

Diabetes and COVID-19: Risks, Management, and Learnings From Other National Disasters

Diabetes Care 2020;43:1695–1703 | https://doi.org/10.2337/dc20-1192

Jamie Hartmann-Boyce, ¹ Elizabeth Morris, ² Clare Goyder, ² Jade Kinton, ³ James Perring, ³ David Nunan, ¹ Kamal Mahtani, ¹ John B. Buse, ⁴ Stefano Del Prato, ⁵ Linong Ji, ⁶ Ronan Roussel, ^{7,8,9} and Kamlesh Khunti ¹⁰

Evidence relating to the impact of COVID-19 in people with diabetes (PWD) is limited but continuing to emerge. PWD appear to be at increased risk of more severe COVID-19 infection, though evidence quantifying the risk is highly uncertain. The extent to which clinical and demographic factors moderate this relationship is unclear, though signals are emerging that link higher BMI and higher HbA_{1c} to worse outcomes in PWD with COVID-19. As well as posing direct immediate risks to PWD, COVID-19 also risks contributing to worse diabetes outcomes due to disruptions caused by the pandemic, including stress and changes to routine care, diet, and physical activity. Countries have used various strategies to support PWD during this pandemic. There is a high potential for COVID-19 to exacerbate existing health disparities, and research and practice guidelines need to take this into account. Evidence on the management of long-term conditions during national emergencies suggests various ways to mitigate the risks presented by these events.

People with diabetes (PWD) have been identified as being at increased risk of serious illness from COVID-19. COVID-19 also presents substantial indirect risks to PWD through disruptions in health care and lifestyle factors. Understanding these risks and best ways to mitigate them in the short and longer term is key to facilitating informed decision-making during and after the COVID-19 pandemic.

Evidence relating to COVID-19 and diabetes is limited but continuing to emerge. In this Perspective, we summarize evidence identified through rapid reviews. We consider direct and indirect risks posed to PWD by COVID-19 and management considerations for PWD both with and without COVID-19 infection. Recognizing limitations in evidence related to COVID-19, we also bring together leaders in diabetes care from countries with high rates of COVID-19, highlighting experiences from the most affected countries including Italy, France, China, the U.K., and the U.S.

DIABETES AND RISKS FROM COVID-19

COVID-19 Infection: Contracting the Disease

It is unclear if PWD are more likely to contract COVID-19. PWD are considered at increased risk of infection generally, which has been extended to COVID-19 (1). Community testing for COVID-19 remains limited; hence, data predominantly come from hospitalized cohorts. Systematic reviews primarily consisting of data from China have estimated rates of 8% (95% CI 6–11%) (2), 7.87% (95% CI 6.57–9.28%) (3), and 9.7% (95% CI 6.9–12.5%) (4) of diabetes in people hospitalized with COVID-19. The percentage hospitalization appears higher in the U.S., where from February 12 to 28 March 2020, PWD accounted for 10.9% of all COVID-19 patients (similar to the proportion of the U.S. population with diabetes), 24% of hospitalized cases (non–intensive care unit

¹Centre for Evidence-Based Medicine, Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, U.K.

 Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, U.K.
 Medical Sciences Division, University of Oxford, Oxford, U.K.

⁴University of North Carolina School of Medicine, Chapel Hill, NC

⁵Department of Clinical and Experimental Medicine, Section of Metabolic Diseases and Diabetes, University of Pisa, Pisa, Italy

^bPeking University Diabetes Center, Peking University People's Hospital, China

⁷Federation de Diabetologie, Bichat Hospital, Assistance Publique—Hôpitaux de Paris, Paris, France ⁸INSERM, UMR_S 1138, Centre de Recherche des Cordeliers, Paris, France

⁹UFR de Médecine, Université de Paris, Paris, France

¹⁰Diabetes Research Centre, University of Leicester, Leicester, U.K.

Corresponding author: Jamie Hartmann-Boyce, jamie.hartmann-boyce@phc.ox.ac.uk

Received 19 May 2020 and accepted 19 May 2020

This article is part of a special article collection available at https://care.diabetesjournals.org/collection/diabetes-and-COVID19.

© 2020 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. More information is available at https://www.diabetesjournals.org/content/license.

[ICU]), and 32% of ICU admissions (5). A recent (preprint) U.K. study found uncomplicated diabetes to be the second most common comorbidity (19%) in patients hospitalized with COVID-19; complicated diabetes is reported in a figure only but prevalence looks to be approximately 6.5% (6).

COVID-19 Infection: Disease Severity

Though issues with study quality and imprecision make it extremely difficult to quantify, current data suggest that COVID-19 is associated with worse outcomes in PWD. Reports that aggregate data from multiple centers are summarized in Table 1. There is a notable paucity of data on what moderates the relationship between diabetes and COVID-19 severity. Increased age, being male, hypertension, and cardiovascular comorbidities

are associated with increased risks for COVID-19 severity (7) and are likely to be closely related to diabetes status. It is plausible that BMI (8), ethnicity (9), type of diabetes, diabetes control, and certain medications (10) all may also play a role. In two cohort studies (France and the U.K., U.K. study preprint) in PWD hospitalized with COVID-19, higher BMI was positively associated with worse COVID-19 outcomes when compared with people with BMI 25-29.9 kg/m² (11,12). Data on diabetes type and COVID-19 outcomes are only beginning to emerge, but preliminary (not yet peer reviewed) data from England (see Table 1) suggest risks may be higher in people with type 1 diabetes compared with type 2 (though risk was increased in all PWD regardless of type) (12). Data on glucose control and COVID-19 outcomes are discussed below.

Association Between Blood Glucose Control and COVID-19 Outcomes

There are limited data to date on the association between blood glucose control and COVID-19 outcomes. A retrospective study of 451 people with COVID-19 with diabetes and/or hyperglycemia from the U.S. reported that people with uncontrolled hyperglycemia had longer length of stay and higher mortality compared with people without diabetes or uncontrolled hyperglycemia (13). Another retrospective study of people with type 2 diabetes from China reported that wellcontrolled blood glucose correlated with improved outcomes in infected patients (14). Worse infection may predispose to more difficulty managing blood glucose, so the causal mechanism behind correlations between glucose control and worse COVID-19 outcomes is unclear.

