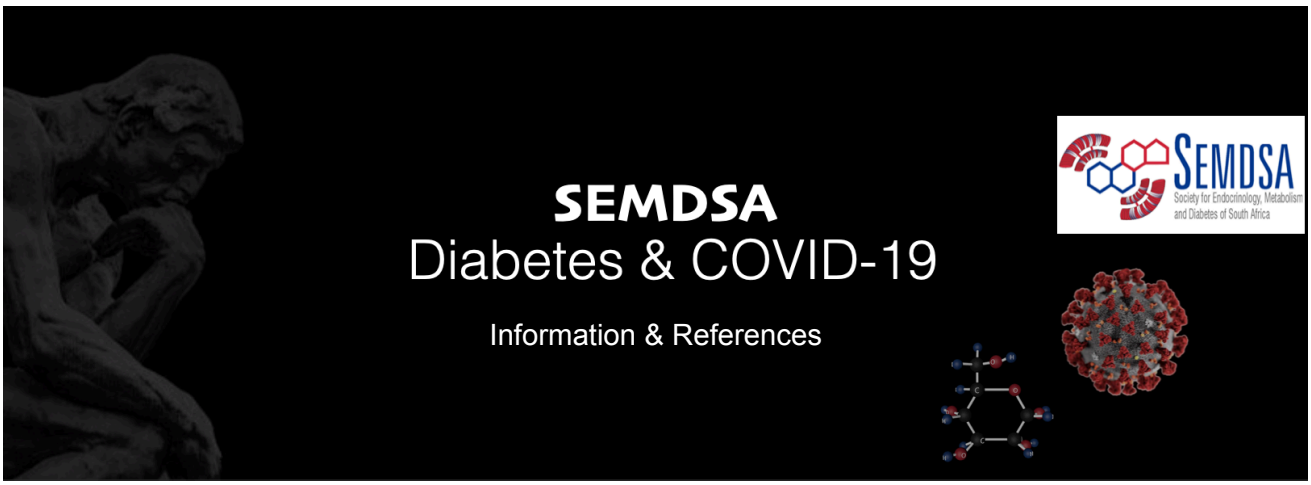

SEMDSA recognises that patients with underlying conditions such as hypertension, diabetes, obesity and cardiovascular disease are at high risk of **severe** COVID-19 (Coronavirus disease 2019). This evidence has been gathered from international data in regions where the burden of disease has been high. Early observations in South Africa are in keeping with these trends.

With this in mind there is a responsibility to educate patients with underlying conditions on this risk, emphasise precautions to prevent infection, and continue to aggressively and responsibly manage metabolic goals of therapy which may reduce risk of severity of potential COVID-19 infection, and yet at the same time manage traditional complications. Those identified as severely ill should be timeously referred for inpatient care.

The following information has been compiled to assist health care workers in making real time decisions with safety and reassurance. Please note that information is constantly changing and being updated - links to useful online information which provide more detailed guidance are mentioned below. Relevant articles and useful links to video material will also be posted on the SEMDSA website (www.semdsa.org.za)

This document contains hyperlinks to articles and references of importance, simply click on the link and you will be guided to the article / video. A summary of useful links appears at the end of the document.

Background :

Patients with diabetes are at increased risk of severe COVID-19 infection and the risk of fatal outcome is increased by up to 50%. This risk appears to mainly affect patients with type II diabetes mellitus. An increase in severity has not been noted in patients with type I diabetes mellitus, however these patients may be at increased risk of diabetic ketoacidosis (DKA). An increased prevalence of DKA has been reported in this group with COVID-19 infections. It is important to note that an elevated HbA1c in patients with type I and type II diabetes mellitus compromises the immune system rendering them more susceptible to **any** infectious disease.

Practical Guidelines

General :

- Prevention of COVID-19 infection - follow WHO, NICD guidelines on hand sanitising, physical distancing and mask wearing. (http://www.health.gov.za/index.php/component/phocadownload/category/628-clinical-management-of-suspected-or-confirmed-covid-19-disease)
- Continue standard of care, educate on risk and importance of optimal metabolic control.
- Dietary guidelines, exercise, weight loss measures should continue to be applied, diabetes self management and education (DSME's) should be emphasised.
- Optimise current therapy as necessary, intensify metabolic control in patients who are not infected with SARS-CoV-2.
- Strict abidance of blood pressure and lipid control.
- Consider need for insulin initiation / intensification.
- Caution with premature discontinuation of therapy.
- Use of **Telemedicine** to maintain self containment may be necessary.
- Patients without diabetes, particularly those at risk for metabolic disease should be monitored for new onset diabetes that might be triggered by the virus

Outpatient care of patients with diabetes and COVID-19:

- Educate patients on the importance of optimal metabolic control
- Optimise current therapy if appropriate
- Continue statin and ACE I/ARB therapy
- Do not discontinue therapy prematurely (see appendix on assessing severity and sick day rules)
- Use **telemedicine** if possible to maintain maximal self containment

Therapeutic aims for outpatient care :

- Plasma glucose 4-8mmol/L
- HbA1c < 7% (general) or agreed upon individualised target
- Avoid hypoglycaemia
- For those using CGM and where possible TIR(Time in Range : 3-9mmol/L) should be more than 70%.

