

Effectiveness of Early Remdesivir Initiation in Patients With Immunocompromising Conditions Hospitalized With COVID-19 by Variant Era, Severity of Immunosuppression, and Age

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Conclusions

- Using methods that reduce bias due to time-varying confounding, informative censoring, and immortal person-time, this study found that the risk of in-hospital mortality was lower for patients with immunocompromising conditions who received early remdesivir compared with those who received no remdesivir regardless of age, SARS-CoV-2 variant era, and severity of immunosuppression
- This study highlights the importance of timely remdesivir administration to improve survival outcomes in people with immunocompromising conditions who are hospitalized with COVID-19

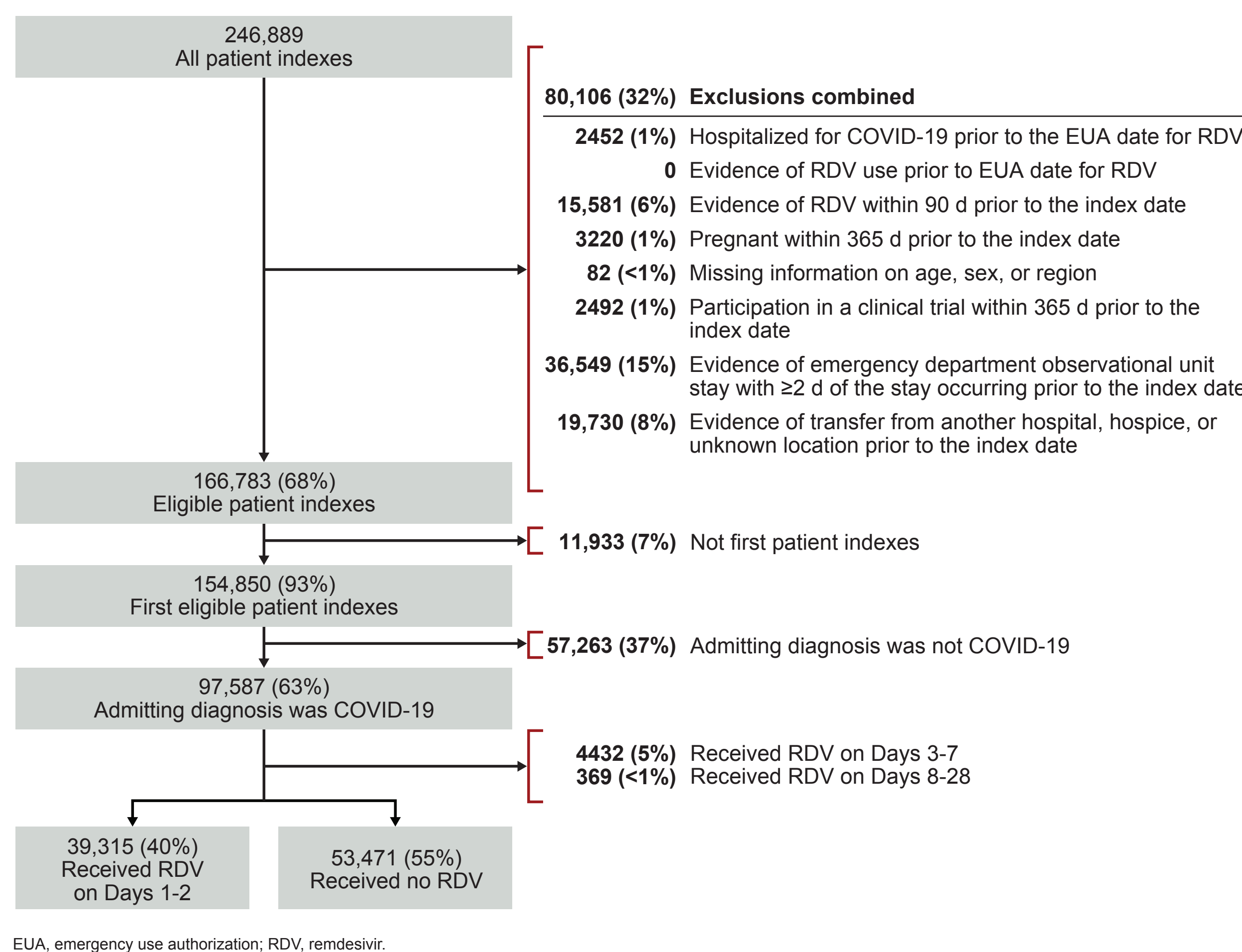
Plain Language Summary

- People with immunocompromising conditions are more likely to develop severe COVID-19, and early treatment with remdesivir has been shown to reduce the risk of dying
- This study consistently found that early initiation of remdesivir after being hospitalized with COVID-19 was associated with a lower risk of dying across subgroups determined by age, SARS-CoV-2 variant era, and level of immunosuppression
- These findings confirm the importance of early remdesivir treatment for improving survival in people with immunocompromising conditions who are hospitalized with COVID-19

