

# The role of modelling in planning and budgeting for South Africa's COVID-19 response

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Given the potential impact that model projections may have on decision-making, uncertainty in projections must be communicated clearly to decision-makers through reasoned discussion on robust and more sensitive model findings.

The unprecedented health response to the South African COVID-19 epidemic saw expert virologists, clinicians, epidemiologists and modellers coming together to provide scientific insight and expertise in the management of the epidemic. One such group was the South African COVID-19 Modelling Consortium, established in late March 2020 to support government's planning and budgeting for COVID-19-related health care. Here we report on the approach taken to modelling cases, hospital admissions, deaths and costs in a situation of substantial uncertainty, the processes supported by the models, and the lessons learnt for future pandemics.

We developed two tools: the National COVID-19 Epi Model (NCEM) and the National COVID-19 Cost Model (NCCM). The NCEM is a stochastic compartmental transmission model developed to project incidence of COVID-19 across the provinces (and later, districts) of South Africa. The model follows a generalised Susceptible-Exposed-Infectious-Removed structure accounting for disease severity (asymptomatic, mild, severe and critical cases) and treatment pathways (out-patient and in-patient [ICU and non-ICU care]). The NCCM uses NCEM outputs and information on

likely need for and baseline availability of resources such as human resources at all care levels, oxygen, oxygen delivery devices, SARS CoV-2 tests, infection control and prevention infrastructure, and public-sector costs to project the total COVID-19 resource needs and budget impact.

Between March and September 2020, we created 38 sets of updates to the models which were shared with stakeholders in the National and Provincial Departments of Health, National Treasury and other partners. We published four sets of short- and long-term NCEM projections and the model code, and created an online dashboard with data and visualisations of all outputs. NCCM results were used to inform the COVID-19 Special Adjustment Budget. Regularly updated assumptions included contact and mobility rates, case fatality, severity, types of hospital care and length of stay, resource availability, costs, and the impact of behavioural factors such as adherence to restrictions.

The South African COVID-19 epidemic provided an opportunity for disease modelling to be a source of scientific evidence for decision-making.

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## Introduction

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On 5 March 2020, the first positive case of COVID-19 in South Africa was reported by the South African National Department of Health (NDoH), at a time when just over 100 000 cases had been reported worldwide.<sup>1,2</sup> One year and multiple waves of infection later, 220 countries and territories have reported over 150 000 000 cases and 3 100 000 deaths cumulatively.<sup>3</sup> In South Africa, by 6 March 2021, COVID-19 cases had been detected in all 52 districts, reaching over 1 500 000 reported cases and 50 000 reported deaths in the public and private sector combined.<sup>4</sup> However, excess deaths at the time, estimated at more than 145 000, indicate that the true COVID-19 mortality had been substantially higher.<sup>5</sup> The health response to the South African epidemic was unprecedented, with expert virologists, clinicians, epidemiologists and modellers coming together to provide scientific insight and expertise in the management of the epidemic. One such group was the South African COVID-19 Modelling Consortium (SACMC).

The SACMC was established at the end of March 2020 at the request of the NDoH to coalesce expertise in disease modelling and adjacent fields to support the development of transmission models that could project the spread of the disease in South Africa. Mathematical modelling of infectious diseases is a powerful tool for evidence-informed decision-making. Through the *in silico* simulation of disease, models may be used to inform planning and budgeting by projecting epidemiological outcomes and associated costs under a set of assumptions/scenarios.

The consortium, with its core group of experienced infectious disease and economic modellers, worked together to establish two models to project incidence, deaths, resource needs, and the required health budget to support policy and planning. Co-ordinated by the National Institute for Communicable Diseases, the SACMC incorporated local data on COVID-19 cases, severity and mortality into the models. The output from these models served to inform the public and decision-makers, ranging from members of the National COVID-19 Co-ordinating Council chaired by the country's President, the Ministerial Advisory Committee on COVID-19 advising the Minister of Health, the Incident Management Team, staff in the NDoH and National Treasury, and implementers and planners in the Provincial Departments of Health.

This chapter describes the approach taken to modelling both cases and costs in a situation of substantial uncertainty, the processes supported by the models, and the lessons learnt for future pandemics. It also provides an overview of the model results and the consortium's recommendations at the different stages of the country's COVID-19 epidemic. The timeframe under consideration is March to September 2020 – the period of the first wave of COVID-19. While the SACMC continued to support NDoH

with additional analysis and modelling during subsequent waves of infection, this chapter provides a comprehensive review of the role of epidemiological modelling and costing during the first wave only.

## Methodology

In the early stages of the epidemic, the most pressing need was for short- and long-term projections of COVID-19 cases, particularly in terms of how quickly infection would increase and spread between provinces. Estimates of the expected number of severe and critical cases leading to hospital admission, as well as estimates of the resources needed for their care, were urgently required. Lastly, it was necessary to compute the required cost and budgets for the health sector response to the epidemic at provincial and national level, in order to inform planned adjustment budgets and stimulate the flow of resources around the country. To fulfil these needs, the SACMC developed the National COVID-19 Epi Model (NCEM), a stochastic compartmental transmission model following a generalised Susceptible-Exposed-Infectious-Removed structure that accounts for disease severity (asymptomatic, mild, severe and critical cases) and treatment pathways (out-patient, in-patient non-ICU and ICU care).<sup>6</sup>

The National COVID-19 Cost Model (NCCM), a companion model, used epidemiological outputs from the NCEM on severe and critical cases to project total COVID-19 resource needs and associated impact on the national and provincial health budgets by incorporating information on resource needs (including their baseline availability and how they scale with the size of the epidemic) and public-sector costs. The resources considered include human resources at all care levels, oxygen, oxygen delivery devices, hospital beds, SARS-CoV-2 diagnostic tests, and infection control and prevention infrastructure. Both private and public health sector capacity was incorporated, although prices were based on the public sector, given the type of contracting arrangements under negotiation throughout the first wave.

Uncertainty in NCEM model projections was taken into account through presenting results as point estimates with uncertainty ranges; uncertainty in NCCM projections were represented by several scenarios informed by the main NCEM scenarios, and the likelihood of moderately severe cases presenting for Primary Health Care services. The SACMC produced a total of 38 updates (11 updates to the NCEM and 27 updates to the NCCM) during the first wave of COVID-19.

