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Age of Onset of Mental Disorders

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Mood and anxiety disorders have an earlier age of onset than most other medical conditions. They often emerge during critical windows for psychological and social development and can interfere with completion of education, initiation of careers, and establishment of relationships. An improved understanding of their age of onset is important since intervention in the early stages of these disorders may provide an opportunity to enhance outcomes.

This issue of *The Canadian Journal of Psychiatry* includes 2 systematic reviews examining the age of onset of mental disorders. The first, by de Lijster et al.,[1] examines the ages of onset of various anxiety disorders, and the second, by Dagani et al.,[2] examines the interval between onset of bipolar disorders and the initiation of management. Together, these articles provide substantial gains over the previous state of knowledge (and previous narrative reviews) due to their adoption of strong methodological and reporting standards for systematic reviews. An example of the systematic approach is seen in the Dagani et al.'s use of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). This ensures comprehensive reporting, a feature that is also in evidence in the de Lijster et al. article. A detailed and clearly articulated literature search strategy is implemented in both articles. Dagani et al.'s use of the Newcastle-Ottawa Scale to assess study quality is another strong methodological feature.

These systematic approaches to summarising the literature have distinct advantages over traditional narrative reviews. Narrative reviews, for example, are subject to 'file drawer' effects, in which experts rely too much on their own collection of favorite studies, resulting in an unbalanced view of the underlying literature. de Lijster et al.[1] note that prior narrative reviews of the same topic have reported younger average ages of onset than they found in their systematic review. A possible explanation is that advocates of early intervention may have overemphasised studies that report younger ages of onset. Systematic reviews seek to eliminate, or at least evaluate, such sources of bias.

Dagani et al.[2] find evidence of publication bias in the form of a significant Eggers test, suggesting that studies reporting longer intervals between onset of bipolar disorders and the start of their management may be more likely to be published than studies reporting a shorter interval. Publication bias differs from the file drawer effect described above. Publication bias is not an issue of failing to include certain studies but rather a failure of some studies to be published at all. Systematic review methods do not always have a solution to this problem, but they at least provide a set of tools to identify and better understand it.

Almost all research studies are subject to errors that may arise by chance—in other words, due to sampling variability. Most seek to quantify such error using statistical techniques such as confidence intervals. As sample sizes become larger, vulnerability to random error diminishes due to the law of large numbers, and estimates become more precise, having narrower confidence intervals. This is the fundamental rationale for conducting meta-analysis as a component of systematic reviews. By pooling together the results of individual studies, more precise estimates can be made. However, not all variability between studies is due to sampling variability. There may be differences between studies that arise from their study design characteristics or the ways in which their protocols were implemented. Differences between studies often arise for unknown reasons. Meta-analytic methods are useful not only for gaining precision through pooling but also for identifying reasons for differing study results through the use of techniques such as meta-regression. Both of these studies use random-effect models, acknowledging that the age of onset varies between people (as represented by the standard errors of the estimated mean ages of onset) and also between studies, such that each study is seen as a member of a distribution of study results rather than as an estimate of a single underlying 'fixed' effect. This approach provides a more realistic statistical representation of the underlying literature.

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de Lijster et al.[1] identify a mean age of onset of anxiety disorders of 21.3 years, but they also document considerable variability depending on the specific anxiety disorder in question. Using random-effects meta-regression models, they also report that the age of onset is younger when prospective study designs are used, as opposed to retrospective ones. This finding may represent recall bias. As people's recollection of the age of onset of their disorders may not be accurate, they may overestimate their age at the time of onset of their disorder. The authors also report that estimates from more highly developed countries suggest an earlier age of onset than those of less developed countries. They speculate that this may occur due to a confounding of effects of study design and the development index. More highly developed countries may more often conduct prospective rather than retrospective studies, creating the impression of an earlier age of onset when in reality the effect may be due to differences in study design. Theoretically, the meta-regression approach could disentangle such confounded effects by simultaneously including indicators of level of development and study type (prospective versus retrospective). Currently, there are not enough published studies to allow this, but as additional literature accumulates, deeper and deeper insights will be possible.

Dagani et al.[2] report some parallel results. They find that studies using systematic approaches to establishing illness chronology report longer intervals between onset and management. This may reflect inaccurate recollection of illness onset when nonsystematic approaches are relied upon, another example of recall bias. However, they also find an apparently paradoxical result: there is a longer interval when onset is defined in terms of episodes rather than symptoms. Logically, one suspects that prodromal symptoms should precede distinct episodes of illness, such that longer rather than shorter intervals would be expected when onset is defined in terms of symptoms.

The most striking finding by Dagani et al.[2] is a 6-year delay between the onset of bipolar disorder and the start of its management. Intuition suggests that this interval may provide an opportunity for earlier and more effective intervention. However, it should be remembered that the interval between onset and management can only be assessed in respondents who eventually develop a bipolar disorder. Efforts at early intervention can have unexpected drawbacks such as false-positive diagnoses, which may lead to unnecessary treatment and associated risks. Resources devoted to earlier detection preclude other uses of those resources. One might hope that increasing mental health literacy would in itself shorten the interval between onset and management. Unfortunately, more recent studies (in which levels of literacy are presumably higher) were found to have a longer rather than shorter interval between onset and management. If increasing mental health literacy is causing people to seek help earlier, this may be offset by its facilitation of earlier personal recognition of onset symptoms and episodes.

Both of these studies are good examples of the knowledge gains made possible by careful application of systematic review methods. As the underlying literature continues to grow, the importance of systematic reviews will also continue to grow. By providing more precise estimates and identifying reasons for variation between studies, these investigations extend familiar research concepts from individual studies to an entire literature. As the literature grows, these methods will permit deeper insights into these important clinical and public health issues, much as larger studies of individual people can usually provide deeper insights than smaller studies. For this reason, *The Canadian Journal of Psychiatry* has been increasingly publishing systematic reviews and meta-analyses. This trend is likely to continue into the future.

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