Article title: Inpatient Care Costs of COVID-19 in South Africa's Public Healthcare System
Journal name: International Journal of Health Policy and Management (IJHPM)
Authors' information: Ijeoma Edoka[1]*, Heather Fraser[1], Lise Jamieson[2], Gesine Meyer-Rath[2,3], Winfrida Mdewa[1]

[1]SAMRC Centre for Health Economics and Decision Science-PRICELESS SA, School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa.

[2]Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa.

[3]Department of Global Health, School of Public Health, Boston University, Boston, MA, USA.
(*Corresponding author: Ijeoma.Edoka@wits.ac.za)

Supplementary File 1

This material provides a detailed breakdown of the inputs used in estimating cost per patient per day for each resource item, for each level of care – general wards, high care wards (HCW) and intensive care units (ICU).

Diagnostics

Haematology, chest x-rays and biochemistry laboratory testing are assumed to be performed on each admission of a patient with severe or critical COVID-19 disease, and as clinically indicated to monitor for complications, such as acute respiratory distress syndrome, acute kidney injury, acute cardiac injury and septic shock. It was assumed that the SARS CoV-2 Polymerase Chain Reaction (PCR) test would be conducted in general and high care wards, prior to a patient's transfer to ICU, and thus this cost was excluded from ICU. Diagnostics included in this analysis (Table S1) and the frequency with which they are administered were identified from South African and WHO clinical management guidelines, as well as from published studies and expert consultations.[1–5] Unit costs for most diagnostics were obtained from previously published estimates in South Africa and from the South African National Health Laboratory Service (NHLS).[6,7] Unit costs from previous years were inflated to 2020 prices using the Consumer Price Index. [8]

In the probabilistic sensitivity analysis (PSA), average quantity of diagnostic test used per day was varied over a range determined by the frequency of each diagnostic test and the length of hospital stay. For example general and high care wards, the frequency of tests required were varied between daily and once every three days, where the base case required each test every two days. Details of all the ranges used in the PSA are provided in Table S1. To restrict the random draws from 0 to 1, a Beta distribution was fitted to average quantity per day in the PSA.

The length of stay was varied in the PSA, using a lognormal distribution, over a specified range reported by the South African COVID-19 Modelling Consortium. [9] The impact of the length of stay parameter on the final results was also assessed in a scenario analysis, where the lowest and highest value in the range was used as the input.

Therapeutics

Therapeutics for managing hospitalised COVID-19 were categorized into antibiotics/antimicrobials, corticosteroids, anticoagulants and nutritional support (Table S2.) Drugs and quantity requirements included in the analysis were obtained from published studies, clinical guidelines and expert consultations .[3,10–12] Unit prices were obtained from the National Department of Health Master Procurement Catalogue.[13,14] The proportion of patients requiring each therapy was obtained from a review of clinical studies on clinical outcomes of severe or critical COVID-19 patients.[10,15–18] Uncertainty in these proportions were assessed in the PSA, using the confidence intervals provided in the clinical studies (Table S2) to fit Beta distributions to these inputs.

Table S1. Inputs for Diagnostics Costs (2020 USD)

(1) Resource input	Hospital ward applicable	(2) Frequency	(3) Average quantity per day[a] (range)	(4) Unit cost	Cost per patient per day	Source
Chest X-ray	General ward	3 over duration of hospitalisation	0.6 (0.3 - 1)	15.05[b]	9.03	(1)[4] (2) [10,19] (3) [10,19] (4) [20]
	High Care and ICUU CPAP	Every two days	0.5 (0.33 - 1)		7.52	
	ICU NIV / IMV	Daily	1 (0.75 - 1)		15.05	
Full blood count	General wards, High care wards and ICU CPAP	Every two days	0.5 (0.33 -1)	3.85	1.93	(1) [4] (2) [10] (3) [10] (4) [7]
	ICU NIV / IMV	Daily	1 (0.75 - 1)		3.85	
Urea	General wards, High care wards and ICU CPAP	Every two days	0.5 (0.33 -1)	2.02	1.01	(1) [3] (2) [10] (3) [10] (4) [7]
	ICU NIV / IMV	Daily	1 (0.75 - 1)		2.02	
CRP	General wards, High care wards and ICU CPAP	Every two days	0.5 (0.33 -1)	4.7	2.49	(1) [2] (2) [10] (3) [10] (4) [7]
	ICU NIV / IMV	Daily	1 (0.75 - 1)		4.97	
ESR	General wards, High care wards and ICU CPAP	Every two days	0.5 (0.33 -1)	2.34	1.18	(1) [2] (2) [10] (3) [10]

