Review of life course outcomes: Quality tables

Page

Table 3.1A (i). Description and quality assessment of studies included in review of infant size/growth and SIDS 3-5
Table 3.1A (ii). Summary data extracted from studies included in review of infant size/growth and SIDS 6-7
Table 3.1B (i). Description and quality assessment of studies included in review of infant size/growth and childhood cancer 8
Table 3.1B (ii). Summary data extracted from studies included in review of infant size/growth and childhood cancer 8
Table 3.1C (i). Description and quality assessment of studies included in review of infant size/growth and respiratory disease 9
Table 3.1C (ii). Summary data extracted from studies included in review of infant size/growth and respiratory disease 10
Table 3.1D (i). Description and quality assessment of studies included in review of infant size/growth and autism 11
Table 3.1D (ii). Summary data extracted from studies included in review of infant size/growth and autism 11
Table 3.2A (i). Description and quality assessment of studies included in review of infant size/growth and childhood obesity 12-14
Table 3.2A (ii). Summary data extracted from studies included in review of infant size/growth and childhood obesity 15-16
Table 3.3A (i). Description of studies included in review of infant head size/growth and cognitive development 17-22
Table 3.3A (ii). Summary data extracted from studies included in review of infant head size/growth and cognitive development 23-27
Table 3.3B (i). Description of studies included in review of growth faltering in infancy and cognitive development 28-34
Table 3.3B (ii). Summary data extracted from studies included in review of growth faltering in infancy and cognitive development 35-40
Table 3.3C (i). Description of studies included in review of infant size/growth in weight or height and cognitive development 41-43
Table 3.3C (ii). Summary data extracted from studies included in review of infant size/growth in weight or height and cognitive development 44-46
Table 3.3D (i). Description of studies included in review of infant size/growth and motor development 47-49
Table 3.3D (ii). Summary data extracted from studies included in review of infant size/growth and motor development 50-51
Table 4.1A (i). Description and quality assessment of studies included in review of infant size/growth and insulin dependent diabetes mellitus 52-53
Table 4.1A (ii). Summary data extracted from studies included in review of infant size/growth and insulin dependent diabetes mellitus 54-55
Table 4.1B (i). Description and quality assessment of studies included in review of infant size/growth and mental illness 56
Table 4.1B (ii). Summary data extracted from studies included in review of infant size/growth and mental illness 57
Table 5.1A (i). Description and quality assessment of studies included in review of infant size/growth and IHD 58-59
Table 5.1A (ii). Summary data extracted from studies included in review of infant size/growth and IHD 60-61
Table 5.1B (i). Description and quality assessment of studies included in review of infant size/growth and cerebrovascular disease 62
Table 5.1B (ii). Summary data extracted from studies included in review of infant size/growth and cerebrovascular disease 62
Table 5.1C (i). Description and quality assessment of studies included in review of infant size/growth and non-insulin dependent diabetes mellitus (NIDDM) 63
Table 5.1C (ii). Summary data extracted from studies included in review of infant size/growth and NIDDM mellitus 64
Table 5.1D (i). Description and quality assessment of studies included in review of infant size/growth and adult cancer 65
Table 5.1D (ii). Summary data extracted from studies included in review of infant size/growth and adult cancer 66
Table 5.1E (i). Description and quality assessment of studies included in review of infant size/growth and osteoarthritis 67
Table 5.1E (ii). Summary data extracted from studies included in review of infant size/growth and osteoarthritis 67
Table 5.1F (i). Description and quality assessment of studies included in review of infant size/growth and mental illness 68
Table 5.1F (ii). Summary data extracted from studies included in review of infant size/growth and mental illness 69
Table 5.2A (i). Description and quality assessment of studies included in review of infant size/growth and adult obesity 70-73
Table 5.2A (ii). Summary data extracted from studies included in review of infant size/growth and adult obesity 74-75
Table 5.3A (i): Description and quality assessment of studies included in review of infant size/growth and non-health-related quality of life 76
Table 5.3A (ii): Summary data extracted from studies included in review of infant size/growth and non-health-related quality of life 76

Table C: Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

3.1A: SIDS studies 77
3.1B: Childhood cancer studies 77
3.1C: Respiratory disease studies 78
3.1D: Autism studies 78
3.2A: Childhood obesity studies 79
3.3A: Studies of HC and cognitive development 80-81
3.3B: Studies of failure-to-thrive and cognitive development 82-83
3.3C: Studies of weight or height and cognitive development 84
3.3D: Motor development studies 85
4.1A: Insulin dependent diabetes mellitus studies 86
4.1B: Mental illness studies 86
5.1A: IHD studies 87
5.1B: Cerebrovascular disease studies 87
5.1C: NIDDM studies 88
5.1D: Adult cancer studies 88
5.1E: Osteoarthritis studies 89
5.1F: Mental illness studies 89
5.2A: Adult obesity studies 90-91
5.3A: Non-health-related quality of life studies 91

Abbreviations used in tables

The following table summarises common abbreviations used throughout appendix 10

Abbreviation	Term in full	Abbreviation	Term in full
BMI	Body mass index	Mo	Months
btwn	Between	Popn	Population
Bwt	Birthweight	SES	Socio-economic status
Diffs	Differences	Ss	Subjects
Excl	Exclusion criteria	Vars	Variables
FU	Follow-up	VLBW	Very low birthweight
Gest	Gestational age	Wt	Weight
Growth vel	Growth velocity	Yr	Year
HC	Head circumference		
Ht	Height		
Incl	Inclusion criteria		
LBW	Low birthweight		
M'ments	Measurements		

Table 3.1A (i). Description and quality assessment of studies included in review of infant size/growth and SIDS

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis*
Williams (1990)[15] *Arch Dis Child* South Island, New Zealand MEDLINE	Case-control study comparing the growth of SIDS victims with matched controls. Population based; set in 3 health dists over 5 years. Sample was all SIDS deaths for which relevant info was available.	136 cases identified during 1979-84; 136 controls drawn from same infant health clinics (no further info). All Ss were full-term; bwt given by infant feeding method (normal wts). Exclusion criteria stated, but no reasons. No sex or race info. Adequate info on original cohort and exclusions. 52% FU of target for cases; no info on controls. Incl/excl Ss compared for bwt, length, HC – no diffs. Mothers of excl Ss older on average though. Very little baseline info.	Infancy: Various wt m'ments with timing criteria; ascertained by clinic nurses during home visits (no further info). No rounding info, but smoothing splines used to generate a weight for each 2-wk period. Outcome: SIDS diagnosis based on national statistics info cross-checked with coroners' records. Independent review & diagnosis by 2 of the authors.	Tables of means & diffs in size and growth betw gps, controlling for infant feeding. *t*-stats and *p*-values given, but no ORs. Matching on sex, bwt & infant feeding; but not SES or maternal smoking.
Brooks (1994)[16] *Pediatrics* Avon, UK MEDLINE	Retrospective case-control study comparing the postnatal growth preceding SIDS deaths with that of matched controls. Popn. based; set in 4 health dists over 2 years. Sample was all SIDS deaths satisfying study criteria.	78 cases who died during 1987-89; 139 controls drawn from case's health visitor's list (closest in DOB). Mean bwt and gest. age given; both normal. Good info on original cohort and exclusions, with reasons & flow chart. 80% FU of target cases; no controls lost, but those corresponding to lost cases were excluded. Info on sex but not race. Incl/excl Ss compared for various factors incl. bwt, gest age, age at death & SES – no sig diffs. Cases & controls differed for gest. age & maternal smoking, but these were controlled for in analysis. Baseline info good.	Infancy: A median of 7 (2 to 20) live weight measures (excluding birth) per infant, used to derive growth measures. Ascertained in homes by health visitors. No rounding info given. Outcome: SIDS diagnosis by autopsy according to standard protocol in one of 2 hospitals. Results discussed at multidisciplinary case review conference; Beckwith criteria used.	Tables of means & diffs in growth betw gps, controlling for gest age, maternal smoking, infant feeding and age at death. *p*-values given. Matching on age, time of year & area of residence; but not sex, SES or maternal smoking.
Williams (1996)[17] *Acta Paediatr* Various, New Zealand MEDLINE	Case-control study comparing growth velocity in SIDS victims & matched controls. Popn. based; set in various health dists over 3 years. Sample was all SIDS deaths for which relevant info was available.	309 cases who died during 1987-90; 1491 controls randomly selected from all births in study region (except the <1% of home births). Mean bwt normal. Gest. age not given, but adjusted for. Non-participants: numbers & reasons given; sig diffs from incl. Ss on race, maternal smoking & SES (more minorities of lower health & SES excluded). Sig diffs betw. cases & controls for bwt, gest. age, infant feeding, race & SES. 64% FU of target cases; 83% of controls. Although many vars compared for diffs, only bwt has figures given at baseline.	Infancy: All Ss had bwt & ≥1 further body wt measure. Measured in clinics by nurses; info in records held by parents. Growth (weight gain) calculated. No rounding info given. Outcome: SIDS diagnosis by regional pathologist & paediatrician according to agreed protocol. Reviewed by study pathologist where in doubt. PM in 97.7% of cases.	Tables of means & diffs betw gps in size (wt) & growth (wt gain from birth to last m'ment). Also tables of estimated growth in 9 4-wk periods using curve fitting. Randomisation tests for race, maternal smoking and infant feeding (no sig diffs); stratification for sex; adjustment for gest. age.

Table 3.1A (i) (continued). Description and quality assessment of studies included in review of infant size/growth and SIDS

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis*
Peterson (1974)[18] *Am J Epidemiol* King County, WA, USA MEDLINE	Case-control study investigating growth patterns of SIDS cases. Population based (for cases at least); set in a single US county. Time period unclear. Sample was all SIDS cases in the county.	362 cases identified since 1965. 2 control groups selected purposefully from different sources: a public clinic deemed to serve 'disadvantaged' infants (n=118) and a private practice deemed to serve 'advantaged' infants (n=270). Selection process for controls not random or systematic. Controls are therefore a major source of potential bias. Bwt given for 155 of the cases & all controls; normal. No gest. age info. No info on incl/excl criteria, target popn or %FU. No sex or race info; nothing on SES except for indirect info for controls by virtue of the type of clinic they attended. No other baseline info.	Infancy: cases: size at death (PM wt, ht, HC); growth rate (estimated using linear regression by age at death); controls: serial m'ments from birth to 6mo for each infant, from clinic records. No rounding info. Outcome: SIDS diagnosis based on PM, all done by or attended by a single pathologist to a standard protocol. No further info.	Tables of growth rates based on linear regression; p-values for diffs betw cases & each of the control gps. Scattergrams comparing cases' wt, ht & HC in 6 age categories with ref popn. No consideration of confounders.
Jorgensen (1982)[19] *Acta Paediatr Scand* Copenhagen, Denmark MEDLINE	Case-control study comparing the growth & development of SIDS victims with matched controls. Population based; set in 1 city over 15 years. Sample was all SIDS deaths in the city for which relevant info was available.	131 cases born during 1956-71; 524 matched controls selected otherwise at random from health visitors' files. Mean bwt normal; no gest. age info given. 94% FU of target cases; no info for controls. No info on non-participants, but less important as only 8 Ss lost. Sig diffs betw. cases & controls for wt & length at birth, for both sexes. Infant feeding measured, but nothing on maternal smoking or SES.	Infancy: Size (wt) at monthly intervals (1,2,3,4 & 6mo). Ascertained in homes by health visitors; linear interpolation sometimes used. Growth (weight gain) calculated. No rounding info given. Outcome: SIDS diagnosis using police report, thorough PM, and use of Beckwith criteria.	Tables of mean growth (wt gain) in each month; sig of diffs stated. Matched for sex & age; separate analysis also adjusts for bwt & infant feeding.
Blair (2000)[20] *Arch Dis Child* Various, UK MEDLINE	Case-control study investigating patterns of infant growth that may influence the risk of SIDS. Popn. based; set in 5 geog. regions over 3 years. Ss drawn from a larger infant death study over same time period.	247 cases who died during 1993-6; 1110 controls drawn from case's health visitor's list (2 next older and 2 next younger). Median gest. age given; normal. Bwt given only in form of z-scores. No info given on non-participants. Sig diffs betw. cases and controls for bwt, sex and gest. age. No race info. 68% FU of target cases; 76% of controls. Little baseline data given, especially for demographic variables.	Infancy: All Ss had ≥ 2 live weight measures (could include birth). Converted to z-scores. Ascertained from community, primary care, hospital, and parent held records. No rounding info given. Outcome: Diagnosis of SIDS by multidisciplinary committee following autopsy, according to standard protocol. Clear definition of SIDS given.	Tables of means & diffs in size and growth betw gps, controlling for bwt. ORs and p-values given. Also regression for growth, controlling for many conf vars, incl infant feeding, sex, SES and parental smoking. Matching on age only.

Table 3.1A (i) (continued). Description and quality assessment of studies included in review of infant size/growth and SIDS

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis*
Naeye (1976)[21] *Am J Dis Child* Various, USA MEDLINE	Case-control study investigating potential antecedents of SIDS. Hospital based; drawn from 14 US medical institutions over 7 years. Ss drawn from a larger perinatal study over same time period.	125 SIDS cases born during 1959-66; 375 matched controls drawn from same perinatal study (but no further info on control selection). Cases also compared to all 53,721 study infants surviving neonatal period with relevant data. All Ss were full term; no bwt info given. No info given on non-participants. 28 cases (22%) had size data in infancy (due to death & loss to FU); no info for controls. Excellent baseline info incl. sex, race & SES; sig diffs betw. cases & matched controls for bwt, mothers' age & maternal smoking, as well as various neonatal factors (e.g. Apgar).	Infancy: 1 live weight measure at 4mo for surviving infants not lost to FU. Ascertained from records of perinatal project; no further info given. No rounding info given. Outcome: SIDS diagnosis by *single* investigator according to a clear definition, having reviewed all clinical and PM material – no discussions or conferences.	Very little of interest to the review – comparison of cases' size percentile with popn. standards. No adjustment of confounders. Matching on age, sex, gest. age, race, place of birth & SES, but N/A to analysis of interest.
Froggatt (1971)[22] *Brit J Prev Soc Med* Northern Ireland, UK From reference list	Case-control study into the epidemiology of SIDS, as part of a larger SIDS study. Popn. based; setting is whole of N. Ireland over 2 years. Sample was SIDS deaths examined by certain pathologists & satisfying strict inclusion criteria.	162 cases ascertained during 1965-67, of which 129 were used in the analysis of interest, giving a FU of 79% for cases. 162 controls drawn from birth register (next like-sexed birth in same admin. area), but not used in analysis of interest. Bwt & gest. age normal, but no raw data given. Sex & mean age at death also given, but no further baseline info. No info on non-participants except numbers & reasons, but estimated "completeness of ascertainment" of around 85-90% across study region.	Infancy: PM* weights used; "weight increment" calculated using PM weights & those of (live) standard population series at each month of age. Outcome: PM by one of 4 trained forensic pathologists; no info on whether or how records of PM were reviewed, or who by.	Little of interest. Table comparing mean weights & "weight increments" of pooled SIDS cases with standard population series at each month of age. No consideration of confounders.

* PM = "post-mortem"

Table 3.1A (ii). Summary data extracted from studies included in review of infant size/growth and SIDS

Details	*Subjects*			*Findings*				*Do SIDS infants grow differently?*
	Numbers	FU info*	Mean age at death (days)					
Williams (1990)[15] *Arch Dis Child* South Island, New Zealand MEDLINE	136 cases 136 controls ratio = 1:1	52% NG 7.0	BF¶: 88.8 (range 29 – 322) NBF: 77.0 (31 – 157)	Difference in **growth vel** (g/day). Cases – controls (mean; *p*-value)	Birth to last live obs.	Penultimate 2 wks	Last obs. to death	**Yes. Growth** rates for SIDS are significantly lower than controls just before death. Elsewhere, effect is present but not significant. Effect more prominent in non-breastfed group.
				Breastfed Non-breastfed	-0.9 (*p*=0.54; NS) -3.0 (*p*=0.07; NS)	+0.0 (*p*=1.0; NS) -3.1 (*p*=0.10; NS)	-6.3 (*p*=0.03) -12.8 (*p*=0.01)	
Brooks (1994)[16] *Pediatrics* Avon, UK MEDLINE	78 cases 139 controls ratio = 1:2 ‡ due to discarding of controls matched with excluded cases, rather than losses to FU	80% 73%‡ NG	103.6 (SD¶ = 9.71)	Difference in **growth vel** (g/day). Cases – controls (mean; 95% CI)	Birth to last live obs.	Between last 2 live obs.		**No**. No significant differences in **growth** velocity between case & controls in any of the given growth periods.
				All subjects	-1.1 (-4.7, 2.6) NS	+6.6 (-0.7, 13.2) NS		
Williams (1996)[17] *Acta Paediatr* Various, New Zealand MEDLINE	309 cases 1491 ctrls ratio = 1:4	64% 83% NG	111 (SD = 64.2)	Difference in **growth vel.** (g/day). Cases – controls (mean; *p*-value)	Birth to last live obs. (crude)	In each of 9 4-wk periods (estimated)		**Inconclusive. Growth** rates were mostly not significantly different. Significant size differences exist, but these may be due to differences in birthweight.
				Males Females	-0.8 (*p* = 0.33; NS) 2.0 (*p* = 0.01)	NS NS		
				Difference in **size** (weight) at 3 mo, 6 mo, penultimate obs. (mean = 61 days) and final obs. (mean = 86 days) was significant (*p*<0.05) for both sexes, except for females at 6 mo.				
Peterson (1974)[18] *Am J Epidemiol* King County, WA, USA MEDLINE	362 cases 388 controls ratio = 1:1	NG NG NG	NG	Difference in **growth vel.** from 2 to 180 days (from linear regressn.) cases – controls (mean; *p*-value)	Weight (g/day)	Length (mm/day)	Head circ. (mm/day)	**Inconclusive. Growth** rates for SIDS cases were significantly lower than those of one set of controls ('advantaged') but not those of the other ('disadvantaged'), so probable confounding by SES.
				Disadvantaged controls (*n* = 118) Advantaged controls (*n* = 270)	-2.52 (NS) -5.48 (*p*=0.0005)	-0.05 (NS) -0.18 (*p*=0.003)	-0.01 (NS) -0.06 (NS)	

* Percentage FU of target cases; percentage FU of target controls; incidence rate per 1,000 live births in study region. NG = "Not given".

Table 3.1A (ii) (continued). Summary data extracted from studies included in review of infant size/growth and SIDS

Details	*Subjects*			*Findings*				*Do SIDS infants grow differently?*
	Numbers	FU info*	Mean age at death (days)					
Jorgensen (1982)[19] *Acta Paediatr Scand* Copenhagen, Denmark MEDLINE	131 cases 524 controls ratio = 1:4	94% -- 0.92	132 (range 10 – 359) (median = 120)	Differences in **growth** (weight gain in g) for each month from the 3rd onward between cases and controls, for both sexes: NS.				**No.** No statistical evidence for any **growth** differences between cases and controls in infancy in either sex.
Blair (2000)[20] *Arch. Dis. Child.* Various, UK MEDLINE	325 cases 1292 ctrls ratio = 1:4	68% 76% 0.77	91 (median) (IQR¶ 55 – 150)	OR per unit **change in z-score**, adjusted for age & number of obs; 95% CI.	Birth to last live obs. (247 cases; 1110 controls)	Birth to penul-timate live obs † (73 cases; 320 controls)	Penultimate to final live obs. † (73 cases; 320 controls)	**Yes**. Odds ratios for SIDS are significantly higher for 'poor' **growth** than for 'normal' **growth**. Association seems to be partly explained by bwt, but adjusting for bwt does not affect the overall association.
				Certain subsets of subjects	1.85 (1.44, 2.39)	1.69 (1.17, 2.43)	1.46 (1.04, 2.06)	
				Plus: OR of SIDS for 'poor' (≥1 SD downward change) compared to 'normal' growth (<1 SD downward change, or upward change) betw. birth & last live obs within 2 wks of death, for 119 cases & 531 controls, adjusting for *all* potential confounders: OR = 1.89 (1.15, 3.08), $p < 0.01$.				
Naeye (1976)[21] *Am. J Dis. Child.* Various, USA MEDLINE	125 cases 375 controls ratio = 1:3	-- -- 2.1	Not stated; range 14 – 548	**Size** (weight) at 4 months for 28 (22% of 125) SIDS victims still alive at that time was at the 20th percentile compared to reference population. No statistical tests or analysis.				**Inconclusive**. What evidence there is suggests SIDS cases are of smaller **size** in infancy, but no statistical analysis.
Froggatt (1971)[22] *Brit J Prev Soc Med* N. Ireland, UK MEDLINE	148 cases 148 controls ratio = 1:1	79% N/A 2.4	126.7 (median 96.6)	Mean **size** (necropsy weight) of cases lies between the 10th and 50th percentiles of the reference population in each month from birth onwards (except in the 10-12mo and 14mo groups; however, the numbers of cases are extremely small in these groups)				**Inconclusive**. Evidence to suggest smaller **size** among cases than general popn., but no statistical analysis, and PM weights used.

* Percentage FU of target cases; percentage FU of target controls; incidence rate per 1,000 live births in study region
¶ BF = breastfed; NBF = non-breastfed; SD = standard deviation; IQR = inter-quartile range; NS = not significant; OR = odds ratio; CI = confidence interval given
† When both these variables are included in the same model, "Birth to penultimate live obs" remains significant (OR=1.60, p=0.02) whilst "Penultimate to final live obs." becomes non-significant.

Table 3.1B (i). Description and quality assessment of studies included in review of infant size/growth and childhood cancer

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Suminoe (1999)[23] *J Pediatr* Kyushu-Okinawa district, Japan EMBASE	Retrospective cohort study of growth up to diagnosis in **childhood cancer** patients. Setting is the Cancer Registry of a single district. Sample was all patients in study region diagnosed at under 19 years.	1596 childhood cancer patients (911 males) diagnosed during 1985-94. Only 292 of these of interest to the review however (those diagnosed at under 1 year). Bwt normal & not sig. diff. from Japanese popn, although that for subset of males with neuroblastoma was significantly greater. Sex info and age at diagnosis given, but no further baseline info. Excl criteria fairly clear. 93% FU. No info on non-participants, other than numbers and reasons, but this is less important with such a high %FU.	Infancy: size (ht & wt) at diagnosis, obtained from Cancer Registry records; growth (change in size from birth to diagnosis). No further info; reliability unclear. No rounding or blinding info. Outcome: diagnosis of cancers of any type. "**All cancers**", "**neuroblastoma**" and "**acute lymphoblastic leukaemia**" (ALL) used for the analysis of interest. No further info on ascertainment.	Change in wt SD scores from birth to diagnosis (in subgroup diagnosed before 1 yr of age) allows comparison with general popn. No consideration for confounders. No direct measure of assoc.

Table 3.1B (ii). Summary data extracted from studies included in review of infant size/growth and childhood cancer

Details	*Design and Participants*				*Main Findings*			*Conclusion*
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (days) (SD*)	Outcome	Change in weight z-score betw. birth & diagnosis (< 1yr)	Weight z-score at diagnosis (< 1yr)	
Suminoe (1999)[23] *J Pediatr* Kyushu-Okinawa district, Japan EMBASE	292 (57% male)	93%	3.16 (NG*)	NG*	All childhood cancers (*n*=292)	+0.08 (NS)	+0.08	**Positive** assoc. betw. rapid **infant growth** and neuro-blastoma
					ALL (*n*=27)	+0.31 (p=0.20; NS)	+0.55	
					Neuroblastoma (*n*=175)	+0.20 (p=0.03)	+0.20	
					- Detected by MS (*n*=103)	+0.31 (*p*<0.01)	+0.22	
					- Others (*n*=30)	-0.07 (NS)	-0.03	

Table 3.1C (i). Description and quality assessment of studies included in review of infant size/growth and respiratory disease

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Victora (2001)[24] *Int J Epidemiol* Pelotas, Brazil From expert	Prospective cohort study of assoc. betw. infant growth and **morbidity** from diarrhoea or lower respiratory infection in infancy. Almost popn. based – source popn. was all hospital births in a single city, but non-hospital births accounted for less than 1% of total.	3587 Ss born in Pelotas, Brazil in 1982. Mean bwt & gest. age not given, but 6% had bwt <2.5kg, 5% were preterm and 14% were SGA. 51% male; no race info. SES info given: most Ss came from families earning < 6 times the minimum wage; most mothers had < 9yrs educ. 61% FU. Original cohort & study Ss compared on sex, SES (family income, maternal age & educ.), low bwt, preterm & SGA; low bwt & low SES Ss slightly more likely to be lost to FU.	Infancy: weight at 0 & 20mo measured using standard equipment during home visits. No info on observers or reliability. Converted to z-scores using NCHS reference. Fast growth defined as change in wt *z*-score of ≥ 0.66 from 0-20mo. Outcome: morbidity (hospital admission) from respiratory disease or diarrhoea during 1985 (mean age 42mo) by maternal recall in 1986. Validation sub-study showed > 90% agreement betw. recall & hosp case-notes.	Prevalence of hospital admission for diarrhoea and lower respiratory infection by 0-20 weight gain category (fast vs normal/slow). P-values given for difference. Stratified for SGA/AGA, but no adjustment for confounders.
Yoon (1997)[25] *Am J Clin Nutr* Metro Cebu, Phillipines MEDLINE	Prospective longitudinal study of assoc. betw. size and **mortality** from diarrhoea or acute lower respiratory infection (ALRI) in infancy. Setting was a random sample of administrative geog. areas; target popn. was all births in these areas during the study period.	9942 Ss born during 1988-91 in 33 administrative regions (7 urban, 26 rural) of the Phillipines. Mean bwt & gest. age not given, but around 18% had bwt ≤2.5kg. No sex, race or other baseline info. A survival approach was used, with Ss leaving the study if they die, reach 24mo of age, or migrate from the study region. 9942 Ss represents all Ss born in study area during study period, of whom 63% were still being followed at end of study period. No info comparing those migrating or lost to FU with remaining Ss.	Infancy: size (wt & ht) measured at 4, 9, 14, 20 & 23mo. Wt to nearest 100g; ht to nearest 0.1cm. Wt-for-age, ht-for-age & wt-for-ht *z*-scores derived. Measured using standard equipment in homes, but no info on observers. Outcome: Mortality from diarrhoea or ALRI, from post-mortem interview with mother carried out by midwives or local health workers. No further verification of cause of death.	Cox proportional-hazards regression for mortality, by most recent wt-for-age *z*-score measurement, adjusted for infant feeding, SES & maternal educ. Trends in prevalences & rate ratios by wt-for-age category given, plus attributable risks.
Fonseca (1996)[26] *Bull. World Health Organ.* Fortaleza, Brazil From expert	Case-control study of assoc. betw. malnutrition and **morbidity** from pneumonia in infancy. Cases from a single large public city hospital; controls from same neighbour-hoods as cases, by door-to-door enquiries by a field worker. Source popn. was all Ss aged 0-23mo diagnosed with pneumonia & seen at the outpatient clinic of the hosp.	650 cases of pneumonia & 650 controls, recruited during 1989-90. Recruitment took place only 3 days per wk to limit sample size – since the days rotated, this amounts to random sampling. No baseline info given, but SES was low – hosp. catered mainly for low-income families, & >50% of city popn. lived in shanty towns. Excl. criteria clear, both for cases & controls, & sought to minimise selection bias. No specific %FU info, but states that >99% of houses of potential Ss were located, with only 1 refusal. No comparisons betw. cases & controls or incl. & excl. Ss on important variables.	Infancy: size (wt & ht) at age 0-23mo, measured at admission or consultation at hosp. for cases, & at home using standard portable equipment for controls. No info on observers or reliability. Wt-for-age, wt-for-ht & ht-for-age *z*-scores derived. Outcome: morbidity from pneumonia at age 0-23mo. Chest x-rays taken & examined by paediatric radiologist. Potential controls excluded if respiratory rate was ≥40 or ≥50 breaths per minute (depending on age).	Matched-pairs analyses and McNemar's χ^2 test used; odds ratios and 95% CIs calculated from tabluations. Matched on neighbourhood & age. Also, conditional logistic regression controlling for family income, parental educ. & previous episode of pneumonia. Also, crowding, parental smoking, age & sex considered in crude analyses.

