Systematic review: the effects of growth hormone on athletic performance

CRD summary
The authors concluded that the limited evidence available suggests that growth hormone may alter body composition, but has minimal effect on key athletic performance and may be associated with impaired exercise capacity and increased adverse events. The review was generally well-conducted and the conclusions are likely to be reliable.

Authors' objectives
To evaluate the effects of growth hormone on athletic performance in healthy and physically fit young adults.

Searching
MEDLINE, EMBASE, SPORTDiscus and the Cochrane Library were searched to October 2007; the search terms were reported. The reference lists of retrieved articles were handsearched. The search was restricted to studies reported in the English language.

Study selection
Randomised controlled trials (RCTs) comparing growth hormone therapy with no growth hormone therapy were eligible for inclusion, provided they enrolled at least 5 participants. Studies in which growth hormone was administered as a treatment for a specific illness were excluded. The review included studies of growth hormone given either as a single subcutaneous (sc) or intravenous dose, or in a longer-term sc regimen. The mean daily dose was 36 μg/kg and the mean treatment duration in studies that used multiple doses was 20 days (range: 4 to 84); only 3 studies continued for longer than 30 days. Eligible studies included participants living in the community, with a mean or median age between 13 and 45 years. Studies that specifically included people with a medical condition were excluded. The participants in the included studies were typically male with a mean age of 27 years. They were typically healthy, with a mean maximum oxygen intake (VO\textsubscript{2max}) of 51 mL/kg per minute, and lean, with a mean body mass index of 24 kg/m\textsuperscript{2}.

Studies were required to report at least one of the following outcomes: body composition (e.g. body weight, lean body mass), strength (e.g. biceps or quadriceps strength), basal metabolism (e.g. basal metabolic rate, heart rate), exercise capacity (e.g. exercising lactate levels, exercising bicycling speed) or adverse events. The term 'lean body mass' was used in the review to include 'fat-free mass', while the term 'basal metabolic rate' was used to include 'resting energy expenditure'. Studies concerned only with growth hormone secretagogues were excluded.

One author screened the titles and abstracts of identified articles and retrieved potentially relevant studies. Two reviewers then independently reviewed the retrieved studies.

Assessment of study quality
The following criteria were used to assess study validity: baseline similarity of the groups, placebo control, concealment of allocation, specified eligibility criteria, blinding of the participants, blinding of the clinicians, reporting of point estimates and variability, and intention-to-treat analysis.

Two reviewers independently assessed study validity, with any discrepancies resolved by consensus.

Data extraction
For continuous outcomes, the authors calculated the mean difference between the change scores in the two study groups. Where studies did not report the variance of change scores, it was calculated from the variance of baseline and final scores. Where baseline data were not available (e.g. for basal metabolic outcomes), the final scores of the two groups were compared. For binary data, the number of events in each group was extracted. If the data were reported graphically, a graph-digitising programme was used to extract the data.

Two reviewers independently extracted the data, with any discrepancies resolved by consensus. Study authors were
Methods of synthesis
Where studies were clinically similar, the results were pooled to calculate weighted mean differences (WMDs) and standardised mean differences for each outcome, using random-effects models. Since the results were similar for both measures, only WMDs were presented in the review, along with 95% confidence intervals (CIs). Where clinical heterogeneity precluded meta-analysis, the studies were combined in a narrative which reported the p-values from individual study results.

Results of the review
Twenty-seven RCTs (44 articles) were included (n=440), 15 of which used a crossover design. The studies were small (mean n=15) and none described adequate allocation concealment. The groups were similar at baseline in 20 studies, 23 used placebo control, 11 specified eligibility criteria, 23 blinded the participants, 20 blinded the clinicians, 24 reported point estimates and variability, and 18 used intention-to-treat analysis. Drop-out rates were low, with 98% of participants completing the study protocol.

