Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Abbott 1982 82277019	Location: US Setting: In-patient Mean age: 11±3 y Age range: 4-18 y Mean height: ND Height range: 81-132 cm Male: 64% Race: White 82%, Black 18% Enrolled: ND Evaluated: 11 Number of sites: 1	Short stature due to growth hormone deficiency and/or other pituitary hormone deficiency	None	Isolated short stature	Prospective cross-sectional cohort
Angehrn 1979 80093987	Location: Switzerland Setting: ND Mean age: 4±2.2 y Age range: ND Mean height, SDS: –4.4±1.0 Male: 80% Race: ND Enrolled: ND Evaluated: 20 Number of sites: 1	Russell-Silver syndrome: Height < 2 SDS Low normal growth velocity Low birth weight Moderate bone age retardation Small triangular face and skull of large appearance	None	RSS	Prospective longitudinal cohort

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Frisch 1990 90350511	Location: Austria Setting: Clinic Mean age: 12±3 y Age range: 6.8-15.7 y Mean height, SDS: –2.5±0.9 Height range, SDS: –4.5 to –0.9 Male: 67% Race: ND Enrolled: ND Evaluated: 23 Number of sites: 1	Isolated GH deficiency, or Multi-pituitary hormone deficiency	None	GH deficiency	Prospective cross-sectional
Gordon 1984 84214634 Gordon 1982 82268405	Location: US Setting: Pediatric endocrinology clinic Mean age: Cases 10±2.2 y Controls 10±2.1 y Age range: Case 6-12 y Control 6-12 y Mean height, SDS: <5th percentile Male: 83% Race: ND Mean SES: 3.5 (Hollinghead) Enrolled: ND (23 controls) Evaluated: 24 (23) Number of sites: 1	Cases - Constitutional short stature < 5th percentile height Skeletal maturation delayed > 13 months Height velocity > 4 cm/y Controls - Normal height Matched for age, IQ, SES and sex	Cases - Abnormal GH studies Psychiatric history Controls - Psychiatric history	Isolated short stature	Prospective cross-sectional cohort

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Holmes 1986 Holmes 1985 86060101	Location: US Setting: Pediatric endocrinology clinic Mean age, initial: 12 y Mean age, follow-up: 15 y Age range: ND Mean height, SDS: < –2 Male: ND Race: ND SES: Middle class 21% Enrolled: 76 Evaluated: 47 Number of sites: 1	Height < –2 SDS Patients at pediatric endocrinology clinic	Additional medical diagnoses (e.g., IDDM)	Isolated short stature: GH deficiency (17) Constitutional delay (21) Turner syndrome (9)	Prospective longitudinal cohort (Mean 3.1 y Range 2.2-4.0 y)
Kranzler 2000 20102780	Location: US Setting: Region Mean age: 10±1.4 y Age range: 6-12 y Mean height, SDS: Referred –2.7±1.0 Non-referred –1.7±0.5 Controls +0.1±0.4 Height range, SDS: Referred –4.5 to –1.3 Non-referred –3.2 to –1.3 Controls –0.7 to +0.7 Male: 51% Race: ND Enrolled: ND Evaluated: 61 (29 controls) Number of sites: 2	Referred Cases - Height < 5th percentile Pediatric endocrinology clinics (n=27) Non-referred - Identified in local public schools as shortest 10% of class (n=34) Controls - Height in middle 50% At local public schools.	IQ < 75 Serious psychiatric or medical problem English not primary language	Isolated short stature	Prospective cross-sectional cohort

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Lai 1994 95243689	Location: UK Setting: Clinic Mean age: 9±2 y Age range: ND Mean height, SDS: –2.2±1.5 Male: 80% Race: White 95%; West Indian 5% SES: 80% Middle-class or higher Enrolled: 30 Evaluated: 25 Number of sites: 3	Russell-Silver Syndrome (met 3 of 5 criteria) Age 6-12 y	None	RSS	Prospective cross-sectional
McCauley 1987 87161055 McCauley 1986 86141341	Location: US Setting: Pediatric endocrinology clinic Mean age: Turner 13±2.4 y SS 13±2.8 y Age range: ND Mean height: Turner 52±5.0 in SS 53±4.5 in Male: 0% Race: White 94%, Black 6% SES:41±16 (Hollingshead revised) Enrolled: 23 (22 controls with SS) Evaluated: 33 total Number of sites: 1	Cases - Turner syndrome Followed at Endocrine and Genetics Clinics Controls - Girls with height < 5th percentile from cause other than Turner syndrome Followed at Endocrine and Genetics Clinics	Verbal IQ < 79-80	Turner syndrome (17) Isolated short stature (16)	Prospective cross-sectional cohort

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Meyer-Bahlburg 1978 78184456	Location: US Setting: Pediatric endocrine clinic Mean age: GH def 12 y Multi-hormone def 13 y Age range: GH def 4-18 y Multi-hormone def 6-18 y Mean height, SDS: GH def –3.6 Multi-hormone def –3.9 Height range, SDS: GH def –4.8 to –2.4 Multi-hormone def –6.0 to –1.9 Male: 73% Race: ND Enrolled: 29 Evaluated: 22 (age ≤ 18 y; 29 total) Number of sites: 1	Isolated growth hormone deficiency, or Multiple hormone deficiency	None	Isolated growth hormone deficiency (9 total) Multiple hormone deficiency (13 total)	Prospective cross-sectional cohort
Pollitt 1964	Location: US Setting: Endocrine clinic Mean age: ND Age range: 3-16 y Mean height: ND Height range: 70-126 cm Male: 40% Race: ND Enrolled: ND Evaluated: 15 Number of sites: 1	Significant short stature thought to be due to growth hormone deficiency – either pan-hypopituitary or isolated Pediatricians thought were well-adjusted psychologically and had cooperative parents	None	Isolated short stature	Prospective cross-sectional cohort

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Robinson 1983 84052395	Location: US Setting: Region Mean age: ND Age range: 7-15 y Mean height: ND Male: 0% Race: ND Enrolled: 9 Evaluated: 9 Number of sites: ND	Monosomy X karyotype (45, X) and partial monosomy X	None	Turner Syndrome Monosomy (6) Partial monosomy (3)	Prospective cross-sectional cohort
Ross 1997 97320537	Location: US Setting: ND Mean age: 9.5 y Age range: ND Mean height: ND Male: 0% Race: 87% White SES: 47 (Hollingshead) Enrolled: ND Evaluated: 40 Number of sites: 2	Turner syndrome, confirmed by karyotyping Age ≥5 and <12 y	Estrogen treatment Androgen treatment	Turner syndrome	Prospective cross-sectional cohort (derived from RCT of GH treatment)
Rovet 1985	Location: Canada Setting: Clinic Mean age: 14±1 y Age range: ND Mean height: 139±9 cm Male: 100% Race: ND Enrolled: 27 Evaluated: 25 Number of sites: 1	Height more than 2 SD below mean	History of familial short stature	Isolated short stature	Prospective cross-sectional

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Siegel 1986	Location: US Setting: Endocrinology clinic Mean age: 12±2.3 y Age range: 6-16 y Mean height, SDS: < –2 Male: 71% Race: ND SES, Social position: High 5%, High average 21%, Average 31%, Low average 33%(14), Low 10% Enrolled: 53 Evaluated: 42 Number of sites: 2	Idiopathic hypopituitarism	Deprivation dwarfism Craniopharyngioma Age < 6 y IQ < 30	Isolated short stature GH def (28) Multiple hormone def (14)	Prospective cross-sectional cohort
Siegel 1994	Location: US Setting: Endocrinology clinic Mean age: GHD 11±2.7 y ISS 11±2.6 y Control 11±2.8 y+ Age range: ND Mean height, SDS: GHD –2.7±0.6 ISS –2.8±0.6 Control +0.1±0.9 Male: 75% Race: White 91% Enrolled: 177 (90 controls) Evaluated: 177 (90) Number of sites: 27	Cases - Height < 3rd percentile Controls - Normal height	Known mental impairment Severe psychiatric Chronic medical illness Non-English speaking Short stature secondary to systemic disease, tumor, or genetic abnormalities	Isolated short stature GH Def (87) Idiopathic SS (90)	Prospective cross-sectional cohort

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Siegel 1998 98356098	Location: US Setting: Clinic Initial mean age: 10 y Control 11 y Initial mean height: TS 120±13 cm GHD/ISS 125±12 cm Control 145±17 cm Male: 0% Race: ND Enrolled: 88 (Controls 67) Evaluated: 47 (25) Number of sites: ~27	Cases - Girls with Turner syndrome, GH deficiency, or idiopathic short stature Controls - Matched for age and socioeconomic status	Did not follow through with 3 y of GH therapy	Turner syndrome (22) GH deficiency (13) Idiopathic short stature (12)	Prospective longitudinal cohort (3 y)
Skuse 1997 Gilmour 1996 96408881 Skuse 1994 95252652	Location: UK Setting: Growth clinics Mean age: Case 8±1.5 y Control 9±1.4 y Age range: Case 6-11 y Control 2-11 y Mean height, SDS : Case –2.5±0.3 Control –0.3±1.1 Male: 72% Race: ND SES (Parent profession): 59% advantaged/professional ; 14% clerical/craft; 14% manual Enrolled: 31 (25 controls) Evaluated: 22 (22) Number of sites: 2	Cases - Height < 5th percentile (< –2 SDS) Height velocity over the last year above –1.5 SDS Age 6-11 y Prepubertal Controls - From each case's school class, matched for age, sex, and SES	Cases - Bone age delayed > 2 y Medical treatment for growth retardation Russell-Silver children who had IQ < 72	Isolated short stature (15) Russell-Silver syndrome (7)	Prospective cross-sectional cohort

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Stathis 1999 20099119	Location: Australia Setting: Region Mean age: 5.5 y Age range: 4-6 y Mean height: <3rd percentile Male: 53% Race: ND Enrolled: ND Evaluated: 113 (3,178 controls) Number of sites: 1	Cases - Height < 3rd percentile Age 4-6 y Controls - Height between 10th and 90th percentile Age 4-6 y	PPVT-R score < 50 Cerebral palsy Other serious neurological disorder	Isolated short stature	Prospective cross-sectional cohort
Steinhausen 1976 77086274	Location: Germany Setting: Inpatient Mean age: SS 14±2.7 y Control 14±2.6 y Age range: SS 9-18 y Control 9-18 y Mean height, SDS: <3rd percentile Male: 81% Race: ND SES: Lower class 59%, Middle class 41% Enrolled: ND Evaluated: 32 (32 controls) Number of sites: 1	Cases - Height < 3rd percentile Controls - Age and sex matched from local schools with "normal" stature	None	Isolated short stature GH deficiency (16) Constitutional delay (16)	Prospective cross-sectional cohort

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Tanner 1975 75217260	Location: UK Setting: Growth disorder clinic Mean age: ND Age range: 1.4-10 y Mean height, SDS: –3.6 Height range, SDS: –6.3 to –2.2 Male: 56% Race: ND Enrolled: 39 Evaluated: 39 Number of sites: 1	Russell-Silver syndrome Height < –2 SDS Adjusted birth weight ≥ 2 SD below the mean of the Tanner-Thomson standard	None	RSS	Unclear
Voss 1994 Voss 1991 92151680 Downie 1997 97159125 Downie 1996 96408882	Location: UK Setting: Region Mean age: ND Age range: Data at ages 5-6 y, 7-9 y, 11-13 y, mean 13 y (see comments) Mean height (age 5-6 y), SDS: Case –2.3±0.3 Control +0.1±0.6 Mean height (mean age 13, No GH): Case 139 cm Control 155 cm Male: 54% Race: ND SES: Class I/II 20%; Class III 49%; Class IV/V 31%; 25% unemployed fathers Enrolled: 140 (140 controls) Evaluated: 140 (140) (See comments) Number of sites: 1	Cases - Height <3rd percentile, starting school between 1985 and 1986 Controls - From same school class Height between 10th and 90th percentile Matched for age, sex and school class	Cases - Organic disease (e.g., Turner syndrome or celiac disease); Immigrant parents Controls - None	Isolated short stature	Prospective longitudinal cohort (up to 9 y)

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease/Condition Type (N)	Study Design (Duration)
Wilson 1986	Location: US Setting: ND Mean age: ND Age range: 6-17 y Mean height, SDS: ND Male: ND Race: ND Enrolled: ND Evaluated: 6,768-7,119 (all heights) Number of sites: ND	National Health Examination Survey (NHES): 1963-1965: 7,119 children 6-11 y 1966-1970: 6,768 adolescents 12-17 y	None	Isolated short stature	Prospective cross-sectional cohort
Young-Hyman 1986	Location: US Setting: Endocrine clinic Mean age: 12 y Age range: ND Mean height, SDS: ND Male: 78% Race: ND SES: Upper middle class Enrolled: 27 Evaluated: 27 Number of sites: 1	Children with SS who presented to endocrine clinics for evaluation	Chronic health problem Mental disability	Isolated short stature	Prospective cross-sectional cohort

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part II

Author, Year	Predictors	Predictor Measures	Outcomes	Outcome Measures
Abbott 1982 82277019	Isolated short stature	ND	Cognitive/Academic	IQ (WISC) Academic achievement (WRAT) Visual-motor skills (Developmental Test of Visual-Motor Integration)
Angehrn 1979 80093987	Russell-Silver syndrome	Height < –2 SDS, low normal growth velocity, low birth weight for gestational age, moderate bone age retardation, ty pical small triangular face, and large skull	Cognitive/Academic	IQ (ND)
			Psychomotor	Psychomotor development (Denver developmental screening test)
Frisch 1990 90350511	Isolated short stature/GH deficiency Hypopituitary GH deficiency	GH peak < 5 ng/ml in 2 stimulation tests	Cognitive/Academic	IQ (HAWIK & HAWIE, German version of Wechsler IQ test) Academic performance (Repetition of grade)
			Behavioral/Psychological	Personality structure tests (Freiburger Personality Questionnaire, Giessen Test) Sociability, Social activity, Neuroticism (Hamburger Neuroticism-Extroversion Scales)
Gordon 1984 84214634	Isolated short stature	Height < 5th percentile	Cognitive	IQ (WISC-R) Math, reading, comprehension (PIAT)
			Behavioral	School adjustment, Internalization (CBCL – Teacher)
Gordon 1982 82268405				
Holmes 1986	Isolated short stature: CGD (21)	Retarded bone age, growth velocity within 2 SD of normal for age, projected adult height normal	Cognitive/Academic	IQ (WISC-R)
Holmes	GHD (17)	Maximum GH ≤ 7 ng/ml on 9 samples		

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part II

Author, Year	Predictors	Predictor Measures	Outcomes	Outcome Measures
1985 86060101	TS (9)	ND		
Kranzler 2000 20102780	Isolated short stature	Referred: Height < 5th percentile Non-referred: Height < 10th percentile of class	Cognitive/Academic	Verbal and non-verbal intelligence (K-BIT) Educational achievement (KTEA brief form)
			Behavioral	Adaptive and problem behaviors (BASC – Teacher)
Lai 1994 95243689	Isolated short stature	Russell-Silver syndrome	Cognitive/Academic	IQ (WISC) Reading comprehension (Neale Analysis of Reading Ability) Arithmetic comprehension (ND) Cognitive processing (Matching Familiar Figure Test) Special educational needs
McCauley 1987 87161055	Turner syndrome	Karyotype showing absence of all or part of an X chromosome	Cognitive	IQ (WISC)
			Behavioral	Behavior factor (Piers-Harris Scale – Children self-report)
McCauley 1986 86141341	Isolated short stature	Height < 5th percentile	Psychological	Depression (Children's Depression Inventory)
Meyer-Bahlburg 1978 78184456	Isolated growth hormone deficiency, and multiple hormone deficiency	GH deficient or panhypopituitary	Cognitive	IQ (WISC)

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part II

Author, Year	Predictors	Predictor Measures	Outcomes	Outcome Measures
Pollitt 1964	Hypopituitary short stature	Panhypopituitary Isolated GH deficiency Turner syndrome Primordial Undiagnosed	Cognitive	IQ (WISC Scale for Children – age > 5 y)
Robinson 1983 84052395	Turner Syndrome	45, X monosomy or partial monosomy on karyotype from chromosomal exam of amniotic membrane	Cognitive	IQ (Wechsler Preschool and Primary Scale of Intelligence) Language development ("A comprehensive speech and language evaluation")
			Physical Development	Neuromuscular maturation (Bruininks-Oseretsky Test of Motor Proficiency)
Ross 1997 97320537	Turner syndrome	Karyotype 45,X	Cognitive/Academic	IQ (WISC-R) Academic achievement (WART - reading)
Rovet 1985	Isolated short stature	SD from mean	Cognitive	IQ (WISC)
Siegel 1986	Hypopituitary isolated short stature	GH secretion < 7 ng/dL, delayed bone age, growth < 4 cm in past year, height < –2 SDS or below the 3rd percentile	Cognitive/Academic	IQ (WISC-R) Academic achievement (WRAT) Visual-motor integration skills (Bender Visual-Motor Gestalt Test: a significant visual-motor integration deficit was defined as if the developmental score was < 16th percentile, and four or more errors were significant indicators of brain injury)
Siegel 1994	Isolated short stature GH deficient Idiopathic short stature	Height < 3rd percentile	Cognitive/Academic	IQ (Slosson Intelligence Test) Academic achievement (WRAT - revised)

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part II

Author, Year	Predictors	Predictor Measures	Outcomes	Outcome Measures
Siegel 1998 98356098	Isolated short stature	Turner syndrome GHD/ISS	Cognitive/Academic	IQ (Slosson Intelligence Test) Academic achievement (WRAT - revised)
Skuse 1997 Gilmour 1996 96408881 Skuse 1994 95252652	Isolated short stature and Russell-Silver syndrome	Height < –2 SDS	Cognitive	IQ (WISC for children – version III)
			Behavioral	Competence and self-concept (Harter Self Perception Profile for Children, Harter Pictorial Scale of Perceived Competence and Social Acceptance for Young Children, CHIPS)
Stathis 1999 20099119	Isolated short stature	Height < 3rd percentile	Cognitive	Receptive vocabulary (PPVT-R, which correlates closely with intellectual ability)
Steinhausen 1976 77086274	Isolated short stature	Height < 3rd percentile GH deficiency or no endocrine disease	Cognitive/Academic	Primary mental abilities (LPS) IQ (WISC) Academic performance (Grade level for age) School achievement (ND)
			Behavior	Extraversion and Neuroticism (Hamburg Neuroticism Extraversion Scale)
Tanner 1975 75217260	Russell-Silver syndrome	Height < –2 SDS, adjusted birth weight< –2 SDS, no other obvious cause of short stature	Cognitive/Academic	IQ (ND) Academic achievement (Grade repetition)

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part II

Author, Year	Predictors	Predictor Measures	Outcomes	Outcome Measures
Voss 1994 Voss 1991 92151680	Isolated short stature	Height < 3rd percentile	Cognitive/Academic	IQ (Short form IQ scale of the British Ability Scales) Attainment (Word reading and basic number skills scales of British Ability Scales)
Downie 1997 97159125 Downie 1996 96408882			Behavioral	Behavioral problems (Rutter's Behavior Questionnaire – Teacher) Locus of control (Nowicki and Strickland scale)
Wilson 1986	Isolated short stature	Height < 5th percentile	Cognitive/Academic	IQ (WISC) Academic achievement (WRAT)
Young-Hyman 1986	Isolated short stature	ND	Cognitive	IQ (WISC-R) Visual-motor integration skills (Bender Visual-Motor Gestalt Test)

