NCEM v4.0 (District Model): Supplementary information

This document provides a technical overview of the National COVID-19 Epi Model (NCEM) provincial model. The model described in this document is the district-level NCEM model, created by the <u>South African COVID-19 Modelling Consortium</u>. There is also a separate document, the <u>NCEM Provincial Model Code Guide</u>, that gives an overview of the structure of the model code for the Provincial Model; the district model code has a similar structure. If there are any queries regarding the model or the code, please contact us on: <u>info@sacovid19mc.co.za</u>.

Model equations

The model describes the temporal evolution of the following state variables:

Variable	Definition
S	number of susceptible individuals
Ε	number of exposed but not yet infectious individuals
I_A	number of asymptomatic individuals (infectious)
I_P	number of presymptomatic individuals (infectious)
I_M	number of mildly and moderately ill individuals (infectious)
I _{ST}	number of individuals who are or will become severely ill and will access treatment but are not yet hospitalised (infectious)
$I_{S\bar{T}}$	number of individuals who are or will become severely ill but will not access treatment (infectious)
H_1	number of severely ill individuals who are hospitalized in the general (non-ICU) ward
H_2	number of individuals who are work will be come critically ill currently in the general (non-ICU) ward
C_{V1}	number of individuals who are critically ill, will eventually die, and are currently in the ICU (ventilator resourced)
C_{V2}	number of individuals who are critically ill, will eventually recover, and are currently in the ICU (ventilator resourced)
$C_{\bar{V}1}$	number of individuals who are critically ill, will eventually die, and are currently in the ICU (not ventilated)
$C_{\bar{V}2}$	number of individuals who are critically ill, will eventually recover, and are currently in the ICU (not ventilated)
<i>H</i> ₃	number of individuals who have been critically ill, will recover, and have been discharged from the ICU but remain in hospital for step-down care
W_H	number of severely ill individuals who have sought hospitalization but could not be accommodated
W_V	number of critically ill individuals who require a ventilator-resourced ICU bed but could not be accommodated
$W_{ar{V}}$	number of critically ill individuals who require a non-ventilator-resourced ICU bed but could not be accommodated

R number of individuals who are no longer infectious / recoverd and/or discharged

- *D* number of individuals who have died
- I_{M_d} cumulative number of *confirmed* mild / moderate infections
- I_{S_d} cumulative number of *confirmed* severe and critical infections
- $N total number of individuals in the population (S + E + I_A + I_P + I_M + I_{ST} + I_{S\bar{T}} + H_1 + H_2 + C_{V1} + C_{V2} + C_{\bar{V}1} + C_{\bar{V}2} + H_3 + R + W_S + W_V + W_{\bar{V}})$
- *X* dummy variable representing mild and moderate cases who will be tested before they are tested
- *Y* dummy variable representing severe and critical cases who will be tested before they are tested

The following equations describe the dynamics of transmission and disease progression within each district, *x*:

