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Review

Management of patients with diabetes and obesity in the COVID-19 era: Experiences and learnings from South and East Europe, the Middle East, and Africa



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ARTICLE INFO

Article history:

Received 4 November 2020

Received in revised form

2 December 2020

Accepted 7 December 2020

Available online 10 December 2020

Keywords:

Diabetes

Obesity

ABSTRACT

The COVID-19 pandemic has had a major effect on healthcare during 2020. Current evidence suggests that, while individuals with diabetes and obesity are no more prone to SARS-CoV-2 infection than those without, the risk of hospitalisation if someone has diabetes or obesity and then contracts COVID-19 is three times higher – and 4.5 times higher if they have diabetes and obesity. We assembled a panel of experts from South and East Europe, the Middle East, and Africa to discuss the challenges to management of diabetes and obesity during and post the COVID-19 pandemic. The experience and learnings of this panel cover a heterogeneous patient population, wide range of clinical settings, healthcare organisations, disease management strategies, and social factors. We discuss the importance of timely and effective disease management via telemedicine, providing reassurance and guidance for patients unable or unwilling to visit healthcare settings at this time. We

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<https://doi.org/10.1016/j.diabres.2020.108617>

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COVID-19
Pandemic
Management
Consensus

address the use of novel therapies and their role in managing diabetes and obesity during the pandemic, as well as the importance of controlling hypoglycaemia and preventing cardiovascular complications, particularly in vulnerable people. Finally, we consider post-COVID-19 management of diabetes and obesity, and how these learnings and experiences should impact upon future clinical guidelines.

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1. Introduction

Coronavirus disease 2019 (COVID-19) was declared a pandemic by the World Health Organization (WHO) in March 2020. Nine months later, the underlying virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), continues to spread and have a devastating effect on global healthcare and economies.

Reports have shown that the risk of severe disease and/or death from COVID-19 is exacerbated in people with underlying factors such as older age or chronic conditions including diabetes, obesity, hypertension, and cardiovascular (CV) diseases [1,2]. An apparent gender disparity has also been observed, with a significantly greater risk of mortality following SARS-CoV-2 infection in men than in women [3]. While the prevalence of SARS-CoV-2 infection among people with diabetes appears relatively low [4], the risk of hospitalisation if a patient has diabetes or obesity (body mass index [BMI] ≥ 30 kg/m²) and then contracts COVID-19 is three times higher compared with people without diabetes or obesity [5]. Furthermore, if someone has both of these conditions, or severe obesity (BMI ≥ 40 kg/m²), the risk is 4.5 times higher compared with those without these conditions [5]. Approximately 30% of hospitalised patients who died from COVID-19 had diabetes or uncontrolled hyperglycaemia [6–8], and >40% of patients hospitalised due to COVID-19 can present with obesity as a comorbidity [9]. An association between hyperglycaemia at the time of hospital admission for COVID-19 and disease severity has been observed; however, it is not yet known whether this hyperglycaemia is a result of, or a contributing factor to, the severity of COVID-19 [10]. It therefore appears that, while diabetes may not increase the risk of SARS-CoV-2, it may worsen the outcome of COVID-19 [4]. The

physiological mechanisms driving the link between diabetes or obesity with COVID-19 are not clear, but an immunocompromised status, and an exacerbated inflammatory state and its frequent coagulation response, as well as some peculiarities of SARS-CoV-2 to affect β -cells – causing a reduction of insulin secretion and inducing a significant production of cytokines, causing insulin resistance – are likely to play a role, as is increased vascular permeability, a known complication of diabetes [11,12]. Furthermore, diabetes is associated with increased lung expression of angiotensin-converting enzyme 2 (ACE2; the receptor by which SARS-CoV-2 seems to infect cells) and increased circulating levels of proteases that facilitate SARS-CoV-2 fusion with host cells, indicating that it may be easier for the virus to infect the lung of a patient with diabetes compared with an individual without diabetes [13,14].

The contribution of obesity and diabetes to COVID-19 disease severity and mortality is recognised globally [15–18] and, accordingly, local guidelines and recommendations have been produced [19–22] to help the medical community tailor the management of their patients to the additional challenges posed by the pandemic. However, given the rapidly evolving COVID-19 landscape, current advice is mostly based on clinical experience, and there will be a need in due course for clear, practical, evidence-based guidelines. In the meantime, it is just as important for the medical community to continue sharing best practice for the management of COVID-19 based on experiential learning, and particularly for those patients who are most prone to severe forms of COVID-19. Here, we summarise the key clinical learnings and practical advice from an expert panel of clinicians working in South and East Europe, the Middle East, and Africa on the management of diabetes and obesity during the COVID-19 pandemic, as well as a perspective on the post-COVID-19 era. The experience

and learnings of this expert panel cover a heterogeneous patient population, as well as a wide range of clinical settings, healthcare organisations, disease management strategies, and social factors.

