Folate Augmentation of Treatment – Evaluation for Depression (FolATED): randomised trial and economic evaluation

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Depression is common and serious. Only half of sufferers respond well to antidepressants. There is reason to hope that folic acid, which helps mothers and babies in pregnancy, will help. We conducted the clinical trial known as FolATED to test whether adding folic acid to antidepressants makes them work better and also gives good value for money. We also studied genetic and other scientific aspects of depression.

We aimed to recruit 450 adults from across Wales with confirmed moderate or severe depression for which they were taking or about to start antidepressants, but without other serious illness. Our target was for 360 (80%) of them to complete carefully designed questionnaires about their mental health on three occasions over 6 months. We actually recruited 475, and analysed 440 (93%) of them. Once a day for 12 weeks these participants added an extra pill to their antidepressants. For half of them, chosen at random, this pill contained 5 mg of folic acid. For the other half this pill looked the same but did not contain any folic acid. Only one person knew who had which pill.

Unfortunately the reported health of those who received active pills did not improve any more than the health of those who took inactive pills. So there is now no reason to believe that folic acid strengthens antidepressants. Fortunately recent research suggests that methylfolate may be better at this. So FolATED has undermined guidelines that advocate folic acid for depression, but suggested another way forward.
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