purification process and pasteurisation, that can affect the treatment outcomes. The lactoferrin dose used in previous studies varied widely from a fixed dose of 100 mg per day[4] to a maximum dose of 300 mg/kg per day.[7] It is not clear which is the best lactoferrin dose. Kaufman and colleagues[8] in the USA have done a safety and tolerability study in 30 very low birthweight infants randomly assigned to daily 100, 200 or 300 mg/kg of bovine lactoferrin. The authors found that the intervention was safe,[8] and detected bovine lactoferrin levels in plasma and urine, and high levels in saliva, with all three doses.[9] The timing of the lactoferrin administration is also important because early administration might better protect by promoting cell proliferation and maturation of the immature infant gut, decreasing intestinal permeability and preventing bacterial translocation from the gut to the bloodstream.

The LIFT meta-analysis, despite including their own study and the ELFIN study, both without significant results, concluded that bovine lactoferrin supplementation does reduce the risk of late-onset sepsis. Therefore, lactoferrin is still a treatment option to reduce late-onset sepsis in preterm infants; however, additional research is needed to improve the certainty in the evidence, and before it becomes a standard of care in the neonatal units. An ideal design would be a multicentre trial in infants born weighing less than 1500 g, assessing the effect of daily 100, 200, and 300 mg/kg lactoferrin doses, and using the same commercial lactoferrin, same control groups, and same outcome definition (including both culture-confirmed and clinically-defined sepsis with the same clinical, laboratory, and treatment criteria). Ideally this trial should be done in low-income and middle-income countries with the highest burden of neonatal infections, where the potential benefit is expected to have the largest effect.

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ADHD management during the COVID-19 pandemic: guidance from the European ADHD Guidelines Group

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See Online for appendix

The coronavirus disease 2019 (COVID-19) pandemic is creating unprecedented challenges at every level of society. Individuals with neurodevelopmental disorders, such as attention-deficit hyperactivity disorder (ADHD), are particularly vulnerable to the distress caused by the pandemic and physical distancing measures, and they might display increased behavioural problems. The crisis also poses several important questions for clinicians on how best to deliver care within the new restrictions. Therefore, the European ADHD Guidelines Group (EAGG) has developed guidance on the assessment and management of ADHD during the COVID-19 virus pandemic (see full guidance in the appendix).

Given the requirement for physical distancing, all relevant service provision should continue via telephone or appropriate online video technology, in line with current recommendations for the use of telepsychiatry (eg, guidance from the UK Royal College of Psychiatrists[1] or the American Psychiatric Association[2]). The COVID-19 crisis can be particularly challenging for adolescents, and even more so for those with ADHD. Schools and teachers should try to monitor all their students but should include

those with ADHD, especially adolescents, as a priority group, because of their disorganisation and increased level of risk. For example, are they participating in online classes, and are they submitting their tasks? Are there concerns about their social and emotional wellbeing?

For families with children with ADHD, the EAGG recommends the use of behavioural parenting strategies because they improve parenting and have beneficial effects in reducing oppositional defiant and disruptive behaviour, which is common in ADHD.[3] Under the current circumstances, when face-to-face support is not possible, parents will have to rely on self-help versions of evidence-based systems. The efficacy of some of these systems are supported by trial evidence.[4–6] Some online systems have also been shown to have value.[7] However, parents must be cautious and avoid paying for untested applications that could do more harm than good. The EAGG guidelines highlights six essential messages (appendix p 14), including building the child's self-confidence and making sure all family members know what is expected of them. In relation to other non-pharmacological strategies, individuals using neurofeedback or cognitive training should be encouraged to continue practising transfer exercises during homework and new challenges.

Individuals with ADHD should, if clinically indicated and as recommended in standard national guidelines, be offered the opportunity to start on a pharmacological treatment after completion of the initial assessment or, if already on medication, continue with this as usual. Being prevented access to pharmacological treatment after the initial assessment or failure to continue ongoing medication could increase health risks related to COVID-19, because behaviour related to ADHD could become more disorganised and poorly controlled at this time, adversely impacting the ability to comply with requirements for physical distancing. We hope that regulatory authorities will allow for some flexibility around restrictions to accessing ADHD medications during the COVID-19 outbreak to ensure that patients receive their medication in a timely manner.

Parents of children with ADHD and adolescents or adults with ADHD should avoid increasing doses or adding doses (beyond those prescribed) to manage a crisis or stress related to confinement. Similarly, the use of antipsychotic medications to manage disruptive behaviour or the use of sedatives when not clinically indicated should be avoided. In our previous recommendations,[8] we stated that "the risk-benefit balance of drug holidays during weekends must be taken into account and better investigated". Given that family confinement and physical distancing might exacerbate ADHD-related risks, we see no strong rationale to introduce weekend drug holidays during the current crisis.

Routine cardiovascular clinical examination and face-to-face monitoring for individuals with ADHD without any cardiovascular risk factors could be postponed until routine face-to-face visits are reinstated, because currently the risks of conducting face-to-face assessments in this patient group outweigh the benefits of cardiac monitoring. If possible, monitoring of blood pressure and heart rate using home blood pressure machines is recommended, following the guidance detailed in the appendix (p 15). Patients should contact their prescribers should they experience any emerging cardiovascular symptoms (eg, chest pain, prolonged palpitations, and breathing difficulties), or any other concerning symptoms.

Although sleep-onset delay is a possible adverse event during psychostimulant treatment, sleep disruption can be caused by other factors that could be associated with the COVID-19 outbreak, such as stress, late-morning waking, and disruption of daily routines. Appropriate sleep hygiene should be implemented or reinforced in preference to increasing the doses of melatonin beyond the therapeutic range (up to 5–6 mg nocte each night[9]).

Headache can occur during treatment with psychostimulants. Given the uncertainty around possible unfavourable effects of ibuprofen in patients with COVID-19,[10] paracetamol should be preferred over ibuprofen for pain management.

In summary, COVID-19 and the related physical distancing measures are presenting many challenges for children, young people, and their families, and these challenges are likely to be considerably greater for those with ADHD. It will therefore be important to draw upon the strategies routinely recommended in parent-focused ADHD interventions, as well as mental-wellbeing interventions for children and young people. The inability to do routine, face-to-face clinical visits to initiate and monitor medication should not be viewed as an absolute contraindication to pharmacotherapy. Instead, the risks and benefits of initiating or maintaining medication under the COVID-19 restrictions implemented in some countries should be carefully considered. If the use of

medication is deemed desirable, strategies for remote monitoring should be implemented.

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The immune system of children: the key to understanding SARS-CoV-2 susceptibility?

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Humanity has repeatedly faced epidemics of known and novel pathogens and the immune system has adapted to survive. Since severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a new zoonotic pathogen, there is no pre-existing immunity and the whole of humanity is susceptible to infection and developing COVID-19 disease.

Adults can be infected with different outcomes, from asymptomatic, mild, moderate to severe disease, and death. Children can also be infected by SARS-CoV-2, but most paediatric cases with laboratory-confirmed SARS-CoV-2 infection are mild; severe COVID-19 disease in children is rare.[1]

Children are more vulnerable to other infections; thus, the important question arises—why are children less susceptible to COVID-19 disease compared with adults? So far, there is no evidence of a lower degree of expression or function of the SARS-CoV-2 receptor (namely ACE2) in