Study design	Country	Number of studies	Number of participants	Outcome measure	Risk estimate
Systematic review and meta-analysis (2)	Multiple	8	3,076	Risk of diabetes in severe patients compared with nonsevere patients	OR 2.07, 95% CI 0.89-4.82
Systematic review and meta-analysis (63)**	Multiple	9	2,103	Risk of diabetes in severe patients compared with nonsevere patients	OR 2.67, 95% CI 1.91–3.7
Systematic review and meta-analysis (4)	Multiple	6	1,527	Risk of diabetes in severe/ICU patients compared with nonsevere (non-ICU) patients	RR 2.21, 95% CI 0.88-5.57
Meta-analysis (64)	China	12	2,018	Diabetes rate ratio among patients with more severe versus those with less severe infection	Rate ratio 2.26, 95% CI 1.47–3.49
Chinese Centers for Disease Control and Prevention report (65)	China	n/a	72,314	Case fatality rate	7.3% in PWD (compared with 2.3% overall)
U.S. Centers for Disease Control and Prevention report (5)	U.S.	n/a	74,439	Not hospitalized Hospitalized, not in ICU Admitted to ICU	PWD = 6% of all COVID-19 cases PWD = 24% of all COVID-19 cases PWD = 32% of all COVID-19 cases
Multicenter cohort study (66)	China	n/a	191	Risk of in-hospital death in PWD compared with those without (unadjusted)	OR 2.85, 95% CI 1.35–6.05
Retrospective review (67)	China	n/a	1,590	Likelihood of reaching composite end point (admission to ICU, intensive ventilation, or death) in PWD compared with those without (age- and smoking status—adjusted)	HR 1.59, 95% CI 1.03-2.45
Retrospective cohort study (15)**	U.K.	n/a	17,425,445 (5,683 deaths attributed to COVID-19)	Risk of in-hospital death in PWD compared with those without (age-, sex-, and comorbidities-adjusted)	$\begin{aligned} &\text{HbA}_{1c} <& 7.5\% \text{ (58 mmol/mol);} \\ &\text{HR 1.50, 95\% Cl 1.40-1.60.} \\ &\text{HbA}_{1c} \geq & 7.5\% \text{ (58 mmol/mol);} \\ &2.36 \text{ (2.18-2.56)} \end{aligned}$
Population cohort study (12)**	U.K.	n/a	61,414,470 (23,804 COVID- 19-related deaths)	Risk of in-hospital death in PWD compared with those without (adjusted for age, sex, deprivation, ethnicity, geographical region)	Type 1 diabetes OR 3.50 (95% CI 3.15–3.89); type 2 diabetes OR 2.03 (95% CI 1.97–2.09)

HR, hazard ratio; OR, odds ratio; RR, risk ratio. *Definition of severe disease was often not clear; we report here what was reported in the primary literature. Many of the systematic reviews include overlapping studies and have issues with quality and reporting. **Preprint — methods and data have issues with quality and reporting. **Preprint — methods and data have issues with quality and reporting. **Preprint — methods and data have issues with quality and reporting. **Preprint — methods and data have issues with quality and reporting. **Preprint — methods and data have issues with quality and reporting. **Preprint — methods and data have issues with quality and reporting. **Preprint — methods and data have issues with quality and reporting. **Preprint — methods and data have issues with quality and reporting. **Preprint — methods and data have issues with quality and reporting is a supplication of the preprint ofnot been subject to peer review.

Two recent U.K. studies (both preprint) reported that diabetes was independently associated with a higher risk of death that increased with higher HbA_{1c} (12,15). Compared with people without diabetes, one study reported that PWD with HbA_{1c} >7.5% (58 mmol/mol) had a higher chance of in-hospital death than those with HbA_{1c} < 7.5% (< 7.5% HR 1.50 [95% CI 1.40-1.60], \geq 7.5% HR 2.36 [2.18-2.56]) (15). In a separate analysis, PWD with $HbA_{1c} > 10\%$ (86 mmol/mol) had a higher risk of in-hospital death related to COVID-19 than those with an HbA_{1c} of 6.5-7% (48-53 mmol/mol) (HbA_{1c}>10% compared with HbA_{1c} 6.5-7% adjusted HR 2.19 [95% CI 1.46-3.29] for type 1 diabetes, 1.62 [95% CI 1.48-1.79] for type 2; in patients with type 2 diabetes, a significant difference was also detected when comparing HbA_{1c} values >7.5%[59 mmol/mol] to the reference category) (12). These data suggest that diabetes control preinfection has a role to play in COVID-19 outcomes. In contrast, a French observational study in PWD hospitalized with COVID-19 did not find an association between long-term glucose control and COVID-19 outcomes but had a smaller sample (11).

Indirect Risks to PWD Posed by COVID-19

Health care services, and in some cases access to medication and supplies, have been disrupted by COVID-19. Evidence from other national emergencies shows that such disruptions can lead to worse diabetes outcomes during and after these events (16-18). Diet and physical activity are mainstays of diabetes self-management and can reduce risk of worse outcomes in PWD and those with cardiometabolic multimorbidities (19). Though yet to be addressed by the COVID-19 literature, the pandemic presents significant disruption to both: a U.S. survey of PWD found more than a third of respondents reported their diet is now less healthy, and half report exercising less (20). The current pandemic and social isolation are likely to increase rates of anxiety and depression, which may also lead to poor adherence to medications and worsening of risk factor control (21,22).

MANAGING DIABETES DURING THE COVID-19 PANDEMIC

Reducing Risk from COVID-19

There is little evidence on how PWD can reduce their risk during the COVID-19

pandemic beyond following general infection control guidance within each country. More frequent blood glucose monitoring (in people who self-monitor) has been suggested, though it is unclear what evidence was used to make these recommendations (1).

Considerations for Diabetes Management in All PWD

Figure 1 summarizes specific considerations for diabetes management during national emergencies.

