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## EARLY INTERVENTION IN PSYCHOSIS DURING THE COVID-19 PANDEMIC: MAUDSLEY RECOMMENDATIONS

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## Introduction

The COVID-19 pandemic has had dramatic effects on worldwide healthcare systems, and its psychiatric and neuropsychiatric effects have been well documented in the general population (Rogers et al., 2020) and in specific populations such as healthcare workers (Salazar de Pablo et al., 2020). Globally, intense pressures on inpatient beds in the acute physical health setting have had a knock-on effect on mental health pathways and provision, with mental health provider organisations sometimes temporarily shutting selected community services, including Early Intervention for Psychosis (EI) teams. EI services encompass First-Episode of Psychosis (FEP) services (Correll et al., 2018) for those with a first onset illness and Clinical High Risk for Psychosis services (CHR-P) for young individuals with subtle symptoms of the disorder (Catalan et al., 2020; Fusar-Poli et al., 2020b). This report draws on twenty-years' clinical experience gained by EI services in South London and Maudsley NHS Trust (established in 2001) (Fusar-Poli et al., 2020a; Fusar-Poli et al., 2020c) to provide four pragmatic recommendations for EI services during the COVID-19 pandemic. It should be noted that EI services are targeted at people with severe mental disorders, who are at higher risk of needing acute psychiatric care, including hospitalisation.

## Recommendation 1

*EI services for psychosis should prepare for an increase in activity because of the potentially higher risk of psychosis during the COVID-19 pandemic*

The COVID-19 pandemic is likely to lead to an increased incidence of psychosis, via three potential mechanisms.

1.1 As pointed out in a recent review (Kępińska et al., 2020), the association between viruses such as influenza and symptoms of major mental illness has been recognised as far back as 1732. The clearest illustration of a putative relationship remains the Spanish influenza epidemic of 1918-19, Menninger reporting data on patients admitted over a 3 month period to the Boston Psychopathic Hospital, finding 25 of 80 people admitted acutely following influenza fulfilling criteria for dementia praecox (i.e. a narrow Kraepelinian definition of non-affective psychosis), as opposed to delirium and other psychoses (Menninger, 1919). Notably, further studies of 175 people with post-influenza psychoses at the same hospital indicated 50 cases of dementia praecox, followed up for one to five years, indicated a significant proportion (35) were noted to have a complete recovery, 5 to have some improvement, 5 no change, and 5 a worsening of their condition. The length of symptoms and clinical case presentations counts against these cases being ascribed to a prolonged delirium (Menninger, 1926). In the early weeks of the COVID-19 epidemic in London, we have observed a suspected increase of cases of psychotic disorders in our healthcare system-in particular among middle-age men-currently under investigation, and which contrasts with the equal sex distribution seen in our catchment

area. This would also suggest that EI services during COVID-19 pandemic may relax entry age criteria (worldwide these are typically restricted to 14-35 years), in keeping with recent Department of Health guidance (Chandra et al., 2018), to allow early detection and treatment of psychosis onset in older individuals.

1.2 Examination of factors related to the current pandemic points to increased cumulative risk for the development of psychotic disorders. These factors include, but are not restricted, to those contributing to the incidence of the current infection (urban environment), those related to necessary interventions, e.g. social distancing (social fragmentation and loneliness (Smith and Lim, 2020)), and general factors related to the pandemic, such as social isolation, which contribute to social inequalities, in particular in vulnerable groups (see below). It is clear that the infection is more likely to occur in urban environments, and these are already associated with increased risk of psychosis at least in Northern Europe, with an odds ratio of 2.19 (95% CI 1.55-3.09) (Radua et al., 2018). Social fragmentation (a prerequisite of social distancing, one of the main public health interventions in the current pandemic) has detrimental effects on mental health (Brooks et al., 2020). Social isolation increases the risk of psychosis, with an odds ratio of 12.8 (95% CI 5.71-28.88) in the most fragmented area compared to the least fragmented (Allardyce et al., 2005). This effect appears to exist irrespective of rural or urban environment. Added to this should be the general risk conferred by psychosocial stress, life events, including trauma (Radua et al., 2018).