	ICU NIV / IMV	Daily	1 (0.75 - 1)		2.36	(4) [7]
Blood gas analysis	General wards, High care wards and ICU CPAP	Every two days	0.5 (0.33 -1)	4.07	2.03	(1) [3] (2) [19] (3) [19] (4) [6]
	ICU NIV / IMV	Daily	1 (0.75 - 1)		4.07	
HIV	General ward	Once per admission	0.04	0.58	0.07	(1) [21] (2) Expert opinion (3) [9] (4) [6]
	High care ward, ICU CPAP / NIV		0.13 (0.08 -0.25)		0.08	
	ICU IMV		0.06 (0.03 – 0.1)		0.04	
TB Sputum microscopy, culture and susceptibility	General ward	Once per admission	0.13 (0.08 -0.25)	3.21	0.40	(1) [21] (2) Expert opinion (3) [9] (4) [6]
	High care ward, ICU CPAP / NIV		0.14 (0.08 – 0.33)		0.46	
	ICU IMV		0.06 (0.03 – 0.1)		0.20	
SARS CoV-2PCR	General wards	One required for duration of hospitalisation [1]	0.13 (0.08 -0.25)	24.04	3.00	(1) Expert opinion (2) [1] (3)[9] (4) [22]
	High care wards		0.14 (0.08 – 0.33)		3.44	

Note: For most inputs, a different source was used for each component of the input. Thus for each row, the number attached to the column header corresponds to each citation in the source column.

Abbreviations: CPR, C-Reactive Protein; PCR, Polymerase Chain Reaction; ICU: Intensive Care Unit; CPAP: Continuous Positive Airway Pressure; NIV: Non-Invasive Ventilation; IMV: Invasive Mechanical Ventilation

[a]Estimated using average length of stays: 8 (4 - 12) days for general ward; 7 (3 - 12.6) days for HCW and ICU without ventilation; 16 (9.9 – 30.5) days for ICU with invasive mechanical ventilation [9]

[b] The cost obtained from UPFS is specific to chest x-rays, we assume this covers the appropriate number of films required

Table S2. Inputs for Therapeutic Agent Costs (2020 USD)

(1) Resource input	(2) Therapy	(3) Proportion of patients receiving therapy (CI)	(4) Dose	(5) Quantity used per day	(6) Unit cost	Wards applicable	Cost per patient per day	Source
Antibiotics/ antimicrobials	Ceftriaxone	72% (56 – 88)	1g IV daily	1	0.37 per 1 g vial	All	1.02	(1) [18] (2) [12 23] (3) [15] (4) [12] (5) [12 23] (6) [13]
	Clarithromycin		500mg 12 hourly	4	0.26 per 250mg dose			
Corticosteroids	Dexamethasone	100%[a]	6mg per day	1.5	0.38 per 4mg vial	General wards [b]; HCW and ICU	0.57	(1) [18] (2) [18] (3)[35] (4) [12] (5)[17] (6) [13]
Anticoagulation	Enoxaparin	65% (56 – 75)	Regular: 40mg daily	1	2.54 for 40mg injection	All	4.32	(1) [18] (2) [24] (3) [25] (4)[24] (5)[25] (6)[13]
		35% (25 – 44)	High dose: 120mg daily	3				
Enteral nutrition	Standard bag with electrolytes	100%	Total Parenteral Nutrition: 1 bag daily	1.00	47.79 per bag [c]	ICU	47.79	(1)[26] (2) [25] (3) [24] (4) [24] (5) [13]

Note: For most inputs, a different source was used for each component of the input. Thus for each row, the number attached to the column header corresponds to each citation in the source column.

