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**Authors' Response to Brailon's Comment on: "Limited Evidence for Risk Factors for Proarrhythmia and Sudden Cardiac Death in Patients Using Antidepressants**

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## Authors' Response to Braillon's Comment on: "Limited Evidence for Risk Factors for Proarrhythmia and Sudden Cardiac Death in Patients Using Antidepressants: Dutch Consensus on ECG Monitoring"

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We thank Dr. Braillon for his comments on our article [1]. Dr. Braillon questions whether we should minimize the risk of proarrhythmia and sudden cardiac death in relation to antidepressants with recommendations for electrocardiogram monitoring or avoid the use of antidepressants all together and mainly treat patients with depression with psychotherapy [2]. We agree with Dr. Braillon that psychotherapy (cognitive behavioral therapy) is an alternative first-line treatment option for depression with at least better and prolonged effects regarding relapse prevention relative to antidepressants [3–5]. However, the aim of our article was to aid physicians and patients who have collaboratively decided to start antidepressant therapy to treat depression either as monotherapy or in combination with psychotherapy [1, 6]. We describe a set of recommendations for estimating and minimizing the risk of proarrhythmia and sudden cardiac death after the choice for pharmacological therapy above other treatment options has been made [1].

For decades, there has been a debate about the efficacy, effectiveness, and benefit-harm ratio of antidepressants. A recent systematic review and network analysis that was not yet available when Prescrire published its list of drugs to avoid in 2017 [7] represents the most comprehensive analysis of the evidence base for antidepressant efficacy and acceptability ever performed [8]. Based on 552 trials and over 116,000 participants, Cipriani et al. found that all 21 antidepressants included in the meta-analysis were more efficacious than placebo in adults with major depressive disorder, while few differences were found between the antidepressants and placebo when tolerability was concerned [8]. In fact, treatment with antidepressants can be lifesaving. Patients with major depressive disorder more often die from suicide than from proarrhythmia or sudden cardiac death. Although the risk of intentional overdosing as a consequence of psychiatric disease is always present, the literature currently available shows that adults aged over 25 years treated with any class of antidepressant have a lower risk of suicidality compared with placebo [9, 10]. We agree with Dr. Braillon that risks associated with any drug

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could be prevented by avoiding such agents and considering alternatives (e.g., psychotherapy) instead. Considering the data from the aforementioned meta-analyses, however, the suggested market withdrawal for antidepressants such as citalopram, escitalopram, and venlafaxine [7] is, in our opinion, too far reaching.

Once the choice for antidepressant therapy has been made, in our opinion, it is important to minimize the risk of proarrhythmia and sudden cardiac death. Currently, the only way to achieve risk minimization with respect to these adverse effects of antidepressants is to monitor the electrocardiogram based on risk factors such as older age, female sex, or aberrant potassium levels. We provide clear and readily applicable recommendations for performing electrocardiogram screening and monitoring in daily clinical practice, thereby meeting a need of clinicians that we identified.

We hope we were able to clarify the issues raised by Dr. Braillon and would like to thank him again for his reflections on our work.

### Compliance with Ethical Standards

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**Patient consent** Patient consent was not applicable for this letter.

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