Results

- Overall, 97,587 patients were eligible for the study (**Figure 1**)
 - 4801 patients initiated RDV between Days 3 and 28 of their hospitalization; these patients were allowed to contribute person-time to the study, but the sample size was too small for inclusion in the current analysis
 - 39,315 patients initiated RDV during the first 2 days of their hospitalization, and 53,471 patients did not receive RDV during their hospitalization

Figure 1. Patient Attrition



- Demographic and clinical characteristics at admission for each subgroup are shown in **Tables 1** through **3**
 - The most common immunosuppressive conditions across subgroups were solid malignancy and rheumatologic and inflammatory conditions
 - Across all subgroups, greater proportions of patients in the early RDV group were on oxygen support and were on dexamethasone compared with the no RDV group at baseline

Table 1. Demographic and Clinical Characteristics at Admission by Age

	Age Category			
	12-64 y	≥65 y	Early RDV (n = 17,266)	No RDV (n = 36,205)
Age, y, median (Q1, Q3)	56 (49, 61)	55 (47, 60)	77 (71, 93)	78 (72, 93)
Sex, female, n (%)	7169 (54)	9369 (54)	12,585 (48)	18,368 (51)
Comorbidities, n (%)				
Blood disorder	88 (1)	140 (1)	77 (<1)	101 (<1)
Cancer (excluding nonmelanoma skin cancer)	2989 (23)	3836 (22)	10,499 (40)	14,365 (40)
Chronic kidney disease	2083 (16)	4034 (23)	7512 (29)	13,356 (37)
Chronic liver disease	1835 (14)	2622 (15)	1864 (7)	2692 (7)
Chronic lung disease	5914 (45)	7868 (46)	12,683 (49)	17,131 (47)
Diabetes (type 1 or 2)	5142 (39)	7385 (43)	11,090 (43)	16,554 (46)
Cardiovascular disease	8836 (67)	12,121 (70)	21,590 (83)	31,084 (86)
Alzheimer disease/dementia	134 (1)	354 (2)	2959 (11)	5692 (16)
Obesity	5666 (43)	7081 (41)	7410 (28)	9737 (27)
Stroke or cerebrovascular disease	1456 (11)	2553 (15)	5495 (21)	9134 (25)
Substance use disorder	2732 (21)	4753 (28)	3509 (13)	5082 (14)
Tobacco use	3868 (29)	5939 (34)	9451 (36)	13,217 (37)
Disability	5085 (38)	7521 (44)	12,645 (48)	19,414 (54)
Mood disorder or schizophrenia	3549 (27)	5321 (31)	5882 (23)	8995 (25)
Tuberculosis infection	17 (<1)	30 (<1)	26 (<1)	55 (<1)
Baseline oxygen support, n (%)				
No oxygen	9317 (70)	13,128 (76)	18,086 (69)	27,389 (76)
Low-flow oxygen	1920 (14)	1922 (11)	4403 (17)	4585 (13)
High-flow oxygen	1324 (10)	1408 (8)	2649 (10)	3030 (8)
Mechanical ventilation or ECMO	666 (5)	808 (5)	950 (4)	1201 (3)
Immunosuppressive condition, n (%)				
HIV/AIDS	443 (3)	655 (4)	167 (1)	197 (1)
Hematologic malignancy	516 (4)	609 (4)	1597 (6)	1887 (5)
Other immune condition	1689 (13)	2549 (15)	2241 (9)	3438 (9)
Solid malignancy	6881 (52)	8315 (48)	17,625 (68)	23,946 (66)
Organ transplant	1188 (9)	1648 (10)	1025 (4)	1271 (4)
Rheumatologic/inflammatory condition	6102 (46)	8709 (50)	10,602 (41)	15,661 (43)
Baseline medication, n (%)				
Oral antiviral (eg, nirmatrelvir/ritonavir, molnupiravir)	0	6 (<1)	2 (<1)	27 (<1)
Glucocorticoid (eg, dexamethasone)	8425 (63)	5898 (34)	15,894 (61)	12,170 (34)

ECMO, extracorporeal membrane oxygenation; Q1, first quartile; Q3, third quartile; RDV, remdesivir.

