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Background

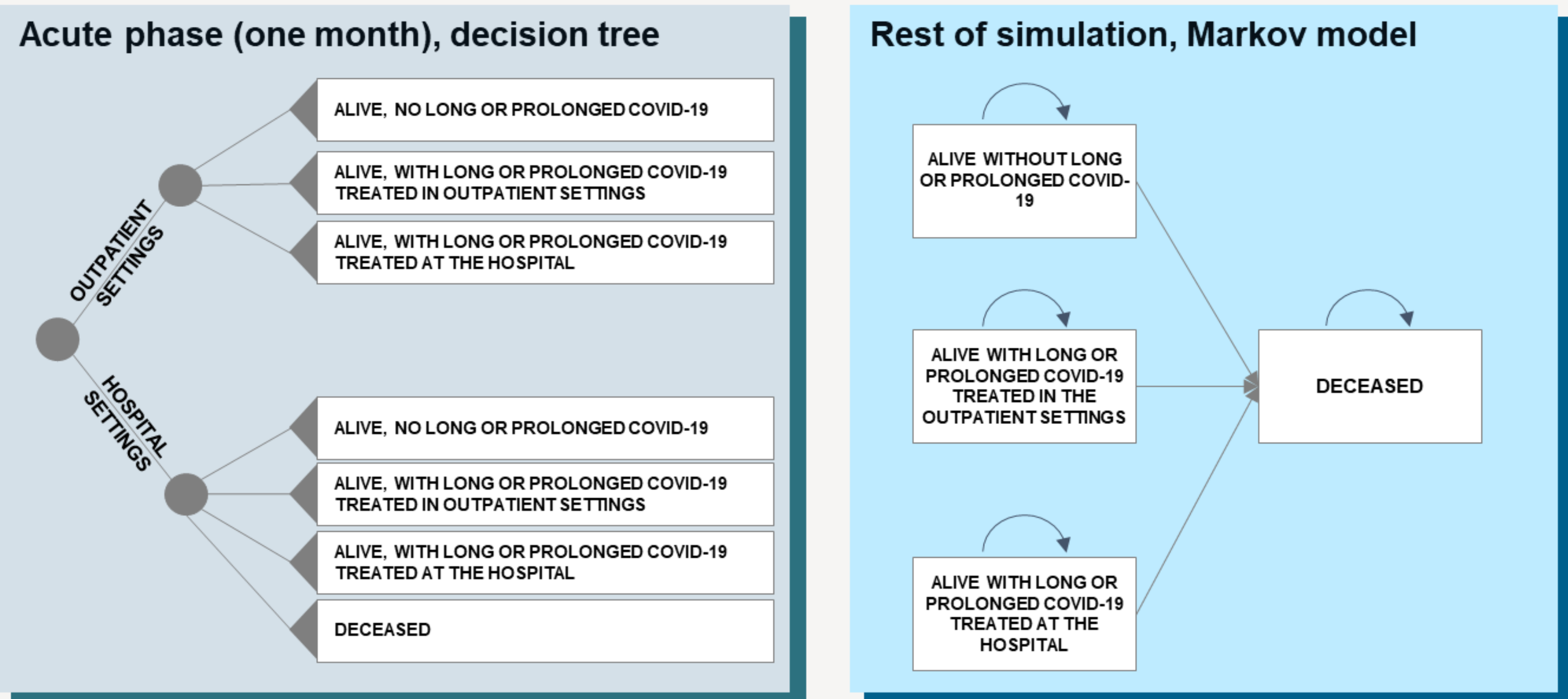
- The health situation caused by COVID-19 is very dynamic, both globally and in France. The arrival of new variants leads to changes in the positioning of treatments and vaccines offer an increased protection against severe forms. In this context, it appears useful, even necessary, to estimate the health and economic burden of COVID-19, to support future choices of resource allocation and to possibly allow comparison with other diseases.
- The aim of this study is to provide initial answers by presenting the results of a simple but flexible simulation model to assess the public health impact of COVID-19 in French patients initially treated in the outpatient settings and having at least one risk factor for severe disease. The population of interest is represented by the population of the Ronapreve® (casirivimab & imdevimab) temporary authorisation for use (ATU) cohort<sup>1</sup>. Various scenarios analyses were explored to assess the impact on the results of the assumptions made.

