Effectiveness and cost-effectiveness of height-screening programmes during the primary school years: a systematic review

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ABSTRACT

Objective: To determine the effectiveness and cost-effectiveness of height screening (of children aged 4 to 11) to identify height-related conditions.

Design: Systematic review and economic modelling.

Setting and intervention: We included published and unpublished screening studies of any design, except case reports, conducted in any setting that measured children's height as part of a population-level assessment. Studies were identified by electronic database searches, contact with experts and from bibliographies of retrieved studies.

Participants: Children aged between 4 and 11 years.

Outcome measures: Diagnostic yield of height-related conditions and change in quality of life, as measured by quality-adjusted life years (QALYs), for early versus late treatment of underlying conditions.

Results: Twelve studies described a height-screening programme and provided data on the diagnostic yield of newly diagnosed height-related conditions. Where reported, yield for growth-hormone deficiency (per 1000 children screened) ranged from 0.05 (1 in 20 000) to 0.62 (approximately 1 in 1500) and for Turner syndrome (per 1000 children screened) was between 0.02 (1 in 50 000) and 0.07 (approximately 1 in 14 000). As a secondary gain, children with other potentially treatable conditions were identified; diagnostic yields ranged from 0.22 to 1.84 per 1000 children screened. Three studies did not detect any new cases, but all of these studies had methodological limitations. Economic modelling suggested that height screening is associated with health improvements and is cost effective for a willingness to pay threshold of £30 000 per QALY.

Conclusions: This review indicates the utility and acceptable cost-effectiveness of height screening arising from increased detection of height-related disorders and secondary pick-up of other undiagnosed conditions. Further research is needed to obtain more reliable data on quality of life gains and costs associated with early interventions for height-related conditions. The exact role of height-screening programmes in improving child health remains to be determined.

A child's height and weight is well established as an indicator of general health and well-being. Assessment of height and weight can lead to the identification of treatable disorders in the apparently normal child. Despite this, children with a treatable cause of abnormal growth are frequently diagnosed at a late age or treatment is initiated at a late stage.[1–5] The role of height-screening programmes for primary-school-aged children in identifying height-related disorders is currently unclear and uncertainties exist about the most appropriate age(s) at which to measure and the measurement strategies to adopt to minimise late referrals.

Regular screening of children's height does not aim to detect a single pathology. There are a number of conditions that may lead to decreased or increased growth rate and/or short or tall stature. Conditions in which stature outside the normal range is often the only or most significant presenting feature are growth-hormone deficiency (GHD) and Turner syndrome (TS), and it is these conditions that are used to justify height screening.[6] However, new cases of a number of other conditions may be identified as a consequence of height screening. Short stature may result from hypothyroidism, psychosocial deprivation, intrauterine growth retardation or other chronic illness. It many instances, however, short stature has no underlying pathology and may be genetic or have no obvious explanation (idiopathic short stature or ISS). Tall stature is a feature of a number of syndromes (eg, Marfan and Klinefelter) and may also indicate treatable endocrine disorders. Early detection and diagnosis of organic causes of abnormal growth is important to optimise final adult height and minimise the health impact of any underlying condition.[2 7–9] Where possible, treatment will be provided for the underlying condition. In cases where the condition is not treatable, early diagnosis can allow for discussion with the family and child, and counselling can be initiated to minimise adverse psychological effects.

There is no standard "cut-off" used for defining short or tall stature. Diagnosis of abnormal growth is usually based on a child's height measurement outlying recommended percentile points on a population-specific growth chart.[10] In the UK, a height below the 0.4th centile of the UK 1990 charts has been recommended to define short stature and a height above the 99.6th centile to define tall stature in need of further investigation.[6] The Child Health Subcommittee of the UK National Screening Committee recommended in 2004 that a single height and weight measurement should be taken at or around the time of school entry and that the 0.4th centile for height should be used to initiate referral.[11] However, historically, routine growth-screening practices have varied across the UK[12], and adherence to current guidance is unknown. Looking outside the UK, variations in practice also exist between countries.[13 14]

METHODS

Our objective was to perform a systematic review of the effectiveness and economic modelling of height screening in primary-school-aged children (4 to 11 years) to identify height-related conditions. The review also included screening for obesity, but this paper focuses on stature only.