Table 3.1C (ii). Summary data extracted from studies included in review of infant size/growth and respiratory disease

Details	*Design and Participants*				*Main Findings*					*Conclusion*
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (days) (SD*)						
Victora (2001)[24] *Int J Epidemiol* Pelotas, Brazil From expert	3587 (51% male)	61%	6% had bwt <2.5kg	5% were preterm	Variable ('growth' = change in weight *z*-score)	SGA (*n*=516)		AGA (*n*=3071)		**Inverse** assoc. betw. **infant growth** and risk of morbidity from LRI in AGA infants; otherwise **inconclusive**.
						Diarrhoea	LRI	Diarrhoea	LRI	
					N	212	304	2333	738	
					Growth 0-20mo ≥ 0.66	1.90%	4.70%	1.00%	3.60%	
					Growth 0-20mo < 0.66	0.00%	2.30%	0.70%	1.50%	
					p for difference	*p* = 0.06	*p*=0.21 (NS)	*p*=0.46 (NS)	*p* = 0.006	
					p for trend (across 3 growth categories)	*p* < 0.05	*p*=0.09 (NS)	*p* < 0.05	*p* < 0.05	
Yoon (1997)[25] *Am J Clin Nutr* Metro Cebu, Phillipines MEDLINE	9942 (% male not given)	N/A	18% had bwt ≤2.5kg	NG*	RRs (95% CIs) & attributable risks for mortality assoc. with a 1-unit decrease in most recent wt-for-age *z*-score, using Cox PH regression, adjusted for infant feeding, mother's educ, toilet facility & previous birth interval					**Inverse** assoc. betw. **infant growth** and risk of mortality from diarrhoea or ALRI
					Age range	Diarrhoea		ALRI		Either	
						RR	AR	RR	AR	RR	AR
					6-11mo	1.9 (1.3, 2.7)	37.7	1.5 (0.9, 2.5) – NS	22.7	2.4 (1.6, 3.6)	55.8
					12-23mo	1.6 (0.9, 3.2) – NS	35.9	3.3 (1.4, 7.8)	85.4	2.5 (1.3, 4.7)	69.4
					0-23mo	1.6 (1.3, 2.1)	NG	1.7 (1.3, 2.3)	NG	2.0 (1.5, 2.6)	NG
					Also given: RRs by wt-for-age z-score category (-1 to 0, -2 to -1, -3 to -2, ≤-3) compared to *z*-score >0 – definite dose-response trends shown.						

Details	*Design and Participants*			*Findings*				*Summary of trend*
author (pub. year); journal; location; source	No. of Subjects	FU info	Mean age at diagnosis					
Fonseca (1996)[26] *Bull. World Health Organ.* Fortaleza, Brazil From expert	650 cases 650 controls ratio = 1:1	NG* NG*	range 0 to 23mo	Size variable	% prevalence in control gp. of z-score < -3	OR (95% CI) for z-score < -3 compared to ≥ 3	χ^2 test for trend in OR over 4 or 5 categories of size var.	**Inverse** assoc. betw. **infant size** and risk of morbidity from pneumonia.
				Wt-for-ht *z*-score	0.9%	6.75 (1.88, 24.27)	χ^2 = 30.28; p < 0.001	
				Ht-for-age *z*-score	8.4%	5.05 (2.92, 8.74)	χ^2 = 30.94; p < 0.001	
				Wt-for-age *z*-score	9.5%	4.57 (2.93, 7.13)	χ^2 = 60.10; p < 0.001	
				NB: ORs (incl. those used for test for trend) adjusted for family income, parental educ. & previous episode of pneumonia. Tabulations and ORs for all of the size variable categorisations also given in the study.				

Table 3.1D (i). Description and quality assessment of studies included in review of infant size/growth and autism

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Courchesne (2003)[27] *JAMA* San Diego, USA MEDLINE	Retrospective cohort study of infant **head size** in autistic children compared to reference standards. Source popn was recruited for earlier studies on MRI data – potential for selection bias.	48 Ss with autism spectrum disorder (ASD) recruited from community advertisements & referrals at age 2-5yrs. No sex info; 92% white. Mean bwt normal; all Ss were full term. No SES or any other baseline info. Only incl. criterion was ASD diagnosis. No %FU info, but states that study (ASD) sample is "about half" of original sample. No comparison with non-participants.	Infancy: size and growth (HC) at ages 1-2mo, 3-5mo & 6-14mo, obtained from medical records from clinics and hospitals. No further info. HC data converted to *z*-scores using CDC standard growth charts. Outcome: ASD at 2-5yrs (mean 31mo), using one of 4 standard diagnostic tests and clinical observation, "completely independently" of infant size measurement	*z*-scores and *p*-values for HC, used to compare ASD Ss to reference populations. No consideration of confounders.

Table 3.1D (ii). Summary data extracted from studies included in review of infant size/growth and autism

Details	*Design and Participants*				*Main Findings*			
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)	General Description			Conclusion
Courchesne (2003)[27] *JAMA* San Diego, USA MEDLINE	15 (80% male)	≈ 25	3.43 (0.13)	All were full-term	Timing	HC size *z*-score	HC growth (from previous timepoint)	**Positive** association between increased **infant head size** and **growth** and autism spectrum disorder
					3-5mo (n=15)	z = +0.18; NS	*z* = +0.66; NS	
					6-14mo (n=15)	z = +1.01; *p* = 0.001	*z* = +0.83; *p* < 0.05	
					15-28mo (n=9)	z = +1.10; *p* = 0.02	*z* = +0.09; NS	
					Body length and weight at birth for the study Ss did not significantly deviate from the reference population at any timepoint. Comparison with 31 Ss from the Fels Longitudinal Study for HC growth from birth to 6-14mo: ASD Ss: z = +1.82; Fels Ss: *z* = +0.76; *p* for diff < 0.001.			

Table 3.2A (i). Description and quality assessment of studies included in review of infant size/growth and childhood obesity

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Stettler (2002)[28] *Pediatrics* Various, USA MEDLINE	Retrospective analysis of a prospective cohort, of assoc. betw. rapid infant growth and risk of childhood obesity. Setting was 12 university hospitals. Source popn. was the offspring of a random sample of pregnant mothers registered on a national perinatal study.	19,397 Ss born during 1959-65 to mothers registered with the perinatal project. 50% male; 48% white. All Ss were born at term; mean bwt normal. Other baseline info given, incl. birth order, size at FU, & maternal BMI & educ. 70% FU; however, term gestation (37-42wks) was an incl. criterion, so Ss with unknown gest. (mostly births before 1962) were excluded. Study Ss compared to non-participants: no sig diffs for sex or gest. age, but study Ss more likely to be black, have higher bwt, an older sibling, and a mother with higher BMI & education.	Infancy: size (weight) at 1yr; growth (wt gain per month from birth to 4mo). No further info. Outcome: overweight at age 7yrs, defined as BMI >95th percentile for age & sex, using CDC growth charts. No further info.	Logistic regression giving ORs and 95% CIs for risk of overweight at 7yrs by rate of weight gain from birth to 4mo, and wt at 1yr. Adjustment for bwt, maternal BMI & educ. and others. Infant feeding considered in a separate analysis with 5479 Ss – including it did not significantly alter the results.
Poskitt (1977)[29] *BMJ* Dudley, UK MEDLINE	Prospective cohort study of assoc. betw. obesity in infancy and in early childhood. Popn. based; original cohort was a 10% sample of infant popn in Dudley county borough.	203 Ss born during 1968-70 from an original sample of around 20 infants from each welfare clinic in the borough. 49% male; all Ss white British – this may be due to selection bias. All Ss had bwts ≥2.5kg; no mean bwt or gest. age info. SES distn. similar to that of 1966 census for Dudley. Incl/excl fairly clear. 68% FU. Numbers and reasons for losses & exclusions given, but no comparisons with study Ss.	Infancy: size (ht & wt) at around 5mo, measured by a single researcher using standard equipment at welfare clinics. Shukla (percentage ht-for-wt ratio) & Eid (percentage wt at age when ht is at 50th centile) indices used, using Tanner reference standards. Outcome: same measurements, at around 5yrs.	Numbers & percentages given in text, allowing contingency tables and ORs and RRs for risk of childhood obesity for obese infants compared to non-obese infants. No consideration of confounding factors.
Stettler (2002)[30] *Int J Obesity* Seychelles MEDLINE	Retrospective cohort study of assoc. betw. rapid infant growth and risk of childhood obesity. Target popn was all Ss in all schools on the islands in one of 4 specific school grades (years).	2573 Ss who were in one of 4 specific school grades in 1999. Of the 5514 Ss with outcome measurements, 49% were male, and mean bwt & gest. age were normal. No race info, but parental size & educ. given, plus family size & birth order. No incl. criteria other than relevant measurements. 39% FU. States that losses mainly due to nurse unavailability, and analyses using imputed values for missing data gave similar results to those presented, so local generalisability was good.	Infancy: size (weight) at birth & 1yr, obtained from medical records, measured by clinic nurses. Growth over 1st year calculated as diff between 1yr wt & bwt. Outcome: overwt & obesity at 4.5 to 17.4yrs, defined using International Obesity Task Force criteria for age & sex (corresponding to 25 & 30kg/m^2 at 18yrs). Ht & wt measured at schools using standard equipment by trained & supervised nurses.	Logistic regression giving ORs and 95% CIs for risk of childhood overweight & obesity by first-year weight gain, adjusting for sex, age, parental occupation & maternal BMI. Other vars, including bwt, gest. age & first-born status, assessed in a separate analysis & found not to be associated with outcome.

Table 3.2A (i) (continued). Description and quality assessment of studies included in review of infant size/growth and childhood obesity

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Mellbin (1973)[31] *Brit J Prev Soc Med* Uppsala, Sweden MEDLINE	Retrospective cohort study of assoc. betw. infant weight gain and risk of childhood obesity. Popn based; source popn. was all 7-yr-olds in schools in a single city for whom infant health records available.	972 Ss starting elementary school in the autumn of 1970 in city of Uppsala. 48% male; mean bwt normal. No further baseline info, incl. race & gest. age. No incl. criteria other than being in school & having suitable infant health records – clearly stated. 76% FU. States that losses were mainly due to incomplete health records from being born elsewhere or spending a large part of their infancy in day nurseries, but no further non-participant info.	Infancy: growth (wt gain over 1st year of life). Wt measured in clinics using standard equipment, but no info on people or reliability. 'Rapid' growth defined in 3 different ways – main model used a total wt gain of ≥7.5kg. Outcome: Overwt at 7yrs, defined as wt 10-20% above standard wt for ht, using charts of Tanner. Obesity defined as wt >20% above standard. Same procedure as in infancy.	Relative risks for childhood obesity by infant weight gain ('rapid' or 'normal'), plus contingency tables. 3 different definitions of 'rapid' weight gain used. No consideration of confounding factors.
Eid (1970)[32] *BMJ* Sheffield, UK Reference list	Retrospective cohort study of assoc. betw. infant weight gain and risk of childhood obesity. Source popn was births in a single city hospital, but target popn was infants following one of 3 specific growth patterns.	224 Ss born at Jessop hospital in Sheffield in 1961 with specific growth patterns. 54% male; no race info. Mean bwt normal; all Ss had gest. age ≥38wks. No further baseline info. Original incl/excl criteria fairly clear, but authors state that only a subset of original cohort were "intended for study" – presumably those with the specific growth patterns, although not made clear. 47% FU of this smaller target popn. These losses compared with study Ss for bwt within each growth category; no sig diffs.	Infancy: growth (wt gain over first 6mo of life). Data obtained from baby clinics - no further info. 'Rapid' growth defined as wt gain >90th percentile; 'average' = around 50th percentile; 'slow' = <10th percentile. Outcome: Obesity/overwt at around 8yrs. Obesity defined as wt >20% over expected for ht and sex; overwt = wt >10%. Most Ss measured at the hospital using standard procedure & equipment; data obtained from school records for the rest.	Contingency tables comparing numbers of obese children in each of the infant growth categories, from which ORs or RRs can be derived. Also tables controlling for bwt, infant ht & parental overweight. Sex, infant feeding, bwt & parental overwt related to outcome – no sig results. No actual adjustment for confounders.
Asher (1966)[38] *Arch Dis Child* Birmingham, UK Reference list	Retrospective cohort study and case-control study of obesity in infancy & early childhood, but design not entirely clear. Source popn. was children who attended infant welfare centres "in various parts of Birmingham", but not adequately defined.	137 Ss who attended welfare clinics "regularly" from infancy to ≥3yrs; no further baseline info at all. Since source popn is also ill-defined, selection bias is likely. Also: 21 cases of infant obesity & 24 controls from same source popn. Mean bwt normal, with no sig diff betw. cases & controls. No further baseline info. 55% FU for cases, 63% for controls – these losses all due to unavailable school medical records.	Infancy: size (wt & ht) at 6mo. Data from infant welfare centre records; no further info. Obesity defined as wt >90th centile for cohort, but as wt >97th centile for case-control. Authors state that 90th was used for cohort instead of 97th due to small cell counts. Outcome: obesity at 3 to 5yrs, defined similarly to that in infancy. Ht & wt data from school medical records. Rounding considered likely.	Numbers & percentages given in text, allowing contingency tables and ORs and RRs for risk of childhood obesity for obese infants compared to non-obese infants. No consideration of confounding factors.

Table 3.2A (i) (continued). Description and quality assessment of studies included in review of infant size/growth and childhood obesity

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Mei (2003)[34] *Sozial- & Praventivmedizin* Various, USA MEDLINE	Longitudinal cohort study of the tracking of obesity from infancy into childhood. Source popn. was records from a large-scale national child health database.	380,518 Ss born during 1985-90 and participating in one of various publicly funded health & nutrition programs that contribute to the national database. Small risk of selection bias since "programs with variations in eligibility and take-up" were used. 51% male; 47% non-Hispanic white. Mean bwt normal; no gest. age info. All were low-income, but no further SES or other baseline info. Incl/excl criteria clearly stated – lack of relevant data or extreme wt-for-ht scores. 78% FU. No comparisons betw. study Ss and non-participants.	Infancy: size (wt & ht) betw. 0 & 11mo. Measured according to WIC protocols by trained staff. Wt rounded to nearest ¼lb; ht to nearest ¼in. All m'ments done twice; must agree to within the above amounts. Scale of study & lack of inter-observer reliability info means measurement bias possible. Obesity defined as wt-for-ht ≥95th percentile using CDC standards. Outcome: obesity at each of 12-23mo, 24-35mo, 36-47mo & 48-59mo. Procedure & obesity definition as for infancy.	Percentages and relative risks given for childhood obesity by infant obesity category. No errors or confidence intervals given, but presumably all significant due to scale of study. Stratified for bwt; sex & race examined in separate analyses, but no actual adjustment for confounders.
Johnston (1978)[35] *Am J Dis Child* Philadelphia, USA Reference list	Prospective cohort study of assoc. betw. 1-yr wt & obesity in early adolescence. Source popn was a single city hospital contributing to a large national perinatal study.	798 Ss registered into the study in infancy during 1960-65. 51% male. No bwt or gest. age info. All were black. No further baseline info. Main incl. criterion was extreme relative wt (high or low) at 1yr. 84% FU of Ss fulfilling this criterion. No comparisons betw. study Ss and non-participants.	Infancy: 1-yr wt regressed on 1-yr ht; only Ss with wt-for-ht < -1 (low) or > +1 SD (high) relative to original cohort of 6600 were included. Data ascertained as for Stettler (2002). Outcome: Obesity at 9-15yrs, defined in 2 different ways: (1) triceps skinfold >90th centile for age, sex & race; (2) relative wt (= predicted wt/actual wt) ≥120%, using US Health Examination Survey data in both cases. No info on ascertainment of data.	Cell counts for obesity in each age group from 9 to 15yrs for low & high relative weight at 1yr, stratified for sex. ORs and RRs able to be calculated. No consideration of confounders other than sex.
Wilkinson (1977)[36] *Lancet* Newcastle-upon-Tyne, UK Reference list	Case-control study of infant size amongst obese & non-obese children. Source popn. for both cases & controls was a larger longitudinal study of child development.	48 cases & controls, individually matched for age, sex & school, all born during 1960-62 & all taking part in a larger study. 42% male; no race info. No bwt or gest. age info given apart from the fact that 20% had bwts-for-gest. age >90th centile. SES profile was roughly similar to that of larger study popn, but more cases than expected were from ? social classes. 30% FU for cases (& therefore for controls, as individually matched), all due to missing infant size data. All Ss fulfilling obesity criteria were originally selected as cases.	Infancy: size (weight) at 6mo & 1yr, from child health clinic records. No further info. Weights compared to reference charts of Tanner*. Outcome: obesity at 10yrs, defined as wt-for-ht >97th centile using tables of Scott*. Controls defined as wt-for-ht 25th-75th centile. Data collected as part of the larger study; no further info.	Numbers & percentages of cases & controls defined as obese at 6mo and 1yr. No statistical analysis. Parental size, SES & family structure compared betw. cases & controls for Ss born in 1961.

Table 3.2A (ii). Summary data extracted from studies included in review of infant size/growth and childhood obesity

Details	*Design and Participants*			*Size of effect measure (relative risk unless otherwise stated)*				
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Birthweight (kg) & gestation (wks)	Exposure(s)	Outcome	Other info	RR (95% CI)	Summary of trend
Stettler (2002)[28] *Pediatrics* Various, USA MEDLINE	19,397 (50% male)	70	Both median (25th to 75th percentile): Bwt: 3.23 (2.41 to 4.20) GA: 40 (37 to 42)	Weight at 1yr (100g) Growth from birth to 4mo (100g/mo)	BMI > 95th percentile for age and sex	Unadjusted Adjusted Unadjusted Adjusted N.B. Adjustment was for sex, birthweight, maternal BMI & education, the other size/growth variable, and others.	Odds ratios: 1.05 (1.04, 1.05) 1.50 (1.38, 1.63) 1.29 (1.25, 1.33) 1.17 (1.11, 1.24)	Positive association (**growth**)
Poskitt (1977)[29] *BMJ* Dudley, UK MEDLINE	203 (49% male)	68	All birthweights were ≥ 2.5kg	Percentage weight at age when height is at 50th centile, measured at around 5mo (>120%)	Same, at around 5yrs		9.38 (1.64, 53.6)	Positive association (**size**)
Stettler (2002)[30] *Int J Obesity* Seychelles MEDLINE	5514 (49% male)	47	Both median (10th to 90th percentile): Bwt: 3.13 (2.54 to 3.74) GA: 40 (38 to 40)	Weight gain during the 1st year of life (kg)	Obesity, using International Obesity Task Force charts at ages 4.5 to 17.4yrs	Unadjusted Adjusted N.B. Adjustment was for age, sex, maternal BMI and parental occupation.	1.62 (1.39, 1.88) 1.59 (1.29, 1.97)	Positive association (**growth**)
Mellbin (1973)[31] *Brit J Prev Soc Med* Uppsala, Sweden MEDLINE	465 males 507 female	76	Birthweights (mean; SD) 3.50 (0.50) 3.37 (0.54)	Weight gain over 1st year of life ≥ 7.5kg Weight gain over months 1-4 & 9-12 >97th percentile for age	Weight > 20% above standard for height at 7yrs	Males Females Males Females	2.32 (0.76, 7.07) – NS 1.72 (0.60, 4.94) – NS 16.9 (4.70, 61.0) 1.33 (0.46, 3.86) – NS	Inconclusive (**growth**)
Eid (1970)[32] *BMJ* Sheffield, UK Reference list	224 (54% male)	47	Birthweight (mean) 3.41	Weight gain >90th percentile over first 6mo of life	Weight >20% over expected for height and sex at around 8yrs		4.05 (0.94, 17.5) – NS	No significant association (**growth**)
Asher (1966)[38] *Arch Dis Child* Birmingham, UK Reference list	137 (no sex info) 21 cases 24 controls	NG 55 63	NG Birthweight (mean; SD) 3.6 (0.56) 3.3 (0.56)	Weight >90th centile at 6mo Weight >97th centile at 6mo	Weight >90th centile at 3-5yrs Weight-for-height >97th centile at 5yrs		9.33 (0.52, 167) – NS 6.56 (2.90, 14.8)	Inconclusive (**size**)

Table 3.2A (ii) (continued). Summary data extracted from studies included in review of infant size/growth and childhood obesity

Details	*Design and Participants*			*Size of effect measure (relative risk unless otherwise stated)*				
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Birthweight (kg) & gestation (wks)	Exposure(s)	Outcome	Other info	RR (95% CI)	Summary of trend
Mei (2003)[34] *Sozial- & Praventivmedizin* Various, USA MEDLINE	380,518 (51% male)	78	Birthweight (mean; SD) 3.26 (0.60)	Weight-for-height ≥ 95th percentile at 0-11mo (1) Weight-for-height ≥ 95th percentile at 12-23 mo (2)	Weight-for-height ≥ 95th percentile at 24-35 mo (3) Weight-for-height ≥ 95th percentile at 36-47 mo (4)	(1) and (3) (1) and (4) (2) and (3) (2) and (4)	3.3 (NG) 2.9 (NG) 6.5 (NG) 5.2 (NG)	Positive association (**size**)
				Also: Relative risks are highest in the low-birthweight group (< 2.5kg) and lowest in the high-birthweight group (≥ 4kg). However, the high-birthweight group had the highest prevalence of becoming/remaining overweight at later ages.				
Johnston (1978)[35] *Am J Dis Child* Philadelphia, USA Reference list	798 (51% male)	84	No info given	Weight-for-height > +1 SD at 1yr, compared to < –1 at 1yr.	At 9-15yrs: Relative wt (predicted wt/actual wt) ≥120% Triceps skinfold >90th centile for age, sex & race	 Males Females Males Females	 3.75 (2.15, 6.54) 4.06 (2.52, 6.53) 2.97 (2.03, 4.35) 2.70 (1.74, 4.17)	Positive association, for both sexes (**size**)
				NB: Similar data also given for each age from 9 to 15yrs individually.				
Wilkinson (1977)[36] *Lancet* Newcastle-upon-Tyne, UK Reference list	48 cases 48 controls (42% male)	30% 30%	20% had bwts-for-gest. age >90th centile; no further info	Measurement 6mo weight (n=48) 12mo weight (n=42)	OR for obesity: 2.00 (0.88, 4.56) – NS 1.62 (0.63, 4.15) – NS			No association (**size**)

Table 3.3A (i). Description of studies included in review of infant head size/growth and cognitive development

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Koller (1997)[39] *Pediatrics* New York, USA MEDLINE	Prospective cohort study of VLBW Ss, identifying patterns of cognitive dev. and their assoc. with vars including infant **head size**. Setting was 3 NICUs. Target popn. was 203 Ss "recruited" from the NICUs.	203 VLBW (<1.5kg) infants born during 1975-89. Mean bwt given; mean gest. age was quite low (30.9wks). 45% male; 9% white (mostly Afr-Am & Latino). Maternal education also given at baseline; only 26% had any higher educ. No explicit incl/excl criteria. Clusters (see 'Analysis') defined using 203 Ss, but head size m'ments only available for 150; thus %FU seen to be 74%. No comparisons betw. those Ss with & without head size data, nor any other non-participant info.	Infancy: Size (HC*) at 1yr (corrected age), measured at NICU. No further reliability info, but head circ. categorised as ≤ or > 10th percentile using growth charts by sex. Outcome: Cognition, ascertained using Bayley MDI (12 & 24mo), Stanford-Binet IQ (3 or 4yrs) and Wechsler WISC-R (5 or 6yrs). No further reliability info.	Cluster analysis used to identify 5 groups with relatively similar patterns of cognitive dev. Various vars incl. 1-yr head size, sex & maternal educ. compared separately across clusters using ANOVA and chi-squared tests. No SES or infant feeding info.
Ford (1986)[40] *Early Hum. Dev.* Melbourne, Australia PsycINFO/ MEDLINE	Prospective longitudinal study of ELBW Ss exploring outcomes incl. sensory & cognitive dev. in relation to poor post-natal growth & IUGR. Set in a single hospital; target popn. was survivors at 2yrs.	83 ELBW (<1kg) infants born during 1977-82. Unclear as to whether source popn of 257 were all that could have been selected. Mean bwt given; mean gest. age was very low (27.5wks). No sex info. All Ss were Caucasian; SES profile was normal. Only incl. criteria were ELBW & survived to 2yrs; no discussion. 97% FU. Stated that the 3 losses to FU were all AGA with normal growth when last seen, and that their inclusion would have little effect on results or conclusions.	Infancy: Size (wt, ht & HC*) at 2yrs, measured by a paediatrician. Info on methods & rounding (wt to 0.1kg; ht/length to 0.1cm). Outcome: Cognition (Bayley MDI) at 2yrs ascertained by psychologist, plus presence of motor or sensory disability assessed by same paediatrician as took size m'ments.	Tables of numbers & percentages of Ss with disabilities and mean MDI by 2yr wt. Tables of certain health vars by 2yr wt, but no important confounders considered. Linear regression giving correlation coeffs betw. head size & MDI at 2yrs.
Fisch (1976)[41] *Am J Dis Child* Minnesota, USA MEDLINE	Prospective cohort study using Minnesota data from the larger perinatal study used in Nelson. Investigated factors assoc. with 7-yr IQ, incl. infant size. Setting was a single university hospital; source popn. unclear.	2023 infants born at University of Minnesota hospitals 1959-66. Mean bwt normal & gest. age normal. No sex info. 94% white. States that SES profile representative of general popn, but no data given. Incl/excl criteria clearly stated. %FU unclear, as size of original Minnesota cohort not given. Numbers given for each analysis suggest losses to FU, but no info given.	Infancy: Size (ht, wt & HC*) at 4mo & 1yr, measured by trained nurse but no further reliability info. Outcome: Cognition (Wechsler WISC short form) at 7yrs. No further reliability info.	Tables of means & correlations betw. infant size (continuous) & IQ, categorised as 'superior' (≥ 120), 'average' (80-119) & low (≤ 79). Many other vars, incl. parental education & IQ, SES, family income compared betw. IQ gps, but no adjustment for them with infant size.