2. Methodology

An international panel was assembled with experts from Algeria, Croatia, Israel, Italy, Poland, Romania, Russia, Serbia, Slovenia, South Africa and Turkey. A Virtual Expert Forum Meeting took place on 24th August 2020, in which we discussed our experiences and learnings relating to the management of patients with diabetes and/or obesity during and after the COVID-19 pandemic, as well as relevant local and national guidelines. A further meeting was held on 3rd September 2020, in which the experiences and opinions from the Virtual Expert Forum Meeting were refined, and a consensus was reached. The manuscript was drafted based on the outputs of these meetings and reviewed by all authors. The manuscript does not have the claim to be a systematic review, and the recommendations are based on the experts' opinion.

3. Management of patients with diabetes and obesity during the COVID-19 pandemic

In response to the COVID-19 pandemic, governments across South-East Europe, the Middle East, and Africa, much like the rest of the world, have imposed quarantine measures and national/local lockdowns. A quick and effective response to the pandemic in many countries within these regions, however, is challenging given local limitations such as the lack of infrastructure, limited resources, conflicts, and poor preparedness capacity [23]. As a result, patients with diabetes and obesity have had reduced contact with their healthcare providers and have experienced an overall decline in the quality of management of their disease. Under these conditions, treatment adherence, routine glucose monitoring, and healthy eating habits are difficult to maintain, and patients are generally performing less exercise. To counteract these tendencies, in some countries, plans to develop a network of centres dedicated to patients with diabetes and COVID-19 were proposed [24].

Telemedicine, predominantly in the form of virtual clinics between patients and physicians, and online/phone consultations, has played a critical role in disease management during the COVID-19 pandemic. In some countries, telemedicine was implemented relatively quickly while, in other countries that were short of pre-existing infrastructure, it took longer to establish a reliable telemedicine service, potentially at the expense of a decline in disease management and patient wellbeing. For instance, in Romania, an online application, Telediabet.ro, has been developed to educate patients about the importance of monitoring their diabetes and comorbidities while also providing free telemedicine consultations, and another application to provide guidance regarding complications, diet, and wellbeing is in development. When lockdown began in Turkey, the Turkish Diabetes Foundation initiated a telemedicine service in which diabetologists, dietitians, and nurses replied to individual questions from

patients via mail, telephone, and online contacts. During this service, the most common issues were diabetic distress and titration of insulin dosages. Data privacy and accuracy were also key challenges when setting up the telemedicine systems. Another example comes from Italy, where these factors, as well as clinical safety issues and technical tools for clinicians, are considered in a telemedicine guideline from the Italian Ministry of Health, and some scientific societies have generated a protocol for the management of patients with diabetes via telemedicine during the COVID-19 pandemic. Although telemedicine is not expected to replace physical clinics in the post-pandemic future, it is likely that it will remain in use as an additional tool to help disease management, particularly as it offers benefits to the patient, such as reduced travel time and cost, as well as the opportunity for more frequent monitoring. Care should be taken to arrange an in-person visit for issues that prove difficult to resolve via telemedicine.

Notwithstanding the feat of implementing supportive telemedicine systems, patients considered in need of in-person consultations or hospitalisation should be encouraged to attend. In Serbia, for example, although outpatient services reopened at the beginning of June, only half of patients have attended these services, as the rest are afraid to visit the clinic. Consequently, there was a delay in the effective treatment of their disease and complications, and a large rise in the number of patients with diabetes visiting the emergency unit – a return to normal disease management is needed. However, convincing patients to attend clinics/hospitals is not straightforward, since they are generally afraid of SARS-CoV-2 infection and, consequently, avoid hospitals/clinics that they feel might place them at high risk of infection. Generally, patients with diabetes and obesity who have not contracted COVID-19 should continue to be treated according to global and local guidelines, with frequent blood glucose monitoring and a reminder of the value of healthy eating, exercise, and vitamin/mineral supplementation. In Israel, for example, the decision to give vitamin D was taken very early, before strong evidence was available to support its use in the management of SARS-CoV-2 infection (potential mechanisms by which vitamin D may reduce the risk of COVID-19 include lowering viral replication rates, the induction of antimicrobial peptides, and regulation of inflammatory responses [25,26]).