Effectiveness review

The systematic review was undertaken in accordance with the Centre for Reviews and Dissemination (CRD) guidelines.[15] We accepted studies of any design with the exception of case reports. To allow direct relevance to the UK population, studies had to include children aged between 4 and 11 years in Western Europe, North America or Australia/New Zealand (excluding studies of aboriginal populations). Target conditions were GHD, TS, juvenile hypothyroidism (JH), psychosocial growth failure and clinical conditions associated with tall stature (including precocious sexual maturation, Klinefelter and Marfan syndromes). Studies had to measure children's height as part of a population-level assessment. Accepted outcomes measures were the diagnostic accuracy of height screening (sensitivity and specificity), "diagnostic yield" of height-related conditions, age at diagnosis, route to diagnosis and patient-management outcomes such as referral.

Studies were identified by searching through an extensive range of bibliographic databases from their inception to July 2005 (supplemental table 1). We attempted to identify further studies by contacting clinical experts and by examining the reference lists of all full publication articles retrieved. Unpublished information on current practice and audit data were sought by directly contacting all Primary Care Trust (PCT) leads in child health/community paediatrics and all Strategic Health Authority (StHA) leads in child health services in England and Wales. Published and unpublished studies in any language were eligible for inclusion. The full search strategy is available from the authors on request.

Study selection, data extraction and quality assessment were performed by one reviewer, using standardised forms, and checked by a second. A review-specific tool was developed to assess the methodological quality of studies reporting a "diagnostic yield" on the basis of the number of children screened, the number found to be below/above a threshold for height and the number subsequently diagnosed with a height-related condition. In this type of study, only short or tall children are followed up, and therefore complete diagnostic accuracy data are not available. The methodological tool and results of the quality assessment are reported in supplemental table 2.

The number of cases of all conditions detected (new, existing or unclear) and reported in the included studies was extracted. Detection rates of new cases were calculated separately for the height-related conditions detailed above and for all new cases of any condition that can present with short stature.

Diagnostic yield data could not be pooled using meta-analytic techniques owing to heterogeneity of ages screened and charts and thresholds used. Studies were, therefore, combined in a narrative synthesis.

Economic modelling

The economic modelling aimed to find the most cost-effective approach to height screening and the diagnosis and treatment of underlying causes of short stature. Raw data from 10 diagnostic yield studies, for new cases detected, were pooled to provide probability distributions for each included condition. Effectiveness data for treatments of the underlying target conditions were obtained from supplementary searches of the literature.

Available data were used to model lifetime costs and outcomes following, as close as was feasible, the NICE guidelines for economic modelling.[16] An NHS perspective was adopted. Screening, referral and treatment costs were included in the analysis. Cost data were derived from the literature,[17–19] Department of Health Reference Costs[20] and UK Social Services.[21] Costs were reflated to 2006 values, using the Consumer Price Index from the Personal and Social Services Resource Use (PSSRU) data set.[22] A discount rate of 3.5% was used when necessary.[23]

A cost–utility (cost/QALY) analysis was conducted; a QALY represents a year of life, adjusted for its quality or perceived value. The model compared two strategies: screening for short stature at entry to school (age 5) with no screening. Tall-stature conditions were excluded owing to their low prevalence and wide variation in diagnosis and treatment. In the screening strategy, referred patients were assumed to be diagnosed and treated early according to their underlying condition. In the no screening strategy, short-stature cases were assumed to be identified later through visits to the GP. The underlying assumption of the model, therefore, is that those found early will receive appropriate treatment with associated gain in QALYs compared with those found later through normal clinical practice. Full details of the modelling are reported elsewhere.[24]

QALY estimates were derived from the literature[25 26] and augmented by estimates from the expert clinical panel advising the systematic review. Early detection and treatment were assumed to provide, over a lifetime, five additional QALYs for GHD, TS and psychosocial conditions, and 2.5 additional QALYs for ISS and JH. No screening (with late detection and treatment) was assumed to provide half the QALY gains, that is, 2.5 years for GHD, TS and psychosocial conditions, and 1.25 for ISS and JH. In the sensitivity analysis, all QALY gains were varied to reflect uncertainty in the estimates.