Abbreviations: CPAP: Continuous positive airway pressure ventilation; HCW: High care wards; ICU: Intensive care unit.

[a] Based on RECOVERY trial preliminary results, dexamethasone is recommended for all patients receiving respiratory support [18]

[b] Patients receiving supplemental oxygen only [18]

[c] Median price of 3 different options for Adult parenteral nutrition, in absence of estimate for enteral nutrition

Treatment of Complications

Complications resulting from COVID-19, and their incidence, were identified from published studies (Table S3). Complications considered in this analysis include acute cardiac injury, acute liver failure, septic shock and acute kidney injury (Table S3). We assumed that all patients with these complications would receive care in ICU, and thus these costs were only included in estimates of total ICU daily costs. We used the South African Standard Treatment Guidelines to identify treatment regimens and resources required for managing septic shock, acute liver failure and acute cardiac injury.[25] Unit costs for each resource were obtained from the South Africa Master Procurement Catalogue (2020).[13,14] Finally, costs for renal replacement therapy and for acute kidney injury were obtained from the South Africa Uniform Patient Fee Schedule (2019).[20] Treatment costs for acute respiratory distress syndrome are discussed in the following sub-section.

Proportions of patients being affected by each complication (incidence rates) were obtained from a review of clinical studies on outcomes in patients with COVID 19. [15,16,27] We assumed that 50% of septic shock cases would be resolved through providing fluids, while 50% of cases would require vasoconstrictive agents. Similarly, we assumed that 50% of patients with acute cardiac injury would require primary percutaneous coronary intervention (PCI), while 50% would be managed conservatively using medication (fibrinolysis, aspirin and morphine).

In the PSA, the incidence rates of each complication was varied using the confidence intervals presented in the clinical studies, with Beta distributions fitted to these inputs. Where confidence intervals were not available from the clinical study (as was the case with the incidence rate for pneumothorax only), the rate was varied by +/-50%.

Table S3. Inputs for Treatment of Complications Costs (2020 USD)

(1) Complication	(2) Incidence of complication [CI]	(3) Therapy	(4) Proportion requiring therapy	(5) Quantity used per day [25]	(6) Cost per dose	Cost per patient per day	Source
Septic shock	19.7% [4%-28%]	Fluids (sodium chloride 0.9%)	50%	500ml IV over 30 minutes	0.26	14.76 [a]	(1) [28] (2) [28] (3) [25] (4) Assumption (5) [25] (6) [13]
		Vasoconstrictive agents (epinephrine)	50%	576ml per day	149.93		
Acute kidney injury (end stage, requiring dialysis)	6.8% [1% – 17%]	Renal replacement therapy	100%	24 hours of therapy per day	126.57	8.61 [a]	(1) [29] (2) [29] (3) [25] (4) Assumption (5) Assumption (6) [20]
Acute liver failure	26.5% [9% – 41%]	Lactulose	100%	10–30 mL 8 hourly	5.25	0.17 [a]	(1)[30] (2) [30] (3) [25] (4) Assumption (5) [25] (6) [13]
Acute cardiac injury	20% [16% - 24%]	Primary percutaneous coronary intervention (PCI)	50%	Once-off intervention	4367.53	62.55 [b]	(1) [31] (2) [31] (3) [25] (4) Assumption (5) Assumption (6) [32]
						27.64 [c]	

		Fibrinolysis (streptokinase)	50%	1.5MU IV, once-off	2.94	6.84 [b]	(1) [31] (2) [31] (3) [25] (4) Assumption (5) [25] (6) [13]
		Aspirin		150mg - 300 mg	0.009		
		Morphine		10mg	0.20*	2.94 [c]	
Pneumothorax	0.66% [0.33% – 0.99%]	Intercostal drain	100%	One per admission	4.83	0.004 [b] / 0.002 [c]	(1) [33] (2) [33] (3) [25] (4) Assumption (5) Assumption (6) [34]

Note: For most inputs, a different source was used for each component of the input. Thus for each row, the number attached to the column header corresponds to each citation in the source column.

[a] All ICU patients

[b] ICU patients on CPAP or NIV

[c] ICU patients on invasive mechanical ventilation

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