Self-management

There is little information on the effectiveness of self-management/self-education during the pandemic. A variety of online services have been implemented but have yet to be assessed (see EXPERIENCES FROM COUNTRIES WITH HIGH RATES OF COVID-19). The wider literature on care of long-term conditions during national emergencies suggests a role for educational materials (23). Evidence for interventions aiming to optimize self-management in PWD that are potentially feasible in disaster contexts include mobile phone apps (24), web- or computer-based interventions (25), text messaging (26,27), and selfmonitoring of blood glucose (28,29). The latter two show the most promise based on the available literature. However, the interventions tested may not be widely available or may require health care resources to be set up. In addition, choice of format should be tailored to patient preferences, which will vary by age and sociodemographic group (30).

Diabetes Services

Guidelines for routine diabetes care during the COVID-19 pandemic vary by country. Themes are summarized in Table 2. Studies of remote consultations have generally found positive results, though their generalizability to the current pandemic may be limited (31). Within diabetes, there is little evidence to support or oppose remote support (32,33).

Mental Health and Diabetes-Related Distress

There are overarching concerns about the impact of the COVID-19 pandemic on mental health and well-being (34,35). PWD are more prone to mental health issues than the general population (36). Adherence to treatment can worsen when people are distressed or have depression (21), as seen both during and after disasters (37,38). We found no evidence directly pertaining to management

of diabetes-related anxiety or distress during this pandemic. In the general literature, there is mixed evidence on interventions to reduce diabetes-related distress, and the vast majority of interventions tested involve face-to-face contact—an unsuitable format in the current context (39).

Managing COVID-19 in PWD

Management of PWD with COVID-19 generally follows standard sick-day rules. Considerations that may be specific to COVID-19 are summarized below.

Medication

Most COVID-19-related consensus statements recommend stopping metformin and sodium-glucose cotransporter 2 inhibitors (SGLT2i) during acute illness and following the sick-day rules. Dipeptidyl peptidase 4 inhibitors (DPP-4i), glucagonlike peptide 1 receptor agonists (GLP-1RA), and insulin are the preferred options in particular for hospitalized patients (see Fig. 2) (40,41). There has been some discussion regarding use of ACE inhibitors and angiotensin receptor blockers (ARBs) being associated with worse outcomes in COVID-19, particularly in PWD. However, in view of data showing potential benefits, the current recommendation is to continue with these therapies (40).

A number of studies are currently testing chloroquine/hydroxychloroquine for prevention or management of COVID-19. Careful glucose monitoring will be required in PWD due to these drugs' antidiabetic properties, with the potential risk of hypoglycemia that is associated with increased risk of cardiac arrhythmia, cardiovascular events, and mortality (42).

Management in Hospital

Guidance emphasizes the importance of referring to local specialist diabetes teams and of managing hyperglycemia (43). A narrative review suggests insulin is the preferred agent for control of hyperglycemia in this context (1). In the U.S., a major early focus for hospital management was to move inpatient care for PWD to "virtual" formats where possible, to reduce the need for personal protective equipment. This included use of electronic health records to interrogate data, telephone communication between diabetes care providers and inpatients and hospital staff, expanded "diabetes self-management protocols" allowing selected inpatients to monitor their own glucose and self-administer

Contact with HCPs

Telecare for all consultations that can be done remotely Priorities include new T1D diagnosis, vulnerable patients, high-risk situations. Depending on capacity, may defer other appointments but recognize that this may in effect be cancellation

Face-to-face for urgent podiatry and ophthalmology; high-risk pregnancy; teaching blood glucose monitoring for urgent reasons; newly diagnosed T1D; initiation of insulin therapy in critical cases; blood tests whose results may change treatment



Throughout: patient education; clear point of contact for all patients; reiteration of sick-day rules; repeat prescriptions for 28-day supplies (or longer); proactive review of patients

Figure 1—Considerations for diabetes management during national emergencies. T1D, type 1 diabetes.

insulin with oversight and advice from the virtual care team, and, in some institutions, initiating inpatient continuous glucose monitoring and/or flash systems. To minimize the need for ICU beds, several institutions launched subcutaneous insulin protocols for the treatment of diabetic ketoacidosis on floors with adequate nursing staffing. Virtual diabetes care teams focused on supporting transitions to lower levels of care or outpatient settings.

EXPERIENCES FROM COUNTRIES WITH HIGH RATES OF COVID-19

We summarize here experiences from five countries that have had significant COVID-19 outbreaks.

China

During the outbreak in China, many PWD were unable to access health care providers (HCPs) or medical supplies due to stay-at-home orders or quarantine. Hospitals reduced the number of appointments drastically. To mitigate the impact of those changes on diabetes management, several organizations issued guidance to PWD on how to cope with the situation (44,45). The guidance developed by the Chinese Geriatric Endocrine Society mainly focused on prevention and early discovery of hyperglycemic crises and management of medications and provided detailed instructions on how to get access to certified internet-based medical services through smartphones (45). If PWD urgently needed to see an

HCP in hospital, detailed guidance on how to prepare for consultations before leaving home and minimize exposure to the virus were given en route and during the hospital visit. Guidance was promoted in the form of reading material and lectures given by medical professionals through internet-based public media such as Baidu Health (an equivalent of Google in China) and the WeChat mobile app. An expert recommendation on insulin treatment of hyperglycemia in patients affected with COVID-19 was developed

France

On 12 March, President Macron ordered most people to stay at home, especially "at-risk" groups, including PWD. Many PWD were struck by the announcement and were not expecting to be publicly identified as such, without answers to basic questions. On 18 March, a group of HCPs and researchers from the Federation of Diabetology launched a web app, CoviDIAB, to provide PWD with diabetesspecific, scientifically based information and to provide support. This free service includes access to a frequently updated media library and to live webinars with nurses, physicians, and experts. Twice a week, registrants also receive short questionnaires about COVID-19 symptoms and tests for anxiety/depression. If indicated, registrants automatically receive a notice suggesting medical contact, and phone calls may follow. At the time of

writing, tens of thousands of patients were registered. Empathy was a driving principle in design, and comments suggest that the service helps people to understand and self-manage their individual risk and to limit disruption in lifestyle and care. An evaluation will indicate to what extent it reduces the burden of disease. Recommendations have been formulated by the Frenchspeaking Diabetes Society (Société Francophone du Diabète) to promote the intensification of glycemic control by remote support by professionals and frequent self-monitoring. However, extremely limited evidence was available to guide both patients and HCPs. In response, a group of physicians and researchers from 50 French hospitals designed and launched a large register to collect data on PWD hospitalized with COVID-19 and their prognosis (COVID-19 and Diabetes Outcomes [CORONADO], NCT04324736, ClinicalTrials.gov). Recruitment has exceeded expectation; early results are now available (11).