During the pandemic, an increase in hypoglycaemia, and even in severe hypoglycaemia, in patients with type 2 diabetes has also been reported in our countries, consistent with other reports in the literature [27]. It is likely that reduced glucose monitoring and lack of physician consultations might be driving this finding. Hypoglycaemia management is critical to the successful treatment of patients with diabetes and should be carefully monitored, particularly in vulnerable people, during the pandemic. The use of novel ultra-long-acting basal insulins should be promoted, as they provide glycaemic control with low hypoglycaemic risk in patients with type 1 or type 2 diabetes [28]. In addition, from our experience and reported data [29], patients with COVID-19 with (or without) diabetes often exhibit hyperglycaemia upon hospital admission, which is likely to be attributed to direct virus-induced decrease in insulin secretion and increase in insulin resistance by SARS-

CoV-2 [11]. Given the poor prognosis of COVID-19 in patients with hyperglycaemia [4,10], it seems imperative to gain control over hyperglycaemic excursions during the early phase of COVID-19 infection. This is particularly important for vulnerable populations, including frail patients and those with gestational diabetes; patients with type 1 diabetes should also be reminded of the risk of diabetic ketoacidosis should they experience excessive hyperglycaemia. Conversely, a recently published study in Italy demonstrated that patients with type 1 diabetes using flash glucose monitoring during lockdown experienced significantly fewer hypoglycaemic events and time below range, while no changes were observed in time in range or time above range [30]. These changes in glycaemic control were associated with increased access to food (particularly sweets) during lockdown.

Furthermore, given that diabetes and obesity are often associated and are accompanied by other cardiometabolic risk factors, a comprehensive approach should be implemented in patients with COVID-19 and those conditions toward a reduction of their cardiometabolic risk. This is indeed highlighted by reports calling for congruence between treatment approach and the significant cardiometabolic potential of COVID-19 [15]. According to the CORONADO study, BMI was positively associated with a combined outcome of tracheal intubation and/or death within 7 days of admission in patients with COVID-19 and diabetes [31]. This places particular emphasis on targeting patients with both diabetes and obesity, thereby increasing their monitoring, priority in testing, and treatment to control comorbidities [2]. Consideration should also be given to whether individuals with diabetes and obesity should be prioritised for national COVID-19 vaccination programmes, when they are available.

Generally, in patients with type 2 diabetes, glucose-lowering medications (and medications for other metabolic conditions) must be reviewed carefully, and insulin therapy should be initiated early, especially in the presence of acute illness and if corticosteroid therapy is being considered. Telemedicine can be used to initiate, monitor, and titrate insulin accordingly. Some guidance suggests that modifying glucose-lowering drugs may be beneficial (particularly reducing use of metformin and sodium/glucose cotransporter-2 [SGLT-2] inhibitors, to reduce the risk of acute metabolic decompensation, such as lactic acidosis and diabetic ketoacidosis, and increasing use of incretin-based therapies due to their overlapping mechanisms with SARS-CoV-2), but that insulin treatment should be continued under all scenarios [19,22,32–36]. In Croatia, during the pandemic, guidance was updated so that patients with BMI > 30 kg/m² could be prescribed glucagon-like peptide-1 receptor agonists (GLP-1 RAs; previously only accessible to patients with BMI > 35 kg/m²) and, for those with type 2 diabetes and established CV disease, GLP-1 RAs could be given if their BMI was > 28 kg/m². Therefore, the use of GLP-1 RAs has been extended to help control weight gain and glycaemia in patients with COVID-19 and diabetes. Given that severe COVID-19 can precipitate CV complications (myocardial infarction, myocarditis, heart failure, and arrhythmias), the cardioprotective effects of GLP-1 RAs [37] should also be considered when individualising treatment regimens.

4. Post-COVID-19 management of patients with diabetes and obesity

It is reasonable to believe that established, safe, and effective vaccines against SARS-CoV-2 will herald a post-COVID-19 era. This eagerly awaited period will be celebrated, but it should also be treated as a time for reflection, for consolidating our learnings, and improving not only the intricacies but the foundations of the management of our patients. In many patients during the pandemic, we have observed a decline in good general self-management (e.g. lack of exercise, unhealthy eating, non-compliance with treatment), and it might take time for patients to re-familiarise themselves with good practice. It is, therefore, conceivable that we might observe a rise in the burden of diabetes and obesity complications after the pandemic. Accordingly, the allocation of resources will need to be carefully prioritised, and we believe efforts will need to be focussed on those patients who have had, and might continue to have, reduced access to health-care (e.g. adolescents and the elderly). Conversely, patients who contracted and recovered from COVID-19 will also need careful attention. We envisage a further challenge to the healthcare system in the form of a 'post-COVID-19 syndrome' where people continue to suffer from poor health, including lung, cardiometabolic, and mental health complications, following acute COVID-19; care teams will need to prepare for this. The shortage, however, of diabetes-trained healthcare professionals, acknowledged during the pandemic, will need to be addressed, possibly through training of medical staff, to help effectively manage these patients and achieve glucose control – particularly in patients in the intensive care unit, where poor glucose control may be a key factor in poor outcomes [10,15].