## Parameters and data sources

The parameters driving the NCEM evolved as the scientific knowledge base on COVID-19 grew. Parameter values were originally based on literature and data from other countries, as well as expert opinion within the SACMC through extensive and ongoing input from clinicians, virologists, intensivists and epidemiologists. The parameters required for modelling focused on the epidemiological pathway of

infection and the types, duration and outcomes of hospital treatment. Many of these assumptions were later updated when South African data became available.

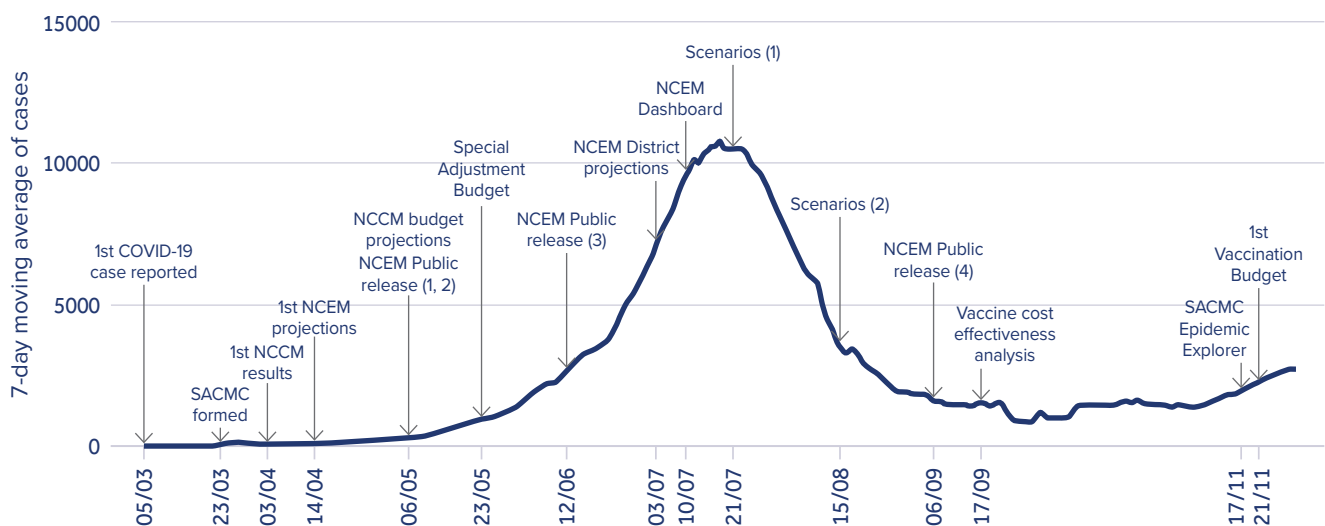
The NCCM used three types of input data: the type and required quantities of resources such as the need for inpatient beds projected by the NCEM, staff at all levels of care, oxygen and delivery devices, diagnostic tests, and infection control and prevention infrastructure; the prices of these resources in the public sector; and – where additional quantities of these resources were required, such as hospital beds and ventilators – the baseline availability in the public and private sector that could be dedicated to the COVID-19 health response. All costs were evaluated from the perspective of the provider – the South African government – although COVID-19 testing and care were provided in both the public and the private health sectors.

## Key findings

### Developing the NCEM

Between end-March and early September 2020, the SACMC developed 11 sets of updates to the epidemiological models which were shared with stakeholders in the National and Provincial Departments of Health, National Treasury, and other partners such as the National Ventilator Project and Reserve Bank. We published four sets of short- and long-term NCEM projections, released the model code, and created an online dashboard with data and visualisations of all outputs for use by Department of Health planners and other decision-makers. Figure 1 represents the timeline of the modelling projections.

Figure 1: Timeline of modelling updates from the SACMC



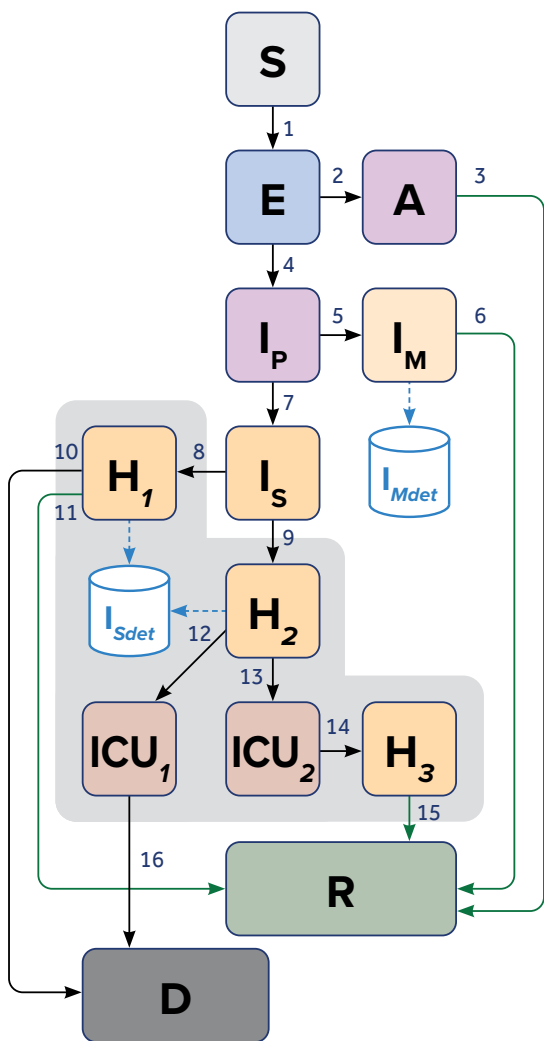
Between these frequent updates, four significant versions of the NCEM stand out as examples of the adaptive nature of disease modelling, exemplified by changes in the treatment of major sources of uncertainty. These versions are described first, followed by the model findings.

