

## EDITORIALS

## Antidepressant induced weight gain

Lifestyle advice and weight monitoring are sensible responses to this important side effect

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Antidepressant prescriptions (mainly selective serotonin reuptake inhibitors and serotonin-noradrenaline reuptake inhibitors) have increased greatly in recent decades: from 61.9 to 129.9 prescriptions per 1000 person years between 1995 and 2011 in the United Kingdom alone.<sup>1</sup> Similarly, in the United States prescription rates increased from 6.8% to 13% of the population between 1999 and 2011.<sup>2</sup> Whatever the reasons (including new clinical indications and increased duration of maintenance treatment<sup>3</sup>) increasing use of antidepressants raises concerns about tolerability and harm. The risk of weight gain associated with antidepressant treatment has received particular attention because of the increased risk of chronic disease and mortality related to being overweight and obese.<sup>4</sup>

While the short term risk of weight gain has been well described,<sup>5</sup> the longer term risk (>1 year) remains poorly investigated. In a linked article, Gafoor and colleagues (doi:10.1136/bmj.k1951) help fill this gap by investigating the long term population impact of antidepressant prescriptions on weight gain in a large cohort of more than 300 000 people.<sup>6</sup> The absolute risk of weight gain without antidepressant use was 8.1 per 100 person years, whereas the risk in people prescribed antidepressants was 11.2 per 100 person years. This translates into a number needed to harm of 59—or one extra weight gain episode for every 59 patients treated, assuming that the association is causal.

This level of risk might look modest, but the effect at population level could be substantial. If roughly 13% of the UK population take an antidepressant, many thousands of people will gain weight each year because of their treatment. Clinicians should discuss the possibility of weight gain with patients who need antidepressants, provide concomitant lifestyle advice on diet and exercise to minimise the risk, and monitor patients' weight and metabolic variables for the duration of treatment. Increasing physical activity may also improve symptoms of depression.<sup>7</sup>

Antidepressants are known to be effective, and they remain the cornerstone of treatment for moderate or severe episodes of major depression.<sup>8</sup> While low intensity psychosocial interventions and individual or group cognitive behavioural therapy may be preferable for people with mild depression, antidepressant treatment should be always offered to those with moderate or severe depression—ideally in combination with a

high intensity psychological intervention such as cognitive behavioural therapy or interpersonal therapy.<sup>9</sup>

Shared decision making is important when deciding between treatment options, to take full account of patient preferences and priorities, including the choice of specific antidepressant. The different agents have similar efficacy but noticeably different tolerability profiles.<sup>9 10</sup> Until better tolerated drug treatments are available, efforts should be focused not on reducing use of antidepressants but on minimising the risk of weight gain and other associated side effects such as sexual dysfunction.

The next step is to quantify the risk of weight gain associated with specific antidepressants. Although some progress has been made to identify agents associated with higher and lower risk of weight gain,<sup>5</sup> the study by Gafoor and colleagues shows how difficult it is to identify long term differences between agents, because of the many other factors contributing to change in weight over time, such as comorbidities, smoking status, and social deprivation. As with all population studies, confounding cannot be ruled out.

Another complication is that obesity likely increases the risk of depression (particularly in adolescents),<sup>11 12</sup> as well as depression increasing the risk of obesity,<sup>13</sup> resulting in a reciprocal risk. Finally, a genetic predisposition likely contributes to risk of weight gain in people taking antidepressants.<sup>14</sup> Some patients may be more genetically predisposed to gain weight irrespective of the antidepressant prescribed.

Currently, we are still unable to identify patients at higher risk of weight gain with antidepressants. Hopefully it will be possible in the not too distant future to identify a genetic predisposition and recognise those at higher risk before treatment is started. In these patients we can then prescribe the antidepressant least likely to cause weight gain, monitor weight and metabolic variables carefully, and provide concomitant lifestyle advice to minimise weight gain. Until then, we should give lifestyle advice and consider monitoring everyone taking these agents.

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