The successful treatment of COVID-19 might rely on addressing not only the respiratory aspects of the disease but also the exacerbation of comorbidities and their complications. Similarly, the treatment of diabetes should not only address fluctuations in glucose levels but the full suite of concomitant cardiometabolic factors that affect disease prognosis. To this goal, we believe modern glucose-monitoring devices and glucose-lowering medications with additional weight and CV/renal benefits (e.g., GLP-1 RA and SGLT-2 inhibitors) will be key for the future management of diabetes and obesity. In our countries, access to these innovative drugs must be improved and, where they are available, their use should be broader and not exclusive to the most vulnerable of patients. Although there is some awareness of modern alternatives, many physicians across our countries continue to prescribe only those drugs they are most familiar with. We suggest that emphasis on earlier management of diabetes and obesity across all patients, leveraging all available modern medications, would help address clinical inertia, improve prognosis, and lower the overall risk of infection, thus also helping patients become less vulnerable to the daunting potential of future pandemics.

The importance of weight control in patients with diabetes, and clearly in those with concomitant obesity, cannot be underestimated. Between 1980 and 2015, the prevalence of obesity in the Middle East increased from 12% to 20%,

and in Africa from 6% to 13%, and rising trends are likely to continue unless significant measures are taken [38]. After the COVID-19 pandemic, particularly in patients with type 2 diabetes, there will be a need to raise individual awareness of how weight gain was managed during the pandemic, the consequences of uncontrolled weight gain, and the necessary steps to achieve a healthy lifestyle. Importantly, a more aggressive treatment approach to obesity is needed. As recently emphasized, obesity cannot just be seen as a risk factor for diabetes but also as a disease itself, and the deserved spotlight it has gained during the COVID-19 pandemic must continue [39].

Telemedicine and technology have been quickly recognised as invaluable tools during the pandemic, and their use should be maximised and integrated with in-presence visits as we move into the post-pandemic era, helping patients gain prompt access to medical guidance but also to ease the burden on healthcare professionals in primary and secondary care. Online patient education programmes and smartphones should be better utilised to improve patient and disease management, covering matters such as introducing flash/continuous glucose monitoring into patient regimens and dosing guidance for new treatments. Emphasis on raising awareness of the impact of weight gain, CV events, and other organ damage through digital platforms is also needed. We encourage pharmaceutical and medical device companies to take a lead role to help further develop effective and secure online consultation systems, to support patient education where the need is highest, and to provide greater access to the latest advances in diabetes treatment and technology.

5. Impact of COVID-19 on scientific guidelines

In our countries, most specialists dealing with diabetes and obesity are using the International Diabetes Federation and American Diabetes Association/European Association for the Study of Diabetes guidelines, along with local or national guidelines. In addition, several national guidelines and recommendations have been developed during the COVID-19 pandemic, to complement those issued at international level. For instance, an important point to take into further account is the change to how we should monitor glycaemic control, given that we and others have observed a reduction in the use of HbA_{1c} to track diabetes control during the pandemic [40]. Clear, practical evidence-based guidelines for the management of patients with diabetes and obesity with or without COVID-19 are indeed needed, and the adoption of existing international guidelines must be promoted to any extent possible.

We emphasise that the reduction of cardio-renal-metabolic risk is even more important now during the COVID-19 era than before and, in parallel, increased guidelines implementation is needed, for better disease control and to prevent diabetes- and obesity-related acute and chronic complications. Future research will be needed to understand the association and risks between diabetes and obesity and infectious diseases, such as COVID-19. This will allow an individualised approach based on the risk level for contracting COVID-19 or adversely affecting COVID-19 out-

comes. It will also help determine whether patients with diabetes should be prioritised for a COVID-19 vaccine when they become available. Establishing clear treatment pathways and possible combinations of antidiabetic treatment and current medication for COVID-19 will be critical, as there is, for example, limited long-term evidence on the safety and efficacy of COVID-19 off-label drugs, such as hydroxychloroquine, in patients with diabetes [34,41].

Identified gaps that should be stressed in any prospective guidelines for patients with COVID-19 and diabetes and obesity are shown in Table 1 and Table 2, respectively.

6. Final thoughts

The COVID-19 pandemic has dramatically changed the global healthcare landscape, and many questions are being raised, from how patients with diabetes and obesity should access ongoing care, to the optimal treatment of patients contracting COVID-19, to what we should expect after the pandemic subsides. Sub-optimal management of diabetes and obesity are likely to persist following lockdowns and to worsen in places where lockdowns need to remain or be reinstated; therefore, the medical community will need to be prepared to tackle the significant burden of diabetes- and obesity-related complications that will ensue after the pandemic. In this article, we provide insights, learnings, and a consensus of opinion into these topics and beyond, specific to our countries within South and East Europe, the Middle East, and Africa, but we hope our observations will have broader relevance across the medical community.

Sharing meaningful clinical experience across the different countries – as has happened within our expert panel – not only to specialists but to healthcare professionals in general is even more important now during the COVID-19 era than before. For instance, this will help to prevent increased episodes of severe hypoglycaemia and to more effectively control hyperglycaemia due to unhealthy lifestyle or poor therapeutic adherence. Even more importantly, it will help to identify risk factors for unfavourable outcomes of the infection, as some patients have no symptoms at all while others suffer badly. Medical response has to adapt quickly to the evolving COVID-19 landscape, and the need for timely advice and sharing of best practice is at its highest. The implementation of key learnings will need to be swift to improve disease control and prevent acute and chronic complications in our patients. Importantly, now more than ever, a comprehensive approach to the reduction of cardiometabolic risk is needed in patients with diabetes and obesity with or without COVID-19.