Italy

The first cases COVID-19 in Italy were recorded early in February. Tragically, Italy has suffered among the highest numbers of deaths in the world (47). At the time of this writing, the death rate in Italy was estimated at 122.52 per 1,000 infections, i.e., a 10-fold higher rate than in Germany (14.14 per 1,000 infections) (48). This could be due to demographic features of the Italian population, which include a large proportion (23%) of people aged ≥65 years (49). From 9 March, social confinement rules were issued includ-ing restricted access to outpatient clinics. Access to diabetes clinics has been limited to urgent cases, and remote contacts via telephone or video teleconsultation have been officially approved and reimbursed by the National Health System. Prescriptions of glucose-lowering agents requiring specialist approval (DPP-4i, SGLT2i, GLP-1RA, and new basal insulin analogs) were automatically renewed until the end of May. Special joint recommendations have been promptly issued by the Italian Society of Diabetes (SID), the Association of Italian Diabetologists (AMD), the Italian Society of Endocrinology (SIE), and the Italian Society of Pediatric Endocrinology (SIEDP) (50). The same organizations have opened a Facebook page entitled "One hour with

Service	Recommendations			
Inpatient diabetes services	 Inpatient diabetes services will need to continue and potentially increase capacity, with need for team approach re: glycemic control and nutritional status, and consideration of "virtual visits" for reviews (see MANAGEMENT IN HOSPITAL) (68). 			
Urgent/acute diabetes care (outpatient)	 Face-to-face consultations should continue in the following circumstances: a new diagnosis of T1D; urgent insulin start where symptomatic, HbA_{1c} >10% (86 mmol/mol), or ketones detected, teaching blood glucose monitoring for urgent reasons; or in cases where physical examination is essential (e.g., foot ulcer, infection, some points in pregnancy) (69). Virtual (telephone, video, or e-mail) consultations should be used in the following circumstances: follow-up of new T1D diagnoses; vulnerable patients (recent hospital admission, recurrent severe hypoglycemia, HbA_{1c} >11% [99 mmol/mol]); intensive follow-up in high-risk situations; or where risk of attending an appointment face-to-face is greater than the benefits (69).* 			
Routine diabetes care	 Consider routine diabetes care delivered virtually in the context of broader long-term condition management and prioritization, taking into account individual risk factors and clinical needs (68). The following should be deferred: routine appointments where diabetes is stable and well-managed; face-to-face structured group education courses; flash glucose monitoring start sessions; where the risk of attending an appointment is greater than the benefits; and where deferring appointments will not compromise clinical care (69). 			
Foot services for PWD	 May need to continue at full capacity with consideration of moving support to remote forms where possible (68); many of these services are essential (70). Access to in-person support should continue for those with acute or limb-threatening problems (70) or where physical examination is essential (69). All new referrals should ideally be reviewed within 24 h (70). 			
Pregnancy services for PWD	 May need to continue at full capacity with consideration of moving support to remote forms where possible (68). In-person support will be essential for physical examinations and/or teaching blood glucose monitoring at some points in pregnancy (69). 			
Blood tests for PWD	 Urgent blood test monitoring should continue (e.g., declining renal function, raised potassium, low sodium) (69). 			
Eye screening for PWD	 This was not mentioned in the guidance reviewed but we understand in most affected countries eye screening has been halted in view of high risk of transfer. Of note, evidence indicates that risk stratifying is possible (71). 			

AMD, SID, and SIEDP" allowing PWD and their relatives to contact specialists (51). A government web page providing simple and pragmatic recommendations has been created focusing on disruptions to physical activity and diet as a result of social confinement (52). At the time of writing, discussions were ongoing regarding restarting clinical activities and how to organize post-COVID diabetes clinics.

U.K.

Over 90% of PWD in the U.K. are managed in primary care, by enhanced diabetes-skilled primary care physicians, nurses, and health care assistants. These models have shown to be effective in reducing hospitalizations, outpatient attendance, and admissions for diabetes-related complications (53). In March, the government issued guidance on social distancing and self-isolation (54). In England, people considered especially clinically vulnerable (including some but

not all PWD) were contacted by the government with advice on shielding. All people at high risk, including PWD, were advised to only leave the house for limited periods for essential shopping and one form of exercise (55). The Primary Care Diabetes Society and the Association of British Clinical Diabetologists have issued guidance on managing PWD in primary care (56). The national charity Diabetes UK has been active in giving advice to PWD through their website and social media. Both primary and secondary care are providing emergency and routine follow-up using telephone or video consultations including support for mental well-being, though there are some regional variations. Social media channels have been set up where HCPs are sharing experience in managing people in the community and hospital and exchanging new guidance. A number of self-management education programs have been made freely available. There are also discussions regarding longer-term plans to

phase in face-to-face consultations for routine chronic disease management.

U.S.

The lack of universal health coverage poses additional challenges to PWD and their care providers during the COVID-19 pandemic in the U.S. There has been an almost wholesale switch to virtual care for outpatient appointments, but there are many failings in this approach. Phone visits provide a much lower rate of reimbursement than video visits, but many of the most vulnerable patients have inadequate equipment or connectivity to support video visits. Contacts with certified diabetes educators by phone or video are not reimbursed. Additional efforts have been made to communicate with PWD at home to ensure that they are safe. Laboratory and physical exam monitoring of complications has virtually ceased for most patients as long as they symptomatically remain well.