#### Version 1 (April–May 2020)

Version 1 was developed at the start of the epidemic, approximately 12 weeks into the pandemic and one month into the period of community transmission within South Africa. Thus, central assumptions were based on international data and regularly updated expert opinion. Transmissibility of infection was assumed to be the same in all nine provinces, and uncertainty with respect to the

future impact of lockdown restrictions was represented by an optimistic and a pessimistic scenario. Given that the main aim at the time was to inform the NDoH and others about how many cases would require hospitalisation, and if and when hospital capacity would be breached, it was assumed that all severe and critical cases would access a hospital bed, thereby providing an estimate of anticipated need. The NCEM version 1 allowed SARS-CoV-2 to propagate as a single wave through the population as there was no reasonable basis to predict or parametrise any of the potential mechanisms, or the timing thereof, which would result in multiple waves. The model structure is depicted in Figure 2; the model code is available on the SACMC website.<sup>7</sup>

Figure 2: National COVID-19 Epidemiological Model (version 1 structure)



## Model States

<b>S</b>	Susceptible	
<b>E</b>	Exposed (not infectious)	
<b>A</b>	Infected, asymptomatic	
<b>I<sub>P</sub></b>	Infected, pre-symptomatic	
<b>I<sub>M</sub></b>	Infected, mild	
<b>I<sub>S</sub></b>	Infected, severe, untreated	
<b>Hospitalised</b>	<b>H<sub>1</sub></b>	Infected, severe, general ward (never ICU)
	<b>H<sub>2</sub></b>	Infected, severe, general ward (pre-ICU)
	<b>ICU<sub>1</sub></b>	Infected, critical, high-care/ICU (non-survivor)
	<b>ICU<sub>2</sub></b>	Infected, critical, high-care/ICU (survivor)
	<b>H<sub>3</sub></b>	Infected, severe, general ward (post-ICU)
<b>R</b>	Removed (recovered)	
<b>D</b>	Died	
<b>I<sub>Mdet</sub></b>	Detection of mild cases (laboratory confirmed)	
<b>I<sub>Sdet</sub></b>	Detection of severe cases (laboratory confirmed)	

## Model Flows

- Force of infection
- Latent period till asymptomatic infectiousness
- Duration of asymptomatic infectiousness
- Latent period till pre-symptomatic infectiousness
- Mild cases
- Duration of infectiousness (mild cases)
- Severe cases
- Hospitalisation of severe cases
- Hospitalisation of critical cases (prior to ICU)
- Mortality (severe, hospitalised cases)
- Duration of hospitalisation (severe cases)
- Progress from severe to critical (ICU admission)
- Progress from severe to critical (ICU admission)
- Duration of ICU stay for survivors
- Duration of hospitalisation post-ICU
- Mortality (critical, ICU cases)

Source: Silal et al. 2020.<sup>6</sup>

### Version 2 (June–July 2020)

In version 2, spatial heterogeneity in transmission was taken into account, and the model was developed for the district level. Transmission and hospital admission rates were tailored to be specific to each of the nine provinces and, in the four largest provinces, were estimated at the district level. By incorporating limited hospital admissions data, the model enabled an account of locally observed severity of infection and its impact on the use of inpatient facilities. The model was thus usable for producing case, hospital and mortality projections for each of the 52 districts in South Africa. By May 2020, it had become clear that demand for hospital beds was likely to exceed available beds, even at high projected levels of availability (90% of intensive care unit (ICU) beds, and 70% of general ward beds excluding maternity and psychiatry beds). In this version, the discrepancy between demand and supply of beds and the related impact on mortality was modelled as a series of ‘waiting’ compartments to represent individuals in need of a hospital or ICU bed but unable to occupy one due to capacity constraints (Figure 3). Given limitations in test availability, the model also accounted for a shift in testing policy that prioritised hospitalised patients over the previously attempted community testing, and projected detected cases under both general and more limited testing.

### Version 3 (August 2020)

To version 3, we added aspects of behavioural responses to the epidemic by the population, in order to factor in the earlier-than-expected peak in the Western Cape. This modification acknowledged the phenomenon that members of society experience different risks and exhibit heterogeneous behavioural patterns, introducing substantial variation in the number of secondary infections generated by index cases, with highly connected individuals becoming infected earlier in the epidemic and infecting more contacts. This phenomenon was modelled by adapting the transmission function (force of infection) to be inflated at the start of the epidemic, but to decrease as immunity builds up in the most connected individuals early on.

### Version 4 (September 2020)

Version 4 was produced in response to ongoing uncertainty regarding healthcare-seeking and availability of hospital beds. Two additional scenarios representing the *need* for and the (much lower) actual *use* of hospital beds for severe and critical COVID-19 cases were added, as well as the potential mortality impact of not receiving necessary care,

