

Cost-effectiveness of Nirmatrelvir/Ritonavir in high-risk Swedish adults including post-acute COVID syndrome (PACS) from a societal perspective

Martina Aldvén¹, Marcelina Kadziela¹, Christian Gerdesköld Rappe², Arash Rahimi², Fredrik O.L. Nilsson²

Affiliations: 1 Quantify Research, Stockholm, Sweden, 2 Pfizer Sverige, Stockholm, Sweden

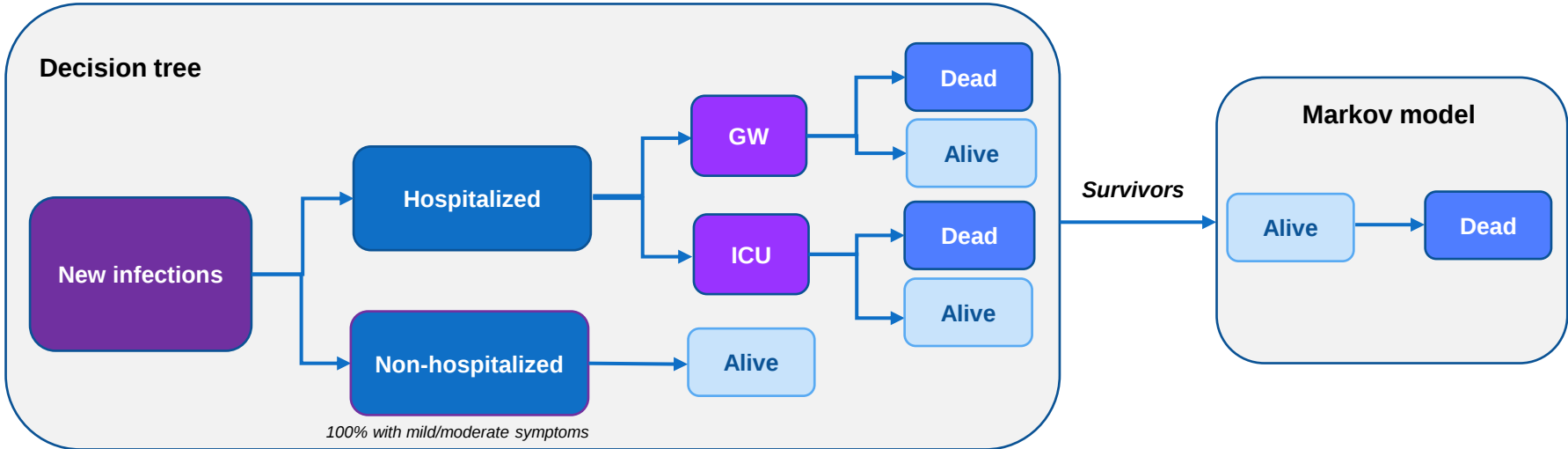
OBJECTIVE

Not only may SARS-CoV-2 infection result in immediate respiratory symptoms, but it can also lead to post-acute COVID-19 syndrome (PACS), lasting several months after recovery. Nirmatrelvir/ritonavir (NV/r) is an antiviral agent recommended for adults at increased risk of progression to severe COVID-19, regardless of vaccination status. Both the pivotal EPIC-HR [1] and real-world evidence (RWE) [i.a. 2,3,4] have shown that NV/r is efficacious in improving patient health outcomes. This study explores the potential cost-effectiveness of NV/r compared to no anti-viral treatment from a societal perspective in Sweden, utilizing recently published RWE (based on data from a omicron-variant dominated period) for mortality and relative risk reductions.

METHODS

A closed-cohort, static cost-effectiveness model was developed using a decision tree for the first year, and a Markov model for the life-time horizon. The model accounted for symptom days, hospitalizations, intensive care unit (ICU) and general ward (GW) admissions, quality of life (QoL), mortality, treatment- and PACS costs (health care and productivity losses). Overview of the model is shown in **Figure 1** and general inputs and treatment effectiveness parameters used in the base case in **Table 1**.

Figure 1. Model overview.



The cost-effectiveness was assessed for 60-year-old patients by varying the underlying risk of hospitalization (1-5%), effectiveness of NV/r in relative reduction of hospitalization and death (53.6%-89.6%) and average healthcare cost per PACS case (SEK 0 / 25000 / 50000). The underlying risk of hospitalization was varied to reflect outcomes of patients at different risk levels in the real-world clinical setting. The healthcare costs incurred due to PACS were varied substantially due to the uncertainty of actual healthcare costs.