Table 2. Demographic and Clinical Characteristics at Admission by Variant Era

	Variant Era					
	Pre-Delta		Delta		Omicron	
	Early RDV (n = 16,248)	No RDV (n = 24,288)	Early RDV (n = 7701)	No RDV (n = 6573)	Early RDV (n = 16,368)	No RDV (n = 22,610)
Age, y, median (Q1, Q3)	71 (60, 79)	71 (60, 80)	67 (56, 77)	68 (57, 78)	74 (64, 82)	74 (63, 82)
Sex, female, n (%)	7870 (48)	12,537 (52)	4082 (53)	3442 (52)	7802 (51)	11,758 (52)
Comorbidities, n (%)						
Blood disorder	54 (<1)	107 (<1)	21 (<1)	23 (<1)	90 (1)	111 (<1)
Cancer (excluding nonmelanoma skin cancer)	5204 (32)	8027 (33)	2375 (31)	2054 (31)	5909 (38)	8120 (36)
Chronic kidney disease	3856 (24)	8057 (33)	1438 (19)	1842 (28)	4301 (28)	7491 (33)
Chronic liver disease	1503 (9)	2378 (10)	703 (9)	687 (10)	1493 (10)	2249 (10)
Chronic lung disease	7211 (44)	10,990 (45)	3158 (41)	2881 (44)	8228 (54)	11,128 (49)
Diabetes (type 1 or 2)	6913 (43)	11,275 (46)	2853 (37)	2730 (42)	6466 (42)	9934 (44)
Cardiovascular disease	12,399 (76)	19,609 (81)	5483 (71)	5000 (76)	12,544 (82)	18,596 (82)
Alzheimer disease/dementia	1114 (7)	2860 (12)	387 (5)	496 (8)	1592 (10)	2690 (12)
Obesity	5742 (35)	8059 (33)	2651 (34)	2186 (33)	4683 (30)	6573 (29)
Stroke or cerebrovascular disease	2607 (16)	5096 (21)	1084 (14)	1228 (19)	3260 (21)	5363 (24)
Substance use disorder	1971 (12)	3831 (16)	1210 (16)	1299 (20)	3060 (20)	4705 (21)
Tobacco use	4735 (29)	7950 (33)	2366 (31)	2347 (36)	6218 (40)	8859 (39)
Disability	6472 (40)	11,679 (48)	2911 (38)	2891 (44)	8347 (54)	12,365 (55)
Mood disorder or schizophrenia	3595 (22)	6373 (26)	1691 (22)	1686 (26)	4145 (27)	6257 (28)
Tuberculosis infection	12 (<1)	41 (<1)	10 (<1)	7 (<1)	21 (<1)	37 (<1)
Baseline oxygen support, n (%)						
No oxygen	10,944 (67)	18,006 (74)	5336 (69)	4850 (74)	11,123 (72)	17,661 (78)
Low-flow oxygen	2907 (18)	3303 (14)	1154 (15)	749 (11)	2262 (15)	2455 (11)
High-flow oxygen	1596 (10)	1999 (8)	817 (11)	656 (10)	1560 (10)	1783 (8)
Mechanical ventilation or ECMO	799 (5)	980 (4)	394 (5)	318 (5)	423 (3)	711 (3)
Immunosuppressive condition, n (%)						
HIV/AIDS	258 (2)	416 (2)	107 (1)	111 (2)	245 (2)	325 (1)
Hematologic malignancy	694 (4)	992 (4)	388 (5)	300 (5)	1031 (7)	1214 (5)
Other immune condition	1518 (9)	2759 (11)	718 (9)	719 (11)	1694 (11)	2509 (11)
Solid malignancy	10,118 (62)	14,448 (59)	4660 (61)	3896 (59)	9728 (63)	13,917 (62)
Organ transplant	631 (4)	1158 (5)	361 (5)	376 (6)	1221 (8)	1385 (6)
Rheumatologic/inflammatory condition	6966 (43)	11,141 (46)	3256 (42)	3018 (46)	6482 (42)	10,211 (45)
Baseline medication, n (%)						
Oral antiviral (eg, nirmatrelvir/ritonavir, molnupiravir)	0	0	0	0	2 (<1)	33 (<1)
Glucocorticoid (eg, dexamethasone)	10,984 (68)	8658 (36)	5417 (70)	2934 (45)	7918 (52)	6476 (29)

ECMO, extracorporeal membrane oxygenation; Q1, first quartile; Q3, third quartile; RDV, remdesivir.

