Brief Practical Recommendations for the Management of Diabetes in Patients with COVID-19

Stefan R Bornstein SR[1,2,3,4], Francesco Rubino[2,5], Kamlesh Khunti K[6], Geltrude Mingrone[2,7,8], David Hopkins[9], Andreas L Birkenfeld[1,2,10,11], Bernhard Boehm[12,13], Stephanie Amiel S[2], Richard IG Holt[14], Jay S Skyler[15], J Hans DeVries[16,17], Eric Renard[18], Robert H Eckel[19], Paul Zimmet[20], George Alberti[21], Josep Vidal[22], Bruno Geloneze[23], Juliana C Chan[24], Linong Ji[25], Barbara Ludwig[1,3,4,26]

[1] Department of Medicine III, University Hospital Carl Gustav Carus, Dresden, Germany.

[2] Department of Diabetes, School of Life Course Science & Medicine, King's College London, London, UK.

[3] University Hospital Zurich, Department of Endocrinology and Diabetology, Zurich, Switzerland.

[4] Paul Langerhans Institute Dresden (PLID) of the Helmholtz Center Munich at the University Hospital Carl Gustav Carus and Faculty of Medicine of the TU Dresden, Dresden, Germany, German Center for Diabetes Research (DZD e.V.), Neuherberg, Germany

[5] King´s College Hospital, Bariatric and Metabolic Surgery, London, UK.

[6] Diabetes Research Centre, University of Leicester, Leicester, UK.

[7] Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy.

[8] Università Cattolica del Sacro Cuore, Rome, Italy.

[9] Institute of Diabetes Endocrinology and Obesity, King's Health Partners, London, UK.

[10] University Hospital Tübingen, Department of Diabetology, Endocrinology and Nephrology, Tübingen, Germany.

[11] Institute for Diabetes Research and Metabolic Diseases of the Helmholtz Centre Munich at the University of Tübingen, Tübingen, Germany

[12] Tan Tock Seng Hospital, Department of Endocrinology, Singapore, Singapore.

[13] Lee Kong Chian School of Medicine, Nanyang Technological University Singapore, Singapore..

[14] Human Development and Health, Faculty of Medicine, University of Southampton, UK.

[15] Diabetes Research Institute, University of Miami Miller School of Medicine, Miami, Florida.

[16] Amsterdam UMC, University of Amsterdam, Endocrinology, Amsterdam, the Netherlands

[17] Profil Institute for Metabolic Research, Neuss, Germany

[18] Montpellier University Hospital and Institute of Functional Genomics, CNRS, INSERM, University of Montpellier, Montpellier, France

[19] University of Colorado Anschutz Medical Campus, Division of Endocrinology, Metabolism, and Diabetes, 12801 East 17th Avenue, Aurora, CO 80045, USA.

[20] Monash University, Department of Diabetes, Central Clinical School, Melbourne, Australia.

[21] Imperial College, London, UK.

[22] Centro de Investigación Biomédica en Red en Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Barcelona, Spain.

[23] Obesity and Comorbities Research Center (OCRC), Laboratory of Investigation in Metabolism and Diabetes (LIMED)/Gastrocentro, Universidade de Campinas (UNICAMP), Campinas – SP, Brazil.

[24] Department of Medicine and Therapeutics, Hong Kong Institute of Diabetes and Obesity and Li Ka Shing Institute of Health Science, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong SAR, China.

[25] Department of Endocrinology and Metabolism, Peking University People's Hospital, Peking University Diabetes Center, Beijing 100044, People's Republic of China.

[26] DFG-Center for Regenerative Therapies Dresden, Technische Universität Dresden, Dresden, Germany.

Abstract

Diabetes is one of the most important comorbidities linked to the severity of all three known human pathogenic coronavirus infections, including SARS-CoV2. Patients with diabetes have an increased risk of severe complications including Adult Respiratory Distress Syndrome (ARDS) and multi-organ failure. Depending on the global region, 20 – 50 % of patients that passed away in the COVID-19 pandemic suffered from diabetes.
Given the importance of the link between COVID-19 and diabetes, we have formed an international panel of experts in the field of diabetes and endocrinology to provide some guidance and practical recommendations in the current situation. We aim to briefly provide insight into potential mechanistic links between the novel corona virus infection and diabetes, present practical management recommendations and elaborate on the special needs of different patient groups.