Model structure and input data

Model structure

- Data from the literature suggest that the age of patients can affect the risk of hospitalisation and the risk of death during hospitalisation<sup>2,3</sup>, and that it is the main factor in the development of a severe form. Therefore, the model is stratified by age, considering the following subgroups: under 50 years, 51-60 years, 61-80 years, and over 80 years.
- Patients enter the model with a COVID-19 infection treated in the outpatient settings with at least one risk factor for developing a severe form.
- To ensure an appropriate simulation of the patient pathway, the model is made out of two parts (Figure 1). The first part reflects the acute phase of COVID-19 (one month), with a decision tree in which patients are either still treated in the outpatient settings or hospitalised. The second part simulates the life of patients over 2 years, using a Markov chain in which patients can be "alive without long or prolonged COVID-19", "alive with long or prolonged COVID-19 treated in outpatient settings", "alive with long or prolonged COVID-19 treated at the hospital", or "deceased".

Figure 1. Model structure



Input data

- The input data come from the following sources: ATU cohort of Ronapreve® (casirivimab & imdevimab), National French hospitalized claims database (PMSI) and Experts opinion

Table 1. Summary of the input data

	Value for each age group				Source
	<50 years	51-60 years	61-80 years	>80 years	
Baseline characteristics					
Age group (%)	25.78	17.09	35.46	21.67	ATU
Male (%)	44.00	50.30	55.70	47.10	ATU
Mean age at the start of the simulation (years)	36.70	55.10	70.20	86.90	ATU
Clinical input during the acute phase (decision tree)					
Hospitalisation probability (%)	11.23	15.15	26.63	49.20	ATU
Type of hospitalisation (%)					PMSI
Standard or no oxygen	84.34	81.98	84.01	97.16	
Non-invasive ventilation	2.88	3.13	2.72	1.13	
Mechanical ventilation	12.78	14.90	13.27	1.71	
Mortality (%)					PMSI
Standard or no oxygen	1.28	2.59	11.79	29.71	
Non-invasive ventilation	2.40	3.46	22.30	64.40	
Mechanical ventilation	11.49	19.09	42.62	69.03	
Clinical input during the long term phase (Markov model) – per cycle					
Distribution of patients after a severe COVID-19 treated in outpatient settings (%)					Experts Experts Calcul
No long or prolonged COVID-19	70.00	65.00	60.00	50.00	
Long or prolonged COVID-19 treated in the outpatient settings	25.00	25.00	30.00	30.00	
Long or prolonged COVID-19 treated at the hospital	5.00	10.00	10.00	20.00	
Distribution of patients after a severe COVID-19 treated at the hospital (%)					Experts Calcul PMSI
No long or prolonged COVID-19	60.00	50.00	40.00	35.00	
Long or prolonged COVID-19 treated in the outpatient settings	22.81	28.37	35.71	47.87	
Long or prolonged COVID-19 treated at the hospital	17.19	21.63	24.29	17.13	
Costs					
Hospitalisation during the acute phase (mean, €)					PMSI
Standard or no oxygen	4 948	5 036	5 118	4 932	
Non-invasive ventilation	9 808	10 995	10 763	8 181	
Mechanical ventilation	14 245	14 848	15 571	12 373	
Long or prolonged COVID-19 treated at the hospital (mean, €)	18 609	21 247	21 386	7 317	PMSI
Long or prolonged COVID-19 treated in the outpatient settings (mean, €)		902.81			Experts + estimations

References

1 - Autorisation temporaire d'utilisation de cohorte. Résumé du rapport de synthèse périodique n°5 <https://ansm.sante.fr/uploads/2022/01/21/20220121-atuc-ronapreve-resume-rapport-n05.pdf>  
2 - Docherty AB et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ. 2020;369:m1985. doi: 10.1136/bmj.m1985.  
3 - Madjid M et al. Potential Effects of Coronaviruses on the Cardiovascular System: A Review. JAMA Cardiol. 2020; 5(7): 831-840. doi: 10.1001/jamacardio.2020.1286.

Results

Base case

- Estimated number of hospitalisations: 256 for 1000 patients in acute phase and 382 for 1000 patients in total.
- Estimated number of deaths in acute phase: 37 for 1000 patients.
- Estimated number of long or prolonged COVID-19: 407 for 1000 patients.
- The total estimated cost per patient is 4 280€: 1 578€ in acute phase and 2 702€ during the long or prolonged COVID-19.