Body composition: when the studies were pooled, lean body mass increased significantly more in the intervention groups than in controls (WMD 2.1 kg, 95% CI: 1.3, 2.9, p<0.01; 11 RCTs). There was no statistically significant difference between the groups in changes in weight (9 RCTs) or fat mass (10 RCTs).

Strength: muscle strength was measured after 42 or 84 days’ treatment. When the studies were pooled, there was no statistically significant difference between the intervention group and controls in measures of quadriceps and biceps strength (2 RCTs, n=40), nor was any statistically significant difference found between the groups across seven other muscle groups (1 RCT).

Basal metabolism: daily basal metabolic rate was significantly higher in the intervention group than in controls (WMD 141 kilocalories/day, 95% CI: 69, 213, p<0.001; 7 RCTs). Resting respiratory exchange ratio/respiratory quotient and resting heart rate were significantly lower in the intervention group (respectively: WMD -0.02, 95% CI: -0.03, -0.01, p=0.001; 7 RCTs and WMD 3.8 beats per minute, 95% CI: 0.2, 7.4, p<0.05; 11 RCTs). The only significant statistical heterogeneity found was for the outcome of resting heart rate (p=0.01; I²= 55%): when only studies with a duration of more than 14 days were included, the heterogeneity was no longer evident (I²=22%).

Exercise capacity: 6 RCTs measured exercise capacity but were not pooled because of differences in the exercise interventions used. Three RCTs measured lactate levels after a single dose of growth hormone; these were not pooled because of clinical heterogeneity. Two individual RCTs reported a significantly higher lactate level in the intervention groups compared with controls (p<0.001). Exercising levels of fatty acids and glycerol were both significantly higher in the intervention groups in all relevant studies (p<0.05; 3 RCTs). Heart rate was significantly increased (p<0.02) in two of the 4 RCTs that measured this outcome, and maximum inspiratory pressure at rest was significantly increased (p<0.05) in the single relevant study. None of the relevant studies found a statistically significant difference between the groups for the outcomes of exercising respiratory rate quotient or respiratory quotient (4 RCTs) and VO₂max (2 RCTs), bicycling speed, exercising energy expenditure, or power output (1 RCT each).

Adverse events: there was a higher rate of adverse events in the intervention group than in controls, especially soft tissue oedema (44% versus 1%; 8 RCTs) and fatigue (35% versus 0%; 4 RCTs).

Sensitivity analyses were performed. The results of 3 meta-analyses were sensitive to the removal of a single study: there was a statistically significant increase in weight in the intervention group when one of 9 RCTs was removed, and the outcomes of fat mass and resting heart rate became non significant when a single RCT was removed from each.

There was little indication of publication bias.

Authors' conclusions
The limited evidence available suggests that growth hormone may alter body composition, but has minimal effect on

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key athletic performance and may be associated with impaired exercise capacity and increased adverse events.

**CRD commentary**
The review objective and inclusion criteria were clear. Relevant sources were searched, although the restriction to English language studies may have meant that some studies were missed. In addition, there was little attempt to identify unpublished studies, thereby introducing the potential for publication bias. The authors reported no evidence of publication bias from inspection of the funnel plots; however, these plots were not presented in the report. Appropriate criteria were used to assess study validity and adequate information was provided about the primary studies. Steps were taken to minimise error and bias by having more than one reviewer independently extract the data and assess study validity, but the process used to select studies for inclusion was unclear. The decisions on which study outcomes to pool statistically appear appropriate. Suitable statistical methods were used for the meta-analysis and to assess heterogeneity and publication bias. The review was generally well-conducted and the conclusions are likely to be reliable.

**Implications of the review for practice and research**
Practice: The authors stated that growth hormone does not seem to improve strength, it may impair athletic performance, and it is frequently associated with adverse events in healthy young people.

Research: The authors stated that research is needed to determine the effects of growth hormone on athletic performance and physiological outcomes. Evidence is particularly sparse among women and over the long term. Growth hormone protocols used in real-world settings should be identified and evaluated.

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