Introduction

Over the last three months, we have been facing an unprecedented pandemic of COVID-19 caused by a novel coronavirus, SARS-CoV-2, that has now become a global catastrophe. Recent data suggest that majority of people with coronavirus disease 2019 (COVID-19) have comorbidities with diabetes, cardiovascular disease and hypertension being the most prevalent comorbidities [1]. A significant association with worse outcomes is seen in people with these comorbidities [1]. Studies have also shown that COVID-19 is associated with hyperglycemia particularly in the elderly with type 2 diabetes [2]. In view of many uncertainties with COVID-19, a faculty of representatives from primary and specialist care have developed a consensus document on management of diabetes for people at risk of or with confirmed COVID-19 for use in both primary and specialist care. The brief practical recommendations authored by this group were convened virtually. The recommendations are based on queries that have been highlighted by clinical experience, questions that have been raised by colleagues and social media and recommendations guided by using focused-literature review. Clinical decision making in management of diabetes is already complex and in normal circumstances we recommend clinicians follow guidelines for management of people with diabetes. However, these recommendations consider specific points of management of people with diabetes who are at risk or have been infected COVID-19.

Why is COVID-19 infection more frequent and severe in people with diabetes?

Diabetes is a major risk factor for the development of severe pneumonia and a septic course due to virus infections and occurs in around 20% of patients [3, 4]. Also in Middle East Respiratory Syndrome (MERS-CoV) diabetes was identified as a major contributor to disease severity and mortality [5]. There is evidence from epidemiologic observations in regions heavily affected by SARS-CoV2 and reports from the Centers for Disease Control and Prevention (CDC) and other national health centers and hospitals that the rate of diabetes and lethal outcome of COVID-19 is up to 50% higher [6-8]. There are several hypotheses to explain the increased incidence and severity of COVID-19 infection in people with diabetes. In general, people with all forms of diabetes are at increased risk of infection because of defects in innate immunity affecting phagocytosis, neutrophil chemotaxis and cell-mediated immunity; however, it is possible that the high frequency of diabetes in serious cases of COVID-19 reflects the higher prevalence of type 2 diabetes in older people. Furthermore, diabetes in older age is associated with more

cardiovascular disease, which in itself could help to explain the association with fatal outcomes of COVID-19.
There are at least two specific mechanisms that may play a role in COVID-19 infection. First, to gain entry to its target cells, the SARS-CoV2 virus hijacks an endocrine pathway that plays a crucial role in blood pressure regulation, metabolism and inflammation [9]. A specific angiotensin-converting-enzyme, ACE2 has been identified as the receptor for the coronavirus spike protein. ACE2 has protective effects mainly with regard to inflammation. COVID-19 infection reduces ACE2 expression inducing cellular damage, hyperinflammation and respiratory failure [9]. Acute hyperglycemia has been shown to upregulate ACE2 expression on cells which might facilitate viral cell entry. However, chronic hyperglycemia is known to downregulate ACE2 expression making the cells vulnerable to the inflammatory and damaging effect of the virus. Furthermore, the expression of ACE2 on pancreatic beta cells may lead to a direct effect on beta cell function [10-12]. Although these findings have not been verified in humans, this implies that diabetes may not only be a risk factor for a severe form of COVID-19 disease but infection may induce a new onset diabetes [10-12]. Potential beta cell damage caused by the virus leading to insulin deficiency is further supported by the recent observation of Italian colleagues and co-authors who have reported frequent cases of severe diabetic ketoacidosis (DKA) at the time of hospital admission. Another important observation by the co-authors from various centres in different countries affected by COVID-19 is the tremendous insulin requirement in patients with a severe course of the infection. To what extent COVID-19 plays a direct role in this high insulin resistance is unclear. However, the extent of insulin resistance in patients with diabetes as reported by the co-authors seems disproportionate compared to critical illness caused by other conditions.

