is the threat of interaction of setting and sample (Gray, 2021). Multiple research analyses and tests were used in this study, which prevent the threat of mono-operational bias and monomethod bias from occurring (Gray, 2021). Overall, the research study does have promising data that suggests that it is helpful in determining the efficacy of RDV in the treatment of Covid-19, however its' validity does cause concern.

The ninth article shows that there was little to no clinical improvement that occurred from the administration of RDV in patients diagnosed with severe Covid-19. Table 9 will provide additional information regarding this article, with a critical review following afterwards.

Table 9

Article 9: Little to no clinical improvement from RDV

Clinical course and disease outcome in patients with severe Covid-19 receiving Remdesivir	
Purpose/Problem	The research study was conducted to examine the effect RDV had when given to patients hospitalized with Covid-19 (Raeisi et al., 2022).
Sample	103 patients that met the inclusion criteria and that were hospitalized for severe symptoms of Covid-19 were placed into either a control or RDV group (Raeisi et al., 2022).
Concepts	RDV has been one of the first line treatments chosen for the treatment of Covid-19, however there are still studies ongoing

	on the efficacy in treating and preventing the progression of Covid-19 (Raeisi et al., 2022).
Design	Non-randomized clinical trial study, interventional.
Instruments	Chi-square tests, independent t-test and repeated measures analysis of variance were performed with a p value lass than 0.l05 being considered as statistically significant (Raeisi et al., 2022).
Results	No statistically significant difference was found between the control and RDV group regarding the rate of mortality and discharge (Raeisi et al., 2022). No clinical improvement, no positive correlation between RDV treatment and Covid-19.
Implications for Advanced Practice Nursing	Since there was found to have not statistically or clinical difference between the two groups, it could do more harm than good to prescribe the RDV therapy in patients, especially those that are at higher risk due to comorbid conditions.
Comments	The study itself never mentioned any limitations, however some were still identified. No concerns about validity.

The title of this article clearly identifies the concept of the research; however, it doesn't mention the type of research that was performed. Within this article, the different levels of infection are clearly classified as mild, moderate, severe, and vital; mild group includes patients that have mild upper respiratory tract infection symptoms such as dry cough, mild fever, core throat, headache, myalgia but without dyspnea and possible radiological identifiable manifestations (Raeisi et al., 2022). The moderate group of patients would present with symptoms such as dyspnea, persistent cough, tachycardia with positive radiological manifestations of infection (Raeisi et al., 2022). The severe group would exhibit dyspnea with a respiratory rate greater than 30 breaths per minute with possible blood oxygen levels less than 90 percent and needing supplemental oxygen (Raeisi et al., 2022). Lastly, the vital group will have conditions such as respiratory failure, septic shock, or the beginning of organ failure and will need MV (Raeisi et al., 2022). The purpose of this study was to determine if RDV would work to prevent patients from advancing from a less severe class of Covid-19 to a higher level of infection (Raeisi et al., 2022).

This research was performed out of south-west Iran, in a hospital located in Shahrekord (Raeisi et al., 2022). Inclusion criteria for patients in this research study were hospitalized patients aged 18 years or older with a positive Covid-19 test; the patients also needed to have supportive oxygen/ventilation or have positive pulmonary infiltration that was detected by radiological studies (Raeisi et al., 2022). Patients were excluded if their live enzymes were five times higher than normal or had a glomerular filtration rate less than 30 mL/min (Raeisi et al., 2022). The study included 103 patients, where 52 were placed in the control group and 51 in the RDV group (Raeisi et al., 2022). The study sampling/placement was nonequivalence and non-randomized (Raeisi et al., 2022). The mean age for the RDV group was statistically significantly higher than that of the control group; with an average age difference of greater than 10 years older in the experimental group as opposed to the control group (Raeisi et al., 2022).

The patients within the RDV group received a loading dose intravenously on day one, and then subsequent maintenance doses intravenously on days two through five (Raeisi et al., 2022). Throughout the study, the patients were assessed on days 1, 5, 10 and 14 for any clinical improvement or deterioration; on these days the patients' blood would be analyzed for levels of liver enzymes, platelet aggregation, kidney function and inflammatory markers to assess for organ possible organ damage/failure (Raeisi et al., 2022). After these initial examinations, the patients would be followed throughout the rest of the study, which lasted 3 months in total.

The first endpoint was the discharge of the patient, either related to clinical improvement and no longer needing additional treatment, or through death of the patient (Raeisi et al., 2022). The secondary endpoint was any adverse event for patients throughout the duration of the study; patients that were hospitalized up to day 14 of longer were all under observation, with important

outcomes including ICU admission, mortality, and the interval between onset of symptoms and recovery (Raeisi et al., 2022).

