

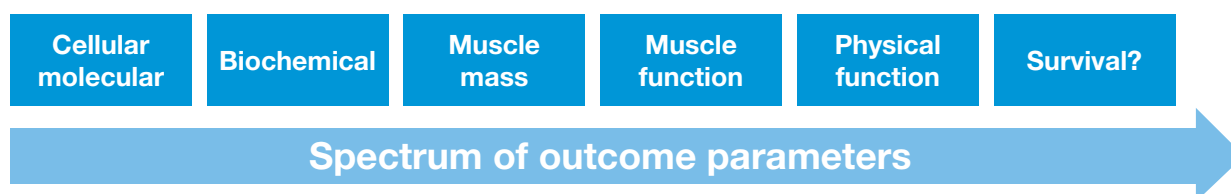
## Medical treatment: what to expect in the near future

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Sarcopenia in older individuals results from progressive deterioration of muscle quantity and quality with advancing age. These age-related changes have been attributed to factors that variously interfere with neuromuscular transmission, muscle fiber synthesis and assembly, excitation-contraction coupling, and metabolism.<sup>1</sup> This wide range of mechanisms underlying muscle loss and weakening presents numerous targets for drug therapy. While no drugs have yet been developed specifically for sarcopenia therapy, some existing drugs and some emerging drugs have potential for treating age-related muscle wasting. It is important to recognize that physical activity and good nutrition can help slow the rate of neuromuscular impairments, but even active and otherwise healthy older adults can exhibit progressive loss of muscle mass and strength, changes that affect ability to perform activities of daily living.

Drugs for sarcopenia can be identified from (1) published drug trials, (2) testing drugs with known anabolic effects in people with sarcopenia, (3) planned trials of new drugs and other strategies, and (4) rational development of new agents. To date, published studies of growth hormone,<sup>2</sup> testosterone,<sup>3</sup> dehydroepiandrosterone (DHEA),<sup>4-5</sup> vitamin D,<sup>6</sup> and a growth hormone *secretagogue* (MK677),<sup>7</sup> have some benefits in some populations. However, most studies showed only limited functional benefits and some unacceptable side effects. Since age-related decreases in circulating anabolic hormones and growth factors contribute to the emergence of sarcopenia, a rational treatment approach is to replace or enhance function of these hormones/factors. Nandrolone and testosterone replacements, insulin-like growth factor, and ciliary neurotrophic factor are currently undergoing testing for ability to offset the sarcopenic phenotype.<sup>1</sup> Growth factor secretagogue ghrelin and its analogues<sup>8</sup> are also being tested, as are drugs that inhibit the effects of myostatin, a factor responsible for muscle weakening with age.<sup>9</sup> Other studies are underway to test beta-agonists and ACE inhibitors for their abilities to reduce impairments associated with sarcopenia.

Nutrition has long been recognized to play a role in recovery from illness or injury, so other trials are examining how nutritional regimens can be used alone or in combination with exercise. Such studies include an omega-3 fatty acid-enriched protein-energy supplement, EAA supplementation, and HMB supplementation with resistance training, as reviewed by Stout.<sup>10</sup> All treatments must undergo testing in well-designed safety and efficacy trials in older populations, and these trials must use relevant endpoints. Development of a reliable clinical definition of sarcopenia, use of consistent inclusion criteria, and use of sensitive and relevant outcome parameters are essential to interpreting and comparing sarcopenia treatment strategies. In particular, it is important to differentiate between parameters that are markers of muscle change and those that represent functional ability and quality of life; improvements in these latter parameters are the differences that really matter to older people with sarcopenia (Figure 1).



**Figure 1. Relevant outcome parameters in elderly people with sarcopenia**

Since sarcopenia is a complex condition, it is unlikely that any single drug will prevent or reverse age-related sarcopenia. Instead, treatment strategies in the future will likely include a combination of nutrition, exercise, and possibly drug treatment.

### Take-home messages

- A wide range of mechanisms underlie muscle loss and weakening in older adults, thus affording many potential targets for drug therapy.
- Candidate drugs for treating sarcopenia include anabolic hormones and growth factors, growth hormone secretagogues, neurotrophic factors, inhibitors of muscle breakdown, and beta agonist or ACE-inhibitory agents; nutrition supplements and exercise regimens are also undergoing testing in people with sarcopenia.
- Treatment strategies in the future will likely include a combination of nutrition, exercise, and possibly drug treatment.

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### Discussion

**Juergen Bauer:** I think we should recommend vitamin D supplementation already. Although the data are not completely certain, there have been new supportive meta-analyses in the field. Studies that showed no vitamin D effects were using too-low doses or were done in populations with very low risk. If you look at a high-risk population, you can show good effects with vitamin D supplementation. So I would use supplementation because it's very safe. For trials measuring other sarcopenia treatments, I think it may be wise to supplement study populations with vitamin D before the start of the trial (2-4 months at least).

**Alfonso Cruz:** I would also go for vitamin D, because even if it doesn't help people with sarcopenia, vitamin D is good for bones and is recommended for older women and probably men. I also agree that correct levels of vitamin D are warranted before starting trials. Many people incorrectly believe vitamin D comes from the sun, but it must be put in the body first [precursors must first be available in the skin, where they are converted to active metabolites by exposure to sunlight]. This is a message that must be sent to our patients.

We know that vitamin D deficiency and low levels are prevalent in many countries, even surprising ones (southern Europe). The Seneca study was a natural experiment. In northern countries of Europe, people had higher levels of vitamin D, which were linked to systematic supplementation of vitamin D in dairy products. So if you buy milk in northern Europe, it has more vitamin D. In southern Europe, supplemented milk is more expensive, so many people don't buy it, and their vitamin D levels are lower.

**Juergen Bauer:** I don't think you can manage vitamin D deficiency solely on natural intake, especially in older people. Supplementation is necessary.

**Servet Ariogul:** We do vitamin D screening in our geriatric outpatient clinics, but it is an expensive test. Therefore, only patients at risk, or patients with osteoporosis should be screened. That's my recommendation.

**Irit Hermesh:** When you are talking about osteopenic patients, it is no longer screening, it is treatment. Screening procedures are for the average-risk population. Vitamin D deficiency is prevalent – 50 percent and maybe 60 percent or more in obese patients. It's really very cost-effective to find out who is deficient and treat them before osteoporosis develops.

**Juergen Bauer:** There is a big debate about the cost-effectiveness of vitamin D screening. Screening is very expensive, but then we can treat only those with deficiency. On the other hand, it may actually be easier and cheaper to take an alternative approach—treating the entire population with a cheap form of vitamin D? Despite considerable debate about which is more cost effective, we do not have a [pharmaco-economic] study that answers the question.