

## Drugs or diet: what approach is most effective in improving knee osteoarthritis prognosis?

“When combined with trauma, obesity leads to serious deterioration of the knee osteoarthritis, a fate, which is particularly common in sportsmen. Being overweight is all the more interesting as this by principle is a modifiable factor throughout life.”

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Abundant documentation has been gathered on the importance of being overweight in the occurrence and progression of knee osteoarthritis (knee OA) [1]. The association has been demonstrated both for the risk of acquiring knee OA and, once there, for the progression of disease. When combined with trauma, obesity leads to serious deterioration of the knee OA [2], a fate, which is particularly common in sportsmen. Being overweight is all the more interesting as this by principle is a modifiable factor throughout life.

A large proportion of the adult population, up to one in three or even one in two, now struggle with being overweight or obesity. When combined with degeneration of weight bearing joints as in knee OA, it seems quite natural to include weight reduction as a fundamental part of the strategy in treatment and rehabilitation. Accordingly, guidelines for knee OA consistently advocate nonpharmacological treatments with weight loss as the primary approach with almost universal agreement among physicians. The NIH guidelines recommend that, in order to achieve 10% weight loss over 6 months, overweight patients (BMI 27–35 kg/m<sup>2</sup>) should aim for a decrease of 300–500 kcal/day (1300–2100 kJ/day), resulting in weight loss of about 250–500 g/week. For more severely obese patients (BMI >35 kg/m<sup>2</sup>), deficits of up to 500–1000 kcal/day (2100–4200 kJ/day) are required for weight loss of about 500–1000 g/week. When obesity is combined with knee OA, activity tends to decrease even more, which implies further inactivity-induced reduction in lean body mass. Accordingly, in a weight loss program such participants would have to

compensate for the lower activity by reducing energy intake even further to obtain a similar weight loss as knee healthy subjects [3].

Of primary importance, applying a GRADE approach to a nonpharmacological strategy demonstrates the obvious advantage of inflicting a treatment with apparently no major adverse effects [4]. By contrast, other treatments, whether medical or surgical, carry risks of varying degrees of severity. Even with a popular medication obtainable over-the-counter, paracetamol, the liver toxicity after over dosage is evidently a cause for concern. Also, with the regular prescribed doses of nonsteroidal anti-inflammatory drugs (NSAIDs), long-term use not only increases gastrointestinal bleeding, it also augments the risk of cardiovascular adverse events. Similarly, surgery includes the risk of development of chronic pain and even death. Thus, apart from considerations of costs, the large-scale utility of knee OA treatments is restricted by the risk of rather severe adverse events. Treatment may even be regarded as a lottery with a limited number of successful outcomes and this leads many patients to discard the doctors' solution in favor of alternative-complementary therapies.

### Structural changes

Disease modification in osteoarthritis (DMOA), in other words, an arrest or even reversal of the degeneration, by any given treatment has yet to be demonstrated [5]. Preliminary data have indicated improvement in the quality of cartilage in patients with knee trouble after a weight loss by gastric bypass [6]. In spite of a decrease in clinical symptoms, no



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such effect was demonstrated in patients with overt knee OA, even after a major weight reduction over time [7]. On the other hand, nor has DMOA been demonstrated with a pharmaceutical approach. Evidence even points at a negative impact on further development of knee OA under the influence of various – possibly too effective – analgesic treatments [8,9].

### Pain & disability

From the patient's perspective, pain relief remains the primary outcome of knee OA treatment. In the short term, weight loss has an effect size on pain in OA equal to the best pharmaceutical alternatives and in some studies a continuing benefit for at least a year has been shown [10–12]. To reach a significant pain reduction, the weight loss should be at least 5%, preferably 10% [13]. Paracetamol or NSAIDs, may have an almost similar impact in the short term, while a lasting effect on OA pain has not been demonstrated for these simple analgesics [14]. A significant weight loss has a small effect on self-reported disability [15]. Also, the weight loss improves gait, which increases in speed and stride during walking [16,17]. The reduced loading on the knee, however, does not seem to affect the degeneration of the joint. With respect to analgesics, a similar rather small effect has been found across most studies [18]. Inflammation in knee OA has been suggested to be essential for the pain accompanying the disease [1], while it still remains to be shown whether anti-inflammatory treatments can be used for prolonged and relevant periods of time, and, in that event, if such therapy might arrest the degeneration of the joints.

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### Methods for weight loss

Long-term use of medications for the treatment of obesity may lead to additional weight loss of 3–9%. Safety considerations, however, for currently available products point at a general indication for these drugs as short-term adjuncts in a transition phase, while patients are learning a sounder dietary behavior to reach an acceptable weight loss [19]. It has been demonstrated quite convincingly that, in knee OA, weight loss must be reached using dietary approaches. Knees are in general too painful to allow significant loss of calories by running. Thus, while

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concomitant exercise may yield better outcomes with respect to pain, it has no importance for the weight loss *per se* [12,20]. In knee OA, a well-tested diet, the ‘Copenhagen program’, gives on average a 10% weight loss in the majority of the participants. A 16-week run-in period with nutritionally complete meal replacement products in a very-low or low calorie diet kicks off the weight loss and this may be maintained for a very long time if subjects are supported throughout. More than 80% of the participants adhere to follow-up group sessions, in which participants are offered support from a dietitian and from other participants, and one meal replacement product per day throughout the year [11,20]. Again, from a GRADE and shared decision-making perspective, this conservative method is almost without adverse effects in contrast to gastric bypass surgery.

The need for constant vigilance to sustain behavioral changes in the face of pressures to regain weight emphasizes the challenges faced by even the most motivated patients. Currently, among ‘obesiologists’ it is generally accepted that there is a need for adjunctive therapies that can help patients who are not able to lose or sustain sufficient weight loss to improve health with lifestyle interventions alone. At this point, pharmacologic weight loss/maintenance therapy is considered appropriate for some individuals as an adjunct to lifestyle interventions to facilitate weight loss and prevent weight regain, but data from randomized controlled trials in patients with knee OA are lacking.

### Conclusion

In conclusion, weight loss should be recommended for people with concomitant knee OA and obesity. Analgesic drugs have a place in individual cases, but may be regarded as care supplementary to effective weight loss. Trials on pharmacologic weight loss/maintenance strategies for patients with knee OA, would be valuable and should be initiated.

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