ECMO, extracorporeal membrane oxygenation; Q1, first quartile; Q3, third quartile; RDV, remdesivir.

Table 3. Demographic and Clinical Characteristics at Admission by Severity of Immunosuppression

	Severity of Immunosuppression			
	Mild		Moderate/Severe	
	Early RDV (n = 32,344)	No RDV (n = 44,650)	Early RDV (n = 6971)	No RDV (n = 8821)
Age, y, median (Q1, Q3)	71 (61, 80)	73 (62, 82)	67 (58, 76)	68 (57, 77)
Sex, female, n (%)	16,205 (50)	23,135 (52)	3549 (51)	4602 (52)
Comorbidities, n (%)				
Blood disorder	131 (<1)	189 (<1)	34 (<1)	52 (1)
Cancer (excluding nonmelanoma skin cancer)	10,121 (31)	14,110 (32)	3367 (48)	4091 (46)
Chronic kidney disease	7486 (23)	14,054 (31)	2109 (30)	3336 (38)
Chronic liver disease	2753 (9)	4066 (9)	946 (14)	1248 (14)
Chronic lung disease	14,324 (44)	19,807 (44)	4273 (61)	5192 (59)
Diabetes (type 1 or 2)	13,189 (41)	19,924 (45)	3043 (44)	4015 (46)
Cardiovascular disease	24,694 (76)	35,752 (80)	5732 (82)	7453 (84)
Alzheimer disease/dementia	2708 (8)	5368 (12)	385 (6)	678 (8)
Obesity	10,515 (33)	13,541 (30)	2561 (37)	3277 (37)
Stroke or cerebrovascular disease	5626 (17)	9758 (22)	1325 (19)	1929 (22)
Substance use disorder	4515 (14)	7508 (17)	1726 (25)	2327 (26)
Tobacco use	10,011 (31)	15,004 (34)	3308 (47)	4152 (47)
Disability	13,819 (43)	21,606 (48)	3911 (56)	5329 (60)
Mood disorder or schizophrenia	7294 (23)	11,498 (26)	2137 (31)	2818 (32)
Tuberculosis infection	29 (<1)	62 (<1)	14 (<1)	23 (<1)
Baseline oxygen support, n (%)				
No oxygen	22,812 (71)	34,210 (77)	4591 (66)	6307 (71)
Low-flow oxygen	5040 (16)	5201 (12)	1283 (18)	1306 (15)
High-flow oxygen	3195 (10)	3638 (8)	778 (11)	800 (9)
Mechanical ventilation or ECMO	1297 (4)	1601 (4)	319 (5)	408 (5)
Immunosuppressive condition, n (%)				
HIV/AIDS	246 (1)	339 (1)	364 (5)	513 (6)
Hematologic malignancy	1122 (3)	1406 (3)	991 (14)	1100 (12)
Other immune condition	2564 (8)	4124 (9)	1366 (20)	1863 (21)
Solid malignancy	20,000 (62)	26,736 (60)	4506 (65)	5525 (63)
Organ transplant	1122 (3)	1623 (4)	1091 (16)	1296 (15)
Rheumatologic/inflammatory condition	14,134 (44)	20,742 (46)	2570 (37)	3628 (41)
Baseline medication, n (%)				
Oral antiviral (eg, nirmatrelvir/ritonavir, molnupiravir)	1 (<1)	29 (<1)	1 (<1)	4 (<1)
Glucocorticoid (eg, dexamethasone)	20,462 (63)	15,082 (34)	3857 (55)	2986 (34)

ECMO, extracorporeal membrane oxygenation; Q1, first quartile; Q3, third quartile; RDV, remdesivir.

