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Title: Severe mental illness and European COVID-19 vaccination strategies

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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. Ethical, neuroscientific, and public health considerations have been emphasized to prioritise individuals with severe mental illness (i.e., psychotic disorders, bipolar disorders, and severe major depressive disorders).¹⁻³ We systematically reviewed national COVID-19 vaccine deployment plans across 20 European countries (cfr. Appendix).

Eight of 20 countries’ national vaccine strategy documents explicitly mentioned psychiatry or mental illness. Several countries prioritised institutional residents, which may include severe mental illness (Table 1). Only four countries (Denmark, Germany, the Netherlands, and the UK) had some form of higher vaccination priority for outpatients with severe mental illness. Additionally, Latvia, Romania, Spain, and Sweden prioritised outpatients with disabilities, possibly including severe mental illness, whereas the Czech Republic and Sweden stipulated behavioural or mental problems possibly hindering pandemic regulation adherence as priority indication.

A European Centre for Disease Control and Prevention survey found most European countries used a combination of epidemiological data, mathematical modelling, guidelines, ethical considerations, and published research findings to define specific morbidities for vaccine prioritisation.⁴

Examples of approaches with positive outcomes for severe mental illness include:

The UK used an Oxford University evidence-based algorithm to calculate the number of vaccinations needed to prevent one death.⁵ Importantly, this QCovid® algorithm (<https://qcovid.org/>; Copyright © 2020, University of Oxford), based on April-June 2020 UK data, explicitly includes severe mental illness among its risk predictors, and so does the UK vaccination strategy.. Preliminary data however indicate vaccination coverage for patients with severe mental illness is lagging behind that of other co-morbidity groups.⁶

Denmark and the Netherlands initially omitted mental disorders from their COVID-19 vaccination strategies. After a large nationwide cohort study found that severe mental illness and use of antipsychotics were associated with an increased risk for 30-day mortality (adjusted OR 2.5; 95%CI 1.2-5.1 and 3.3; 95%CI 2.3-4.8, respectively),⁷ the Danish Health Authority urged healthcare practitioners to refer for priority vaccination patients with psychotic disorders and other individuals with complex severe mental illness deemed to be at particular high risk by the treating physician. The Netherlands increased prioritisation of severe mental illness patients following advocacy from mental health associations.⁸

The German federal research institute performed an “umbrella review” of published systematic reviews and meta-analyses to inform the federal ministry of health’s selection of risk comorbidities.⁹ However, evidence on psychiatric morbidity had not yet been systematically summarized at that time and was therefore not included in the resulting strategy. Following a recent update of its literature review, in which severe mental illness was found to be one of the few medical comorbidities with OR >2.0 for COVID-19 hospitalisation and mortality, the strategy now explicitly includes severe mental illness in the highest risk group of medical comorbidities.⁹

Multiple high-quality studies have demonstrated odds ratios for comorbid severe mental illness, and schizophrenia in particular, to equal or even surpass those of other risk comorbidities included for prioritisation (Table 1).^{7,10} Evidence-based policy would then require severe mental illness be included in the list of risk comorbidities. Yet several sources of bias may have caused the risks associated with severe mental illness to be overlooked by most countries. Firstly, mental disorders are often not included as predictors in COVID-19 outcome studies. Secondly, studies specifically investigating the risks of psychiatric comorbidity were not yet summarized in systematic reviews or meta-analyses and therefore ignored by some national strategies and mathematical models.

In summary, there is a compelling medical, ethical, and economic case for targeted early vaccination for the vulnerable group of patients with severe mental illness. Our joint recommendations, representing professionals, patients, and families, are clear and urgent: (1) explicit inclusion of both inpatients and outpatients with severe mental illness in medical priority groups for COVID-19 vaccination, (2) meaningful patient- and family organisational participation in developing vaccination plans, and (3) engagement of peer workers in providing vaccination education to patients.