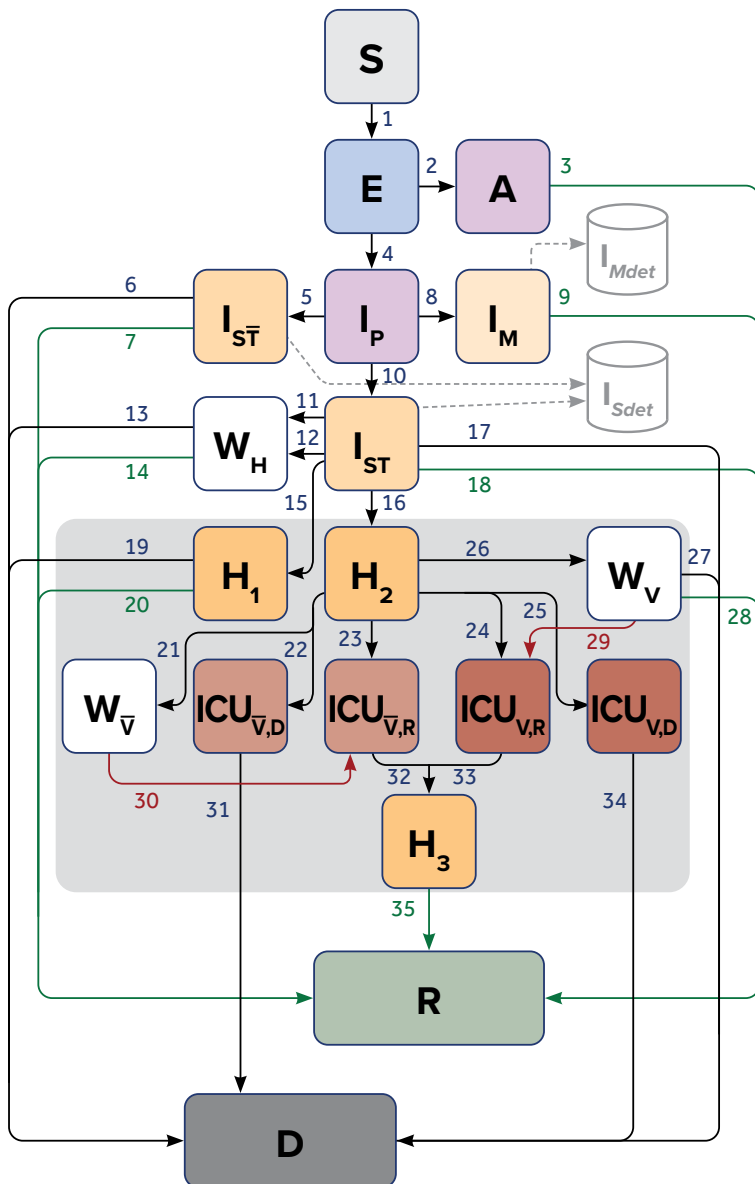
either because of patients not having access to care or due to care capacity itself having been breached. These additional deaths occurring outside of hospitals were parameterised by assuming that 80% of the weekly excess mortality from natural causes estimated by the South African Medical Research Council (SAMRC), was due to COVID-19.<sup>5</sup> The SAMRC’s analysis compared current natural deaths from the vital registry to projections based on mortality in the same calendar week in previous years. While not all excess deaths are attributable to COVID-19, the congruence of spatiotemporal patterns of excess deaths, confirmed COVID-19 cases and officially reported COVID-19 deaths, and consultation with experts, indicated that the bulk of excess deaths at the time were likely to have occurred as a result of COVID-19 rather than from collateral causes. Estimates of the likelihood of mortality due to untreated COVID-19 were determined by a panel of intensive care specialists and experts working with the NDoH to increase COVID-19 healthcare capacity. The foundational model structure for versions 2, 3 and 4 are depicted in Figure 3, with the model code available at the SACMC website.<sup>7</sup>

### Developing the NCCM

The NCCM was set up to estimate the six-month budget for the NDoH response to COVID-19 between April and September 2020, allocating costs at the level of the provinces as well as the NDoH, incremental to existing resources such as hospital beds and staff contingents. The NCCM was updated with the latest NCEM results whenever they became available and incorporated additional interventions deemed necessary by policymakers and planners. Examples of such requests included temporary in-patient infrastructure such as field hospitals and add-on clinic space, dexamethasone treatment, and high-flow nasal cannula treatment.

Prices and quantities were updated for cost items as new tenders and data on real resource use became available; for example, in July we adjusted our initial assumptions regarding in-patient length of stay downwards based on data from the South African hospital surveillance database, DATCOV. Overall, we developed 27 versions of the NCCM throughout the first wave, representing rapid changes in the required quantity and prices of inputs, models of care, and usage data. Here we report on the version used from the end of May to partially inform the COVID-19 adjustment health budget.

Figure 3: National COVID-19 Epidemiological Model (versions 2, 3, 4 Basic structure)



## Model States

<b>S</b>	Susceptible	
<b>E</b>	Exposed (not infectious)	
<b>A</b>	Infected, asymptomatic	
<b>I<sub>P</sub></b>	Infected, pre-symptomatic	
<b>I<sub>M</sub></b>	Infected, mild	
<b>I<sub>ST</sub></b>	Infected, severe, untreated	
<b>I<sub>ST</sub></b>	Infected, severe, seeking treatment	
<b>W<sub>H</sub></b>	Infected, severe, waiting for hospital bed	
<b>Hospitalised</b>	<b>H<sub>1</sub></b>	Infected, severe, general ward
	<b>H<sub>2</sub></b>	Infected, severe, general ward pre-ICU
	<b>W<sub>v</sub></b>	Infected, critical, waiting for ICU, no ventilation
	<b>ICU<sub>v,D</sub></b>	Infected, critical, in ICU, not ventilated, non-survivor
	<b>ICU<sub>v,R</sub></b>	Infected, critical, in ICU, not ventilated, survivor
	<b>W<sub>v</sub></b>	Infected, critical, waiting for ICU & ventilated
	<b>ICU<sub>v,R</sub></b>	Infected, critical, in ICU, ventilated, survivor
	<b>ICU<sub>v,D</sub></b>	Infected, critical, in ICU, ventilated, non-survivor
	<b>H<sub>3</sub></b>	Infected, severe, general ward (post-ICU)
	<b>R</b>	Removed (recovered)
<b>D</b>	Died	
<b>I<sub>Mdet</sub></b>	Detection of mild cases (laboratory confirmed)	
<b>I<sub>Sdet</sub></b>	Detection of severe cases (laboratory confirmed)	

## Model Flows

- Force of infection
- Latent period (until asymptomatic infectiousness)
- Recovery (duration of asymptomatic infectiousness)
- Latent period (until asymptomatic infectiousness)
- Development of severe symptoms, does not seek treatment
- Death of severe, untreated case
- Recovery: duration of severe cases infectiousness
- Development of mild symptoms
- Recovery: duration of mild case's infectiousness
- Development of severe symptoms, seeks treatment
- Severe case waiting for a hospital bed (if bed capacity reached)

- Critical case waiting for a hospital bed (if bed capacity reached)
- Death while waiting for hospital bed (excess mortality)
- Recovery while waiting for hospital bed
- Severe case admitted to hospital
- Critical case admitted to hospital (pre-ICU progression)
- Death of severe case while seeking treatment
- Recovery of severe case while seeking treatment
- Death of severe case in general hospital bed
- Recovery of severe case in general hospital bed
- Critical case in hospital, waiting for ICU admission (no ventilation)
- Progression to ICU admission (no ventilation), non-survivor
- Progression to ICU admission (no ventilation), survivor

- Progression to ICU admission (with ventilation), survivor
- Progression to ICU admission (with ventilation), non-survivor
- Critical case in hospital, waiting for ICU admission (ventilation)
- Death of critical case while awaiting ICU & ventilation
- Recovery of critical case while awaiting ICU & ventilation
- Waiting critical case needing ventilation admitted to ICU
- Waiting critical case not needing ventilation admitted to ICU
- Death of critical case from ICU (not ventilated)
- Critical case discharged from ICU (non-ventilation) to general ward
- Critical case discharged from ICU (ventilated) to general ward
- Death of critical case from ICU (ventilated)
- Recovery of critical case (discharged from hospital)