* HC = "head circumference"

Table 3.3A (i) (continued). Description of studies included in review of infant head size/growth and cognitive development

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Fernandez-Carrocera (2003)[42] *Nutrition Research* Mexico City, Mexico EMBASE	Nested case-control study based on cohort of Ss from a single NICU, assessing assoc. betw. neurological impairment and factors incl. IUGR & infant size. Target popn. was a random sample of all suitable IUGR infants plus equal no. of matched controls.	154 Ss (77 IUGR cases, 77 controls) hospitalised at birth in a single NICU. Cases randomly selected from all IUGR Ss fulfilling incl. criteria; controls paired by gest. age (+/- 1wk). Mean bwt of cases very low (<1.5kg); that of controls low (<2.5kg). Mean gest. age was borderline preterm (36wks). No sex info; all parents were Mexican. Incl/excl criteria stated clearly. All selected Ss were used, but no info on size of original cohort or representativeness of sample.	Infancy: Size (wt, ht & HC*) at 1yr; growth (change in size betw. birth & 1yr relative to birth size). All m'ments by same researcher according to standard methods. Outcome: Well-validated neurologic, neuromotor, communication & psychological evaluations at 1yr. 'Neurological alteration' presumably defined as ≥1 abnormal result, though this is unclear. No info on observers.	Numbers, percentages & unadjusted ORs of Ss with 1-yr 'neurological alteration' by factors incl. low wt-for-age & low HC at 1yr. Stepwise logistic regression controlling for IUGR & SES (head of family unemployed).
Pryor (1996)[43] *J Reprod. Infant Psychol.* **Auckland, New Zealand** PsycINFO	Prospective longitudinal study comparing SGA and AGA Ss. Also examines correlation betw. **head size** & cognition in infancy. Set in a single hospital. Source popn. unclear as Ss were "recruited".	64 infants (46 SGA and 18 AGA) "recruited" at birth from neonatal wards. Mean bwt & gest. age normal for AGA. SGA Ss had borderline low bwt (mean 2552g) and normal gest. age (although sig. diff from AGA Ss). 48% male (similar %s in SGA/AGA subgps). Maternal age & smoking status also given. No explicit incl/excl criteria except AGA & SGA definitions. 75% FU at 12mo. No info on non-participants or original source popn.	Infancy: Size (wt, ht & HC*) at 12mo. Description of instruments given, but nothing else. No rounding info. Outcome: Cognition (Bayley MDI & PDI) at 1yr, plus composite Infant Behaviour Record (IBR). No further reliability info.	Stepwise regression analyses for SGA & AGA subgps separately, adjusting for exercise in pregnancy, mutual object & global affection (considered comparable to maternal educ.). SES found not to be correlated with exercise in pregnancy, but was not then included in regression.
Camp (1990)[44] *Dev. Behav. Pediatr* Denver, USA MEDLINE	Cross-sectional study assessing the assoc. betw. size and attentional behaviour in infancy. Set in a single pediatric clinic. Target popn was all 4-6mo old infants attending the clinic when an examiner was present.	57 infants attending a university hospital paediatric clinic. Mean bwt was normal; no gest. age info. 49% male. Age at time of clinic visit ranged from 15.1 to 28.5wks (3.5-6.5mo); no mean age given. No further baseline info. No incl/excl. criteria. In return for participation, families were not charged for that clinic visit. "There were no refusals." Hence no %FU info. No info on size of source popn. or representativeness of sample relative to all infants attending clinic.	Infancy: Size (wt, ht & HC*) at time of clinic visit. Measured at clinic; no further info. Outcome: Measures of attention to visual stimuli at time of clinic visit, referred to as 'Initial Fixation' and 'Response Decrement'. Detailed info on procedure and reliability.	Matrix of correlations betw. outcomes and all infant size measures plus sex & age. Stepwise multiple regression, using potentially all variables, giving *F*-, *p*- & r^2-values. No confounders considered important by this review were assessed.

* HC = "head circumference"

Table 3.3A (i) (continued). Description of studies included in review of infant head size/growth and cognitive development

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Nelson (1970)[45] *Dev. Med. Child Neurol.* Various, USA MEDLINE	Prospective cohort study of assoc. of head size in infancy with childhood IQ. Setting was 12 university hospitals. Source popn. was the offspring of a random sample of pregnant mothers registered on a national perinatal study.	9379 subjects born during 1959-64. Mean bwt not given, but over 90% of Ss had bwts ≥2500g. No gest. age info, but no exclusions made on basis of gestation. Ss mostly urban. 51% male; 44% white. Incl/excl criteria stated briefly; no discussion. %FU unclear, but likely to be low, since 60,000 pregnant women originally registered. No info on non-participants, but SES profile (given in earlier paper§) seems to be fairly representative of US population.	Infancy: Size (HC*) at 1 year, measured using standard procedure. No further reliability info. Rounded to nearest whole centimetre below. Outcome: Cognition (Stanford-Binet IQ) at 4yrs. Use of test flawed, as standardisation popn. was all white, and likely to have been better educated than the study Ss.	Tables of mean 4-yr IQ by 1-yr head size, sex, race and maternal education. Tables of mean 1-yr head size by 4-yr IQ, race and sex. No statistical analysis at all, so no formal adjustment for confounders.
Lasky (1981)[46] *Child Development* Rural villages in Guatemala. MEDLINE	Prospective cohort study exploring correlations betw. infant size & behavioural dev. Setting was 4 rural villages in a developing country; target popn. was all live births in the villages during study period.	709 subjects born (alive) during 1969-73. No baseline data, but description of setting states that breast-feeding was universal and undernutrition endemic. Bwt also differed by sex, but no data given. No explicit incl/excl criteria. Since betw. 284 and 419 Ss used in different analyses, %FU was betw. 40% & 59%. No non-participant info.	Infancy: Size (wt, ht, HC*, skinfold) at 6, 15 & 24mo. All m'ments taken by trained & standardised researchers; detailed info of methods & reliabilities (all high) given. Outcome: Composite Infant Scale (CIS)† at 6, 15 & 24mo. Scale standardised for Guatemalan popn, and details of procedure & reliability (high) given.	Multiple regression analyses giving correlation coeffs for assoc. betw. all combinations of age and size measure and CIS; for wt & ht controlling for wt or ht at earlier ages; and betw. CIS & various other factors incl. sex, bwt & parental size (but not infant feeding).
Lucas (1992)[47] *NEJM* Various, UK PsycINFO	Prospective data, from VLBW participants in a nutritional RCT, exploring correlations betw. infant size & later cognition. Setting was medical facilities in 5 UK towns & cities; target popn. was all participants in the RCT with relevant data.	926 VLBW (<1.5kg) infants born since 1983. Bwt & gest. age data given for some of the 5 centres, & suggest that mean gest. age was quite low (30-32wks). No further baseline info. Incl/excl criteria for RCT given in detail in a previous paper. Between 338 and 773 Ss used in analyses, giving %FU range of 37% to 83%. No info on non-participants in different analyses, except that data from some of the 5 centres sometimes missing.	Infancy: Size (HC*) at 9 & 18mo. No further info, but should be adequate if done as part of a RCT. Outcome: Cognition, ascertained by Knobloch's Developmental Quotient‡ (9mo), Bayley MDI (18mo) and WISC-R (7½-8yrs). As for infancy measures, no reliability info but should be adequate.	Correlations between infant head size and cognition at 3 different ages. Multiple regression to assess relation betw. infant head size and bwt, SES & neonatal risk factors, but no direct adjustment. No infant feeding or maternal IQ info.

* HC = "head circumference"

§ see Myrianthopoulos NC, French KS. An application of the US Bureau of the Census socioeconomic index to a large, diversified patient population. *Soc. Sci. Med.* 1968;**2**:283-99.

† a composite measure of mental and motor development constructed by selecting items from various well-known infant development scales including Bayley, Gesell and Stanford-Binet. See Stott ZH, Ball R. Infant and preschool mental tests: review and evaluation. *Monograph of the Society for Research in Child Development* 1965;**30**

‡ see Knobloch H, Pasamanick B, Sherard ES Jr. A developmental screening inventory for infants. *Pediatrics* 1966;38 Suppl:1095-108

Table 3.3A (i) (continued). Description of studies included in review of infant head size/growth and cognitive development

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Ernhart (1987)[48] *Psychol Rep* Cleveland, USA PsycINFO	Prospective cohort study, following up Ss from an alcohol-related birth defect study, assessing the assoc. betw. size and cognition in infancy & young childhood. Setting & source popn. unclear.	359 infants from an alcohol-related birth defect study. No bwt info, but all were full-term (>37wks). 37% were black; all were "disadvantaged", and 50% of mothers had alcohol-related problems (by design of earlier study). Attrition & missing data mean that betw. 219 and 264 Ss used in different analyses, so %FU is betw. 61% & 74%. No info on non-participants or original source popn.	Infancy: Size (wt, ht & HC*) at 6mo, 1yr & 2yrs. No further info, and no rounding info. Outcome: Cognition, ascertained by Bayley MDI (6 mo, 1yr & 2yrs) and Stanford-Binet IQ (3yrs) at home by trained examiners.	Correlation coeffs. betw. each size measure at each of 6mo, 1yr & 2yrs and cognition at each of 6mo & 1, 2 & 3yrs, both unadjusted and adjusted for 37 potential confounders incl. sex, race & maternal IQ (plus SES of all Ss is known to be low). *p*-values given.
Stathis (1999)[49] *Dev. Med. Child Neurol.* Brisbane, Australia MEDLINE	Prospective cohort study of ELBW Ss, assessing relationship betw. **head size** in infancy and learning & cognition at school age. Set in a single hospital. Target popn. was all healthy ELBW discharges.	87 ELBW (< 1kg) infants born during 1977-88. Mean bwt given; mean gest. age was very low (27.7wks). 36% male. Incl/excl criteria stated briefly; no discussion. 28% FU. Losses to FU compared to study Ss in terms of bwt, HC at birth & during infancy, and gest. age – no sig diffs. Low education & intellectual ability and disabilities more prevalent amongst mothers lost to FU, but diffs not stat sig. 6-yr GCI only available for 70 Ss, of which 3 more excl. due to severe disability. No info on the 17 without GCI info, but none of the further 3 Ss had abnormal head sizes in infancy.	Infancy: Size (HC*) at 4, 8, 12 & 24mo, measured at hospital research unit. No further reliability info. No rounding info given. Outcome: Learning problems "at school age", ascertained by ANSER questionnaire completed by teachers† (no info on whether trained or standardised); cognition at age 6 years, ascertained by McCarthy GCI.	Tables of percentages of Ss with various academic problems, and mean GCIs, by head size in infancy. Logistic regression giving ORs for learning diffs; linear regression for mean GCI. Both adjusted for many confounders, incl. sex & parental educ but not SES or infant feeding.
Hack (1986)[50] *Pediatrics* Cleveland, USA MEDLINE	Later FU of SGA Ss from cohort in study by Hack (1982), assessing relationship betw. **head size** in infancy and childhood IQ. Target popn. was all those surviving to 3yrs.	139 SGA VLBW (< 1.5kg) infants admitted to an NICU during 1977-78. Same source popn. as in Hack (1982). Mean bwt given; mean gest. age was very low (29.1wks). 47% male; 52% had black mothers. Other maternal and perinatal vars given at baseline, incl. maternal age & educ. Main excl. criterion was SGA; stated clearly with discussion. 45% FU. Numbers & reasons given for losses to FU, but no comparisons with study Ss.	Infancy: size (ht, wt & HC) at corrected ages 8 & 20mo. Wt categorised as normal or subnormal (≥ or < –2 SD) using growth charts of Babson & Benda (1976)*. No info on observers or reliability. Growth betw. 8 & 20mo also used in analysis. Outcome: Cognitive development, ascertained by Stanford-Binet scales at 33mo (≈ 3yrs). No info on observers, reliability or blinding.	Tables of means, with F- and *p*-values. ANOVA for growth between 8 & 20mo. 'Path analysis', giving unstandardised partial regression coeff, adjusting for neonatal risk, neurologic impairment, race, SES and "other residual variables".

* HC = "head circumference"
† for details of the questionnaire, see Levine MD (1985). *School Questionnaire for Developmental, Behavioural and Health Assessment of the Elementary School Child*. Boston, MA: The Censor System. Educators Publishing Service.

Table 3.3A (i) (continued). Description of studies included in review of infant head size/growth and cognitive development

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Ong (1997)[51] *Ann Trop Paediatr* Kuala Lumpur, Malaysia MEDLINE	Prospective cohort study comparing VLBW & normal bwt Ss. Also examines relationship betw. head size & neurodev. in infancy. Set in a single hospital. Target popn. was all VLBW Ss & a random sample of normal-bwt Ss from same hospital.	201 infants (103 VLBW, 98 normal bwt) born in a single hospital from late 1989-92. Good baseline info incl. mean bwt & gest. age (VLBW Ss were preterm on average; normal-bwt Ss had normal gest. age) plus sex, race & maternal age. 51% male (48% for VLBW, 53% for normal-bwt). Incl/excl given, but not clearly. 34% FU (25% for VLBW, 56% for normal-bwt). No sig diffs in bwt, gest. age, head size at birth, sex, race or maternal age betw. study Ss & losses to FU in either bwt group (although only small no. of VLBW losses from original popn compared in this way).	Infancy: Size (HC*) at 3, 6 & 12mo, assessed by one of 2 researchers using standard methods & rounded to nearest 0.1cm. No info on inter-observer reliability. Outcome: Cognition (Bayley MDI & PDI) at 1yr, ascertained by a single child psychologist, blind to perinatal course & therefore possibly to infant size data too.	Stepwise multiple regression for 1-yr MDI & PDI, adjusting for various factors incl. maternal education & bwt. SES previously found to be unrelated to 'neurological disability' (not directly relevant to review as incl. factors such as cerebral palsy). Regression coeffs, CIs & p-values given.
Gale (2004)[52] *Brain* Southampton, UK From expert.	Prospective cohort study assessing the assoc. betw. infant **head size** & IQ in childhood. Set in a single antenatal clinic. Target popn. was offspring of all mothers who took part in a previous study.	221 infants whose mothers took part in a study of nutrition during pregnancy during 1992-93. Mean bwt was normal; 7.7% were premature. 53% male; all mothers were Caucasian. Baseline data on size of family, SES, maternal education & infant feeding. Incl. criteria of previous study used, plus FU at 9mo. 40% FU. Losses to FU compared for SES, bwt, & head size at various ages; no sig diffs from study participants. No info on original selection of mothers.	Infancy: Size (HC*) at 9mo, converted to SD score. Growth (birth to 9mo) assessed by regressing 9-mo head size on head size at birth. Good procedures followed; inter-observer reliability good. Outcome: Cognition (Wechsler WAIS) at 9yrs, assessed at home by member of research team. No inter-observer reliability info.	Multivariate linear regression giving coeffs for increase in IQ for each SD increase in infant head size or growth, adjusted for sex, SES, parental education & infant feeding, along with many others. CIs & *p*-values given.
Bendersky (1998)[53] *Clinical Pediatrics* New Brunswick, USA MEDLINE	Prospective cohort study assessing the assoc. betw. **head size** & development in infancy in preterm Ss with & without intra-cranial haemorrhage (ICH). Setting & target popn. unclear.	125 preterm infants born during 1985-87. Mean bwt was very low (<1.5kg); mean gest. age was <32wks. 50% male. SES profile seems normal. No race info. Incl/excl criteria clearly stated. Target popn. "recruited" from larger popn, but no details given. 30% FU of source popn, or 48% of "recruited" Ss. Losses to FU (from "recruited" Ss) compared for ICH prevalence, bwt, gest. age, SES, % firstborn & sex; no sig diffs from study participants.	Infancy: Size (HC*) at 1yr (corrected; mean 11.7mo), categorised into 'low' (≤ –2 SD) or 'normal'. Info on people & method; inter-rater reliability high. Outcome: Cognition (Bayley MDI & PDI) at 1yr ascertained by a single psychologist, blind to ICH status & therefore possibly to infant head size data too.	Tables of numbers & percentages in each cell defined by head size (low or normal) and MDI or PDI, categorised as low (< –2 SD), borderline (< –1 SD) or normal. Multiple regression giving coeffs adjusted for SES and others, but not sex, maternal education or infant feeding.

* HC = "head circumference"

Table 3.3A (i) (continued). Description of studies included in review of infant head size/growth and cognitive development

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Hack (1991)[54] *NEJM* Cleveland, USA Reference list	Extension of study by Hack (1986), with a larger birth cohort and later childhood FU. Assessed relationship betw. **head size** in infancy and childhood IQ.	249 VLBW (< 1.5kg) infants admitted to an NICU during 1977-79. Extension of 1977-78 cohort used in Hack (1986). Mean bwt given; mean gest. age was very low (29.7wks). 50% male; 56% had black mothers. Other maternal and perinatal vars given at baseline, incl. maternal age & educ. No excl. criteria used. 79% FU. Non-participants compared to study Ss on all baseline vars; only sig diff was that mothers of study Ss more likely to be black.	Infancy: as for Hack (1986), but growth betw. 8 & 20mo not used. Outcome: Cognitive development, ascertained by Wechsler WISC-R scale at mean age 8.6yrs. No info on observers, reliability or blinding.	Tables of means and differences, with 95% CIs, for development scores between "normal" & "subnormal" 8-mo HC groups. Hierarchical multiple regression giving unstandardised *β*-coeffs & *p*-values for assoc. betw. 8-mo HC and 8-yr development, adjusting for SES and bwt.

Table 3.3A (ii). Summary data extracted from studies included in review of infant head size/growth and cognitive development

Details	*Design and Participants*				*Main Findings*						
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)	General Description						Conclusion
Koller (1997)[39] *Pediatrics* New York, USA MEDLINE	203 (45% male)	74	1.17 (NG*) VLBW	30.9 (NG*) (Very preterm)	In terms of % of Ss with 1-yr HC* <10th centile: Highest % is for "very low stable" cluster (68%); lowest is for "average stable" (18%). The other 3 clusters, in which cognition changes in some way from 1-6yrs, have %s of betw. 21 & 32%. Chi-sq for trend (across clusters) = 15.3; p<0.005.						**Head size** at one year appears to be positively associated with increased cogntive function up to 6 years of age.
Ford (1986)[40] *Early Hum. Dev.* Melbourne, Australia PsycINFO/ MEDLINE	83 (%male not given)	97	0.86 (0.01) range 0.57 to 0.99 ELBW	27.5 (2.2) range 24-32 (Extremely preterm)		Statistic	p-value				Did not show an association between poor **post-natal growth** and MDI, but sample was relatively small and so may have been underpowered, since raw data suggests otherwise.
					Mean diff in 2-yr MDI by weight (low – normal)	-3.0	NS*				
					2-yr HC* correlation with 2-yr MDI	*r* = 0.03	NS*				
					Raw data: Ss of low 2-yr weight (<3rd %ile) had mean MDI of 87.4, and 22% had an MDI of <69. Corresponding figs for normal 1-yr weight gp were 90.4 and 8.3%. Does seem to be a definite difference.						
Fisch (1976)[41] *Am J Dis Child* Minnesota, USA MEDLINE	2023 (%male not given)	NG*	3.30 (0.54) (Normal)	40 (2.7) (Normal)	Mean diffs (7-yr IQ gp)	Superior – average	p-value	Average – Low	p-value	Correlation with 7-yr IQ	Positive. Larger **head size** assoc with higher 7-yr IQ.
					1-yr HC*	+0.5	p<0.05	+0.3	NS*	0.17	
					1-yr height	+0.3	NS*	+1.4	p<0.05	0.14	
					1-yr weight	0.0	NS*	+0.5	NS*	0.11	
					IQ gps at 7ys: Superior: *n*=258; Average: *n*=1669; Low: *n*=96. 91%FU at 1yr compared to those tested at 7yrs. No *p*-values given for correlations.						
Fernandez-Carrocera (2003)[42] *Nutrition Research* Mexico City, Mexico EMBASE	154 (% male not given)	NG*	2.09 (NG*) LBW	36 (2.0) (Borderline preterm)	Infant size measure		Unadjusted OR (95% CI) for 1-yr neurological alteration				Small **size** (low wt) at 1 year was assoc. with 1-yr neurological alteration (unadj OR); small 1-yr **head size** had a marginal effect. However, logistic regression controlling for IUGR and social factors, suggested otherwise – effect of these may be contained in 'absence of IUGR'?
					Low wt at 1yr (<8.7kg)		5.52 (1.94, 15.70)				
					Low HC* at 1yr (<45cm)		2.58 (1.00, 6.64)				
					When these 2 put into a stepwise logistic regression, they became non-significant; significant vars were IUGR, head of family unemployed, & hospital stay >21days.						

N.B. LBW: < 2500g; VLBW: < 1500g; ELBW: < 1000g. Preterm: <37wks, very preterm: <32wks, extremely preterm: <28wks.
* SD = standard deviation; NG = "not given"; HC = head circumference; NS = "non-significant"

Table 3.3A (ii) (continued). Summary data extracted from studies included in review of infant head size/growth and cognitive development

Details	*Design and Participants*				*Main Findings*	
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)	General Description	Conclusion
Pryor (1996)[43] *J Reprod. Infant Psychol.* Auckland, New Zealand PsycINFO	64 (48% male)	75	2.82 (NG*) (Normal)	39.2 (NG*) (Normal)	Stepwise regression, adding "exercise in pregnancy", then 1-yr HC, then others (so figures given below are partial R- and F-values, adjusting for "exercise in pregnancy"): Group: SGA — R^2: 0.35 (adding 0.12 to "exercise in pregnancy" value); F: 10.4; *p*=0.0002 Group: AGA — R^2: NG*; F: 0.01; NS	For SGA infants, 1-yr **head size** is a significant predictor of 1-yr MDI, accounting for approx 12% of the variance. However, for AGA infants, HC is not significant at all.
Camp (1990)[44] *Dev. Behav. Pediatr* Denver, USA MEDLINE	57 (49% male)	NG*	3.23 (0.49) (Normal)	Not given	Stepwise regression: Initial fixation – best model is Sex + Visit Length. Below, the R^2 value is for the whole model, whilst the F- and p-values refer to the Length term alone. Response decrement: no model involving infant size measures was significant. HC* was not significant in any of these models. Outcome: Initial fixation — R^2 (for whole model; *p*-value): 0.131 (p<0.05); F: 4.05; *p*=0.050	Although growth parameters at the time of the visit accounted for some of the variance in initial fixation and response decrement, **growth** parameters at birth were significantly more important.
Nelson (1970)[45] *Dev. Med. Child Neurol.* Various, USA MEDLINE	9379 (51% male)	NG*	Not given	Not given	Generally, 4-year IQ increased with 1-year HC. An estimate of the average difference in IQ between the smallest-HC group (≤ 43cm) and the largest-HC group (≥ 49cm) is 9 or 10 IQ points. In other words, for each 1cm increase in 1-yr HC, 4-year IQ may be expected to be increased by around 1.5 IQ points. This difference is greatest among those of highly-educated mothers, especially among males, and amongst white subjects. For all HCs and educational levels, black males appeared to have the lowest IQs, and white females the highest. For males of both races there was a tendency for IQ to drop off for the largest HC values; in females this was visible but less pronounced.	HC **size** in infancy appears to be positively associated with later IQ, but no statistical analysis.