Author contributions

All authors provided input at the Virtual Expert Forum Meeting and follow-up meeting. Based on the output of these meetings, the manuscript was prepared with valuable support from Watermeadow Medical. All authors contributed to the critical revision of the article and approved the final article.

Table 1 – Identified gaps that should be addressed in prospective guidelines for patients with COVID-19 and diabetes.

- The early uptake of insulin and modern glucose monitoring and their use in hospitalised patients and those in the ICU
- The guidance for different settings (e.g., primary care, hospitalisation, ICU) and patients' groups (e.g., type 1 diabetes, type 2 diabetes, pre-diabetes, gestational diabetes)
- Updated treatment algorithms and glucose-monitoring guidelines accounting for differences in regional and socioeconomic factors, as well as in access to healthcare (including the latest drugs and technology)
- Optimal incorporation of telemedicine into management strategies
- Updated recommendations for the overall reduction in cardiometabolic risk
- Clear indications of which patients should be treated as outpatients and which should be admitted to hospital
- Consideration as to whether patients with diabetes should be prioritised for national COVID-19 vaccination programmes

ICU, intensive care unit.

Table 2 – Identified gaps that should be addressed in prospective guidelines for patients with COVID-19 and obesity.

- Clear, practical evidence-based recommendations for the management of patients with or without COVID-19
- Updated recommendations for the overall reduction in cardiometabolic risk
- A more aggressive treatment approach to obesity is needed
- Clear indications of which patients should be treated as outpatients and which should be admitted to hospital
- Consideration as to whether individuals with obesity should be prioritised for national COVID-19 vaccination programmes

Funding statement

The authors thank Julie Sawyers of Watermeadow Medical, and Steven Barberini on behalf of Watermeadow Medical, an Ashfield company, part of UDG Healthcare plc, funded by Novo Nordisk, for developing this manuscript based on their discussions at the Virtual Expert Forum Meeting and follow-up meeting, for which the experts received consultancy fees from Novo Nordisk. Editing and submission support were provided by Helen Marshall of Watermeadow Medical, an Ashfield company, part of UDG Healthcare plc, funded by Novo Nordisk.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: 'FG has served as an advisory board member for AstraZeneca; has served as a research investigator for Eli Lilly; has served as a speaker for AstraZeneca and Eli Lilly; has received consulting fees from AstraZeneca, Sanofi, Abbott, Boehringer Ingelheim, Eli Lilly, MedImmune, Merck Sharp & Dohme, Novo Nordisk, and Roche Diabetes Care; and has received grants from Lifescan, Eli Lilly, and Takeda. SB has received grant funding from Merck Sharp & Dohme; has received educational grants from Merck Sharp & Dohme, Novo Nordisk, Sanofi, and Boeringer Ingelheim; has received speaker honorarium from Bayer, Novo Nordisk, Astra Zeneca, Merck Sharp & Dohme, Abbott, and Novartis; and received travel grants from Merck Sharp & Dohme, Bayer and Boeringer Ingelheim. LC has nothing to declare for this manuscript. SD has been involved in international randomized clinical trials with Novo Nordisk, Sanofi, Takeda, and AstraZeneca; and advisory boards for Novo Nordisk, Sanofi, Astra Zeneca, Bristol Myers Squib, Boehringer Ingelheim, Merck Sharp & Dohme, Novartis, and Servier. GG serves on advisory panels for AbbVie, AstraZeneca, Merck Sharp & Dohme, Novo Nordisk, Pfizer, and Sanofi; and is a member of speakers' bureaus for Amgen, AstraZeneca, Berlin Chemie, Boehringer Ingelheim, Eli Lilly, LifeScan, Merck Sharp & Dohme, Novartis, Novo Nordisk, Sanofi, Servier, and Takeda. AJ has served as a consultant and is on speakers' bureaus for AstraZeneca, Boehringer Ingelheim, Eli Lilly, Merck Sharp & Dohme, Novo Nordisk, Medtronic, and Sanofi. NL has nothing to declare for this manuscript. NN has lectured, received honoraria, participated in conferences, advisory boards and clinical trials sponsored by several pharmaceutical companies, including Novo Nordisk, Sanofi, Novartis, and Eli Lilly but declares no conflicts of interest with the drafting of this manuscript. DR is director of Vuk Vrhovac University Clinic for Diabetes, Endocrinology and Metabolic Diseases at Merkur University Hospital, Zagreb, Croatia. He is the president of Croatian Society for Diabetes and Metabolic Disorders of Croatian Medical Association. He serves as an Executive Committee member of the Croatian Endocrine Society, the Croatian Society for Obesity, and the Croatian Society for Endocrine Oncology. He was a board member and secretary of IDF Europe and is currently the Chair of the IDF YLD Programme. He has served as an Executive Committee member of the Diabetes

