Selective reporting of results in guidelines

Taylor and Perera argue persuasively that the 2014 National Institute for Health and Care Excellence (NICE) schizophrenia guideline promotes cognitive–behavioural therapy (CBT) and other psychosocial interventions beyond the evidence. Its conclusions with respect to CBT also seem open to another charge, that of selective reporting: the highlighting of favourable results while unfavourable ones are suppressed.

In its evidence summary (p. 232), NICE states that 'when compared with standard care, CBT was effective in reducing rehospitalisation rates up to 18 months following the end of treatment. NICE actually examined rehospitalisation rates in three of the large series (more than 100) of meta-analyses they carried out (data available at www.nccmh.org.uk). One of these compared CBT with standard care at up to 18 months and found a significant effect (5 trials, 910 patients, RR 0.76, 95% CI 0.61–0.94). Another compared CBT with standard care at 2–4 years and failed to find a significant advantage (2 trials, 513 patients, RR 0.82, 95% CI 0.64–1.05). The third meta-analysis compared CBT with ‘other active treatments’ (which consisted in all but one case of putatively inactive control interventions such as befriending and supportive counselling) at up to 2 years; this was again non-significant (5 trials, 506 patients, RR 1.07, 95% CI 0.86–1.33). The findings of the two negative meta-analyses are not mentioned in the NICE guideline. Neither does NICE mention that CBT was not found to be effective against relapse when compared with either standard care (3 trials, 460 patients, RR 0.85, 95% CI 0.50–1.41) or other active treatments (4 trials, 416 patients, RR 1.05, 95% CI 0.85–1.30). This omission is difficult to understand given the obvious relationship between relapse and rehospitalisation.

NICE goes on to state that ‘CBT was shown to be effective in reducing symptom severity as measured by total scores on items, such as the PANSS and BPRS, both at end of treatment and at up to 12 months’ follow-up’. This was the case in the comparison between CBT and standard care, where there was a significant effect for CBT at the end of treatment (13 trials, 1356 patients, standardised mean difference (SMD) −0.27, 95% CI −0.45 to −0.01) as well as in meta-analyses of 6- and 12-month follow-up data. However, the findings were non-significant in the comparisons between CBT and ‘other active treatments’ both at end of treatment (6 trials, 396 patients, SMD −0.13, 95% CI −0.32 to 0.07) and at all follow-up points. Once again, NICE conveys an impression of uniform evidence of effectiveness against symptoms, whereas the reality is that an entire subset of pre-planned meta-analyses gave negative results.

Selective reporting arises when authors fail to publish data altogether, or when they arbitrarily decide which analyses and results to report in a publication. The NICE 2014 recommendations provided by data sharing between patients, carers and clinicians does not threaten privacy and undermine public trust. Finally, patients, clinicians and NHS commissioners require an agreed framework to evaluate the core features of new technologies including usability, content, safety, clinical- and cost-effectiveness.

These still apply with equal force to the first two digital revolutions.

Does previous experience of antidepressants form the expectations necessary for a placebo response?

Leuchter et al\(^1\)\(^1\) findings extend the current understanding of the placebo response and raise important questions regarding the design of antidepressant trials. An important finding was that expectation of medication effectiveness predicted treatment response in the placebo group only, which suggests that expectations of treatment benefit are required for a placebo response.

It is thought that the placebo response results from an interaction between expectations and learning.\(^2\) In studies of placebo analgesia, experimental paradigms often involve a conditioning procedure to induce an expectation of benefit from treatment. One widely used paradigm involves thermal pain stimulation and application of an inert cream. Following application of the cream, the thermal energy is reduced to non-painful levels to condition the participant to believe the cream has analgesic properties. Subsequently, laser stimulation continues at painful levels, and application of an inert cream. Following application of the cream, the thermal energy is reduced to non-painful levels to condition the participant to believe the cream has analgesic properties. Subsequently, laser stimulation continues at painful levels, and participants report the stimulation as less painful.\(^3\)\(^4\)\(^5\)\(^6\)

The implication is that an expectation of analgesia, induced by exposure to the cream's "analgesic" properties, results in a placebo response.\(^3\) Learning to expect an effect has also been shown to influence emotional processing. Petrovic et al\(^7\) measured responses to aversive pictures in healthy volunteers following administration of placebo "anxiolytic" medication and its reversal, and found that participants reported aversive pictures as less distressing when they thought they had received anxiolytic medication, and more distressing when they believed this had been reversed. This result shows that a learned expectation, induced through exposure to a medication, can cause changes in emotional processing.

In the study reported by Leuchter et al\(^1\),\(^1\) there was a relationship between expectation of benefit and treatment response in the placebo group. However, these patients did not undergo a conditioning procedure to induce an expectation of benefit. What caused these patients to expect a benefit? Could the therapeutic environment and consent process for starting an antidepressant engender a powerful expectation of benefit on its own? Or does this expectation come from previous experience of benefit from antidepressant treatment? The data from this study suggest the latter, as the expectations seemed to be formed at the time of enrolment. We could perhaps answer this question more fully through assessment of the relationship between previous response to antidepressant treatment and placebo response in this trial. It is possible that more patients in the placebo group had previously benefitted from treatment than in the medication group, and if this were so, it would lend support to the idea that previous experience of benefit from antidepressant treatment could cause a placebo antidepressant response. This could be an important consideration in future antidepressant drug trials.

Authors' reply: Huneke & Baldwin raise important points regarding the interpretation of our study results and the relationship of our findings to the broader placebo literature. It is challenging to compare the results from our study with the literature cited by them. As they note, studies of placebo analgesia generally are performed in healthy volunteers not being treated for a chronic illness. Such studies examine the placebo effect, namely the relief of transient, experimentally induced symptoms during manipulation of expectations. By contrast, our study examined placebo response, which involves relief of naturally occurring symptoms of a chronic illness (in this case major depressive disorder, or MDD) within the context of a clinical trial. Because patients with MDD have long courses of illness and treatment, they commonly enter treatment studies with pre-existing expectations and beliefs, and our participants had indeed formed expectations about medications at the time of study enrolment. We concluded that these expectations were probably formed by factors external to the study, and speculated on the role that

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Authors' reply: We thank Dr McKenna (and colleagues) for his interest in our editorial, and respect his long record of research into schizophrenia. His point about the authors of influential national clinical guidelines such as NICE, the British Association for Psychopharmacology (BAP) and the Scottish Intercollegiate Guidelines Network (SIGN) needing to take negative evidence into account is well made, and analogous to the AllTrials movement in pharmacotherapeutics. Schizophrenia is such a common and potentially devastating illness that it is incumbent on mental health professionals such as psychologists and psychiatrists to work together to deliver best-evidenced treatments.

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https://doi.org/10.1192/bjp.207.6.560a Published online by Cambridge University Press