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part III

Author, Year	Associations found	Potential Biases	Comments
Abbott 1982 82277019	Mean (SD) IQ of children with SS due to pituitary hormone deficiency (n=11) was Full Scale = 88 (17), Verbal = 89 (20), Performance = 89 (16), Reading = 88 (17), Spelling = 85 (14), and Arithmetic = 83 (15) Mean (SD) WRAT scores for children with SS (n=11) were Reading = 88 (17), Spelling = 85 (14), and Math = 83 (15) Visual-Motor Integration skills were significantly below average among children with SS	Compared to population norms	Study was government and hospital funded
Angehrn 1979 80093987	Mean (range) IQ for children with SS due to RSS (n=9) was 91 (38 to 110); 3 subjects had low IQs of 85, 83, and 38; an additional 5 subjects were "probably of normal intelligence" Of subjects with RSS, 3 of these children had microcephaly; 3 children had sub-normal IQ, 2 of whom had microcephaly More than half of the psychomotor activities on the Denver developmental screening test occurred at an age > 90th percentile in subjects with RSS (n=14)	Incomplete testing IQ test used not reported Incomplete and unclear reporting Small sample size for IQ data	No data on funding source
Frisch 1990 90350511	The median (range) IQ of children with GHD (n=23) were Full Scale = 115 (68-131), Performance = 114 (61-136), Verbal = 104 (72-128); full score and performance IQ were significantly higher than population norms; verbal IQ was similar to population norms Performance Behavior (zeal and school aversion) was similar in children with GHD (n=20) compared to population norms Sociability in children with GHD (n=20) than population norms; Social activity in children with GHD was similar to population norms (No further data) Emotional Stability (including mood, control, depression) in children with GHD was similar to population norms (No further data) Delayed Schooling was more common in children with multiple pituitary hormone deficiencies and SS (33%) than normal population (2.1%)	Compared to population norms Reporting incomplete	No data on funding source

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part III

Author, Year	Associations found	Potential Biases	Comments
Gordon 1984 84214634 Gordon 1982 82268405	Mean (SD) IQ for children with SS due to constitutional delay (n=24) were total 108 (14), verbal 107 (16), and performance 108 (14). Mean (SD) scores on PIAT for children with SS (n=24) were math 103 (16), reading recognition 102 (11), and comprehension 102 (11); these were, similar to scores among children with normal stature who were matched by IQ (n=23): 103 (9.6), 102 (7.5), and 103 (10), respectively Mean (SD) teacher CBCL scores for children with SS (n=24) were total 31.2 (26.5) and for controls (n=23) 27.5 (27.6); conduct problem scores were 22.6 (4.3) and 24.1 (6.8), respectively; inattentive/passive 12.7 (4.8) and 12.1 (4.8), respectively; hyperactive 13.7 (5.9) and 11.9 (4.3), respectively; and socialization 14.7 (2.5) and 14.3 (3.0), respectively	Comparisons of cognitive function between short children and controls of questionable value since controls were matched for overall IQ No outline of the statistical analyses used in the paper; therefore, it is hard to evaluate the significance	Study was government and private funded There is no evidence that these behavior problems constitute a disability The subjects and controls were matched for IQ and had equal school performance
Holmes 1986 Holmes 1985 86060101	Mean (SD) Verbal IQ in children with isolated SS (n=47) was 102 (13); among these children, those with GH deficiency (n=17) verbal IQ was 97 (13), those with constitutional delay (n=21), 104 (14) and those with TS (n=9), 103 (14); these were all similar to population norms	40% non-participation rate Those declining participation more likely to have constitutional delay and to have received optimal treatment benefits Study presented only partial data, focusing on significant results IQ compared only to population norms	No data on funding source

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part III

Author, Year	Associations found	Potential Biases	Comments
Kranzler 2000 20102780	Mean (SD) IQ scores of referred children with SS (n=27) were Verbal = 101 (16), Matrices = 106 (14), and Composite = 103 (14); of non-referred children with SS (n=34) were Verbal = 104 (15), Matrices = 105 (14), and Composite = 105 (14); and of normal controls (n=29) were verbal = 110 (12), matrices = 110 (17), and composite = 112 (13); Post hoc analysis found that referred short children had significantly lower Verbal IQ than normal controls; other comparisons were statistically similar Mean (SD) composite and spelling Educational Achievement (KTEA) scores were similar for referred short children, 106 (18) and 105 (15), non-referred short children, 107 (19) and 104 (19); and, controls, 114 (17) and 102 (17). Mean (SD) mathematics and reading KTEA scores were lower for referred short children, 107 (21) and 104 (15) and for non-referred short children, 105 (19) and 106 (18) than for controls, 121 (20) and 115 (18). Teacher ratings on BASC for Externalizing behavior, Internalizing behavior, School Problems composite, Behavior symptoms index and Adaptive Skills composite were each similar among referred short children, non-referred short children and normal controls	Study of cognitive skills excluded children with low IQ Definition of non-referred short children sample vague Predominantly post hoc analyses	Study was government, privately and pharmaceutical funded
Lai 1994 95243689	The mean (SD) IQ of children with RSS (n=25) were Full Scale = 86 (24), range 46-130, Verbal = 89 (23), range 52-141, and Performance = 84 (24), range 47-127; these were significantly lower than population norm, 100 (15) In children with RSS, larger Head Circumference was significantly associated with higher IQ (r=0.5-0.6) Reading Comprehension in children with RSS was delayed by a mean of 15.4 months; Arithmetic Competence was delayed by a mean of 7 months Cognitive Processing, measured by reaction time and error scores in children with RSS (n=22) was similar to normal controls from an earlier study (n=90) Special Education needs were necessary in 9 (36%) children with RSS, primarily in reading and language skills; 12 (48%) children received speech therapy	Compared to population norms and controls from prior study	No data on funding source

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part III

Author, Year	Associations found	Potential Biases	Comments
McCauley 1987 87161055 McCauley 1986 86141341	Mean verbal and performance IQ (SD) for girls with TS (n=17) were 95 (11) and 91 (10), respectively; those IQ (SD) scores for girls with SS not due to TS (n=16) were 100 (12) and 108 (14), respectively. The difference in performance IQ between the groups was significant; however, both groups had verbal and performance IQ scores within 1 SD of the mean Girls with TS had significantly lower performance on arithmetic, digit span, picture completion, object assembly, and coding subscales than girls with SS; performance on other subscales were similar for the two groups Self-reported Piers-Harris behavior factor and Children's Depression Inventory scores were similar in girls with TS and girls with SS; "Although the TS children indicated low self-concept they did not endorse features of clinical depression."	Excluded children with low IQ	Study was hospital funded
Meyer-Bahlburg 1978 78184456	Mean IQ of children with isolated GHD (n=13) was 101, and of children with multiple hormone deficiency (n=9) was 102 Patients with multiple hormone deficiencies have somewhat lower IQs than patients with isolated GHD, after controlling for SES	Compared to population norms	No data on funding source
Pollitt 1964	Mean (SD) IQ for children over age 5 with SS (n=13) were total 103 (16), verbal 103 (15), and performance 102 (16); These IQ scores were not significantly different than normal IQ	Compared to population norms	No data on funding source Descriptive study
Robinson 1983 84052395	Mean (SD) IQ of girls with TS (n=9) were Full Scale = 87 (20), Verbal = 93 (25), and Performance = 83 (12). Siblings (n=17) had significantly higher Full Scale IQ = 111 (15) and Performance IQ = 107 (14), but similar Verbal IQ =113 (15). The TS girls were at non-significantly greater risk of developing Language Disorders than their unaffected siblings	Small sample Handwriting problems not defined Methods and results not fully reported Most analyses were done for all subjects (girls and boys with various sex chromosomal anomalies) together	No data on funding source

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part III

Author, Year	Associations found	Potential Biases	Comments
Ross 1997 97320537	Mean (SD) Full scale IQ in girls with TS with GH treatment (n=20) was 98 (14) and without GH (n=20) was 99 (15) Mean (SD) Academic Achievement (WART) reading score in girls with TS with GH treatment (n=20) was 100 (14) and without GH treatment (n=20) was 97 (17), similar to population norms	Indirectly compared to population norms	Study was government funded
Rovet 1985	The mean IQ of boys with SS (n=25) were Verbal = 98, Performance = 102, and Full Scale = 101	Compared to population norms	Study was hospital funded
Siegel 1986	Mean (SD) IQ for children with hypopituitary SS (n=42) were verbal 94 (18), range 52 to 127, and performance 94 (16), range 49-123; Both the verbal and performance IQ were significantly below normal IQ Mean (SD) WRAT scores for children with hypopituitary SS (n=42) were reading 96 (16.9), range 52 to 131, and math 85 (13.9), range 52-126; The WRAT reading score was in normal range, but the WRAT math score was significantly below the normal score (100) Significant visual-motor integration deficits occurred in 11 (26%) of children with hypopituitary SS (n=42), indicating "a significant number of hypopituitary youngsters have visual-motor integration problems."	Compared to population norms Excluded children with severe mental retardation	Study was hospital funded
Siegel 1994	Mean (SD) IQ for children with GHD (n=87) was 110 (16) for children with ISS (n=90) was 107 (19); compared to 116 (15) for control children (n=90); Significantly more GHD children (9%) and ISS children (18%) had IQs < 90, than control children (3%) Mean (SD) WRAT scores for children with GHD (n=87) were reading 103 (18), spelling 98 (17), and math 99 (17); for children with ISS (n=90) were reading 102 (18), spelling 98 (17), and math 96 (21); and for control children (n=90) were reading 105 (14), spelling 103 (14), and math 105 (16) Significantly more ISS children (22%) had a skill deficit in math (score < 80) compared to GHD (10%) and normal children (7%)	Excluded children with "known mental impairment"	No data on funding source

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part III

Author, Year	Associations found	Potential Biases	Comments
Siegel 1998 98356098	The mean IQ of girls with TS (n=22) was 102 (11), and with GHD/ISS (n=25) was 105 (15); these were not significantly different than controls (n=25) with 109 (17). Mean (SD) WRAT scores for children with TS (n=22) were reading 98 (15), spelling 95 (19), and math 90 (16); for children with GHD/ISS (n=25) were reading 105 (18), spelling 99 (21), and math 102 (22); and for control children (n=25) were reading 98 (16), spelling 100 (15), and math 99 (20). No significant differences among groups.	CBCL completed by parent, typically mother	Study was pharmaceutical company funded
Skuse 1997 Gilmour 1996 96408881 Skuse 1994 95252652	Mean (SD) IQ of children with SS (n=22) were Full Scale = 96 (19), Verbal = 95 (20), and Performance = 97 (17); for normal children (n=22), Full Scale = 107 (17), Verbal = 105 (17), and Performance = 108 (17); Children with SS had statistically lower Full Scale IQ and Performance IQ than controls, but statistically similar Verbal IQ Conduct, Global, Physical, Athletic, Social, and Scholastic competencies measured by Teacher CBCL were similar among SS children (n=17) and controls	Excluded Russell-Silver Syndrome children who had low IQ Incomplete reporting of results. Teacher CBCL completed only on subset of subjects	Study was pharmaceutical funded
Stathis 1999 20099119	Mean receptive vocabulary score on PPVT-R test for boys with SS (n=60) was 92, which was significantly lower for normal height boys, 98 (n=1,660) Mean receptive vocabulary score on PPVT-R test for girls with SS (n=53) was 92, which was significantly lower for normal height girls, 95 (n=1,508)	Study of correlation of PPVT-R score to height excluded those with score < 50	No data on funding source PPVT-R score was adjusted for maternal age, education, non-English speaking background, age at evaluation, maternal depression at birth and maternal height

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part III

Author, Year	Associations found	Potential Biases	Comments
Steinhausen 1976 77086274	Mean IQ for children with SS (n=32) were total 103, verbal 102, and performance 103. Primary mental abilities on LPS intelligence test were significantly different among children with SS (n=32) and controls (n=32) for only 2 of 14 measures of intelligence; Spatial orientation was 4.7 for SS children and 6.2 for controls; Speed of closure was 4.4 for SS children and 5.3 for controls Grade level was appropriate in 59% of children with SS (n=17); Academic achievement was adequate in 48% of SS children Among children with short stature (n=32) mean extraversion and neuroticism scores on HANES were 11.4 and 12.9, respectively. These were similar to controls (11.6 and 15.6, respectively).	Not all of the psychological tests are published and validated; the one well-known test (WISC) was used without data in control group Many comparisons with some statistical significance but questionable clinical significance; the intelligence (LPS) and personality (CPQ) variables are not well defined No statistical comparison was done for social and coping behavior; and, school performance; Average scores only No outline of how the subset 17 kids were selected School achievement not defined	No data on funding source
Tanner 1975 75217260	Mean (SD) IQ for children with SS due to RSS (n=11) was 103 (21), range 70-130 Of subjects with RSS and head circumference < 3rd percentile (n=18), 83% were at "normal" schools, 17% were at schools for educationally subnormal children ("usually IQ < 80"); Of subjects with head circumference > 3rd percentile (n=19), all were at normal schools	IQ test not described and performed in only a sub-sample	No data on funding source

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part III

Author, Year	Associations found	Potential Biases	Comments
Voss 1994 Voss 1991 92151680 Downie 1997 97159125 Downie 1996 96408882	Mean (SD) IQ in children aged 7-9 y with SS (n=140)was 102 (15.2) and for controls with normal height (n=140), IQ was 104 (14.1); there was no significant difference between the two groups; there was also no significant difference in Verbal scales, Non-verbal scales, Speed of Information Processing, or Reading or Number Attainment, after controlling for SES Behavior Disturbance (total Teacher RBQ score > 9) occurred in 29% of children aged 7-9 y with SS (n=132), and in 21% of control children (n=132); the difference was not significant; Hyperactivity (Activity subscale score ≥ 3) occurred in 16% of SS children compared to 8% of control children (p=0.003); Mean (SD) Total Behavior scale score for children with SS was 6.2 (6.2), compared to 5.1 (6.5) for control children (NS) Conduct subscale score was 1.2 (2.3) for children with SS, compared to 1.0 (2.1) for control children (NS) Emotional subscale score was 1.2 (1.4) for children with SS, compared to 1.2 (1.7) for control children (NS) Activity subscale score was 1.7 (2.1)for children with SS, compared to 1.1 (1.6) for control children (NS after controlling for SES) Mean (SD) IQ in children aged 13 y with SS, not treated with GH, (n=84-106 for different tests) and controls (n=93-119), were 103 (17) and 109 (16), respectively (p=0.005); Reading Attainment of 44.3 (8.8) and 47.9 (8.5), respectively (p=0.002); Math Attainment of 40.2 (7.2) and 43.5 (9.2), respectively (p=0.003); Locus of Control score of 16.6 (5.0) and 14.3 (5.1), respectively (p=0.001), Behavior score of 6.8 (7.5) and 5.3 (6.8), respectively (NS); The statistical significance of these differences were reduced, but remained significant, after controlling for SES	None noted	Studies were hospital and pharmaceutical funded Downie studies included subsets of subjects in Voss studies; one examined subjects treated with GH; one examined untreated subjects Different sized subsets of subjects, at different ages, analyzed in different articles

Evidence Table 1. Studies Evaluating Short Stature Secondary to Medical Impairment
Part III

Author, Year	Associations found	Potential Biases	Comments
Wilson 1986	Mean IQ (WISC) for children with SS, aged 12-17 (N~350) was 92 Mean IQ (WRAT) for children with SS, aged 12-17 (N~350) was 91 Among children of all heights, aged 6-11 (n=7,119), both WISC and WRAT scores showed a significant but small correlation with height (r=0.18, WISC; r=0.17, WRAT) Among children of all heights, aged 12-17 (n=6,768), both WISC and WRAT scores showed a significant but small correlation with height (r=0.20, WISC; r=0.19, WRAT) "The association between height and IQ scores is less among the subjects with a high family income"	Prevalence and correlation data only Incomplete reporting	Study was government funded
Young-Hyman 1986	Mean (SD) IQ for children with SS (n=27) was 110 (16), range was 85 to 142 Mean (SD) perceptual-motor skill for children with SS (n=27) was significantly delayed at 9.2 y (1.2 y), compared to chronological age 11.8 y	How significance was defined for perceptual-motor skill test was not outlined in the paper	No data on funding source

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Alston 1983	Location: UK Setting: Brittle Bone Society, Health Authorities Mean age: ND Age range: 5-16 y Mean height: ND Male: ND Race: ND Enrolled: 40 (40 controls) Evaluated: 40 (40) Number of sites: ND	Cases - Osteogenesis imperfecta Controls - Same school class or neighborhood as cases, matched for age, sex and social class	None reported	Osteogenesis imperfecta	Prospective cross-sectional cohort
Apajasalo 1998 98163312	Location: Finland Setting: Clinic Mean age: ND Age range: 12-15 y Mean height: ND Male: 42% Race: ND Enrolled: 21 (239 controls) Evaluated: 19 (239) Number of sites: 1	Cases - Diagnosis of skeletal dysplasia Age 12-15 y Controls – Age-matched Helsinki elementary school pupils who completed the HRQOL questionnaire Age 12-15 y	Cases – Incomplete questionnaires	Skeletal dysplasia Achondroplasia Cartilage hair hypoplasia Diastrophic dysplasia	Prospective cross-sectional

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Bailey 1971 72080259	Location: US Setting: Clinic Mean age: ND Age range: 3 days - 72 y Mean height: ND Male: 51% Race: ND Enrolled: ND Evaluated: 41 (no data on number < 21 y) Number of sites: 1	Diagnosis of achondroplasia	None reported	Achondroplasia	Retrospective cross-sectional
Benson 1978 79027354	Location: US Setting: Shriner's Hospital Mean age: ND Initial age range: 1 mo - 16 y Mean height: ND Male: 44% Race: White 94%; Black 6% Enrolled: 143 Evaluated: 126 Number of sites: 1	Diagnosis of osteogenesis imperfecta from 1924 to 1974	Spine X-ray films not available	Osteogenesis imperfecta	Retrospective longitudinal case series (Mean [Range] 5 [0-17] y)

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Bleck 1981 82026195	Location: US Setting: ND Initial mean age: 9y Follow-up mean age: 13 y Initial age range: 3 mo - 21 y Follow-up age range: 4-26 y Mean height: ND Male: ND Race: ND Enrolled: 30 Evaluated: 24 Number of sites: ND	Diagnosis of osteogenesis imperfecta: congenita or tarda	Death Too young to enable a satisfactory follow-up Moved out of the state	Osteogenesis imperfecta	Prospective longitudinal cohort (Mean [Range] 4 [1-15] y)
Brinkmann 1993 94091382	Location: Germany Setting: Clinic Mean age: 9 y Age range: ND Mean height: ND Male: 47%% Race: ND SES: Primarily middle-class Enrolled: 30 (90 controls) Evaluated: 30 (90) Number of sites: 1	Cases - Clinical and radiographic diagnosis of achondroplasia Controls - Closest sibling; Other causes of short stature Matched for age, sex and SES Normal height children, matched for age, sex and SES	None reported	Achondroplasia	Prospective cross-sectional