TreeAge Professional 2005 (TreeAge Software Inc, Williamstown, MA) and MS Excel were used for the model. The model was run using a hypothetical cohort of 594 000 children, which represents the number of 5-year-old children in England and Wales[27] to assess the overall effect on costs and benefits. Probabilistic sensitivity analysis was conducted to evaluate uncertainty in the model's estimates.
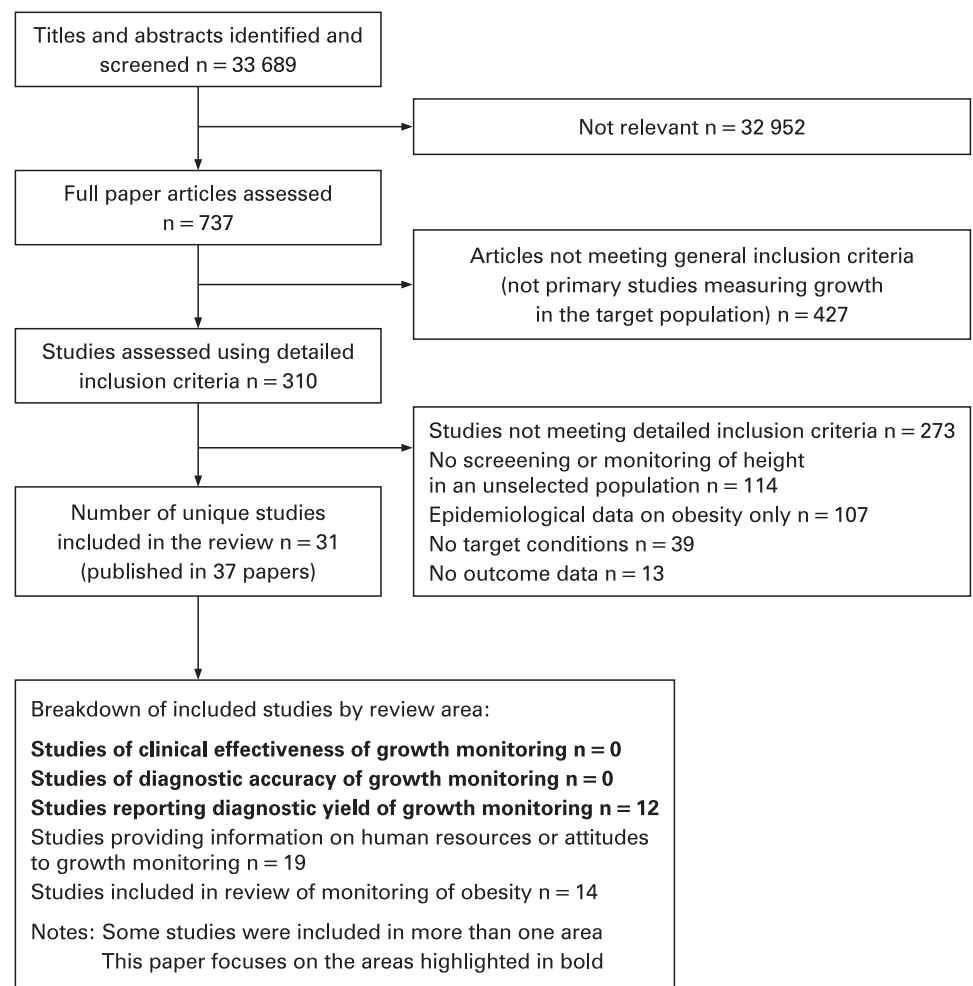
RESULTS

Effectiveness review

Figure 1 shows the flow of studies through the review process and the number of studies excluded at each stage.