A second potential mechanism that may explain the link between COVID-19 and diabetes involves the dipeptidyl peptidase-4 enzyme, which is commonly targeted pharmacologically in people with type 2 diabetes. In cell studies, DPP-4 was identified as a functional receptor for human coronavirus-Erasmus Medical Center (hCoV-EMC), the virus responsible for MERS [13]. Antibodies directed against DPP4 inhibited hCoV-EMC infection of primary cells. DPP4 enzyme is an ubiquitously expressed type II transmembrane glycoprotein. It plays a major role in glucose and insulin metabolism but also increases inflammation in type 2 diabetes [14]. Whether these mechanisms also apply to COVID-19 and whether diabetes treatment with DPP-4 inhibitors in clinical practice influences the course of the infection is currently unknown, but, if these translates to SARS-CoV2, the use of these agents could reduce DPP4 levels and may provide therapeutic opportunities to COVID-19 infection [14].

Clinical Implications

The clinical relevance of these two mechanisms is currently uncertain but healthcare practitioners should be aware of their implications for patients with diabetes. We have compiled a simple flowchart for the metabolic screening and management of patients with COVID-19 and diabetes or at risk for metabolic disease. This includes recommendations regarding both the need for primary prevention of diabetes as well as the avoidance of severe sequelae of diabetes triggered by unidentified or poorly managed diabetes (Fig 1). Moreover, special considerations on anti-diabetes drugs commonly used in patients with type 2 diabetes in view of COVID-19 are presented in Table 1.

Metabolic and Glycemic Control
People with diabetes who have not yet been infected with the SARS-CoV2 virus should intensify their metabolic control as needed as means of primary prevention of COVID-19

disease. This includes continuation and strict abidance with adequate control of blood pressure and lipids. Wherever possible, remote consultations using Connected Health models should be utilized in order to reduce exposure. They should also be encouraged to follow general advice from WHO, the Centers for Disease Control and Prevention (CDC) and state and local governments about hand washing and social distancing.
All patients without diabetes and particularly when at high risk for metabolic disease who have contracted the viral infection need to be monitored for new onset diabetes that may be triggered by the virus. All patients with COVID-19 disease and diabetes require a continuous and reliable glycaemic control as suggested in the flowchart.

Management of Hyperglycemia and Associated Metabolic Conditions
Most patients with type 2 diabetes have other components of the metabolic syndrome including hypertension and dyslipidaemia. It is thus of crucial importance to continue with an appropriate antihypertensive and lipid-lowering regimen in all these patients.
It had been suggested that treatment with ACE inhibitors (ACEI) and angiotensin 2 receptor blockers (A2RB) may increase the expression of ACE2 which could accelerate the entry of the virus to the cells [15]. However, as SARS-CoV2 may impair the protective ACE2/Mas receptor pathway and increase deleterious angiotensin-2 activity, the use of ACEI and (A2RB) could protect against more severe lung injury following infection. On the balance of current evidence, we recommend that patients should continue to take their current antihypertensive regimens including ACEI and A2RB. This view is endorsed by a recent position statement from the European Society of Cardiology and the HFSA/ACC/AHA who also strongly recommended continuation of treatment with ACEI and A2RBs [16].
Statins have been shown to restore the reduction of ACE2 induced by high lipids such as LDL or Lp(a) [17]. Indeed, the pleiotropic anti-inflammatory effects of statins have been attributed to its upregulation of ACE2. However, although we believe that modulation of ACE2 expression is associated with both infection and mortality rates in COVID-19, statins should not be discontinued based on the long-term benefit and moreover the potential for tipping the balance towards a cytokine storm by rebound rises in IL-6 and IL-1ß by discontinuation of statins. Given the close links between diabetes and cardiovascular disease, we recommend control of lipid levels in all patients with COVID-19.

There are certain subgroups of people with diabetes who may require specific consideration. Elevated HbA_{1c} in people with type 1 diabetes compromises immune function rendering them more susceptible to any infectious disease. These individuals will need more intense monitoring and supportive therapy to reduce the risk of metabolic decompensation including DKA in particular those taking sodium glucose co-transporter 2 inhibitors (SGLT2). According to the expertise from the co-authors, there has been an increase in the rate of severe DKA in COVID-19 positive patients with established type 1 diabetes but this might in part be due to delayed hospital admission. Thus, it is crucial to make patients with type 1 diabetes aware of this complication and (re-)educate them about typical symptoms, home-measurement of urine or blood ketones if possible, acute behaviour guidelines and liberal and early inquiry of professional medical advice and sick day rules.
Patients who have undergone transplantation of islets, pancreas and/or kidney on immunosuppressive therapy will be at particularly increased risk; in addition, the potential impact of coronavirus infection on pancreatic function in this group is unknown and it will be important to monitor for a recurrence of insulin requirement in those who are insulin independent post-transplant.