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Cox 1982 83016754	Location: US Setting: Dept of Communicative Disorders Mean age: 10 y Age range: 4-17 y Mean height: ND Male: 53% Race: ND Enrolled: 30 Evaluated: 30 (15 met criteria for current review) Number of sites: 1	Medically diagnosed osteogenesis imperfecta, types I, III or IV	History of head injury Prior surgery Treatment for ear disease Noise exposure (For current review, excluded those age ≥ 18 y)	Osteogenesis imperfecta	Prospective cross-sectional cohort
Daly 1996 96219608	Location: UK Setting: Osteogenesis imperfecta clinic Mean age: 7.4 y Age range: 3.5-16.3 y Mean height: ND Male: 49% Race: ND Enrolled: 59 Evaluated: 51 Number of sites: 1	Patients registered at OI clinic who had been recently seen	No reply to the questionnaire	Osteogenesis imperfecta	Prospective cross-sectional cohort

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Engelbert 1997 Possible overlap with Engelbert 1998, Engelbert 1999 Engelbert 2000 Engelbert 2001	Location: Netherlands Setting: Children's hospital Mean age: Type I OI: 7.3±3.5 y Type III OI: 6.5±2.9 y Type IV OI: 9.1±5.0 y Age range: Type I OI: 2-16 y Type III OI: 2-12 y Type IV OI: 1-17 y Mean height: ND Male: 54% Race: ND Enrolled: 68 Evaluated: 61 Number of sites: 1	Diagnosis of osteogenesis imperfecta Visit source hospital = 1 per year	Parents declined to participate	Osteogenesis imperfecta	Prospective cross-sectional cohort
Engelbert 1998 98366964 Possible overlap with Engelbert 1997, Engelbert 1999 Engelbert 2000 Engelbert 2001	Location: Netherlands Setting: Children's hospital Mean age: 8 y Age range: 1-15 y Mean height, SDS: Type I OI –1.6±1.3 Type III OI –8.0±2.0 Type IV OI –2.8±1.7 Male: 47% Race: ND Enrolled: 47 Evaluated: 47 Number of sites: 1	Children with osteogenesis imperfecta who regularly attended a referral center	None reported	Osteogenesis imperfecta	Prospective cross-sectional cohort

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Engelbert 1999 99381568 Possible overlap with Engelbert 1997, Engelbert 1998 Engelbert 2000 Engelbert 2001	Location: Netherlands Setting: Children's hospital Mean age: Initial: 7.3±3.8 y Follow-up: 9.4±3.6 y Age range: Initial: 1-15 y Follow-up: 3-17 y Mean height: ND Male: 50% Race: ND Enrolled: 54 Evaluated: 44 Number of sites: 1	Diagnosis of osteogenesis imperfecta	Intramedullary fixation surgery within 6 months Any other disability or impairment Parents' refusal in follow-up Unable to be reached Surgical interventions in the last half year of the study	Osteogenesis imperfecta	Prospective longitudinal cohort (Mean [Range] 1.2 [0.7-1.8] y)
Engelbert 2000 20429012 Possible overlap with Engelbert 1997, Engelbert 1998 Engelbert 1999 Engelbert 2001	Location: Netherlands Setting: Children's hospital Mean age: 11.2±5.2 y Type I OI: 10.8±5.8 y Type III OI: 9.4±2.9 y Type IV OI: 13±4.6 y Age range: 1-28 y Type I OI: 1-28 y Type III OI: 5-15 y Type IV OI: 4-20 y Mean height: ND Male: 45% Race: ND Enrolled: 98 Evaluated: 70 Number of sites: 1	Diagnosis of osteogenesis imperfecta Completed questionnaire	Too young to expect walking	Osteogenesis imperfecta	Retrospective cross-sectional cohort

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Engelbert 2001 21334060 Possible overlap with Engelbert 1997, Engelbert 1998 Engelbert 1999 Engelbert 2000	Location: Netherlands Setting: Hospital Mean age: 12.6±3.2 y Age range: 8-16 y Mean height: ND Male: 50% Race: ND Enrolled: 40 Evaluated: 40 Number of sites: 1	Diagnosis of osteogenesis imperfecta	None reported	Osteogenesis imperfecta	Prospective cross-sectional cohort
Falvo 1973 74013834	Location: US Setting: ND Mean age: 13.5 y Age range: 4-34 y Mean height: ND Male: 27% Race: ND Enrolled: ND Evaluated: 11 Number of sites: 1	Diagnosis of osteogenesis imperfecta	None reported	Osteogenesis imperfecta	Unclear

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Fowler 1997 97356792 Possible overlap with Pauli 1995	Location: US Setting: Bone dysplasia clinic Mean age: ND Age range: 1-60 months Mean height: ND Male: 48% Race: White 88%, Black 2%, Hispanic 3%, Korean/Asian/Indian 5% Enrolled: 93 Evaluated: 37 Number of sites: 1	Diagnosis of achondroplasia	None reported	Achondroplasia	Prospective cross-sectional
Pauli 1995 95193803 Possible overlap with Fowler 1997	Location: US Setting: Bone clinic Mean age: ND Age range: Infants, young children Mean height: ND Male: 52% Race: White 85%; Black 3%; Hispanic 4%; Korean 7%; Asian Indian 1% Enrolled: 75 Evaluated: 75 Number of sites: 1	Clinical diagnosis of achondroplasia	None reported	Achondroplasia	Prospective longitudinal (N = 53) and cross-sectional (N = 22) cohorts (To age > 1 y)

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Hecht 1991 92152267	Location: US Setting: Clinic Mean age: 15±5 mo Age range: 8.5-26 mo Mean height: ND Male: 46% Race: ND Enrolled: 13 Evaluated: 13 Number of sites: ND	Infants with clinical diagnosis of achondroplasia	None reported	Achondroplasia	Prospective cross-sectional cohort
Hunter 1998 98299528	Location: Multinational Setting: Clinic Mean age: ND Age range: ND Mean height: ND Male: 49% Race: White 100% Enrolled: 55 (37 controls) Evaluated: 55 (37) Number of sites: 6	Cases - Diagnosis of primary skeletal dysplasia Age < 16-18 y old (by site) Controls - Unaffected siblings	None reported	Skeletal dysplasia	Prospective cross-sectional
Kuurila 2000 20379515	Location: Finland Setting: Dept of clinical genetics Mean age: 10 y Age range: 4-16 y Mean height: ND Male: 42% Race: White Enrolled: 60 Evaluated: 45 Number of sites: 1	Diagnosis of osteogenesis imperfecta Age 4-16 y	Insufficient cooperation No audiometry performed Moderate mental retardation.	Osteogenesis imperfecta	Prospective cross-sectional cohort

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Norimatsu 1982 82163323	Location: Japan Setting: Children's Hospital Initial mean age: ND Follow-up mean age: 15.5 y Initial age range: 12 d - 14 y Follow-up age range: 4-28 y Mean height: ND Male: 68% Race: (Japanese) Enrolled: 30 Evaluated: 22 Number of sites: 1	Osteogenesis imperfecta Treated from 1959 to 1980 Followed by spinal x-ray	None reported	Osteogenesis imperfecta (congenita and tarda)	Retrospective longitudinal case series (Mean [Range] 7.6 [1-20] y)
Poussa 1991 92054945	Location: Finland Setting: Genetics and bone clinics Mean age: ND Age range: 6-20 y Mean height: ND Male: ND Race: White Enrolled: 101 Evaluated: 38 Number of sites: 2	Diagnoses of diastrophic dysplasia Age ≤ 20 y	None reported	Diastrophic dysplasia	Prospective longitudinal cohort 13.5 y

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Reid 1988 89193370 Possible overlap with Stokes 1988	Location: US Setting: Genetics clinic Mean age: ND Age range: < 7 y Mean height: ND Male: ND Race: ND Enrolled: 62 Evaluated: 26 Number of sites: 1	Achondroplasia Age < 7 y Seen in genetics clinic	Seen only in orthopedics clinic (not in genetics clinic)	Achondroplasia	Prospective longitudinal cohort 20-45 mo
Stokes 1988 88110722 Possible overlap with Reid 1988	Location: US Setting: Hospital, genetics clinic, LPA convention Mean age: ND Age range: ND Mean height: ND Male: 50% Race: ND Enrolled: 102 (including adults) Evaluated: 24 children Number of sites: 1	Achondroplasia	Acute medical or surgical problems Hypochondroplasia Technically unsatisfactory spirometry Too young to cooperate with spirometry	Achondroplasia	Prospective cross-sectional cohort
Reite 1972 72182015	Location: US Setting: Clinic Mean age: ND Age range: 6-17 y Mean height: ND Male: ND Race: ND Enrolled: ND Evaluated: 12 Number of sites: 2	Children with “severe” osteogenesis imperfecta	None reported	Osteogenesis imperfecta	Retrospective cross-sectional

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Rogers 1979 79200737	Location: US Setting: Pediatric clinic research unit Mean age: ND Age range: 5 mo – 15 y Mean height: ND Male: ND Race: ND Enrolled: 68 Evaluated: 68 Number of sites: 1	Diagnosis of skeletal dysplasia leading to short stature	Syndromes of low-birth-weight dwarfism Multiple malformations Mucolipidosis or mucopolysaccharidosis Cardiac arrest	Skeletal dysplasia and achondroplasia	Prospective cross-sectional cohort
Ruiz-Garcia 1997 97346439	Location: Mexico Setting: Genetics clinic Mean age: 4.5 y Age range: 3 mo - 17 y Mean height: ND Male: 49% Race: ND Enrolled: 39 Evaluated: 39 Number of sites: 1	"Classical" achondroplasia diagnosed in Genetics Department	History of neurosurgical procedures	Achondroplasia	Prospective cross-sectional cohort

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Shurka 1976	Location: Israel Setting: Pediatric endocrinology clinic Mean age: 15 y Age range: 9-17 y Mean height: 134 cm Height range: 104-157 cm Male: 46% Race: ND SES: Primarily average or high Enrolled: 12 Evaluated: 11 (7 met criteria for current review) Number of sites: 1	Dwarfism due to bone disease	(For current review, age ≥ 18 y)	Bone disease (External chondromatosis, Achondroplasia, Undefined)	Prospective cross-sectional cohort
Skeletal Dysplasia Group 1989 89192477	Location: UK Setting: Workgroup's registers Mean age: ND Age range: 1-15 y Mean height: ND Male: 49% Race: ND Enrolled: 182 Evaluated: 15 (children with Morquio disease) Number of sites: ND	Diagnosis of skeletal dysplasia Adequate cervical spine films (Morquio disease: other disease sub-groups did not meet criteria for current review)	Osteogenesis imperfecta Sclerosing bone dysplasias or tumor-like disorders Malformation syndromes	Morquio disease	Retrospective cross-sectional case series

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Stewart 1989 90125184	Location: Scotland Setting: Dep. Of medical genetics Mean age: ND Age range: 10-19 y Mean height: ND Male: 43% for the larger group Race: ND Enrolled: 56 Evaluated: 56 (13 met criteria for current review) Number of sites: ND	Diagnosed based on their history of spontaneous fractures. Contacted via Brittle Bon Society. For current review, only children aged 10-19 were included	None reported	Osteogenesis imperfecta	Prospective cross-sectional cohort
Thompson 1999 99221075	Location: US Setting: Genetics clinic Mean age: Cases: 89 mo Premature: 107 mo Controls: 111 mo Age range: ND Mean height: ND Male: 52% Race: White 74%, Black 6%, Hispanic 13%, Other 7% SES: Low 31%, Middle 19%, High 50% Enrolled: 16 (21 premature, 17 controls) Evaluated: 16 (21, 17) Number of sites: 1	Cases - clinical and radiographic diagnosis of ACH Premature controls- premature infants with hydrocephalus Normal controls - normally developing children of average stature All - IQ>69	Severe psychiatric disorder Uncontrolled seizure Other neurological disorder Child abuse Sensory deficit Unable to speak English	Achondroplasia	Prospective cross-sectional cohort

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Disease / Condition Type	Study Design Mean Duration (Range)
Waters 1993 94029092	Location: Australia Setting: Sleep lab and clinic Mean age: ND Age range: 1-31 y Mean height: ND Male: 50% Race: ND Enrolled: 20 Evaluated: 20 Number of sites: 1	Patients with dysplasia (implied)	Refusal to participate	Achondroplasia	Prospective cross-sectional cohort

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part II

Author, Year	Predictors	Predictor Measures / Definitions	Outcomes	Outcome Measures
Alston 1983	Osteogenesis imperfecta	ND	Cognitive/Academic	Non-verbal intelligence (Raven's Matrices) Reading (Primary Reading Test, Wide Span Reading Test, or Gapadol Reading Test) Spelling (Graded Word Spelling Test) Writing speed (Number of words written in 5 minutes)
			Motor function	Mobility (Walk vs wheelchair)
Apajasalo 1998 98163312	Achondroplasia	Disproportionate short limbed short stature, characteristic facial features and joint and spine disorders	Physical development	Overall quality of life (Health related quality of life, 16 dimensions) Mobility dimension Vision dimension Hearing dimension
	Cartilage-hair hypoplasia	Congenital disproportionate short-limbed short stature, thin/sparse hair, defective immunity		
	Diastrophic Dysplasia	Severe physical handicap due to short-limbed short stature, progressive joint limitations, kyphoscoliosis, foot deformities		
Bailey 1971 72080259	Achondroplasia	ND	Motor function	Elbow flexion (Angle, Self-reported disability)
Benson 1978 79027354	Osteogenesis imperfecta, mild	Thicker cortical bone with visible trabeculae, not severe osteoporosis of vertebrae	Motor function	Walking ability (Independent walkers, Walked with appliance, Sitter) Scoliosis (spinal curvature on spine radiography)
	Osteogenesis imperfecta, moderate	ND		
	Osteogenesis imperfecta, severe	Thin osteoporotic long bones and severe osteoporosis of vertebrae		

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part II

Author, Year	Predictors	Predictor Measures / Definitions	Outcomes	Outcome Measures
Bleck 1981 82026195	Osteogenesis imperfecta congenita	Severe type	Physical development/Motor function	Independence (0 = No achievement possible 1 = Complete dependence 2 = Partial dependence 3 = Independence through technical help 4 = Completely independent, but not normal in timing, effort expenditure, or external appearance 5 = Normal activity) Mobility efficiency (0 = None 1 = Mobility not functional enough to be used 2 = Moves about immediate surroundings 3 = Travels in the community 4 = Travel beyond the community Activities of daily living (ADL: 0 = No ADL possible 1 = Meets own essential needs 2 = Completes personal care 3 = Household activity possible 4 = Normal ADL) Ambulation (0 = None 1 = Walking possible but not functional enough to be useful 2 = Household walker 3 = Walk outside home but limited to neighborhood 4 = Community walker)
	Osteogenesis imperfecta tarda	ND		

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part II

Author, Year	Predictors	Predictor Measures / Definitions	Outcomes	Outcome Measures
Brinkmann 1993 94091382	Achondroplasia	Short limbs and characteristic skull changes with macrocephaly	Cognitive	Cognitive Abilities Test, German version Verbal component Arithmetic component Reasoning component
			Physical development	Motor development (Months to sit, stand, walk alone) Delayed speech (parental report)
			Sensory	Hearing deficit (parental report)
			Pain	Limb, joint, back pain
Cox 1982 83016754	Osteogenesis imperfecta	Idiopathic bone fragility, blue sclerae, hearing impairment	Sensory	Hearing loss (Pure tone thresholds > 30 dB hearing loss at 250-1,000 Hz and/or > 25 db hearing loss at 2,000-6,000 Hz)
Daly 1996 96219608	Osteogenesis imperfecta Shapiro classification: Congenita A	Fractures at birth, bones radiographically abnormal	Physical development/Motor function	Mobility (Wheelchair, Aided walker, Independent) Patterns of development (Abnormal arrested, Delayed arrested, Normal arrested, Delayed, Normal)

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part II

Author, Year	Predictors	Predictor Measures / Definitions	Outcomes	Outcome Measures
	Congenita B	Fractures at birth, bones radiographically normal		
	Tarda A	First fracture by walking stage, bones narrow, osteopenic		
	Tarda B	First fracture after walking, bones radiographically normal		
	Osteogenesis imperfecta Sillence classification: I A	Autosomal dominant, normal stature, blue sclerae		
	I B	IA plus dentinogenesis imperfecta		
	III	Autosomal recessive, multiple fractures at birth, progressively deforming		
	IV A	Autosomal dominant, bone fragility, normal sclerae		
	IV B	IV A plus dentinogenesis imperfecta		
Engelbert 1997	Osteogenesis imperfecta I, III and IV	Classified according to Sillence method (see Daly 1996, above)	Motor function	Self-care (Pediatric Evaluation of Disability Inventory, PEDI, range 0-100, median 50. Score scaled for children older than 7.5 years such that normal score=100) Mobility (PEDI)
Engelbert 1998 98366964	Osteogenesis imperfecta I, III and IV	Classified according to Sillence method (see Daly 1996, above)	Motor function	Scoliosis (Cobb angle > 40°) Kyphosis (Cobb angle < 10° or > 40°)
Engelbert 1999 99381568	Osteogenesis imperfecta I, III and IV	Classified according to Sillence method (see Daly 1996, above)	Motor function	Level of ambulation (Bleck classification)
Engelbert 2000 20429012	Osteogenesis imperfecta I, III and IV	Classified according to Sillence method (see Daly 1996, above)	Motor function	Level of ambulation (Bleck classification)

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part II

Author, Year	Predictors	Predictor Measures / Definitions	Outcomes	Outcome Measures
Engelbert 2001 21334060	Osteogenesis imperfecta I, III and IV	Classified according to Sillence method (see Daly 1996, above)	Motor function	Self-care (Pediatric Evaluation of Disability Inventory, PEDI, range 0-100. Score scaled for children older than 7.5 years such that normal score=100) Mobility (PEDI) Level of ambulation (Bleck classification)
			Motor function	Joint range of motion: arms, legs (0=normal, 4=maximally decreased) Muscle strength: arms, legs (0=no muscle activity, 5=normal muscle strength)
Falvo 1973 74013834	Osteogenesis imperfecta	Generalized osteoporosis, blue sclerae, dentinogenesis imperfecta, history of fracture	Pulmonary	Pulmonary function tests (Vital capacity (VC), Residual volume (RV), 1-second forced expiratory volume divided by forced vital capacity (FEV_1/FVC)) Arterial blood analysis (Oxygen partial pressure, carbon dioxide partial pressure)
	Mild	No noticeable deformity of long bones		
	Moderate	Bowing of lower extremity long bones only		
	Severe	Bowing of all long bones		
Fowler 1997 97356792	Achondroplasia	ND	Physical development	Motor development (Denver Developmental Screening Test: Months to sit, stand, walk alone)
Pauli 1995 95193803	Achondroplasia	ND	Neurological	Neurological examination (Truncal tone, Limb tone, Arm strength, Leg strength) Neurological history (Developmental delays, Asymmetry, Weakness, Sensory abnormality, Arching / opisthotonus, Clonus, Seizure, Apnea)
			Pulmonary	Polysomnography (Central apnea, Central hypopnea, Obstructive apnea)

