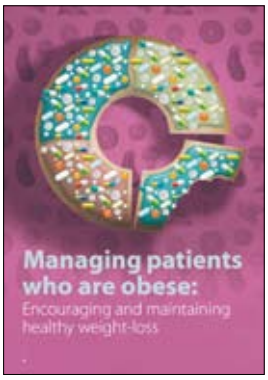

Milk and bone density

Dear Editor

*Can bpac^nz substantiate its claim that "consumption of milk, yoghurt or cheese is associated with improved bone density and a reduced risk of ischaemic heart disease, myocardial infarction and stroke"? ["*Managing patients who are obese", BPJ 65, Dec 2014*] A recent cohort study of 107,000 Swedish adults found almost twice the overall mortality rate and significantly more fractures among women drinking three or more glasses of milk a day. Both men and women had higher rates of cardiovascular mortality with increasing milk consumption. The authors found such a claim may be true for fermented dairy products such as yoghurt and cheese (perhaps because of lower levels of D-galactose) but saying "milk, yoghurt or cheese" may no longer be accurate.*

Reference: Michaëlsson K, et al. Milk intake and risk of mortality and fractures in women and men: cohort studies. BMJ 2014: http://www.bmj.com/content/349/bmj.g6015

***Dr Stephen Hoskin**, General Practitioner*
Te Anau

Response from BPJ editorial team: Milk, yoghurt and cheese are recommended by the Australian Dietary Guidelines (2013) as one of five food groups that people choose from daily to create a varied and nutritious diet.[1] This guideline was the principle source of information for the healthy eating guidance provided in our article "Managing patients who are obese", BPJ 65 (Dec, 2014). Milk, cheese and yoghurt are widely recognised as being good sources of easily absorbed calcium, protein, iodine, vitamin A, vitamin D, riboflavin, vitamin B12 and zinc. However, it is recommended that reduced fat versions of these dairy foods should be chosen on most occasions as full fat milk, cheese and yoghurts increase total fat, saturated fat and overall energy intake.[1]

Specifically regarding milk, yogurt and cheese consumption and cardiovascular risk, the guidelines state:[1]

> *"Coronary heart disease: It is probable that the consumption of at least two serves per day of milk, cheese and yoghurt is associated with a reduced risk of ischaemic heart disease and myocardial infarction.[2]*
>
> *Stroke: It is probable that the consumption of two or more serves per day of milk, cheese and yoghurt is associated with reduced risk of stroke, particularly reduced fat varieties.[2, 3]*
>
> *Hypertension: It is probable that consumption of three serves of low fat milk, cheese and yoghurt is associated with reduced risk of hypertension. The evidence also suggests that consumption of three serves of any milk, cheese or yoghurt products per day is associated with reduced risk of hypertension.[4, 5, 6, 7]"*

The article by Michaelsson *et al* that found an association between milk intake, all-cause mortality and fracture risk was published in October 2014, and therefore would not have been available when the Australian guidelines were compiled. Michaelsson *et al* provided two large patient cohorts in Sweden with food frequency questionnaires which were used to correlate milk intake, either low or full fat, with health outcomes. A dose-dependent increased rate of mortality in females and males was observed, as well as a increased rate of bone fracture in females.[8] This pattern of association was not detected with the consumption of other dairy products.[8] The authors also noted that fermented milk products, such as yogurt and cheese, were associated with reduced mortality and rates of fracture.[8] This observation, combined with other experimental data mainly from animal studies, led the authors to suggest that milk may be harmful due to the potential inflammatory and oxidative properties of D-galactose, a metabolite of lactose.[8] However, currently there is limited evidence concerning the cardiovascular effect of D-galactose.[9] It is possible that the increased fracture rate associated with milk consumption was due to females who were at increased risk of fractures voluntarily increasing their milk consumption and therefore creating a reverse causation phenomenon.

Dietary guidelines are based on rigorous methods of data analysis to ensure that recommendations are a balanced reflection of current evidence. Michaelsson *et al* note that as

their study was observational in design their conclusion that milk consumption within recommended daily quantities may be harmful should be interpreted cautiously. Independent replication is required before these results can be incorporated into population-wide dietary recommendations. As one commentator remarked "a fascinating possibility" has been raised, and randomised controlled trials will assist in determining if this observation is correlation or causation.[9]

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Is phentermine addictive?

Re: "Managing patients who are obese", BPJ 65 (Dec, 2014)

This article is poorly researched and should be re-written. Phentermine abuse or psychological dependence (addiction) does not occur in patients treated with phentermine for obesity. Phentermine treatment does not induce phentermine drug craving, a hallmark sign of addiction. Amphetamine-like withdrawal does not occur upon abrupt treatment cessation even at doses much higher than commonly recommended and after treatment durations of up to 21 years.[1]

In 2005 a randomised, double-blind, placebo-controlled study was performed on 68 relatively healthy obese adults whose body mass index was 25 kg/m^2 or greater. They received phentermine-HCl 37.5 mg or placebo once daily with behavioural therapy for obesity. Mean decrease of both body weight and waist circumference in phentermine-treated subjects were significantly greater than that of placebo group (weight: –6.7 ± 2.5 kg, $p < 0.001$; waist circumference: –6.2 ± 3.5 cm, $p < 0.001$).[2]

Insufficient evidence exists for the use of metformin as treatment of overweight or obese adults who do not have diabetes mellitus or polycystic ovary syndrome.[3]

Dr Nicholas Cooper, *General Practitioner*
[online comment]

Response from BPJ editorial team and Dr Jeremy McMinn, Addiction Specialist: The role of phentermine in the management of patients who are obese is a controversial, and at times polarising, subject; perhaps due to the relatively limited evidence available. There is concern among some addiction experts in New Zealand, about the risks of phentermine. They advise general practitioners not to prescribe phentermine. However, some obesity specialists advocate its use as a short-term, adjunctive treatment for patients who are obese. In the article "Managing patients who are obese: Encouraging and maintaining healthy weight-loss" (BPJ 65) we have attempted to present a balanced view on the subject.

