The potential of individual patient data for research on antidepressant safety and efficacy

de Vries, Ymkje Anna; Roest, Annelieke M; de Jonge, Peter

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The potential of individual patient data for research on antidepressant safety and efficacy

We thank Drs. Braillon and Naudet for their interest in our work on bias in the reporting of harms in antidepressant trials (Braillon and Naudet, 2016). We agree that biased results have been used by pharmaceutical companies to market antidepressants as being safer than they truly are (e.g., Jureidini et al., 2008) and that bias is by no means limited to adverse events. This may be particularly the case for the biased reporting of efficacy and treatment-emergent suicidal behavior in young people, as the authors point out.

The recent re-analysis of Study 329 (Le Noury et al., 2015), a controversial trial of paroxetine for the treatment of depression in young people, shows the potential value of individual patient data (IPD) for improving our understanding of the adverse effects of antidepressants. Because adverse events are often idiosyncratic, individual events are usually coded to preferred, standardized terms before analysis. In our study, we found bias in the reporting of these preferred terms (de Vries et al., 2016a), but bias can also occur in the (inherently somewhat subjective) process of turning an event narrative into a standardized term. For instance, use of the preferred term “emotional lability” diminishes and obscures the seriousness of the actual events, which include self-harm and suicidal ideation (Le Noury et al., 2015). Examination of IPD, including case report forms, is essential to uncover such biases.

We believe that IPD meta-analyses, performed by independent investigators, have the potential to provide answers to many questions regarding antidepressant efficacy and safety, not just with regard to bias. Combining IPD from multiple trials can provide the necessary statistical power to examine rare adverse events, which is often impossible in individual trials. IPD can also be used to examine which patients are more likely to benefit from antidepressants and which patients, by contrast, are more likely to experience side effects. We have, for example, previously used trial-level data to examine the effect of initial severity on antidepressant efficacy for anxiety disorders (de Vries et al., 2016b) and are now working on an IPD meta-analysis examining this question in more detail.

We therefore believe it is a highly positive development that IPD from pharmaceutical trials are becoming more readily accessible (e.g. through ClinicalStudyDataRequest.com, the Yale University Open Data Access (YODA) project, or Pfizer’s own data access system). Obstacles do remain, including the difficulty in combining data from multiple sponsors with different access systems, problems in working with remote desktop systems (Le Noury et al., 2015), and the time investment required, particularly if one is interested in examining adverse event narratives. We share Drs. Braillon and Naudet’s hope that further developments in sharing IPD, including standardization and improvements in ease of access, will enable more researchers to conduct relevant and high-quality IPD re-analyses and meta-analyses.

Conflicts of interest
None.

References


Ymkje Anna de Vries*, Annelieke M. Roest
Interdisciplinary Center Psychopathology and Emotion regulation, Department of Psychiatry, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands
E-mail address: y.a.de.vries@umcg.nl (de Vries)

Peter de Jonge
Interdisciplinary Center Psychopathology and Emotion regulation, Department of Psychiatry, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands
Developmental Psychology, Department of Psychology, University of Groningen, Groningen, The Netherlands

*Correspondence to: Department of Psychiatry University Medical Center Groningen, Hanzeplein 1, 9713 GZ Groningen, The Netherlands.