Title
Recombinant Human Growth Hormone for the Treatment of Growth Disorders in Children: A Systematic Review and Economic Evaluation

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Aim
To assess the clinical and cost effectiveness of recombinant human growth hormone (rhGH) compared with treatment strategies without rhGH for children with growth hormone deficiency (GHD), Turner syndrome (TS), Prader-Willi syndrome (PWS), chronic renal insufficiency (CRI), short stature homeobox-containing gene deficiency (SHOX-D), and being born small for gestational age (SGA).

Conclusions and results
Recombinant human growth hormone is licensed for short stature associated with GHD, TS, PWS, CRI, SHOX-D, and being born SGA. The systematic review included 28 randomized controlled trials (RCTs) in 34 publications. GHD: Children in the rhGH group grew 2.7 cm/year faster than untreated children and had a statistically significantly higher height standard deviation score (HtSDS) after 1 year: –2.3 ± 0.45 versus –2.8 ± 0.45. TS: In one study, treated girls grew 9.3 cm more than untreated girls. In a study of younger children, the difference was 7.6 cm after 2 years. HtSDS values were statistically significantly higher in treated girls. PWS: Infants receiving rhGH for 1 year grew significantly taller (6.2 cm more) than those untreated. Two studies reported a statistically significant difference in HtSDS in favor of rhGH. CRI: rhGH-treated children in a 1-year study grew an average of 3.6 cm more than untreated children. HtSDS was statistically significantly higher in treated children in two studies. SGA: Criteria were amended to include children of 3+ years with no catch-up growth, with no reference to mid-parental height. Only one of the RCTs used the licensed dose; the others used higher doses. Adult height (AH) was approximately 4 cm higher in rhGH-treated patients in the one study to report this outcome, and AH-gain SDS was also statistically significantly higher in this group. Mean HtSDS was higher in treated than untreated patients in four other studies (significant in two). SHOX-D: After 2 years’ treatment, children were approximately 6 cm taller than the control group and HtSDS was statistically significantly higher in treated children. The incremental cost per quality adjusted life-year (QALY) estimates of rhGH compared with no treatment were: 23 196 pounds sterling (GBP) for GHD, GBP 39 460 for TS, GBP 135 311 for PWS, GBP 39 273 for CRI, GBP 33 079 for SGA, and GBP 40 531 for SHOX-D. The probability of treatment of each of the conditions being cost effective at GBP 30 000 was: 95% for GHD, 19% for TS, 1% for PWS, 16% for CRI, 38% for SGA, and 15% for SHOX-D. Statistically significantly larger HtSDS values were reported for rhGH-treated children with GHD, TS, PWS, CRI, SGA, and SHOX-D. rhGH-treated children with PWS also showed statistically significant improvements in body composition. Only treatment of GHD would be considered cost effective at a willingness-to-pay threshold of GBP 20 000 to 30 000 per QALY gained. Future research should include studies exceeding 2 years that report near-final height or final adult height.

Recommendations
See Executive Summary link www.hta.ac.uk/project/1755.asp.

Methods
The systematic review of clinical effectiveness used a priori methods as described in the research protocol. We searched key databases (e.g. MEDLINE, EMBASE, NHS Economic Evaluation Database) for relevant studies (in English) from their inception to June 2009. Relevant conferences, bibliographies of included papers, our expert advisory group, and manufacturers’ submissions to NICE were also consulted to identify additional published or unpublished references. We developed an economic model using the best available evidence to determine cost effectiveness in the UK.

Further research/reviews required
See Executive Summary link www.hta.ac.uk/project/1755.asp.