* SD = standard deviation; NG = "not given"; HC = head circumference

Table 3.3A (ii) (continued). Summary data extracted from studies included in review of infant head size/growth and cognitive development

Details	*Design and Participants*				*Main Findings*				
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (days) (SD*)	General Description				Conclusion
Lasky (1981)[46] *Child Development* Rural villages in Guatemala. MEDLINE	284 to 419 (% male not given)	40-59	Not given	Not given	HC & Mental CIS (unadj.)	r-value			**Size**, both at the time of the outcome measure and earlier, was positively associated with psychomotor performance, but the size of the correlations are modest.
						HC	Weight	Height	
					6mo – 6mo	0.12 ($p < 0.05$)	0.18 ($p < 0.01$)	0.21 ($p < 0.01$)	
					2yrs – 2yrs	0.18 ($p < 0.01$)	0.29 ($p < 0.01$)	0.35 ($p < 0.01$)	
					6mo – 2yrs	0.15 ($p < 0.01$)	0.19 ($p < 0.01$)	0.20 ($p < 0.01$)	
					Also: Mental CIS at 24mo correlated with 24mo-height controlling for 6-mo & 15mo height respectively as r=0.31 (p<0.01) and r=0.26 (p<0.01). Equivalent results for weight were r=0.28 (p<0.01) and r=0.13 (p<0.05). Motor development: Very similar results all round.				
Lucas (1992)[47] *NEJM* Various, UK PsycINFO	926 (% male not given)	37-83	Not given, but VLBW	Not given, but < 32wks (Very preterm)	HC & DQ/IQ (unadjusted)	r-value (*p*-value)	NOTE: Authors suggest that suggest that it is head *size* rather than *growth* that predicts cognitive performance, and that head size is a measure of social and biologic influences rather than neonatal factors.		**Size**, both at the time of the outcome measure and earlier, was positively associated with IQ.
					9mo – 9mo	0.21 ($p < 0.0005$)			
					18mo – 18mo	0.17 ($p < 0.0005$)			
					9mo – 8yrs	0.29 ($p < 0.0005$)			
Ernhart (1987)[48] *Psychol Rep* Cleveland, USA PsycINFO	219 to 264 (% male not given)	61-74	Not given	Not given, but full-term (>37wks)	Size & MDI (adjusted)	*r*-values for correlation			**Size** (weight & height) at 6mo is correlated most strongly with 6-mo IQ, whereas 6-mo HC is only significantly correlated with 3-yr IQ.
						HC*	Height	Weight	
					6mo – 6mo	0.09 (NS)	0.19 (p<0.01)	0.17 (p=0.01)	
					2yrs – 2yrs	0.09 (NS)	0.15 (p<0.05)	0.06 (NS*)	
					2yrs – 3yrs	0.22 (p<0.001)	0.22 (p<0.001)	0.13 (p=0.05)	
					6mo – 3yrs	0.13 (p=0.05)	0.14 (p=0.05)	0.13 (p=0.05)	
					NB Correlations adjusted for sex, race, maternal IQ and others (plus SES of all subjects is known to be low).				

* SD = standard deviation; NS = “non-significant”; HC = head circumference

Table 3.3A (ii) (continued). Summary data extracted from studies included in review of infant head size/growth and cognitive development

Details	*Design and Participants*				*Main Findings*				
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)	General Description				Conclusion
Stathis (1999)[49] *Dev. Med. Child Neurol.* Brisbane, Australia MEDLINE	87 (36% male)	70	0.86 (NG*) ELBW	27.7 (NG*) (Extremely preterm)	Linear regression coefficient, adjusted for sex & parental education (and others), for presence of exposure compared with absence.				**Head size** and **growth** in infancy positively associated with later cognition, and negatively associated with later learning difficulty
					Exposure	Outcome	Coeff. (SE*)	Significance	
					8-mo HC* ≤10th centile	6-yr GCI (IQ points)	–8.30 (NG*)	*p* = 0.04	
Hack (1986)[50] *Pediatrics* Cleveland, USA MEDLINE	139 (47% male)	89	1.19 (0.21) VLBW	29.1 (1.9) (Very preterm)	Unstandardised partial regression coefficient, adjusted for SES (and others), for presence of exposure compared with absence.				**Head size** in infancy positively associated with later IQ; HC change in late infancy (8-20 months) has no effect on later IQ.
					Exposure	Outcome	Coeff. (SE*)	Significance	
					8-mo HC* < –2 SD	3-yr IQ (IQ points)	– 9.963 (3.872)	*p* = 0.01	
Ong (1997)[51] *Ann Trop Paediatr* Kuala Lumpur, Malaysia MEDLINE	201 total; 103 VLBW (51% male; 48% for VLBW)	34 25	1.26 (0.15) VLBW	31.8 (2.85) (Very preterm)	Linear regression coefficient, adjusted for duration of oxygen requirement (bwt, maternal education and others previously shown to be NS), for a unit increase in value of independent variable (VLBW infants only: *n*=103).				**Head size** at 1 year was positively related to developmental status at 1 year **among VLBW S**s in this Malaysian popn.
					Independent variable	Outcomes	Coeff. (SE*)	Significance (95% CI; p-value)	
					1-yr HC* ratio (obs/exp)	1-yr MDI (units) 1-yr PDI (units)	241.6 (52.97) 179.2 (51.84)	(136.7, 346.7); *p*<0.001 (90.25, 295.6); *p*<0.001	
Gale (2004)[52] *Brain* Southampton, UK From expert.	221 (53% male)	40	3.3 (0.6) Normal	Not given, but 7.7% premature	Linear regression coefficient, adjusted for sex, SES, parental education, infant feeding and others, but not bwt) for a unit increase in value of independent variable. Height and weight were not significantly associated with 9-yr IQ.				**Head size** at 9 months and **growth** up to 9 months are positively associated with cognitive function at 9 years of age.
					Independent variables	Outcome	Coeff. (SE*)	Significance (95% CI; p-value)	
					Size at 9mo HC SD score Growth 0-9mo HC SD score	9-yr IQ (IQ points)	1.98 (NG) 2.30 (NG)	(0.34, 3.62); *p*=0.018 (0.56, 4.03); *p*=0.010.	

* SD = standard deviation; NG = “not given”; HC = head circumference; SE = standard error

Table 3.3A (ii) (continued). Summary data extracted from studies included in review of infant head size/growth and cognitive development

Details	***Design and Participants***				***Main Findings***			
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)	General Description			Conclusion
Bendersky (1998)[53] *Clinical Pediatrics* New Brunswick, USA MEDLINE	125 (50% male)	30	1.45 (NG) VLBW	30.9 (NG) (Very preterm)	Multiple linear regression standardized beta weight (SBW) for 1-yr HC SD (adjusted for bwt, earlier head size & others): MDI: 0.23 ($p<0.01$); PDI: 0.27 ($p<0.01$). For MDI, the only variable that has a larger SBW is "medical complications score" (-0.37). For PDI, HC is the strongest, but "medical complications score" (-0.21) and "ICH" (-0.26) aren't far behind. N.B. the 'standardized beta weights' are the regression coefficients we would get if we converted all variables (independent and dependent) to z-scores before doing the regression. They can be compared to judge relative predictive power of independent variables. The closer they are to 1, the stronger their ability to predict the outcome.			**Head size** was an independent predictor of MDI and PDI. Although this study is based on preterm babies, many of whom have ICH, the association is independent of ICH status.
Hack (1991)[54] *NEJM* Cleveland, USA Reference list	249 (50% male)	79	1.18 (0.22) VLBW	29.7 (2.0) (Very preterm)	Mean diff in 8-yr IQ is given as subnormal HC – normal HC at 8mo. Regression coeff is for subnormal 8-mo HC compared to normal HC.			Positive association between increased infant **head size** and IQ, even after adjustment for confounders.
					WISC-R subscale at 8yrs	Mean diff (95% CI) in 8-yr IQ by 8-mo HC	Unstandardised regression coeff (SE*), adjusted for SES, bwt & others	
					Verbal IQ Performance IQ	-10.1 (-16.8, -3.35); $p<0.01$ -8.1 (-14.6, -1.61); $p<0.05$	-7.78 (3.04); $p=0.011$ -7.70 (2.84); $p=0.007$	

Table 3.3B (i). Description of studies included in review of growth faltering in infancy and cognitive development

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Skuse (1994)[55] *J Child Pyschol Psychiatr* London, UK MEDLINE	Prospective longitudinal study with nested case-control study, assessing whether cognition is particularly vulnerable to poor growth in infancy. Popn. based; setting was a single health district. Source popn. was all births registered with participating health clinics in 1 year.	94 Ss (47 NOFT*, 47 non-FTT controls) born in a single inner-city health district in 1986. Mean bwt SD score –0.67; mean gest. age 40wks (normal; preterm infants <37wks were excluded). 49% male; 39% of mothers non-white. Baseline info on maternal IQ & marital status. SES of district was "quite severely disadvantaged". Incl/excl fairly clear. 19% FU of original cohort, due to case-control design, but all available NOFT* Ss included. No info on losses to FU due to migration or missing data. No sig diffs betw. cases & controls by sex, bwt, race & maternal IQ, but controls had greater ht & HC at birth, & had taller mothers.	Infancy: Wt data before 12mo from clinic records. Weighed by clinic nurses using standard equipment, regularly checked for accuracy. WAZ* calculated; FTT defined as WAZ < –1.88 (3rd centile) by 12mo, sustained for ≥ 3mo. Outcome: Cognition & motor development (Bayley MDI & PDI) at 15mo (mean ages 14.6mo for cases; 14.2mo for controls). No further info. Apparently blind for assessment of maternal vars, but otherwise unclear.	Tables of means within groups. MANOVA used to assess diffs. Multiple regression for MDI & PDI, adjusting for bwt. Non-linear regression model for MDI & PDI by sensitivity & severity of growth faltering, adjusted for mother-infant interaction. Maternal IQ found not to affect assoc. Controls pairwise matched on sex, age, race, bwt, ordinal position & SES.
Boddy (2000)[56] *J. Child Psychol. Psychiat.* London, UK MEDLINE	Prospective cohort study with nested case-control study assessing the assoc. betw. FTT in infancy & childhood development. Popn. based; source popn. was all live births in study region in 1 year.	42 cases and 41 comparison infants from a survey of all 1986 live births in an inner-city area of S. London (pop. 140,000). Mean bwt normal; mean gest. age not given, but premature infants excluded. 47% male; 54% of mothers were Caucasian. Baseline data on size of family, SES, maternal education & infant feeding. 86% FU. Losses to FU created a small diff. in bwt betw. cases & controls (they were originally matched). Case gp mothers who took part in the FU were significantly shorter than those in control gp. Also evidence that FTT cases had lower SES, but no stat. tests.	Infancy: Ht & wt at 15mo. Weighed by clinic nurses using standard equipment, regularly checked for accuracy. FTT defined as wt-for-age z-score (WAZ) ≤ 3rd centile at 12mo & growth below 3rd centile for 3 months. Outcome: Cognition (McCarthy GCI) at 6yrs. Assessed at school by one of the authors, a trained psychologist. No blinding info.	Matching on bwt, sex, ordinal position, age at assessment, ethnicity, area of residence. Matched-pairs analysis used in calculating means & diffs. Pearson correlations & linear regression controlling for bwt & maternal IQ. No account made for matching, since whole-sample analysis.
Corbett (1996)[57] *Acta Paediatr* Newcastle-upon-Tyne, UK EMBASE	Prospective follow-up of a subset of Ss from a previous FTT case-control study, assessing the assoc. betw. severity of growth failure & later cognition. Setting was 2 clinics in a single city; source popn. was all infants registered at the clinics that took part in the earlier study.	94 Ss born during late 1985-86, registered in one of 2 district health authority clinics in a single city. Mean bwt & gest. age. not given, but all Ss were born at term, by design. FTT of organic aetiology excluded; other excl criteria clear. No sex info. All Ss were Caucasian. No further baseline info. Original study was a case-control design; details of control selection given and were valid, but many non-FTT Ss were excluded by this design. 81% FU. Numbers & reasons clearly stated. 4 non-participating cases were among the slowest growing, but no further info on non-participants – high risk of bias given small sample size.	Infancy: Wt at various ages up to 18mo ascertained from clinic records. FTT defined as wt centile declining from max achieved at 4-8wks, crossing ≥ 2 centile lines, & remaining at this low level for ≥ 2 measurements over a period of at least 1mo. "Thrive index" also calculated for cases, by regressing a later wt on a baseline wt. Outcome: Cognition (Wechsler WIPPSI-R*) and behaviour (CBC & TRF†) at 6-7yrs. Cognition assessed by 2 psychologists blinded to FTT status & trained in use of test; reliability maintained by observing one another in trials. No info on assessment of behaviour.	Tables of means & diffs betw. FTT cases & controls, with *t*-test. Linear regression, giving coeff for increase in IQ for a unit increase in thrive index, for cases only. No consideration of confounders.

* NOFT = "non-organic failure-to-thrive"; AGA = "appropriate for gestational age"; WAZ = "weight-for-age *z*-score"; WIPPSI-R = "Wechsler Pre-school and Primary Scale of Intelligence – Revised"
‡ see footnotes for Kerr (2000).

Table 3.3B (i) (continued). Description of studies included in review of growth faltering in infancy and cognitive development

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Drewett (1999)[58] *J. Child Psychol. Psychiat*. Newcastle-upon-Tyne, UK PsycINFO	Prospective cohort study with nested case-control study assessing the assoc. betw. FTT in infancy & childhood development. Popn. based; source popn. was all live births in study region in 1 year.	107 cases and 117 comparison infants from a cohort of births in a single city in 1987-88. Mean bwt normal in over 96% of Ss. All were born at term – this was the sole incl. criterion, clearly stated. 39% male; 91% of mothers were Caucasian. Baseline data on size of family, SES, maternal education & infant feeding; no sig diffs betw. cases & controls except that cases had shorter fathers & more prevalent feeding problems. 83% FU (79% of cases, 87% of controls). Numbers & reasons clearly stated. No sig diffs in wt betw. losses to FU & study Ss at any of FU ages (incl. at birth).	Infancy: Wt at 3, 6, 9, 12 &18mo. "Thrive index" calculated for each time point by regressing later wt on baseline wt. FTT defined as thrive index < 5th centile on ≥2 occasions betw. 3 & 18 mo; controls defined as no thrive index value <10th centile. Wts obtained from baby clinic records; weights not available for all Ss at all ages. No further info. Outcome: Cognition (Weschler WISC & WORD scales) at 8yrs. Assessed by one of 2 psychologists blind to FTT status, but no further info.	Tables of means & diffs, plus linear regression controlling for maternal IQ, infant feeding, family size, maternal smoking & parental height. No adjustment for sex. No matching, by design, but controls selected to have similar SES to cases.
Drotar (1985)[59] *J Clin Child Psychol* Cleveland, USA PsycINFO	Prospective cohort study with post-discharge family support interventions for FTT cases, assessing assoc. betw. FTT in infancy & childhood development. Setting was 7 hospitals in same region. Target popn. unclear – Ss were "recruited".	68 Ss hospitalised for FTT, recruited from one of 7 Cleveland area hospitals. No bwt or gest. age info. 65% male; 38% white. All families were working class or received welfare. Baseline info on family characteristics such as size of family, income & maternal educ. Incl/excl criteria clearly stated. Approx. 78% participation (numbers of families given rather than individuals). No sig diffs betw. non-participants & study Ss for demographic characteristics, age, physical growth or cognitive development at study intake.	Infancy: Wt, ht & HC* at study intake (mean 4.9mo), 12 & 18mo. Wasting (% of expected wt-for-ht, grouped into >90%, 80-89%, 70-79% & <70%) & stunting (% of expected ht-for-age, grouped into >95%, 90-95%, 85-89% & <85%) derived. Assessed by "experienced examiners" using standard equipment, but no reliability info. Outcome: Cognition (Bayley MDI), plus behaviour, language ability & 'symbolic play'¶, all at same ages as size/growth measurements. Assessed in family homes; inter-rater reliabilities good. Blind to intervention status, but unclear as to whether blind to infant size/growth as could be same observers.	Stepwise multiple regression models, with regression coeffs, *R*-, *F*- & *p*-values (but no CIs), for change in outcome for a unit change in degree of stunting or wasting. Family income, size & adult-to-child ratio entered into analyses, but no infant feeding or intervention status.
Drotar (1988)[59] *J Pediatr Psychol* Cleveland, USA PsycINFO	Prospective cohort study with post-discharge family support interventions for FTT cases, assessing assoc. betw. FTT in infancy & cognition in childhood. Setting was 7 hospitals in same region. Target popn. unclear – Ss were "recruited".	59 Ss hospitalised for FTT, recruited from one of 7 Cleveland area hospitals. No gest. age info, but all Ss had bwt ≥1.5kg, by design. 66% male; 42% white. SES unclear but presumably low, as for Drotar (1985). Also baseline info on family income & maternal educ. Incl/excl criteria clearly stated. Approx. 65% participation (numbers of families given rather than individuals) – numbers similar but not identical to those given by Drotar (1985). No sig diffs betw. non-participants & study Ss for demographic chars, age, physical growth or cognitive development at study intake (using ANOVA).	Infancy: Wt & ht at hospital admission (1-9mo); info on instruments but nothing further. NOFT* confirmed during hospitalisation using standard criteria incl. wt <5th percentile, wt gain in hospital, decrease in wt gain from birth to <5th percentile & absence of organic aetiology. Outcome: Cognition (Stanford-Binet IQ) at 36mo (range 36-40mo), assessed by experienced examiners blind to other info about Ss (presumably including FTT status). Also cognition using Bayley MDI at intake, assessed by trained examiners.	Pearson correlations betw. variables. Hierarchical regression for prediction of 36-mo cognition, using age at onset & duration of NOFT, plus wt-for-ht at intake. Adjusted for family income & maternal education, but not intervention status or any other confounders.

* HC = "head circumference"; NOFT = "non-organic failure-to-thrive"

¶ Behaviour assessed using a version of the Infant Behaviour Record (see Bayley N (1969). *The Bayley scales of infant development manual*. New York: Psychological Corporation). Language ability assessed using a battery used in an earlier study (see White BL, Kohan BT, Antanucci, Shapiro BB (1978). *Experience and environment: Major influences on the development of the young child*. Englewood Cliffs, NJ: Prentice-Hall). 'Symbolic Play Test' – see Lowe M, Costello AJ (1976). *Manual for the symbolic play test*. Windsor, UK: NFER.

Table 3.3B (i) (continued). Description of studies included in review of growth faltering in infancy and cognitive development

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Mackner (1997)[61] *Child Abuse & Neglect* *Baltimore, USA* MEDLINE	Cross-sectional study assessing risk of FTT and neglect for cognitive deficits. Setting was a single paediatric clinic. Target popn. unclear – Ss were selected from a pre-existing sample.	177 Ss (70 with FTT; 23 neglected; 27 both; 57 neither) recruited from a single inner-city paediatric clinic. Mean bwt & gest. age not given, but all Ss were full-term (≥37wks) with bwt AGA*. 58% male; 94% African-American. 73% on income support. Also baseline info on home environment, plus maternal IQ & educ. Eligibility criteria clearly stated. No info on %FU, original sample or the selection method for the present study. Parents of FTT Ss more likely to have been reported to CPS, but sig diffs in maternal IQ & home environment appear to be mostly due to neglect rather than FTT status.	Infancy: FTT defined as wt-for-age <5th centile before 24mo using NCHS growth charts, with no organic aetiology. Non-FTT Ss had same criteria, but with wt-for-age >5th centile. No further info. Outcome: Cognition (Bayley MDI), assessed during clinic visit (at intake – age range 3 to 30mo) by a trained psychologist. No further info.	MDI means within each group. ANCOVA model using group status (neglect & FTT; neglect only; FTT only; neither) as the independent variable. SES, race & maternal educ assessed & found to be NS. Maternal IQ & child age used as covariates.
Mackner (2003)[62] *J Child Psychol Psychiatr* Baltimore, USA PsycINFO	Prospective cohort study with RCT of home intervention for FTT cases, assessing assoc. betw. FTT in infancy & cognitive development in childhood. Setting was a single paediatric clinic. Target popn. unclear – Ss were "recruited".	226 Ss recruited from an inner-city paediatric clinic (128 FTT; 98 non-FTT). Mean bwt & gest. age not given, but all Ss were full-term (≥37wks) with bwt AGA*. 56% male; 92% African-American. 76% on income support. Also baseline info on family size & maternal IQ & educ. Eligibility criteria defining gps clearly stated. 84% participation (no diffs betw. non-participants & study Ss by age, sex or maternal educ); 72% retention rate (compared to at intake) at 6yrs (no diffs betw. losses to FU & study Ss by maternal educ, age, race, marital status, employment, receipt of food stamps or age of child at recruitment).	Infancy: FTT defined as a decline in wt-for-age or wt-for-ht from AGA* to <5th centile at intake. Non-FTT Ss had wt-for-age & wt-for-ht >10th centile at intake. Wt & ht assessed by nurses using appropriate equipment. Outcome: Cognition at 12 & 18mo after intake (FTT only) or 6mo after intake (non-FTT only), and at 3, 4, 5 & 6yrs chronological age. Bayley MDI used before age 3yrs, Stanford-Binet IQ at 3 & 5yrs, Battelle cognitive score† at 4yrs, & Wechsler WPPSI-R at 6yrs*. Assessed by psychologists or supervised psychology students blinded to FTT status. Training (incl. inter-rater reliability) conducted prior to data collection.	Tables of means; diffs betw. groups assessed using ANCOVA, adjusting for age, home environment, intervention status & sex. Hierarchical linear models for prediction of cognitive dev, adjusting for intervention status, family size, home environment, sex & maternal educ.
Kerr (2000)[63] *Child Abuse Negl.* Baltimore, USA MEDLINE	Data from a subset of a prospective longitudinal study of child maltreatment, assessing the assoc. betw. FTT in infancy & childhood development. Setting was inner-city pediatric clinics. Target popn. unclear – mothers were "recruited".	193 infants (64 FTT; 21 maltreated; 28 both; 80 neither) recruited from inner-city paediatric clinics for an earlier study. Info on consent procedures & remuneration for mothers. Mean bwt & gest. age. not given, but incl. criteria included gest. age >36wks & AGA* bwt. Other incl/excl criteria clearly stated. 52% male; 92% African-American; 63% of families on income support. Also baseline data on maternal characteristics. No sig diffs betw. FTT groups for sex, race, SES or maternal educ. No %FU info. 24% of the 193 had missing outcome data from schools, but no demog. diffs betw. Ss with & without this data. No further non-participant info.	Infancy: No info on measurements, but FTT defined as wt-for-age at recruitment < 5th centile using NCHS growth charts. Non-FTT Ss had wt-for-age >10th centile. No info on timing, but all Ss were aged <25mo at recruitment. Outcome: Cognition (Weschler WISC-R), adaptive functioning at school (TRF‡), and behaviour at school (TRF) & at home (CBC‡), all at 6yrs. TRF completed by teachers, CBCL by mothers; no reliability info. Ascertainment of cognition unclear.	Means & diffs betw. FTT groups. ANCOVA model using pairwise comparisons, adjusting for sex & maternal education, but not infant feeding. All Ss were of low SES. Group-matching on age, race, sex & SES.

* NOFT = "non-organic failure-to-thrive"; AGA = "appropriate for gestational age"; WIPPSI-R = "Wechsler Pre-school and Primary Scale of Intelligence – Revised"
† see Newborg J, Stock J, Wnek L, Giubaldi J, Svinicki J (1984). *Battelle Developmental Inventory*. Allen, TX: LINC Associates, DLM Teaching Resources.
‡ TRF = "Teacher's Report Form" – see Achenbach TM (1991). *Manual for the Teacher's Report Form and 1991 profile*. Burlington, VT: University of Vermont, Department of Psychiatry.
CBC = "Child Behaviour Checklist" – see Achenbach TM (1991). *Manual for the Child Behavior Checklist/4-18 and 1991 profile*. (same publisher).

Table 3.3B (i) (continued). Description of studies included in review of growth faltering in infancy and cognitive development

Details (author (pub. year); journal; country; source)	***Design & Setting***	***Participants***	***Measurement***	***Analysis and Confounding***
Kelleher (1993)[64] *Pediatrics* Various, USA MEDLINE	Prospective cohort study of Ss from larger RCT of stimulation & home visit interventions for LBW* preterm infants, with nested case-control analysis at 36mo FU. Setting was 8 university hospitals; source popn. was all members of larger RCT cohort.	771 Ss (180 FTT, 591 non-FTT) from the IHDP† cohort. Mean bwt was 1.8kg (LBW); mean gest. age was 33wks (preterm). 49% male; 53% of mothers were black. Baseline info on maternal vars (age, IQ, height, educ) & home environment (family income, marital status). Incl/excl clearly stated. 78% FU. Numbers & reasons for losses & exclusions from original cohort given. States that losses to FU from target did not differ from study Ss on any of the perinatal vars examined, but no info on exclusions (n=143) due to partial fulfilment of FTT criteria. FTT & non-FTT Ss differed by bwt, SGA & maternal height.	Infancy: Ht, wt & HC* at each clinic visit (4, 8, 12, 18, 24 & 36mo) using standard well-validated methods. No info on observers or inter-rater reliability betw. the 8 centres. FTT defined as meeting formal criteria described in detail, incl. wt < 5th centile on ≥ 2 occasions. Outcome: Cognitive & psychomotor dev. (Bayley MDI & PDI) at 12 & 24mo; CBC‡ at 24 & 36mo; Bates Temperament Scale¶ at 12mo; prosocial behaviour scale at 36mo§. Observers assessing outcomes were blind to infant growth status.	Tables of means, with χ^2- & *t*-tests to assess diffs betw. FTT groups. Maternal educ. & IQ and SES compared but not adjusted for; nothing for infant feeding or intervention status.
Singer (1984)[65] *J Pediatr Psychol* Cleveland, USA PsycINFO	Prospective longitudinal study assessing assoc. betw. FTT in infancy & cognitive development in childhood. Setting was 3 hospitals in same city. Target popn. was 3 gps of 13 Ss of different growth status recruited from hospitals.	39 Ss recruited from 3 local hospitals in Cleveland, including the first 26 FTT Ss identified (13 non-organic, 13 organic) & 13 controls (non-FTT). Mean bwt 2.75kg; mean gest. age 38wks (both normal). Parental educ. also given. No sig diffs betw. gps for any of these, although organic FTT Ss had bwts as low as 1kg. Eligibility criteria defining gps clearly stated. 85% FU at 20mo; 64% at 36mo – mostly due to families moving out of study region. Unusually high attrition in control gp at 36mo. No further non-participant info.	Infancy: FTT status confirmed during hospitalisation – defined by wt <3rd percentile for conceptual age. Wt gain in hospital also a criterion for NOFT*, & presence or absence of organic aetiology defined NOFT & OFT gps. Mean age at initial assessment was 7mo. Outcome: Cognition at 7 & 20mo (Bayley MDI) & 36mo (Stanford-Binet IQ); no further info. Also 'visual recognition memory' (duration of fixation to familiar & novel targets – procedure described; inter-rater reliability good) at 7mo. No blinding info.	Tables of means & diffs betw. groups. ANOVA models for prediction of MDI or IQ, in which effect of parental education, race & 'placement outside the home' considered to varying degrees. Nothing on sex or infant feeding.