Scenario « Age »

- This scenario highlights the impact of the age of patients on the outcomes.
- Estimated number of hospitalisations in acute phase: 112 for 1000 patients among the youngest (<50 years) and 492 for 1000 patients among the oldest (>80 years).
- Estimated number of deaths in acute phase: <10 for 1000 patients among the youngest (<50 years) and >150 for 1000 patients among the oldest (>80 years).

Scenario « Omicron »

- This scenario is based on the assumption that the probability of hospitalisation and its associated mortality rate during the acute phase is reduced by 50% compared to the base case. It leads to a decrease of more than 75% of the estimated number of deaths in acute phase. The impact on the number of long or prolonged COVID-19 is even more significant with a decrease of more than 90%.

Scenario « Not-vaccinated »

- This scenario is based on the assumption that the probability of hospitalisation and its associated mortality rate during the acute phase is increased by 50% compared to the base case. It leads to an increase of more than 120% of the estimated number of deaths in acute phase. However, the impact on the number of long or prolonged COVID-19 is limited because of the decrease of the number of patients alive at the end of the acute phase.

Scenario « Treatments »

- This scenario explores the impact of treatments for mild to moderate COVID-19 in outpatient settings with at least one risk factor for severe disease. A risk ratio (RR) was applied to account for hospitalisations reductions as well as long or prolonged COVID-19 occurrence reductions.
- Estimated total number of hospitalisations: 37 for 1000 patients for the highly effective treatment (RR=0.1) and 187 for 1000 patients for the moderately effective treatment (RR=0.5).
- The total estimated cost per patient is 811€ for the highly effective treatment and 2 475€ for the moderately effective one.

Table 2. Summary of the results

	Base case	Scenario « Age »				Scenario « Omicron »	Scenario « Not-vaccinated »	Scénario « Treatments »		
		<50	51-60	61-80	>80			RR=0.1	RR=0.3	RR=0.5
Life duration – Acute phase (maximum duration of the acute phase is 365,25/12 ≈ 30,4 days)										
Life duration	29.7d	30.4d	30.3d	29.6d	27.6d	30.3d	28.9d	30.4d	30.2d	30.0d
Life duration lost due to COVID-19	0.7d	0.1d	0.1d	0.8d	2.9d	0.2d	1.6d	0.1d	0.2d	0.4d
Life duration - Total										
Life duration	1y 11m 19.1d	2y 0m 18.8d	2y 0m 12.4d	1y 11m 10.3d	1y 7m 14.5d	2y 0m 9.0d	1y 10m 15.7d	2y 0m 13.1d	2y 0m 7.6d	2y 0m 2.2d
Life duration lost due to COVID-19	27.1d	2.2d	5.7d	1m 1d	3m 12.4d	6.8d	2m	2.7d	8.1d	13.6d
Number of hospitalisations for 1000 patients*										
Acute phase	256	112	151	266	492	128	384	26	77	128
Total	382	175	267	394	652	140	512	37	111	187
Number of deaths at the hospital in acute phase for 1000 patients										
Total	37	3	8	43	151	9	83	4	11	18
Number of long or prolonged COVID-19 for 1000 patients										
Requiring a hospitalisation	126	63	116	128	160	12	128	11	34	59
Total	407	310	369	427	475	32	402	39	118	199
Costs per patient (€)										
Acute phase	1 578	705	1 013	1 773	2 507	789	2 368	568	884	1 199
Long or prolonged COVID-19	2 702	2 014	3 313	2 879	1 292	248	2 737	243	747	1 275
Total	4 280	2 718	4 326	4 652	3 799	1 038	5 105	811	1 631	2 475

d: day(s); m: month(s); y: year(s) | \*One patient can have 2 hospitalisations (one in acute phase and one in the long term phase)

Conclusion

- The assessment of the public health impact of COVID-19 in patients with at least one risk factor for severe disease is important to help health policy makers regarding the decisions related to prevention programmes, especially in the context of this pandemic, where health care resources are limited.
- This study shows that the health and economic burden is considerable for the elderly and/or unvaccinated and extends beyond the acute phase of the disease due to the effects and consequences of the long or prolonged COVID-19.
- Strategies aiming to decrease this burden in France are required: the introduction of early treatment in mild and moderate outpatient cases of COVID-19 is one of them.