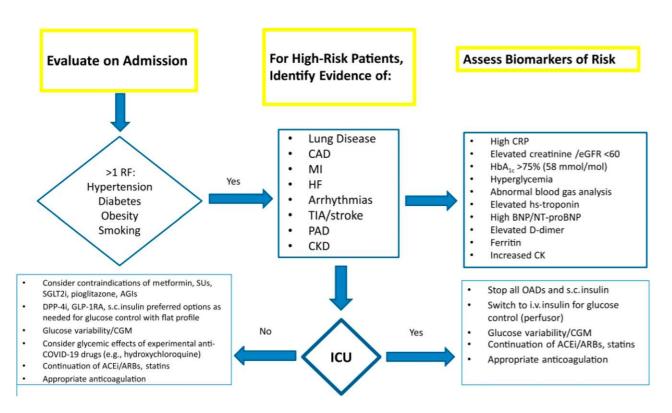


Figure 2—Possible flowchart for management of people hospitalized with diabetes and COVID-19, adapted with permission from Ceriello et al. (49). ACEi, ACE inhibitors; AGIs, α -glucosidase inhibitors; BNP, brain natriuretic peptide; CAD, coronary artery disease; CGM, continuous glucose monitoring; CK, creatine kinase; CKD, chronic kidney disease; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate (mL/min/ 1.73m²); MI, myocardial infarction; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; OADs; oral antidiabetes drugs; PAD, peripheral arterial disease; RF, risk factor; SUs, sulfonylureas; TIA, transient ischemic attack.

Many patients have lost insurance coverage. Prescription fills for diabetes medications are down 10%; a survey of PWD found one in six respondents needing insulin experienced a problem. A similar proportion reported issues with obtaining test strips, and a quarter of respondents reported issues with obtaining pump or continuous glucose monitoring supplies (20). Many pharmaceutical companies have stepped in to increase access to otherwise unaffordable medications. In data available through the end of March, relatively early in the U.S. COVID-19 course, approximately 80% of clinicians reported serious strain and nearly two-thirds were uncertain whether they would be able to keep their practices open due to insufficient financial resources and low volume of reimbursable work. Overall visits (virtual and face-to-face) for chronic asymptomatic care were down \sim 50% (57). As the future course of the epidemic in the U.S. is uncertain and seems likely to persist for many weeks, the threat to PWD is grave. The hope is that new government initiatives and innovation on the part of stakeholders will fill the

emerging cracks in an already fragmented system.

CONSIDERATIONS FOR MANAGEMENT OF LONG-TERM CONDITIONS DURING NATIONAL **EMERGENCIES**

Evidence on the management of longterm conditions during national emergencies suggests various ways to mitigate the risks presented by these events, which predominantly fall under two phases: planning and response (23). These strategies are outlined in Table 3.

AFTER COVID-19

There is much uncertainty as to how the COVID-19 pandemic will end and what will be left in its wake. Disruptions that arise due to national emergencies can lead to increased HbA_{1c} in those affected up to 16 months later, with some evidence that this is particularly the case for people of lower socioeconomic status and those treated with insulin (18,23). A lack of access to routine health care is a leading cause of morbidity and mortality

after disasters; stroke, acute myocardial infarctions, and diabetes complications are all shown to increase after the immediate threat has dissipated (26,58). Services such as diabetes clinics may also rethink their organization to minimize risk of ongoing transmission.

CONCLUSIONS

The need for decisive action creates an important tension when evidence is limited. An example here is the classification of PWD as being at increased risk from COVID-19 and therefore subject to increased preventive measures. Though risk is clearly increased, quantification is scant. There is little to no evidence on potentially moderating factors, despite the fact that these data are routinely collected in data sets used for existing analyses; the results presented are often unadjusted and use single disease categories, ignoring potential differences between type 1 and type 2 diabetes and multimorbidities, which are associated with worse outcomes (59).

In the face of a limited evidence base relating directly to COVID-19, decisions

Table 3—Strategies suggested for mitigating risks to management of long-term conditions during national emergencies (23) Phase Suggested strategy **Planning** • Collaboration, including the role of community-based partnerships • Development of culturally adapted resources for people living with LTCs, including print and web-based educational materials and access to support telephone lines • Access to online self-management education programs • Monitoring for patients using prescription data on assessing adherence to medications • Proactive remote review of patients requiring care for LTCs and their possible needs if health care services are disrupted • Clear point of contact for patient care should disasters/emergencies occur • Improving identification and tracking mechanisms for people living with LTCs Response • Triage and resource allocation • Transfer of care to allied HCPs including nurses and pharmacists • Communication between different agencies • Business continuity plans for pharmacies, and consideration of 30-day supplies from pharmacists • Ensuring access to appropriate foods where supplies may be limited (for people with LTCs impacted by diet) • Dedicated patient transportation or mobile clinics for patients requiring in-person care who may be affected by transport • Continued guidance from patient support groups LTCs, long-term conditions.

can be informed by international experiences to date and, to some extent, from the literature as it relates to other national emergencies. This latter source of evidence shows the toll of disruptions to diabetes care is often most pronounced after the acute phase of the emergency or disaster has passed. In some cases, the excess morbidity and mortality in the aftermath of national emergencies is higher than the toll during the emergency itself. History issues a stark warning here when considering the balance between diverting resources toward the acute COVID-19 crisis and maintaining routine care for people living with longterm conditions.

Finally, in reviewing what has been written on the topic of diabetes and COVID-19, we have been struck by two noticeable absences. The first is the absence of literature on wider contextual factors. PWD are likely to be impacted by COVID-19 just as much outside the health care setting as within it, with particular concerns relating to disruptions to diet and physical activity, increased stress, and burdens on mental health and well-being, yet the literature to date focuses almost exclusively on clinical management. The other unspoken issue in the literature we reviewed is that of inequality. COVID-19 is not an equal-opportunity disease. The burden will disproportionally be borne by people from less-advantaged groups (60). Emerging data also suggest that COVID-19 may pose more of a risk to nonwhite ethnic groups (9). Diabetes discriminates in similar ways, and the

intersection of diabetes and COVID-19 creates a maelstrom in which existing health disparities risk exacerbation with profound and long-lasting consequences. COVID-19 holds a mirror to our health care systems and care of PWD; may we do all we can now to make that reflection favorable in hindsight.

Acknowledgments. Parts of this article are based on Rapid Reviews conducted for the Centre for Evidence-Based Medicine's COVID-19 Evidence Service (23,61,62).