Phentermine is a dopaminergic agonist that acts as an appetite suppressant. Like amphetamine, phentermine is classified as a sympathomimetic drug because it mimics the actions

of neurotransmitters of the sympathetic nervous system. Phentermine was approved for the short-term treatment of obese patients in the United States in 1959.[4] It is subject to the controlled substances act as the United States Drug Enforcement Agency believes that the use of phentermine is associated with a risk of habituation or addiction.[5] However, recently the United States Federal Drug Administration approved the combination of phentermine and topiramate for the long-term treatment of patients who are obese. In Europe, phentermine is not approved for the treatment of patients who are obese due to concerns about its potential to cause addiction, tachycardia and increased blood pressure.[4] In New Zealand, phentermine is indicated as a short-term adjunctive treatment for weight loss in patients with a BMI greater 30 kg/m^2, although it is unsubsidised.[6]

The decision of whether or not to initiate phentermine treatment should take into account the following factors, and should not focus entirely on the medicine's addictive potential or lack of it:

- Phentermine has a substantial number of contraindications
- There is a paucity of research assessing the safety and effectiveness of phentermine
- The studies that have been conducted on phentermine report relatively modest reductions in weight by patients
- Phentermine is not subsidised and the cost of treatment limits the number of patients who this medicine can be prescribed to

Phentermine is contraindicated in patients with: pulmonary artery hypertension, severe cardiac disease, heart valve abnormalities or heart murmurs, moderate to severe arterial hypertension, cerebrovascular disease, hyperthyroidism, a history of psychiatric illness, glaucoma, a history or drug or alcohol abuse, or use of a monoamine oxidase inhibitor within the past 14 days.[6] Phentermine can be prescribed at 15 – 30 mg, once daily, in the morning.[6] Patients should be advised to contact a health professional immediately if they experience symptoms such as breathlessness, chest pain, fainting, swelling in the lower limbs, or a decreased ability to exercise.[6] Prescribers are recommended to consider withdrawing treatment of phentermine at 12 weeks if the patient has lost less than 5% of their pre-treatment bodyweight.[6]

Phentermine is a generic medicine, therefore it is highly unlikely that any industry-sponsored trials will be conducted in the future and the available evidence relating to the use of phentermine is relatively limited. Early studies in monkeys did not indicate that phentermine was associated with addictive potential.[4] A study of 117 obese patients who had been treated with phentermine long-term (1.1 – 21.1 years) at a private obesity centre, and 152 obese patients from the same centre who had been treated with phentermine short-term (4 – 22 days), found that, following neuropsychiatric interviews, all patients were negative for phentermine abuse or psychological dependence.[1] While this study does provide some evidence that phentermine can be used safely, it will need to be replicated in larger patient cohorts before the medicine can be recommended routinely for the treatment of obesity. This study must also be balanced against reports that in Europe phentermine is known as a "street drug", and that it is sold for considerable sums of money both overseas and in New Zealand.[4, 7] Addiction clinicians find that phentermine prescribing is sought disproportionally by patients with addiction difficulties, frequently for reasons that do not reflect a managed weight control programme.

The phentermine debate should also be focused on the medicine's effectiveness as an anti-obesity medicine. A meta-analysis of nine studies published between 1975 and 1999 found that over a treatment period ranging from two to 24 weeks patients treated with phentermine lost an average of 3.6 kg of additional weight compared with placebo.[8] It was concluded that phentermine can produce statistically significant but modest increases in weight loss, in addition to lifestyle interventions.[8] The small 2005 study referred to by Dr Cooper investigated weight loss following a 14-week course of phentermine. Results were compared between 24 people who completed the course of phentermine and 12 people who completed a course of placebo treatment.[2] However, the entry criteria for this study was a BMI > 25 kg/m^2 and the mean BMI for patients allocated phentermine was 29.3 kg/m^2.[2] The commonly accepted definition of obesity is a BMI > 30 kg/m^2.[9]

The two key questions for clinicians who are considering prescribing phentermine are:

- Has the patient adequately trialled lifestyle change previously?

- Are the modest increases in weight loss associated with phentermine clinically significant enough to outweigh any concerns over the cardiovascular adverse effects and/or addictive potential?

These questions can only be answered on an individual patient basis. A patient's addictive potential includes consideration of present or past history of addiction to any substance; family history of addiction; and present or past history of mental illness. The prescriber and patient should have an agreed contract including duration of treatment, treatment goals and how outcomes will be measured. If the benefits of treatment are judged to outweigh the risks then the financial cost to the patient of treatment must also be considered.

In regards to the correspondents comment about metformin, it has not been recommended as an anti-obesity treatment for patients without type 2 diabetes. Weight-loss was highlighted as a beneficial side effect of metformin treatment in patients with diabetes, as diabetes is a common co-morbidity in patients who are obese.

"Metformin is associated with clinically significant weight-loss in patients with type 2 diabetes and is fully-subsidised as an anti-diabetic medicine, however, it is not approved for use as an anti-obesity medicine."

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