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part II

Author, Year	Predictors	Predictor Measures / Definitions	Outcomes	Outcome Measures
Hecht 1991 92152267	Achondroplasia	ND	Cognitive	Mental development index (Bayley Scales of Infant Development) Psychomotor development index (Bayley)
			Pulmonary	Sleep apnea
Hunter 1998 98299528	Chondrodysplasia	ND	Psychological	Depression (Beck Depression Inventories) Anxiety (Speilberger State-Trait Anxiety Inventories)
Kuurila 2000 20379515	Osteogenesis imperfecta I, III and IV	Classified according to Sillence method (see Daly 1996, above)	Sensory	Hearing loss (Pure tone < 20 dB, Conductive < 15 dB)
Norimatsu 1982 82163323	Osteogenesis imperfecta Mild, Moderate, Severe	Per Falvo 1973 (see above)	Motor function	Walking ability (Wheelchair bound, ambulates with assistance) Scoliosis (Mild <30°; Moderate 30°-50°; Severe > 50°, by Cobb's method)
Poussa 1991 92054945	Diastrophic dysplasia	Short-limbed short stature, joint limitations, spinal and foot deformities, dysmorphic earlobes, cleft palate	Motor function	Scoliosis (>10° by Cobb's method)
Reid 1988 89193370	Achondroplasia	ND	Pulmonary	Obstructive sleep apnea (>5 obstructive or >2 central apneas per hour)
			Neurological	Paresis (not defined)
Stokes 1988 88110722	Achondroplasia	Rhizomelia, macrocephaly with midfacial hypoplasia, spinal canal narrowing	Pulmonary	Forced vital capacity
Reite 1972 72182015	Osteogenesis imperfecta	ND	Cognitive	IQ (WISC)

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part II

Author, Year	Predictors	Predictor Measures / Definitions	Outcomes	Outcome Measures
Rogers 1979 79200737	Achondroplasia	ND	Cognitive	IQ (Age< 2 y: Bayley Scales of Infant Development; Age 2-6 y: Stanford-Binet Intelligence Scale; Age 6-15 y: WISC)
	Other skeletal dysplasia	Multiple diagnoses		
Ruiz-Garcia 1997 97346439	Achondroplasia	Autosomal dominant, abnormally short stature, macrocephaly, rhizomelia	Neurological	Neurological examination (Quadriparesis, Weakness, Sensory deficit) Compressive neural syndrome (craniocervical compression, lumbar compression)
			Hearing Loss	Brainstem auditory evoked response
Shurka 1976	Skeletal dysplasia	External chondromatosis, achondroplasia, or undefined	Cognitive	IQ (WISC)
Skeletal Dysplasia Group 1989 89192477	Morquio disease	ND	Neurological	Neurological complications (ND)
Stewart 1989 90125184	Osteogenesis imperfecta	ND	Sensory	Hearing loss (Pure tone < 30 dB, conductive < 15 dB)
Thompson 1999 99221075	Achondroplasia	ND	Cognitive	IQ (WISC-R) Academic achievement (WRAT-R)
			Motor function	Gross motor arm and leg coordination (McCarthy Scales)

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part II

Author, Year	Predictors	Predictor Measures / Definitions	Outcomes	Outcome Measures
			Visual-motor skills	Motor-based design copying task (Beery Test of Visual Motor Integration) Motor-free spatial matching task (Judgment of Line Orientation) Fine motor skills
Waters 1993 94029092	Achondroplasia	ND	Pulmonary	Sleep apnea (> 5 apneic episodes per hour)

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part III

Author, Year	Associations found	Potential Biases	Comments
Alston 1983	In children with osteogenesis imperfecta (n=40) mean non-verbal intelligence (104), reading ability (100) and spelling ability (102) were similar to control children (n=40, 105, 102, 104, respectively). Writing speed was significantly slower (51 words in 5 minutes) compared to controls (61 words). Of children with osteogenesis imperfecta (n=40), 38% required wheelchair use.	None noted	Study was privately funded
Apajasalo 1998 98163312	Among adolescents with skeletal dysplasia (n=19), overall quality of life (HRQOL=92) was significantly lower than in controls (n=239, 95) in univariate and multivariate analyses. Among adolescents with skeletal dysplasias (n=19), the quality of life dimension mobility was significantly lower than for normal children. Children with diastrophic dysplasia and achondroplasia had mean scores of ~81 (from graph); those with cartilage-hair hypoplasia had a mean score of 100. Those with skeletal dysplasia had similar scores to normal children for vision and hearing. Children with diastrophic dysplasia had mean scores of 94 for vision and 93 for hearing; those with achondroplasia had mean scores of 96 and 95, respectively; those with cartilage-hair hypoplasia had mean scores of 96 and 85, respectively. In the analysis of 16 dimensions of quality of life, there were no statistically significant differences among the different groups of children with skeletal dysplasia.	Few definitions of outcome measures Reporting of analyses incomplete	No data on funding source
Bailey 1971 72080259	Infants with achondroplasia, aged 0-2 years, had mean elbow flexion deformity of 11°, ranging from 5°-25°; Children, aged 3-12 years, had mean elbow flexion of 19°, ranging from 10°-40°; adolescents, aged 13-20 years, had mean elbow flexion of 23.5°, ranging from 0°-40°.	No data on actual disability due to limited joint movement specifically in children. Unknown number of subjects in relevant age ranges.	No data on funding source

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part III

Author, Year	Associations found	Potential Biases	Comments
Benson 1978 79027354	Among children with osteogenesis imperfecta (n=126) 48% were wheelchair bound (sitters), 25% walked with appliances, and 28% were independent walkers. Among those children with osteogenesis imperfecta who had spine radiography performed (n=103), 38% had straight spines, 7% had scoliosis between 0°-9°, 19% had scoliosis between 10°-19°, 14% had scoliosis between 20°-49°, 14% had scoliosis between 50°-79°, and 9% ≥ 80°.	Incomplete data available. Incomplete reporting	No data on funding source
Bleck 1981 82026195	Among children with osteogenesis imperfecta congenita, severe type (n=12), mean independence, mobility, activities of daily living, and ambulation scores after orthotic and mobility management were 2.6 (partial dependence-independence through technical help), 3.0 (travels in community), 2.5 (completes personal care-household activity possible), and 0.7 (no ambulation-walking possible but not functional), respectively. Among children with osteogenesis imperfecta tarda (n=12), mean independence, mobility, activities of daily living, and ambulation scores after orthotic and mobility management were 3.4 (independence through technical help-completely independent but not normal), 3.8 (almost travel beyond community), 3.7 (almost normal activities of daily living), and 2.8 (almost walk outside home but limited to neighborhood), respectively.	No statistical analysis.	No data on funding source. No statistical comparison.

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part III

Author, Year	Associations found	Potential Biases	Comments
Brinkmann 1993 94091382	Among children with achondroplasia (n=30), mean Cognitive Abilities Scores were Total 48, Verbal 46, Arithmetic 49, and Reasoning 51. Compared to normal controls (n=30), Total (56), Verbal (54) and Arithmetic (55), children with achondroplasia had significantly lower scores; Reasoning scores (control 55) were not significantly different. Overall comparisons to siblings (n=30) and other short children (n=30) were similar. Children with achondroplasia (n=30) were able to sit alone at a median of 12 months (compared to 7 months for normal controls, n=30), according to parental reports, to stand alone at 14 months (10 months), and to walk alone at 18 months (12 months). Siblings (n=30) and short controls (n=30) had motor development similar to other controls. No statistical analysis reported. Among children with achondroplasia (n=27) 63% were reported by their parents to have hearing deficits, compared to 18% of short controls (n=28) and 19% of normal controls (n=27). Among children with achondroplasia (n=27) 41% were reported by their parents to have delayed speech development, compared to 14% of short controls (n=28) and 7% of normal controls (n=27). Among children with achondroplasia (n=30) limb, joint or back pain was present by parental report in 80%, compared to 43% of short controls (n=30) and 10% of normal controls (n=30).	Limited statistical analyses. No data on sibling controls for factors that were reported by parents.	Study was government funded
Cox 1982 83016754	Of children with osteogenesis imperfecta (n=15) 33% had hearing loss	All subjects from 5 families with history of osteogenesis imperfecta. Limited data on hearing function	Study was university funded

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part III

Author, Year	Associations found	Potential Biases	Comments
Daly 1996 96219608	Among children with osteogenesis imperfecta classified by Shapiro as congenita B (n=31) 19% had abnormal arrested development, 19% had delayed arrested development, 29% had normal arrested development, 29% had delayed development, and 3% had normal development. Among these children, 87% were wheelchair bound and 13% were independent walkers. Among children with osteogenesis imperfecta tarda A (n=15) none had abnormal arrested development, 27% had delayed arrested development, 7% had normal arrested development, 20% had delayed development, and 47% had normal development. Among these children, 27% were wheelchair bound, 13% were aided walkers, and 60% were independent walkers. Too few children had osteogenesis congenita A (n=1) or tarda B (n=4) for analysis. Among (the same sample of) children with osteogenesis imperfecta classified by Sillence as Type I (n=15) none had abnormal arrested or delayed arrested development, 7% had normal arrested development, 27% had delayed development, and 67% had normal development. Among these children, 7% were aided walkers and 93% were independent walkers. Among children with osteogenesis imperfecta Type III (n=29) 21% had abnormal arrested development, 34% had delayed arrested development, 28% had normal arrested development, 17% had delayed development, and none had normal development. Among these children, 97% were wheelchair bound and 3% were independent walkers. Among children with osteogenesis imperfecta Type IV (n=7) none had abnormal arrested development, 14% had delayed arrested development, 14% had normal arrested development, 43% had delayed development, and 29 had normal development. Among these children, 57% were wheelchair bound, 14% were aided walkers and 29% were independent walkers.	Only a parental questionnaire No statistical analysis. Definitions of development unclear	No data on funding source

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part III

Author, Year	Associations found	Potential Biases	Comments
Engelbert 1997	Among children aged ≤ 7.5 years with osteogenesis imperfecta Type I (n=16) mean Self-care Functional Skills score on PEDI (normal median 50) was 39 and mean Mobility score was 31. Among children with Type III (n=8) mean Self-care score was 31 and Mobility score was 5. Among children with Type IV (n=6) mean Self-care score was 37 and Mobility was 48. Among children aged > 7.5 years with osteogenesis imperfecta Type I (n=16) mean Self-care Functional Skills score on PEDI (normal = 100) was 100 and mean Mobility score was 100. Among children with Type III (n=6) mean Self-care score was 70 and mean Mobility was 41. Among children with Type IV (n=9) mean Self-care score was 93 and Mobility was 62.	Interpretation of scales difficult due to different norms used and unclear description of scales No explicit comparison to normal children Unclear how much overlap in sample with other Engelbert papers.	No data on funding source
Engelbert 1998 98366964	Among children with osteogenesis imperfecta scoliosis > 10° was present in 12% of those with Type I (n=17), 63% with Type III (n=16), and 71% with Type IV (n=14). Among children with osteogenesis imperfecta kyphosis < 10° was present in 6% of those with Type I (n=17), 38% with Type III (n=16), and 14% with Type IV (n=14). Among children with osteogenesis imperfecta kyphosis > 40° was present in 6% of those with Type I (n=17), 38% with Type III (n=16), and 14% with Type IV (n=14).	No comparison with normal controls Unclear how much overlap in sample with other Engelbert papers.	No data on funding source
Engelbert 1999 99381568	At follow-up, of children with osteogenesis imperfecta Type I (n=19) 53% were community walkers, 26% were neighborhood walkers, 16% were household walkers, and 5% were exercise walkers. Of children with Type III (n=13) 31% were household walkers, 8% were exercise walkers, 38% were bottom shufflers, 15% could sit unsupported, and 8% could only sit supported. Of children with Type IV (n=10) 10% were community walkers, 10% were neighborhood walkers, 10% were household walkers, 40% were exercise walkers, 20% could weight bear on feet, and 10% were bottom shufflers.	No children with recent intramedullary fixation surgery or other disability or impairments. PEDI scale scores reported for small to very small samples of children. Appears to be earlier subset of data reported earlier in Engelbert 1997. Not analyzed here. Unclear how much overlap in sample with other Engelbert papers.	No data on funding source

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part III

Author, Year	Associations found	Potential Biases	Comments
Engelbert 2000 20429012	At follow-up, of children with osteogenesis imperfecta Type I (n=41) 59% were community walkers without aides, 5% were community walkers with aides, 10% were neighborhood walkers without aides, 12% were household walkers without aides, 7% were household walkers with aides, and 7% were therapy walkers with aides. Of children with Type III (n=11) 9% were neighborhood walkers with aides, 27% were household walkers with aides, 19% were therapy walkers with aides, and 45% were non-walkers. Of children with Type IV (n=18) 28% were community walkers without aides, 11% were community walkers with aides, 6% were neighborhood walkers with aides, 11% were household walkers with aides, 22% were therapy walkers with aides, and 22% were non-walkers.	Unclear how much overlap in sample with other Engelbert papers. No comparison with normal children	No data on funding source.

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part III

Author, Year	Associations found	Potential Biases	Comments
Engelbert 2001 21334060	Among children aged > 8 years with osteogenesis imperfecta Type I (n=17) mean Self-care Functional Skills score on PEDI (normal = 100) was 100 and mean Mobility score was 92. Among children with Type III (n=11) mean Self-care score was 81 and mean Mobility was 55. Among children with Type IV (n=12) mean Self-care score was 100 and Mobility was 67. Among children with osteogenesis imperfecta Type I (n=17) the average child was a community walker without aides. Among children with Type III (n=11) the average child was a therapy walker with aides. Among children with Type IV (n=12) the average child was a household walker without aides. Among children with osteogenesis imperfecta Type I (n=17), the average joint range of motion on a scale of 0 (normal) to 4 (maximally decreased) was 0.5 for arms and 0 for legs. Among children with Type III (n=11) the average arm range of motion was 1.8 and leg range of motion was 3.3. Among children with Type IV (n=12) the average arm range of motion was 1.3 and leg range of motion was 1.7. Among children with osteogenesis imperfecta Type I (n=17), the average muscle strength on a scale of 0 (no muscle activity) to 5 (normal muscle strength) was 4.5 for arms and 4.8 for legs. Among children with Type III (n=11) the average arm strength was 3.5 and leg strength was 3.6. Among children with Type IV (n=12) the average arm strength was 4.5 and leg strength was 3.8.	Unclear how much overlap in sample with other Engelbert papers, especially those with PEDI analyses (1997 and 1999) No comparison to normal children. Meaning of scales unclear.	No data on funding source.
Falvo 1973 74013834	Among children with osteogenesis imperfecta mean pulmonary vital capacity was 85% of predicted normal (n=10), mean residual volume was 119% of predicted normal (n=10), mean FEV_1/FVC was 99% of predicted normal (n=10), mean arterial oxygen partial pressure was 88 mm Hg (n=8), and mean arterial carbon dioxide partial pressure was 35 mm Hg (n=8). "No patient had severe hypoxemia or hypercapnea. Reduction of VC and increase in RV were found only in patients with kyphoscoliosis. Other parameters of pulmonary function were within normal limits."	Limited analyses	Study was government and privately funded.

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part III

Author, Year	Associations found	Potential Biases	Comments
Fowler 1997 97356792	Among children with achondroplasia, by parental report, the mean age of sitting unsupported was 12 months (n=37), the mean age of standing alone was 19 months (n=21), and the mean age of walking alone was 18 months (n=24). "Virtually all fine motor skills were delayed when compared with children without achondroplasia."	Includes subjects in Pauli 1995 Data on motor development from few subjects enrolled in study	No data on funding source
Pauli 1995 95193803	Among children with achondroplasia, 72% had decreased truncal tone (n=39), 70% had decreased limb tone (n=44), 32% had abnormal arm strength (n=40), and 50% had abnormal leg strength (n=40). No child had marked abnormalities in neurological examination. Among children with achondroplasia (n=52) 42% had an abnormality by neurological history. These included disproportionate developmental delays (10%), asymmetries (21%), weakness (14%), sensory abnormalities (4%), arching/opisthotonos (10%), clonus (8%), seizures (8%), and apnea (27%). Among children with achondroplasia (n=35) by polysomnography 40% had mild to severe central apnea, 66% had mild to severe central hypopnea, and 23% had mild obstructive apnea	Earlier subset of subjects in Fowler 1997	Study was hospital funded
Hecht 1991 92152267	Among infants with achondroplasia (n=13) mean BSID Mental Development Index score was 97 (1 or 2 infants had scores <70, text and table disagree) and mean Psychomotor Development Index score was 63 (62% scored <50). Among infants with achondroplasia (n=13) 77% had normal polysomnography. Two infants (15%) had obstructive apnea, 1 had hypoxemia and respiratory acidosis.	5 of 13 patients were initially seen (and thus included) for apnea, motor delay or neurological complication Reporting errors	Study was government funded

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part III

Author, Year	Associations found	Potential Biases	Comments
Hunter 1998 98299528	Among children with chondroplasias (n=55) 7% had moderate or severe depression per the Beck Depression Inventories, which was not significantly different than among normal siblings (11%, n=35). Among children with chondroplasias (n=55) the mean Speilberger Child State Anxiety score was 28.4 and Trait Anxiety score was 32.5, which were significantly lower (implying *less* anxiety) than general population means for boys (31.0 and 36.7, respectively) and girls (30.7 and 38.0, respectively).	None noted	No data on funding source
Kuurila 2000 20379515	Among children with osteogenesis imperfecta (n=45), 7% had hearing loss: 2 children had conductive hearing loss and 1 had sensorineural deafness.	Descriptive study only	No data on funding source.
Norimatsu 1982 82163323	Among children with osteogenesis imperfecta congenita (n=8) 38% were wheelchair bound; the remainder walked with assistance. Among children with osteogenesis imperfecta tarda (n=14) 14% were wheelchair bound; the remainder walked with assistance. Among children with osteogenesis imperfecta congenita (n=8) 88% had severe scoliosis (59°-139°; one had mild scoliosis (17°). Among children with osteogenesis imperfecta tarda (n=14) 21% had severe scoliosis (55°-125°), 14% had moderate scoliosis (32° & 33°), 64% had mild scoliosis (5°-28°).	Multiple subjects were closely related. Descriptive study only	No data on funding source
Poussa 1991 92054945	Among children with diastrophic dysplasia (n=38) 29% had scoliosis. Of those ≤ 10 years (n=17) 6% had scoliosis; of those between 11 and 20 years (n=21) 48% had scoliosis. Those with scoliosis (n=11) had a mean magnitude of curvature of 39° (range 15°-80°).	Descriptive analysis only	No data on funding source. Subjects are part of the study. Descriptive data only.
Reid 1988 89193370	Among children with achondroplasia (n=26) 85% had a history of respiratory abnormalities including pneumonia, loud snoring, cyanotic spells or apnea in the preceding 6 months; 35% had obstructive sleep apnea. Among children with achondroplasia (n=26) 42% had paresis.	Descriptive study only No specific definitions of conditions reported Appears to be subgroup of subjects included in Stokes 1988	No data on funding source

