MAIN OUTCOME MEASURES
Days alive without delirium or coma and percentage of days spent within 1 RASS point of the sedation goal.

RESULTS
Sedation with dexmedetomidine resulted in more days alive without delirium or coma (median days, 7.0 vs 3.0; \( P = 0.01 \)) and a lower prevalence of coma (63\% vs 92\% ; \( P \)).

Patients sedated with dexmedetomidine spent more time within 1RASS point of their sedation goal compared with patients sedated with lorazepam (median percentage of days, 80\% vs 67\%; \( P = 0.04 \)). The 28-day mortality in the dexmedetomidine group was 17\% vs 27\% in the lorazepam group (\( P = 0.18 \)), and cost of care was similar between groups. More patients in the dexmedetomidine group (42\% vs 31\%; \( P = 0.61 \)) were able to complete post-ICU neuropsychological testing, with similar scores in the tests evaluating global cognitive, motor speed, and attention functions. The 12-month time to death was 363 days in the dexmedetomidine group vs 188 days in the lorazepam group (\( P = 0.48 \)).

CONCLUSION
In mechanically ventilated ICU patients managed with individualized targeted sedation, use of a dexmedetomidine infusion resulted in more days alive without delirium or coma and more time at the targeted level of sedation than with a lorazepam infusion.

TRIAL REGISTRATION
Clinicaltrials.gov Identifier: NCT00095251.

This is the largest RCT to date that compares dexmedetomidine, an alpha-2 adrenergic receptor agonist, to conventional sedative therapy (lorazepam in this case) for a prolonged course (120 hours – note that Dex is FDA approved only for

REFERENCE

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Update in Endocrinology
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PITUITARY
Systematic review: the safety and efficacy of growth hormone in the healthy elderly
Ann Intern Med. 2007;220;146;104-15.

AIM
The goal of this study was to evaluate the safety and efficacy of growth hormone therapy in healthy elderly individuals.

METHODS
The data were derived by searching MEDLINE and EMBASE-based databases for English-language, randomized controlled trials comparing growth hormone (GH) with no GH therapy or GH and lifestyle interventions with lifestyle interventions alone. In the selected trials, GH was given for \( \geq 2 \) weeks to community-dwelling participants with a mean age of \( \geq 50 \) years and a BMI of \( \leq 35 \) kg/m\(^2\). Studies utilizing GH as treatment for specific illnesses were excluded.

RESULTS
Thirty-one articles and 18 unique study populations were included. Two hundred twenty participants with a mean age of 69 ± 6 years and a mean BMI of 28 ± 2 kg/m\(^2\) completed respective studies. Compared with those not treated, participants treated with GH had a 2.1-kg decrease in fat mass (95\% CI, -2.8 to -1.35) and a 2.1-kg increase in overall lean body mass (CI, 1.3 to 2.9; \( P < 0.001 \)). There was no significant change in weight, total cholesterol, bone density, or body composition. Persons treated with GH had significantly higher rates of soft tissue edema, arthralgia, carpal tunnel syndrome, and gynecomastia than those not treated. There was no significant difference between the groups.
in impaired fasting glucose or in the development of diabetes mellitus.

CONCLUSION
GH in healthy elderly individuals has little clinical benefit.

IMPACT ON INTERNAL MEDICINE
The GH-induced changes in body composition in healthy, elderly subjects are similar to those reported in adults with GH deficiency. The difference is that in the elderly, clinically important outcomes, like oxygen consumption, lipids, and bone density, are not affected. In addition, the small improvement in lean body mass seen in this study might be due, in part, to fluid retention. Since all of the studies lasted less than 1 year and none examined cancer outcomes, the effect of GH on cancer risk and death cannot be evaluated. GH should not be used to attempt to prevent aging in healthy individuals and should only be used for clearly defined indications, such as adult-onset GH deficiency and in HIV patients with cachexia.

RELATED REFERENCES

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DIABETES
Effect of rosiglitazone on the risk for myocardial infarction and death from cardiovascular causes

AIM
The goal was to compare the effect of rosiglitazone and placebo on cardiovascular outcomes.

METHODS
The data for this meta-analysis were derived from searches of the FDA Web site, a clinical trials registry maintained by the drug manufacturer, and published literature. Forty-two randomized, controlled trials met the selection criteria. The outcomes were myocardial infarction and death from cardiovascular causes.

RESULTS
Overall there was a moderate predominance of men in this study, and mean baseline glycated hemoglobin was approximately 8.2% for rosiglitazone and placebo study groups. The summary odds ratio for myocardial infarction was 1.43 in the rosiglitazone group (95% CI, 1.03-1.9; \(P = 0.03\)) compared with placebo. The odds ratio from death from cardiovascular causes in the rosiglitazone group as compared with control was 1.64 (95% CI, 0.98-2.74; \(P = 0.06\)). Rosiglitazone increased risk for myocardial infarction more than placebo or other drugs but the groups did not differ for cardiac death.

CONCLUSIONS
Rosiglitazone was associated with a significant increase in the risk for myocardial infarction and with an increase in the risk for death from cardiovascular causes that had borderline significance.

IMPACT ON INTERNAL MEDICINE
While this meta-analysis analyzed small, short-duration trials that were not designed to assess cardiovascular outcomes, it did show a 30% to 40% relative increase in the risk for myocardial infarction in patients treated with rosiglitazone. The RECORD trial, designed to examine cardiovascular event as primary outcomes, revealed no statistically significant effect on myocardial infarction (hazard ratio, 1.17 [95% CI, 0.75-1.82]) and confirmed the risk for heart failure (hazard ratio, 2.15 [95% CI, 1.30-3.57]). Even though the data are not definitive about risk for cardiac death and myocardial infarction, rosiglitazone should be used with caution in type 2 diabetes mellitus until randomized trials answer this question. The increase in fluid retention and congestive heart failure with thiazolidinediones led to a ‘black box’ warning in the prescribing information for both rosiglitazone and pioglitazone regarding risk for congestive heart failure, and risk for myocardial infarction with rosiglitazone. The 2008 American Diabetes Association guidelines related to therapy of type 2 diabetes mellitus do not remove either thiazolidinedione from the treatment