1.3 Third, these effects may be more pronounced in ethnic minorities, homeless people and immigrants, which are all independent risk factors for psychosis (Pareek et al., 2020). Recent evidence indicates the COVID-19 pandemic is particularly severe in ethnic minorities, which are highly represented in populations accessing EI services. CHR-P services are ideally placed to investigate the contributions of various risk factors to psychosis (Oliver et al., 2020) in the context of COVID-19 (Kotlicka-Antczak et al., 2020). These services are also engineered to improve early detection and may contribute to address the possible increase in COVID-19 related incidence of psychosis. For example, these services are designed to take care of patients with short-lived psychotic episodes (e.g. Brief and Limited Intermittent Psychotic Symptoms, which overlap with Acute and Transient Psychotic Disorders or Brief Psychotic Disorders) (Fusar-Poli et al., 2016; Fusar-Poli et al., 2017a; Fusar-Poli et al., 2019). Several studies indicate that short-lived psychotic episodes are an emerging clinical phenomenon of the COVID-19 pandemic (D. Agostino et al., 2021; Valdes-Flrido et al., 2020).

## **Recommendation 2**

*FEP services should increase their focus on early interventions and relapse prevention to reduce hospital admissions*

Whilst EI services were originally conceptualised to decrease the duration of untreated psychosis during a FEP, and therefore improve functioning, over the years they have also increasingly focused on relapse prevention (Taylor and Jauhar, 2019).

2.1 This has particular relevance for the current COVID-19 pandemic, as relapses constitute a significant proportion of readmissions to hospital (Taylor and Jauhar, 2019). The literature on the natural history of non-affective psychotic illness (including in the pre-antipsychotic era) suggests that interventions given during the first five years are more likely to impact on short and longer-term outcomes (Fusar-Poli et al., 2017b). These interventions include antipsychotic treatment, intensive care coordination, and psycho-social interventions, which constitute the core components of an EI service. The most recent systematic review and meta-analysis concluded that EI substantially decreased risk of relapse (RR, 0.71; 95% CI= 0.53-0.93) (Correll et al., 2018).

2.2 Around 15% of people within EI services fulfil criteria for bipolar disorder, and many people with first-episode mania come into contact with EI services (Jauhar et al., 2019). These patients are even more likely to be hospitalised than those with first-episode schizophrenia-like psychosis (Chang et al., 2016), and EI services are well placed to reduce their risk of hospitalisation. In the absence of EI services, it is unclear which services will effectively cater to this population and prevent relapse.

2.3 EI services have played a psychoeducational role in the management of substance misuse, specifically cannabis misuse, a significant predictor of relapse. This has relevance to the current pandemic, as people continue to have access to substances, and relapses in this context are likely, and possibly amenable to treatment.

2.4 Lastly, continuity of care and approach is fundamental to keeping patients engaged in treatment. EI services are characterised by this approach. By reconfiguring EI teams and reducing continuity of care due to the current pandemic there is the possibility of decreased engagement with services, and stopping treatment, which is the major cause of relapse, in a population of people whose illness have a high risk of relapse (MacDonald et al., 2018). For example, up to 50% of individuals with an initial brief psychotic episode under the care of CHR-P services are at risk of relapse into persistent psychosis (Fusar-Poli et al., 2016). Therefore, focusing on routine work (including treatment of co-morbid substance misuse), as well as dealing with new incident cases is essential.

### **Recommendation 3**

*Refine physical health guidelines to improve outcomes in EI patients during the COVID-19 pandemic.*

Psychotic disorders are frequently associated with physical co-morbidities, which reduce life expectancy. Specifically, these include vitamin D deficiency, the metabolic syndrome,

diabetes, cigarette smoking and general effects of psychotropic medication offered to this population. Therefore EI services adhere to specific standards for physical health (Chandra et al., 2018), as well as general considerations, which should be refined to meet the COVID-19 circumstances.