* HC = "head circumference"; NOFT = "non-organic failure-to-thrive"; LBW = "low birthweight"
† IHDP = Infant Health & Development Program. See: Infant Health & Development Program. Enhancing the outcomes of low-birth-weight, premature infants. *JAMA* 1990;**263**:3035-42.
‡ CBC = "Child Behaviour Checklist" – see Achenbach TM, Edelbrock CS, Howell CT. Empirically based assessment of the behavioural/emotional problems of 2- and 3-year-old children. *J Abnorm Child Psychol.* 1987;**15**:629-50.
¶ Bates Temperament Scale – see Bates JE. The measurement of temperament. In: Plomin R, Dunn J, eds. (1986). *The study of temperament: Changes, continuities and challenges*. Hillsdale, NJ: Lawrence Erlbaum Assoc.
§ Prosocial behaviour scale – see Scott KG, Hogan AE. Adaptive Social Behaviour Inventory: Infant Health & Development Program study proposal. Presented at the biennial meeting of the Society for Research in Child Development, April 1991.

Table 3.3B (i) (continued). Description of studies included in review of growth faltering in infancy and cognitive development

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Glaser (1968)[66] *Pediatrics* Boston, USA MEDLINE	Retrospective study of FTT infants discharged from a single hospital, assessing later development. Target popn. was all discharges with non-organic FTT.	40 Ss with NOFT* discharged from a single hospital during 1958-65. Mean bwt & gest. age. not given, but incl. criteria included bwt >2.5kg (normal). Other incl/excl criteria clearly stated. 60% male; no race info. 62% were of SES class IV or V†. Also baseline info on family characteristics such as size of family & father's employment. 80% FU. Numbers & reasons clearly stated, but no further info on non-participants.	Infancy: FTT status retrospectively ascertained from hospital records – no info on infant size/growth measures. FTT defined as wt < 3rd centile on admission to hospital (mean age 12.5mo). Outcome: Psychiatric evaluation; cognition (Cattell IQ, Stanford-Binet IQ, Wechsler WISC, Rorschach Inkblot Test) at a single age ranging from 8mo to 11yrs (mean 4.5yrs). No info on observers, reliability or blinding.	Numbers & percentages of Ss with developmental problems; histogram of IQ scores. No statistical analysis, and no consideration of confounders.
Reif (1995)[67] *Isr J Med Sci* Tel Aviv, Israel MEDLINE	Retrospective cohort study with nested case-control study, comparing FTT & normal infants on later development. Setting was a single medical centre; target popn. was all NOFT* diagnoses over an 8-yr period.	61 FTT cases, diagnosed during 1982-90 as having NOFT* at a single medical centre; 65 controls present at the same centre for an unrelated disease. Mean bwt percentile was 39% for cases but normal (51%) for controls. No gest. age info. 53% male. 59% were of Sephardic ethnicity; the remainder were Ashkenazi. Also baseline info on family size & parental educ. Incl/excl criteria clearly stated. 71% FU for cases; no info for controls. Numbers & reasons for losses given, but no further info on non-participants. FTT Ss were smaller at birth & at FU, and had smaller parents.	Infancy: NOFT defined as wt & ht < 5th percentile in ≥ 2 measurements during a period of > 6mo with no organic aetiology, from retrospective review of records. Mean age at diagnosis was 13mo. Outcome: Educational & developmental achievements at 6yrs, ascertained either by developmental assessment & school records (41 cases) or from contact with parents & family physician (20 cases). Outcomes not clearly defined (no info on scales etc.), but states that controls assessed in similar way to cases.	Tables of means, diffs & percentages, with *p*-values. No estimate of effect size, and no consideration of confounders, although some comparisons betw. groups on important variables. Matched for age, sex & race.
Field (1984)[68] *J Pediatr.Psychol.* Philadelphia, USA MEDLINE	Prospective longitudinal study assessing assoc. betw. NOFT* & later development. Setting was a single hospital; target popn. unclear, but was presumably all potential cases admitted to the hospital.	17 infants admitted to a single hospital with growth failure. 35% were preterm with mean bwt 2.0kg (LBW*); the remainder were full-term with mean bwt 3.5kg (normal). 47% male; 65% white. Also baseline info on mother's age, education & marital status, plus child's birth order. A rough social index suggested that 53% of the families were "highly stressed". No incl criteria other than poor wt gain & absence of organic aetiology. No info on target popn, %FU or any non-participants.	Infancy: Wt, ht & HC* measured on admission (mean age 7.5mo), at discharge (mean 28days later) and 1 & 3mo post-discharge. Wt also measured weekly during hospitalisation; wt quotient calculated as 'weight age' divided by chorological age. No info on observers or protocol. No formal FTT definition – just "some measurements of poor weight gain" & "absence of organic findings". Outcome: Cognition (Bayley MDI & PDI) at admission, discharge, and 1, 3 & 6-13mo post-discharge. No further info.	Table of means for outcomes at each FU point. Assoc. betw. growth & developmental status assessed using Pearson correlation coeffs & *post hoc* analysis of ANOVA findings. Race, sex, post-hospital intervention & family stress were unrelated to outcome. Maternal educ & infant feeding not considered.

* HC = "head circumference"; NOFT = "non-organic failure to thrive"; LBW = "low birthweight"
† using the Hollingshead social class scale – see Hollingshead AB, Redlich FC (1958). *Social class and mental illness*. New York: John Wiley & Sons, Inc., p66.

Table 3.3B (i) (continued). Description of studies included in review of growth faltering in infancy and cognitive development

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Hack (1982)[69] *Am J Obstet Gynecol* Cleveland, USA Reference list	Prospective cohort study of VLBW Ss, assessing relationship betw. **head size** in infancy and childhood IQ. Set in a single NICU. Target popn. was all those surviving to 1yr.	192 VLBW (<1.5kg) infants admitted to an NICU during 1977-78. Unclear as to whether source popn of 308 were all that could have been selected. Mean bwt given; mean gest. age was very low (29wks) in AGA Ss & low (32wks) in SGA Ss. 47% male. Of mothers of Ss, 54% were black & 66% were of low social class. Other maternal and perinatal vars given at baseline, incl. maternal age & educ. No excl. criteria used. 94% FU. Numbers & reasons given for losses to FU, but no comparisons with study Ss.	Infancy: Size (ht, wt & HC) at corrected ages 8 and 20 months. Wt categorised as normal or subnormal (≥ or < –2 SD) using growth charts of Babson & Benda (1976)*. No info on observers or reliability. Outcome: Cognitive development, ascertained by Bayley scales at 8mo. No info on observers, reliability or blinding.	Tables of mean development score within subgroups defined by normal or subnormal size at birth, term & 8mo, with *p*-values for diffs. Also correlations with wt at term & 8mo for bwt, SES, race, maternal education and others. No adjustment though.
Mitchell (1980)[70] *Pedatrics* North Carolina, USA Reference list	Retrospective cohort study with nested case-control study assessing the assoc. betw. FTT in infancy & childhood development. Source popn. was all children registered at one of 3 federally-funded health clinics.	12 FTT cases & 16 comparison Ss registered at one of 3 health clinics aged 2-5yrs. Of the original cohort of 312, 50% were male & 71% black. SES of area was low; parental employment, income & marital status given. No bwt info, but 10% were preterm (< 37wks). No excl. criteria used. 74% FU of target popn. for nested case-control study, but only 9% FU of original cohort. No comparison betw. study Ss and rest of original cohort.	Infancy: size (ht, wt & HC) from clinic medical records. No further info. FTT diagnosed at 0-24mo using clearly-stated criteria, based on wt being < 80% of normal for age using Harvard growth charts. Outcome: Development (McCarthy Scales) at 3-6yrs, administered by a single psychologist (one of the authors) blind to previous growth status.	Mean McCarthy scores for cases & comparison Ss, with *p*-values and power calculations. Comparison Ss matched to cases on age, sex, mother's age & marital status, and family problems. Also, stepwise linear regression for prediction of GCI using FTT, age, sex & mother's education – no data given.
Tudehope (1983)[71] *Aust Paediatr J* South Brisbane, Australia MEDLINE	Prospective cohort study of VLBW Ss, assessing relationship betw. infant size & later cognitive development. Set in a single hospital NICU; target popn was all surviving VLBW births during study period.	164 VLBW (<1.5 kg) Ss born 1978-80 in a single NICU. Mean bwt given; mean gest. age was very low (29.4wks) in AGA Ss & low (32.5wks) in SGA Ss. No sex, race or SES info. No incl. criteria other than VLBW. FU rates varied – from 93% at 1yr down to 6.3% at 4yrs. Ss lost in 1st year had inadequate FU data, but no reasons for later attrition, or data comparing non-participants to study Ss.	Infancy: size (wt & HC) at 1yr, measured at growth & development clinic. No info on protocols or observers. Growth in wt from birth to 1yr calculated. Outcome: cognitive development, measured using Griffiths scale (< 3yrs) & McCarthy scale (3-4 yrs) GQs by a psychologist at the clinic. No info on reliability and not clear whether same observer throughout or whether blind to growth status.	Mean GQ at latest assessment given by growth in wt over 1st year stratified into > 3rd & < 3rd percentile, for AGA and SGA Ss separately. Corrected for gest. age, but no other consideration of confounders.

* see Babson SG, Benda GI. Growth graphs for the clinical assessment of infants of varying gestational age. *J Pediatr* 1976;**89**:814.

Table 3.3B (i) (continued). Description of studies included in review of growth faltering in infancy and cognitive development

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Abramson (1991)[72] *Merrill-Palmer Quarterly* Flint and Detroit, MI, USA PsycINFO	Prospective cohort study assessing assoc. betw. FTT and emotional development in infancy. Setting was 2 hospitals in 2 nearby cities. Target population unclear.	12 FTT cases and 12 comparison Ss, all from one of 2 children's hospitals in Michigan. Mean bwt normal (although higher in non-FTT gp); all Ss were full-term and AGA. 42% male; 75% white. Incl/excl criteria given. No info on %FU or target popn. The 12 FTT cases were possibly all the cases available, though this is not clear.	Infancy: FTT defined as weight ≤ 3rd percentile of NCHS growth charts at age 6-25mo (mean 10mo), and a clinical diagnosis of NOFT was made, but no further info given. Outcome: emotional development 2-5wks after hospital discharge, measured by videotaping the infant over an 80min period whilst being variously stimulated, tested & allowed to play. Facial expressions coded using MAX system*. Coding reliabilities betw. the 2 observers were good.	Frequencies of different facial expressions compared between FTT cases and comparison Ss using *z*-tests. P-values given. Cases & comparison Ss matched for sex, race, mother's age, method of payment for health services (SES) & parity. No other adjustment for confounders.
Dykman (2001)[73] *Clinical Pediatrics* Arkansas, USA MEDLINE	Prospective cohort study of childhood cognitive development in NOFT & comparison infants. Target popn. for NOFT Ss was a roster of former patients of a single growth & development clinic. Comparison gp recruited via adverts placed at various public amenities.	27 FTT cases from records of a single children's clinic; 17 comparison Ss from local community. Mean bwt & gest. age not given, but 56% had bwts < 5th percentile. 61% male; 48% white. SES was low in both gps. One exclusion for cerebral palsy; no other excl. criteria, though comparison gp screened so as to group match on age, sex, race & SES. 33% FU for cases. No info on non-participants.	Infancy: FTT defined as weight < 5th percentile of NCHS growth charts, low wt-for-ht ratio, and abnormal weight growth velocity. Median age of Ss was 20mo. Measured at children's clinic; no further info. Comparison gp given routine check-up; none had a history suggestive of NOFT, but no further info. Outcome: cognitive development at 8-12yrs (mean 10yrs), using certain subscales of the Wechsler WISC-III & WIAT and the VMI†. CBCL given to caregivers. Tests carried out at clinic, but no info on observers.	Means and SDs given within FTT and comparison groups, with *p*-values for differences. Also, correlations given betw. potential risk factors such as SES and maternal educ. & IQ and outcome measures. No adjustment for risk factors, despite some significant correlations.

* MAX system: see Izard C. *The maximally discriminative facial coding system (MAX)*. Newark: University of Delaware, Instructional Resources Center; 1979.
† Wechsler WISC-III: see Wechsler D. *Wechsler Intelligence Scale for Children III*. San Antonio, TX: Harcourt Brace Jovanovich, Inc.; 1991.
WIAT: see Wechsler D. *Wechsler Individual Achievement Test*. San Antonio, TX: Harcourt Brace Jovanovich, Inc.; 1992.
VMI: see Beery KE, Buktenica NA. *Developmental Test of Visual Motor Integration*. Cleveland: Modern Currriculum Press; 1989.
CBCL: see Achenbach TM. *Manual for the Child Behavior Checklist/4-18 and 1991 Profile*. Burlington, VT: University of Vermont, Dept. of Psychiatry; 1991.

Table 3.3B (ii). Summary data extracted from studies included in review of growth faltering in infancy and cognitive development

Details	***Design and Participants***				***Main Findings***	
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)	General Description	Summary of trend
Skuse (1994)[55] *J Child Pyschol Psychiatr* London, UK MEDLINE	94 (47 cases, 47 controls) (49% male)	N/A	-0.67 (0.77) (SD score)	39.5 (1.18) (normal; preterm Ss excluded)	Outcome: Mean diff (cases – ctrls): MANOVA for diff: Multiple regression coeff for 6-mo standardised wt (cases only; adjusted for bwt & 15-mo wt) 15-mo MDI: -10.3: *F*=8.07; *p*=0.007: 15.16 (*p* = 0.004) 15-mo PDI: -6.9: 10.79 (*p* = 0.028) Non-linear regression model (cases only; 'sensitivity' = 'decrement in outcome score per unit decrement in weight within each month'): Coeff: (MDI+PDI)/2 (95% CI): MDI only: PDI only Sensitivity at birth: 8.0 (2.1, 13.9): 8.2: 7.7 Change per month in sensitivity: -1.0 (-3.2, 0.0): -1.0: -1.0	**Positive**. **FTT** cases had lower developmental indices at 15mo than controls. Sensitivity of outcome to a unit of growth faltering decreases by 1 unit per month from 8 units at birth.
Boddy (2000)[56] *J. Child Psychol. Psychiat.* London, UK MEDLINE	83 (42 cases, 41controls) (47% male, dist. evenly)	86	3.01 (0.34) 3.11 (0.37) (normal)	Not given, though "premature" infants excluded	Linear regression coefficient for 6-yr cognitive score, adjusted for maternal IQ & bwt, for presence of FTT compared with absence: Outcome: Coeff. (SE*): Significance: % variance explained GCI: 2.200 (3.650): *p* < 0.55 (NS): NG* Quant. Subscale: 3.940 (2.050): *p* < 0.06 (NS): 3.5% Also: Mean diff (cases – controls) in 6-yr GCI = -3.9 (p < 0.10; NS). Bwt & maternal IQ sig. correlated with 6-yr GCI, but not 15-mo size (wt or ht).	**No significant association** found between the 6yr cognition of **FTT** cases and control infants.
Corbett (1996)[57] *Acta Paediatr* Newcastle-upon-Tyne, UK EMBASE	94 (%male not given)	81	Not given	Not given, but all subjects born at term	Linear regression coefficient for 6/7-yr development, not adjusted for confounders, for a unit increase in lowest recorded 'thrive index' value: Outcome: Coeff. (SE*): Significance IQ: 5.8 (2.6): *p* = 0.03 Also: Similar analyses using CBCL & TRF scores as independent vars were NS. Mean diff (cases – controls) in 6/7-yr IQ = -3.7 (*p* = 0.16; NS). No sig diffs for any subscales.	**Inconclusive**. Mean diff. in 6/7-yr IQ betw. **FTT** cases & controls was non-significant, but linear regression for cases showed a positive assoc. betw. thrive index & later IQ.
Drewett (1999)[58] *J. Child Psychol. Psychiat.* Newcastle-upon-Tyne, UK PsycINFO	224 (107 cases, 117 ctrls) 39% male	79 87	Not given, but normal in over 96% of subjects	Not given, though all subjects born at term	Linear regression coefficient for 8-yr cognitive score, adjusted for maternal IQ & whether the FTT possibly or definitely organic, for presence of FTT compared with absence: Outcome: Coeff. (SE*): Significance IQ: -1.67 (1.80): *p* = 0.35 (NS) Reading score: 1.46 (1.94): *p* = 0.45 (NS) Also: Mean diff (cases – controls) in 8-yr IQ = -3.0 (*p* = 0.19; NS). No sig diffs for any subscales, or for maternal IQ.	**No significant association** found between the 8yr cognition of **FTT** cases and control infants.

* SD = standard deviation; NG = "not given"; NS = "non-significant"; SE = "standard error"

Table 3.3B (ii) (continued). Summary data extracted from studies included in review of growth faltering in infancy and cognitive development

Details	***Design and Participants***				***Main Findings***	
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)	**General Description**	**Summary of trend**
Drotar (1985)[59] *J Clin Child Psychol* Cleveland, USA PsycINFO	68 (65% male)	78	Not given	Not given	Stepwise multiple regression; all figures relate to wasting (wt-for-ht) at same age as outcome. Outcome: / Previous entries / / Beta / Significance 12-mo BRS / None / 0.30 / -0.296 / $F = 6.93$; $p < 0.05$ 18-mo MDI / Income / 0.08 / -0.272 / $F = 5.37$; $p < 0.01$ 18-mo BRS / None / 0.25 / -0.253 / $F = 4.04$; $p < 0.05$ 18-mo SPS / Income; adult-child ratio / 0.07 / -0.283 / $F = 6.17$; $p < 0.01$ BRS = "Behavioural Rating Score"; MDI = Bayley mental development index; SPS = "Symbolic play score".	**Positive** association betw. presence of **wasting** in infancy and decrement in 18-mo mental development.
Drotar (1988)[60] *J Pediatr Psychol* Cleveland, USA PsycINFO	59 (66% male)	65	Not given, but all bwts ≥1.5kg (LBW or normal)	Not given	Hierarchical regression analysis for prediction of 36-mo IQ ('admission' was between 1 & 9mo of age): Variable / R increment / R^2 increment (% variance) / Significance **Income & mat educ.** / 0.47 / 0.22 / $F = 9.06$; $p = 0.05$ FTT onset & duration / 0.12 / 0.10 / $F = 3.80$; $p = 0.05$ Wt-for-ht at admission / 0.00 / 0.01 / $F = 0.00$; NS MDI at admission / 0.05 / 0.04 / $F = 3.05$; NS Correlations with 36-mo IQ: Age at onset of FTT, controlling for duration of FTT: $r = 0.38$; $p < 0.005$ Duration, controlling for at age onset: $r = 0.10$; NS.	**Inconclusive**. The inclusion of a variable for age at onset & duration of **FTT** significantly improved the prediction of 36-mo IQ, but the inclusion of wt-for-ht in infancy did not.
Mackner (1997)[61] *Child Abuse & Neglect Baltimore, USA* MEDLINE	177 (58% male)	NG*	Not given, though all bwts were AGA*	Not given, though all subjects born at term (≥37wks)	Mean diff in MDI at admission (age 3-30mo) betw. 'FTT only' (n=70) & 'neither' (n=57): -3.43. t = 0.582; NS. (NB 'maltreatment only & 'both' also given in paper)	**Inconclusive**. Mean diff. in cognition betw. **FTT** cases & controls non-significant, but hard to separate from maltreatment data.

* NG = "not given"; AGA = "appropriate for gestational age"

Table 3.3B (ii) (continued). Summary data extracted from studies included in review of growth faltering in infancy and cognitive development

Details	*Design and Participants*				*Main Findings*	
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)	General Description	Summary of trend
Mackner (2003)[62] *J Child Psychol Psychiatr* Baltimore, USA PsycINFO	226 (128 FTT, 98 controls). (56% male)	84	Not given, though all bwts were AGA*	Not given, though all subjects born at term (≥37wks)	Hierarchical linear model for cognitive score (IQ, MDI etc, depending on age), adjusted for intervention, maternal educ, sex & family size, over all ages from 6mo to 6yrs. Cognition: Intercept — Coeff (SE*) 5.41 (1.72) — Significance $p < 0.01$ Linear change with age — 0.33 (0.07) — $p < 0.001$ Quadratic change with age — -0.016 (0.003) — $p < 0.05$ Mean diffs (cases – controls) change from –3.0 at 15mo to –13.9 at 22mo, down to –3.1 by 6yrs. All significant except at 5 & 6yrs.	**Positive** association betw. presence of **FTT** and later cognition. **FTT** was a significant predictor of both linear & quadratic changes in cognition over time.
Kerr (2000)[63] *Child Abuse Negl.* Baltimore, USA MEDLINE	193 (92 cases, 101 ctrls) 52% male	NG*	Not given, though all bwts were AGA*	Not given, though all subjects born at term (>36wks)	'FTT only' and 'neither' groups only: (NB 'maltreatment only & 'both' also given in paper). 'Mean diff' = cases – controls. 6-yr outcome — Mean diff — Significance Cog dev — -1.97 — $t = 0.40$ (NS) Adaptive func. — -2.00 — $t = 0.59$ (NS) School behav. — +2.58 — $t = 0.23$ (NS) Home behav. — +1.44 — $t = 0.18$ (NS)	**No significant differences** between **FTT** cases and control infants for any of the 6-yr outcomes.
Kelleher (1993)[64] *Pediatrics* Various, USA MEDLINE	771 (180 cases, 591 ctrls) (49% male)	78	1.68 (NG*) (LBW)	33.1 (NG*) (preterm)	Outcome — Mean diff (cases – controls) — p-value for diff 12-mo MDI — -5.8 — $p < 0.005$ 24-mo MDI — -5.5 — $p < 0.005$ 12-mo PDI — -7.3 — $p < 0.005$ 24-mo PDI — -5.7 — $p < 0.005$ 12-mo BTS — +0.5 — NS 24-mo CBCL — -0.6 — NS NB: MDI & PDI = Bayley mental & psychomotor development indices; BTS = Bates Temperament Scale; CBCL = "Child Behaviour Checklist" (the latter two are behavioural)	**Positive**. **FTT** cases had lower developmental indices at 12 & 24mo than controls. However, no significant differences were found for behavioural outcomes.
Singer (1984)[65] J Pediatr Psychol Cleveland, USA PsycINFO	39 (13 NOFT, 13 OFT, 13 controls)	85% at 20mo; 64% at 36mo	2.85 (0.59) 2.38 (0.86) 3.03 (0.69) (all normal)	39 (1.8) 37 (3.5) 38 (1.8) (all normal)	Outcome — Mean diff (NOFT – ctrls) — *t*-test — ANOVA gp comparison 7-mo VRM (%) — +5.5 — $t = 1.53$; NS — $F = 2.1$; NS 7-mo MDI — -42.6 — $t = -6.64$; p<0.001 — $F = 46.5$; $p < 0.001$ 20-mo MDI — -28.5 — $t = -3.72$; p=0.001 — Not given 3-yr IQ — -18.8 — $t = 2.77$; $p = 0.01$ — Not given VRM = "visual recognition memory", measured by % of total duration of fixation to novel targets compared to familiar targets.	**Positive**. **FTT** cases had lower mental development than controls at 7 & 20mo and at 3yrs. However, no significant differences were found for visual recognition memory.

* SD = standard deviation; NG = "not given"; AGA = "appropriate for gestational age"; HC = "head circumference"; SE = "standard error"; (N)OFT = "(non-) organic failure to thrive"

Table 3.3B (ii) (continued). Summary data extracted from studies included in review of growth faltering in infancy and cognitive development

Details	***Design and Participants***				***Main Findings***	
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)	General Description	Summary of trend
Glaser (1968)[66] *Pediatrics* Boston, USA MEDLINE	40 (all FTT) (60% male)	80	Not given, but all bwts >2.5kg (normal)	Not given	15% were mentally retarded (using formal psychological tests) 18% had mild behaviour disorders (e.g. immature speech, excessive shyness, enuresis) IQ scores approx. normally distributed; slight skewing to left. 15% had IQ ≤ 80 pts (borderline or retarded) Approx. mean IQ = 98.25 (normal). Of the 19 Ss in kindergarten/1st grade, 37% of had failed, or were having significant difficulty. 32% found to be "retarded clinically".	**Inconclusive**. No statistical analyses, and IQ histogram showed only a slight skew towards lower scores in **FFT**. (Age range at outcome: 8mo to 11yrs, mean 4.5yrs).
Reif (1995)[67] *Isr J Med Sci* Tel Aviv, Israel MEDLINE	126 (61 cases, 65 controls) (53% male)	71 NG*	39% 51% (percentiles)	Not given	6-yr outcome Learning difficulties Special class Repeated grade Developmental delay	*Prevalence*: Cases: 18%, 1.6%, 3.2%, 11.5%; Controls: 3.1%, 0%, 1.5%, 0%; *p*-value for diff: $p < 0.01$, NS, NS, $p < 0.005$	**Inconclusive**. 6-yr outcomes not well described, and some showed significant differences between **FTT** cases and controls while others did not.
Field (1984)[68] *J Pediatr.Psychol.* Philadelphia, USA MEDLINE	17 47% male	NG*	35% were preterm with mean bwt 2.0kg (LBW); the remainder were full-term with mean bwt 3.5kg (normal).		Correlation betw. change in wt & change in mental quotient, both over total period of FU (up to 6-13mo post-discharge): r=0.64; p=0.003. Similarly for motor quotient: r=0.53; p=0.002. Significant wt increase occurred betw. admission (mean 7.5mo) & discharge (mean 28days later), but significant change in mental quotient not observed until 3mo post-discharge. Sex, race, age, family stress and post-hospital intervention did not affect growth or development variables.	**Inconclusive**. Increase (**growth**) in wt seems to be correlated with increase in mental quotient, but mental quotient shown to only increase several months after the increase in wt.

