

Clinical guidelines for mood disorders: the roads travelled, the road ahead

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Introduction

In December 2015, the Royal Australian and New Zealand College of Psychiatrists (RANZCP) published their latest clinical practice guidelines for mood disorders (Malhi et al., 2015).

Recently, other guidelines on the same topic have been published by important scientific societies: the British Association of Psychopharmacology (BAP) and the Canadian Network for Mood and Anxiety Treatments (CANMAT). Each guideline stemmed from a meeting of experts, which identified relevant new literature, consensus points and areas of uncertainty.

In this commentary, we compare these clinical guidelines, considering why multiple organizations publish guidance on similar topics and discussing what might be done to improve such publications in the future.

Layout

It is notable that the layouts of the publications vary considerably (Table 1). RANZCP and CANMAT guidelines include multiple helpful flowcharts and tables to consolidate the text.

The use of diagrammatic treatment algorithms in these guidelines are particularly useful additions. BAP guidelines are missing such visual aids, but do separate the

recommendations and evidence into different sections, so the key clinical points are presented in a concise manner unobstructed by lengthy discussions of the evidence. A

distinct question-answer format is utilized by the CANMAT unipolar depression guidelines.

Whilst this is undoubtedly helpful in answering specific questions, this approach requires the reader to have a deeper level of prior understanding to put each question into context (for example, the treatment of mild-moderate depression may span multiple questions and separate sections, requiring some prior knowledge to hone in on where this information might be).

Framing the key recommendations

In terms of key recommendations, the guidelines are broadly similar. Moreover, they often cite each other and are based on similar evidence retrieved from similar systematic reviews. This raises the question of why multiple national organizations produce separate recommendations. Should clinicians use the most recent guidance published in the literature or that of their own country, even if older? The value of country-specific guidelines comes from addressing country-specific issues, which might include addressing the needs of minority populations or licensing issues. For example, the RANZCP guidance considers the needs of Māori and Aboriginal and Torres Strait Islander peoples. Whilst sections that discuss minority groups may not be backed up by the same quality of studies as the key recommendations, they serve as a unique and useful anchor point for clinicians encountering such populations.

The example of acute mania

One difference of note is the inclusion of asenapine as a monotherapy for acute mania in the RANZCP and CANMAT guidelines, but not the BAP recommendations. Interestingly, these recommendations are based on similar evidence, with all papers citing the same network meta-analysis (Cipriani et al., 2011). It appears to be the interpretation of the evidence (and not the evidence itself) that has resulted in this difference. The BAP bipolar guideline explicitly state that they “are impressed by the power of network meta-analysis for understanding treatment efficacy”. Therefore, they highly rate the treatments best supported by the network meta-analysis such as haloperidol, olanzapine, risperidone and quetiapine. We agree that network meta-analyses should be positioned amongst the

highest levels of evidence used in clinical guidelines, because they allow all treatments to be compared to one another and ranked, facilitating the selection of a preferred treatment for a specific condition (Leucht et al., 2016). When many different treatment options are available, guideline developers should go beyond pairwise meta-analyses because pairwise meta-analyses are limited by treatments that have been compared directly in individual studies (Rouse et al., 2016).

How to assess the quality of evidence

Assessing the quality of evidence to developing recommendations is very important in guidelines. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach represents a transparent and consistent method of moving from evidence to recommendations, by using explicit, comprehensive criteria for downgrading and upgrading quality of evidence ratings (www.gradeworkinggroup.org). GRADE allows a clear separation between quality of evidence and strength of recommendations, resulting in a pragmatic interpretation of strong versus weak recommendations for clinicians, patients, and policy makers. The BAP bipolar guidelines refer to the GRADE approach (Goodwin et al., 2016). This is a step forward (other mood guidelines used old and non-reliable categories to assess quality), but all future updates should move towards employing the full GRADE approach.

How to implement the guidelines

Whilst the methodology, it should not be forgotten that the end-users are mental health professionals. As such, it is worth considering how guideline developers might also help and promote implementation of guidelines in the future. Technology is increasingly entering the

clinical environment. Recently, the UK Resuscitation Council published its latest guidance in an app format to be used on tablets and mobile phones (www.resus.org.uk/apps/iresus). Technological adaptations may well increase the utilization of such information. Social media may also play a role in getting ideas and feedback from clinicians about published guidance.

Newer medicines are often tested and used as first line treatment, however older drugs can still play a role as second or third line, or in the treatment of patients with resistant illness. It is important to remember that young clinicians may have limited experience with older agents. Therefore, part of any implementation process must be to ensure that those who will use the guidance are comfortable with its recommendations. Trainees should gain appropriate exposure to older medications so that these agents remain available to the patients who need them.

Finally, as the main aim of each guidance is an improvement in patient outcomes, the impact of guidelines should be measured to check whether they have had or will have a tangible benefit for patients. The RANZAP guidance was published following a consultation with patients and the wider public. This is a step in the right direction, ensuring that guidelines reflect what matters to patients. However, authors of future guidelines should consider how they can routinely and systematically monitor the effect of their recommendations. This will help maximize the improvement of patient outcomes and this, after all, is why they are written.

# Item	RANZCP	BAP	CANMAT
Number of documents	1	2 [1 UP + 1 BP]	8 [7 UP +1 BP]
Total length (pages)	120	126 [67 UP + 59 BP]	142 [98 UP + 44 BP]
Length of text (pages)	89	95 [49 UP + 46 BP]	103 [71 UP + 32 BP]
Length of references (pages)	27	31 [19 UP + 12 BP]	47 [34 UP +13 BP]
Length of appendices (pages)	5	3 [3 BP]	0

Table 1: Layout of the guidelines.

Legend. RANZCP: Royal Australian and New Zealand College of Psychiatrists; BAP: British Association of Psychopharmacology; CANMAT: Canadian Network for Mood and Anxiety Treatments; UP: about unipolar depression; BP: about bipolar disorder.

References

Cipriani A, Barbui C, Salanti G, et al (2011) Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. *Lancet* 378: 1306-1315.

Goodwin GM, Haddad PM, Ferrier IN, et al (2016) Evidence-based guidelines for treating bipolar disorder: Revised third edition recommendations from the British Association for Psychopharmacology. *Journal of Psychopharmacology* 30: 495-553.

Leucht S, Chaimani A, Cipriani A, et al (2016) Network meta-analyses should be the highest level of evidence in treatment guidelines. *European Archives of Psychiatry and Clinical Neurosciences* 266: 477-80.

Malhi GS, Bassett D, Boyce P, et al (2015) Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders. *The Australian and New Zealand Journal of Psychiatry* 49: 1087-1206.

Rouse B, Cipriani A, Shi Q, et al (2016) Network Meta-analysis for Clinical Practice Guidelines: A Case Study on First-Line Medical Therapies for Primary Open-Angle Glaucoma. *Annals of Internal Medicine* 164: 674-682.