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part III

Author, Year	Associations found	Potential Biases	Comments
Stokes 1988 88110722	Among children with achondroplasia (n=24) mean forced vital capacity was 72% of predicted, significantly lower than population norms.	Limited details of pediatric sub-sample. Appears to include subjects in Reid 1988	Study funded by government, hospital and private sources
Reite 1972 72182015	Among children with osteogenesis imperfecta (n=12) the mean IQ was 107, ranging from 78-133.	Only children with "severe" osteogenesis imperfecta Incomplete data reported	Study was government and privately funded.
Rogers 1979 79200737	Among school aged children with achondroplasia (n=19) mean Full scale IQ was 96, Verbal IQ was 95, and Performance IQ was 100; 5% had IQ<70. Among preschool aged children with achondroplasia (n=15) mean Full scale IQ was 97; 13% had IQ<70. Among school aged children with other skeletal dysplasias (n=22) mean Full scale IQ was 104, Verbal IQ was 104, and Performance IQ was 103; none had IQ<70. Among preschool aged children with other skeletal dysplasias (n=12) mean Full scale IQ was 100; none had IQ<70.	Descriptive study only	Study was government funded
Ruiz-Garcia 1997 97346439	According to summary table, among children with achondroplasia (n=39) 59% had hypotonia, 15% had quadriparesis, 31% had weakness, and 10% had a sensory deficit. According to text, 49% had hypotonia, 13% had quadriparesis, 26% had weakness, and 5% had sensory deficit. In additon, 31% had compressive neural syndromes (18% craniocervical, 13% lumbar). According to the text, among children with achondroplasia (n=32), 50% had abnormal hearing as tested by brainstem auditory evoked response.	No definitions of outcomes Results reported in text differ from results reported in table Descriptive study only.	No data on funding source
Shurka 1976	Among children with skeletal dysplasias (n=7) mean Full scale IQ was 102, Verbal IQ was 103, and Performance IQ was 99.	Very small sample size. Multiple, poorly defined causes of dwarfism.	No data on funding source

Evidence Table 2. Studies Evaluating Short Stature Secondary to Skeletal Dysplasia
Part III

Author, Year	Associations found	Potential Biases	Comments
Skeletal Dysplasia Group 1989 89192477	Among children with Morquio disease (n=15) 33% had "known neurological complications."	Limited data reported Conditions and outcomes not defined Only subset met criteria for inclusion in SSA report	No data on funding source
Stewart 1989 90125184	Among children with osteogenesis imperfecta (n=13), 15% had hearing loss.	Incomplete reporting Descriptive only	Study was private funded
Thompson 1999 99221075	Among children with achondroplasia mean WISC-R Verbal IQ was 94 (n=16), Performance IQ was 101 (n=16), WRAT-R Spelling score was 88 (n=14), Arithmetic was 89 (n=15), and Sentence writing was 80 (n=12). These scores were all statistically similar to normal controls (IQ ND, Spelling 97, Arithmetic 96, Sentence writing 95, n=17). Among children with achondroplasia (n=13) Gross Motor Arm Coordination score on McCarthy Scales was 73 and Leg Coordination was 79, significantly lower than normal controls (93, 104, respectively; n=13). Among children with achondroplasia (n=13) visual motor skills were significantly lower (Beery 82, JLO 85) than among normal controls (Beery 92, JLO 100, n=12). Various measures of fine motor skills were similar between the two groups.	Biased sample as some children dropped who were unable to complete the testing for many measures and excluded children with IQ<69.	Study was government funded. Subjects were recruited as part of larger previous study of hydrocephalus
Waters 1993 94029092	Among children with achondroplasia (n=20) 75% had > 5 apneic episodes per hour of sleep.	Descriptive study only	No data on funding source

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Asthma – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Balfour-Lynn 1986 87074993	Location: UK Setting: Pediatric asthma clinic Initial mean age: 7.5 y Initial age range: 2-12 y Follow-up mean age: 21 y Follow -up age range: 13-26 y Mean height: ND Male: 68% Race: ND SES: ND Enrolled: 66 Evaluated: 66 Number of sites: 1	Chronic perennial asthma	None reported	Asthma	Prospective longitudinal cohort (Mean 8.9 y)
Cernelc 1975 76016195 [Also in cardiac section]	Location: Yugoslavia Setting: Clinic Mean age: ND Mean height: ND Male: ND Race: ND SES: ND Enrolled: ND Evaluated: 337 Number of sites: ND	Asthmatic children with normal or pathological lung function tests	None reported	Asthma	Prospective cross-sectional

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Asthma – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Ferguson 1982 82190765	Location: Canada Setting: Regional Mean age: ND Age range: ~3-17 y Mean height: ND Male: 89% Race: ND SES: ND Enrolled: 36 Evaluated: 36 Number of sites: 1	Children with a diagnosis of asthma and short stature (height < 3rd percentile)	None reported	Asthma	Preliminary study of a prospective longitudinal study
Hauspie 1979 80114229	Location: Belgium and Hungary Setting: Sanatorium; Asthma clinic Mean age: ND Age range: 3-16 y Mean height: ND Male: 100% Race: ND SES: ND Enrolled: 1107 Evaluated: 1107 Number of sites: 2	Hungary : asthmatic boys residing in the National Sanatorium for Children Belgium: boys with chronic aspecific respiratory affection, asthma or asthma and eczema.	None reported	Asthma /Respiratory disease	Retrospective cross-sectional cohort

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Asthma – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Klein 1991 91314975	Location: US Setting: Clinic Mean age: 8.5 y Age range: 2-15 y Mean height: ND Male: ~ 69% Race: ND SES: ND Enrolled: 176 Evaluated: 176 Number of sites: 4	Children with moderately severe, non-steroid-dependent asthma	> 6 short courses of steroids during previous year	Asthma	Prospective cross-sectional
Martin 1981 82110081	Location: Australia Setting: Region Initial age: 7 y Follow-up ages: 10 y, 14 y, 21 y Mean height: ND Male: 63% Race: ND SES: ND Enrolled: 375 Evaluated: 315 Number of sites: 1	Asthmatic children Aged 7 y in 1964	None reported	Asthma	Prospective longitudinal cohort (14 y follow-up)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Asthma – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
McNicol 1970 71076839	Location: Australia Setting: Unclear Ages: 7 and 10 y Mean heights: 123 cm (age 7 y); 138 cm (age 10) Male: ND Race: ND SES: ND Enrolled: 226 Evaluated: 226 Number of sites: ND	Asthmatic children	None reported	Asthma	Prospective longitudinal cohort (Ages 7 and 10)
Neville 1996 96427603	Location: UK Setting: Pediatric practices Mean age: ND Age range: 3.5-13 y Mean height: ND Male: 57% Race: ND SES: “Broad range” Enrolled: 2915 Evaluated: 699 Number of sites: 12	Tayside Childhood Asthma Project (1990-92) Possible asthma, based on medication prescriptions, from chart review Age 3.5-13 y Height and weight measurements available	Loss to follow-up	Asthma	Secondary analysis of prospective longitudinal cohort

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Asthma – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Rona 1980 81025712	Location: UK Setting: Schools Mean age: ND Age range: 5-11 y Mean height: ND Male: 68% Race: ND SES: Proportionally more lower SES areas Enrolled: 102 Evaluated: 102 Number of sites: 28	Parental reporting of asthma in last 12 months	None reported	Asthma	Retrospective cross-sectional cohort
Sant'Anna 1996 97295750	Location: Brazil Setting: Pediatric immunology clinic Mean age: ND Age range: 6 mo - 16 y Mean height: ND Male: 58% Race: ND SES: ND Enrolled: 514 Evaluated: 514 Number of sites: 1	Children with asthma followed in Division of Allergy, Clinical Immunology and Rheumatology	Phenotypical deviations Clear changes in body proportions Other chronic diseases Rash and/or atopic dermatitis	Asthma	Retrospective cross-sectional case series

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Asthma – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Spock 1965	Location: US Setting: Pediatrics department Mean age: 7 y Age range: 4-12 y Mean height: ND Male: 65% Race: White SES: ND Enrolled: 200 Evaluated: 200 Number of sites: 1	Children with bronchial asthma Age > 4 y at the first visit Followed for minimum of 3 y	Concomitant chronic illness Cyproheptadine use	Asthma	Retrospective longitudinal cohort (19 y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Asthma – Part II

Author, Year	Severity of Illness Groups	Outcomes
Balfour-Lynn 1986 87074993	Treatment required to control asthma • Bronchodilators alone or children whose asthma resolved before puberty • Sodium cromoglycate and bronchodilators in children whose asthma did not improve at puberty • Steroids and bronchodilators	Initial growth retardation (not defined) Growth along centile lines Final adult height Percentile, based on Tanner and Whitehouse growth chart
Cernelc 1975 76016195	Pulmonary function tests • Normal • Pathological (not defined)	Height by age (linear regression) Compared to normal values for Slovenian children
Ferguson 1982 82190765	Asthma symptom score, based on frequency of wheezing in past year, duration of wheezing, level of therapy required, and bronchodilator medication days in past year (16 point scale) • Mild: score 1-7 • Moderate: score 8-12 • Severe: score 13-16	Height Percent average height for age
Hauspie 1979 80114229	Hungarian sample: Ovsáth's system, based on based on frequency of attacks, seriousness of dyspnea, duration of dyspnea, and number of symptom-days per year • Class II: Less severe • Class III: More severe • Class IV: Most severe Belgian sample: Disease diagnosis • Chronic aspecific respiratory affection • Asthma • Asthma and eczema Belgian sample: Treatment required to control asthma: • No corticotherapy • Interrupted corticotherapy • Continuous corticotherapy for at least 6 months	Height Z-scores
Klein 1991 91314975	Asthma severity score (by event), based on hospitalization and medication requirements in previous year (score: 0-60) • Mild: score < 25 • Moderate/severe ≥ 25	Height Height percentile Based on National Center for Health Statistics Growth Chart

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Asthma – Part II

Author, Year	Severity of Illness Groups	Outcomes
Martin 1981 82110081	Asthma grade, based on frequency and recency of wheezing • Grade A: ≤ 5 episodes of wheezing • Grade B: > 5 episodes of wheezing but no wheezing within 12 months of exam • Grade C: Episodic asthma over a number of years and wheezing within 12 mo of exam • Grade D: Very frequent or chronic unremitting asthma	Percentage of subjects <10th percentile Based on Australian Department of Health Anthropometric tables At ages 10, 14, and 21 y
McNicol 1970 71076839	Asthma grade, based on frequency and recentness of asthma episodes • Grade I: ≤ 5 episodes of asthma • Grade II: ≤ 20 episodes of asthma or no asthma within 12 mo of exam • Grade III: >20 episodes and still having asthma within 12 mo of exam	Height
Neville 1996 96427603	Asthma severity (British Thoracic Society treatment steps), based on medication requirements • Step 1: Beta-agonist only in past year • Step 2: Beta-agonist and cromoglycate • Step 3: Beta-agonist and low dose inhaled steroid • Step 4: Beta-agonist and > 400 μg/day inhaled steroid	Height SDS, based on control group within study
Rona 1980 81025712	Frequency of asthma episodes • ≤ 2 episodes in the past year • ≥ 3 episodes in the past year Hospitalization for asthma	Height SDS, based on Scottish and English norms • Unadjusted • Adjusted for parents' height, social class, number of siblings Height gain, cm/year • Unadjusted • Adjusted
Sant'Anna 1996 97295750	Asthma severity, based on the International Consensus Report on Diagnosis and Treatment of Asthma • Mild • Moderate • Severe	Percentage with short stature < 3rd percentile, based on National Center of Health Statistics, US, 1977

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Asthma – Part II

Author, Year	Severity of Illness Groups	Outcomes
Spock 1965	Clinical status (not defined) • Poor • Fair • Good • Excellent	Linear growth rate Percentage of normal, based on Stuart and Wetzel's anthropometic charts

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Asthma – Part III

Author, Year	Associations found	Potential Biases	Comments
Balfour-Lynn 1986 87074993	Comparing children whose asthma was controlled with bronchodilators alone or had resolved at puberty (n=18, Group I) with those whose asthma required sodium cromoglycate and had not resolved at puberty (n=19, Group II), and with those whose asthma required treatment with steroids (n=29, Group III), there was no statistical difference in growth retardation at the start of the study. However, "growth retardation" was not defined. Of children in Group I, 2 of 18 (11%) had initial height < 10th percentile. Of children in Group II, 1 of 19 (5%) had initial height < 10th percentile. Of children in Group III, 3 or 29 (10%) had initial height < 10th percentile. No child had height < 3rd percentile. All children "grew along expected centile lines without appreciable deviation, from initial age (mean 7.5 y) until age 10 y, regardless of treatment required. 30 of 66 (45%) children had "physiological decelerating growth velocity pattern of delayed puberty." No data are reported regarding association with asthma severity. Comparing the three groups of asthmatic children, based on treatment requirements, no statistical difference was found in final adult height. Possible minor trend toward taller adult height from Group I to II to III seen in graph.	Severity of asthma based on treatment used, not objective measures Reported data incomplete Study sample poorly defined 6 subjects lost to follow up prior to obtaining final adult height but were followed for mean 8.3 years (6.3-14.6 y)	No data on funding source
Cernelc 1975 76016195	Asthmatic children with normal pulmonary function tests (n=225) were not significantly different in height for age compared to asthmatic children pathological pulmonary function tests (n=112). No data on growth velocity.	Limited data and analysis Study sample poorly defined	No data on funding source Data on asthmatic children with bronchiectasis (n=22) not included because children reported to be both significantly and not significantly more likely to have growth retardation
Ferguson 1982 82190765	The percentages of average normal height for age (50th percentile) of short children whose asthma was mild (n=19, 90.7%), moderate (n=13, 90.2%) and severe (n=4, 88.5%) were not significantly different among the three groups. No significant correlation was found between symptom score and percentage of average normal height for age of individual subjects (r=0.20). No data on growth velocity	Study limited to children with height < 3rd percentile, however results reported as percentage of average normal height	Study was government and private funded.

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Asthma – Part III

Author, Year	Associations found	Potential Biases	Comments
Hauspie 1979 80114229	Mean height of Class II (relatively mild) Hungarian asthmatic boys (n=222) is normal (~ 0 SDS, from graph). The mean height of Class III asthmatic boys (n=253) was significantly lower (~ –0.3 SDS) and that of Class IV asthmatic boys (n=25) was even lower (~ –0.9 SDS). "A gradually increasing degree of growth retardation in relation to the seriousness of the disease can be observed." In a separate sample of Belgian asthmatic boys, those with chronic aspecific respiratory affection (n=204) had normal mean height (~ –0.1 SDS, from graph). Those with asthma (n=323) were statistically significantly but minimally shorter (~ –0.2 SDS) and those with asthma and eczema (n=80) were even shorter (~ –0.4 SDS). Belgian asthmatic boys requiring no corticotherapy (n=245) and requiring interrupted corticotherapy (n=130) had normal mean height (~ –0.1 SDS, from graph). Those who required continuous corticotherapy (n=16) were statistically shorter (~ –0.5 SDS). No data on growth velocity.	Chronic aspecific respiratory affection includes illnesses other than asthma. Data reported mostly in graphical format only Study limited to boys	No data on funding source.
Klein 1991 91314975	Children (n=176 total) with mild asthma (ND on n) had mean ± SD height of 145±10 cm; those with moderate asthma were on average 148±10 cm. The height difference was not significantly different. No data reported on children with severe asthma. "There was no relationship between the severity of asthma (as assessed by a clinical and medications score) and the height percentile." Reported data are incomplete. No data on growth velocity	Reported data very incomplete. Mean heights reported as 44.8 cm and 47.8 cm. We understood this to mean 144.8 cm and 147.8 cm, however, reported numbers may refer to percentiles. Children requiring > 6 short courses of steroids within previous year excluded.	No data on funding source

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Asthma – Part III

Author, Year	Associations found	Potential Biases	Comments
Martin 1981 82110081	The prevalence rates of height < 10th percentile in 10 years old children whose asthma was rated Grade A (mild, n=64), Grade B (moderate, n=88), Grade C (severe, n=106), and Grade D (very severe, n=57) were 9%, 8%, 8%, and 15% respectively. Only children with very severe asthma had significant higher prevalence of height < 10th percentile at age 10 y compared to non-asthmatic children (n=62, 4%). The prevalence of short stature in the asthmatic children when they were 14 years old was similar to when they were 10 years old. Height < 10th percentile in Grade A asthmatics was 6%, Grade B 5%, Grade C 5%, and Grade D 17%. Only children with very severe asthma had significant higher prevalence of height < 10th percentile at 14 years of age compared to non-asthmatic children (1%). At age 21 years, the prevalence of short stature was similar among all asthma grades. Height < 10th percentile Grade A asthmatics was 15%, Grade B 15%, Grade C 9%, and Grade D 19%. There was no difference in the prevalence of height < 10th percentile at 21 years of age, between the 4 groups and non-asthmatic children (12%). No direct data on growth velocity	None noted.	No data on funding source
McNicol 1970 71076839	The mean heights of children at both ages 7 and 10 years were the same (123-124 cm at age 7 years; 137-139 cm at age 10 years) regardless of frequency of asthmatic episodes among 276 asthmatic children and 94 non-asthmatic controls. No significant difference was found between controls and any degree of asthma severity. No data on growth velocity	None noted	No data on funding source
Neville 1996 96427603	Asthmatic children who used only beta agonists (n=537) had a mean height of +0.04 SDS. Those who used beta agonists and cromoglycate (n=64) had a mean height of +0.04 SDS. Those who used beta agonists and low dose inhaled steroids (n=39) had a mean height of +0.08. Those who used beta agonists and > 400 µg/day inhaled steroids (n=59) had a mean height of –0.38. Only those on high dose inhaled steroids were significantly shorter than normal. No data on growth velocity.	Large number of potential subjects excluded due to missing height data Statistical analysis implied only Asthma severity based on medication use	Study was government, privately, and pharmaceutical funded

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Asthma – Part III

Author, Year	Associations found	Potential Biases	Comments
Rona 1980 81025712	Among children with asthma episodes, those with ≤ 2 episodes in previous year (n=33) were not significantly shorter (–0.1 SDS, – 0.2 SDS, respectively) than controls (n=4334) in both unadjusted model and model adjusted for parental height, social class, and number of siblings. Those with ≥ 3 asthma episodes in previous year (n=69) were significantly shorter (–0.4 SDS) than controls in both models. Overall, "there was a highly significant negative relationship between unadjusted [and adjusted] height and number of [asthma] episodes. "Hospitalization for asthma was more closely associated with shorter stature for boys than for girls, but the number of children hospitalized was too small for useful analysis." In adjusted model, height velocity was non-significantly lower in boys with ≤ 2 asthma episodes per year (n=22, 5.34 cm/y) and with ≥ 3 episodes per year (n=41, 5.57 cm/y) than non-asthmatic boys (n=1873, 5.72 cm/y), and in girls with ≤2 episodes per year (n=9, 5.67 cm/y) and with ≥ 3 episodes per year (n=16, 5.50 cm/y) than non-asthmatic girls (n=1552, 5.93 cm/y).	Retrospective survey of parents (for medical history) and school records Logic of adjusting for number of siblings unclear.	Study was government funded.
Sant'Anna 1996 97295750	The prevalence of short stature (< 3rd %tile) in children with mild asthma (n=211, 6%) was non-significantly lower than those with moderate asthma (n=154, 11%) and severe asthma (n=149, 11%). No data on growth velocity	Multiple height-related exclusion criteria	No data on funding source
Spock 1965	The mean linear growth rate in percentage of normal was 109% for asthmatic patients with excellent clinical status (n=68), 107% for asthmatic patients with good clinical status (n=86), 102% for asthmatic patients with fair clinical status (n=30), and 97% for asthmatic patients with poor clinical status (n=16). The correlation between severity of clinical status and the linear growth rate in percentage of normal was not statistically significant. "No statistically significant correlation was found between the duration and/or severity of asthmatic symptoms and growth impairment for height or weight."	Degree of clinical status not defined The percentage of children requiring steroids was unusually low at 12%	No data on funding source.

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Cardiac Disease – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Baum 1980 81065058	Location: US Setting: Clinic Mean age: 3.8±1.0 y Age range: ND Mean height: 99 cm Male: 77% Race: ND SES: ND Enrolled: 26 Evaluated: 26 Number of sites: 1	Diagnosis of acyanotic congenital heart disease Age 2 to 6 y	None reported	Congenital heart disease: Patent ductus arteriosus Ventricular septal defect Atrial septal defect Pulmonic stenosis Aortic stenosis Atrioventricular canal Pulmonary artery band Right ventricular band Mitral stenosis Mitral insufficiency	Prospective cross-sectional cohort
Cernelc 1975 76016195 [Also in asthma section]	Location: Yugoslavia Setting: Clinic Mean age: ND Mean height: ND Male: ND Race: ND SES: ND Enrolled: ND Evaluated: 22 Number of sites: ND	Children with congenital heart disease with or without cyanosis	None reported	Congenital heart disease: Not defined	Prospective cross-sectional

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Cardiac Disease – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Feldt 1969 69176079	Location: US Setting: Clinic Mean age: ND Age range: 1 wk - 17 y Mean height: ND Male: ND Race: ND SES: ND Enrolled: 463 Evaluated: 311 Number of sites: 1	Diagnosis of congenital heart disease	Trisomy 21 Gonadal dysgenesis Clinically recognized maternal rubella syndrome	Congenital heart disease: Ventricular septal defect Tetralogy of Fallot Aortic stenosis Pulmonary stenosis	Prospective longitudinal cohort (5 mo)
Levy 1977 78125814	Location: US Setting: Cardiology clinic Mean age: ND Age range: ND Mean height: ND Male: 50% Race: ND SES: ND Enrolled: 1,210 Evaluated: 777 Number of sites: ND	Diagnosis of ventricular septal defect	None reported	Ventricular septal defect	Retrospective longitudinal cohort (mean[range] 6.4 [4-8] y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Cardiac Disease – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Strangway 1976 76101945	Location: Canada Setting: Cardiology clinic Mean age: ND Age range: < 2-11 y Mean height: ND Male: ND Race: ND SES: ND Enrolled: 568 Evaluated: 568 Number of sites: 1	Diagnosis of congenital heart disease	Additional major congenital lesion Mental retardation Undergone corrective surgery Acute or chronic intercurrent illness	Congenital heart disease: Tetralogy of Fallot Ventricular septal defect Atrial septal defect Pulmonary stenosis Aortic stenosis Coarctation of aorta Patent ductus arteriosus Arterioventricular canal MIscellaneous	Retrospective longitudinal cohort (5 y)
White 1970 72024496	Location: US Setting: Adolescent cardiac clinic Mean age: ND Age range: 12-18 y Mean height: ND Male: ND Race: White 96% SES: Generally middle class Enrolled: 80 Evaluated: 80 Number of sites: 1	Diagnosis of congenital heart disease Age < 19 y	Tetralogy of Fallot with total corrective surgery	Congenital heart disease: Ventricular septal defect Atrial septal defect Patent ductus arteriosus Pulmonary stenosis Aortic stenosis Coarctation of aorta Aortic insufficiency Undiagnosed acyanotic	Prospective cross-sectional

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Cardiac Disease – Part II

Author, Year	Predictors (N)	Outcomes
Baum 1980 81065058	Heart Failure (not defined)	Height by age (linear regression) Height percentile Based on National Center for Health Statistics growth charts
Cernelc 1975 76016195 [Also in asthma section]	Cyanosis	Height by age (linear regression) Compared to normal values for Slovenian children
Feldt 1969 69176079	Pulmonic valve pressure gradient Aortic valve pressure gradient Tetralogy of Fallot lesion severity • Hematocrit • Oxygen saturation (cyanosis) • Magnitude of right to left shunt • History of hypoxemia Ventricular septal defect shunt severity • Pulmonary vascular disease (pressure)	Growth failure preoperative height (and weight) ≤ –2 SDS Height SDS based on Reed and Stuart, 1959
Levy 1977 78125814	Ventricular septal defect severity • I: Trivial to mild, pulmonary artery mean pressure < 20 mm Hg • II: pulmonary artery mean pressure ≥ 20 mm Hg and pulmonary to systemic resistance ratio < 0.20 • III-IV: Severe: pulmonary artery mean pressure ≥ 20 mm Hg and pulmonary to systemic resistance ratio ≥ 0.20	Height SDS
Strangway 1976 76101945	Cardiac problems • Cyanosis • Cardiac enlargement (cardiothoracic ratio > 59% age < 2 y, > 55% age >2 y) • Congestive heart failure	Height velocity fraction of the normal mean for the same age and sex

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Cardiac Disease – Part II

Author, Year	Predictors (N)	Outcomes
White 1970 72024496	Cyanosis	Short stature, height < 2nd percentile

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Cardiac Disease – Part III

Author, Year	Associations found	Potential Biases	Comments
Baum 1980 81065058	Children with congenital heart disease with early heart failure (n=12) were significantly shorter for age than asymptomatic children (n=14). On average, children age 2-6 years with heart failure were 5-9 cm shorter than those without. The differences in height were greater with older age. Six (50%) of the 12 children with early heart failure had height below the 5th percentile, while none of the 14 asymptomatic children had height below the 10th percentile. No data on growth velocity.	None noted	No data on funding source.
Cernelc 1975 76016195 [Also in asthma section]	Children with congenital heart disease and cyanosis (n=11) were significantly more likely to be short for age than normal population, as opposed to children with congenital heart disease without cyanosis (n=11) who were not significantly different in height for age than normal population.	Limited data and analysis Study sample poorly defined	No data on funding source
Feldt 1969 69176079	Among children with aortic or pulmonary stenosis (n=73), those "with mild pressure gradients (< 50 mm Hg) across either the pulmonic or the aortic valve usually were of normal weight and height. In contrast, patients with severe valvular gradients were more likely to have severe growth failure." The severity of growth failure of children with Tetralogy of Fallot (n=83) "was not related to any criteria for seveity of the lesion such as hemaglobin value, oxygen saturation…, magnitude of right to left shunt, or history of hypoxemic spells." Specifically height SDS was not associated with hemoglobin level. Among children with ventricular septal defect (n=155) "there was no correlation between the extent of growth failure and the degree of pulmonary vascular disease assessed either at cardiac catheterization of from pressure measurements taken at the time of operation." No data correlated height velocity to severity of disease.	No statistical analyses Growth retardation included both short stature and low weight	Study was government funded.
Levy 1977 78125814	For children with ventricular septal defect, the mean initial height SDS for those with mild disease (n=492) was –0.23 SDS, for those with moderate disease (n=170) –0.63 SDS, and for those with severe disease (n=115) –0.86. The height of children in each category was statistically significantly lower than normal children. The statistical significance of the association between height and severity of disease is implied only.	Reporting of statistical analyses unclear and incomplete	Study was government funded.

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Cardiac Disease – Part III

Author, Year	Associations found	Potential Biases	Comments
	No data on growth velocity		
Strangway 1976 76101945	Among children aged 0 to 2 years with congenital heart disease (n=181), height velocity percentile was significantly lower in children with cyanosis (–14%) than those without cyanosis (+7%), was similar in children with cardiac enlargement (+2%) as without cardiac enlargement (+1%), and was non-significantly lower in children with congestive heart failure (–20%) than without congestive heart failure (+2%). Among children aged 2 to 11 years with congenital heart disease (n=387), height velocity percentile was similar in children with cyanosis (+10%) as those without cyanosis (+7%), was similar in children with cardiac enlargement (+15%) as without cardiac enlargement (+6%), and was non-significantly lower in children with congestive heart failure (–13%) than without congestive heart failure (+7%).	Because of the calculation of height velocity, some subjects missing follow-up measures of height were excluded from analyses.	Study was government funded.
White 1970 72024496	Among children with congenital heart disease, height < 2nd percentile was more common among those with cyanosis (n=27, 19%) than those without cyanosis (n=53, 2%)	No statistical analyses performed Reporting of data unclear	Study was partial government funded.

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Insulin Dependent Diabetes Mellitus – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Arreola 1991 93191566	Location: Mexico Setting: Outpatient diabetes clinic Mean age: ND Age range: 1-16 y Mean height: ND Male: ND Race: ND SES: ND Enrolled: 198±8 each year (1984-1988) Evaluated: 198±8 each year Number of sites: 1	Patients with type I diabetes seen at outpatient diabetes clinic from 1984 to 1998 Age 1-16 y	None reported	Insulin dependent diabetes	Retrospective longitudinal cohort (4-5 y)
Court 1982 83021090	Location: UK Setting: Region Mean age: 13±3.7 y Age range: ND Mean height, SDS: –0.69 Male: 54% Race: ND SES: ND Enrolled: 121 Evaluated: 111 Number of sites: ND	Children with diabetes attending clinics in the Newcastle region	None reported	Diabetes (implied insulin dependent)	Retrospective cross-sectional cohort

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Insulin Dependent Diabetes Mellitus – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Herber 1988 88180314	Location: UK Setting: Pediatric diabetic clinic Initial mean age: 10 y Follow-up mean age: 13 y Age range: ND Initial height, SDS: –0.24±1.16 Follow-up height, SDS: –0.20±1.08 Male: 64% Race: ND SES: ND Enrolled: 67 Evaluated: 67 Number of sites: 1	Patients with Type I diabetes who have attended the pediatric diabetic clinic for at least 3 years	None reported	Insulin dependent diabetes	Retrospective longitudinal cohort (3 y)
Izumi 1995 96105591	Location: Japan Setting: Summer camp Initial mean age: ND Follow-up mean age: 14 y Age range: ND Mean height: ND Male: 40% Race: ND SES: ND Enrolled: 385 Evaluated: 107 Number of sites: ND	Children participated in Summer camp program More than 3 determinations of Hgb_A1c Age < 18 y at final examination.	None reported	Insulin dependent diabetes mellitus	Retrospective longitudinal cohort (18 y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Insulin Dependent Diabetes Mellitus – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Jivani 1973 73134278	Location: UK Setting: Children's hospital Mean age: ND Age range: 9 mo - 13 y Mean height: ND Male: 46% Race: ND SES: ND Enrolled: 116 Evaluated: 104 Number of sites: 1	Children with diabetes > 3 y follow-up	Other condition which might have affected growth (12 subjects with fair control were not analyzed)	Diabetes (implied insulin dependent)	Retrospective longitudinal cohort (mean [range] 7 [3-13] y)
Pitukcheewanont 1995 96136504	Location: US Setting: Clinic Mean age: 11.5±3.8 y Age range: ND Mean height: ND Male: 49% Race: White 100% SES: ND Enrolled: 82 Evaluated: 82 Number of sites: 1	Type I diabetes	< 3 visits during study Other problems that might affect growth (thyroid disease, cerebral palsy, foster care placement, methylphenidate therapy) Precocious or delayed puberty	Insulin dependent diabetes	Retrospective longitudinal cohort (6 y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Insulin Dependent Diabetes Mellitus – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Rosenbloom 1982 83032889	Location: US Setting: Clinic Mean age: ND Age range: ND Mean height: ND Male: ND Race: ND SES: ND Enrolled: 309 Evaluated: 142 Number of sites:8	Children with Type I diabetes Pre-puberty Duration of DM >3 y	None reported	Insulin dependent diabetes mellitus	Prospective longitudinal cohort (ND)
Salardi 1987 87127000	Location: Italy Setting: Pediatric clinic Mean age: 7.4±3.6 y Age range: 0.7-15 y Mean height: ND Male: 44% Race: ND SES: ND Enrolled: 79 Evaluated: 79 Number of sites: 1	Children with Type I diabetes	None reported	Insulin dependent diabetes mellitus	Prospective longitudinal cohort (Mean [Range] 4.5 [1-10.7] y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Insulin Dependent Diabetes Mellitus – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Soliman 1996 96412723	Location: Oman Setting: Diabetes clinic Mean age: 9 y Age range: 2-12 y Mean height: ND Male: ND Race: ND SES: ND Enrolled: 47 Evaluated: 45 Number of sites: 1	Prepubertal children with diagnosis of Type I diabetes mellitus	Intra-uterine growth retardation Systemic or endocrine disease Dysmorphic trait Central nervous system irradiation Hypothyroid	Insulin dependent diabetes mellitus	Prospective longitudinal cohort (1 y)
Vanelli 1992 93052062	Location: Italy Setting: Diabetes unit Mean age: ND Age range: 1.5-21 y Mean height: ND Male: 0% (analyzed) Race: ND SES: ND Enrolled: 204 Evaluated: 42 Number of sites: 1	Diabetic children referred to diabetes clinic at diagnosis Treated with daily insulin Subset analysis of girls who became diabetic at onset of puberty	Endocrinological disease affecting linear growth	Insulin dependent diabetes mellitus	Prospective longitudinal cohort (ND)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Insulin Dependent Diabetes Mellitus – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Wise 1992 92387067	Location: US Setting: Pediatric diabetes clinic Mean age: ND Age range: ND Mean height: ND Male: ND Race: ND SES: ND Enrolled: 122 Evaluated: 122 Number of sites: 1	Children and adolescents with diabetes	Other problems that might affect growth (thyroid disease, cerebral palsy, foster care placement, methylphenidate therapy, or precocious or delayed onset of puberty)	Insulin dependent diabetes mellitus	Prospective longitudinal cohort

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Insulin Dependent Diabetes Mellitus – Part II

Author, Year	Severity of Illness Groups	Outcomes
Arreola 1991 93191566	Diabetes control • HgbA1c • Poor control: HgbA1c > 11% • Good control: HgbA1c < 11%	Height velocity cm/month
Court 1982 83021090	Diabetes control (text unclear) • Poor control: Glucosuria (>2%) frequency >75% or 24 hour urine glucose > 50 g • Good control: Glucosuria frequency < 10% or 24 urine glucose < 20 g	Height SDS, based on Tanner 1976 Growth velocity SDS
Herber 1988 88180314	HgbA1c	Change in height SDS
Izumi 1995 96105591	HgbA1c category • <10.0% • 10.0-12.4% • ≥12.0% (unclear why overlap)	Height SDS, based on Japanese Ministry of Education statistics
Jivani 1973 73134278	Diabetes control • Poor: Ketonuria, glycosuria up to 5% at clinic, BS > 250 mg/dL, severe or frequent hypoglycemic reactions • Good: No ketonuia, ≤ 1% glycosuria at clinic, blood sugar < 150 mg/dL, rare mild hypoglycemic reactions	Height percentile, based on Tanner, 1966
Pitukcheewanont 1995 96136504	HgbA1c	Height SDS, based on National Center for Health Statistics Height velocity, SDS
Rosenbloom 1982 83032889	Limited joint mobility (“associat[ed with] early microvascular complications) • None • Mild: Involving 1 or 2 interphalangeal joints, 1 large joint, or only the metacarpophalangeal joints bilaterally • Moderate/Severe: Involving 3 or more interphalangeal joints or 1 finger joint and 1 large joint bilaterally or cervical spine involvement or obvious hand deformity at rest	Height percentile, based on National Center for Health Statistics < 25%

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Insulin Dependent Diabetes Mellitus – Part II

Author, Year	Severity of Illness Groups	Outcomes
Salardi 1987 87127000	HgbA1c	Height SDS, based on Tanner's centiles Height velocity SDS, based on Tanner's centiles
Soliman 1996 96412723	Diabetes control • HgbA1c < 10% • HgbA1c > 10%	Height velocity SDS, based on age-matched population
Vanelli 1992 93052062	Diabetes severity (apparently post hoc grouping) • Lower insulin requirement: Mean ± SD insulin 37±1.5 U/m²/day; HgbA1c 10±1.8% • Higher insulin requirement: Insulin 42±0.5 U/m²/day; HgbA1c 9±2.4%	Peak height velocity (during pubertal growth) cm/year
Wise 1992 92387067	HgbA1c level categories • 6.0-7.9 • 8.0-9.9 • 10.0-11.9 • 12.0-13.9 • 14.0-15.9 • 16.0-21.9	Height velocity Change in SDS, based on National Center for Health Statistics

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Insulin Dependent Diabetes Mellitus – Part III

Author, Year	Associations found	Potential Biases	Comments
Arreola 1991 93191566	Children with diabetes with HgbA1c > 11% (no data on number of subjects) had significantly lower height velocity (0.54 cm/month, from graph) compared to those with HgbA1c < 11% (0.22 cm/month). There was a significant correlation between HbA1c level and height velocity.	True number of subjects included not reported.	No data on funding source
Court 1982 83021090	For children with diabetes that was under poor control (n=57) mean height (–0.96 SDS) was significantly lower than those under good control (n=54, –0.22 SDS). Mean height velocity was significantly lower for children under poor control (–1.22 SDS) than those under good control (–0.61 SDS).	Determination of diabetes control based on glucosuria frequency and 24 hour urine glucose instead of HgbA1c	No data on funding source.
Herber 1988 88180314	In children with diabetes (n=67), "no significant effect on [change in height] was apparent with differing levels of HgbA1c."	Specific data on height SDS in relation to HbA1c levels was not given. Overall good control (mean HbA1c levels at commencement 10.2%; mean HbA1c levels at end 9.9%.	No data on funding source.
Izumi 1995 96105591	Among children with diabetes, mean height of those with HgbA1c < 10% (n=28) was –0.54 SDS, of those with HgbA1c of 10-12.4% (n=53) was –0.76, and of those with HgbA1c ≥ 12% (n=26) was –0.75. Height was not significantly associated to HgbA1c level. No data on height velocity.	Categories of severity of diabetes overlapping. Unclear if statistical analysis based on groups or on individual HgbA1c levels	No data on funding source.
Jivani 1973 73134278	The mean height percentile among girls with diabetes with poor control (n=22) was 38% and among those with good control (n=34) was 40%. There was no significant difference between the two groups. The mean height percentile among boys with diabetes with poor control (n=19) was 35% and among those with good control (n=29) was 29%. There was no significant difference between the two groups. Among both boys and girls with diabetes, height velocity was not associated with level of diabetes control	Eligibility criteria unclear. Age of children at time of follow-up analysis unclear. Statistical analysis unclear. Determination of diabetes control based on factors other than HgbA1c	No data on funding source. The text and table of the criteria for assessment of diabetic control were not concordant.

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Insulin Dependent Diabetes Mellitus – Part III

Author, Year	Associations found	Potential Biases	Comments
Pitukcheewanont 1995 96136504	Among children with type I diabetes (n=82), there was no association between mean HgbA1c and mean height SDS in univariate analysis. In multivariate analysis, controlling for age of diabetes onset and initial height, there remained no association between HgbA1c and height. There was no association between mean HgbA1c and mean height velocity at any Tanner stage in univariate analysis.	Retrospective analysis	No data on funding source.
Rosenbloom 1982 83032889	Diabetic children with mild (n=31), moderate (n=19) or severe (n=24) limited joint mobility were significantly more likely to be below the 25th percentile for height (~75%, from graph) than those without limited joint mobility (n=68, ~37%)). However, the correlation between HgbA1c and joint mobility was poor. No data on height velocity	Joint mobility is a poor proxy for severity of diabetes. Only looked at quartiles of height.	Study hospital funded
Salardi 1987 87127000	In children with insulin dependent diabetes (n=79), height SDS and height velocity SDS were not significantly correlated with HgbA1c.	Only summary of results reported.	Study was government funded
Soliman 1996 96412723	Children with diabetes whose HbA1c < 10% (n=30) had significant higher growth velocity (+0.75 SDS) than DM subject HbA1c > 10% (n=15, –1.6 SDS).	None noted	No data on funding source.
Vanelli 1992 93052062	In a subset of girls who became diabetic at onset of puberty (n=42), the 23 treated with greater amounts of insulin (mean 41.5 U/m²/d) and who had lower mean HgbA1c (8.9%) had significantly higher mean peak growth velocity (8.5 cm/y) than the 19 treated with less insulin (37.3 U/m²/d and higher HgbA1c (10.1%), at 6.9 cm/y.	Study poorly defined. Unclear a priori hypotheses Definitions of sample groups poorly defined Single analysis of subgroup only	No data on funding source
Wise 1992 92387067	Among children with diabetes (n=122) a significant linear relationship was seen between HgbA1c and growth velocity. HgbA1c < 8% was associated with growth acceleration (+0.10 SDS); the most severe growth retardation occurred when HgbA1c levels were > 16% (–0.07 SDS).	None noted	No data on funding source

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
ß-thalassemia – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Constantoulakis 1975 75129833	Location: Greece Setting: Outpatients Mean age: ND Age range: 7 months – 28 y Mean height: ND Male: 58% Race: ND SES: ND Enrolled: 229 Evaluated: 171 Number of sites: 1	Diagnosis of homozygous ß-thalassemia	None reported	ß thalassemia major	Retrospective longitudinal cohort (Range 4-7 y)
Kattamis 1970 71003038	Location: Greece Setting: Clinic Mean age: ND Age range: 1-11 y Mean height: ND Male: 53% Race: ND SES: ND Enrolled: 74 Evaluated: 74 Number of sites: 1	Diagnosis of homozygous β-thalassemia	Clinical picture of thalassemia intermedia and hemoglobin between 7-10 g/dL Age > 11 y	ß thalassemia major	Prospective cross-sectional cohort

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
ß-thalassemia – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Madeddu 1978 78167848	Location: Italy Setting: Clinic Mean age: ND Age range: 2-13 y Mean height: ND Male: 46% Race: ND SES: ND Enrolled: 50 Evaluated: 50 Number of sites: 1	Homozygous ß thalassemia	None reported	ß thalassemia major	Prospective cross-sectional

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
ß-thalassemia – Part II

Author, Year	Severity of Illness Groups	Outcomes
Constantoulakis 1975 75129833	Multiple linear regression including • Mean hemoglobin level over previous 2-4 years • Total blood transfused since birth • "Index of severity of disease" based on amount of blood transfused during previous 2 years • (Age)	Height percentiles, based on various Greek sources
Kattamis 1970 71003038	β-thalassaemia severity • Group I: Pre-transfusion hemoglobin > 8 g/dL, frequent transfusions • Group II: Unable to follow regularly, pre-transfusion hemoglobin 6-8 g/dL, either very low SES or had to travel "very long distance" for transfusion • Group III: Transfused only when hemoglobin < 6 g/dL, usually < 5 g/dL	Height percentile, based on Children's Medical Center, Boston growth chart
Madeddu 1978 78167848	Hemoglobin concentration between two transfusions	Height percentile, based on Tanner, 1962

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
ß-thalassemia – Part III

Author, Year	Associations found	Potential Biases	Comments
Constantoulakis 1975 75129833	Among children with ß-thalassemia major (n=171) there was a trend toward lower height percentiles being associated with low hemoglobin levels and severity of disease; however, neither was statistically significant in a linear regression controlling for age. Total blood transfused since birth was not associated with height. No data on height velocity.	No data on hemoglobin levels, total blood transfused since birth, and index of severity of disease. Provides only the regression results. Definition of the severity of the disease unclear. Large numbers of subjects were not included in analyses. No explanation. Model adjusted for non-independent variables.	No data on funding source
Kattamis 1970 71003038	Children with mild ß-thalassemia major (n=38) had significantly higher mean height percentile (56%) than children with moderate (n=14, 22%) and severe (n=22, 7%) disease. No data on height velocity.	Thalassemia severity based on how low hemoglobin allowed to fall before transfusion	No data on funding source
Madeddu 1978 78167848	Children with ß thalassemia major who were < 3rd percentile for height (n=18) had mean hemoglobin of 6.6 g/dL, which was not significantly lower than those whose height was 3rd -25th percentile (n=12, 7.2 g/dL) and whose height was 25th-75th percentile (n=19, 7.0 g/dL) (One child had height above 75th percentile). No data on height velocity.	Cross-sectional study cannot evaluate previous degree of anemia	No data on funding source

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Inflammatory Bowel Disease – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Farmer 1979 80023814	Location: US Setting: Clinic Mean age: ND (41% < 16 y) Age range: < 20 y Mean height: ND Male: ND Race: ND SES: ND Enrolled: 522 Evaluated: 522 Number of sites:1	Crohn's disease established by clinical, radiographic and/or histological means Age < 20 y Diagnosis made form 1955-1974	Unable to obtain follow-up data	Crohn's disease	Retrospective longitudinal case series (Mean 7.7 y)
Griffiths 1993 93345883	Location: Canada Setting: Clinic Mean age: 11±2.3 y Age range: 5 - 17 y Mean height, SDS: –1.1±1.3 Male: 66% Race: ND SES: ND Enrolled: 100 Evaluated: 100 Number of sites: 1	Diagnosis of Crohn's disease Tanner stage 1 or 2	Transferred after initial diagnosis and referred for consultation only	Crohn's disease	Retrospective longitudinal case series (≥ 2 y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Inflammatory Bowel Disease – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Saha 1998 98182041	Location: Finland Setting: Pediatrics department Mean age: 7 y Age range: ND Mean height: ND Male: 43% Race: ND SES: ND Enrolled: 47 Evaluated: 47 Number of sites: 1	Diagnosis of inflammatory bowel disease	None reported	Inflammatory bowel disease: Ulcerative colitis Crohn's disease	Retrospective longitudinal cohort (13 y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Inflammatory Bowel Disease – Part II

Author, Year	Severity of Illness Groups	Outcomes
Farmer 1979 80023814	Location of Crohn's disease • Ileocolic pattern • Colon pattern • Small intestine pattern • Anorectal pattern	Short stature Height < 3rd percentile, based on growth charts
Griffiths 1993 93345883	Severity of gastrointestinal symptoms over given year • Quiescent: No symptoms, normal complete blood count and sedimentation rate • Mild: Some symptoms, no prednisone treatment needed • Moderate: Intermittent exacerbations requiring prednisone or nutritional support • Severe: Chronic unremitting symptoms requiring prednisone or alternate treatment Location of Crohn's disease • Small bowel • Ileocecal • Ileocolic • Colon	Height velocity cm/year Percent with growth retardation < 4 cm/year Height SDS, based on National Center for Health Statistics Change in height SDS
Saha 1998 98182041	Severity of Crohn's disease/ulcerative colitis 12 point scale based on number of relapses, exacerbations, medications and need for surgery (correct scoring mechanism not clear) • Mild: 1-3 points • Moderate: 4-6 points • Severe: ≥ 7 points	Height SDS, based on Finnish population mean Height velocity SDS

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Inflammatory Bowel Disease – Part III

Author, Year	Associations found	Potential Biases	Comments
Farmer 1979 80023814	Among children with Crohn's disease likelihood of short (< 3rd height percentile) was not related to location of disease. Of those with ileocolic disease (n=175) 7% were short; of those with colonic disease (n=162) 8% were short; of those with small intestine disease (n=151) 6% were short; of those with anorectal disease (n=34) 9% were short. No data on height velocity	No statistical analyses. "Severity" based on location of disease	No data on funding source
Griffiths 1993 93345883	Among children with Crohn's disease, "severity of gastrointestinal symptoms was the major factor influencing linear growth during the first two years [after diagnosis]. Height velocity significantly decreased with increasing gastrointestinal symptoms during both year and year two, after adjusting for corticosteroid use. During year one, height velocity of children with quiescent disease (n=14) was ~5.7 cm/year (from graph), with mild disease (n=54) was ~4.6 cm/year, with moderate disease (n=23) was ~3 cm/year, and with severe disease (n=9) was ~2.7 cm/year. During year two, height velocity of children with quiescent disease (n=23) was ~7.3 cm/year, with mild disease (n=44) was ~4.5 cm/year, with moderate disease (n=24) was ~4 cm/year, and with severe disease (n=8) was ~4.1 cm/year. Among children with Crohn's disease who were followed to maturity, initial and ultimate height were not associated with disease severity. Initial and ultimate height severity were –0.88 and –0.43 SDS for those with mild disease (n=26), –1.17 and –1.15 SDS for those with moderate disease (n=15), –1.48 and –0.70 SDS for those with moderate or severe disease with sustained remission (n=14), and –1.12 and –1.37 SDS for those with chronically severe disease (n=12). Among children with Crohn's disease who were followed to maturity, change in height was significantly associated with disease severity. Change in height was 0.58 SDS for those with mild disease (n=26), 0.03 SDS for those with moderate disease (n=15), 0.68 SDS for those with moderate or severe disease with sustained remission (n=14), and –0.11 SDS for those with chronic severe disease (n=12). Among children with Crohn's disease, at year two (n=100), disease location was not significantly associated with height velocity (cm/year) or percentage with height velocity < 4 cm/year. Among those with long-term follow-up (n=65), disease location was not associated with initial height SDS, ultimate height SDS, or change in height SDS.	Retrospective	No data on funding source

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Inflammatory Bowel Disease – Part III

Author, Year	Associations found	Potential Biases	Comments
Saha 1998 98182041	Among children with ulcerative colitis (n=29), mean overall change in height over 4 years was –0.16 SDS for those with mild disease, –1.09 SDS for those with moderate disease, and –1.74 SDS for those with severe disease. This trend did not reach statistical significance. The overall change in height velocity was significantly greater in those with mild disease (+1.14 SDS) than those with moderate disease (+0.39 SDS) and those with severe disease (+0.12 SDS). Among children with Crohn's disease (n=18), mean overall change in height over 4 years was +0.51 SDS for those with mild disease, –0.27 SDS for those with moderate disease, and –0.11 SDS for those with severe disease. This trend did not reach statistical significance. The overall change in height velocity was significantly greater in those with mild disease (+0.42 SDS) than those with moderate disease (+0.09 SDS) and those with severe disease (–1.09 SDS).	Height outcomes are difficult to interpret. Numbers of subjects in each category not reported.	Study was hospital and privately funded.

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Juvenile Rheumatoid Arthritis – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Bernstein 1977 87026009	Location: US Setting: Clinic Mean age: ND Initial age range: 1-12 y Mean height: ND Male: 24% Race: ND SES: ND Enrolled: 31 Evaluated: 31 Number of sites: 1	Children with diagnosis of juvenile rheumatoid arthritis	None reported	Juvenile rheumatoid arthritis	Retrospective longitudinal cohort (mean [range] 6.6[2.3-11] y, up to age of 15)
Polito 1997 97283189	Location: Italy Setting: Pediatric clinic Initial mean age: 7 y Follow-up mean age: 12 y Age range: ND Initial mean height, SDS: +0.34 Follow-up mean height, SDS: –0.05 Male: 26% Race: ND SES: ND Enrolled: 58 Evaluated: 58 Number of sites:1	Children with active juvenile rheumatoid arthritis for ≥ 1 y Follow-up for ≥ 1 y	Steroid use Growth hormone therapy	Juvenile rheumatoid arthritis: Pauciarticular onset Systemic onset Polyarticular onset	Retrospective longitudinal case series (≥ 1 y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Juvenile Rheumatoid Arthritis – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Saha 1999 99374796	Location: Finland Setting: Hospital based clinic Mean age: 4 y Age range: 0.9-11 y Mean height: ND Male: 36% Race: ND SES: ND Enrolled: 64 Evaluated: 64 Number of sites: 1	Children with mild to moderate juvenile onset chronic arthritis Prepuberty Followed for ≥ 1 y	Ullrich-Turner syndrome	Juvenile rheumatoid arthritis: Pauciarticular onset Systemic onset Polyarticular onset	Retrospective longitudinal case series (1-11 y, until age 12 y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Juvenile Rheumatoid Arthritis – Part II

Author, Year	Severity of Illness Groups	Outcomes
Bernstein 1977 87026009	Mode of onset of juvenile rheumatoid arthritis • Systemic • Polyarticular • Pauciarticular	Mean percent change in height per year
Polito 1997 97283189	Type of juvenile rheumatoid arthritis • Systemic • Polyarticular • Pauciarticular Number of joints affected (systemic or polyarticular only) Sum of periods of time with disease flares (systemic or polyarticular only) joint swelling, tenderness, functional impairment, ESR > 25 mm/hr) Functional class, not defined (systemic or polyarticular only)	Change in height SDS, based on Tanner 1976 Change in height SDS per year
Saha 1999 99374796	Severity of juvenile chronic arthritis score 6 point scale based on local anti-inflammatory administrations and number of systemic antirheumatics • Mild: Score 1-3 • Moderate: Score ≥ 4 Type of disease • Pauciarticular • Polyarticular • Systemic • Iridocyclitis	Height velocity SDS, based on Tanner 1966 Height SDS

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Juvenile Rheumatoid Arthritis – Part III

Author, Year	Associations found	Potential Biases	Comments
Bernstein 1977 87026009	Among children with juvenile rheumatoid arthritis, those with systemic disease (n=13) had significantly greater mean change in height per year (–0.85%) than those with polyarticular disease (n=9, +0.04%) and those with pauciarticular disease (n=9, –0.01%).	Definition of outcome measure (percent change in height per year) not well defined	Study was privately funded.
Polito 1997 97283189	Among children with juvenile rheumatoid arthritis, those with pauciarticular disease (n=21) were less likely to lose > 1 height SDS between first and last visits (0%) than those with systemic disease (n=19, 26%) or those with polyarticular disease (n=18, 28%). No statistical analysis was performed. Among children with either systemic or polyarticular disease (n=37), change in height SDS per year was not associated with number of affected joints but was associated with the sum of the periods of disease flares. Children in functional class I (not defined) had significantly smaller change in height SDS per year (–0.01 SDS) than those in functional class II (–0.06 SDS)	Retrospective analysis Inclusion criteria was no steroids, thus children with most severe disease, were excluded. Functional class not defined.	No data on funding source
Saha 1999 99374796	Among children with juvenile rheumatoid arthritis (n=64), by multivariate analysis of covariance "the most obvious decrease in [height] velocity was seen in children with polyarthritis and growth velocity was affected slightly more in children with moderate than mild disease," adjusting for sex and duration of disease. "Heights were more affected in children with polyarthritis and the severity of the disease had an additive effect," adjusting for glucocorticoid use and duration of disease.	Exclusion criteria unclear. No children with severe arthritis. Limited reporting of data. Statistical significance of relevant findings not reported.	Study hospital and privately funded

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Chronic Kidney Disease / Kidney Failure – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Claris-Appiani 1989 91002131	Location: Italy Setting: ND Mean age: 1.6-9 y Age range: ND Mean height: ND Male: 65% Race: ND SES: ND Enrolled: 17 Evaluated: 17 Number of sites: ND	Children with chronic kidney disease Pre-dialysis Stable	Acute obstruction Pyelonephritis Hypertension Hyposthenuria Salt wasting Steroid treatment	Chronic kidney disease Stage 3 Stage 4	Prospective longitudinal cohort
Ismaili 2001 21219717	Location: Belgium Setting: Pediatric nephrology Initial mean age: 6 mo Follow-up mean age: 4 y Age range: ND Mean height: ND Male: 55% Race: ND SES: ND Enrolled: 11 Evaluated: 11 Number of sites: 1	Infants with kidney dysplasia and chronic kidney disease	Obstructive renal dysplasia	Chronic kidney disease Kidney dysplasia Stage 4 Stage 5	Retrospective longitudinal cohort (4 y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Chronic Kidney Disease / Kidney Failure – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Karlberg 1996 96384503	Location: Europe Setting: Pediatric nephrology clinics Mean age: ND Age range: 0-5 y Mean heights (various ages), SDS: –1.05 to –3.09 Male: 70% Race: ND SES: ND Enrolled: 73 Evaluated: 61 Number of sites: 22	Onset of chronic kidney disease age < 6 mo GFR < 3 SD below mean for age ≥ 2 height measurements before age 1 y and followed until at least age 3 y	Primary glomerulonephropathy Systemic metabolic disorder	Chronic kidney disease Stage 4 Stage 5	Prospective longitudinal case series (Mean [Range] 7.3 [3-16] y)
Konrad 1995 96162281	Location: Europe Setting: Pediatric nephrology clinics Initial mean age: 1.7 y Initial age range: 1-8 y Follow-up man age: 5.6 y Follow-up age range: 2-9 y Mean height: ND Male: 59% Race: ND SES: ND Enrolled: 67 Evaluated: 58 Number of sites: 22	Autosomal recessive polycystic kidney disease Prepuberty Girls ≤ 9 y old Boys ≤ 10 y old Age ≥ 1 y at first assessment ≥ 1 y follow-up Subset of Karlberg, 1996 [#226] and Schaefer, 1996 [#3001]	Single growth measurement only	Autosomal recessive polycystic kidney disease Stage 1 Stage 2 Stage 3 Stage 4	Prospective longitudinal case series (≥ 1 y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Chronic Kidney Disease / Kidney Failure – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Schaefer 1996 96384504	Location: Europe Setting: Pediatric nephrology clinics Initial median age: 2.6 y Initial age range: 0-8 y Follow-up age: ~ 10 y Height range, SDS: –4.2 to +4.1 Male: ND Race: White 96%, Arab or Asian 4% SES: ND Enrolled: 500 Evaluated:321 Number of sites: 22	Born between 1970 and 1992 Marked reduction in functional kidney mass	Primary glomerulonephropathy Systemic metabolic disorder	Chronic kidney disease Stage 4 Stage 5	Prospective longitudinal case series (Median [Range] 3.3 [0.5-10] y)
Norman 2000 21024968	Location: UK Setting: Clinic Mean age: ND Age range: 2-17 y Mean height: ND Male: 63% Race: ND SES: ND Enrolled: 95 Evaluated: 95 Number of sites: 1	Children scheduled for GFR measurements	Congenital growth abnormalities Receiving dialysis	Chronic kidney disease Stage 1 Stage 2 Stage 3 Stage 4	Prospective cross-sectional cohort