- The cumulative incidence of in-hospital mortality by subgroup at Days 14 and 28 is shown in **Table 4**

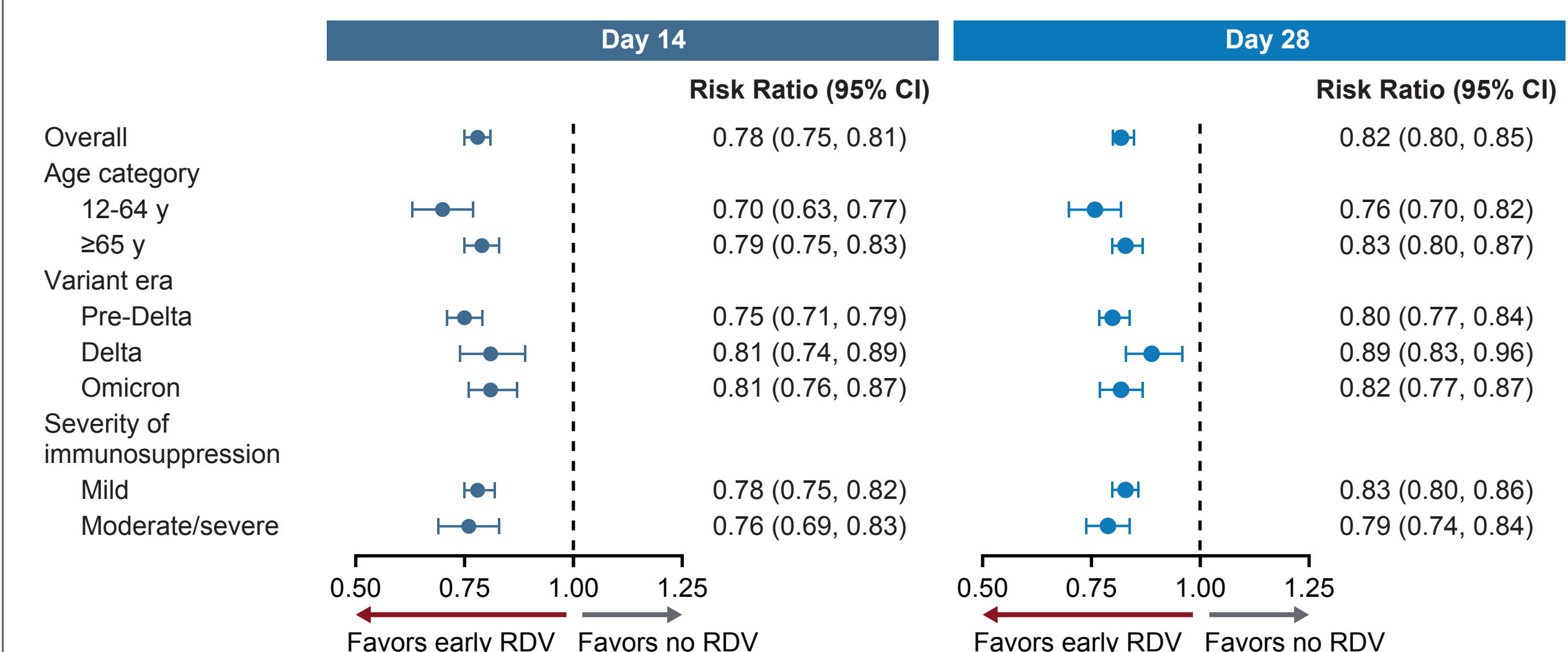
Table 4. Cumulative Incidence of In-Hospital Mortality by Age, Variant Era, and Severity of Immunosuppression

Cumulative Incidence, %	Day 14		Day 28	
	Early RDV	No RDV	Early RDV	No RDV
Overall	9.22	11.84	13.66	16.56
Age category				
12-64 y	3.89	5.58	7.13	9.41
≥65 y	11.78	14.96	16.79	20.11
Variant era				
Pre-Delta	10.07	13.50	15.23	18.98
Delta	11.13	13.70	17.87	20.01
Omicron	7.62	9.38	10.37	12.68
Severity of immunosuppression				
Mild	9.06	11.60	13.44	16.21
Moderate/severe	9.96	13.13	14.60	18.52

RDV, remdesivir.

