

Agomelatine – is it another reboxetine? Another case of publication bias

I read the special article about agomelatine with interest.¹ The authors state that controlled studies have suggested a favourable efficacy and tolerability profile of agomelatine in depression. This statement is not entirely accurate.

The article has missed the negative studies and is a glaring example of publication bias, issues that have been highlighted in a recent meta-analysis.² This meta-analysis of placebo-controlled trials of agomelatine in depression included unpublished trials and concluded that agomelatine is unlikely to be clinically superior to placebo. I am part of a group which has recently submitted a systematic review for the Cochrane Collaboration where we compared the efficacy of agomelatine with other antidepressant drugs in depression. Agomelatine did not seem to provide any significant advantage in efficacy. We also found evidence of publication bias. We contacted Servier, maker of agomelatine, for the unpublished trials, but did not receive any response. Furthermore, Servier has not provided data to the National Institute for Health and Care Excellence (NICE); hence NICE has not recommended agomelatine use.³

The article states that more data are needed to assess the effectiveness of agomelatine in real-world conditions. However, the fact is that agomelatine's efficacy in controlled trials is not yet established. Almost all the studies have been sponsored by Servier or Novartis, the company which marketed it in the USA.

Reboxetine is a classic example of publication bias; in this case mostly positive studies were published. Many years after its introduction, in 2010, the unpublished data was accessed and a meta-analysis found reboxetine to be an ineffective and potentially harmful antidepressant drug.⁴ It is time that drug companies disclose all data from all trials irrespective of the outcome so the efficacy of a drug can be judged objectively.

- 1 Whiting D, Cowen PJ. Drug information update: agomelatine. *Psychiatrist* 2013; **37**: 356–8.
- 2 Koesters M, Guaiana G, Cipriani A, Becker T, Barbui C. Agomelatine efficacy and acceptability revisited: systematic review and meta-analysis of published and unpublished randomised trials. *Br J Psychiatry* 2013; **203**: 179–87.
- 3 National Institute for Health and Clinical Excellence. *Agomelatine for the Treatment of Major Depressive Episodes (Terminated Appraisal)* (Technology Appraisal TA231). NICE, 2011.
- 4 Eyding D, Lelgemann M, Grouven U, Hrter M, Kromp M, Kaiser T, et al. Reboxetine for acute treatment of major depression: systematic review and meta-analysis of published and unpublished placebo and selective serotonin reuptake inhibitor controlled trials. *BMJ* 2010; **341**: c4737.

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Authors' response: By taking part of a single sentence out of context, Sumeet Gupta misrepresents our article. We wrote: 'Controlled studies have suggested favourable efficacy and tolerability profiles; however, agomelatine is not without its controversies, with recent meta-analyses showing only marginal advantages over placebo' (our italics). We also stated that, 'although narrative reviews of the efficacy of agomelatine emphasise its superior efficacy relative to placebo and certain other antidepressants such as sertraline and fluoxetine, formal

meta-analyses have found these effects to be less convincing and of uncertain clinical significance' (the meta-analysis by Koesters *et al*¹ had not been published when we submitted our article, so we relied on that of Singh *et al*² which reaches similar conclusions). Merely reading the abstract is enough to encounter the phrase: 'Current meta-analyses show marginal clinical benefits of agomelatine relative to placebo'. Overall, our conclusion is similar to that of Koesters *et al*¹: 'The present systematic review found that acute treatment with agomelatine is associated with a difference of 1.5 points on the HRSD. This difference was statistically significant, although the clinical relevance of this small effect is questionable'.

Drug companies are often accused, with justification, of making exaggerated and misleading claims. Their critics should avoid emulating them.

Declaration of interest: P.J.C. has been a paid member of advisory boards for Eli Lilly, Lundbeck and Servier.

- 1 Koesters M, Guaiana G, Cipriani A, Becker T, Barbui C. Agomelatine efficacy and acceptability revisited: systematic review and meta-analysis of published and unpublished randomised trials. *Br J Psychiatry* 2013; **203**: 179–87.
- 2 Singh SP, Singh V, Kar N. Efficacy of agomelatine in major depressive disorder: meta-analysis and appraisal. *Int J Neuropsychopharmacology* 2012; **15**: 417–28.

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A leaflet to improve knowledge and attitudes to help-seeking for mental illness among Muslims

Help-seeking for mental illness is problematic among Muslim communities in Western countries.^{1,2} We set out to develop a leaflet on attitudinal and knowledge barriers to help-seeking for mental illness in UK Muslims, working with a local voluntary organisation (SMART), the Royal College of Psychiatrists (RCPsych) and the Muslim Council of Britain. In the leaflet, we addressed known barriers to help-seeking such as cultural and traditional beliefs, knowledge of and familiarity with formal services, perceived societal stigma, and the use of informal indigenous resources.³ An Islamic religious leader checked the content for religious accuracy and we ensured the design was culturally consistent. A draft of the leaflet was piloted with a focus group of six Muslim men, then re-drafted using their feedback to produce the final version.