The increasing number of patients with type 2 diabetes and concomitant fatty liver disease will most likely have an increased risk for a more pronounced inflammatory response including "cytokine storm" and should be considered at increased risk of severe COVID-19 disease. Therefore, screening for hyperinflammation using laboratory trends (e.g, increasing ferritin, decreasing platelet counts, hsCRP, or erythrocyte sedimentation rate) are of crucial importance and might also help to identify subgroups of patients for whom immunosuppression (steroids, immunoglobulins, selective cytokine blockade) could improve outcome.
The majority of patients with type 2 diabetes are living with overweight or obesity. BMI is an important determinant of lung volumes, respiratory mechanics, and oxygenation during mechanical ventilation, especially in the supine position. Therefore, patients with obesity and diabetes may be at specific risk of ventilatory failure and complications during mechanical ventilation. Indeed, first clinical experience with young patients with obesity and COVID-19 support this notion. Furthermore, individuals with obesity or with diabetes have an altered innate and adaptive immune response, characterized by a state of chronic and low-grade inflammation as characterized by higher levels of the pro-inflammatory leptin and lower anti-inflammatory adiponectin [18]. In addition, obesity is often associated with physical inactivity leading to aggravated insulin resistance. This condition per se impairs immune response against microbial agents including macrophage activation and inhibition of pro-inflammatory cytokines, and leads to a dysregulation of the immune response contributing to obesity-linked complications [19].

Finally SARS-CoV-2 may induce long-term metabolic alterations in patients who had been infected with the virus as has been reported previously with SARS virus [20]. Therefore, a careful cardio-metabolic monitoring of patients who have survived severe COVID-19 disease might be necessary.

Surgical Treatment of Type 2 Diabetes (Metabolic Surgery)
Provision of elective surgical procedures – including metabolic surgery – is being postponed at many hospitals around the world in order to increase capacity for inpatients beds and acute care. *Postponing elective metabolic surgery during the outbreak of COVID-19, however, is advisable regardless of issues of hospital capacity.* In fact, patients with type 2 diabetes and obesity are at increased risk of complications of COVID-19 [19], compounding the potential negative influence of surgical stress in the recovery period. Furthermore, although specific data are not available, there are plausible concerns that pneumoperitoneum and the use of haemostatic instruments during laparoscopy (by far the most common approach used in metabolic surgery due to its ability to reduce morbidity and mortality) may lead to viral aerosolization, thus increasing the risk of Covid- transmission to both patients and staff.

It is unclear if patients with type 2 diabetes who have had metabolic surgery will be protected relative to their peers who have not undergone surgical treatment simply due to better glycemic control [21]. However, metabolic surgery could induce nutritional deficiencies, including reduced absorption of vitamins and micronutrients, which play important roles in the regulation of immune and stress response [22]. Although there are no data to date to suggest that patients who had metabolic surgery are at greater risk of infection and/or complications from COVID-19, it is advisable that these patients receive particular attention and close monitoring.

Implications for Healthcare Professionals (HCPs) with diabetes
It is of particular importance to highlight the subgroup of people with diabetes who work as HCPs. Given the expectation that COVID-19 infection may be much more common among the sick than is diagnosed, HCP with diabetes should be deployed away from front line clinical

duties where possible. Where this is not possible or desirable, particular care to use high grade protection is essential or even increased protection levels should be used.