$$\begin{aligned} \frac{dS_x}{dt} &= -\Phi_x S_x \\ \frac{dE_x}{dt} &= \Phi_x S_x - \gamma_1 E_x \\ \frac{dI_{A_x}}{dt} &= p_a \gamma_1 E_x - r_1 I_{A_x} \\ \frac{dI_{P_x}}{dt} &= (1 - p_a) \gamma_1 E_x - \gamma_2 I_{P_x} \\ \frac{dI_{ST_x}}{dt} &= (1 - p_m_x) p_{t_x} \gamma_2 I_{P_x} - \tau_s I_{ST_x} \\ \frac{dI_{ST_x}}{dt} &= (1 - p_m_x) (1 - p_{t_x}) \gamma_2 I_{P_x} - r_8 I_{ST_x} \\ \frac{dH_{1x}}{dt} &= \alpha_{1x} \left(1 - \frac{p_{c_x}}{1 - p_{m_x}} \right) \tau_s I_{ST_x} - r_3 H_{1_x} \\ \frac{dH_{2x}}{dt} &= \alpha_{1x} \frac{p_{c_x}}{1 - p_{m_x}} \tau_s I_{ST_x} - \tau_p H_{2_x} \\ \frac{dC_{V1x}}{dt} &= \alpha_{2x} p_{v_x} d_{cv_x} \tau_p H_{2_x} - \mu_v C_{V1_x} \\ \frac{dC_{V2x}}{dt} &= \alpha_{2x} (1 - p_{v_x}) d_{c\bar{v}_x} \tau_p H_{2_x} - \mu_v C_{V2_x} \\ \frac{dC_{V1x}}{dt} &= \alpha_{2x} (1 - p_{v_x}) d_{c\bar{v}_x} \tau_p H_{2_x} - \mu_v C_{V1_x} \\ \frac{dC_{V2x}}{dt} &= \alpha_{2x} (1 - p_{v_x}) d_{c\bar{v}_x} \tau_p H_{2_x} - \mu_v C_{V1_x} \\ \frac{dC_{V2x}}{dt} &= \alpha_{2x} (1 - p_{v_x}) (1 - d_{c\bar{v}_x}) \tau_p H_{2_x} - r_{10} C_{\bar{v}2_x} \\ \frac{dH_{3x}}{dt} &= r_9 C_{V2x} + r_{10} C_{\bar{v}2_x} - r_5 H_{3x} \end{aligned}$$

$$\begin{aligned} \frac{dR_x}{dt} &= r_1 I_{A_x} + r_2 I_{M_x} + (1 - d_{s_x}) r_3 H_{1_x} + r_5 H_{3_x} + \left(1 - \frac{p_{c_x} d_{C\bar{T}}}{1 - p_{m_x}} - \frac{p_{s_x} d_{S\bar{T}}}{1 - p_{m_x}}\right) r_8 (W_{H_x} + I_{S\bar{T}_x}) \\ \frac{dD_x}{dt} &= d_{s_x} r_3 H_{1_x} + \mu_V C_{V1_x} + \mu_{\bar{V}} C_{\bar{V}1_x} + \left(\frac{p_{c_x} d_{C\bar{T}}}{1 - p_{m_x}} - \frac{p_{s_x} d_{S\bar{T}}}{1 - p_{m_x}}\right) r_8 (W_{H_x} + I_{S\bar{T}_x}) + r_9 W_{V_x} + r_{10} W_{\bar{V}_x} \\ \frac{dW_{H_x}}{dt} &= (1 - \alpha_1) \tau_s I_{ST} - r_8 W_{H_x} \\ \frac{dW_{V_x}}{dt} &= (1 - \alpha_2) p_{v_x} \tau_p H_2 - r_9 W_{V_x} \\ \frac{dW_{\bar{V}_x}}{dt} &= (1 - \alpha_2) (1 - p_{v_x}) \tau_p H_2 - r_{10} W_{\bar{V}_x} \\ \frac{dX_x}{dt} &= d_m p_{m_x} \gamma_2 I_{P_x} - \Delta_m X_x \\ \frac{dI_{M_d}}{dt} &= \Delta_n X_x \\ \frac{dI_{M_d}}{dt} &= \Delta_s Y_x \end{aligned}$$

where the force of infection, Φ_{χ} , is defined as

$$\Phi_{x} = \frac{\beta_{x} \delta_{x,t} \left(\zeta I_{A_{x}} + \zeta I_{P_{x}} + I_{M_{x}} + I_{ST_{x}} + I_{S\bar{T}_{x}} + W_{H_{x}} \right)}{N_{x}}$$

and $p_{c_{\chi}} = 1 - p_{m_{\chi}} - p_{s_{\chi}}$.

Key parameter values

Tables 2 and 3 below show the values of key parameters used to inform the model. Parameter values have been selected for use by an expert panel of clinicians on the SA COVID-19 Modelling Consortium and updated with inputs from recent South African data where indicated. Parameter values that are provided as ranges only differ by province.

Table 1 Results of NICD analysis of estimated	national and provincial	reproductive numbers [1,3]*
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Restriction level	National	Eastern Cape	Gauteng	KwaZulu Natal	Western Cape
None (R ₀)	2.5 (2, 3)	2.5 (2, 3)	2.5 (2, 3)	2.5 (2, 3)	2.5 (2, 3)
Level 5 Rt ²	1.3	1.4	1.2	1.1	1.5
	(1.0, 1.6)	(1.1, 1.7)	(1.0, 1.4)	(0.9, 1.43	(1.2, 1.8)

Level 4 R _t : NICD R _t estimates calibrated to fit hospital-based provincial deaths ²	1.6 (1.3, 1.9)	1.6 (1.2, 1.8)	1.8 (1.4, 2.2)	1.6 (1.3, 1.9)	1.6 (1.3, 1.9)
	Other Provinces	Eastern Cape	Gauteng	KwaZulu Natal	Western Cape
Level 3 (1–30 June): increase in contacts (relative to previous period) estimated from a decrease in residential mobility ³	(21.1%, 26.0%)	21.0% (16.8, 25.2)	4.3% (3.4, 5.2)	20.5% (16.4, 24.6)	8.1% (6.5, 9.7)
Level 3 (1 July – 17 August): increase in contacts (relative to previous period) estimated from a decrease in residential mobility ³	(0.5%, 2.5%)	3.0% (2.4, 3.6)	1.8% (1.4, 2.2)	0.8% (0.6, 1.0)	6.6% (5.3, 7.9)
Level 2 (18 August ->): increase in contacts (relative to previous period) estimated from a decrease in residential mobility ³	(3.3%, 5.8%)	5.4% (4.3, 6.5)	1.7% (1.4, 2.0)	4.8% (3.8, 5.8)	3.1% (2.5, 3.7)

 * We utilised national estimates where provincial data was too sparse. R₀, and R_t for Level 5 and Level 4 from symptom onset date adjusted for testing volumes

Table 3. Key model parameters

	Parameter	Value (range)	Sources	
Infection severity	Proportion of cases that are asymptomatic	75% (70% - 80%)	[9-12]	
	Relative infectiousness of asymptomatic	80% (77.5%, 82.5%)	[13-15]	
	cases		Estimated through calibration to admissions and fatalities count data (DATCOV) [4]	
	Mild to moderate cases among the symptomatic	ne (94.55% - 97.13%) Estin calib	Estimated through calibration to	
	Severe cases among the symptomatic	(2.58% - 5.00%)	admissions and fatalities count data	
	Critical cases among the symptomatic	(0.18% - 0.55%)	(DATCOV) [4]	
	Fatal cases among the admitted (general)	(6.82% - 20.28%)	Estimated from NICD COVID-19	
	Fatal cases among the admitted (ICU ventilated)	(43.01% - 85.03%)	Hospital Sentinel Surveillance database	
	Fatal cases among the admitted (ICU non-ventilated)	(22.73% - 43.35%)	(DATCOV) [4] & Western Cape Line	
	Proportion of cases in ICU requiring ventilation	(19.44% - 51.47%)	List Data (SPV) [16]	
	Fatal cases among the critically infected requiring ventilation, <i>in the absence of appropriate care</i>	100%	Expert opinion of clinicians convened by the National	