European countries’ vaccination strategies try to balance ethical and scientific evidence, but for individuals with severe mental illness an evidence-policy disconnect remains. Most of these patients are treated in the community,

yet these individuals are overlooked by the majority of European COVID-19 vaccination strategies. Information collected in this report is not definitive or exhaustive. Countries are still developing vaccination plans and strategies may change as knowledge evolves. EU member states have been asked to share best practices for prioritisation through the Health Security Committee, coordinated by the European Commission.

We therefore call on the European authorities (Council, Parliament and Commission), as well as national health authorities and the scientific community to take note of the summarized evidence and recommendations outlined in this paper, and to correct this intolerable inequality.

References

1. De Hert M, Mazereel V, Detraux J, Van Assche K. Prioritizing COVID-19 vaccination for people with severe mental illness. *World Psychiatry* 2021; **20**(1):54-55.
2. De Picker LJ, Yolken R, Benedetti F, et al. Viewpoint | European COVID-19 exit strategy for people with severe mental disorders: too little, but not yet too late. *Brain, Behavior, and Immunity* 2021. doi: 10.1016/j.bbi.2021.01.008
3. Warren N, Kisely S, Siskind D. Maximizing the Uptake of a COVID-19 Vaccine in People With Severe Mental Illness: A Public Health Priority. *JAMA Psychiatry* 2020. doi: 10.1001/jamapsychiatry.2020.4396
4. European Centre for Disease Prevention and Control. Overview of COVID-19 vaccination strategies and vaccine deployment plans in the EU/EEA and the UK – 2 December 2020. Stockholm: ECDC; 2020. URL: <https://www.ecdc.europa.eu/en/publications-data/overview-current-eu-eea-uk-plans-covid-19-vaccines> (accessed Jan 14th, 2021).
5. Clift AK, Coupland CAC, Keogh RH, et al. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. *BMJ* 2020; **371**: m3731.
6. MacKenna B, Curtis HJ, Morton CE, et al. Trends, regional variation, and clinical characteristics of COVID-19 vaccine recipients: a retrospective cohort study in 23.4 million patients using OpenSAFELY. medRxiv 2021: 2021.01.25.21250356. [preprint]
7. Reilev M, Kristensen KB, Pottegard A, et al. Characteristics and predictors of hospitalization and death in the first 11 122 cases with a positive RT-PCR test for SARS-CoV-2 in Denmark: a nationwide cohort. *Int J Epidemiol* 2020; **49**(5): 1468-81.
8. De Jonge H, Nederlands Ministerie van Volksgezondheid, Welzijn en Sport. COVID-19 vaccinatiestrategie update stand van zaken. Parnassusplein 5, 2511 VX Den Haag, the Netherlands; 2021. <https://www.rijksoverheid.nl/documenten/kamerstukken/2021/01/04/kamerbrief-over-covid-19-vaccinatiestrategie-update-stand-van-zaken> (accessed Jan 7th, 2021).
9. Robert Koch Institut. Beschluss der STIKO zur 2. Aktualisierung der COVID-19-Impfempfehlung und die dazugehörige wissenschaftliche Begründung. 2021. *Epidemiologisches Bulletin* 5/2021. URL: https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2021/Ausgaben/05_21.pdf (accessed Feb 3rd, 2021).
10. Nemani K, Li C, Olfson M, et al. Association of Psychiatric Disorders With Mortality Among Patients With COVID-19. *JAMA Psychiatry* 2021. doi:10.1001/jamapsychiatry.2020.4442

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Author contributions

LDP, CP and ML conceptualized the study. LDP, ES, AS, JB and MCD collected and reviewed the data on country national vaccination strategies. IB, FB, BV, PFP, MEB and RT performed a literature search of the effect of psychiatric comorbidities on COVID-19 outcomes. JB, HK and MM created the best-practice recommendations. All authors provided feedback and helped revise the manuscript.