The highest rate of fever was recorded on the first day and the least one was observed on the tenth day of the study within both study groups (Raeisi et al., 2022). The highest prevalence of cough/dyspnea was recorded on the first day within both study groups, and the least was seen in days 10 for control and 14 for RDV group (Raeisi et al., 2022). The patients' white blood cell count (WBC) increased up until day 14 for the RDV group, whereas it only increased until day 10 for the control group (Raeisi et al., 2022). Even so, there was no statistically significant difference between the two values found between the two groups in the previous areas (Raeisi et al., 2022).

It has been well known that patients that had comorbid conditions, such as hypertension and diabetes, are at higher risk of having severe Covid-19. However, there was no significant difference seen in this research study between the control group and the RDV group regarding the mortality and discharge rates for patients with comorbid conditions (Raeisi et al., 2022). There was not statistically significant difference in the duration of hospitalization, nor the rate of ICU admission between the two groups of patients, even those with comorbidities (Raeisi et al., 2022). Overall, patients with severe Covid-19 were examined in both the control and experimental groups, however there was no significant difference seen between those received RDV and those received standard of care treatment (Raeisi et al., 2022).

In terms of validity, the study used several different units of measurement, which prevents the possibility of mono-operational and monomethod bias from occurring (Gray, 2021). Another concern was regarding the age differences in the two groups, where those in the RDV group were statistically significantly higher than those in the control group; this puts the research

at risk for homogeneous sample, interaction of selection and treatment, and interaction of setting and sample (Gray, 2021). The study was also with a small number of participants, which creates the possibility for low statistical power (Gray, 2021). The t-test (a parametric test) was used in this research study, which prevents the risk for violated assumptions of statistical tests (Gray, 2021). The treatment methods for both the control group and the experimental group were clearly identified and did not change throughout the study, which prevented the possibility of unreliable implementation of the treatment (Gray, 2021). Lastly, the groups were not randomized in their selection of participants, which places the study at risk for random heterogeneity of participants (Gray, 2021). Overall, even though the research study did have useful information, it is concerning that it has so many threats to validity.

The last article showed that there was no clinical evidence of increased survival rates in patients that received RDV therapy. Table 10 will provide additional information regarding this article, with an analysis following afterwards.

Table 10

Article 10: No evidence of increased survival

Efficacy of Remdesivir-containing therapy in hospitalized Covid-19 patients: A prospective clinical experience	
Purpose/Problem	To obtain real-world data on the efficacy of RDV in the treatment of hospitalized patients with Covid-19 (Russo et al., 2021).
Sample	A total of 407 Covid-19 positive patients were selected through their EHR to be placed in this research study. 113 received standard of care treatment and 294 patients received RDV therapy (Russo et al., 2021).
Concepts	RDV became one of the first line treatment, alongside steroids such as DXM, for the treatment of Covid-19. However, the true efficacy of this treatment has yet to be studied in the real-world treatment of Covid-19.
Design	This was a non-interventional observational prospective study (Russo et al., 2021).

Instruments	Propensity score density plot and a Love plot were generated to examine the balance of scores and distributions between the two groups (Russo et al., 2021). Also, Welch's t test was used assuming unequal variances to evaluate continuous independent variables, and Pearson's Chi-square of Fisher's exact test was used for categorical variables (Russo et al., 2021). Kaplan-Meier curve was used to compare 30-day survival of patients in both study groups (Russo et al., 2021). Multivariate Cox regression was used to analyze need for additional therapy methods in both study groups (Russo et al., 2021).
Results	There was no difference found in the rate of mortality between the two groups either (Russo et al., 2021). No evidence of increased rates of survival, no positive correlation between RDV and Covid-19 treatment.
Implications for Advanced Practice Nursing	If there is no clinical indication that RDV is improving the care of the patients, then there is no clinical indication to prescribe this medication to the patients diagnosed with Covid-19.
Comments	The study had some major limitations and the validity of the research is concerning.

The title of the article clearly identified the purpose and type of research that was performed to determine the efficacy of RDV in the treatment of Covid-19 patients. This research was a non-interventional prospective observational study that was performed on patients admitted to University Hospital of Rome between October 2020 through February 2021 and diagnosed with positive Covid-19 (Russo et al., 2021). However, patients that required HFNC/NIV or MV at the time of initial admission were excluded from this analysis (Russo et al., 2021). Data for this research study was extracted from the patients' EHR and they were followed until either discharge or death; those that were discharged were followed for an additional 30 days to assess clinical outcomes (Russo et al., 2021).