Relative reduction of hospitalization and death were sourced from two NV/r real-world studies [2,3]. Variation in effectiveness of NV/r in different RWE studies may be due to differences in time since symptom onset to treatment initiation. Studies that do not account for this tend to have lower effectiveness estimates. The effectiveness estimates are highest (89.6%) in patients tested within 5 days of symptom onset and who started treatment on the test day [2], which is in line with clinical practice. Despite the evolution of COVID-19 variants NV/r has shown, both in RWE and in-vitro studies, to retain its effectiveness [20].

Quality-adjusted life years (QALYs) and costs were accumulated over the patients' life expectancy and the incremental cost-effectiveness ratio (ICER) was calculated. Several scenario analyses were performed to test the robustness of the results.

Table 1. Model inputs.

BASE CASE INPUTS	
Mean baseline age (at COVID-19 infection)	60 years
Annual discount rate (costs & health benefits) [5]	3%
Survival general population [6]	Sweden (2022)
Medication cost per case – Paxlovid [7]	SEK 9,915
Cost per day at GW [8]	SEK 7,144
Cost per day at ICU [9]	SEK 66,793
Baseline utility at age 60 [10]	0.8072
Disutility, per day – Non-Hospitalized [11]	-0.290
Disutility, per day – Hospitalized [11]	-0.640
Disutility, total QALY loss – PACS [11]	-0.340
Proportion ICU [12]	2.80%
Proportion inpatient mortality [12]	8.6%
Proportion PACS in non-hospitalized [13]	5.7%
Proportion PACS in hospitalized [14]	17.5%
Symptom days in non-hospitalized [15]	6.87
Length of stay at GW (days) [16]	6
Length of stay at ICU (days) [17]	6
Average societal cost per PACS case [18]	SEK 25,705
TREATMENT EFFECTIVENESS	
Reduction in symptom days non-hospitalized [19]	24%
Reduction of length of stay, hospitalization [3]	30%
Reduction in proportion requiring ICU [3]	65%
REDUCTION IN NUMBER OF HOSPITALIZATIONS AND DEATHS	
Low – treatment within 30 days of positive test [2]	53.6% (6.6-77.0)
Low-intermediate [3]	63.0% (43.0-77.0)
Medium – treatment within 5 days since the onset of symptoms [2]	79.6% (33.9-93.8)
High – treatment initiated same day as test within 5 days of symptom onset [2]	89.6% (50.2-97.8)

RESULTS

The ICERs ranged from SEK 18,552 to SEK 651,798 depending on underlying hospitalization risk, treatment effectiveness estimates and health care PACS cost (**Table 2**). Changing the relative effectiveness of NV/r from high (89.6%) to low (53.6%) increased the ICER by around SEK 45,000 (* in Table 2) in the highest hospitalization risk (5%) and around SEK 150,000 (** in Table 2) in the lowest hospitalization risk (1%) for the three different levels of average PACS costs.