Special Considerations on Use of Diabetes Drugs

While it may be of general importance to optimise glycemic control to reduce the risk of severe COVID-19 disease, there are some specific considerations around treatment modality (Tab. 1). Although, lactic acidosis associated with metformin or euglycemic or moderate hyperglycemic diabetic ketoacidosis associated with SGLT-2 inhibitors are rare events, we recommend these drugs should be discontinued for patients with severe symptoms of COVID-19 to reduce the risk of acute metabolic decompensation [23]. Importantly, discontinuing these drugs is not recommended prophylactically for out-patients with diabetes without any symptoms of infection or in the absence of evidence for a serious course of COVID-19. Also, at present, there is no convincing evidence that DPP-4 inhibitors should be discontinued. Further analyses on affected patients with various diabetes treatment and COVID-19 may allow to elucidate the effects of DPP-4 inhibitors [14]. Importantly, where drugs are discontinued, the alternative treatment of choice is insulin where this is feasible [23].

Given the multiple stresses associated with COVID-19 including but not limited to respiratory failure, the defects in insulin secretion and the frequent occurrence of diarrhoea and sepsis, most patients will require insulin and especially since many cases are reported with very high insulin consumption, this will need to be managed by intravenous infusion [24]. Considerable care is required in fluid balance as there is a risk that excess fluid can exacerbate pulmonary oedema in the severely inflamed lung. Furthermore, potassium balance needs to be considered carefully in the context of insulin treatment as hypokalaemia is a common feature in COVID-19 (possibly related to hyperaldosteronism induced by high levels of angiotensin 2) and may be exacerbated following initiation of insulin [24].

We do realize that all our reflections are based on expert opinion, awaiting the outcome of randomized clinical trials. Executing clinical trials under challenging circumstances has been proven feasible with COVID-19 and trial networks to provide evidence based therapies are arising [25]. It will be of importance to look at subgroups with diabetes in particular to investigate if some of the various approaches would be particularly effective in diabetes or ask for particular attention in patients with diabetes due to potential antidiabetic effects [26].

Contributors

All authors did the literature search and drafted sections of the manuscript. SRB and BL combined and edited the drafts, and supervised the manuscript, BL prepared table and figure of the manuscript. All authors subsequently and repeatedly revised the final manuscript.

Declaration of interests

This article was not funded by any organisation. SA reports that she serves on Advisory Boards for Novo Nordisk, Abbott and Medtronic. All other authors declare no competing interests.