Source: Silal et al. 2020.<sup>8</sup>

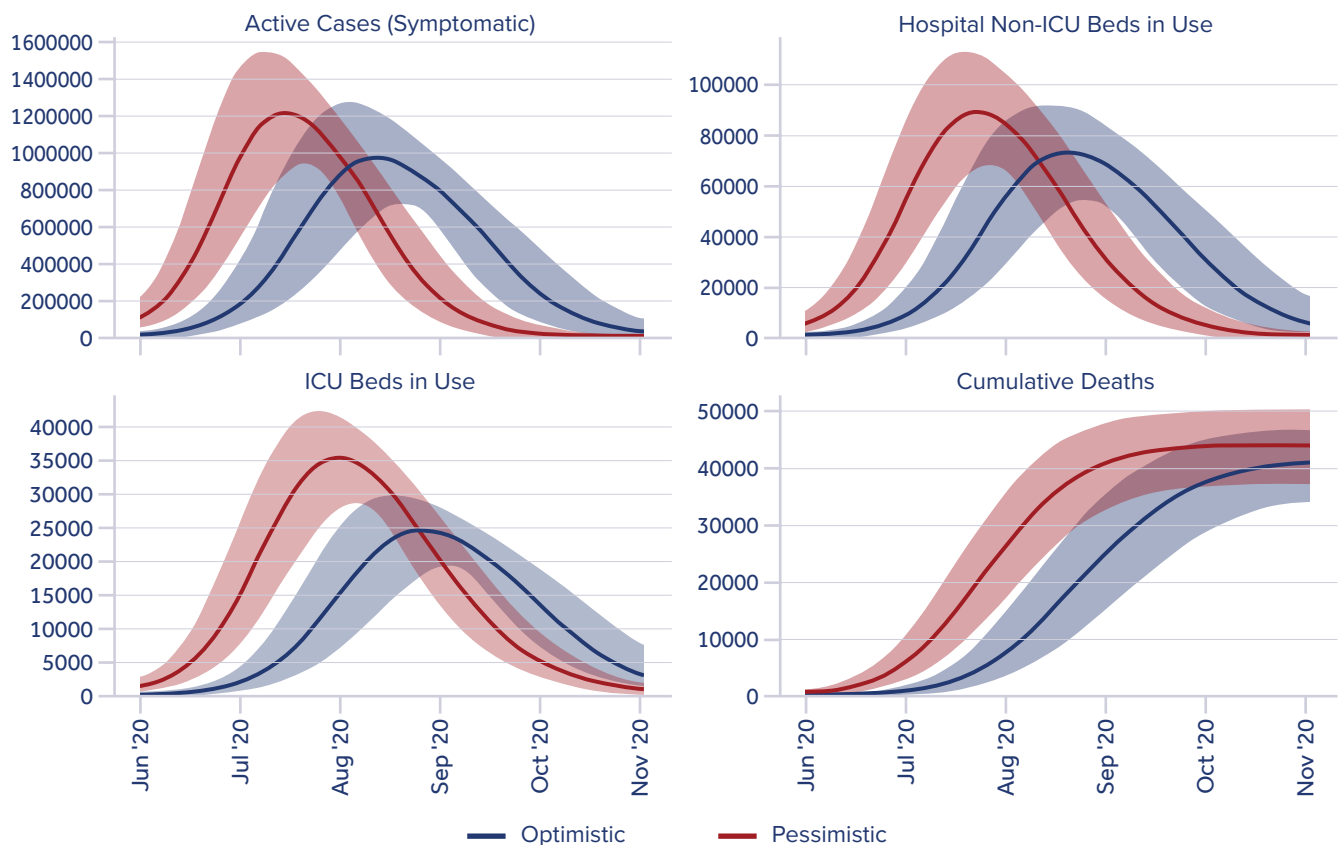
## NCEM findings

The findings of the models were communicated to policymakers and planners in the South African government and were subsequently presented in publicly available reports.<sup>6,8-10</sup> For ease of reference, the findings are summarised as follows.

In May 2020 (NCEM version 1), the model projected between 8.01 and 8.62 million laboratory-confirmed cases, and 40 223 and 43 759 deaths, in the optimistic and pessimistic scenarios, respectively, by 1 October. Nationally, active cases were estimated to peak in early to mid-July in

both scenarios, with a maximum number of between 72 281 and 77 899 hospital beds, and 31 656 and 24 150 ICU beds in use at peak (Figure 4). The single wave projected by the NCEM v1 model over-estimated the hospital bed requirements. Short-term model projections released in May indicated that the number of hospital and ICU beds required by the end of May would still be within national capacity. Short-term projections released a month later, however, projected breaches in hospital capacity in the Western and Eastern Cape, which were borne out by media reports of individual facilities reaching capacity or being under severe pressure.<sup>11-13</sup>

Figure 4: NCEM v1: Projected cases, hospital beds and deaths



Source: Silal et al. 2020.<sup>6</sup>

The NCEM version 2 – accounting for variation in timing and level of peaks of the epidemics between the provinces and districts in each province – projected the overall national peak in cases to occur at a similar time to the peak in version 1’s optimistic scenario, but at a lower level. Despite this lower projected peak, the reduced need for general hospital and ICU beds at a national level was still expected to overwhelm available capacity in all provinces. We noted that increasing capacity to accommodate patients in hospital could allow the country to more effectively leverage new therapeutic options such as high-flow oxygen and dexamethasone which could potentially improve mortality outcomes.<sup>14</sup>

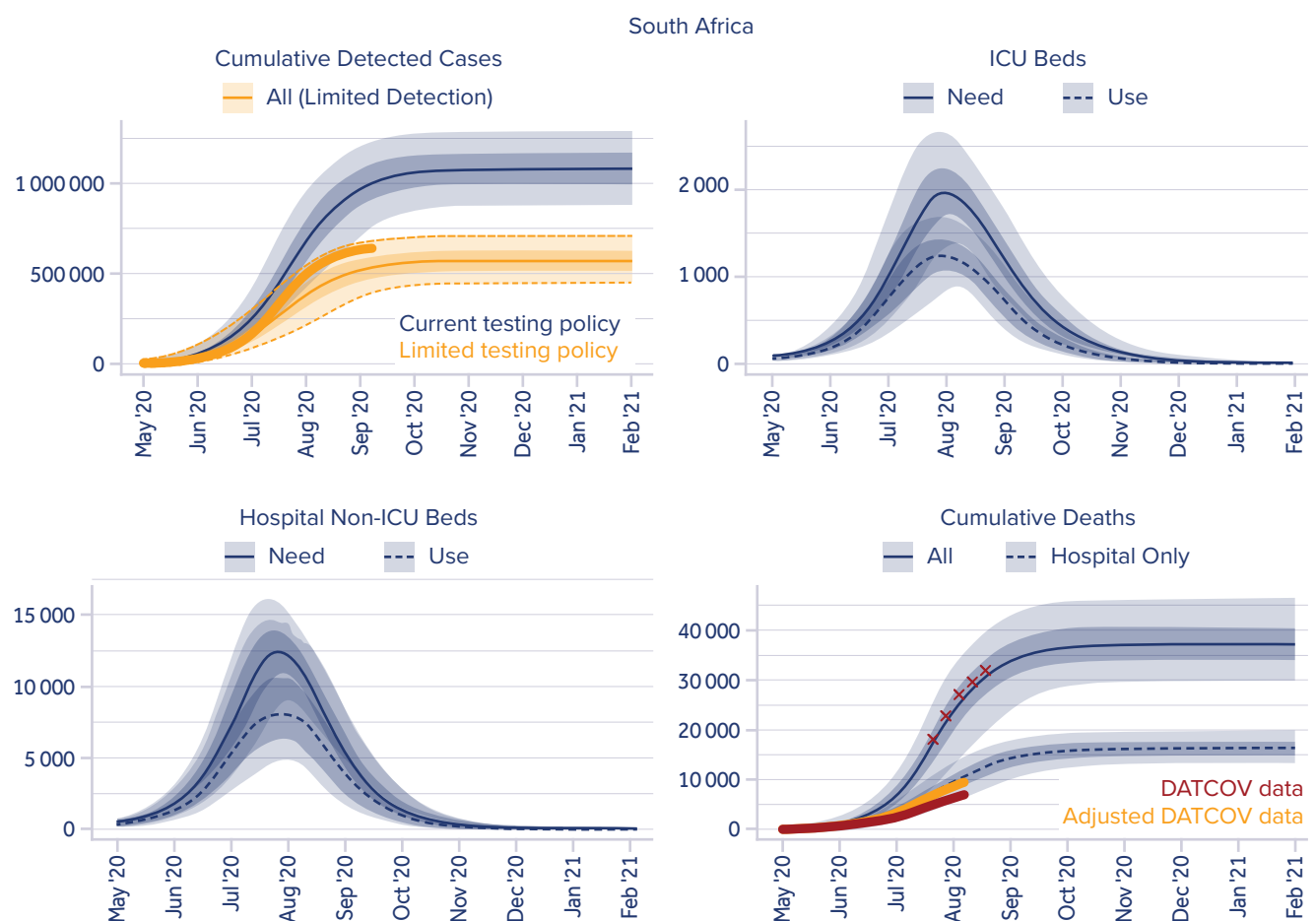
In version 3, four scenarios capturing different behavioural aspects were developed for the four provinces with the most advanced epidemics, namely Western Cape, Eastern Cape, Gauteng and KwaZulu-Natal. The earlier-than-expected peaking of the case curve in the Western Cape, with its associated reduced daily deaths and admissions, highlighted the need to interrogate the difference between the version 2 projections and actual case and death data. We considered a number of phenomena that could potentially account for this discrepancy: reduced susceptibility to infection; behavioural response to increasing mortality; behavioural heterogeneity; and better adherence to protective measures (mask-wearing and

physical distancing, for example) during the relaxation of restrictions. The analysis found that each of these phenomena could produce earlier and/or lower peaking of cases than the original projections, leading to the conclusion that it was most likely a combination of factors that was producing this earlier-than-expected peak.

NCEM version 4 projected that there would be 16 million SARS-CoV-2 infections (asymptomatic and symptomatic) by December 2020, equating to 26.7% (uncertainty range: 24.1%–29.3%) of the population. Under the limited testing scenario, cumulative detected cases were projected to continue to grow until 1.2 million in early November, and only

marginally so thereafter. The maximum number of non-ICU hospital beds in use at national level was projected to be reached in early August, at approximately 8 000 beds (with 12 500 beds estimated to have been needed). There was, however, considerable variation between provinces and substantial uncertainty. The peak number of ICU beds in use was projected to be reached around the same time, at approximately 1 100 beds (when more than 2 000 beds would have been needed). COVID-19 deaths occurring both in and out of hospital were projected to continue to increase until early November, when the cumulative number of all deaths would reach 37 000 (of which 16 000 would have been in hospital), with the growth thereafter estimated to be very low.

Figure 5: NCEM v4: Projected cumulative detected cases, general and ICU hospital beds and cumulative deaths in the first wave of COVID-19 in South Africa



The red crosses in the bottom right-hand panel correspond to 80% of cumulative excess deaths. Source: Silal et al. 2020.<sup>8</sup>

## Discussion

### NCCM findings

The NCCM version in use from the end of May (that partially informed the Adjustment Budget) found that the budget required for the COVID-19 health response for 2020/21 would

be 29 billion Rand and 38 billion Rand, under the optimistic or pessimistic scenario, respectively, of NCEM's version 1. In both scenarios, the largest drivers of costs were additional ICU beds and the staff required to care for critically ill COVID-19 patients, personal protective equipment, and infrastructure projects such as additional out-patient space for testing and isolation of cases at clinics, and pre-fabricated 30-bed wards to be used to rapidly expand in-patient capacity.