Funding. This work was not funded. E.M. and C.G. are funded by Wellcome Trust fellowships. J.B.B. is supported by grants from the National Institutes of Health (UL1TR002489 and P30DK124723). K.K. acknowledges support from the National Institute for Health Research (NIHR) Applied Research Collaboration East Midland (NIHR ARC-EM) and the NIHR Leicester Biomedical Research Centre.

The views expressed are those of the authors and not those of the universities, the NIHR, or the U.K. Department of Health and Social Care.

Duality of Interest. J.B.B. reports nonfinancial support and other from Adocia, AstraZeneca, Dance Biopharm, Dexcom, Eli Lilly, Fractyl, GI Dynamics, Intarcia Therapeutics, Lexicon, Mann-Kind, Metavention, NovaTarg, Novo Nordisk, Orexigen, PhaseBio, Sanofi, Senseonics, vTv Therapeutics, and Zafgen; grants and nonfinancial support from AstraZeneca, Eli Lilly, Intarcia Therapeutics, Johnson & Johnson, Lexicon, Medtronic, NovaTarg, Novo Nordisk, Sanofi, Theracos, Tolerion, and vTv Therapeutics; personal fees from Cirius Therapeutics Inc. and CSL Behring; and personal fees and other from Mellitus Health, Pendulum Therapeutics, PhaseBio, and Stability Health, outside the submitted work. R.R. reports grants, personal fees, and nonfinancial support from Sanofi, personal fees and nonfinancial support from Merck Sharp & Dohme, personal fees from AstraZeneca, grants and personal fees from Novo Nordisk, personal fees from Janssen, personal fees from Eli Lilly, personal fees from Abbott, personal fees from Medtronic, grants and personal fees from Diabnext, and personal fees from Mundipharma, outside the submitted work. K.K. has received grants from Bohringer Ingelheim, AstraZeneca, Novartis, Novo Nordisk, Sanofi, Eli Lilly, Merck Sharp & Dohme, and Servier, outside the submitted work. K.K. has served as a consultant, speaker, or an advisory board member for AstraZeneca, Bayer, Napp Pharmaceuticals, Eli Lilly, Merck Sharp & Dohme, Novartis, Novo Nordisk, Roche, Berlin-Chemie AG/Menarini Group, Sanofi, Servier, and Boehringer Ingelheim. No other potential conflicts of interest relevant to this article were reported. Author Contributions. J.H.-B., E.M., C.G., D.N., K.M., and K.K. were involved in concept and design. J.H.-B., E.M., C.G., J.K., and J.P. reviewed studies for inclusion and extracted relevant data. J.B.B., S.D.P., L.J., R.R., and K.K. contributed experiences from individual countries. J.H.-B. drafted the remainder of the article. All authors edited and approved the final manuscript. J.H.-B. had full access to all data and final responsibility for the decision to submit for publication.

References

- 1. Gupta R, Ghosh A, Singh AK, Misra A. Clinical considerations for patients with diabetes in times of COVID-19 epidemic. Diabetes Metab Syndr 2020;14:211–212
- 2. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV2: a systematic review and meta-analysis. Int J Infect Dis 2020;94:91–95
- 3. Emami A, Javanmardi F, Pirbonyeh N, Akbari A. Prevalence of underlying diseases in hospitalized patients with COVID-19: a systematic review and meta-analysis. Arch Acad Emerg Med 2020;8:e35
- 4. Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin Res Cardiol 2020;109:531–538
- 5. CDC COVID-19 Response Team. Preliminary estimates of the prevalence of selected underlying

- health conditions among patients with coronavirus disease 2019 - United States, February 12-March 28, 2020. MMWR Morb Mortal Wkly Rep 2020;69:382-386
- 6. Docherty AB, Harrison FM, Green CA, et al. Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol. 28 April 2020 [preprint]. medRxiv. DOI: 10.1101/2020.04.23.20076042
- 7. Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. BMJ 2020; 368:m1198
- 8. Stefan N, Birkenfeld AL, Schulze MB, Ludwig DS. Obesity and impaired metabolic health in patients with COVID-19. Nat Rev Endocrinol 2020:2020:1-2
- 9. Khunti K, Singh AK, Pareek M, Hanif W. Is ethnicity linked to incidence or outcomes of covid-19? BMJ 2020;369:m1548
- 10. Aronson JK, Ferner RE. Angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers in COVID-19. 22 March 2020. Available from: https://www.cebm.net/covid-19/ angiotensin-converting-enzyme-ace-inhibitors-andangiotensin-receptor-blockers-in-covid-19/. Accessed 1 May 2020
- 11. Cariou B, Samy H, Wargny M, et al. Phenotypic characteristics and prognosis of inpatients with COVID-19 and diabetes: the CORONADO study. Diabetologia. 29 May 2020 [Epub ahead of print] DOI: 10.1007/s00125-020-05180-x
- 12. NHS England. Type 1 and type 2 diabetes and COVID-19 related mortality in England. 20 May 2020. Available from: https://www.england.nhs .uk/publication/type-1-and-type-2-diabetes-andcovid-19-related-mortality-in-england/. Accessed 21 May 2020
- 13. Bode B, Garrett V, Messler J, et al. Glycemic characteristics and clinical outcomes of COVID-19 patients hospitalized in the United States. J Diabetes Sci Technol.9 May 2020 [Epub ahead of print]. DOI: 10.1177/1932296820924469
- 14. Zhu L, She Z-G, Cheng X, et al. Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. Cell Metab 2020;31:1068-1077

15. The OpenSAFELY Collaborative; Williamson

- E. Walker AJ. Bhaskaran KJ. et al. OpenSAFELY: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. 7 May 2020 [preprint]. medRxiv. DOI: 10.1101/2020.05.06.20092999 16. Saulnier DD. Brolin Ribacke K. von Schreeb J. No calm after the storm: A systematic review of human health following flood and storm disasters, Prehosp Disaster Med 2017;32:568-579
- 17. Fonseca VA, Smith H, Kuhadiya N, et al. Impact of a natural disaster on diabetes: exacerbation of disparities and long-term consequences. Diabetes Care 2009;32:1632-1638
- 18. Ng J, Atkin SL, Rigby AS, Walton C, Kilpatrick ES. The effect of extensive flooding in Hull on the glycaemic control of patients with diabetes. Diabet Med 2011:28:519-524
- 19. Chudasama YV, Zaccardi F, Gillies CL, et al. Leisure-time physical activity and life expectancy in people with cardiometabolic multimorbidity and depression. J Intern Med 2020;287:87-99
- 20. dQ&A. Impact of COVID-19 on the diabetes community in the United States, 2020. Available from https://d-qa.com/impact-of-covid-19-on-theusa-diabetes-community/?utm_source=Closer+Look+