Search strategy and selection criteria

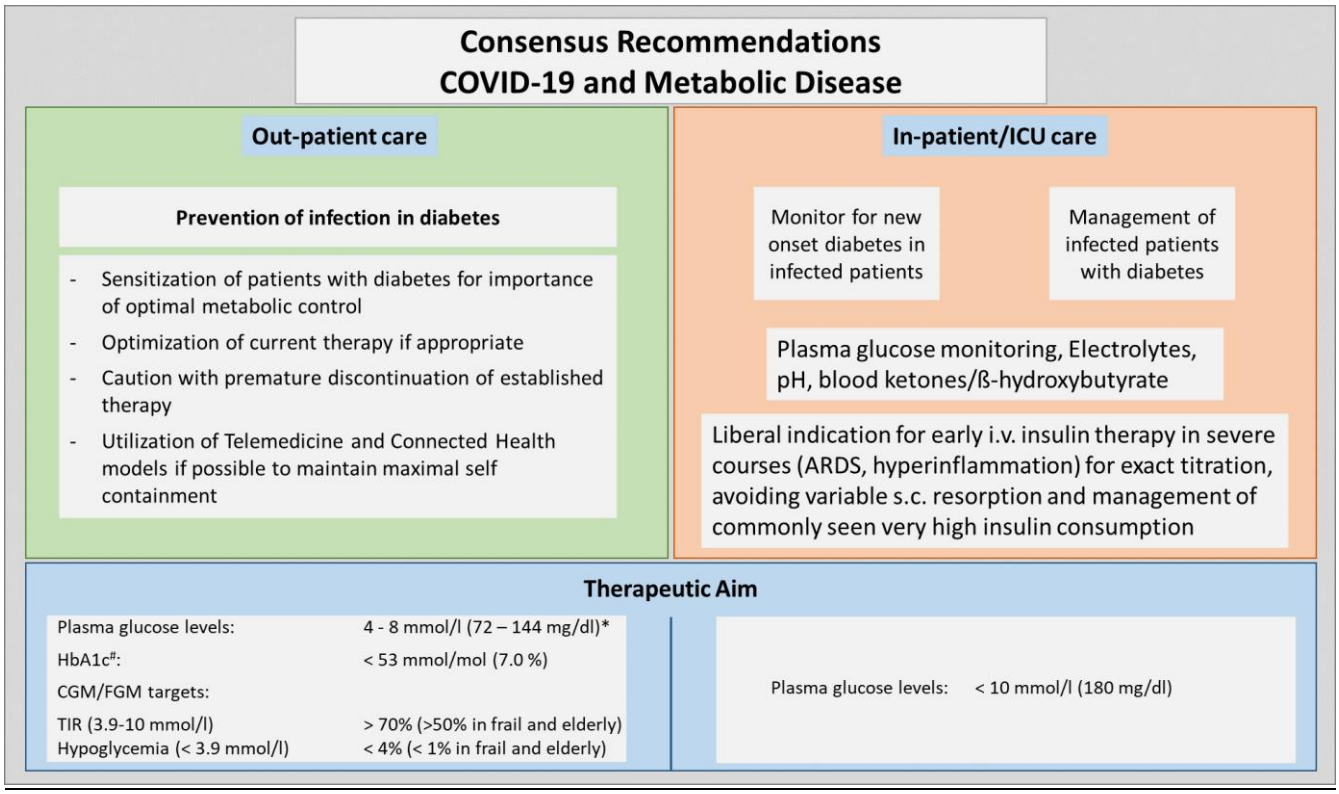
We identified the references for this publication through searches of PubMed for articles published between Apr 29 2009, and April 5, 2020, using combinations of the terms "coronavirus", "COVID-19", "SARS-CoV-2", "nCoV", "diabetes", "risk factors", "severe acute respiratory syndrome", "acute respiratory distress syndrome", and "co-morbidities". We reviewed guidelines for the management of COVID-19 published by WHO, ADA, and the US Centers for Disease Control and Prevention. We added articles through searches of the authors' personal files. We also reviewed relevant references cited in retrieved articles. Articles published in English, Italian and Chinese were included. The final reference list was generated on the basis of relevance to the topics covered in this publication, with the aim of highlighting the multiple challenges the health care professionals from practitioners to intensive care staff might face in the management patients with diabetes and at risk of or with COVID-19, and providing practical recommendations for the care of this vulnerable subgroup.

References

1. Chen Y, Gong X, Wang L, Guo J. Effects of hypertension, diabetes and coronary heart disease on COVID-19 diseases severity: a systematic review and meta-analysis. *medRxiv* 2020: 2020.03.25.20043133.
2. Xue T, Li Q, Zhang Q, et al. Blood glucose levels in elderly subjects with type 2 diabetes during COVID-19 outbreak: a retrospective study in a single center. *medRxiv* 2020: 2020.03.31.20048579.
3. Hespanhol VP, Barbara C. Pneumonia mortality, comorbidities matter? *Pulmonology* 2019.
4. Zou Q, Zheng S, Wang X, et al. Influenza A-associated severe pneumonia in hospitalized patients: Risk factors and NAI treatments. *International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases* 2020; **92**: 208-13.
5. Memish ZA, Perlman S, Van Kerkhove MD, Zumla A. Middle East respiratory syndrome. *Lancet (London, England)* 2020; **395**(10229): 1063-77.
6. https://www.cdc.gov/mmwr/Novel_Coronavirus_Reports.html. 2020.
7. https://www.iss.it/en/coronavirus. 2020.
8. Remuzzi A, Remuzzi G. COVID-19 and Italy: what next? *Lancet (London, England)* 2020.
9. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell* 2020.
10. Bindom SM, Lazartigues E. The sweeter side of ACE2: physiological evidence for a role in diabetes. *Molecular and cellular endocrinology* 2009; **302**(2): 193-202.
11. Roca-Ho H, Riera M, Palau V, Pascual J, Soler MJ. Characterization of ACE and ACE2 Expression within Different Organs of the NOD Mouse. *International journal of molecular sciences* 2017; **18**(3).
12. Yang JK, Lin SS, Ji XJ, Guo LM. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. *Acta diabetologica* 2010; **47**(3): 193-9.
13. Raj VS, Mou H, Smits SL, et al. Dipeptidyl peptidase 4 is a functional receptor for the emerging human coronavirus-EMC. *Nature* 2013; **495**(7440): 251-4.
14. Iacobellis G. COVID-19 and diabetes: Can DPP4 inhibition play a role? *Diabetes research and clinical practice* 2020; **162**: 108125.
15. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *The Lancet Respiratory medicine* 2020.
16. de Simone GNMoECoH. Position Statement of the ESC Council on Hypertension on ACE-Inhibitors and Angiotensin Receptor Blockers https://www.escardio.org: European Society of Cardiology; 2020.
17. Shin YH, Min JJ, Lee JH. The effect of fluvastatin on cardiac fibrosis and angiotensin-converting enzyme-2 expression in glucose-controlled diabetic rat hearts. 2017; **32**(5): 618-27.
18. Andersen CJ, Murphy KE, Fernandez ML. Impact of Obesity and Metabolic Syndrome on Immunity. *Advances in nutrition (Bethesda, Md)* 2016; **7**(1): 66-75.
19. Luzi L, Radaelli MG. Influenza and obesity: its odd relationship and the lessons for COVID-19 pandemic. *Acta diabetologica* 2020.
20. Wu Q, Zhou L, Sun X, et al. Altered Lipid Metabolism in Recovered SARS Patients Twelve Years after Infection. 2017; **7**(1): 9110.
21. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial. *Lancet (London, England)* 2015; **386**(9997): 964-73.