* NG = "not given"

Table 3.3B (ii) (continued). Summary data extracted from studies included in review of growth faltering in infancy and cognitive development

Details	***Design and Participants***				***Main Findings***					
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)	General Description					Conclusion
Hack (1982)[69] *Am J Obstet Gynecol* Cleveland, USA Reference list	192 (47% male)	94	1.19 (NG*) VLBW	29.6 (NG*) (Very preterm)	Group		Mean diff in DQ by 8-mo wt (subnormal – normal)		Diff in % neurological impairment	Positive association betw. absence of **FTT** and development for AGA Ss; less so for SGA Ss.
					AGA; appr. at term (n=83) AGA; small at term (n=71) SGA; appr. at term (n=3) SGA; small at term (n=35)		-20 (p<0.001) -15 (p=0.001) N/A – zero cell count -7 (p=0.27 – NS)		+37 (p<0.01) +15 (p<0.01) N/A – zero cell count +19 (p<0.01)	
Mitchell (1980)[70] *Pedatrics* North Carolina, USA Reference list	28 (50% of 312 male)	74	NG*	10% were preterm (< 37wks)		Mean diff (FTT cases – controls)		Power (probability of detecting a 10pt difference if it exists)		No signficent differences between **FTT** cases and controls.
					Motor GCI	-4.4 (NS) -5.0 (NS)		0.87 0.64		
					In a stepwise linear regression for GCI, controlling for age, sex & maternal education, FTT was found *not* to predict GCI or any subscale score (data not given).					
Tudehope (1983)[71] *Aust Paediatr J* South Brisbane, Australia MEDLINE	131 AGA 33 SGA (no sex info)	94	1.18 (0.22) 1.19 (0.24) VLBW	29.4 (2.1) 32.5 (2.7) Preterm		Infant growth status (0-1yr wt)	*n*	Mean 1-yr HC (cm) (*p*-value for diff)	Mean GQ (latest age) (*p*-value for diff)	Positive association betw. absence of **FTT** and development for AGA Ss; less so for SGA Ss.
					AGA	Adequate (> 3rd centile) Retarded (< 3rd centile)	105 26	46.3 45.2 ($p < 0.001$)	102.9 94.1 ($p < 0.001$)	
					SGA	Adequate (> 3rd centile) Retarded (< 3rd centile)	23 10	47.1 44.5 ($p < 0.001$)	98.3 95.0 (NS)	
Abramson (1991)[72] *Merrill-Palmer Quarterly* Flint and Detroit, MI, USA	24 (12 FTT; 12 controls) 42% male	NG*	2.86 (0.61) 3.42 (0.55)	NG* NG*	Expression	Frequency (SD) FTT	Control	*p*-value for diff.		**No association** for overall expressivity, but **FTT** cases showed more negative emotions and lower face actions than controls.
					Overall expressivity	NG*	NG*	NS*		
					Positive emotion	45 (23)	67 (26)	$z = 1.88$; $p < 0.06$ (NS)		
					Negative emotion	22 (15)	9 (7)	$z = 2.54$; $p < 0.01$		
					Discrete emotions: **all NS** apart from 'dissmell': †	7 (6)	3 (3)	$z = 1.91$; $p < 0.05$		
					Upper face actions	53 (23)	55 (22)	NS*		
					Lower face actions	32 (26)	48 (24)	$z = 2.07$; $p < 0.05$		
					Self-comforting	14 (16)	5 (6)	$z = 1.80$; $p < 0.07$ (NS)		
					Aversion of eye gaze	NG*	NG*	$z = 2.31$; $p < 0.05$		
					Vocalizations	12	15	NS*		

** NG = not given; NS = non-significant*

† 'dissmell' = an expression somewhere between disgust and contempt, used by neonates in response to a bad smell for example

Table 3.3B (ii) (continued). Summary data extracted from studies included in review of growth faltering in infancy and cognitive development

Details	***Design and Participants***				***Main Findings***					
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)	General Description					Conclusion
Dykman (2001)[73] *Clinical Pediatrics* Arkansas, USA MEDLINE	44 (27 FTT; 17 controls) 61% male	33%	Not given, but 56% had bwts < 5th percentile	NG*	Outcome	Mean (SD)				
						FTT	Control	Difference (FTT – control)	*p*-value	
					WISC IQ	76.3 (14.3)	88.6 (12.7)	-12.3	$p < 0.01$	Inconclusive
					VMI SS	81.4 (10.5)	89.1 (13.1)	-7.7	$p < 0.01$	
					Reading SS	84.7 (12.7)	89.8 (11.0)	-5.1	NS	
					Spelling SS	87.5 (16.3)	91.7 (13.0)	-4.2	NS	
					Arithmetic SS	86.7 (17.1)	87.2 (10.3)	-0.5	NS	
					CBCL Internalising	61.7 (12.5)	55.4 (11.9)	+6.3	NS	
					CBCL Exernalising	62.5 (10.0)	49.8 (8.8)	+12.7	$p < 0.001$	

** NG = not given; NS = non-significant*

Table 3.3C (i). Description of studies included in review of infant size/growth in weight or height and cognitive development

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Berkman (2002)[74] *Lancet* Lima, Peru MEDLINE	Prospective cohort study of childhood cognitive function in previously stunted infants. Source popn. was offspring of a random sample of pregnant women in the censused community.	143 Ss whose mothers were enrolled during 1989-91 whilst in the final trimester of pregnancy. No bwt or gest. age info. 53% male; no race info. Info on education of Ss & parents, plus family income & career, also given. Source popn. was a slum community, so low SES. Only incl. criterion was regular FU in infancy. 68% FU; reasons for losses given. Non-participants & study Ss compared for stunting prevalence & SES – no sig. diffs.	Infancy: size (wt & ht) every 30days from 0 to 2yrs, measured by fieldworkers according to standard protocols. No reliability info. Wt-for-age & ht-for-age *z*-scores calculated using WHO reference data; wasting defined as wt-for-age z-score < -2; stunting as ht-for-age z-score < -2. Outcome: 9-yr cognitive function, using Weschler WISC-R. Administered by 6 trained & supervised psychology interns.	Multivariate ANOVA models giving *β*-coefficients, 95% CIs and p-values for assoc. betw. stunting & 9-yr cognition, adjusted for paternal education & Ss' school type.
Monckeberg (1972)[75] *Am J Clin Nutr* Santiago, Chile MEDLINE	Cross-sectional study of assoc. betw. size and cognitive development in infancy. Popn. based; sample consisted of a random sample from a slum area and a middle-class comparison gp.	110 Ss randomly sampled from a slum community – low SES. Parental IQ, education & income given, but no other baseline info. Authors state that ethnic profile of study Ss is similar to national. No info on size of source popn, %FU, or comparisons betw. study Ss and non-selected Ss.	Infancy: size (wt, ht & HC) on entry to study (age 1-3yrs). Ascertainment unclear; could be medical records or data from a previous study. Wt-for-age & growth deficit for ht & HC (=real size/expected size for age) calculated using Iowa standard. Outcome: mental development at 1-3yrs, ascertained using Gesell scales*. No info on observers or reliability.	Mean DQ scores within malnourished (wt-for-age <3rd centile) & well-nourished groups (>10th centile), with *p*-values for differences. Scatter plots with correlation coefficients & *p*-values for assoc. betw. DQ and ht & HC growth deficits.
Paine (1984)[76] *Dev Psychol* Brasília, Brazil PsycINFO	Prospective study with cross-sectional analysis of assoc. betw. height & cognitive function at 4 time points in infancy. Set in a single hopsital; sampling method unclear.	80 Ss born during 1975-78 in a single teaching hospital. All were born at term. 36% were SGA, with low mean bwt (<2.5kg); the remainder were AGA, with mean bwt normal. SES, maternal age & ht also given – no sig diffs betw. gps, but no info on whether representative of wider community. No sex or race info. No info on size of source popn, selection method or %FU.	Infancy: size (height) at 4, 8, 12 & 18mo, measured at outpatient clinic by a single trained nurse's aid using standardised techniques. Outcome: psychomotor development (DQ) at same time points as above, ascertained by a single observer (one of the authors) using Gesell scales*.	Correlation coefficients, with *p*-values, betw. length and DQ at each of the 4 time points, within separate SGA and AGA groups. Bwt and SES controlled for. Also, hierarchical multiple correlation coeffs given for DQ using length, bwt & SES.
Gherpelli (1993)[77] *Arq Neuropsiquiatr* Sao Paulo, Brazil MEDLINE	Prospective cohort study of SGA Ss, assessing relationship betw. size & neurological development in infancy. Setting unclear, but probably a single hospital NICU; selection method unclear.	37 SGA Ss born during 1984-86. Mean bwt was low (2.0kg); mean gest. age was normal. 43% male; 47% white. "Most" Ss were from low SES families. Incl/excl. criteria clearly stated. 44% FU. Non-participants compared to study Ss on sex, race, SES, bwt & gest. age – no sig diffs. However, potential diffs in infant size cannot be known.	Infancy: size (weight) at 1yr, measured by a single observer (one of the authors). No further info. Outcome: 1-yr neurological development, by examination & use of Denver Developmental Screening Test, carried out by a single observer (one of the authors). Not blind to infant size status.	Correlations, with *p*-values, between 1-yr weight < 2.5 percentile and whether developmentally or neurologically "normal" or "abnormal" at 1yr.

*see Gesell A, Amatruda C (1947). *Developmental diagnosis: normal and abnormal development.* New York: Harper & Row.

Table 3.3C (i) (continued). Description of studies included in review of infant size/growth in weight or height and cognitive development

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Ross (1983)[78] *J Pediatr* New York, USA Reference list	Prospective cohort study of VLBW Ss, assessing relationship betw. infant growth & neuro-behavioural outcome. Source popn. was admissions to the perinatology dept. of a single hospital.	86 VLBW (<1.5kg) Ss admitted to a perinatology dept. during 1978-79. Mean bwt given; mean gest. age was very low (<29wks). All were AGA. 50% male; 45% white. "About half" from middle- or upper-class families (using Hollingshead scale). No info on size of source popn, method of selection or %FU.	Infancy: size (wt, ht & HC) at 3, 6, 9 & 12mo, measured using standard equipment at the study centre. No info on observers or reliability. Wt measured to nearest 100g; ht & HC to nearest 0.5cm. Outcome: neuro-behavioural development at 12mo, ascertained using Bayley scales by a single psychologist "without knowledge of perinatal condition".	Mean wt, ht & HC given at each of 3, 6, 9 & 12mo for premature Ss with low (<85) & high (≥85) Bayley scores, and for term Ss. P-values given in text. Association of SES, bwt, gest. age & other perinatal factors to 12-mo size investigated, but not adjusted for.
Rose (1994)[79] *Child Development* Bombay, India PsycINFO	Cross-sectional study assessing the assoc. betw. size & cognitive development in infancy. Source popn. was attendees of a single well-baby clinic.	183 Ss, recruited from a single well-baby clinic during Oct-Dec 1984. Mean bwt was low normal; no gest age info. 60% male; no race info. Maternal size & education, birth order & family income also given. "Many" families unskilled, though some Ss from families who would normally have private healthcare were recruited. "Nearly all" Ss were breastfed. No incl/excl criteria used; study Ss represented "virtually all" of the source popn, though no %FU given. No info on non-participants.	Infancy: size (ht, wt & HC) measured at 5-12mo using standard techniques. Reliability ensured by averaging of repeated measurements & use of inter-rater reliabilities (all high). "Underweight" defined as weight-for-age < -1 SD, using NCHS standards. Outcome: behavioural development (visual recognition memory & cross-modal transfer) at 5-12mo, assessed using standard techniques by 2 observers with good inter-rater reliability.	Mean fixation times to novel shapes following varying amounts of visual or tactual familiarisation, within "adequate" & "underweight" groups, with *p*-values given for difference from chance. ANOVA and regression models used to assess potential confounders: bwt, maternal size, parental education & income all considered, but no size-of-effect measures presented.
Corbett (2004)[80] Unpublished Newcastle-upon-Tyne, UK From expert	Prospective cohort study assessing the relationship between infant size and educational achievement in childhood. Source popn. was all live births in study region in 1 year.	1724 Ss born during 1987-88 in a single city. Of the original 3652 Ss, 94% were born at term (>36wks), and bwt was normal compared to UK 1990 growth standards. No sex or race info. Townsend deprivation scores varied from –6.25 to +8.98. No excl. criteria used. 47% FU. Ss with incomplete data compared to study Ss: "very similar" on gest age, bwt & late weight SDS, but those with incomplete outcome data had lower SES scores, whilst those with incomplete weight data had poorer outcomes. No info on the remaining losses to FU.	Infancy: size (weight), routinely measured throughout infancy. Data obtained from child health clinic records. Converted to SD* scores for age & sex, adjusted for gest. age if <37wks, using 1990 UK growth standards. "Late infancy" wt defined as latest available wt SDS betw. 9 & 24mo. Outcome: educational achievement at 10yrs, using 4 well-validated tests (measuring 'problems of position', 'picture vocabulary', reading & maths). No info on observers or reliability though.	Multiple regression giving unstandardised coeffs & 95% CIs for change in outcome score assoc. with a 1 unit change in late infancy weight SD score, adjusted for gestation., bwt & SES (Townsend deprivation score).

Table 3.3C (i) (continued). Description of studies included in review of infant size/growth in weight or height and cognitive development

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Whaley (1998)[81] *Dev Behav Pediatr* Embu, Kenya PsycINFO	Longitudinal cohort study assessing relationship betw. infant size and childhood motor development. Source popn. was 3 sub-areas of a geog. district; sampling approach unclear.	132 Ss born during a 17-mo period in a defined geog. region of Kenya. Mean bwt z-score was < 1 SD using 'normal' growth charts; no gest. age info. 55% male; all Ss from Embu tribe. Diet, lifestyle & SES of region described. Incl/excl criteria clearly described. %FU ranged from 96% to 78% at different FU points. No info on non-participants, but the relatively low attrition reduces the risk of bias.	Infancy: size (ht, wt & arm circumference) measured monthly over first 6mo using standard procedures. No info on observers or reliability. Size-for-age data calculated each month for each of ht, wt & arm circ. Outcome: mental development at 30mo, ascertained using Bayley Mental Scale by 2 trained & supervised local women. Close agreement on scoring.	Correlation coefficients and p-values given for association betw. each infant size measure and outcome at 30mo. No consideration of confounders.
Latal-Hajnal (2003)[82] *J Pediatr* Zurich, Switzerland MEDLINE	Prospective cohort study of VLBW Ss, assessing relationship betw. size and motor development in infancy. Source popn. was all live-born VLBW Ss from a single maternity hospital.	219 VLBW (<1.5kg) Ss recruited from a single maternity hospital in 3 phases: 1983-85, 1988-89 and 1992-94. 40% were SGA; mean bwt & gest. age given within SGA & AGA groups. Ss "almost completely" white; no sex info. No excl. criteria used. 64% FU of all births; 94% FU of survivors. No info on non-participants, but losses (as opposed to deaths) were minimal.	Infancy: size (wt, ht & HC) at age 2yrs, measured "according to standard anthropometric procedures". No further info. Outcome: 2-yr mental development, ascertained using Bayley Mental Scale at the hospital by paediatricians experienced with the tests. Possible blinding: "examiners not involved in the neonatal care of the study Ss".	Correlation coeffs & *p*-values betw. all size variables and PDI. Mean PDI given by size category (stratified at 10th percentile), with chi-square testing. Logistic regression for PDI <84pts by weight percentile category, adjusted for sex, SES, gest. age & others, stratified for bwt.
Upadhyay (1992)[83] *Indian Pediatrics* Varanasi district, India Reference list	Prospective cohort study, with cross-sectional analyses, of assoc. between degree of malnutrition (wt-for-age) & cognitive development in infancy. Setting is 10 villages in same region; target population unclear.	224 Ss born during 1981-83 in 10 villages in a single Indian rural 'block' (geog. district – popn. 120,000). No baseline info for Ss, but states that for 'block' as a whole, 26% of infants have bwt <2.5kg, and SES is low. 36% FU. No excl. criteria except lack of continuous FU data (< 4 data points out of 5). No data comparing non-participants to study Ss, but states that "general characteristics of these villages are almost representative of the rural population of this part of the country".	Infancy: Wt, ht and mid-arm, chest & head circumference at 4, 16, 28, 40 & 52wks, all measured using standard techniques & equipment. No info on place, observers or reliability though. Malnutr. defined using wt-for-age percent of NCHS 50th centile: Normal: >= 80% (of NCHS 50th centile); Grade I: <80 to 70%; Grade II: <70 to 60%; Grade III: <60%. Outcome: Developmental Quotient (DQ) at 4, 16, 28, 40 & 52wks. No further info.	Means and standard deviations within malnourishment groups. Also ANOVA model giving *F*- and *p*-values between groups, controlling for 'environment', including parental occupation, educ & health, infant feeding, SES & others.

Table 3.3C (ii). Summary data extracted from studies included in review of infant size/growth in weight or height and cognitive development

Details	***Design and Participants***				***Main Findings***				***Summary of trend***
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)					
Berkman (2002)[74] *Lancet* Lima, Peru MEDLINE	143 (53% male)	68	NG*	NG*	Category	Numbers (stunted vs reference)	*β*-coefficient for change in 9-yr WISC score; 95% CI; *p*-value		Positive association with later cognition for severe **stunting** (compared to less severe or no stunting), and for longer-term stunting (compared to short-term stunting).
					Age at first stunting event (compared to "never stunted"):				
					6-17mo vs "never stunted" or age <6mo or ≥ 18mo	36 of 107	-4.3 (-8.3, -0.5); p=0.031		
					Stunting prevalence (months per year)				
					Continuous measure ≥ 2mo vs < 2mo	143 38 of 105	-0.6 (-1.3, +0.1); p=0.162 – NS -4.2 (-8.0, -0.4); p=0.032		
					Stunting severity ("severe" compared to "never stunted" or "not severe"):				
					All ages 0-11mo ≥ 12mo	10 of 133 5 of 138 10 of 107	-5.4 (-12.4, +1.6); p=0.129 – NS +0.1 (-10.7, +10.9); p=0.989 – NS -10.0 (-17.5, -2.4); p=0.011		
					All adjusted for inter-tester variability, paternal education, school type, grade retention & grade level.				
Monckeberg (1972)[75] *Am J Clin Nutr* Santiago, Chile MEDLINE	110 (no sex info)	NG*	NG*	NG*	Variable	Well-nourished (n=14) – malnourished (n=76)	Height deficit (correlation)	HC deficit (correlation)	Positive assoc. between **infant size** and DQ
					General DQ Motor dev	Diff= +16; p<0.0001 Diff= +21; p<0.0001	*r* = 0.56; *p*<0.001 --	*r* = 0.60; *p*<0.001 --	
					NB. Both size and DQ were measured at 1-3yrs.				
Paine (1984)[76] *Dev Psychol* Brasília, Brazil PsycINFO	51 AGA 29 SGA	NG*	3.25 (0.43) 2.16 (0.24)	≥ 37wks ≥ 37wks (term)	Correlation coeffs & *p*-values betw. height & DQ, controlling for bwt & SES:				Positive assoc. between **infant size** and DQ for SGA Ss, (except in late infancy), but no assoc. for AGA Ss.
					Age (mo)	SGA	AGA	*p* for diff betw. SGA & AGA	
					4 8 12 18	0.57 (*p*<0.05) 0.46 (*p*<0.05) 0.50 (*p*<0.05) 0.36 (NS)	0.08 (NS) -0.09 (NS) 0.02 (NS) 0.15 (NS)	*p* = 0.008 *p* = 0.006 *p* = 0.010 *p* = 0.169 (NS)	
					Hierarchical multiple correlation analysis (order of entry: bwt; SES; height): For AGA infants, either bwt significantly predicts DQ and adding SES & height does not better the prediction, or none of the variables significantly predict DQ. For SGA infants, height is always a significant predictor; bwt never is. SES also predicts DQ at ages 8 & 18mo, but height improves the prediction in both cases.				

* SD = standard deviation; NG = "not given"; HR = hazard ratio; OR = odds ratio; CI = confidence interval; NS = not significant

Table 3.3C (ii) (continued). Summary data extracted from studies included in review of infant size/growth in weight or height and cognitive development

Details	***Design and Participants***				***Main Findings***				***Summary of trend***
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)					
Gherpelli (1993)[77] *Arq Neuropsiquiatr* Sao Paulo, Brazil MEDLINE	37 (43% male)	44	2.02 (range 1.03 – 2.58) LBW	37.4 (range 32 – 40)	Outcome	% abnormal at 1yr	*p*-value for correlation with 1-yr weight < 2.5 percentile		Positive assoc. between increased **infant size** and normal development
					Neurologic (examination) Developmental (DDST)	32.5% 25.0%	*p* = 0.0001 *p* = 0.0011		
Ross (1983)[78] *J Pediatr* New York, USA Reference list	86 (50% male)	NG*	1.16 (0.21) VLBW	29 (1.8) Very preterm	Differences in size analysed using ANOVA, controlling for bwt. All differences were significant (p<0.05) except 12-mo HC for females. Outcome measured at 12mo.				Positive assoc. between increased **infant size** and normal development.
						Mean size diff (low Bayley score – normal Bayley score)			
					Variable	3mo	6mo	9mo	12mo
					Wt (g) – males Wt (g) – females Ht (cm) – males Ht (cm) – females HC (cm) – males HC (cm) – females	-474 -551 -2.5 -3.9 -1.8 -1.3	-722 -330 -1.6 -1.5 -1.7 -1.2	-712 -808 -4.0 -2.3 -1.5 -0.6	-1002 -851 -2.2 -2.2 -1.7 -0.2 (NS)
Rose (1994)[79] *Child Development* Bombay, India PsycINFO	183 (60% male)	NG*	2.76 (NG) (Low-normal)	NG*	Outcome	ANOVA, controlling for age & familiarisation time:	Regression, controlling for bwt, age, parental educ & previous illness (extra variance explained):		Positive assoc. between increased **infant size** and normal development.
					Visual recognition Cross-modal transfer	F(1, 160) = 14.8, p < 0.001 F(1, 160) = 9.19, p < 0.01	8% (p < 0.05) 7% (p < 0.05)		
					All figures are for addition of extra "weight" variable, categorised into "normal" and "underweight". Normal weight infants showed proportions of their attention on the novel object that were significantly different from chance.				
Corbett (2004)[80] Unpublished Newcastle-upon-Tyne, UK From expert	1724 (no sex info)	47	Range (SD score): -4.1 to +3.1 (Normal)	94% born at term	10-yr outcome	Unstandardised coeff (95% CI) for unit change in "late infancy" weight SD score			Positive assoc. between increased **infant size** and normal development, **but** only significant for one subscale.
					Problems of position Picture vocabulary Reading Maths	0.30 (-0.2, 0.8) – NS 0.68 (0.2, 1.1); p=0.003 0.39 (-0.1, 0.8) – NS 0.36 (-0.1, 0.8) – NS			

* SD = standard deviation; NG = "not given"; HR = hazard ratio; OR = odds ratio; CI = confidence interval; NS = not significant

Table 3.3C (ii) (continued). Summary data extracted from studies included in review of infant size/growth in weight or height and cognitive development

Details	***Design and Participants***				***Main Findings***	***Summary of trend***
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)		
Whaley (1998)[81] *Dev Behav Pediatr* Embu, Kenya PsycINFO	132 (55% male)	78 to 96	*z*-score: -0.23 (0.98)	NG*	Correlation coefficients & p-values for infant size against 30-mo Bayey mental development. Age/variable: Upper arm circ. / Weight-for-age / Height-for-age Growth faltering slope: NG (NS) / NS at any age / NS at any age 0-6mo: 0.20 (p<0.05) 1-2mo: NG (NS) 3-4mo: 0.21 (p<0.05) 5-6mo: NG (NS)	Slight positive assoc. between **size** (arm circ.) and later development, but only for certain ages. No assoc. otherwise.
Latal-Hajnal (2003)[82] *J Pediatr* Zurich, Switzerland MEDLINE	219 (no sex info)	64 or 94	1.02 (NG*) VLBW	29.0 (NG) Very preterm	Mean MDI diff by 2-yr size (low – normal) for each of wt, ht & HC, adjusted for gest. age, SES, sex, multiple birth & others. Bwt category / 2-yr weight / 2-yr height / 2-yr HC Low bwt (< 10%): -3.5 (NS) / -8.3 (p<0.05) / -0.9 (NS) Normal bwt: -6.8 (p<0.05) / +1.5 (NS) / +1.2 (NS) Logistic regression for 2-yr MDI < 84 for low 2-yr weight compared to normal 2-yr weight, adjusted for sex, multiple birth, SES, gest. age & others: Bwt category / OR (95% CI) / Significance Low bwt (< 10%): 1.08 (0.28, 4.11) / *p* = 0.91 (NS) Normal bwt: 1.84 (0.44, 7.69) / *p* = 0.40 (NS)	Slight positive assoc. between **infant size** later development, but only for certain m'ments. No association when regression used.
Upadhyay (1992)[83] *Indian Pediatrics* Varanasi district, India Reference list	224 (% male not given)	36	NG	NG	*F*-ratios and *p*-values in ANOVA: 'nutrition' refers to the 4 malnourishment groups, whilst 'environment' includes parental occupation, educ & health, infant feeding, SES & others. Age (wks) / Nutrition gp effect / Nutrition + environment gp effect 16: 6.01 (*p* < 0.01) / 0.68 (NS) 28: 15.18 (*p* < 0.01) / 1.35 (NS) 40: 12.85 (*p* < 0.01) / 0.43 (NS) 52: 35.52 (*p* < 0.01) / 0.95 (NS) Subscales (motor, adaptive, langauge & personal-social): after addition of environmental factors, none were significant at any age, except 'motor' at 40wks (*F*=3.63, *p*<0.01) and 'language' at 28wks (*F*=2.22, *p*<0.05).	After adjustment for confounders, **no association** between degree of **malnourishment** and cognitive development.

Table 3.3D (i). Description of studies included in review of infant size/growth and motor development

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Astbury (1986)[38] *Dev Med Child Neurol* Melbourne, Australia MEDLINE	Prospective cohort study of AGA VLBW Ss, assessing relationship betw. growth and motor & cognitive development in infancy. Source popn. was surviving discharges from a single hospital NICU.	235 AGA VLBW (<1.5kg) Ss discharged from a single NICU during 1977-80. Mean bwt given; mean gest. age normal. 49% male; no race info. 48% of fathers had occupations at/above the level of skilled worker. No excl. criteria used. 94% FU; all losses due to failure to attend for assessment. No comparisons betw. non-participants and study Ss. Unclear whether source popn is representative of all VLBW infants or whether all such Ss were enrolled.	Infancy: Size (wt, ht & HC) at discharge (mean age 63days) and 2yrs, carried out by 2 of the authors (a paediatrician & a psychologist). 2-yr wt categorised by <10th & >10th centile. No further info. Growth (change in wt, ht & HC) from discharge to 2yrs also assessed. Outcome: 2-yr motor development, using Bayley PDI. Same observers as for infancy m'ments. No further info.	Means and p-values for differences in motor development between the 2-yr weight categories. No adjustment for confounders, although SES & infant feeding were compared betw. the 2-yr wt groups.
Connors (1999)[84] *J Paediatr Child Health* Brisbane, Australia MEDLINE	Prospective cohort study of ELBW Ss, assessing relationship betw. poor growth and motor development in infancy. Source popn. was surviving discharges from a single hospital.	226 ELBW (<1kg) Ss discharged from a single hospital during 1987-92. Mean bwt given; mean gest. age was extremely preterm (<28wks). 45% male; no race info. Maternal age, education & marital status also given. No excl. criteria used. 88% FU; reasons for losses given. Non-participants compared to study Ss on important variables – mothers of study Ss likely to be better educated & married, leaving potential for bias.	Infancy: Size (weight) at 2yrs, measured in hospital using standard equipment. No info on observers or reliability. Categorised into <3rd, 3rd – 9th & ≥10th centile using NCHS growth charts. Outcome: 2-yr motor development, using Neurosensory Motor Developmental Assessment (NSMDA). No info on observers or reliability.	Cell counts of NSMDA 'borderline' & '≥ mild' scores, with chi-square test & p-value. Also multiple logistic regression for NSMDA score, adjusting for feeding difficulty & maternal education.
Jaffe (1982)[85] *Clinical Paediatrics* Haifa, Israel MEDLINE	Cross-sectional study assessing relationship betw. overweight & motor development in infancy. Source popn. was a random sample of Ss attending infant welfare clinics in a single city.	135 Ss aged 6-18mo randomly sampled from attendees of infant welfare clinics in a single city. LBW & premature infants excluded, but mean bwt & gest. age not given. No sex or race info, or any other baseline data. 99% FU of target sample; no info on original popn. from which Ss were sampled though. Reasons & infant size data given for the 1 loss to FU.	Infancy: size (wt & ht) at 6-18mo. Equipment & procedure given, but no info on observers or reliability. Wt & ht used to calculate Sveger's Index: overweight defined as index of 111-120, obesity as > 120. Outcome: motor development at 6-18mo, ascertained using Sheridan Stycar schedule by a single observer (one of the authors). "Delay" defined as an age lag of ≥ 3mo in any of the 4 spheres of development in the schedule.	Numbers and percentages of Ss with normal & "delayed" development by weight category ("normal", "overweight" & "obese"). Chi-square test used, giving *p*-values.
Kohlhauser (2000)[86] *Clinical Paediatrics* Vienna, Austria PsycINFO	Prospective cohort study of VLBW Ss, examining predictors (incl. HC) of development in infancy. Source popn. was surviving discharges from a single hospital NICU.	76 VLBW (<1.5kg) Ss admitted to a single NICU during 1994-95. Mean bwt given; mean gest. age was very preterm (<32wks). 50% male; no race info. 84% of parents married; parental age & education and birth rank info also given. Only incl. criterion was regular FU in infancy. 77% FU; reasons for losses given. No comparison betw. non-participants and study Ss.	Infancy: size (HC) at 1yr, measured by a single observer during clinic visit. No further info. Outcome: Development at age 1-2yrs, assessed using Griffiths scales by psychologists; no further info.	ANOVA models and correlations giving p-value for association betw. 1-yr HC and 1-2yr development. Bwt and SES also assessed in relation to outcome, but no formal adjustment.

Table 3.3D (i) (continued). Description of studies included in review of infant size/growth and motor development

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Whaley (1998)[81] *Dev Behav Pediatr* Embu, Kenya PsycINFO	Longitudinal cohort study assessing relationship betw. infant size and childhood motor development. Source popn. was 3 sub-areas of a geog. district; sampling approach unclear.	132 Ss born during a 17-mo period in a defined geog. region of Kenya. Mean bwt z-score was < 1 SD using 'normal' growth charts; no gest. age info. 55% male; all Ss from Embu tribe. Diet, lifestyle & SES of region described. Incl/excl criteria clearly described. %FU ranged from 96% to 78% at different FU points. No info on non-participants, but the relatively low attrition reduces the risk of bias.	Infancy: size (ht, wt & arm circumference) measured monthly over first 6mo using standard procedures. No info on observers or reliability. Size-for-age data calculated each month for each of ht, wt & arm circ. Outcome: motor development at 6 & 30mo, ascertained using Bayley Motor Scale by 4 trained & supervised local women. Close agreement on scoring.	Correlation coefficients and p-values given for association betw. each infant size measure and outcome at both 6 & 30mo. No consideration of confounders.
Latal-Hajnal (2003)[82] *J Pediatr* Zurich, Switzerland MEDLINE	Prospective cohort study of VLBW Ss, assessing relationship betw. size and motor development in infancy. Source popn. was all live-born VLBW Ss from a single maternity hospital.	219 VLBW (<1.5kg) Ss recruited from a single maternity hospital in 3 phases: 1983-85, 1988-89 and 1992-94. 40% were SGA; mean bwt & gest. age given within SGA & AGA groups. Ss "almost completely" white; no sex info. No excl. criteria used. 64% FU of all births; 94% FU of survivors. No info on non-participants, but losses (as opposed to deaths) were minimal.	Infancy: size (wt, ht & HC) at age 2yrs, measured "according to standard anthropometric procedures". No further info. Outcome: 2-yr motor development, ascertained using Bayley Motor Scale at the hospital by paediatricians experienced with the tests. Possible blinding: "examiners not involved in the neonatal care of the study Ss".	Correlation coeffs & *p*-values betw. all size variables and PDI. Mean PDI given by size category (stratified at 10th percentile), with chi-square testing. Logistic regression for PDI <84pts by weight percentile category, adjusted for sex, SES, gest. age & others, stratified for bwt.
Tenovuo (1988)[37] *Neuropediatrics* Turku, Finland Reference list	Prospective cohort study of SGA Ss, assessing risk factors, incl. infant head size, for developmental status. Source popn. was catchment area of a hospital, accounting for 10% of all annual deliveries in Finland.	463 SGA (bwt <10th percentile for gest. age) Ss born during 1981-82 in the catchment area of a single hospital. Mean bwt & gest. age not given, but all bwts were >0.5kg, and only 6% were preterm. No sex or race info. No excl. criteria used other than SGA & bwt limit. 89% FU; main reason given was movement to other parts of the country. No comparison betw. non-participants and study Ss.	Infancy: size (HC) at 2yrs, measured at child welfare clinics by nurses or doctors. No info on techniques or inter-observer reliability. Outcome: developmental delay at 2yrs, ascertained using Denver Developmental Screening Test* by paediatricians at the hospital or health centre doctors. No reliability info. Tests were scored "normal", "doubtful" or "abnormal".	Cell counts of Ss classed as "normal" or "abnormal or doubtful" at 2yrs by 2-yr HC percentile, classified as "<2.5 percentile", "2.5-10" & ">10". Chi-square test for independence carried out, and *p*-value given. No consideration of confounders.
Hack (1991)[54] *NEJM* Cleveland, USA Reference list	Extension of study by Hack (1986), with a larger birth cohort and later childhood FU. Assessed relationship betw. **head size** in infancy and childhood IQ.	249 VLBW (< 1.5kg) infants admitted to an NICU during 1977-79. Extension of 1977-78 cohort used in Hack (1986). Mean bwt given; mean gest. age was very low (29.7wks). 50% male; 56% had black mothers. Other maternal and perinatal vars given at baseline, incl. maternal age & educ. No excl. criteria used. 79% FU. Non-participants compared to study Ss on all baseline vars; only sig diff was that mothers of study Ss more likely to be black.	Infancy: as for Hack (1982). Outcome: Visual & fine motor development at mean age 8.6yrs, ascertained by Bender Gestalt and Purdue Pegboard Tests†. No info on observers, reliability or blinding.	Tables of means and differences, with 95% CIs, for development scores between "normal" & "subnormal" 8-mo HC groups. Hierarchical multiple regression giving unstandardised *β*-coeffs & *p*-values for assoc. betw. 8-mo HC and 8-yr development, adjusting for SES and bwt.

Table 3.3D (i) (continued). Description of studies included in review of infant size/growth and motor development

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Simon (1993)[87] *Clinical Pediatrics* Alabama, USA MEDLINE	Retrospective cohort study assessing relationship betw. **catch-up head growth** and motor development in VLBW infants. Setting was a single NICU.	48 AGA VLBW (< 1.5kg) infants discharged from a single NICU during 1985-87. Mean bwt given; mean gest. age was very low (28.5wks). No sex, race or other baseline info. Very clear incl. criteria given. 94% FU. No info on non-participants, but %FU was very high. However, the target popn. was 'retrospectively selected' – no info on selection criteria or on the popn. from which selection took place.	Infancy: size (HC) at 1, 3, 6 & 12mo after discharge from NICU, corrected for gest. age. Catch-up head growth defined as HC recovering to 5th percentile using NCHS growth charts. Measured at NICU by same nurse on each visit. Outcome: mental & motor development at 12mo corrected age, using DDST, MDI & PDI. Administered by trained professionals, blinded both to each other & to previous growth status.	Ss grouped into 'normal' & 'abnormal' motor function at 12mo corrected age. Mean & SD for age at catch-up head growth given within each group. Positive & negative test predictive values given betw. catch-up head growth and 12-mo motor delay. No consideration of confounding factors.
Cheung (2001)[88] *Int J Epidemiol* Lahore, Pakistan MEDLINE	Large-scale prospective cohort study assessing relationship between growth in the first 6 months of infancy with gross and fine motor development. Source population was infants born between 1984-87 in 4 areas of Lahore (village, periurban slum, urban slum and upper middle-class).	1476 infants born 1984-87 in one of the 4 areas of Lahore. Mean gestational age was 39 weeks and only 3% were preterm. Mean wt-for-length at birth and sex reported. Excl. criteria clearly stated (death, migration and small number with extreme anthropometric measurements). Also some loss to FU due to missing data. 69% of all births and 81% FU of target popn. Some non-participant info but not on losses due to missing or extreme data.	Infancy: Length measured according to standard procedures by trained fieldworkers with inter-observer differences checked regularly. Wt-for-length SDS and length SDS used to assess PN wasting and stunting respectively. Outcome: fine and gross motor developmental milestones (age at independent walking (10 steps), building tower of 3 bricks). Mean age indep walking and building 3-cube tower=17.8mo and 13.8mo respectively.	Logistic regression analysis, adjusted for SES, bwt, sex, gestational age. Survival analysis to deal with censored data (loss to FU before milestones reached). Time ratios calculated, indicating relation of a unit change in indep var on the age at achieving milestone (e.g. unit change 0.9 means one unit increase indep var is associated with 10% decrease in age achieving milestone).

* see Frankenburg WK, Dodds JB. The Denver developmental screening test. *Pediatrics* 1967;**71**:181-6. The test includes items on motor development (walking, eating, dressing), sensory development (vision, hearing) and cognitive development (comprehension). The analysis relevant to this review involved overall development and did not address these subgroups individually.
† see Koppitz EM. *The Bender Gestalt test for young children. Vol. 2.* New York: Grune & Stratton, 1975 and Wilson BC, Iacoviello JM, Wilson JJ, Risucci D. Purdue pegboard performance of normal preschool children. *J Clin Neuropsychol* 1982;**4**:19-26.

Table 3.3D (ii). Summary data extracted from studies included in review of infant size/growth and motor development

Details	***Design and Participants***				***Main Findings***				***Summary of trend***
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)					
Astbury (1986)[38] *Dev Med Child Neurol* Melbourne, Australia MEDLINE	235 (49% male)	94	1.20 (0.22) VLBW	29 (2) Very preterm	2-yr outcome PDI Gross motor age (mo) Fine motor age (mo)	Mean diff in outcome score (low 2-yr wt – normal 2-yr wt) -5.7 (p=0.03) -2.5 (p<0.001) -1.9 (p<0.01)			Positive assoc. between increased **infant size** (weight) & improved motor development.
Connors (1999)[84] *J Paediatr Child Health* Brisbane, Australia MEDLINE	226 (45% male)	88	0.82 (0.13) ELBW	27.0 (2.2) Extreme-ly preterm	Multiple logistic regression for "normal/borderline" NSMDA compared to "mild or above" for 2-yr wt < 10th centile vs ≥ 10th centile, adjusted for maternal education, feeding difficulty & others: OR = 3.4; 95% CI = (1.1, 11.2) Adding gest age, SGA status & infant feeding did not significantly alter the association. After addition of birthweight: OR = 3.3; 95% CI = (0.9, 10.0) – NS.				Positive association between **size** and motor development, but effect **mostly due to birthweight**.
Jaffe (1982)[85] *Clinical Paediatrics* Haifa, Israel MEDLINE	135 (no sex info)	99	NG*	NG*	Infant wt category Normal Obese/overwt Overwt Obese	*n* 79 56 45 11	% delayed motor development at 6-18mo 9% 30% 29% 36%	A chi-square test for independence concluded that the "fat" Ss had a significant delay compared to "normal" Ss ($p < 0.05$)	Inverse association between **infant size** and prevalence of normal motor development.
Kohlhauser (2000)[86] *Clinical Paediatrics* Vienna, Austria PsycINFO	76 (50% male)	77	1.04 (NG*) VLBW	28.8 (NG) Very/extr. preterm	Risk factors for poor developmental outcome at 1-2yrs: Neuromotor development (no, mild, severe) HC at 1 year (<3rd centile compared to > 3rd) Bwt (0.5-1kg, 1-1.5kg) Gest. age (25-28wks, 29-32wks)		$p = 0.03$ $p = 0.04$ $p = 0.31$ (NS) $p = 0.28$ (NS)		Positive assoc. betw. increased **infant head size** & improved development.
Whaley (1998)[81] *Dev Behav Pediatr* Embu, Kenya PsycINFO	132 (55% male)	78 to 96	*z*-score: -0.23 (0.98)	NG*	Correlation coefficients & p-values for infant size against 6-mo Bayey motor development. No correlations with 30-mo Bayey motor development were significant.				Positive assoc. with motor development for *some* **infant size** measurements at *some* ages, but **inconclusive** overall.
					Age/variable	Upper arm circ.	Weight-for-age	Height-for-age	
					Growth faltering slope 0-6mo 1-2mo 3-4mo 5-6mo	0.19 (p<0.05) 0.19 (p<0.05) NG (NS) NG (NS) 0.26 (p<0.01)	NS at any age	NS at any age	

* SD = standard deviation; NG = "not given"; OR = odds ratio; CI = confidence interval; NS = not significant

Table 3.3D (ii) (continued). Summary data extracted from studies included in review of infant size/growth and motor development

Details	***Design and Participants***				***Main Findings***	***Summary of trend***
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)		
Latal-Hajnal (2003)[82] *J Pediatr* Zurich, Switzerland MEDLINE	219 (no sex info)	64	1.02 (NG*) VLBW	29.0 (NG) Very preterm	Mean PDI diff by 2-yr size (low – normal) for each of wt, ht & HC, adjusted for gest. age, SES, sex, multiple birth & others. Bwt category: Low bwt (< 10%) / Normal bwt 2-yr weight: -11.9 (p<0.001) / -13.2 (p<0.001) 2-yr height: -11.7 (p<0.01) / -15.7 (p<0.001) 2-yr HC: -4.2 (NS) / -8.4 (p<0.05) Logistic regression for 2-yr PDI < 84 for low 2-yr weight compared to normal 2-yr weight, adjusted for sex, multiple birth, SES, gest. age & others: Bwt category: Low bwt (< 10%) / Normal bwt OR (95% CI): 4.32 (0.70, 26.51) / 5.77 (1.15, 29.0) Significance: *p* = 0.12 (NS) / *p* = 0.04	Positive assoc. between **infant size** and motor development. Assoc. is stronger among normal bwt Ss than LBW Ss.
Tenovuo (1988)[37] *Neuropediatrics* Turku, Finland Reference list	463 (no sex info)	89	All > 0.5kg	6% were preterm (<37 wks)	2-yr HC (percentile) / 2-yr development (counts; %): Normal / Abnormal or doubtful < 2.5: 35 (8%) / 4 (31%) 2.5 to 10: 69 (15%) / 3 (23%) > 10: 346 (77%) / 6 (46%) χ^2 - test for independence: χ^2 = 9.99 on 2df; *p* = 0.007	Positive assoc. between **head size** and development in infancy.
Hack (1991)[54] *NEJM* Cleveland, USA Reference list	249 (50% male)	79	1.18 (0.22) VLBW	29.7 (2.0) (Very preterm)	Mean diff in 8-yr motor dev is given as subnormal HC – normal HC at 8mo. Regression coeff is for subnormal 8-mo HC compared to normal HC. Motor development at 8yrs: Mean diff (95% CI) in 8-yr motor dev by 8-mo HC Visual motor: +0.8 (-0.62, 2.26); NS Fine motor: -0.3 (-1.05, 0.46); NS	No association betw. infant **head size** and **childhood** motor development.
Simon (1993)[87] *Clinical Pediatrics* Alabama, USA MEDLINE	48 (% male not given)	94	1.09 (range 0.66 – 1.48) VLBW	28.5 (range 25 – 32wks) (Very preterm)	Motor performance at 12mo (corrected for gestation): Normal (n=37) / Abnormal (n=11) / *p* for diff Mean catch-up time (mo): 3.7 (3.1) / 7.7 (2.1) / *p* < 0.05 % catch-up by 6mo: 89% (n=37) / 27% (n=3) / *p* < 0.05 Catch-up growth by 6mo as a predictor for motor delay at 12mo: Positive predictive value: 0.73 Negative predictive value: 0.84	Positive association between catch-up **growth** and motor development
Cheung (2001)[88] *Int J Epidemiol* Lahore, Pakistan MEDLINE	1014 (53% male)	81	NG	39 (NG) Only 3% <37 weeks	*Time ratio (95% CI): Independent walking / Building a 3-cube tower Postnatal wasting: 0.97 (0.96, 0.98) / 0.98 (0.97, 0.99) Postnatal stunting: 0.96 (0.94, 0.97) / 0.99 (0.98, 1.00) Where postnatal wasting =6mo wt-for-length SDS – birth wt-for-length SDS Postnatal stunting=6mo lengthSDS – birth length SDS	Inverse association between **infant growth** and achievement of developmental milestones. Poorer growth led to slower achievement of milestones. Time ratio indicator relation of unit change in the independent variable on age at achieving the milestone

* SD = standard deviation; NG = "not given"; OR = odds ratio; CI = confidence interval; NS = not significant

Table 4.1A (i). Description and quality assessment of studies included in review of infant size/growth and insulin dependent diabetes mellitus

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Johansson (1994)[89] *Diabetologia* Southeast Sweden	Case-control study comparing infant growth of i**nsulin dependent diabetics** with matched controls. Cases from paediatric clinics; popn-based controls matched by geog region. Source popn. was all diabetic patients treated at the clinics at time of study.	297 cases diagnosed during 1974-88; 792 controls drawn from national popn. register but matched to cases by geog region. Cases had slightly lower bwt than controls but not significantly (-0.16SD vs -0.05 SD, p=0.09). No further baseline info. Exclusion criteria stated, but no reasons. 90% FU of target for cases, 81% for controls. No info on non-participants, but %FUs are high, and target popn was all cases in study region & time period.	Infancy: Size (ht & wt) m'ments obtained from child welfare records and read as SD from growth charts and approximated to nearest 0.5 SD line at various ages. Growth (change in weight SD score from birth) used in analysis. Outcome: Insulin dependent diabetes. No info on diagnosis, but age at onset = timing of 1st insulin injection, from paediatric records.	Tables of means & diffs in growth betw cases & controls, with *p*-values and CIs for mean diffs calculated using *t*-tests. Also, diffs in growth betw. cases & controls compared in terms of sex, age of mother and infant feeding. Matching on age, sex & geog. region.
Hypponen (1999)[90] *Diabetes Care* Finland	Case-control study comparing infant size & growth of i**nsulin dependent diabetics** with matched controls. Popn-based; cases & controls from same source (entire Finnish popn). Source popn. was all Finnish children ≤14yrs diagnosed as diabetic during period of study.	435 cases diagnosed from Sep 1986 to Apr '89; 386 controls drawn from same source popn. All Ss were full-term (premature Ss were excluded); bwts were normal with no sig diff betw. cases & controls. 53% of cases & controls were male. Excl criteria clear. 54% FU for cases; 48% for controls. No info on non-participants or comparisons with study Ss, and losses to FU were high. Cases & controls compared for various SES & neonatal variables; no sig diffs.	Infancy: Size (wt) measurements at 3, 6 & 9mo obtained from well-baby and child health records. No further info, but same approach for cases as controls. Growth (change in weight) also used in analysis. Outcome: Insulin dependent diabetes. No further info, although presumably diagnosed at a medical facility.	Means & diffs in wt betw cases & controls given by sex and early introduction of formula feeding given, with p-values & CIs. Also, longitudinal logistic regression used for repeated measurements, with adjustment for formula feeding, giving ORs with 95% CIs. Matching on birth-date & sex.
Hypponen (2000)[91] *Diabetes Care* Finland	As for Hypponen (1999)	586 cases diagnosed from Sep 1986 to Apr '89; 571 controls drawn from same source popn. Cases & controls compared for bwt (normal), % born prematurely, plus various family & parental vars; no sig diffs (figures given). 53% of cases & controls were male. No explicit incl/excl criteria. 73% FU for cases; 71% for controls. No info on non-participants or comparisons with study Ss.	Infancy: Size (wt & ht) m'ments at various ages obtained from well-baby and child health records, converted to SD scores. No further info, but same approach for cases as controls. Outcome: Insulin dependent diabetes. No info on diagnosis, but confirmed with auto-antibody testing.	Fitted means & diffs in wt & ht SD score betw cases & controls by sex, with *p*-values, using longitudinal polynomial models. Also, logistic regression giving ORs adjusted for sex, age & the corresponding value of the other size measure (wt or ht) at ages 1 & 2yrs. Matching on birth-date & sex.

Table 4.1A (i) (continued). Description and quality assessment of studies included in review of infant size/growth and insulin dependent diabetes mellitus

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Baum (1975)[92] *Lancet* Oxford, UK	Case-control study comparing infant size of **insulin dependent diabetics** with a comparison group. Cases from a paediatric clinic; setting of controls is unclear. Source popn. was all children attending the clinic.	35 cases attending a single clinic; 80 controls randomly selected from "a larger group currently under study in Oxford for other purposes" – no further info, so potential for bias. Cases & controls all had normal bwts and were full-term (cases according to mother's recollection). 63% of cases & 50% of controls were male; no further baseline info. No sig diffs in bwt between cases & controls for either sex. 33% FU for cases, no info for controls. No info on non-participants or comparisons with study Ss.	Infancy: Size (wt) at 6 & 12mo, from infant welfare clinic records as retrieved by parents. Correction made for weight of clothing at time of measurement; supplied by parents' recall (cases only – no info for controls). Outcome: Insulin dependent diabetes. No further info, although presumably diagnosed at a medical facility.	Mean wts (& SDs) for cases & controls given separately by sex, with *p*-values for diffs calculated using *t*-tests. Could be said to be matched on bwt and gest. age.
DiLiberti (2002)[93] *Pediatrics* Wisconsin, USA	Cross-sectional study comparing infant size of **insulin dependent diabetics** with an unmatched comparison group. Cases from a paediatric clinic; controls from national survey. Target popn. was all diagnoses at the clinic satisfying incl/excl criteria.	446 cases diagnosed during 1988-98 at a single clinic; 10,522 unmatched controls from entire US popn (NHANES III). 51.3% of cases were male; no info for controls but presumably close to 50%. No further baseline info. Excl criteria clear: 'other medical conditions affecting growth' for both cases & controls, plus presence of diabetes for controls. 99% FU for cases, 75% for controls. No info on representativeness of cases, but %FU was high, & target popn was all suitable cases.	Infancy: Size (height) at 1 & 2yrs, measured at the clinic by a trained nurse with the same stadiometer (cases only – no info for controls). Converted to *z*-scores using data from controls. Outcome: Insulin dependent diabetes. No info on diagnosis, but age at onset = time of initiation of insulin therapy.	Tables of mean *z*-scores for diffs betw. cases & controls, both by sex and adjusted for sex, using linear regression modelling. Logistic regression giving ORs at 1 and 2yrs for risk of developing diabetes assoc. with each 1 SD increase in height (no CIs or *p*-values though). No matching.
Ramachandran (1994)[94] *Diabetes Res Clin Pract* Madras, India.	Cross-sectional study comparing infant size of **insulin dependent diabetics** at onset with a comparison group. Cases from a diabetes research centre; comparison data from standard growth charts. Source popn unclear.	48 cases aged 1-5yrs at onset, of which an unknown number were aged 1-2yrs. Size of comparison group unknown, but presumably fairly large. 50% of cases & controls were male. States that Ss "were from different income group families and were representative of the socio-economic groups in the general population" – no data though. Incl. criteria fairly clear, but no info on source popn, %FU or non-participants.	Infancy: Size (height) of cases at 1 & 2yrs (onset of diabetes), measured at research centre; no further info. Height of controls from standard charts of Indian Council of Medical Research. Outcome: Insulin dependent diabetes at 1 & 2yrs. No info on diagnosis, but confirmed at research centre by medical tests.	Not much of relevance to the review. Charts comparing ht of cases & controls separately by sex; no stat. analyses; authors deemed it unnecessary as differences small. Matching on age and sex.
Bruining (2000)[95] *Lancet* SW Netherlands Reference list	Case-control study comparing infant size of **insulin dependent diabetics** with controls. Cases identified using diabetes register complied by regional paediatricians & a children's hospital register; controls were healthy siblings of cases.	91 cases identified during 1995-98; 125 healthy siblings of cases. A comparison gp of 2151 healthy Ss was also used to calculate *z*-scores. Ss in all 3 gps were of non-immigrant Dutch origin. Cases & controls had "normal" bwt, length & BMI 2-4wks after birth, but no data given. Parental heights "not substantially different" from national standards. No further baseline info. No incl/excl stated. 50% FU for cases; no info for controls. No non-participant info.	Infancy: An average of 20 m'ments of ht & wt betw. 2wks & 5yrs, obtained from child health clinic records by parents. National reference values used to convert ht & BMI data to SD scores for each child. Outcome: Insulin dependent diabetes at a mean age of 8.3yrs. Based on registers claiming 95% ascertainment, but not confirmed with testing.	*z*-scores for height & BMI size and growth for cases & controls with respect to a healthy comparison group. *P*-values given for differences from zero. No matching or consideration for confounders.