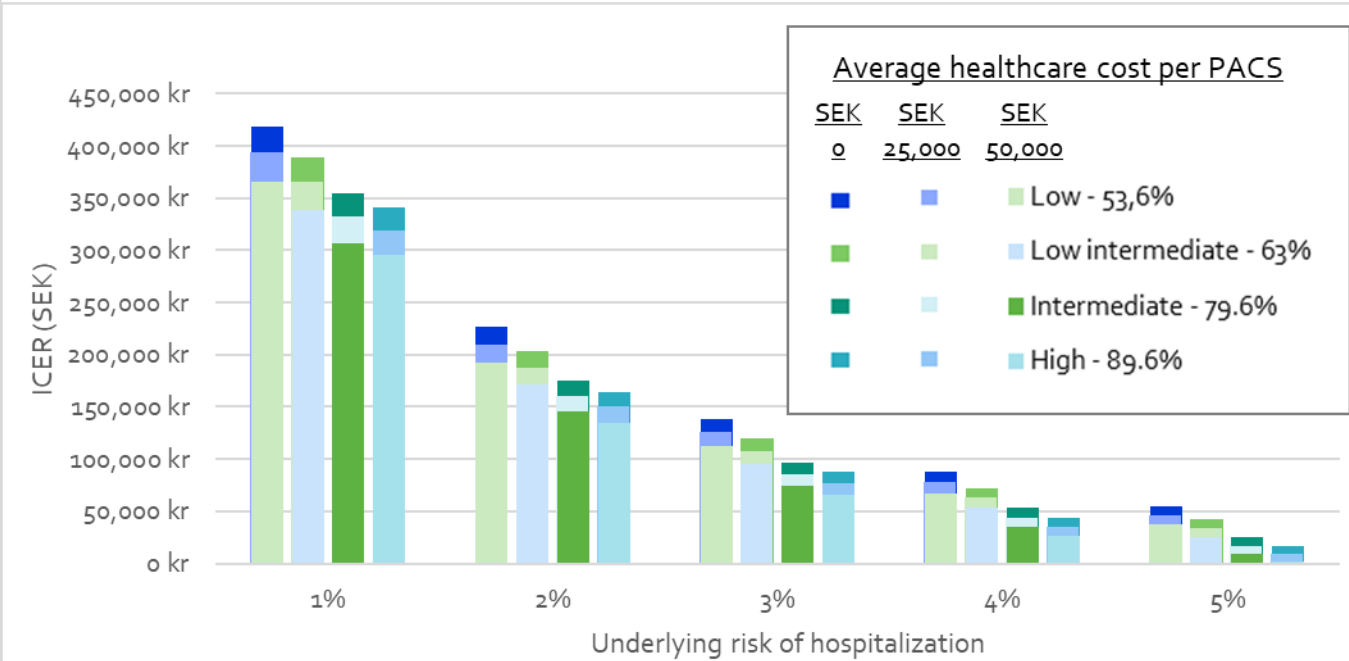
Four scenarios explored the potential impact of NV/r relative risk reduction on PACS. The first scenario analysis, where NV/r reduces the risk of PACS by 26% [13], decreased the cost per QALY substantially with the ICER ranging up to SEK 418,886 (**Figure 2**). A second scenario analysis, excluding societal costs, resulted in ICERs ranging from SEK 98,752 to SEK 614,127. A third scenario, testing the outer limits of the confidence interval of the relative risk reduction on PACS [13], resulted in ICERs ranging from SEK 2,758 to 437,657 when a 23% reduction was applied and from a dominant ICER to SEK 407,142 when a 28% reduction was applied.

The fourth scenario tested the proportion of PACS cases at 12 months (hospitalized 11.1% and non-hospitalized 0.7%) [13] and resulted in ICER ranging from SEK 4,129 to 423,330 and SEK 13,186 to 602,425, respectively.

Table 2. Base-case analysis, no NV/r relative risk reduction on PACS.

PACS cost	Effectiveness	Underlying risk of hospitalization				
		1%	2%	3%	4%	5%
0 SEK	Low - 53,6%	651,798**	301,343	174,071	108,275	68,079*
	Low intermediate - 63%	589,415	265,701	148,997	88,843	52,151
	Intermediate - 79.6%	521,476	225,589	119,714	65,305	32,172
	High - 89.6%	498,120**	210,505	107,820	55,097	23,007*
25000 SEK	Low - 53,6%	650,280**	299,726	172,417	106,603	66,394*
	Low intermediate - 63%	587,777	263,965	147,226	87,053	50,351
	Intermediate - 79.6%	519,597	223,609	117,698	63,270	30,126
	High - 89.6%	496,070**	208,347	105,624	52,881	20,779*
50000 SEK	Low - 53,6%	648,762**	298,108	170,763	104,930	64,710*
	Low intermediate - 63%	586,139	262,229	145,454	85,263	48,550
	Intermediate - 79.6%	517,719	221,629	115,681	61,234	28,079
	High - 89.6%	494,020**	206,190	103,428	50,666	18,552*

Figure 2. Scenario analysis 1, NV/r relative risk reduction on PACS included.



CONCLUSION

Given the prevailing willingness-to-pay (WTP) thresholds in Sweden for moderate health conditions, this study, utilizing recently published RWE, suggests that NV/r compared to no anti-viral treatment is cost-effective in high-risk Swedish adults. The results were robust in sensitivity analyses. Only in patient groups with a very low (~1%) underlying risk of hospitalization *and* either assuming no NV/r impact on PACS, no PACS societal costs or a very low proportion of PACS in non-hospitalized patients, NV/r may not be cost-effective. In all other scenarios tested, the ICERs were below the WTP thresholds.

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DISCLOSURES

This study was funded by Pfizer AB. M Aldvén and M Kadziela are employed by Quantify Research, which has been contracted by Pfizer to conduct this study. C Gerdesköld, A Rahimi and F Nilsson are employed by Pfizer AB.