Smoking and COVID-19: Unravelling the risks and signposting resources

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As I write this, it is frightening to realise that the one-year anniversary of the start of the COVID-19 pandemic is upon us. As the second wave continues to impact all aspects of our professional and personal lives, and we struggle to juggle vaccination sessions and to meet demand for remote and face-to-face consultations, well done to everyone for making the time to read this editorial.

From the beginning of the pandemic we have ensured that the journal contains resources that support us in managing diabetes in these challenging times. In this issue, Clare Hambling on behalf of PCDS and together with colleagues from the Association of British Clinical Diabetologists (ABCD) and Diabetes UK, share "COVID-19 and diabetes: Update for primary care in response to the ongoing coronavirus pandemic". It contains information in an easy-to-read and implement format, and links to resources that will help us work more efficiently and effectively in delivering diabetes care right now. Our *Diabetes Distilled* summaries of interesting and important papers in this issue explore mortality and metformin in relation to COVID-19, cardiovascular disease and low-carbohydrate diets.

Smoking cessation – more important now than ever?

Previous studies have identified that smoking predisposes to bacterial and viral respiratory infections, and early in the pandemic the World Health Organization issued a statement warning that smoking could increase the risk and severity of COVID-19. Epidemiological data from a small systematic review of studies from China, which has been widely cited, suggested that people who smoke may be at higher risk both of acquiring SARS-CoV-2 and of developing severe COVID-related complications (Vardavos and Nikitara, 2020). However, other authors have explored whether there is instead a "smoker's paradox", with smokers being at lower risk of COVID infection and severe disease (Usman et al, 2020) or if this is purely a result of confounding in the studies. People with diabetes in my clinics recently have shared media coverage of both viewpoints, encouraging me to delve a little deeper into the evidence.

The OpenSAFELY study (Williamson et al, 2020) of a large GP practice population demonstrated that, after adjusting for confounders such as age and sex, smokers had significantly increased risk of COVID-related death compared to never smokers (hazard ratio, 1.14 [95% confidence interval, 1.05–1.23]). A very large prospective population cohort study (Hopkinson et al, 2021) involving 2.4 million users of the ZOE COVID Symptom Study app concluded that smokers were more likely to report classic symptoms of COVID-19 and that smoking is associated with increased risk of developing symptomatic COVID-19. Smokers with a positive COVID test result using the app had higher symptom burden and were more likely to need to attend hospital compared with those who did not smoke.

Possible mechanisms by which smoking may have protective effects (Usman et al, 2020) include that nicotine could potentially offer an anti-inflammatory effect by inhibiting production of inflammatory cytokines, while leaving anti-inflammatory cytokines unchanged. Chronic inflammation as occurs in smokers may result in a less reactive immune system and decreased production of inflammatory cytokines, so smokers may be relatively protected against the COVID-19 "cytokine storm syndrome". Production of nitrous oxide during smoking may inhibit replication and entry of SARS-CoV-2 virus. Changes in angiotensin-converting enzyme 2 (ACE2) expression are cited as possibly contributing to both potentially harmful and protective effects, partly attributable to SARS-CoV-2 attachment and access into the body. Smokers have more hand-to-mouth/face movements, something

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"A systematic review and meta-analysis of 25 studies exploring pre-operative smoking cessation demonstrated that as little as four weeks of cessation prior to surgery had a significant positive impact on respiratory complications."

we have all been warned to avoid during the pandemic. Smoking damages the epithelial cells lining the airways, interfering with normal ciliary action and increasing risk of respiratory infection. Finally, smoking increases the risk of heart disease, stroke and COPD, which have all been identified as risk factors for worse outcomes in those contracting COVID-19.

The authors of the "smoker's paradox" paper concluded that, although further research was indicated, suggestions of protective benefits from smoking should be viewed with extreme caution (in the same way we view such findings in those with inflammatory bowel disease).

Although data on the benefits of smoking cessation in changing outcomes of COVID infection are limited at this stage, there is some evidence extrapolated from surgical studies that four weeks of cessation may have benefits in decreasing need for intubation amongst those with COVID (Eisenberg and Eisenberg, 2020).

Even if smoking had any beneficial protective effects against COVID-19, these are unlikely to outweigh the proven adverse effects from smoking as outlined in "How to help people with diabetes stop smoking" in this issue. Not everyone will believe this is the right time to quit and, indeed, many people tell us they have been smoking more heavily during lockdown and relying on smoking as a guilty pleasure and for support. But, for those facing financial difficulties, there could be an important incentive to motivate them to quit. Surgical waiting lists are at an all-time high so, when normal services resume, many of our smokers will be heading for long-awaited surgery. A systematic review and meta-analysis of 25 studies exploring pre-operative smoking cessation demonstrated that as little as four weeks of cessation prior to surgery had a significant positive impact on respiratory complications (Wong et al, 2012), while other surgical studies demonstrated greater post-operative need for ventilation and development of complications amongst smokers compared to non-smokers (Turan et al, 2011).

Smoking cessation support services have worked remotely throughout the pandemic, and are willing and waiting to take our patients' calls. From my experience, all that many people need to encourage them to take action is an extra nudge and a number to phone, both easily supplied remotely.

In this issue

ABCD has recently published their position statement summarising the cardiovascular impact of DPP-4 inhibitors, GLP-1 receptor agonists and SGLT2 inhibitors (Basu et al, 2021). With so many cardiovascular outcome trials in widely different baseline populations and the large number of new studies with SGLT2 inhibitors in mixed populations with and without type 2 diabetes, staying on top of the data and implications for our personal practice is challenging. Some of the SGLT2 inhibitor studies have resulted in licence changes and more are likely to follow, providing much greater scope to use this class of drugs not only for glucose-lowering, but to provide benefits in cardiovascular disease, heart failure and reducing progression of kidney disease. For those less confident in using these newer drugs, our "How to use GLP-1 RAs safely and effectively" in the previous issue of the journal and "How to use SGLT2 inhibitors safely and effectively" in this issue provide traffic-light tables to help simplify and safety-net our prescribing. David Morris' interactive case study provides hands-on experience of managing diabetic nephropathy using these newer drugs.

Mental health problems amongst people with and without diabetes have increased during the pandemic, and particularly during the prolonged lockdown associated with this second wave, so Peter Bagshaw's At a Glance Factsheet gives a useful overview. With restricted access to dentists, gum disease may be contributing to poor glycaemic control and Ashana Gupta and colleagues remind us to consider this in our consultations. Finally, for those who were not able to attend the highly successful virtual Scottish Conference of the PCDS last year, I would encourage you to take a look at the on-demand sessions here. Thank you to our speakers who contributed their key messages to our conference report, which you can read here.

I hope you all enjoy using the tools and

resources in this issue to help support you in continuing to deliver quality diabetes care during these challenging months, where worry about loved ones, weather and workload conspire to wear us down. Stay safe – spring will be here soon! ■

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"All that many people need to encourage them to take action [to stop smoking] is an extra nudge and a number to phone, both easily supplied remotely."