and Nutrition Study Group of the EASD and currently serves as an Executive Committee member of the Diabetes and Cardiovascular Disease Study Group of the EASD. He has served as Principal Investigator or Co-Investigator in clinical trials for AstraZeneca, Eli Lilly, Merck Sharp & Dohme, Novo Nordisk, Sanofi Aventis, Solvay, and Trophos. He has received honoraria for speaking or advisory board engagements and consulting fees from Abbott, Amgen, AstraZeneca, Bauerfeund, Bayer, Boehringer Ingelheim, Eli Lilly, Lifescan – Johnson & Johnson, Novartis, Novo Nordisk, Merck Sharp & Dohme, Pfizer, Pliva, Roche, Salvus, Sanofi Aventis, and Takeda. APS has given talks, attended conferences, and participated in advisory boards and clinical trials sponsored by Astra Zeneca, Merck Sharp & Dohme, Medtronic, Novo Nordisk, Roche Diabetes, Sanofi, Boehringer Ingelheim, Coca-Cola, Eli Lilly and Janssen. She is currently Vice-President, National Diabetes Commission, Ministry of Health, Romania. IR has attended advisory boards for AstraZeneca, Eli Lilly and Company, Merck Sharp & Dohme, Novo Nordisk, and Sanofi. He has acted as a consultant for AstraZeneca, Insuline Medical, Medial Early-Sign Ltd, CamerEyes Ltd, Exscopia, Orgenesis Ltd, BOL, Glucome Ltd, DarioHealth, Diabot, and Concenter BioPharma. He has attended speakers' bureaus for AstraZeneca, Eli Lilly and Company, Merck Sharp & Dohme, Novo Nordisk, and Sanofi; and is a stock/shareholder of Glucome Ltd, Orgenesis Ltd, DarioHealth, CamerEyes Ltd, Diabot, and BOL.'

REFERENCES

- [1] Kumar A, Arora A, Sharma P, Anikhindi SA, Bansal N, Singla V, et al. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. *Diabetes Metab Syndr* 2020;14:535–45. <https://doi.org/10.1016/j.dsx.2020.04.044>.
- [2] Malik VS, Ravindra K, Attri SV, Bhadada SK, Singh M. Higher body mass index is an important risk factor in COVID-19 patients: a systematic review and meta-analysis. *Environ Sci Pollut Res Int* 2020:1–9. <https://doi.org/10.1007/s11356-020-10132-4>.
- [3] Stoian AP, Toth PP, Kempler P, Rizzo M. Gender differences in the battle against COVID-19: impact of genetics, comorbidities, inflammation and lifestyle on differences in outcomes. *Int J Clin Pract* 2020:e13666. <https://doi.org/10.1111/ijcp.13666>.
- [4] Fadini GP, Morieri ML, Longato E, Avogaro A. Prevalence and impact of diabetes among people infected with SARS-CoV-2. *J Endocrinol Invest* 2020;43:867–9. <https://doi.org/10.1007/s40618-020-01236-2>.
- [5] Centers for Disease Control and Prevention. Assessing risk factors for severe COVID-19 illness. 2020. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/assessing-risk-factors.html> [last accessed: 28 October 2020].
- [6] Bode B, Garrett V, Messler J, McFarland R, Crowe J, Booth R, et al. Glycemic characteristics and clinical outcomes of COVID-19 patients hospitalized in the United States. *J Diabetes Sci Technol* 2020;14:813–21. <https://doi.org/10.1177/1932296820924469>.
- [7] Giardullo S, Zerbini F, Perra S, Muraca E, Cannistraci R, Lauriola M, et al. Impact of diabetes on COVID-19-related in-hospital mortality: a retrospective study from Northern Italy. *J Endocrinol Invest* 2020:1–8. <https://doi.org/10.1007/s40618-020-01382-7>.