- Subscribers + 2018&utm_campaign = 4285f7ac19-2020-04-19_WIR_4%2F13-4%2F1704_18_2020&utm_ medium=email&utm term=0 c55d924bf1-4285f7ac19-409220105. Accessed 24 April 2020 21. Grenard II. Munias BA. Adams II. et al. Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis. J Gen Intern Med 2011;26:1175-
- 22. Qiu J, Shen B, Zhao M, Wang Z, Xie B, Xu Y. A nationwide survey of psychological distress among Chinese people in the COVID-19 epidemic: implications and policy recommendations. Gen Psychiatr 2020;33:e100213
- 23. Hartmann-Boyce J, Mahtani KR. CEBM: Supporting people with long-term conditions (LTCs) during national emergencies. Available from: https://www.cebm.net/covid-19/supporting-peoplewith-long-term-conditions-ltcs-during-nationalemergencies/. Accessed 18 April 2020 2020
- 24. Aminuddin HB. Jiao N. Jiang Y. Hong J. Wang W. Effectiveness of smartphone-based selfmanagement interventions on self-efficacy, selfcare activities, health-related quality of life and clinical outcomes in patients with type 2 diabetes: a systematic review and meta-analysis. Int J Nurs Stud. 8 February 2019 [Epub ahead of print]. DOI: 10.1016/j.ijnurstu.2019.02.003
- 25. Pal K. Eastwood SV. Michie S. et al. Computerbased diabetes self-management interventions for adults with type 2 diabetes mellitus. Cochrane Database Syst Rev 2013 3:CD008776
- 26. Huang L, Yan Z, Huang H. The effect of short message service intervention on glycemic control in diabetes: a systematic review and meta-analysis. Postgrad Med 2019;131:566-571
- 27. Sahin C, Courtney KL, Naylor PJE, E Rhodes R. Tailored mobile text messaging interventions targeting type 2 diabetes self-management: a systematic review and a meta-analysis. Digit Health 2019;5:2055207619845279
- 28. Xu Y, Tan DHY, Lee JY-C. Evaluating the impact of self-monitoring of blood glucose frequencies on glucose control in patients with type 2 diabetes who do not use insulin: a systematic review and meta-analysis. Int J Clin Pract 2019;73:e13357
- 29. Malanda UL, Welschen LMC, Riphagen II, Dekker JM, Nijpels G, Bot SDM. Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin. Cochrane Database Syst Rev 2012;1:CD005060
- 30. Woolley AK, Chudasama Y, Seidu SI, et al. Influence of sociodemographic characteristics on the preferred format of health education delivery in individuals with type 2 diabetes mellitus and or cardiovascular disease: a questionnaire study. Diabet Med 2020:37:982-990
- 31. The Health Foundation. Using virtual consultations in the fight against COVID-19: Interview with Professor Trish Greenhalgh, 30 March 2020. Available from https://www.health.org .uk/news-and-comment/newsletter-features/usingvirtual-consultations-in-the-fight-against-covid-19. Accessed 18 April 2020
- 32. Farrell K, Holmes-Walker DJ. Mobile phone support is associated with reduced ketoacidosis in young adults. Diabet Med 2011;28:1001-1004
- 33. Viana LV, Gomes MB, Zajdenverg L, Pavin EJ, Azevedo MJ; Brazilian Type 1 Diabetes Study Group. Interventions to improve patients' compliance with therapies aimed at lowering glycated

- hemoglobin (HbA1c) in type 1 diabetes: systematic review and meta-analyses of randomized controlled clinical trials of psychological, telecare, and educational interventions. Trials 2016;17:94
- 34. World Health Organisation. Mental Health and psychosocial considerations during the COVID-19 outbreak. 18 March 2020. Available from https:// www.who.int/docs/default-source/coronaviruse/ mental-health-considerations.pdf. Accessed 18 April 2020
- 35. Shelvin M, McBride O, Murphy J, et al. Anxiety, depression, traumatic stress, and COVID-19 related anxiety in the UK general population suring the COVID-19 pandemic. 18 April 2020 [preprint]. PsyArXiv DOI: 10.31234/osf.io/hb6nq
- 36. The All-Party Parliamentary Group for Diabetes (APPG Diabetes). Diabetes and Mental Health. Available from: https://www.diabetes .org.uk/resources-s3/2018-08/Diabetes%20and% 20Mental%20Health%20%28PDF%2C%205.7MB% 29.ndf. Accessed April 18, 2020
- 37. Krousel-Wood MA, Islam T, Muntner P, et al. Medication adherence in older clinic patients with hypertension after Hurricane Katrina: implications for clinical practice and disaster management. Am J Med Sci 2008;336:99-104
- 38. Khan Y, Albache N, Almasri I, Gabbay RA. The management of diabetes in conflict settings: Focus on the Syrian crisis. Diabetes Spectr 2019;
- 39. Chew BH, Vos RC, Metzendorf MI, Scholten RJ, Rutten GE. Psychological interventions for diabetes-related distress in adults with type 2 diabetes mellitus. Cochrane Database Syst Rev 2017;9:CD011469
- 40. Ceriello A, Standl E, Catrinoiu D, et al.; Diabetes and Cardiovascular Disease (D&CVD) EASD Study Group. Issues of cardiovascular risk management in people with diabetes in the COVID-19 era. Diabetes Care 2020;43:1427-1432
- 41. Bornstein SR, Rubino F, Khunti K, et al. Practical recommendations for the management of diabetes in patients with COVID-19. Lancet Diabetes Endocrinol 2020; 8:546-550
- 42. Wondafrash DZ, Desalegn TZ, Yimer EM, Tsige AG, Adamu BA, Zewdie KA. Potential effect of hydroxychloroquine in diabetes mellitus: A systematic review on preclinical and clinical trial studies. J Diabetes Res 2020;2020:5214751
- 43. NHS London Clinical Networks, Management of diabetes in emergency department during coronavirus pandemic. Available from https:// www.england.nhs.uk/london/wp-content/uploads/ sites/8/2020/04/Covid-19-Management-of-diabetesin-emergency-department-crib-sheet-updated-150420.pdf. Accessed 18 April 2020
- 44. Weiqing W, Zhongyan S, Guang W, et al. Expert recommendations for diabetes management in primary care during COVID-19 pandemic. Zhonghua Neifenmi Daixie Zazhi 2020;36:185-190
- 45. Linong J, Guangwei L, Qiuhong G, et al. Guidance on diabetes management in elderly during COVID-19 pandemic. Chin J Diabetes 2020:28:1-6
- 46. Linong J, Jiajun Z, Zhiguang Z, et al. Recommendation on insulin treatment in diabetes patients affected with COVID-19. Chin J Diabetes 2020;28:1-5
- 47. Remuzzi A, Remuzzi G. COVID-19 and Italy: what next? Lancet 2020;395:1225-1228
- 48. Euronews. Coronavirus statistics: latest numbers on COVID-19 cases and deaths, 2020.