3.1 The need for face-to-face physical health checking should be considered on a case by case basis, with a risk-benefit analysis. To reduce the length of face-to-face examinations, we also recommend collecting remotely personal/family history for physical health illnesses, lifestyle review and weight checks. Appointments between patients should also be carefully scheduled to facilitate social distancing and avoid prolonged waiting periods in common areas. Any existing or emergent physical health co-morbidities associated with a greater risk of COVID-19 complications: diabetes, obesity, hypertension, cardiovascular and respiratory disease should be identified and managed, in collaboration with primary care, with appropriate shielding advice and arrangements put in place.

3.2 EI patients are three times more likely to have vitamin D deficiency than their peers (Crews et al., 2013), and this can be worsened by prolonged lockdowns. There is evidence that vitamin D supplementation enhances the function of the immune system and reduces the risk of developing respiratory infections (Martineau et al., 2017). EI services in the SLaM NHS Trust have recently recommended short-term top-up vitamin D supplementation for working-age adult in-patients without contraindications: community EI services are better placed to offer longer-term supplementation strategies.

3.3 The role of cigarette smoking. Assisting EI patients with smoking cessation is particularly important during the COVID epidemic. EI clinicians should assume that smoking habits would reduce to some extent in-patients with COVID-19 related respiratory infections and stop with associated hospital admission. Dose reductions should, therefore, be considered with drugs that may be influenced by smoking: olanzapine, fluvoxamine, duloxetine, fluphenazine, benzodiazepines, tricyclic antidepressants, haloperidol, and carbamazepine (clozapine is covered in more depth below).

3.4 The role of early weight gain and development of the metabolic syndrome in early psychosis is readily acknowledged. During the pandemic there will be increased propensity for weight gain in this population, given the decreased level of activity seen in the general population. Therefore monitoring of weight, which can be done remotely, is recommended, and thought in regard to psychotropic medication as well as lifestyle factors (diet and exercise, within the home) would seem reasonable measures.

3.5 Most psychotropic drugs and some medications used to treat COVID-19, such as antimicrobials, antimalarials, and antiretrovirals, are associated with increased risk of prolonging QTc (in addition to the risk conferred by antipsychotics, with the exception of aripiprazole, cariprazine, lurasidone and paliperidone which appear to have negligible effects),

putting EI patients at higher acute and longer-term risk of life-threatening ventricular arrhythmias. Therefore, a repeat electrocardiogram should be considered. Furthermore, thought should also be given to possible interactions between psychotropic medication and putative treatments for COVID-19 (Bishara et al., 2020).

3.6 COVID-19 related symptoms should be distinguished from neuroleptic malignant syndrome (NMS), especially in the case of autonomic instability, fever, dyspnoea, and change in the level of consciousness, though we acknowledge rates of potential misdiagnosis are unknown. This is relevant to EI as a risk factor for NMS is recent initiation of a new neuroleptic drug. A thorough physical examination combined with a rapid COVID-19 antigen test is paramount to exclude the presence of severe muscle rigidity and/or autonomic instability.

3.7 COVID-19 symptoms in patients taking clozapine can be difficult to distinguish from myocarditis. This has relevance for EI as it occurs more commonly in the first 1-2 months from initiation, and neutropenic sepsis occurs more often in the first year. After that period, a possible extension of full blood count monitoring could be considered. In the UK, those taking clozapine with fever are advised to be immediately tested for both agranulocytosis and coronavirus, especially when they also suffer from coughing, sore throat, shortness of breath and a runny nose. Moreover, in those patients with COVID-19 infection, clozapine dose should be decreased, by about 25% in those at high risk of relapse, with monitoring (Siskind et al., 2020). Where a low white cell count occurs in the presence of a normal neutrophil level in the context of COVID-19 infection, it is thought that clozapine can be safely continued (Bishara et al., 2020).