- [8] Stoian AP, Pricop-Jeckstadt M, Pana A, Ileanu B-V, Schitea R, Geanta M, et al. Death by SARS-CoV 2 - a Romanian COVID-19 multi-centre comorbidity study. Preprint from Research Square 2020: DOI:10.21203/rs.3.rs-38098/v1.
- [9] Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA* 2020;323:2052–9. <https://doi.org/10.1001/jama.2020.6775>.
- [10] Sardu C, D'Onofrio N, Balestrieri ML, Barbieri M, Rizzo MR, Messina V, et al. Hyperglycaemia on admission to hospital and COVID-19. *Diabetologia* 2020;63:2486–7. <https://doi.org/10.1007/s00125-020-05216-2>.
- [11] Ceriello A, De Nigris V, Praticchizzo F. Why is hyperglycemia worsening COVID-19 and its prognosis?. *Diabetes Obes Metab* 2020. <https://doi.org/10.1111/dom.14098>.
- [12] Kaur S, Tripathi DM, Yadav A. The enigma of endothelium in COVID-19. *Front Physiol* 2020;11:989. <https://doi.org/10.3389/fphys.2020.00989>.
- [13] Caruso I, Giorgino F. The diabetic lung: An easy target for SARS-CoV-2?. *Diabetes Metab Res Rev* 2020:e3346. <https://doi.org/10.1002/dmrr.3346>.
- [14] Catrinou D, Ceriello A, Rizzo M, Serafinceanu C, Montano N, Stoian AP, et al. Diabetes and renin-angiotensin-aldosterone system: implications for covid-19 patients with diabetes treatment management. *Farmacia* 2020;68. <https://doi.org/10.31925/farmacia.2020.3.1>.
- [15] Ceriello A, Standl E, Catrinou D, Itzhak B, Lalic NM, Rahelic D, et al. Issues of cardiovascular risk management in people with diabetes in the COVID-19 era. *Diabetes Care* 2020;43:1427–32. <https://doi.org/10.2337/dc20-0941>.
- [16] Caballero AE, Ceriello A, Misra A, Aschner P, McDonnell ME, Hassanein M, et al. COVID-19 in people living with diabetes: an international consensus. *J Diabetes Complications* 2020;34:107671. <https://doi.org/10.1016/j.jdiacomp.2020.107671>.
- [17] Frühbeck G, Baker JL, Busetto L, Dicker D, Goossens GH, Halford JCG, et al. European Association for the Study of Obesity position statement on the global COVID-19 pandemic. *Obesity Facts* 2020;13:292–6. <https://doi.org/10.1159/000508082>.
- [18] Puig-Domingo M, Marazuela M, Giustina A. COVID-19 and endocrine diseases. A statement from the European Society of Endocrinology. *Endocrine* 2020;68:2–5. <https://doi.org/10.1007/s12020-020-02294-5>.
- [19] Ministry of Health of the Russian Federation. ВРЕМЕННЫЕ МЕТОДИЧЕСКИЕ РЕКОМЕНДАЦИИ, ПРОФИЛАКТИКА, ДИАГНОСТИКА, И ЛЕЧЕНИЕ НОВОЙ КОРОНАВИРУСНОЙ ИНФЕКЦИИ (COVID-19). 2020. Available at: https://static-0.rosminzdrav.ru/system/attachments/attaches/000/050/584/original/03062020_%D0%9CR_COVID-19_v7.pdf [last accessed: 28 October 2020].
- [20] Rahelić D, Matić T, Skelin M, Klobučar Majanović S, Bakula M, Deškin M, et al. Recommendations of the Working group of the Croatian Society for Diabetes and Metabolic Disorders of the Croatian Medical Association for people with diabetes and healthcare professionals in the Republic of Croatia during COVID-19 pandemic. *Liječnički vjesnik* 2020;142:85. <https://doi.org/10.26800/LV-142-3-4-14>.
- [21] Türkiye Diyabet Vakfı (Turkish Diabetes Foundation). COVID-19 Pandemi diyabet izelme ve tedavi kriterleri. Uzlaşi raporu. 2020. Available at: <https://www.turkdiabet.org/images/Covid-19veDiyabetYonetimi.pdf> [last accessed: 28 October 2020].
- [22] Polskie Towarzystwo Diabetologiczne (Diabetes Poland). Nowy koronawirus SARS-Cov-2, COVID-19 a Cukrzyca. 2020. Available at: https://cukrzyca.info.pl/aktualnosci/nowy_koronawirus_sars_cov_2_covid_19_a_cukrzyca [last accessed: 28 October 2020].
- [23] Belkhadir J. COVID-19 and diabetes from IDF MENA region. *Diabetes Res Clin Pract* 2020;166. <https://doi.org/10.1016/j.diabres.2020.108277>.
- [24] El-Malky A, Alharbi A, Alsaqabi A, Alghammdi W, Albalawi Y, Al-khalaf T, et al. COVID-19 specialized diabetes clinic model for excellence in diabetes care: scientific perspective. *Clin Diabetol* 2020;9:208–11. <https://doi.org/10.5603/DK.2020.0032>.
- [25] Grant WB, Lahore H, McDonnell SL, Baggerly CA, French CB, Aliano JL, et al. Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. *Nutrients* 2020;12. <https://doi.org/10.3390/nu12040988>.