Inpatient care or Intensive care of COVID-19 patients

- Monitor for hyperglycaemia / new onset diabetes
- Monitor plasma glucose, electrolytes, pH, blood ketones
- Liberal indication for early intravenous insulin therapy (IVI) in severe cases (ARDS, hyperinflammation)
- Benefits of IVI insulin therapy :
  - exact titration
  - avoid variable subcutaneous tissue absorption due to peripheral perfusion changes
  - assists with managing very high insulin consumption that is commonly seen

Therapeutic aims for inpatient care :

Good inpatient glycemic control lowers mortality
Aim : 3.9 - 10 mmol/L

Medication considerations :

Metformin

Dehydration and lactic acidosis may occur if patients are dehydrated, so patients should stop taking the drug and follow sick day rules

During illness, renal function should be carefully monitored because of the high risk of chronic kidney disease or acute kidney injury

Sulphonylureas

Monitor for hypoglycaemia if patient is unwell with reduced intake or vomiting
May need to adjust dose
More frequent glucose monitoring may be necessary

Sodium-glucose-co-transporter 2 (SGLT2) inhibitors

These include dapagliflozin and empagliflozin in South Africa

Risk of dehydration and diabetic ketoacidosis during illness, so patients should stop taking the drugs and follow sick day rules

Avoid initiating therapy during respiratory illness

Carefully monitor renal function for acute kidney injury

Glucagon-like peptide-1 (GLP-1) receptor agonists

These include exenatide, liraglutide and dulaglutide

Dehydration is likely to lead to a serious illness so patients should be closely monitored

Encourage adequate fluid intake and regular meals

Dipeptidyl peptidase-4 (DPP-4) inhibitors

These include saxagliptin, sitagliptin and vildagliptin

Well tolerated and can be continued

Pioglitazone

Stop in severely ill patients with haemodynamic instabilty, or hepatic or cardiac decompensation

Insulin

Insulin therapy should not be stopped

Regular self-monitoring of blood-glucose every 2–4 hours should be encouraged, or continuous glucose monitoring

Carefully adjust regular therapy if appropriate to reach therapeutic goals according to diabetes type, co-morbidities, and health status

Specific medications :

Statement on ACE I's / ARB's

ACE I's and ARB's have been shown to increase the expression of ACE 2 receptor (ACE2) which SARS-CoV-2 binds to gain entry into lung cells. This raised the possibility of and increased risk and severity of COVID-19 in patients on treatment with these medications. However, once internalised, SARS-CoV-2 impairs the ACE2 receptor pathway and increases deleterious angiotensin-2 activity. The continued use of ACE I's/ARB's may mitigate this deleterious effect.

Blood pressure (BP) management should be maintained, even short term escalations in BP may lead to increased cardiovascular risk. **Patients are encouraged to continue the use of this class of medication, unless specific contraindications arise (eg. hypotension, hyperkalaemia, acute kidney injury).**

This view is endorsed by international associations such as European Society of Cardiology (ESC) and American Heart Association (AHA) and is congruent with advice from the South African Department of Health

Statin therapy

Statin therapy has long term benefits, pleiotropic effects (anti-inflammatory), and cardiovascular risk reduction.
There is a possibility of an increased risk of transaminitis and myositis.
An individualized decision on risk and benefit is recommended.

Aspirin
The risk of cardiovascular disease is higher during COVID infection.
Continue for patients using aspirin for secondary prophylaxis, unless contraindications arise.

Legal (Consent Forms, T & C's)
Click to link to Elsabe Klinck Associates Website

Inpatient Care Algorithm
Click to download algorithm

Telemedicine Guidance
Click to download pdf

Sick Day Rules
Click to download

Assessing Severity of COVID-19:

Please refer to Department of Health **outline on managing COVID-19** (reference made on which patients may be managed at home)

The following table taken from WHO Guidance on the management of COVID-19 is also helpful in assessing severity :