Available from https://www.euronews.com/ 2020/04/04/covid-19-coronavirus-breakdown-ofdeaths-and-infections-worldwide. Accessed 20 April 2020

- 49. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. JAMA 2020;323:1775–1776 50. SIE Società Italiana di Endocrinologia. Emergenza COVID, 2020. Available from http://societaitalianadiendocrinologia.it/html/cnt/emergenza-covid.asp. Accessed 5 April 2020
- 51. SID Società Italiana di Diabetologia. One hour with AMD, SID and SIEDP [in Italian], 2020. Available from http://www.siditalia.it/progetto-un-ora-con-amd-sid-siedp. Accessed 5 April 2020
- 52. Ministero della Salute. Nuovo coronavirus in Italia, 2020. Available from http://www.salute.gov.it/nuovocoronavirus. Accessed 20 April 2020
- 53. Seidu S, Davies MJ, Farooqi A, Khunti K. Integrated primary care: is this the solution to the diabetes epidemic? Diabet Med 2017;34:748–750 54. Public Health England. Guidance on shielding and protecting people who are clinically extremely vulnerable from COVID-19, 2020. Available from https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19. Accessed 15 April 2020
- 55. NHS. People at higher risk from coronavirus, 2020. Available from https://www.nhs.uk/conditions/coronavirus-covid-19/advice-for-people-at-high-risk/. Accessed 24 April 2020
- 56. Association of British Clinical Diabetologists. COVID-19 (Coronavirus) information for health-care professionals, 2020. Available from https://abcd.care/coronavirus. Accessed 24 April 2020 57. IQVIA. Monitoring the impact of COVID-19 on the pharmaceutical market. Available from

- https://www.iqvia.com/-/media/iqvia/pdfs/files/iqvia-covid-19-market-tracking-us.pdf? _=1587334105503. Accessed 19 April 2020 58. Mokdad AH, Mensah GA, Posner SF, Reed E, Simoes EJ, Engelgau MM; Chronic Diseases and Vulnerable Populations in Natural Disasters Working Group. When chronic conditions become acute: prevention and control of chronic diseases and adverse health outcomes during natural disasters. Prev Chronic Dis 2005;2:A04
- 59. Zemedikun DT, Gray LJ, Khunti K, Davies MJ, Dhalwani NN. Patterns of multimorbidity in middle-aged and older adults: An analysis of the UK biobank data. Mayo Clin Proc 2018;93: 857–866
- 60. Royal College of Physicians. COVID-19 and mitigating impact on health inequalities. Available from https://www.rcplondon.ac.uk/news/covid-19-and-mitigating-impact-health-inequalities. Accessed 18 April 2020
- 61. Hartmann-Boyce J, Morris E, Goyder C, et al. Diabetes and risks from COVID-19. Available from https://www.cebm.net/covid-19/diabetes-and-risks-from-covid-19/. Accessed 18 April2020 62. Hartmann-Boyce J, Morris E, Goyder C, et al. Managing diabetes during the COVID-19 pandemic. Available from https://www.cebm.net/covid-19/managing-diabetes-during-the-covid-19-pandemic/. Accessed 18 April 2020
- 63. 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. 30 March 2020 [preprint]. medRxiv. DOI: 10.1101/2020.03.25.20043133 64. Fadini GP, Morieri ML, Longato E, Avogaro A. Prevalence and impact of diabetes among people infected with SARS-CoV-2. J Endocrinol Invest 2020;43:867–869;
- $65.\ \mbox{Wu}$ Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019

- (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020;323:1239–1242 66. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054–1062
- 67. Guan WJ, Liang WH, Zhao Y, et al.; China Medical Treatment Expert Group for COVID-19. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Eur Respir J 2020;55:2000547
- 68. NHS; Royal College of Physicians; Association of British Clinical Diabetologists. Clinical guide for the management of people with diabetes during the coronovirus pandemic (19 March 2020, Version 2). Available from https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/speciality-guide-diabetes-19-march-v2-updated.pdf. Accessed 18 April 2020
- 69. NHS London Clinical Networks. Outpatient appointment prioritisation for specialist diabetes departments during the coronavirus pandemic. Available from: https://www.england.nhs.uk/london/wp-content/uploads/sites/8/2020/04/4.-Covid-19-Diabetes-Outpatient-Appointment- Prioritisation-Crib-Sheet-27032020.pdf. Accessed 18 April 2020 70. NHS London Clinical Networks. Clinical strategy for service management of diabetic foot units during the COVID-19 pandemic. Available from https://www.england.nhs.uk/london/wp-content/uploads/sites/8/2020/04/5.-Covid-19-Clinical-Strategy-for-MDFTs-Crib-Sheet-02042020.pdf. Accessed 18 April 2020
- 71. Leese GP, Stratton IM, Land M, et al.; Four Nations Diabetic Retinopathy Screening Study Group. Progression of diabetes retinal status within community screening programs and potential implications for screening intervals. Diabetes Care 2015;38:488–494