- [26] Martineau AR, Forouhi NG. Vitamin D for COVID-19: a case to answer?. *Lancet Diabetes Endocrinol* 2020;8:735–6. [https://doi.org/10.1016/s2213-8587\(20\)30268-0](https://doi.org/10.1016/s2213-8587(20)30268-0).
- [27] Shah K, Tiwaskar M, Chawla P, Kale M, Deshmane R, Sowani A. Hypoglycemia at the time of Covid-19 pandemic. *Diabetes Metab Syndr* 2020;14:1143–6. <https://doi.org/10.1016/j.dsx.2020.07.003>.
- [28] Ratner RE, Gough SC, Mathieu C, Del Prato S, Bode B, Mersebach H, et al. Hypoglycaemia risk with insulin degludec compared with insulin glargine in type 2 and type 1 diabetes: a pre-planned meta-analysis of phase 3 trials. *Diabetes Obes Metab* 2013;15:175–84. <https://doi.org/10.1111/dom.12032>.
- [29] Zhang Y, Li H, Zhang J, Cao Y, Zhao X, Yu N, et al. The clinical characteristics and outcomes of patients with diabetes and secondary hyperglycaemia with coronavirus disease 2019: A single-centre, retrospective, observational study in Wuhan. *Diabetes Obes Metab* 2020;22:1443–54. <https://doi.org/10.1111/dom.14086>.
- [30] Caruso I, Di Molfetta S, Guarini F, Giordano F, Cignarelli A, Naticchio A, et al. Reduction of hypoglycaemia, lifestyle modifications and psychological distress during lockdown following SARS-CoV-2 outbreak in type 1 diabetes. *Diabetes Metab Res Rev* n/a:e3404. [10.1002/dmrr.3404](https://doi.org/10.1002/dmrr.3404).
- [31] Cariou B, Hadjadj S, Wargny M, Pichelin M, Al-Salameh A, Allix I, et al. Phenotypic characteristics and prognosis of inpatients with COVID-19 and diabetes: the CORONADO study. *Diabetologia* 2020;63:1500–15. <https://doi.org/10.1007/s00125-020-05180-x>.
- [32] Papachristou S, Penlioglou T, Stoian AP, Papanas N. COVID-19 and sodium-glucose cotransporter 2 inhibitors: no fear to attempt?. *Exp Clin Endocrinol Diabetes* 2020. <https://doi.org/10.1055/a-1235-5617>.
- [33] Stoian AP, Papanas N, Prazny M, Rizvi AA, Rizzo M. Incretin-based therapies role in COVID-19 era: evolving insights. *J Cardiovasc Pharmacol Ther* 2020;25:494–6. <https://doi.org/10.1177/1074248420937868>.
- [34] Stoian AP, Catrinou D, Rizzo M, Ceriello A. Hydroxychloroquine, COVID-19 and diabetes. Why it is a different story. *Diabetes Metab Res Rev* e3379. [10.1002/dmrr.3379](https://doi.org/10.1002/dmrr.3379).
- [35] Federația Asociațiilor Diabeticilor din România. Ghidul pentru persoanele cu diabet în perioada epidemiei de coronavirus. 2020. Available at: <http://fad.ro/wp-content/uploads/2016/07/GHID-diabet-si-coronavirus-2020.pdf> [last accessed: 28 October 2020].
- [36] Ministerul Sănătății Comisia de Diabet Zaharat NșBM. Managementul hiperglicemiei în condiții de spitalizare pentru infecția cu noul coronavirus (SARS-COV-2); 2020. Available at: <http://www.ms.ro/wp-content/uploads/2020/04/Recomand%C4%83ri-privind-managementul-hiperglicemiei-%C3%AEn-condi%C8%9Bii-de-spitalizare-pentru-infec%C5%A3ia-cu-SARS-COV-2.pdf> [last accessed: 28 October 2020].
- [37] Sachinidis A, Nikolic D, Stoian AP, Papanas N, Tarar O, Rizvi AA, et al. Cardiovascular outcomes trials with incretin-based medications: a critical review of data available on GLP-1 receptor agonists and DPP-4 inhibitors. *Metabolism*

- 2020;111:154343. <https://doi.org/10.1016/j.metabol.2020.154343>.
- [38] Chooi YC, Ding C, Magkos F. The epidemiology of obesity. *Metabolism* 2019;92:6–10. <https://doi.org/10.1016/j.metabol.2018.09.005>.
- [39] Clément K, Coupaye M, Laville M, Oppert JM, Ziegler O. COVID-19: a lever for the recognition of obesity as a disease? The French experience. *Obesity (Silver Spring)* 2020;28:1584–5. <https://doi.org/10.1002/oby.22924>.
- [40] Fragala MS, Kaufman HW, Meigs JB, Niles JK, McPhaul MJ. Consequences of the COVID-19 pandemic: reduced hemoglobin A1c diabetes monitoring. *Popul Health Manag* 2020. <https://doi.org/10.1089/pop.2020.0134>.
- [41] Infante M, Ricordi C, Fabbri A. Antihyperglycemic properties of hydroxychloroquine in patients with diabetes: Risks and benefits at the time of COVID-19 pandemic. *J Diabetes* 2020;12:659–67. <https://doi.org/10.1111/1753-0407.13053>.