Table 2. Clinical syndromes associated with COVID-19

Mild illness	Patients uncomplicated upper respiratory tract viral infection may have non-specific symptoms such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion, or headache. Rarely, patients may also present with diarrhoea, nausea, and vomiting (3, 11-13). The elderly and immunosuppressed may present with atypical symptoms. Symptoms due to physiologic adaptations of pregnancy or adverse pregnancy events, such as dyspnea, fever, GI-symptoms or fatigue, may overlap with COVID-19 symptoms.
Pneumonia	**Adult** with pneumonia but no signs of severe pneumonia and no need for supplemental oxygen. **Child** with non-severe pneumonia who has cough or difficulty breathing + fast breathing: fast breathing (in breaths/min): < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40, and no signs of severe pneumonia.
Severe pneumonia	**Adolescent or adult:** fever or suspected respiratory infection, plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO_2 ≤ 93% on room air (adapted from *14*). **Child** with cough or difficulty in breathing, plus at least one of the following: central cyanosis or SpO_2 < 90%; severe respiratory distress (e.g. grunting, very severe chest indrawing); signs of pneumonia with a general danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions *(15)*. Other signs of pneumonia may be present: chest indrawing, fast breathing (in breaths/min): < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40 *(16)*. While the diagnosis is made on clinical grounds; chest imaging may identify or exclude some pulmonary complications.
Acute respiratory distress syndrome (ARDS) *(17-19)*	**Onset:** within 1 week of a known clinical insult or new or worsening respiratory symptoms. **Chest imaging** (radiograph, CT scan, or lung ultrasound): bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules. **Origin of pulmonary infiltrates**: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echocardiography) to exclude hydrostatic cause of infiltrates/oedema if no risk factor present. **Oxygenation impairment in adults** *(17, 19)*: • Mild ARDS: 200 mmHg < PaO_2/FiO_2[a] ≤ 300 mmHg (with PEEP or CPAP ≥ 5 cmH_2O, or non-ventilated) • Moderate ARDS: 100 mmHg < PaO_2/FiO_2 ≤ 200 mmHg (with PEEP ≥ 5 cmH_2O, or non-ventilated) • Severe ARDS: PaO_2/FiO_2 ≤ 100 mmHg (with PEEP ≥ 5 cmH_2O, or non-ventilated) • When PaO_2 is not available, SpO_2/FiO_2 ≤ 315 suggests ARDS (including in non-ventilated patients). **Oxygenation impairment in children:** note OI = Oxygenation Index and OSI = Oxygenation Index using SpO_2. Use PaO_2-based metric when available. If PaO_2 not available, wean FiO_2 to maintain SpO_2 ≤ 97% to calculate OSI or SpO_2/FiO_2 ratio: • Bilevel (NIV or CPAP) ≥ 5 cmH_2O via full face mask: PaO_2/FiO_2 ≤ 300 mmHg or SpO_2/FiO_2 ≤ 264 • Mild ARDS (invasively ventilated): 4 ≤ OI < 8 or 5 ≤ OSI < 7.5 • Moderate ARDS (invasively ventilated): 8 ≤ OI < 16 or 7.5 ≤ OSI < 12.3 Severe ARDS (invasively ventilated): OI ≥ 16 or OSI ≥ 12.3.
Sepsis *(5, 6)*	Adults: life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection.[b] Signs of organ dysfunction include: altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output (5, 20), fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, or laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate, or hyperbilirubinemia. Children: suspected or proven infection and ≥ 2 age- based systemic inflammatory response syndrome criteria, of which one must be abnormal temperature or white blood cell count.
Septic shock *(5, 6)*	Adults: persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP MAP ≥ 65 mmHg and serum lactate level > 2 mmol/L. Children: any hypotension (SBP < 5th centile or > 2 SD below normal for age) or two or three of the following: altered mental state; tachycardia or bradycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children); prolonged capillary refill (> 2 sec) or feeble pulse; tachypnoea; mottled or cool skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia (21).

Summary of linked references :

1. **JAMA** Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area
2. **Circulation** : Association of Inpatient Use of Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers with Mortality Among Patients With Hypertension Hospitalized With COVID-19
3. **NEJM** Renin–Angiotensin–Aldosterone System Inhibitors and Risk of Covid-19
4. **NEJM** Renin–Angiotensin–Aldosterone System Inhibitors in Patients with Covid-19
5. **Lancet** Practical recommendations for the management of diabetes in patients with COVID-19
6. **Cell Metabolism** Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes
7. **Endocrine Reviews** Coronavirus Infections and Type 2 Diabetes—Shared Pathways with Therapeutic Implications
8. SA Department of Health COVID-19 Guideline
9. Sick Day Rules
10. Inpatient & DKA Management
11. Telemedicine
12. National Institute for Communicable Diseases (NICD) COVID-19 Guidelines
13. COVID-19 Coronavirus South African Resource Portal
14. Diabetes UK Coronavirus and diabetes
15. American Diabetes Association: Diabetes and Coronavirus
16. Sick Day Rules
17. Inpatient & DKA Management
18. Telemedicine for Diabetes

(Members section) – Articles of interest

19. **Lancet** Practical recommendations for the management of diabetes in patients with COVID-19
20. **Diabetologia** Prevention and management of COVID-19 among patients with diabetes: an appraisal of the literature
21. **JAMA** Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area
22. **Circulation** : Association of Inpatient Use of Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers with Mortality Among Patients With Hypertension Hospitalized With COVID-19
23. **NEJM** Renin–Angiotensin–Aldosterone System Inhibitors and Risk of Covid-19
24. **NEJM** Renin–Angiotensin–Aldosterone System Inhibitors in Patients with Covid-19
25. **Cell Metabolism** Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes
26. **Endocrine Reviews** Coronavirus Infections and Type 2 Diabetes—Shared Pathways with Therapeutic Implications
27. **OpenSAFELY**: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients.