Excess weight is the strongest factor in the risk and severity of obstructive sleep apnea (OSA) (1). Two decades ago, prospective observational studies reported that a 10% weight gain over 4 years is associated with a 32% increase in the apnea–hypopnea index (AHI) and, conversely, a 10% weight loss predicts a 26% decrease in AHI (2). More recently, randomized controlled trials (RCTs) with up to 4-year follow-up indicated that weight loss is associated with decreased OSA severity with an average change in AHI of 0.78 events/h for every kilogram of weight lost, and that a small proportion of patients can achieve remission of OSA (AHI < 5 events/h) (3, 4).

In this issue of the *Journal*, Kuna and colleagues (pp. 221–229) report on change in AHI at 10-year follow-up in Sleep AHEAD (Action for Health in Diabetes), a multicenter RCT of 306 middle-aged and older adults with overweight or obesity and type 2 diabetes (5). Participants who had OSA at baseline (*n* = 264; AHI ≥ 5 events/h, mean age 61.3 yr, and mean body mass index 36.6 kg/m²) were randomized to receive either intensive lifestyle intervention (ILI) aimed at reducing body weight by at least 10% within 1 year or diabetes support and education (DSE) as part of standard care (control group). This is the longest RCT to date reporting on OSA trajectories in adults undergoing a lifestyle weight management program. Added strengths include the rigorous RCT design, AHI assessment by polysonomography at baseline and Years 1, 2, 4, and 10, and the use of high standards to minimize inter scorer variability.

There are several noteworthy findings in this report by Kuna and colleagues. The authors found that the greater reductions in body weight and AHI in the ILI group compared with DSE, which were evident at 1-, 2-, and 4-year follow-ups (6), persisted at 10-year follow-up, albeit with some attenuation over time (Table 1). Of note, despite a significantly greater weight loss by 3.6 kg with ILI over DSE at 10 years, the reduction in AHI favoring ILI by 4.0 events/h did not reach statistical significance between intervention arms. Nevertheless, considering all follow-up visits, the overall intervention effect resulted in a 7.4 events/h greater reduction in AHI with ILI. At 10-year follow-up, for every kilogram of weight lost in ILI participants relative to baseline, the AHI decreased by 0.68 events/h compared with 0.54 events/h in DSE participants (*P* value not reported). From Year 4 to Year 10, both groups showed reductions in weight and AHI, and curiously, for every kilogram of weight lost during this period, the AHI decreased by 3.1 events/h in ILI compared with 3.8 events/h in DSE. This suggests that unmeasured factors between 4-year and 10-year follow-ups may have contributed to the observed modestly greater intervention effects on AHI in the control group. At 10 years, the remission of OSA was more common in ILI (34.4%) than in DSE (22.2%) participants, particularly in those who had mild to moderate OSA. Taken together, the findings by Kuna and colleagues highlight the importance of weight management in OSA, particularly in patients with type 2 diabetes, regardless of type of intervention used to achieve weight loss. Indeed, weight loss by either medical or surgical approaches has beneficial effects on OSA severity and glycemic control, and it can potentially cure OSA in some patients (4).

Interestingly, the authors found that although the change in weight predicted the improvement in AHI over time, weight loss alone did not explain the full extent of the intervention effects on OSA severity. Additionally, changes in waist circumference, a surrogate marker of visceral adiposity, did not independently influence AHI. So, what could be the potential explanations for these intriguing weight-independent intervention effects? In Sleep AHEAD, lifestyle intervention focused on modifications of diet and physical activity, and perhaps these healthier lifestyle behaviors contributed to the reduction in AHI. In adults from diverse backgrounds, diet quality is associated with OSA severity, after adjusting for confounders (7). To our knowledge, diet data are not available from Sleep AHEAD. Also, independent of body habitus, level of exercise is associated with OSA severity (8). Although physical activity data were not included in this report by Kuna and colleagues, the authors previously found that cardiorespiratory fitness does not predict change in AHI at 4-year follow-up, after adjusting for change in weight (9). There is evidence from RCTs to suggest that diet-only, exercise-only, and combined diet and exercise interventions all attenuate OSA severity despite highly variable changes in weight (10). These weight-independent effects of intervention on OSA severity are likely due to multifactorial mechanisms that may modulate upper airway stability, chemoreceptor sensitivity, visceral adiposity, neuroendocrine control, sleep quality, and other aspects of OSA pathophysiology, which are yet to be discovered (10–12).

It is worth noting that these new insights from Sleep AHEAD by Kuna and colleagues should be interpreted cautiously given some limitations. First, the sleep studies were missing in about half of the participants at the 10-year follow-up. The authors performed post hoc statistical analyses (e.g., multiple imputations and weighing for missingness) in an attempt to address this drawback. Sensitivity analyses in 96 participants who had complete AHI data at 10 years would have been useful to further support the authors’ conclusions. Second, 16% of patients were receiving continuous positive airway pressure treatment for OSA, which may partly bias measured outcomes. Third, the potential effects of changes in medications that commonly influence weight (13), in particular the use of oral antidiabetic agents or insulin in this diabetic population, could be confounders. Lastly, Sleep AHEAD involved older adults with overweight/obesity and type 2 diabetes, which may limit the generalizability to more diverse populations.

Weight loss is frequently recommended to patients with OSA with overweight and obesity (4). Although Kuna and colleagues found no statistically significant difference in OSA severity at
Table 1. ILI versus DSE

|                      | 1-yr Follow-up |   | 2-yr Follow-up |   | 4-yr Follow-up |   | 10-yr Follow-up |
|----------------------|----------------|---|----------------|---|----------------|---|-----------------|
|                      | ILI Group      |   | DSE Group      |   | ILI Group      |   | DSE Group       |   | ILI Group      |   | DSE Group       |   |                  |
| Polysomnography, n (%)† | 103 (82)       |   | 116 (83)       |   | 99 (79)        |   | 111 (80)       |   | 82 (66)        |   | 83 (60)        |   | 67 (54)         |   | 67 (48)         |
| Change in weight, kg†  | −10.7          |   | −0.5           |   | −7.4           |   | −0.8           |   | −5.1           |   | −0.9           |   | −7.1           |   | −3.5           |
| Change in AHI, events/h† | −5.5           |   | 4.3            |   | −3.6           |   | 4.4            |   | −3.8           |   | 4.0            |   | −9.9           |   | −5.9           |
| Change in waist circumference, cm† | −9.0           |   | −0.6           |   | −5.9           |   | −0.7           |   | −3.4           |   | 0.2            |   | −2.1           |   | 1.6            |
| Remission of OSA, %‡  | 13.6           |   | 3.5            |   | Data not published |   | Data not published |   | 20.7           |   | 3.6            |   | 34.4           |   | 22.2           |

Definition of abbreviations: AHI = apnea-hypopnea index; DSE = diabetes support and education; ILI = intensive lifestyle intervention; OSA = obstructive sleep apnea.

Data are means unless otherwise specified.

†The number (% of total) of participants who had available polysomnography data among n = 264 total participants who were randomized.

‡Change from baseline; all comparisons are statistically significant between the ILI and DSE groups except for change in AHI at 10-year follow-up.

Data not published.

10-year follow-up between active and control intervention arms, their overall conclusions clearly support the potential benefit of weight loss on OSA severity in the long term with the possibility of remission of OSA in some patients. These findings also provide an important message that lifestyle modifications combining healthy diet and exercise should be integral to OSA management, particularly in patients with type 2 diabetes. Further research efforts should focus on testing whether lifestyle interventions for weight loss combined with continuous positive airway pressure treatment of OSA lead to synergistic effects in mitigating cardiometabolic consequences of OSA (14). ■

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References

1. Jordan AS, McSharry DG, Malhotra A. Adult obstructive sleep apnoea. Lancet 2014;383:736–747.
2. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA 2000;284:3015–3021.
3. Mitchell LJ, Davidson ZE, Bonham M, O’Driscoll DM, Hamilton GS, Truby H. Weight loss from lifestyle interventions and severity of sleep apnoea: a systematic review and meta-analysis. Sleep Med 2014;15:1173–1183.
4. Joosten SA, Hamilton GS, Naughton MT. Impact of weight loss management in OSA. Chest 2017;152:194–203.
5. Kuna ST, Rebboussin DM, Strotmeyer ES, Millman RP, Zammit G, Walkup MP, et al.; Sleep AHEAD Research Subgroup of the Look AHEAD Research Group. Effects of weight loss on obstructive sleep apnea severity: ten-year results of the sleep AHEAD study. Am J Respir Crit Care Med 2021;203:221–229.
6. Kuna ST, Rebboussin DM, Borradaile KE, Sanders MH, Millman RP, Zammit G, et al.; Sleep AHEAD Research Group of the Look AHEAD Research Group. Long-term effect of weight loss on obstructive sleep apnea severity in obese patients with type 2 diabetes. Sleep 2013;36:641–649A.
7. Reid M, Maras JE, Shea S, Wood AC, Castro-Diehl C, Johnson DA, et al. Association between diet quality and sleep apnea in the Multi-Ethnic Study of Atherosclerosis. Sleep 2019;42:zsy194.
8. Peppard PE, Young T. Exercise and sleep-disordered breathing: an association independent of body habitus. Sleep 2004;27:480–484.
9. Kline CE, Rebboussin DM, Foster GD, Rice TB, Strotmeyer ES, Jakicic JM, et al.; Sleep AHEAD Research Group of the Look AHEAD Research Group. The effect of changes in cardiorespiratory fitness and weight on obstructive sleep apnea severity in overweight adults with type 2 diabetes. Sleep 2016;39:317–325.
10. Edwards BA, Bristow C, O’Driscoll DM, Wong AM, Ghazi L, Davidson ZE, et al. Assessing the impact of diet, exercise and the combination of the two as a treatment for OSA: a systematic review and meta-analysis. Respirology 2019;24:740–751.
11. Ifitkhar IH, Kline CE, Youngstedt SD. Effects of exercise training on sleep apnea: a meta-analysis. Lung 2014;192:175–184.
12. Smith PC, Mong JA. Neuroendocrine control of sleep. Curr Top Behav Neurosci 2019;43:353–378.
13. Domecq JP, Prutsky G, Leppin A, Sonbol MB, Altayar O, Undavalli C, et al. Clinical review: drugs commonly associated with weight change: a systematic review and meta-analysis. J Clin Endocrinol Metab 2015;100:363–370.
14. Chirinos JA, Gurubhagavatula I, Teff K, Rader DJ, Wadden TA, Townsend R, et al. CPAP, weight loss, or both for obstructive sleep apnea. N Engl J Med 2014;370:2265–2275.
15. Foster GD, Borradaile KE, Sanders MH, Millman R, Zammit G, Newman AB, et al. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. Arch Intern Med 2009;169:1619–1626.

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