The primary endpoint of this study was the impact of RDV-containing therapy on 30-day mortality in hospitalized patients with Covid-19 PNA (Russo et al., 2021). The secondary endpoint was the impact of RDV-containing therapy on the need for HFNC/NIV or MV on patients diagnosed with positive Covid-19 PNA (Russo et al., 2021). To reduce the impact of

treatment selection bias in the estimation of treatment effects; propensity score matching was conducted, and variables were selected for inclusion in the propensity score based on the potential impact on receiving RDV and the association with mortality (Russo et al., 2021). A propensity score density plot and a Love plot were generated to examine the balance of propensity scores and the covariate distribution between the two clinical groups (Russo et al., 2021). To evaluate the demographic factors, Welch's t-test was used for continuous variables and the Pearson's Chi-square or Fisher's exact test was used for categorical variables (Russo et al., 2021). Multivariate analysis was used to identify independent predictors of 30-day mortality and the need for NIV or MV (Russo et al., 2021). Matched bivariate analysis was conducted using a conditional logistic regression model and survival was analyzed by Kaplan-Meier curves (Russo et al., 2021). All tests that were performed were two-tailed, and a p-value less than 0.05 was considered as statistically significant (Russo et al., 2021).

In the study, a total of 407 patients were monitored, with 113 being in the control group and 294 in the experimental group received RDV (Russo et al., 2021). Overall, a total of 61 patients were treated during their hospital stay with HFNC/NIV or MV (Russo et al., 2021). There were no statistically significant differences found between the two groups in terms of their 30-day survival rate (Russo et al., 2021). Also, the study showed that neither group had a decreased incidence of the need for HFNC/NIV or MV, however it was identified that those placed on MV had increased rates or mortality (Russo et al., 2021). The study ended up determining that the use of RDV in hospitalized patients with Covid-19 was not associated with a significant increase in survival rates or a reduced need for HFNC/NIV or MV (Russo et al., 2021).

This study had several limitations: since this study was done only in one location, the results might be affected by local practice in the management of Covid-19 (Russo et al., 2021). Secondly, critically ill elderly patients with fatal disease were excluded from receiving NIV/MV and only a total of 61 patients in the study received HFNC/NIV or MV (Russo et al., 2021). Thirdly, the analysis found within this study should be taken cautiously, as it did not include randomized groups and could have been affected by confounding factors (Russo et al., 2021). Lastly, this study had a small sample size, with a much larger portion receiving RDV therapy, which could have skewed the results (Russo et al., 2021). However, it is important to note that the comparison of patients treated with RDV as opposed to standard of care was based on a robust statistical methodology that was appropriate for a non-randomized observational cohort study (Russo et al., 2021).

In terms of validity, there are some concerns that need to be mentioned. The sample size is quite small, with a major proportional difference between the control group and the experimental group. Specifically, 72% of the research sample group was part of the experimental group, and only 28% consisted of the control group (Russo et al., 2021). This places the study at risk for inappropriate sample and homogenous sample (Gray, 2021). When looking closer at the experimental group, it is also concerning that 80% of those patients were male, which also places the study at risk for homogenous sample (Gray, 2021). Because of the small sample size, the study is at risk for low statistical power (Gray, 2021). Even though these concerns for the validity are present, the research did have compelling data regarding the effects of RDV treatment for Covid-19 patients (Russo et al., 2021).

Implications on Nursing Practice

After reviewing all the articles that were selected for the critical literature review and after analyzing all articles, six were found to show a positive response to RDV therapy. Of the four that were found to have no clinical improvement related to RDV therapy, one of those articles were found to have concerns regarding their validity. As a result, it can be determined after reviewing all the literature, that RDV is, in fact, beneficial in the treatment of patients diagnosed with Covid-19 (Russo et al., 2021). Currently, clinical guidelines state that RDV should be given to patients diagnosed with Covid-19 that are either immunocompromised, at high risk for severe disease, and that are not yet requiring supplemental oxygen (National Institute of Health [NIH], 2023).

At the beginning of the pandemic, there became a great need for an increased number of healthcare workers in the field as the number of patients diagnosed with severe Covid-19 disease increased. In response to the pandemic creating a need for more practitioners and healthcare workers in general, APRNs were given more flexibility and practice authority (Stucky et al., 2020). This concept goes hand in hand with how RDV therapy and its implications on treating patients with Covid-19 affects the APRN field. When given greater prescriptive and practice authority, the APRN can provide care to the patient that is both evidence-based, but also providing the most well-rounded care that is seen in nursing.

RDV shines a light into the dark that has become healthcare since the beginning of the Covid pandemic. With its offering of reducing the severity and longevity of the disease for many patients, this can also decrease the burden placed on the healthcare system. Overall, it can be seen through the evidence-based research studies reviewed that RDV is found to be beneficial and safe for the patient diagnosed with Covid-19. With the ability to write this prescription for

patients admitted to the hospital with Covid-19, the APRN can help to reduce the length of stay, the severity, and reduce the possibility of worsening outcomes for the patient.

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