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Chronic Kidney Disease / Kidney Failure – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Rizzoni 1984 85010647	Location: Italy Setting: Pediatric clinic Mean age: 6 y Age range: < 6 mo - 15 y Initial mean height, SDS: –1.6 Follow-up mean height, SDS: –1.5 Male: 69% Race: ND SES: ND Enrolled: 47 Evaluated: 47 Number of sites: 1	Children with GFR < 70 ml/min/1.73 m^2 ≥ 1 bone age determined Follow-up for ≥ 1 y	Proteinuria Nephrotic syndrome Steroid treatment	Chronic kidney disease Stage 2 Stage 3 Stage 4 Stage 5	Retrospective longitudinal case series (Mean [Range] 4.3 [1-12] y)
Schärer 1999 20068988	Location: US Setting: Clinic Mean age: 4.5 y Age range: 1.2-10 y Mean height: ND Male: 67% Race: ND SES: ND Enrolled: 45 Evaluated: 38 Number of sites: ND	Prepubertal children with idiopathic nephrotic syndrome	Chronic kidney failure	Idiopathic nephrotic syndrome	Prospective longitudinal cohort (Mean [Range] 9.0 [2-19] y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Chronic Kidney Disease / Kidney Failure – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Tejani 1983 84068349	Location: US Setting: Pediatric nephrology clinic Mean age at onset: Steroid resistant 7.7±3.7 y; Steroid sensitive, 3.5±2.5 y Age range at onset: 10 mo - 15 y Mean height: ND Male: 42% Race: White 16%, Black 50%, Hispanic 33% SES: ND Enrolled: 25 Evaluated: 24 Number of sites: 1	Nephrotic syndrome Biopsy-proven focal segmental sclerosis Biopsy performed because of lack of response to steroids or relapse after treatment with steroids	Diffuse increase in mesangial cells or with mesangial deposition of immunoglobulin	Focal segmental sclerosis	Retrospective longitudinal case series (Steroid resistant: 7±5 y; Steroid sensitive: 13±8 y))
Tsau 1989 90155156	Location: Taiwan Setting: Hospital Mean age of onset: 5 y Age range: ND Mean height: ND Male: 83% Race: Chinese SES: ND Enrolled: 52 Evaluated: 52 Number of sites: 1	Nephrotic syndrome beginning before age 15 y Followed up for at least 2 y	Development of chronic kidney insufficiency	Nephrotic syndrome	Retrospective longitudinal cohort (5.5±2.8 y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Chronic Kidney Disease / Kidney Failure – Part II

Author, Year	Severity of Illness Groups	Outcomes
Claris-Appiani 1989 91002131	GFR, Schwartz formula estimate	Height SDS, based on Tanner 1976 Growth velocity per year SDS
Ismaili 2001 21219717	Chronic kidney disease severity, Schwartz formula estimate and direct measurement • GFR < 15 mL/min/1.73 m^2 • GFR > 15 mL/min/1.73 m^2	Height SDS, based on Tanner 1966
Karlberg 1996 96384503	GFR, age-specific Schwartz formulae estimates	Height SDS, based on normal Swedish children
Konrad 1995 96162281	GFR, Schwartz formula estimate Chronic kidney disease severity • GFR < 60 mL/min/1.73 m^2 • GFR > 260 mL/min/1.73 m^2	Height SDS, based on First Zurich Longitudinal Growth Study
Schaefer 1996 96384504	GFR, age-specific Schwartz formulae estimates Chronic kidney disease severity • GFR < 25 mL/min/1.73 m^2 • GFR > 25 mL/min/1.73 m^2	Height SDS Height velocity SDS
Norman 2000 21024968	Chronic kidney disease severity, based on GFR direct measurements • Normal: GFR > 75 mL/min/1.73 m^2 • Mild: GFR 50-75 mL/min/1.73 m^2 • Moderate: GFR 25-50 mL/min/1.73 m^2 • Severe: GFR < 25 mL/min/1.73 m^2	Height SDS, based on normal UK population
Rizzoni 1984 85010647	GFR, estimate or direct measurement	Height SDS, based on Tanner 1976 Height velocity, cm/year

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Chronic Kidney Disease / Kidney Failure – Part II

Author, Year	Severity of Illness Groups	Outcomes
Schärer 1999 20068988	Final kidney status • Reached final height in absence of kidney function deterioration or ESRD • Reached final height with serum creatinine > 1.2 mg/dL after age 13.6 years • (Lost to follow-up before kidney function deterioration -- not evaluated in this report) • Developed ESRD before reaching adult height Idiopathic nephrotic syndrome severity (mean serum albumin level and serum protein level)	Height SDS Change in height SDS
Tejani 1983 84068349	Responsiveness (improvement of proteinuria) of focal segmental sclerosis to steroids • Steroid responsive: Complete remission within 8 wk of prednisone, persisting for 2 mo after cessation of treatment • Steroid resistant: No remission after 8 wk of treatment	Growth retardation Height for age < 5th percentile at follow-up
Tsau 1989 90155156	Nephrotic syndrome severity • Less favorable clinical courses, including frequent relapsing, steroid-dependent, and steroid-resistant nephrotic syndromes • Had responded to steroid therapy initially with occasional or no relapse	Change in Height SDS, based on Department of Health, Taiwan Growth velocity index Ratio of actual growth velocity to normal growth velocity for age (% of expected growth)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Chronic Kidney Disease / Kidney Failure – Part III

Author, Year	Associations found	Potential Biases	Comments
Claris-Appiani 1989 91002131	Among children with pre-dialysis chronic kidney disease (n=17) there was a significant positive correlation between height SDS and creatinine clearance. In multivariate analysis, height velocity was not associated with creatinine clearance, controlling for bone age, BUN, change in BUN, PTH, calcitriol, caloric and protein intake.	Univariate analysis only was performed for height. No univariate analysis for height velocity and creatinine clearance. Creatinine clearance not independent of other variables. Far too few subjects for multivariate analysis	No data on funding source
Ismaili 2001 21219717	Among infants with chronic kidney disease with GFR < 15 mL/min/1.73 m^2 at age 6 months (n=5) mean height did not improve between age 6 months (–2.6 SDS) and 4 years (–2.3 SDS). Among those with GFR > 15 mL/min/1.73 m^2 (n=6) mean height increased from age 6 months (–2.6 SDS) to 4 years (–1.4 SDS).	Small sample size	No data on funding source.
Karlberg 1996 96384503	Among children with chronic kidney disease (n=47) change in height SDS between 9 months and 2 years was not associated with GFR in a multiple linear regression. Among infants with chronic kidney disease (n=14) change in height SDS during the "first postnatal months of life" were not associated with GFR.	No data on variables in model. Many children not included in all analyses	Study was pharmaceutical funded. Same dataset as Schaefer 1996
Konrad 1995 96162281	Among girls with autosomal recessive polycystic kidney disease, those with GFR < 60 mL/min/1.73 m^2 (n=9) had mean height of –2.1 SDS; those with higher GFR (n=15) had mean height of –0.3 SDS. Boys with GFR < 60 mL/min/1.73 m^2 (n=10) had mean height of –1.5 SDS; those with higher GFR (n=24) had mean height of –0.5 SDS. There was a significant correlation between GFR and height SDS among girls but not among boys. No data on height velocity.	None noted	No data on funding source. Subset of Karlberg, 1996 [#226] and Schaefer, 1996 [#3001]

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Chronic Kidney Disease / Kidney Failure – Part III

Author, Year	Associations found	Potential Biases	Comments
Schaefer 1996 96384504	Among children with chronic kidney disease (n=321) height velocity was positively correlated with GFR among 6 year olds and among children of 4 other age groups (of 9 age groups total). Children with GFR > 25 mL/min/1.73 m^2 had consistently higher annual height velocities than children with lower GFR. Children with GFR > 25 mL/min/1.73 m^2 were taller (mean height –1.65 SDS) than those with lower GFR (–2.79 SDS).	Numbers of children analyzed with GFR > 25 mL/min/1.73 m^2 and with lower GFR not reported Results for specific age groups not reported	Study was pharmaceutical funded. Same dataset as Karlberg 1996
Norman 2000 21024968	Among children with chronic kidney disease, those with GFR > 75 mL/min/1.73 m^2 (n=35) had mean height of +0.40 SDS, those with GFR 50-75 mL/min/1.73 m^2 (n=23) had mean height of –0.34 SDS, those with GFR 25-50 mL/min/1.73 m^2 (n=19) had mean height of –0.58 SDS, those with GFR < 25 mL/min/1.73 m^2 (n=18) had mean height of –1.52. Those with moderate and severe chronic kidney disease had significantly lower height than those with normal GFR. No data on height velocity	None noted	No data on funding source.
Rizzoni 1984 85010647	Among children with chronic kidney disease (n=47) there was no association between GFR and growth velocity. or height SDS.	Limited data reported	No data on funding source
Schärer 1999 20068988	Children with nephrotic syndrome who reached final height without deterioration of kidney function (n=16) had a mean change in height SDS from onset of kidney disease to final height of +0.27 SDS; those who developed serum creatinine > 1.2 mg/dL before reaching final height (n=8) had a mean change in height SDS of –0.08 SDS; those who developed ESRD before reaching final height (n=9) had a mean change in height of –1.35 SDS. Children who developed ESRD had a significant decrease in their height SDS compared to other groups. Among children with steroid resistant nephrotic syndrome in whom steroid therapy was stopped before puberty (n=16) change in prepubertal height SDS and height velocity SDS correlated positively and significantly with total protein and albumin levels.	Analyses performed on only subgroups of subjects Categorization of children by severity of disease is retrospective. Categorized only after reaching final height. Serum albumin and protein are poor markers of disability-related severity of disease	No data on funding source.

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Chronic Kidney Disease / Kidney Failure – Part III

Author, Year	Associations found	Potential Biases	Comments
Tejani 1983 84068349	In children with focal segmental sclerosis, those with steroid responsive disease (n=10) were significantly less likely to have short stature (< 5th percentile) than those with steroid resistant disease (n=14) despite greater steroid doses among the former. No data on growth velocity	Detailed results not reported.	No data on funding source
Tsau 1989 90155156	Among children with nephrotic syndrome, those with relapsing disease (n=29) had significantly lower height velocity (80% of normal) and change in height SDS (–0.63 SDS) than those without relapsing disease (n=23, 104%, +0.19 SDS). This association was true for up to 7 years of follow-up	Cannot distinguish the effect of steroid use from severity of disease. Those with relapsing disease required significantly longer duration of steroid use (8 months) than those without relapsing disease (4 months).	No data on funding source

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Human Immunodeficiency Virus – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Brettler 1990 91011887	Location: US Setting: Hemophilia clinic Median age: 8 y Age range: 2.5-15 y Mean height: ND Male: 100% Race: ND SES: ND Enrolled: 36 Evaluated: 36 Number of sites: 1	Hemophilia HIV infection 2 y of growth data before HIV diagnosis Age ≤ 12.5 y in 1980	None reported	HIV (with hemophilia)	Prospective and retrospective longitudinal cohort (ND)
Matarazzo 1994 95143841	Location: Italy Setting: Pediatric clinic Median age: 2.6 y Age range: 0-8 y Mean height: ND Male: 49% Race: ND SES: ND Enrolled: 24 Evaluated: 24 Number of sites: 1	Perinatal HIV infection	None reported	HIV	Prospective longitudinal cohort (24 mo)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Human Immunodeficiency Virus – Part II

Author, Year	Severity of Illness Groups	Outcomes
Brettler 1990 91011887	Progression to AIDS or ARC (not defined)	Growth failure Decrease in ≥ 15 percentile points in height or weight for age for 2 consecutive years
Matarazzo 1994 95143841	Clinical condition • Stable: not defined • Clinical deterioration: not defined	Height SDS, based on Tanner 1966 Height velocity SDS

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Human Immunodeficiency Virus – Part III

Author, Year	Associations found	Potential Biases	Comments
Brettler 1990 91011887	Among boys with hemophilia and HIV infection "progression to AIDS or [AIDS related complex]" was more common in those with "growth failure" over 2 years (n=9, 55%) than those with normal growth (n=27, 7%). In multivariate analysis, "growth failure was the strongest prognostic variable" for progression to AIDS or AIDS related complex, adjusted for CD4, p24 antigenemia, and possibly other variables.	Methods, predictors and outcomes poorly defined Variables included in multivariate analysis not reported Definition of growth failure includes weight	No data on funding source
Matarazzo 1994 95143841	Among children with perinatal HIV infection (n=24), those with stable disease courses (n=14) had mean height at 1 year follow-up of –0.7 SDS, mean height at 2 year follow-up of –0.7 SDS, mean height velocity at 1 year follow-up of +1.2 SDS, and mean height at 2 year follow-up of +0.4 SDS. Children with unstable disease courses (n=10) had lower heights and height velocities. Mean height at 1-year follow-up was –2.0 SDS, mean height at 2 year follow-up of –2.6 SDS, mean height velocity at 1 year follow-up of –2.6 SDS, and mean height at 2 year follow-up of –3.0 SDS. "At follow-up [after 2 years], most children with normal growth maintained a stable clinical condition, whereas those with growth reduction showed progression in the severity of the disease….Growth failure was a simple, sensitive predictor of clinical course [stable condition vs clinical deterioration]."	Direct comparison of children with stable and unstable disease had to be calculated from reported raw data. Clinical condition not defined. No statistical analysis.	Study was government and privately funded

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Atopic Dermatitis / Eczema – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Massarano 1993 93312068	Location: UK Setting: Pediatric clinic Mean age: 6 y Age range: 2.3-12 y Mean height: ND Male: 68% Race: ND SES: ND Enrolled: 68 Evaluated: 68 Number of sites: 1	Diagnosis of eczema Prepubertal	Chronic non-atopic disease which would limit growth	Atopic eczema	Prospective cross-sectional cohort
Patel 1988 99014336	Location: UK Setting: Pediatric clinic Mean age: 5.5±0.3 (SEM) Age range: 2-10 y Mean height, initial, SDS: +0.1±0.1 (SEM) Mean height, follow-up, SDS: –0.1±0.2 (SEM) Male: 55% Race: ND SES: ND Enrolled: 80 Evaluated: 80 Number of sites:1	Atopic dermatitis that began before age 1 y Prepubertal, age 2-11 y Referred by pediatrician or dermatologist because of severity of disease	Systemic steroids	Atopic dermatitis	Prospective longitudinal cohort (2 y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Atopic Dermatitis / Eczema – Part II

Author, Year	Severity of Illness Groups	Outcomes
Massarano 1993 93312068	Maximum percentage of skin surface area affected by atopic eczema (erythema, vesicle, and crusts) Subgroups by percentage of skin surface area affected • < 50% • > 50%	Height SDS, based on Tanner 1966
Patel 1988 99014336	Percentage body surface area affected by atopic dermatitis • < 50% • > 50% Coexistence of disease • With asthma • Without asthma	Height SDS, based on Tanner 1966 Height velocity SDS

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Atopic Dermatitis / Eczema – Part III

Author, Year	Associations found	Potential Biases	Comments
Massarano 1993 93312068	Among children with atopic eczema (n=68), in a multivariate regression analysis, height SDS was correlated with surface area of eczema, controlling for parental height, diet, duration of eczema, treatment and asthma. Those children with < 50% of skin affected (n=41) had mean height of +0.11 SDS; those with 50% of skin affected (n=27) had significantly shorter mean height of –0.83 SDS. No height velocity data.	None noted	No data on funding source
Patel 1988 99014336	Among children with atopic dermatitis height SDS and height velocity SDS "did not differ between patients with < 50% body surface area (n=43) involvement and those with ≥ 50% body surface area involvement (n=37)…and between patients without asthma (n=36) and those with asthma (n=44)."	Complete results not reported. No statistical analyses reported.	No data on funding

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Miscellaneous Diseases – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Evliyaoglu 1996 97097381	Location: Turkey Setting: Pediatric hematology clinic Mean age: 10 y Age range: 5.5-15 y Mean height, percentile: 20±22% Height range, percentile: 3-75% Male: ND Race: ND SES: ND Enrolled: 24 Evaluated: 24 Number of sites: 1	Homozygote sickle cell anemia	None reported	Homozygous sickle cell anemia	Prospective cross-sectional cohort
Rasat 1995 95372015	Location: New Zealand Setting: ND Median age: 15 y Age range: 2-31 y Mean height: ND Male: 50% Race: ND SES: ND Enrolled: 16 Evaluated: 9 Number of sites: 1	Congenital adrenal hyperplasia diagnosed and treated at one hospital between 1962 and 1993	None reported	Congenital adrenal hyperplasia	Retrospective longitudinal case series (Median [Range] 14 [2-31] y)

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease
Miscellaneous Diseases – Part I

Author, Year	Demographics	Inclusion Criteria	Exclusion Criteria	Types of Diseases / Conditions	Study Design (Duration)
Samson-Fang 1998 99066563	Location: US Setting: Rehabilitation center Mean age: 4.5 y Age range: 1-12 y Mean height, SDS: -1.2±1.5 Male: 53% Race: White 80%, Black 20% SES: ND Enrolled: 175 Evaluated: 81 Number of sites: 1	Children with cerebral palsy Age < 10 years old at the mid-point of assessing growth interval Minimum time interval of measurements of 0.8 years	Genetic disorders Complicating medical issues	Cerebral Palsy	Retrospective cross-sectional cohort

Evidence Table 3. Association of Decreased Growth Velocity with Severity of Disease

Miscellaneous Diseases – Part II

Author, Year	Severity of Illness Groups	Outcomes
Evliyaoglu 1996 97097381	Severity of sickle cell anemia • Mild: No blood transfusion or crises • Severe: Blood transfusion needed early in life, frequent crises	Height percentile (not defined)
Rasat 1995 95372015	Number of episodes of biochemical escape from congenital adrenal hyperplasia suppression (morning 17-OH Progesterone > 60 nmol/L) • < 3 episodes over at least 2 years • > 3 episodes	Height SDS. based on Tanner 1966
Samson-Fang 1998 99066563	Cerebral palsy cognitive impairment • Cognitive impairment: Learning disability, or delay in problem solving or receptive language skills • No cognitive impairment Type of cerebral palsy • Spastic • Extrapyramidal • Mixed Ambulatory status • Ambulatory: Functionally ambulated with or without aids at home • Non-ambulatory	Growth velocity SDS, based on Rikken 1992

Association of Decreased Growth Velocity with Severity of Disease
Abbreviations

Author, Year	Associations found	Potential Biases	Comments
Evliyaoglu 1996 97097381	Among children with sickle cell anemia, those with mild disease (n=12) had significantly greater mean height percentile (22.5%) than those with severe disease (n=12, 17.3%). No data on height velocity	Only mild and severe sickle cell. Height measurement (percentile) not clear. Unclear why all children had low height percentile	No data on funding source
Rasat 1995 95372015	Among children with congenital adrenal hyperplasia there was no significant difference in final height SDS in those with < 3 biochemical escape episodes (n=4) and those with > 3 episodes (n=5). No data on height velocity.	Very small numbers Results shown only graphically.	No data on funding source
Samson-Fang 1998 99066563	Among children with cerebral palsy those with cognitive impairment (n=62) had significantly lower mean growth velocity (–1.25 SDS) than those with no cognitive impairment (n=19, –1.25 SDS)) Those age ≥ 2 years who were non-ambulatory (n=35) had significantly lower mean growth velocity (–1.20 SDS) than those who were ambulatory (n=37, –0.35 SDS). There was no significant difference in mean height velocity among those with spastic disease (n=22, mean height velocity = –0.69 SDS), those with extrapyramidal disease (n=36, –0.86 SDS), and those with mixed disease (n=22, –1.50 SDS)	Exclusion criteria limit most severe impairments due to cerebral palsy	Study was privately funded.