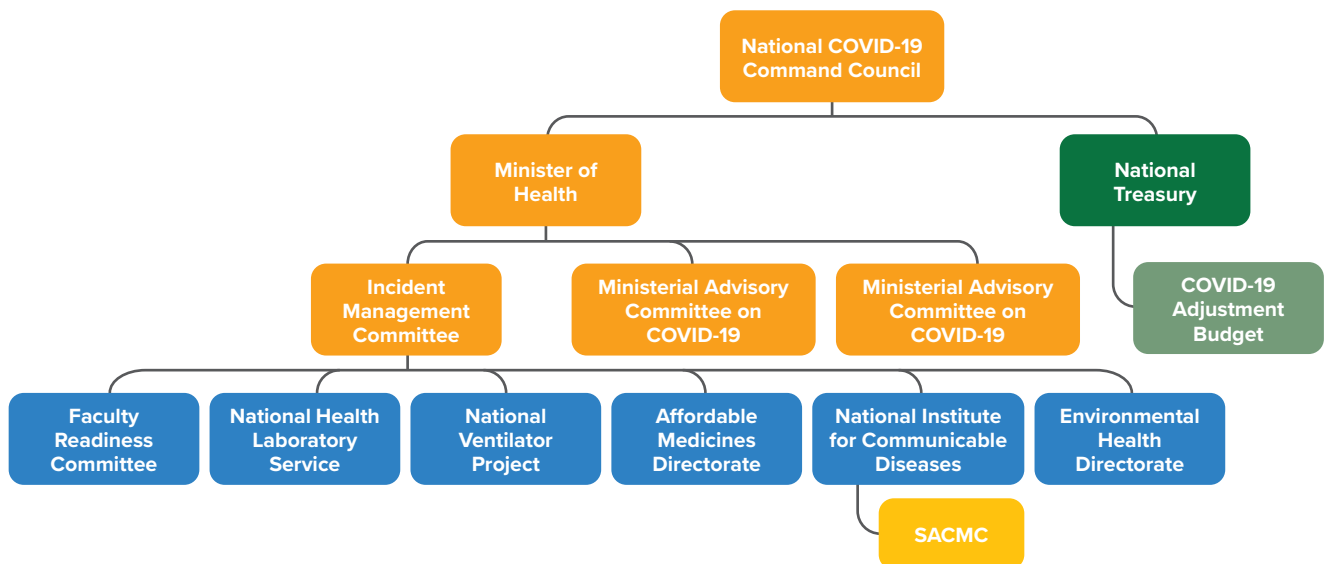
## Users of the NCEM and NCCM

The primary beneficiaries of the modelling projections were the different departments within and related to the NDoH that used the information to support planning (Figure 6). Usage examples included the quantification of drug volumes for in-patient and out-patient care at facilities; the estimation of additional mortuary and graveyard spaces by the Environmental Health Department; costing of ventilation equipment for public and private hospitals in South Africa through the National Ventilator Project; supporting the prediction of the macro-economic impact of the epidemic under different scenarios by the Reserve Bank; estimated testing kits required by the National Health Laboratory Service; and the planning and staffing of field hospitals and facilities in general.

Through continuous adaptation and collaboration with stakeholders, the SACMC was able to support decision-

making and planning at several levels of government throughout the epidemic. For example, outputs of our cost and budget models in particular were used by the National Treasury to make decisions with regard to the additional budget allocation required to manage the COVID-19 epidemic. Model projections were used to inform the Special Adjustment Budget tabled in June, which allocated about R21.5 million to Provincial Departments of Health (and to a much smaller amount, the NDoH for central functions such as surveillance and Port Health programmes), through a combination of increased lending and reprioritisation of committed funds from other departments and within the health budget.<sup>15</sup> An additional R4.5 billion was gained through adjustments at the provincial level.<sup>15</sup> About 68% of the total R25 billion thus generated was in addition to the original health budget.<sup>15</sup> For more information, please see the chapter by Blecher et al.<sup>16</sup> in this Review.

Figure 6: Primary users of the NCEM and NCCM outputs



The colours used signify recipients of scenarios for decision-making (orange), inputs for planning (blue), and inputs for budgeting (green).

## Conclusions

The modelling response to SARS-CoV-2 pandemic demonstrated the value of disease and budget modelling for decision-making and planning processes, but also provided numerous opportunities for improvement and lessons in how to make modelling more useful.

### Uncertainty is the only certainty in modelling

At the start of the epidemic, when modelling was likely to have been most needed, very little was known about transmissibility of infection, symptomatic profiles and susceptibility to infection. SARS-CoV-2 was likened to other coronaviruses in the first attempts to estimate

infection fatality rates, reproductive numbers, and other quantities of interest. As the virus spread from China to Europe, much speculation existed as to how Africa, with younger populations but generally weaker health systems, would be affected. Even locally, the first versions of the NCEM and NCCM relied almost entirely on the international experience of COVID-19, and only subsequent versions were able to incorporate local data on cases, hospital admissions and deaths. Over the course of 2020, much of the 'unknown' at the start of the epidemic became 'known' – or rather 'slightly more well understood'. For example, the role of comorbidities in COVID-19 deaths was investigated in the Western Cape, supplying an indication for the rest of the country without being applicable to all provinces.<sup>17</sup>

Additionally, while meta-analyses and systematic reviews have been conducted to assess the role of children in the spread of SARS-CoV-2<sup>18,19</sup> and the clinical profile of infection,<sup>20–22</sup> considerable uncertainty remains. Other essential inputs to the modelling process remained ‘unknowable’ through the epidemic. Non-identifiability of parameters affecting transmission, such as the probability of transmission, age-related susceptibility, the degree of behavioural heterogeneity, and the impact of public health interventions (PHIs), meant that it was impossible to isolate the contribution of these factors at different stages of the epidemic. Human behaviour and its response to the epidemic are equally unknowable – yet assumptions had to be made, or gleaned from imperfect data, in order to produce models.

Even on the decline of the epidemic curve, there was much uncertainty in the remaining course of the epidemic in terms of its duration and consequences, and some of this uncertainty remains. For example, it was not yet known whether those already infected would have long-lasting or short-term immunity, and whether this immunity would offer complete or partial protection. SARS-CoV-2 transmission remains largely dependent on the proportion of the population vaccinated or with prior infection, and individual behaviour – in particular, the ability and willingness of the population to adopt preventative measures like mask-wearing and physical distancing whilst going about their daily lives.

