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In a Comment from Samuele Cortese and colleagues[1] on the Review by Papola and colleagues that describes the 2023 changes to the WHO Model List of Essential Medicines (EML),[2] Cortese and colleagues focus on the EML committee's decisions not to support the inclusion of methylphenidate as an essential medicine for the treatment of ADHD in children and adolescents. Two applications were made to WHO, one in 2018 and one in 2020, to include methylphenidate in the EML. Both applications were rejected by the EML committee due to uncertainty about the quality of the evidence and the benefit to harm balance of methylphenidate over long-term use (ie, 52 weeks and beyond). Cortese and colleagues state that the first decision by WHO in 2018 to not add methylphenidate to the EML was largely based on our Cochrane review published in 2015.[3] It is a bit disheartening to observe our work being referenced in a manner that does not accurately reflect the content of our review,[3] the findings of which were supported by our 2023 update.[4] Moreover, the risks of adverse events[5] are discounted by Cortese and colleagues by reference only to recent observational evidence (rather than a more comprehensive assessment of harms in observational studies and randomised clinical trials).[1]

To accept a long-term pharmacological treatment for children when there is no strong evidence of effects is problematic.[3,4,5,6]

The latest EML for children was released by WHO on July 26, 2023.[7] In the context of mental disorders, changes to the EML for children involved the eradication of the substances chlorpromazine, haloperidol, and fluoxetine. With these alternations, the current EML contains no medications of any kind to treat mental disorders in children younger than 12 years, which aligns with current evidence.[8,9]

WHO sends an important signal regarding the evidence required for medications to be accepted in the EML.[7] WHO indicates that precautions are warranted regarding any pharmacological treatment of mental disorders for children younger than 12 years. From an evidence-based perspective, we believe the precautions to be an ethical and sound stance.

WHO emphasises that decision makers in national health-care systems should seize the revision of the EML mental health section as an opportunity to take actions that improve the evidence base of both pharmacological and psychosocial interventions. Now, more than ever, mental health treatments should be firmly placed on health-policy agendas worldwide, and these treaments should be based on solid evidence.

JPR, OJS, and CG have been co-authors of a Cochrane systematic review on methylphenidate for children with ADHD. All other authors declare no competing interests.

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Authors' reply

Sébastien Ponnou and colleagues and Ole Jakob Storebø and colleagues expressed concerns around our plea for methylphenidate to be included in the

WHO Model List of Essential Medicines (EML).

Ponnou and colleagues claim that methylphenidate is an amphetamine analogue with addictive potential. Methylphenidate has—as does dexamfetamine—a very different pharmacology to stimulant drugs that are misused, such as methamphetamine and cocaine. These differences, primarily pharmacokinetic in nature, reduce drug-liking effects, misuse potential, and the development of addiction. Substantial evidence suggests that, when used therapeutically, stimulant treatments for ADHD do not increase, and might even protect against, the likelihood of later substance use problems.[1]

Both Ponnou and colleagues and Storebø and colleagues claim that there is a low level of certainty about evidence on the efficacy of methylphenidate for reducing symptoms of ADHD. That claim is based on Storebø and colleagues' meta-analyses of methylphenidate, which used an idiosyncratic application of the Cochrane risk of bias tool.[2] We believe that data from randomised clinical trials are clear: methylphenidate is not only efficacious, it is among the most efficacious drugs in all of medicine.[1]

Both Ponnou and colleagues and Storebø and colleagues express concerns about the long-term effectiveness and safety of methylphenidate. Their claim that there is no strong evidence for the long-term effectiveness of methylphenidate ignores data from relapse prevention studies, which demonstrate the persistence of clinically meaningful benefits for people with ADHD with continued long-term methylphenidate treatment.[3] Findings from many naturalistic studies, from multiple medical registries around the world, also document longer-term effects of methylphenidate across key real-world outcomes, including decreased risk of suicide, car accidents, and unintentional injuries.[1]

The ADDUCE study,[4] which confirmed the safety of methylphenidate over a 2-year period in children and adolescents, found that long-term methylphenidate use was associated with small increases in heart rate and blood pressure, but these increases were present only during the day and recovered overnight. A recent observational study found that longer cumulative use of methylphenidate, for up to 14 years, was associated with a statistically significant increased risk of hypertension and arterial disease, but no increased risk for other serious cardiovascular conditions (including heart failure).[5] Although these findings reinforce the recommendations found in all evidence-based guidelines to monitor cardiovascular parameters when prescribing methylphenidate, they are not an argument to withhold such an effective treatment from those who would benefit.

Safety and efficacy data have been reviewed in great depth by regulators (eg, the US Food and Drug Administration and the European Medicines Agency), the developers of evidence-based national guidelines (eg, the UK National Institute for Health and Care Excellence and the American Academy of Pediatrics), and government agencies who have endorsed these guidelines (eg, the Australian National Health and Medical Research Council). These groups all conclude that methylphenidate is safe and effective and should be considered as a first-line pharmacological treatment for ADHD. Although WHO has not yet agreed to include methylphenidate on the EML, they do support the use of methylphenidate as a treatment for ADHD, including in non-specialist settings within low-income and middle-income countries. The 2023 WHO Mental Health Gap Action Programme guideline for mental, neurological, and substance use disorders makes a clear recommendation that methylphenidate should be considered for children aged 6 years and older who have ADHD, noting specifically that, "methylphenidate treatment shows substantial effects on symptom reduction".[6]

A crucial perspective missing from the Correspondence of Ponnou and colleagues and Storebø and colleagues is the voice of people with lived experience of ADHD. Listening to what those with lived experience are saying is essential for evaluating evidence and determining policy. When preparing our original Correspondence for *The Lancet Psychiatry*, we consulted with seven large lived-experience associations from across the world.[7] These associations were unanimous in recognising the crucial role methylphenidate has had in improving the lives of people with ADHD, and supporting inclusion of methylphenidate in the EML. As clinicians and researchers, we cannot ignore their message.

We hope that members of the WHO EML committee evaluating methylphenidate will, in the future, take into account both the scientific evidence and the views of people with lived experience of ADHD.

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Physical health metrics are essential for establishing the effectiveness of eating disorder treatment

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The set of outcomes and measures for eating disorders proposed in Amelia Austin and colleagues' Position Paper[1] is commendable, as it covers the important aspects of mental wellbeing and overall quality of life. Nonetheless, integrating physical health outcomes into this set is essential, given that eating disorders can have severe, potentially irreversible physical consequences, including the risk of premature mortality.[2] In the past 4 years, anorexia nervosa has been redefined as a metabo-psychiatric disorder.[3] Therefore, the inclusion of metabolic factors is key for assessing treatment efficacy.

Austin and colleagues noted that BMI was initially considered as an outcome measure but was subsequently discarded due to poor consensus. Despite criticism of BMI as a metric for assessing obesity, low BMI is associated with physical risks in both medical emergencies and long-term complications and is included in both the DSM-5 and ICD-11 diagnostic systems for assessing the severity of anorexia. Addressing malnutrition is crucial for preventing long-term complications, enhancing physical and mental wellbeing, and ensuring optimal functioning. Furthermore, even though a healthy BMI at discharge is a strong predictor of good outcomes in anorexia nervosa,[4] the mean BMI at discharge is approximately 17 kg/m^2 in the UK,[5] which could contribute to poor patient outcomes. BMI is a low-cost and accessible tool for a wide range of health-care settings, including those with scarce resources, and can thus facilitate international comparisons of outcomes.

Individuals with bulimia nervosa require outcome measures that