Twelve studies described a screening programme that aimed to identify height-related conditions and provided a diagnostic yield of new cases.[18 28–38] Eight studies were conducted in the UK,[18 28 30 32–35 37] one in Sweden,[36] one in Spain,[29] one in Germany[38] and one in the United States.[31] Only two studies[36 38] included conditions relating to tall stature, the remainder aimed to identify conditions of short stature only. A brief overview of the programmes reported and their protocols is given in tables 1 and 2.

The number of children measured ranged from 1592[18] to 114 881.[31] The percentage of eligible children measured ranged from 45%[29] to 90%,[28] where reported. The majority of the screening programmes were based on a single screen of the

Figure 1 Chart showing the flow of studies through the review process.

children's height to detect height-related conditions. Five studies measured children of the same age group[18 28 32 34 35] whereas seven studied a cross section of ages using single or serial measurement, but providing results only for the entire cohort rather than by age group.[29–31 33 36–38] Three studies described programmes measuring children at primary-school entry only (ages 4–5)[28 32 34] One study measured children at age 3 and 4.5 years.[30] Five other studies described screening programmes involving children of primary-school age (but not restricted to school entry).[18 29 31 33 35] Two studies included a group of older children as well as those at primary school.[36 37] The study conducted in Germany[38] differed from the others in that it involved a national network of paediatric practices and a computerised monitoring system into which routine height measurements for all children aged 0 to 18 were input on an ongoing basis.

Collectively, the studies' strengths were in reporting a clearly defined selection procedure, providing details of eligibility for the study and indicating whether the sample was random or a whole cohort based on age group and/or region. A description of a reproducible protocol for taking and interpreting height measurements was provided by the majority of the studies. However, almost half of the studies failed to measure >80% of the study sample. Three further studies did not explicitly state the number of eligible children, only the number measured; it therefore was not possible to assess their level of coverage. Full quality assessment of all the included studies is provided in supplemental table 2. In addition to the methodological issues detailed in the table, four studies did not have a sufficiently large sample size, given the

estimated prevalence of the height-related conditions under consideration, to detect one case of a target condition.[18 28 29 35]

Table 3 lists the number of new cases detected, as reported by each study. Where reported, yield for newly diagnosed GHD (per 1000 children screened) ranged from 0.05[30] to 0.62.[38] Where reported, for newly diagnosed Turner syndrome yield (per 1000 children screened) was between 0.02[33] and 0.07.[38] As a secondary gain, height screening identified children with other potentially treatable conditions with a range of detection rates (per 1000 children screened) from 0.22[31] to 1.84.[38] Three studies did not detect any new cases of any conditions[18 34 36] but all of these had important methodological limitations such as small sample size or high attrition rates at follow-up.

Owing to limitations in the design of included studies, the age or ages at which screening might be most beneficial were unclear. However, the larger, more robust studies of school-entry screening indicated that a single measure at this age might identify new cases at a rate of between 0.54[30] and 0.56[32] per 1000 children screened. It was unclear from the studies that included older age groups what might be the incremental gain from further screening. The diagnostic yield of two of the larger studies of primary-school-aged children may not be reliable as it was unclear whether a number of cases were new or previously diagnosed.[31 33]

Economic modelling

The incremental cost–utility of height screening at school entry compared with no screening was £9 900 per QALY. This is well

Table 1 Overview of height-screening programmes

Study details	Selection procedure	No. measured (% of eligible)	Gender – no. males (%) and ethnicity	Measured age(s)
Agwu (2004), UK[28]	All children in one school year (Sept 1999 to Aug 2000) in the Sandwell district (87 schools) were eligible	3474 (90%)	1729 (50%) Caucasian 75% Other ethnicity 25%	A single measurement of reception-class children aged 4 to 5
Ahmed (1995), UK[30]	All Oxfordshire children measured as part of their routine development checks were eligible. The study took place from 1988 to 1994	20 338 (66%)	11 808 (58%)	A single measurement of two groups of children, aged 3 years (n = 11 603) and 4.5 years (n = 11 477). 2742 of these children were measured at both ages to determine height velocity
Aszkenasy (2005), UK[34]	Audit of all children in the area measured as per routine school-entry height-monitoring policy over three school entry years: (1999–2001)	9338 (83%)	NR	A single measurement of three cohorts of children at primary-school entry
Banerjee (2003), UK[18]	Audit of all children born between September 1992 and August 1993 and measured in the school year September 1998 to August 1999 in the Rhondda and Taff Ely area	1592 (68%)	NR	A single measurement of children aged around 6 years (range 5 years 3 months to 6 years 8 months)
Cernerud (1994), Sweden[36]	Random samples of school classes receiving routine health-surveillance height monitoring were selected	7129 (NR)	NR	A single measurement of two groups of children, aged 10 (n = 3239) and 14 (n = 3890)
de la Puente (1999), Spain[29]	Primary care teams linked to three hospitals in the province of Barcelona were invited to participate. The eight that elected to participate had to screen all children born between 1986 and 1987 under their jurisdiction	2084 (45%)	1093 (52%)	A single measurement of a group of children aged between 5 and 8: aged 5 years (n = 10), 6 years (n = 811), 7 years (n = 1234) and 8 years (n = 26)
Hearn (1995), UK[37]	All primary and secondary school entrants in Hackney over three school entry years (1990–1992) were eligible	9549 (79%)	NR	A single measurement of two groups of children. Primary school entrants had a mean age of 5 years 3 months (n = 6421). Secondary school entrants group had a mean age of 11 years 8 months (n = 3128)
Keller (2002), Germany[38]	Height data submitted over a two-year period from Sept 1998 by paediatricians in practice, or in paediatric group practice or public health school physicians participating in the CrescNet collaborative network were eligible	60 984 (NR)	31 021 (51%)	Data were reported for children and adolescents who had been measured at least once. Males had a mean age of 8.15 years (range 0–18.77 years) and females had a mean age of 8.3 years (range 0–19.28 years)
Lacey (1974), UK[35]	All children born during 1960–62 to mothers living in Newcastle were eligible	2256 (45%)	NR	A single height measurement at the age of 10
Lindsay (1994), US[31]	Schools from the state of Utah were randomly selected and invited to participate. 251 schools representing 38/40 school districts agreed and were required to measure all children from kindergarten to fifth grade	11 4881 (81%)	59 087 (51%)	Serial measurements were taken to assess height and growth velocity. The first measurement was of children aged between 5 and 11. 79 495 of these children participated in the second measurement 12 months later.
Vimpani (1981), UK[33]	All second and third year (and fourth in Aberdeen) primary-school pupils attending education authority and some independent schools in Edinburgh, Glasgow and Aberdeen were screened over 5 months in 1975–6	48 221 (NR)	24 670 (51%)	A single height measurement of children aged between 6 and 9 years.
Voss (1992), UK[32]	All children in the districts of Winchester and Southampton entering local authority primary schools in two consecutive years (1985/7) were eligible	14 346 (100%)	NR	Single height measurement in children at school entry aged 5

Table 2 Overview of growth-measurement protocols used in included studies

Study details	Measurer	Method of measuring height	Method of referencing height	Diagnostic threshold
Agwu (2004)[28]	School nurse, SHN support worker	Leicester height measure	UK 1990 charts	<0.4th centile
Ahmed (1995)[30]	Health visitor	Microtoise, Minimetre (Raven), Oxford screening wall charts (Castlemead Publications)	Tanner and Whitehouse 1965	(1) < −2 SDS (referral to auxologist) (2) < −3 SDS (referral to consultant) (3) SDS decrease between measurements (referral to auxologist)
Aszkenasy (2005)[34]	School nurse	Leicester height measure	0.4th centile tables based on UK 1990 charts	<0.4th centile
Banerjee (2003)[18]	Classroom assistant, health visitor	Leicester height measure	UK 1990 charts	<0.4th centile
Cernerud (1994)[36]	School nurse	Fixed vertical backboard with scale and horizonal blade	Reference data used by schools in the region (unspecified)	Height or height for weight outside 2 SDS, or change of >0.5 SDS/year
de la Puente (1999)[29]	NR	Accustat wall-mounted stadiometer	Growth charts for Catalonia	Less than or equal to the 3rd centile
Hearn (1995)[37]	School nurse	Minimeter (Raven)	Tanner and Whitehouse, 1965	<3rd centile
Keller (2002)[38]	Practising paediatrician	Standiometer (Dr Keller system)	German synthetic norm curve	<3rd centile or >97th centile
Lacey (1974)[35]	School nurse	NR	Tanner and Whitehouse, 1965	1st cohort: <3rd centile 2nd cohort: < −3 SDS
Lindsay (1994)[31]	Trained volunteer	Accustat stadiometer	NR	1st phase: < −2 SDS 2nd phase: <3rd centile and growth rate <5 cm/year
Vimpani (1981)[33]	Investigator	Harpenden portable anthropometer	Tanner and Whitehouse, 1965	⩽ −2.5 SDS
Voss (1992)[32]	School nurse	Portable wall-mounted microtoise	Tannerand Whitehouse, 1965	<3rd centile

SDS, standard deviation scores.

within accepted willingness to pay thresholds for the UK (usually £20–30 000 per QALY). Probabilistic sensitivity analysis indicated that the screening programme was cost-effective over 100% of the model's data distributions for a willingness to pay threshold of £30 000 per QALY. In other words, all projections of the model produced incremental cost per QALY values under £30 000. The majority of costs were incurred in referrals and treatment.

DISCUSSION
Statement of principal findings
This review has shown the clinical utility of height screening in terms of increased detection of height-related disorders in children between the ages of 4 and 11 years. We found an incremental yield of between 0.22 and 1.84 per 1000 children screened of undiagnosed treatable conditions including GHD, Turner syndrome, juvenile hypothyroidism and psychosocial growth failure, amongst others. School-entry studies suggested

a new case yield of between 0.54 and 0.56 per 1000 children screened.

Reasons for the differences in yield between studies were not clear. The age at which the children were measured is, of course, a significant factor, but differences in yield could also be due to methodological limitations in the study, features of the sample measured or unknown contextual factors (such as previous/existing monitoring/screening not described in the study).

Economic modelling indicated that height screening is cost-effective according to accepted willingness to pay thresholds in the UK of £20–30 000 per QALY.

Strengths and weaknesses of the study
This is, to our knowledge, the first systematic review to specifically address the effectiveness of height screening to detect height-related conditions in primary-school-aged children. We have used rigorous systematic review methodology to address an important aspect of child health. The review

Table 3 Detection of new cases

Study	Age of children (years)	No. children screened	No. of new cases (yield per 1000)				
			Growth hormone deficiency	Turner syndrome	Juvenile hypothyroidism	Psychosocial short stature	All conditions
Agwu 2004[28]	4–5	3474	2 (0.58)		1 (0.29)	1 (0.29)	4 (1.15)
Ahmed 1995[30]	3, 4.5	20 338	1 (0.05)			1 (0.05)	11 (0.54)
Aszkenasy 2005[34]	4–5	9338					
Banerjee 2003[18]	6	1592					
Cernerud 1994[36]	10, 14	7129					
de la Puente 1999[29]	5–8	2084					2 (0.96)
Hearn 1995[37]	5, 11	9549	2 (0.21)			2 (0.21)	11 (1.15)
Keller 2002[38]	0–19	60 984	38 (0.62)	4 (0.07)	2 (0.03)	3 (0.05)	112 (1.84)
Lacey 1974[35]	10	2256	1 (0.44)			1 (0.44)	4 (1.77)
Lindsay 1994[31]	5–11	114 881	16 (0.14)	6 (0.05)	3 (0.03)		25 (0.22)
Vimpani 1981[33]	6–9	48 221	9 (0.19)	1 (0.02)	1 (0.02)		11 (0.23)
Voss 1992[32]	5	14 346	1 (0.07)		1 (0.07)		8 (0.56)
	Range of yield per 1000		0–0.62	0–0.07	0–0.29	0–0.44	0–1.84
	Population prevalence per 1000		0.25*	0.2†	0.69‡	?§	?§

*1 in 4000 UK 9 year olds. †1 in 2500 live female births. ‡1 in 1450 people under the age of 22 in UK. §Unknown.

included a comprehensive search strategy and extensive attempts to obtain unpublished studies. However, it remains possible that we have not identified all relevant height-screening programmes given that some may not have been formally evaluated.

This review was unable to fully define the role of height-screening programmes in terms of the effectiveness and cost-effectiveness of various measurement strategies, owing to weaknesses in the available evidence. Firstly, and most significantly, no controlled studies were found evaluating height screening versus no height screening for the detection of height-related conditions. Secondly, no studies were found that reported on the diagnostic accuracy of height-screening programmes for the identification of height-related conditions. The review was based on studies of diagnostic yield that only followed-up children found to be outside the normal height range. Such studies are incomplete in that they only present true positive (number of cases identified) and false positive (number of unnecessary referrals) results. Children found to be of normal height were not followed up, so false negatives (number of cases missed by screening) and true negatives cannot be determined. The available diagnostic yield studies were heterogeneous in terms of the age of participants at screening, methods of measurement and thresholds used for referral. The majority of studies were based on one-off screening for height disorders so the relative merits of serial monitoring strategies cannot be determined. In addition, the majority of studies had further methodological limitations that might affect the reliability of their diagnostic yield estimates: failure to measure >80% of their sample and insufficient sample size, given the estimated prevalence, to detect one case of a height-related condition.

Although the findings of the economic modelling suggest that height screening is justifiable, the analysis was not able to capture any potential harmful effects of screening associated with negative labelling and inappropriate further referral. Data used to populate the model had a number of additional limitations and therefore the results need to be treated with caution. In particular, there is considerable uncertainty associated with the estimates used to derive QALY gains for early versus late detection and treatment, as these were based on previously published estimates from only two studies and expert opinion. QALY gains used in the model attempted to reflect the increases in health-related quality of life as a result of increases in final height. Data were not available to capture all quality of life gains as a result of treatment. However, although these limitations exist it should be noted that the growth-hormone-related QALY gains in a previous study,[25] used to inform the present model, were given cautious acceptance by NICE in the compilation of guidelines for growth-hormone treatment in children.[39] Sensitivity analyses considered this uncertainty by attaching a plausible distribution to QALY gains, which is reflected in the results of the model. Full details of the methods and results of the modelling are provided in the published HTA report.[24]

Unanswered questions and future research

This review strongly points to the need for further research. The role of height screening, alone or in conjunction with other child-health surveillance, needs to be fully defined. Large-scale, long-term controlled trials are needed to determine the optimum strategy. Such trials should evaluate overall benefits and harms alongside costs. Diagnostic accuracy studies could address the relative diagnostic performance of different

> ### What is already known on this topic
>
> ► Height screening has the potential to identify height-related conditions such as growth-hormone deficiency and Turner syndrome, which may present with short stature.
> ► Early identification of height-related conditions is beneficial.

> ### What this study adds
>
> ► Height-screening programmes in primary-school-aged children are likely to be cost-effective and to give an additional yield of undiagnosed height-related conditions. They can lead to additional detection of other undiagnosed conditions for which short stature is a secondary presentation.
> ► Further research is needed to determine health utility gains and costs. There is a need for controlled studies to evaluate the exact role of height-screening programmes in improving child health and appropriate measurement strategies to adopt.

screening strategies for the identification of height-related disorders. However, long-term follow-up of both short and normal children would be required to derive sensitivity and specificity estimates and to improve the validity and methodology of future economic-modelling studies.

In future, research should report all factors that might affect detection rates. Studies should clearly report the following details: selection criteria for participants, attempts to contact those eligible, methods used to ensure and check the competence of measurers, a reproducible protocol to ensure consistency of measurements, coverage, measurement error, measurement and follow-up results for all participants. Empirical studies of quality of life gains associated with the early detection and treatment of height-related conditions are warranted to improve long-term cost–utility estimates.

The research described would lend support to the findings of this review and would clarify the role of height screening in improving child health.

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