Given the potential impact that model projections may have, it is of utmost importance that this uncertainty is communicated clearly to decision-makers, through reasoned discussion on where the model findings are robust, and particularly where model outputs are more sensitive. At the SACMC, each report was prefaced with a section on context for interpreting projections that detailed what the model could and could not project. This context was communicated more effectively through several engagements with policymakers.

Additionally, regular updates to models that incorporate new data and updated methods can highlight key areas of sensitivity. As an example, NCEM v3 and subsequently NCEM v4 were made in direct response to differences between model projections and observed data, where the models were adapted to explore (NCEM v3) and include (NCEM v4) behavioural characteristics. In this way, when model projections deviated widely from observed data, models were adapted following investigation of drivers of these differences, usually through incorporating new data or adding epidemiological features to the model.

### **Mathematical modelling is more than just mathematics**

Disease modelling, although essentially mathematical in nature, requires input from numerous other domains in order to be relevant and useful. To this effect, the SACMC was established by the National Institute for Communicable Diseases, on behalf of the NDoH, to bring together disease modellers, epidemiologists, virologists, clinicians,

economists, and public health specialists from academic, non-profit, and government institutions across South Africa. The mandate of the group was to provide data for model development, and assess and validate model projections to be used for planning. The regular meetings and networks established in this consortium provided much-needed insight throughout the modelling process.

### **An agile and rapid response is necessary to remain useful**

In a non-epidemic setting, it can typically take many months to years to develop and calibrate a disease model and run a variety of scenario analyses to make projections. The entire disease modelling process, from problem definition through the review of previous models and literature, data collation, model development, to verification and validation of results, was meticulously followed. Disease modelling in the setting of an epidemic caused by a rapidly transmissible and highly fatal pathogen required following this same process, but at unprecedented speed. Decisions that had to be made often required modelling input within a week or two, and if that input was not provided, the decisions would have been made without model input. Therefore, in order to remain useful, we had to choose model structures that were sufficiently complex to be parameterised and answer the required questions, whilst being able to be processed efficiently. The SACMC produced a total of 38 updates (11 updates to the NCEM and 27 updates to the NCCM) over the course of six months. This regular updating not only allowed new modelling output to be adopted routinely but, more importantly, allowed emerging knowledge and data on SARS-CoV-2 and feedback from policymakers to be incorporated into subsequent updates. It is equally important to have an established channel of communication so that modelling output may be fed into decision-making processes and decision-makers can stipulate needs for modelling with ease, thereby accelerating the response time to minimise the impact on severe outcomes. It is also important to remember that the role of modellers is to provide but one source of evidence in the decision-making process. It is often the case that decision-makers will undertake a series of consultations based on multiple sources of evidence before concluding on a course of action.

### **Measured responses**

In situations where urgent input is required, it becomes easy to fall into the trap of responding in a reactive fashion. In disease modelling, modellers must be acutely aware how model output is used. It is in the hands of the modeller to judge whether sufficient data are available and/or modelling can responsibly support the decisions to be made. At the start of the second wave in South Africa (in October 2020), updated model predictions of the shape and peak of the wave were desired urgently, and the SACMC decided to first assess the driving forces behind the resurgence, considering factors such as increased mobility, PHI fatigue, lower seroprevalence, and new variants. In the absence of additional information at the time (with the B.1.351/Beta

variant announced only in December 2020), the SACMC made the difficult decision to not produce model-based projections, but rather to provide data analysis to develop a set of metrics that could detect and monitor the second wave. Further updates to the NCEM were resumed in anticipation of the third wave and the vaccine roll-out programme. The SACMC continues to support the national COVID-19 response through modelling and analysis during the third wave and beyond.

## Recommendations

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- Managing expectations and communicating uncertainty is of paramount importance when communicating model findings. Through the presentation of figures with uncertainty bands, of both input parameters and results tables, with uncertainty ranges clearly marked, and of scenario and sensitivity analyses, modellers can effectively communicate the uncertainty associated with outputs. Additionally, the sensitivity of model projections to central assumptions and the quality and context of input data should also be communicated.
- A multidisciplinary team should be established to provide the necessary clinical and health system expertise and to assess and validate model structure, calibration and projections. This group of experts proved particularly useful in data-sparse environments.
- Epidemiological models should be paired with cost and budget modelling to maximise usefulness to the planning process. Limited budgets and competing needs for resources are universal. Thus, the impact and effectiveness of scenarios and interventions can be fully realised only if epidemiological modelling is paired with projections of resource needs and costs, and macro-economic impact. This is especially true in the situation of early COVID-19 modelling, where, in the absence of therapeutic interventions or vaccination, re-allocating scarce in-patient resources was the only avenue to improve survival and reduce the population impact.
- Adaptive modelling requires continued interaction with users. In a rapidly evolving epidemic, producing model output that serves the needs of an array of users requires continuous engagement with stakeholders. Establishing relationships and supporting stakeholders' needs accelerates the incorporation of modelling output into decision-making. Modellers should invest time in developing tools to make output more accessible to users. It is also important to determine early on the model outputs required by user groups. During the COVID-19 epidemic in South Africa, we found that estimates of in-patient beds were most useful for planners, while estimated cases and deaths were most relevant for the public.

During the first wave of the epidemic, the SACMC developed models in response to the most urgent needs of decision-makers. Together, the NCEM and NCCM allowed

national and provincial government to plan several months ahead of time, negotiate with manufacturers, and prepare contracts for additional resources. The SACMC continues to serve the planning needs of the government and is currently developing models and scenarios to project future waves and support the national vaccine roll-out.

SARS-CoV-2 is the most disruptive virus the world has faced in the last century. In the absence of previous experience and knowledge of the behaviour of this disease and the impact of measure to control, mathematical modelling and other analytical approaches have played a significant role in the global response to the pandemic. The current heightened global attention provides an opportunity to fundamentally reconfigure and strengthen our preparedness for, and responses to, epidemic risk.

Mathematical modelling of infectious diseases is a powerful tool for evidence-informed decision-making. Models have played a role in supporting decision-making during this pandemic; however, there remains a critical unmet need for evidence-based, strategic decision support of public health policy in the global health arena. This demand is likely to grow, as governments increasingly recognise the benefits of optimising the impact of limited national health budgets through advanced analytical techniques. The further development of local capacity in disease modelling is imperative to sustain the contribution of this domain to support the future health needs of the country.

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