	Fatal cases among the critically infected not requiring ventilation, <i>in the absence of appropriate care</i>	Unchanged: Fatal cases among the admitted (ICU non- ventilated)	COVID-19 Modelling Consortium	
	Fatal cases among the critically infected requiring oxygen, <i>in the absence of appropriate care</i>	100%		
	Fatal cases among the severely infected requiring oxygen, <i>in the absence of appropriate care</i>	90%		
	Probability of seeking hospital-level care for severely and critically ill	(50.00% - 97.00%)	Estimated through calibration to 80% of excess mortality [5]	
Timeframes & treatment	Time from infection to onset of infectiousness	2 days (1.0 - 3.0)	[8, 17-26] with input from the National COVID-19 Modelling Consortium	
durations	Time from onset of infectiousness to onset of symptoms	4 days (3.0 - 5.0)		
	Duration of infectiousness from onset of symptoms	5 days (4.0 - 6.0)	[26, 27]	
	Time from onset of symptoms to testing	4 days (3.0 - 5.0)	[17,18, 28-32]	
	Time from onset of symptoms to hospitalisation	5 days (4.0 - 6.0)		
	Time in non-ICU (never ICU) to death/recovery	8 days (4.0 - 12⋅0)	Lengths of stay: values and ranges	
	Time in non-ICU for those destined for ICU	0 days (0.0 - 2.0)	sourced from NICD COVID-19 Hospital	
	Time in ICU for those ventilated and destined to die	14 days (7.0 - 27.0)	Surveillance database	
	Time in ICU for those never ventilated and destined to die	11 days (7.0 - 18.0)	(DATCOV) [4]	
	Time in ICU for those ventilated and recovered	19 days (15.0 - 37.0)		
	Time in ICU for those never ventilated and recovered	5 days (1.0 - 10.0)		
	Time in non-ICUs for those who were in ICU and recovered	0 days (0.0 - 6.0)		

* A full list of parameters are available in the code.

Basic reproduction number

The expected number of secondary infections produced by a single infection introduced into a naive population (basic reproduction number) can be calculated as:

$$R_{0_x} = \beta_{x,0} \left(\frac{p_a \zeta}{r_1} + \frac{(1 - p_a)}{\gamma_2} + \frac{(1 - p_a)p_{m_x}}{r_2} + \frac{(1 - p_a)(1 - p_{m_x})}{\tau_s} + \frac{(1 - p_{t_x})(1 - p_a)(1 - p_{m_x})}{r_8} \right)$$

In this context, a 'naive' population is the population at the start of the epidemic when (a) there are no previously-infected individuals ($S_x \approx N_x$) and (b) there are no measures or practices in place that reduce the contact rate below baseline ($\delta_{x,0} = 1$). We further assume that at this stage in the epidemic there will be hospital beds available for all severe and critical cases that access care ($\alpha_1 = 1$).

Time-varying reproduction numbers

The reproduction number is assumed to vary over time, reflecting changes in the contact rate that result from both government-enforced and individually-enacted measures. We refer to two types of time-varying reproduction numbers: $R_c(t) = \delta_t R_0$ denotes the hypothetical reproduction number at a given point in time that would be observed in the absence of previously-infected individuals, where δ_t is a proportional reduction from baseline; $R_e(t) = R_c(t)S(t)/N(t)$ denotes the realized reproduction number at a given point in time, taking into account accumulation of infection and immunity in the population.