22. Gombart AF, Pierre A, Maggini S. A Review of Micronutrients and the Immune System-Working in Harmony to Reduce the Risk of Infection. *Nutrients* 2020; **12**(1).
23. https://www.cebm.net/covid-19/managing-diabetes-during-the-covid-19-pandemic/. 2020.
24. Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Critical care medicine* 2013; **41**(2): 580-637.
25. Cao B, Wang Y, Wen D, et al. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. *The New England journal of medicine* 2020.
26. Wondafrash DZ, Desalegn TZ, Yimer EM. Potential Effect of Hydroxychloroquine in Diabetes Mellitus: A Systematic Review on Preclinical and Clinical Trial Studies. 2020; **2020**: 5214751.

Figure 1. Flowchart for Metabolic Screening and Type 1 and 2 Diabetes Management of Patients with COVID-19



* Target levels for lower plasma glucose may be adjusted to 5 mmol/l (90 mg/dl) in frail patients
# HbA1c testing may not be possible at the time, but previous measurements if available allow for differentiation of chronic and acute decompensation

(HbA1c- hemoglobin A1c; TIR- time in range)

Table 1. Special Considerations in suspected or COVID-19 positive Patients with Type 2 Diabetes

Therapy	Special considerations
Metformin	• Dehydration and lactic acidosis likely if dehydrated. Stop and follow sick day rules • During illness monitor renal function as high risk of CKD and AKI
SGLT2 inhibitors Canagliflozin Dapagliflozin Empagliflozin	• Dehydration and DKA risk during illness. Stop therapy and follow sick day rules • Avoid starting during respiratory illness • Monitor renal function including for AKI
GLP-1 receptor agonists Albiglutide Dulaglutide Exenatide-extended release Liraglutide Lixisenatide Semaglutide	• Dehydration likely to lead to serious illness – monitor closely • Encourage adequate fluid intake and regular meals
DPP-4 inhibitors Alogliptin Linagliptin Saxagliptin Sitagliptin	• Well tolerated and can be continued
Insulin	• Do not stop insulin • Encourage regular SMBG 2-4 hourly or CGM • Carefully adjust therapy if appropriate to reach therapeutic goals according to diabetes type, co-morbidities, and current health status (fig. 1)
Utilize Connected health models and telemedicine where possible to continue regular reviews and self-management education programs virtually and ensure patients are adherent to therapy	
Consider potentially metabolically interfering effects of drugs used in the treatment of COVID-19 disease.	
Abbreviations: SGLT- sodium-glucose-co-transporter; GLP- glucagon-like peptide; DPP- dipeptidyl peptidase; CKD- chronic kidney disease; AKI- acute kidney injury; DKA- diabetic ketoacidosis; SMBG- self-monitoring-blood-glucose; CGM- continuous glucose monitoring;	