3.8 In EI patients taking lithium we emphasise general measures, such as need to maintain good fluid intake, particularly if they have fever, vomit or diarrhoea, and maintain lithium use if flu-like symptoms occur (with monitoring of lithium and electrolyte levels, as in general care).

#### **Recommendation 4**

##### *Embed e-Health technology in the detection, assessment and care of EI patients*

eHealth approaches have high levels of patient satisfaction and acceptability in patients with chronic illnesses, as well as their carers. In response to the COVID-19 pandemic, e-mental health can be particularly helpful as it can prevent exposure to additional unnecessary human contact and reduce emergency department overuse (Moazzami et al., 2020).

4.1 We recommend reducing face-to-face contacts during lockdowns and introducing, whenever possible, virtual contacts during EI clinical care. EI patients (FEP and CHR-P individuals) are typically young and usually highly engaged with the digital world (Reilly et al., 2019). There is no substantial evidence of EI patients having difficulties with videoconferencing or experiencing any exacerbation of symptoms because of it (Reilly et al., 2019). In fact, most individuals in EI services are concordant with e-Health technologies, and

it should be acknowledged that younger people are more likely to have smartphones and embrace new technologies.

In some young people, physical distance may actually relieve anxiety and concerns associated with attending appointments. In acute exacerbations or new transitions to psychosis from a CHR-P state, face-to-face care and in-person visits may be irreplaceable. Similarly, adherence to treatments should be monitored with additional caution to avoid loss to follow-up during virtual assessments, which may result in relapses.

4.2 EI services can take advantage of the COVID-19 pandemic to fully implement virtual working policies. Our EI healthcare system is effectively digitised and paper-free, and it is a legal requirement for EI healthcare professionals to keep the local Electronic Health Record (EHR) up to date. The local EHR contains the full clinical records of all patients, which are continually updated throughout their care, regardless of discharges from and/or referrals to other services. The EHR can be accessed remotely by EI clinicians via virtual protected network access, thus respecting local and national confidentiality and privacy policies. The local EHR also allows embedding virtual conferencing platforms that are NHS-compliant for roll-out to EI staff, further facilitating working from home and communicating between patients and medical professionals.

4.3 We also recommend exploring the availability of e-Health therapeutic approaches. For example, there is evidence that e-cognitive behavioural therapy (which is the first-line treatment in CHR-P patients) has similar effect sizes to face-to-face interventions across psychiatric disorders. Additionally, vocational interventions lend themselves well to digital technology and can be implemented easily during periods of lockdown. Therefore, the use of e-Health technology could be seen not only as a means of facilitating care. During the pandemic, but also a way of expanding future services for this patient group, building on the experience during the pandemic.

## **Recommendation 5**

### *Prioritising EI patients in the vaccination campaign*

5.1 On December 2020, European Medicines Agency has approved the first COVID-19 vaccine for authorisation across the European Union, inspiring hope in the face of future waves of the pandemic. The European Union advises prioritising for vaccination “persons whose state of health makes them particularly at risk” for severe COVID-19, but leaves it to member states to decide which medical conditions to prioritise. Although several countries have initiated their vaccination plans, only a few national vaccine strategy documents explicitly mentioned people with severe mental disorders such as those under the care of EI services. In light of the physical health burden and associated risk, we recommend that EI patients are prioritised during vaccination COVID-19 exit strategies. Tailored pandemic management and

vaccination optimization and monitoring plans need to be created to cater to this group as an immediate public health priority and correct any intolerable inequality (De Picker et al., 2021).

### **Conclusions**

In summary, the challenges posed by the COVID 19 pandemic, highlight the importance of EI services, which play a central role in the care of a particularly vulnerable patient group and decrease the burden on already stretched generic mental health systems. Consideration can be given to these recommendations by policymakers, service planners and commissioners, and those who provide mental health care.

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