To evaluate the leaflet, we attended a London mosque at evening prayer time (Isha) and invited members of the congregation to complete a questionnaire before and after reading it. Twenty-five men aged 18–65+ volunteered; there were no women at the mosque at the time. All were Muslim UK residents: 32% Asian/Asian British Pakistani, 20% Asian/Asian British other, 44% other ethnicities combined, 4% gave no response. A statistically significant change was noted in response to two questions: 'I would see a doctor if I felt very sad, worried, scared or was having unusual experiences' ($P = 0.039$) and 'I know what treatments are available for mental illnesses' ($P = 0.010$). Furthermore, 72% of participants thought the leaflet helped them to understand mental illness better, 96% found it easy to read, 88% easy to understand and

72% felt more able to tell others about mental illness after reading it.

The leaflet was posted on the RCPsych website and results were collated from the online feedback. Respondents rated the leaflet on readability, usefulness, respectfulness and design on a scale from 1 (strongly disagree) to 5 (strongly agree). Overall, 103 respondents submitted feedback over a period of approximately 5 months: 10 service users, 6 patient relatives, 4 carers, 11 friends, 65 healthcare professionals, 8 healthcare students, 12 'others'. The mean score for 'readable' was 4.38 (88 responses); the mean score for 'useful' was 4.30 (94 responses); the mean score for 'respectful' was 4.11 (89 responses); and the mean score for 'well-designed' was 4.17 (89 responses), with a score of 4 meaning 'agree'.

Although the evaluation was limited by a small sample size of men only and the lack of follow-up, we concluded that after reading the leaflet, participants assessed themselves as more likely to seek medical help if they were experiencing symptoms of mental illness and more knowledgeable about what treatments are available. They found the leaflet helpful in improving their understanding of mental illness, easy to read and understand, and thought it enabled them to tell others about mental illness. From the online feedback, respondents agreed that the leaflet was readable, useful, respectful and well designed.

The leaflet is available on the RCPsych website: www.rcpsych.ac.uk/healthadvice/problemsdisorders/leafletformuslimsonstress.aspx

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- 2 Loewenthal KM, Cinnirella M, Evdoka G, Murphy P. Faith conquers all? Beliefs about the role of religious factors in coping with depression among different cultural-religious groups in the UK. *Br J Med Psychology* 2001; **74**: 293–303.
- 3 Aloud N, Rathur A. Factors affecting attitudes toward seeking and using formal mental health and psychological services among Arab Muslim populations. *J Muslim Ment Health* 2009; **4**: 79–103.

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Research ethics approval and discrimination

We read with envy Galappathie *et al's* study¹ of detained patients' awareness of the mental health review tribunal (MHRT). We applaud their decision to regard their study as part of service evaluation rather than as a research project requiring National Research Ethics Service Committee (NRES) approval.

We applied for NRES approval for a study asking patients detained under Section 2 or Section 3 of the Mental Health Act 1983 about their views on the chances of the MHRT rescinding their detention if they appealed. The crucial question was 'What do you think are the chances that you will be discharged by the Tribunal if you appeal?'

The NRES which reviewed the application did not have a mental health patients' representative, carers' representative or mental health professional as its member. Therefore, it sought expert opinion from a retired clinical psychologist. The NRES ruled that 'the study should not be done in the acute phase of treatment when participants are detained and it would be more appropriate once they have been discharged. This would remove concerns about the ability of the participants to give informed consent whilst under detention and in a vulnerable condition'.

We appealed against the decision and our application was referred to another NRES which also did not have a mental health patients' representative or carers' representative, but had a psychologist as a member. We attended the review and explained that we endeavoured to assess detained patients' views and that post-discharge retrospective assessment would be futile. We argued that the first principle of the Mental Capacity Act 2005 is the presumption of capacity. The General Medical Council guidance also states that one must not assume that a patient lacks capacity to make a decision solely because of their medical condition, including mental illness. We confirmed that patients who did not have capacity to decide whether to take part in the study will not be offered the opportunity to take part. This second NRES agreed with the first one for the same reasons, that is, detained patients don't have capacity to decide whether to take part in the study.

This is an example of ignorance and consequent stigmatising attitudes held by those in authority, resulting in discrimination against mental health patients, carers and professionals. Members of NRESs believing that those who are mentally ill lack the capacity to make simple decisions could significantly hamper research into mental illness and perpetuate the myth that psychiatry is the most unscientific medical specialty. Mental health professionals and patient groups may share part of the blame by not representing themselves on NRESs.

- 1 Galappathie N, Harsch RK, Thomas M, Begum A, Kelly D. Patients' awareness of the mental health tribunal and capacity to make requests. *Psychiatrist* 2013; **37**: 363–6.

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Mental health screening in police custody – acceptability among detainees

McKinnon *et al*¹ highlight the importance of effective screening of detainees in police custody for mental health problems and draw attention to the emerging provision of liaison and diversion services in police custody. In their study, approximately 28% of detainees from inner city London police stations declined to be interviewed by mental health professionals.

The experience of the criminal justice mental health team which provides liaison services to two police stations in rural North East Essex was similar. Of 573 detainees who were offered an assessment within 14 months of the newly