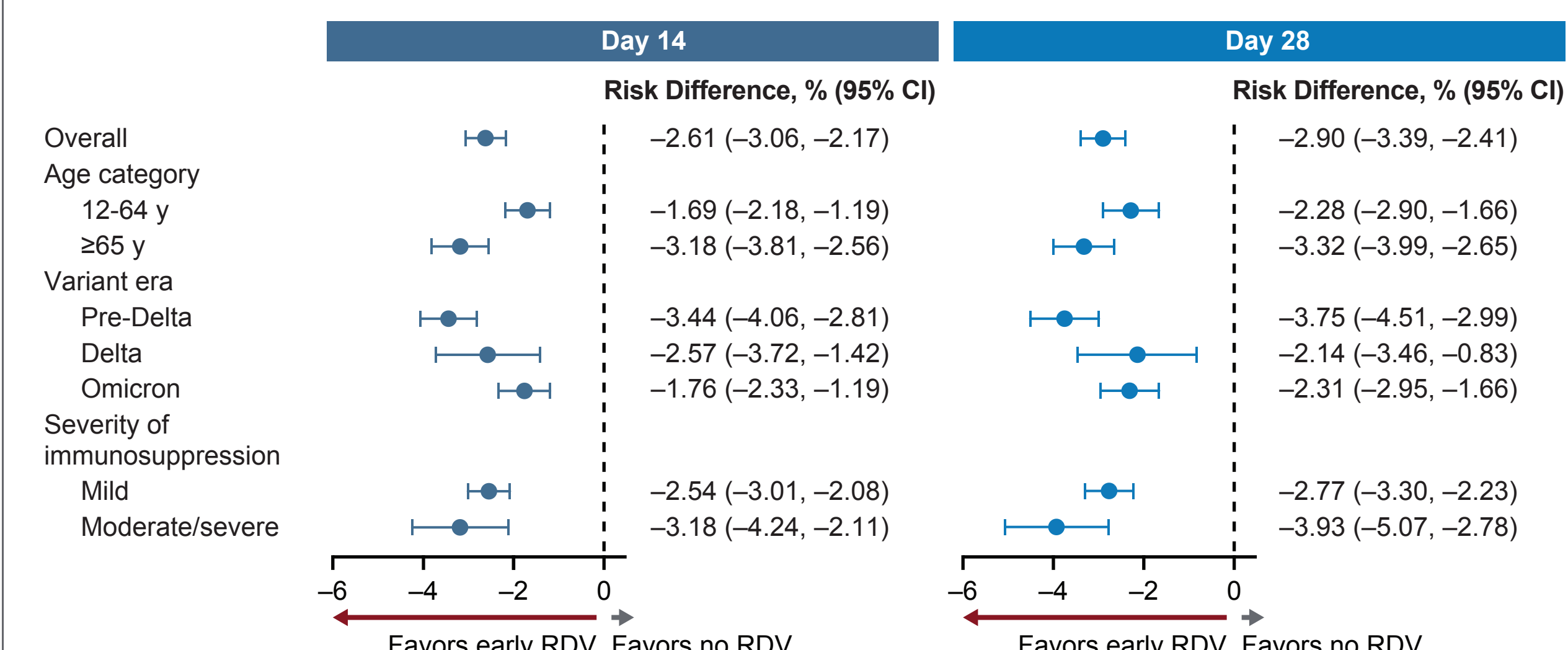
- Overall, initiation of RDV during the first 2 days of hospitalization was associated with a 22% decreased risk of in-hospital mortality at Day 14 and an 18% decreased risk at Day 28 compared with no initiation of RDV (**Figure 2**)
 - Similarly, in-hospital mortality risk was lower with early RDV treatment when the population was stratified by age, variant era, and severity of immunosuppression

Figure 2. Risk Ratios of In-Hospital Mortality for Early RDV Treatment Compared With No RDV Treatment by Age, Variant Era, and Severity of Immunosuppression



- In the overall population, initiation of RDV during the first 2 days of hospitalization was associated with 2.61% and 2.90% absolute reductions in the risk of in-hospital mortality at Days 14 and 28, respectively, compared with no initiation of RDV (**Figure 3**)
 - The risk difference ranged from −1.69% to −3.93% across all subgroups at Days 14 and 28

Figure 3. Risk Differences of In-Hospital Mortality for Early RDV Treatment Compared With No RDV Treatment by Age, Variant Era, and Severity of Immunosuppression



- At Days 14 and 28, the risk ratio of in-hospital mortality for early RDV treatment versus no RDV treatment was stronger for patients aged 12 to 64 years compared with those aged ≥65 years (**Figure 2**)
 - The risk difference was greater for patients aged ≥65 years compared with those aged 12 to 64 years at Day 14 (**Figure 3**); the effect of early RDV treatment on in-hospital mortality compared with no RDV treatment was significantly stronger in patients aged ≥65 years at Day 28 based on the test of homogeneity ($P = 0.021$ on the risk difference scale)
- The risk ratio of in-hospital mortality for early RDV treatment versus no RDV treatment was similar across variant eras (**Figure 2**)