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References

- National Institute for Communicable Diseases. The Daily COVID-19 Effective Reproductive Number (R) in South Africa – week 33 2020. Available from: https://www.nicd.ac.za/wp-content/uploads/2020/08/COVID-19-Effective-Reproductive-Number-in-South-Africa-week-33_draft04.pdf
- National Institute for Communicable Diseases. The Initial and Daily COVID-19 Effective Reproductive Number (R) in South Africa 10 June 2020. Available from: https://www.nicd.ac.za/wp-content/uploads/2020/06/Initial-and-Daily-COVID-19-Effective-Reproductive-Number-R-in-SA-11_6_2020.pdf
- Google LLC "Google COVID-19 Community Mobility Reports". https://www.google.com/covid19/mobility/ Accessed: <26 August 2020>.
- 4. National Institute for Communicable Diseases. COVID-19 Hospital Sentinel Surveillance database (DATCOV). [cited 2020 July 29]. (Unpublished)
- 5. Bradshaw D, et al., Report on weekly deaths in South Africa, 1 January -18 August 2020 (Week 33). 2020, South African Medical Research Council Cape Town, South Africa.
- 6. Boulle, A., et al., Data Centre Profile: The Provincial Health Data Centre of the Western Cape Province, South Africa. International Journal of Population Data Science, 2019. 4(2).
- Moultrie, T., et al. Excess deaths: additional measures and approaches to understanding covid-19 related mortality in South Africa. 2020; Available from https://www.samrc.ac.za/sites/default/files/files/2020-08-12/Excess%20deaths_4%20Aug%202020.pdf
- Peter, A., Huisman, J.S., Sonja, L., Bouman, J.A., Althaus, C.L., Regoes, R.R. and Sebastian, B., 2020. COVID-19 infectivity profile correction. *Swiss Medical Weekly*, 150.
- Inui S, Fujikawa A, Jitsu M, Kunishima N, Watanabe S, Suzuki Y, et al. Chest CT Findings in Cases from the Cruise Ship "Diamond Princess" with Coronavirus Disease 2019 (COVID-19). Radiol Cardiothorac Imaging [Internet]. 2020 Apr 1 [cited 2020 Mar 23];2(2):e200110. Available from: http://pubs.rsna.org/doi/10.1148/ryct.2020200110
- 10. Sutton D, Fuchs K, D'Alton M, Goffman D. Universal Screening for SARS-CoV-2 in Women Admitted for Delivery. N Engl J Med [Internet]. 2020 Apr 13. Available from: https://www.nejm.org/doi/full/10.1056/NEJMc2009316
- Day, M., 2020. Covid-19: four fifths of cases are asymptomatic, China figures indicate. BMJ [Internet]. 2020 Apr 2. Available from: <u>https://doi.org/10.1136/bmj.m1375</u>
- 12. Ing AJ, Cocks C, Green JP. COVID-19: in the footsteps of Ernest Shackleton. Thorax [Internet]. 2020 May 27 [cited 2020 Jun 4]. Available from: <u>http://www.ncbi.nlm.nih.gov/pubmed/32461231</u>
- Li, R., Pei, S., Chen, B., Song, Y., Zhang, T., Yang, W. and Shaman, J., 2020. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2). *Science*, *368*(6490), pp.489-493.

- 14. Furukawa NW, Brooks JT, Sobel J. Evidence Supporting Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 While Presymptomatic or Asymptomatic. Emerg Infect Dis. 2020;26(7):6059.
- 15. Zhou R, Li F, Chen F, Liu H, Zheng J, Lei C, et al. Viral dynamics in asymptomatic patients with COVID-19. Int J Infect Dis [Internet]. 2020;96:288–90. Available from: https://doi.org/10.1016/j.ijid.2020.05.030
- 16. Western Cape Department of Health. Single Patient Viewer Database (SPV). [cited 2020 July 29]. (Unpublished)
- 17. Tindale L, Coombe M, Stockdale JE, Garlock E, Lau WYV, Saraswat M, et al. Transmission interval estimates suggest pre-symptomatic spread of COVID-19. medRxiv [Internet]. 2020 Mar 6;2020.03.03.20029983. Available from: https://www.medrxiv.org/content/10.1101/2020.03.03.20029983v1
- Nie X, Fan L, Mu G, Tan Q, Wang M, Xie Y, et al. Epidemiological Characteristics and Incubation Period of 7015 Confirmed Cases With Coronavirus Disease 2019 Outside Hubei Province in China. J Infect Dis [Internet]. 2020 [cited 2020 Jun 10];1– 8. Available from: <u>https://academic.oup.com/jid/advance-article-abstract/doi/10.1093/infdis/jiaa211/5825699</u>
- Linton NM, Kobayashi T, Yang Y, Hayashi K, Akhmetzhanov AR, Jung S, et al. Incubation Period and Other Epidemiological Characteristics of 2019 Novel Coronavirus Infections with Right Truncation: A Statistical Analysis of Publicly Available Case Data. J Clin Med [Internet]. 2020 Feb 17 [cited 2020 Jun 10];9(2):538. Available from: <u>https://www.mdpi.com/2077-0383/9/2/538</u>
- Thompson RN, Lovell-Read FA, Obolski U. Time from Symptom Onset to Hospitalisation of Coronavirus Disease 2019 (COVID-19) Cases: Implications for the Proportion of Transmissions from Infectors with Few Symptoms. J Clin Med [Internet]. 2020 May 1 [cited 2020 Jun 10];9(5):1297. Available from: <u>https://www.mdpi.com/2077-0383/9/5/1297</u>
- Backer JA, Klinkenberg D, Wallinga J. Incubation period of 2019 novel coronavirus (2019- nCoV) infections among travellers from Wuhan, China, 20 - 28 January 2020. Vol. 25, Eurosurveillance. European Centre for Disease Prevention and Control (ECDC); 2020. Available from:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7014672/

- 22. Jing Q, You C, Lin Q, Hu T, Yu S, Zhou X-H. Estimation of incubation period distribution of COVID-19 using disease onset forward time: a novel cross-sectional and forward follow-up study. medRxiv [Internet]. 2020 Mar 10;2020.03.06.20032417. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7217033/</u>
- Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, et al. The incubation period of coronavirus disease 2019 (CoVID-19) from publicly reported confirmed cases: Estimation and application. Ann Intern Med [Internet]. 2020 May 5;172(9):577–82. Available from: <u>https://www.acpjournals.org/doi/10.7326/M20-0504</u>
- 24. Ganyani T, Kremer C, Chen D, Torneri A, Faes C, Wallinga J, et al. Estimating the generation interval for coronavirus disease (COVID-19) based on symptom onset data, March 2020. Eurosurveillance [Internet]. 2020 Apr 30;25(17). Available from: <u>https://www.eurosurveillance.org/content/10.2807/1560-</u> 7917.ES.2020.25.17.2000257
- 25. Nishiura H, Linton NM, Akhmetzhanov AR. Serial interval of novel coronavirus (COVID-19) infections. Int J Infect Dis [Internet]. 2020 Mar [cited 2020 Mar 16]; Available from: <u>https://linkinghub.elsevier.com/retrieve/pii/S1201971220301193</u>

- 26. He X, Lau EHY, Wu P, Deng X, Wang J, Hao X, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med [Internet]. 2020 May 1;26(5):672–5. Available from: <u>https://www.nature.com/articles/s41591-020-0869-5</u>
- Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. Nature. 2020 May 28;581(7809):465–9. Available from: <u>https://www.nature.com/articles/s41586-020-2196-x</u>
- 28. World Health Organization. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) [Internet]. 2020 [cited 2020 Mar 14]. Available from: <u>https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-oncovid-19-final-report.pdf</u>
- 29. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet [Internet]. 2020 [cited 2020 Mar 14];395:497. Available from:

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30183-5/fulltext

- Gaythorpe K, Imai N, Cuomo-Dannenburg G, Baguelin M, Bhatia S, Boonyasiri A, et al. Report 8: Symptom progression of COVID-19 [Internet]. 2020 Mar [cited 2020 Mar 18]. Available from: <u>https://doi.org/10.25561/77344</u>
- 31. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet [Internet]. 2020 Mar [cited 2020 Mar 14];0(0). Available from: <u>https://linkinghub.elsevier.com/retrieve/pii/S0140673620305663</u>
- 32. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA - J Am Med Assoc. 2020 Mar 17;323(11):1061–9. Available from: <u>https://jamanetwork.com/journals/jama/fullarticle/2761044</u>
- 33. Statistics South Africa. Mid-year district population estimates 2020 (unpublished)
- Data Science for Social Impact Research Group @ University of Pretoria, Coronavirus COVID- 19 (2019-nCoV) Data Repository for South Africa. Available at: <u>https://github.com/dsfsi/covid19za</u>.