See footnote at the end of Table B1.

Table 4.1A (ii). Summary data extracted from studies included in review of infant size/growth and insulin dependent diabetes mellitus

Details	***Design and Participants***			***Findings***				***Summary of trend***
author (pub. year); journal; location; source	No. of Subjects	FU info	Mean age at diagnosis (years)					
Johansson (1994)[89] *Diabetologia* Southeast Sweden MEDLINE	297 cases 792 controls ratio = 1:3	90% 81%	7.3 (approx.) (range 0 to <15)	Cases – controls	0-18mo (Δ wt SD score*)	0-30mo (Δ wt SD score*)		Inverse association between **infant growth** and IDDM, stronger in female**s**
				All Males Females	+0.24 (0.05, 0.43); p=0.012 +0.16 (NS) +0.33 (p < 0.05)	+0.28 (0.07, 0.50); p=0.010 +0.16 (NS) +0.42 (p < 0.05)		
				Other findings: Δ wt SD score from birth to infancy was reduced in breast-fed infants in both case & control group. However, among infants breastfed for a long time, cases gained more weight than controls (e.g. p<0.05 at 5mo).				
Hypponen (1999)[90] *Diabetes Care* Finland EMBASE	435 cases 386 controls ratio = 1:1	54% 48%	8.2 (SD=3.6) (range 0 – 14)	ORs (95% CIs) for weight in highest quartile vs others (adjusted for time introduction of formula feeding: <3mo vs. ≥3mo)				Inverse association between **infant size** and IDDM
					3 months	6 months	9 months	
				All subjects	1.48 (1.1, 2.1)	1.39 (1.0, 1.9)	1.25 (0.9, 1.7); NS	
				Other findings: Interaction of weight and formula feeding was NS.				
Hypponen (2000)[91] *Diabetes Care* Finland MEDLINE	586 cases 571 controls ratio = 1:1	73% 71%	8.1 (median) (range 1.0 – 14.9)	ORs (95% CIs) for 10-unit increase in relative wt or ht (adjusted for sex, birth-date and the other size variable)				Inverse association between **infant size** (relative weight or height) and IDDM
				Infant size	6 months	12 months	18 months	2 years
				Weight Height	1.62 (1.33, 1.98) 1.29 (1.12, 1.50)	1.67 (1.37, 2.03) 1.33 (1.15, 1.56)	1.66 (1.36, 2.02) 1.28 (1.09, 1.52)	1.60 (1.31, 1.93) 1.26 (1.07, 1.48)
				Other findings: The proportion of obese (defined as relative wt >120%) children at 2 years was low, and the association with increased risk of Insulin dependent diabetes was not statistically significant.				
Baum (1975)[92] *Lancet* Oxford, UK MEDLINE	35 cases 80 controls ratio = 1:2	33% Unkn.	Unknown	Diff. in size (weight); cases – controls	6 months	12 months		Inconclusive – all results show an inverse assoc. between **infant size** and IDDM, but not all are significant
				Males (n=22) Females (n=13)	+0.61 (p < 0.05) +0.12 (NS)	+0.63 (NS) +0.82 (p < 0.05)		
				N.B. Numbers of cases refer to birth. At 6mo there were 21 males & 11 females; at 12mo, 15 males & 9 females. Males weighed more than females in every cell except controls at birth, where females weighed slightly more.				
DiLiberti (2002)[93] *Pediatrics* Wisconsin, USA EMBASE	446 cases 10522 ctrls ratio = 1:23	99% 75%	N/A – size measured at onset	Diffs: cases – controls	1 year	2 years		Positive association between **infant size** and IDDM, mostly due to males.
				Diff. in z-score (All) Diff. in z-score (Males) Diff. in z-score (Females) OR (All)	-1.00 (p=0.009) -1.63 (p=0.002) +0.15 (p=0.82; NS) 0.40	-0.05 (p=0.8; NS) -0.20 (p=0.4; NS) +0.26 (p=0.42; NS) 0.97		

* Δ = “change in”; SD = “standard deviation”

Table 4.1A (ii) (contined). Summary data extracted from studies included in review of infant size/growth and insulin dependent diabetes mellitus

Details	***Design and Participants***			***Findings***				***Summary of trend***
author (pub. year); journal; location; source	No. of Subjects	FU info	Mean age at diagnosis (years)					
Ramachandran (1994)[94] *Diabetes Res Clin Pract* Madras, India. MEDLINE	Unknown, but < 48 for cases	Unkn. "	N/A – size measured at onset	Diffs: cases – controls	1 year	2 years		Evidence of an inverse association between **infant size** and IDDM, but no statistical analysis
				Males Females	+4.3 +7.5	+6.3 +4.4		
Bruining (2000)[95] *Lancet* SW Netherlands Reference list	91 cases 125 controls ratio = 1:1	50% Unkn.	8.3 (range 4 – 15)		Cases	Controls	Cases – controls	Inverse assoc. between **infant size** and risk of Insulin dependent diabetes.
				Birthweight	Normal (NG*)	Normal (NG*)	N/A	
				Conditional velocity analysis: values are z-scores for infant growth compared to a healthy Dutch comparison group (n=2151)				
				BMI growth 0-1yr Height growth 0-1yr BMI growth 1-3yrs Height growth 1-3yrs	+0.31 (p=0.002) Normal (NG) +0.09 (p=0.51 – NS) +0.49 (p=0.018)	+0.10 (p=0.17 – NS) Normal (NG) -0.09 (p=0.37 (NS)) +0.47 (p=0.001)	+0.21 N/A +0.18 +0.02	
				Repeated measures analysis				
				1-yr BMI Height after 1yr	NG (p=0.018) NG (p=0.0004)	NG (NS) NG (p=0.0004)	N/A NS	

* NG = “not given”; NS = “non-significant”

Table 4.1B (i). Description and quality assessment of studies included in review of infant size/growth and mental illness

Details (author (pub. year); journal; location; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Drewett (unpubl.)[96] Newcastle-upon-Tyne, UK From author correspondence	Prospective cohort study with nested case-control study assessing the assoc. betw. FTT in infancy and emotional development. Popn. based; source popn. was all live births in study region in 1 year, as for Drewett (1999).	89 FTT cases & 91 comparison infants from a cohort of births in a single city in 1987-88. 37% male. No further baseline info given except size at FU, but Drewett (1999) states that all were born at term (incl. criterion) and mean bwt was normal in >96% of Ss. 67% FU (65% for cases and 68% for comparison). Numbers & reasons for losses given, but no comparisons on important variables.	Infancy: Wt at 3, 6, 9, 12 &18mo. "Thrive index" calculated for each time point by regressing later wt on baseline wt. FTT defined as thrive index < 5th centile on ≥2 occasions betw. 3 & 18 mo; controls defined as no thrive index value <10th centile. Wts obtained from baby clinic records; weights not available for all Ss at all ages. No further info. Outcome: Emotional development at 12yrs, using Self-Perception Profile for Children, Revised Children's Manifest Anxiety Scale and Mood and Feelings Questionnaire (completed by Ss), the Child Behaviour Checklist (completed by parents) and the Teacher's Report Form (completed by teachers)*. No info on observers or reliability.	Means and differences betw. cases & comparison Ss for emotional development scores, with *t*-tests and *p*-values. No consideration of confounding factors. **[NB for the emotional development outcomes, anyway]**

* Self-Perception Profile for Children – see Harter S. The percieved competence scale for children. *Child Development* 1982;**53**:87-97 and Hoare P et al. The modification and standardisation of the Harter self-esteem questionnaire with Scottish school children. *Eur Child Adolesc Psychiatry* 1993;**2**:19-33
Revised Children's Manifest Anxiety Scale – see Reynolds C, Richmond B. What I think and feel: a revised measure of children's manifest anxiety. *J Abnorm Child Psychol* 1978;**6**:271-80 and Mertin P et al. Using North American instruments with British samples: norms for the revised manifest children's anxiety scale. *Child Psychol & Psychiat Rev* 2001;**6**:121-6
Mood and Feelings Questionnaire – see Kent L et al. Detection of major and minor depression in children and adolescents: evaluation of the mood and feelings questionnaire. *J Child Psychol Psychiatry* 1997;**38**:565-73
Teacher's Report Form – see Achenbach TM (1991). *Manual for the Teacher's Report Form and 1991 profile*. Burlington, VT: University of Vermont, Department of Psychiatry.
Child Behaviour Checklist – see Achenbach TM (1991). *Manual for the Child Behavior Checklist/4-18 and 1991 profile*. (same publisher).

Table 4.1B (ii). Summary data extracted from studies included in review of infant size/growth and mental illness

Details	***Design and Participants***				***Main Findings***			**Conclusion**
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (days) (SD*)				
Drewett (unpubl.)[96] Newcastle-upon-Tyne, UK From author correspondence	180 (37% male)	67%	Not given	Not given	12-yr outcome†	Median diff (FTT cases – comparison)	Significance (using t-test or Mann-Whitney U test as appropriate)	**No association** between **FTT** in infancy and childhood emotional development.
					SPPC (global) RCMAS MFQ TRF (total) CBC (total)	0.00 (mean diff) +1.0 +0.5 -1.0 -3.0	*t* = 0.08; *p* > 0.1 – NS* *z* = 1.18; *p* > 0.1 – NS *z* = 0.43; *p* > 0.1 – NS *z* = 0.61; NS *z* = 0.65; NS	

* SD = “standard deviation”; NG = “not given”; NS = “non-significant”.
† SPPC = Self-Perception Profile for Children; RCMAS = Revised Children’s Manifest Anxiety Scale; MFQ = Mood and Feelings Questionnaire; TRF = Teacher’s Report Form; CBC = Child Behaviour Checklist.

Table 5.1A (i). Description and quality assessment of studies included in review of infant size/growth and IHD

Details (author (pub. year); journal; location; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Barker (1989)[4] *Lancet* East Herts, UK MEDLINE	Controlled retrospective cohort study of impaired growth in infancy as a risk factor for IHD. Popn. based but relatively small geog. region (6 health dists). Sample was all births in study region & period traceable on NHSCR.	5654 male births during 1911-30. Mean bwt normal; mean gest. age not given. SES at death given (& infant feeding); no other baseline info or mean age at death. Excl criteria stated but no reasons. 36% FU. Incl Ss had slightly higher weights at birth & 1 year than to those lost to FU – no stat test though. Numbers & reasons for losses given. IHD rates in study region were below national average.	Infancy: size (weight) at 1 yr of age measured by local health visitor and recorded on birth register, but no reliability info. Weight measurements rounded to nearest lb or half-lb. No blinding info. Outcome: mortality from IHD from death certificate (ICD9 used).	SMRs with tests for trend; Cox PH regression. SES at death & infant feeding considered, but not for the analysis of interest. No direct measure of assoc. Graph of RRs by infant feeding and wt at 1 yr.
Eriksson (2001)[5] *BMJ* Helsinki, Finland MEDLINE	Controlled retrospective cohort study of how infant growth modifies assoc. betw. low bwt and CHD risk. Set in a single city univ. hosp. Sample was all survivors with relevant records.	4630 male births during 1933-44. Mean bwt and gest. age normal. No mean age at FU, but Ss would be at least 64 yrs of age. Good anthrop. measures at birth, but no demog. info, and no FU info at all. No clear incl/excl criteria. 84% FU. No comparison of study Ss and those excluded/lost to FU. Child welfare clinic attendance is voluntary, and source hosp. accounts for only 60% of total births in the city – potential for selection bias; however, SES dist. appears similar to that of Helsinki as a whole.	Infancy: size (wt, ht & BMI) at 1 yr of age, from city child welfare clinic records. Weight measurements rounded to nearest 0.5kg; height to nearest 0.5cm. Converted to *z*-scores for some analyses. Outcome: CHD mortality, from national mortality register, or morbidity from hosp. admssn info (no info on reliability). No blinding info.	Cox PH regression giving hazard ratios and tests for trend. Bwt adjusted for, but nothing else.
Fall (1995)[97] *BMJ* East Herts, UK MEDLINE	Retrospective cohort study of assoc. of bwt and wt at 1 yr with CHD prevalence. Setting as for Barker (1989)[1]. Sample was all births in study period with records, still alive and agreeing to participate.	290 males born during 1911-30. Mean bwt normal; gest age not given. No other baseline info at birth, but good info at FU incl age, BMI and smoking (but not alcohol). No clear incl/excl criteria. 25% FU. Incl Ss had slightly higher weights at birth & 1 year than to those lost to FU – no stat test though. Numbers & reasons for losses given. NB: cohort is same for Barker (1989)[1], but outcome is morbidity rather than mortality.	Infant size/growth measurement: as for Barker (1989)[1]. Outcome: prevalence (morbidity) of CHD, with precise definition involving criteria such as Rose/WHO questionnaire, ECG and surgical history). ECG coding was blind to other data; no other blinding info.	Various tables of means & differences betw. gps, controlling for bwt, SES (at birth & at FU) and smoking, and other medical factors at FU. Also logistic regression, adjusting for same vars, giving OR.
Osmond (1993)[98] BMJ East Herts, UK From reference list	Extension of study by Barker (1989)[1] (covering 11 health dists), with a larger cohort of males & a new cohort of females.	5585 females born during 1922-30 and 10141 males born during 1911-30. SES at death given (& infant feeding); no other baseline info or mean age at death (although range given). Excl criteria stated but no reasons. 43% FU (55% for males, 40% for females). Incl. males had slightly higher weights at birth & 1 year than to those lost to FU – no stat test though. No diffs for females. Numbers & reasons for losses given.	As for Barker (1989)[1]	SMRs with tests for trend; Cox PH regression. SES at death & infant feeding considered, but not for the analysis of interest. No direct measure of assoc.

Table 5.1A (i) (continued). Description and quality assessment of studies included in review of infant size/growth and IHD

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Forsen (2004)[99] *Heart* Helsinki, Finland From expert	Retrospective cohort study of how infant growth modifies assoc. betw. low bwt and CHD risk. Set in a single city univ. hosp. Target popn was all survivors with relevant records.	4130 female births during 1934-44. Mean bwt and gest. age normal. No mean age at FU, but Ss would be at least 64 yrs of age. Size & SES at birth, plus education, income & SES given at FU. No clear incl/excl criteria. 75% FU. No comparison of study Ss and those excluded/lost to FU. Authors state that child welfare clinic attendance is voluntary, but that the SES dist. appears similar to that of Helsinki as a whole.	Infancy: size (wt, ht & BMI) from infant welfare clinic records. Converted to *z*-scores, interpolated so as to be at exactly 1 & 2yrs. Outcome: CHD mortality, from national mortality register (ICD 8-10 used), or morbidity from hosp. admission info (no info on reliability). No blinding info.	Cox PH regression giving hazard ratios. Z-scores for ht, wt & BMI calculated at age 1 & 2yrs for cases of NIDDM relative to cohort as a whole. No consideration of confounders.

N.B. 'Source' refers to how the paper was encountered. If it was found in a search of electronic databases, the name of the database is given (e.g. MEDLINE, EMBASE). 'Reference list' would mean that the paper was found in the reference list of a paper already included in the review, whilst 'Author' would mean that the paper was brought to our attention through correspondence with an author of a paper already included in the review, and 'Expert' through correspondence with a scientist considered to be an expert in his or her field.

* CHD and IHD have the same ICD9 codes (410-4)

Table5.1A (ii). Summary data extracted from studies included in review of infant size/growth and IHD

Details	***Design and Participants***				***Main Findings***	***Conclusion***
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (days) (SD*)		
Barker (1989)[4] *Lancet* Herts, UK MEDLINE	5654 males	71	3.59 (0.59)	NG*	Statistic: Data SMR in lowest 1-yr weight (≤ 18lb) category: 104 SMR in highest 1-yr weight (≥ 27lb) category: 81 Chi-sq for trend (p-value): p < 0.002 Approx. % change in risk across categories: 17% Also: simultaneous analysis of bwt and wt at 1 yr for breastfed subjects using Cox PH model (figure)	**Inverse** association – risk decreases with increasing **l-yr size** (weight).
Eriksson (2001)[5] *BMJ* Helsinki, Finland MEDLINE	4630 males	84	3.46 (0.49)	280 (11)	HRs for risk of CHD for Ss in the lowest category for weight at 1 year (≤ 18lb) when compared with those in the highest category (> 26lb): Size measure: Hazard ratio (95% CI): p-value for trend Wt at age 1 year: 1.82 (1.25, 2.64): p<0.0001 BMI at age 1 year: 1.83 (1.28, 2.60): p=0.0004 Ht at age 1 year: 1.55 (1.11, 2.18): p=0.007 Also: HRs adjusted for size at birth: 0.84 (0.75, 0.94) and 0.87 (0.78, 0.96)	**Inverse** association – risk decreases with increasing **1-yr size**.
Fall (1995)[97] *BMJ* Herts, UK MEDLINE	290 males	25	3.59 (0.59)	NG*	OR for CHD among Ss in the lowest category for weight at 1 year (≤ 18lb) when compared with those in the highest category (> 26lb): 3.6 (no estimate of precision). Difference in 1-yr weight between those with CHD and those without (lb) = -1.0 (95% CI -1.8 to -0.1) – i.e. those developing CHD had lower weights at age 1 year. Prevalence of CHD (%) decreased from 27% to 9% as 1-yr weight category increases from ≤18lb to ≥27lb. The approximate risk reduction across each 1-yr weight category was 13%. The p-value for trend was 0.03. When adjusted for bwt and current SES: 0.05; for bwt and SES at birth: 0.02; for bwt and smoking status: 0.01.	**Inverse** association – risk decreases with increasing **1-yr size**
Osmond (1993)[98] *BMJ* Herts, UK MEDLINE	10141 males 5585 female	79 60	3.54 (NG*) 3.41 (NG*)	NG*	Statistic: IHD: Males: Females SMR in lowest 1-yr weight gp: 105: 91 SMR in highest 1-yr weight gp: 42: 76 Chi-sq for trend (p-value): 23.8 (p< 0.002): NS Approx. % change in risk across 1-yr wt gps: 16%: N/A Lowest 1-yr weight group: ≤ 18lb Highest 1-yr weight group: ≥ 27lb	**Inverse** association – risk decreases with increasing **1-yr size** (weight) (males only).

* SD = standard deviation; NG = "not given"; HR = hazard ratio; OR = odds ratio; CI = confidence interval; NS = not significant

Table 5.1A (ii). Summary data extracted from studies included in review of infant size/growth and IHD

Details	***Design and Participants***				**Main Findings**				***Summary of trend***
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (days) (SD*)	Age (yrs)	Height	Weight	BMI	
Forsen (2004)[99] *Heart* Helsinki, Finland From expert	4130 female	75	3.33 (0.46) (0 missing)	280 (11) (292 missing)	1 2	-0.012 (NS) -0.030 (NS)	-0.136 (NS) -0.139 (NS)	-0.171 (NS) -0.174 (NS)	No association between **infant size** and IHD.
					Data are z-scores for cases (n=87) compared to the cohort as a whole (n=4130), for which the mean z-score is set at 0 and the SD at 1. HRs for IHD by 1-yr body size were NS.				

* SD = standard deviation; NG = “not given”; HR = hazard ratio; OR = odds ratio; CI = confidence interval; NS = not significant

Table 5.1B (i). Description and quality assessment of studies included in review of infant size/growth and cerebrovascular disease

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Martyn (1996)[100] *Lancet* Herts, UK MEDLINE	Retrospective cohort study of assoc. betw. infant size and mortality from **stroke**. Popn. based (11 health dists). Sample was all births in study region & period traceable on NHSCR.	10141 males born during 1911-30. No bwt info, but presumably normal as for other Hertfordshire studies. No other baseline info. Incl/excl criteria not given, but presumably similar to other Hertfordshire studies. 44% FU. No info on non-participants. Prevalence of stroke was less than among general population (SMR = 73).	Infant size/growth measurement: as for Barker (1989)[1]. Outcome: mortality from **stroke**, from death certificate (ICD9 used).	SMRs with tests for trend. Infant feeding considered in analysis, but not adjusted for. Percentage reduction in SMR between successive 1-yr wt categories given.

Table 5.1B (ii). Summary data extracted from studies included in review of infant size/growth and cerebrovascular disease

Details	*Design and Participants*				*Main Findings*			*Conclusion*
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (days) (SD*)				
Martyn (1996)[100] *Lancet* Herts, UK MEDLINE	10141 (all male)	44%	Not given	Not given	Statistic	All subjects		**Inverse** association betw. **1-yr** size (weight) & risk of mortality from stroke.
					SMR in lowest 1-yr weight gp: SMR in highest 1-yr weight gp: % reduction in SMR between successive 1-yr wt gps (95% CI):	105 52 14% (2%, 25%)		
					Lowest 1-yr wt gp: ≤ 18lb. Highest 1-yr wt gp: > 26lb.			

Table 5.1C (i). Description and quality assessment of studies included in review of infant size/growth and non-insulin dependent diabetes mellitus (NIDDM)

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Hales (1991)[101] *BMJ* Herts, UK	Retrospective cohort study of assoc. of bwt and wt at 1 yr with prevalence of **NIDDM**. Popn. based but relatively small geog. region (6 health dists). Sample was all births in study region & period traceable on NHSCR.	370 male births during 1920-30. Mean bwt normal; mean gest. age not given. No other baseline info (size at FU given, but not specifically for subgp of interest). Excl criteria stated but no reasons; however, numbers & reasons for losses given. 32% FU. Ss with IGT were slightly lighter at birth & 1 year than those without, but no info specifically for those with NIDDM.	Infancy: Size (weight) at 1yr measured by local health visitor and recorded on birth register, but no reliability info. Measurements rounded to nearest lb or half-lb. Fieldworkers carrying out home visits were blind to infant data; not clear whether clinic workers were blind though. Outcome: NIDDM at 59-70yrs (mean 64yrs). 2-hr glucose tolerance test taken at local clinic; diagnosis assigned according to standard procedure.	For data of relevance: prevalence (numbers & percentages) of diabetes by 1-yr weight category. No statistical analysis at all (though ORs given for risk of IGT). No consideration of confounders.
Eriksson (2003)[102] *Diabetologia* Helsinki, Finland From expert	Retrospective cohort study of assoc. of infant size and prevalence of **NIDDM**. Setting was a single university hospital. Sample was all those with relevant records who were traceable as adults.	8760 Ss born during 1934-44. Mean bwt normal; mean gest. age not given (although stated that gestation not assoc. with prevalence of diabetes). 53% male. No other baseline info. Excl criteria clearly stated; numbers & reasons for losses given. 83% FU. No info on non-participants, but %FU was high so risk of bias is fairly small.	Infancy: Size (wt, ht & BMI) at 1 & 2yrs. Method of ascertainment: as for Eriksson (2001)[2]. Outcome: NIDDM, diagnosed after 40yrs. Cases identified using national register of Ss on diabetes medication, risking bias due to underestimation of cases. Limit of 40yrs chosen to minimise chances of including Type 1 patients, since register does not differentiate.	Tests for trend in 1-yr weight using multivariate logistic regression – only *p*-values are reported though. z-scores for ht, wt & BMI calculated at age 1 & 2yrs for cases of NIDDM relative to cohort as a whole. No consideration of confounders.
Bhargava (2004)[103] *NEJM* South Delhi, India From expert	Prospective cohort study of assoc. of infant size and prevalence of IGT & **NIDDM** in adulthood. Popn based; source popn was all pregnancies in a defined 12km^2 area of south Delhi.	1526 Ss born during 1969-72 on whom baseline data recorded; 1442 of these completed the study. Mean bwt was lower end of normal; mean gest. age normal. 58% male. 15% of parents were illiterate. At FU, around 45% were overweight, 10% obese & among men, 30% smoked and 56% used alcohol (corresponding figs. for women: ≤ 1%). No excl. criteria, but very high attrition – 19% FU. Study Ss had more males, higher maternal literacy & larger mean bwt & birth length – suggests risk of bias, though no stat. analysis.	Infancy: Size (wt, ht & BMI) at 1 & 2yrs. Measured by trained observers using standardised methods, but no info on inter-observer reliability. Outcome: NIDDM, ascertained by glucose tolerance test carried out at a clinic using well-validated procedures. Diabetes defined as fasting glucose of ≥ 126mg/dl or 120-min glucose of ≥ 200mg/dl (=11.1 mmol/l).	Multiple linear and logistic regression giving odds ratios & 95% CIs at 1 and 2yrs for unit increases in ht, wt or BMI z-score. Adjusted for adult BMI, waist-to-hip ratio, sex and age, but not infant feeding.

Table 5.1C (ii). Summary data extracted from studies included in review of infant size/growth and NIDDM mellitus

Details	***Design and Participants***				***Main Findings***	***Summary of trend***
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Birthweight & gestation	Mean age at diagnosis (years)		
Hales (1991)[101] *BMJ* Herts, UK	370 (all male)	32%	Mean bwt: 3.57kg (normal)	64 (range 59 - 70)	Statistic: Data (all subjects) % cases in lowest 1-yr weight (≤ 18lb) cat: 17% % cases in highest 1-yr weight (≥ 27lb) cat: 0% Approx. % change in risk across categories: 28%	No stat. analysis, but visual evidence of inverse association betw. 1-yr **infant size** (weight) & prevalence of NIDDM
Eriksson (2003)[102] *Diabetologia* Helsinki, Finland	8760 (53% male)	83%	Mean bwt: 3.40kg (normal)	> 40	Age (yrs): 1: Height -0.124 (NS), Weight -0.136 (NS), BMI -0.089 (NS); 2: Height -0.122 (NS), Weight -0.135 (NS), BMI -0.093 (NS) Data are z-scores for cases (n=290) compared to the cohort as a whole (n=8760), for which the mean z-score is set at 0 and the SD at 1.	No association between **infant size** and NIDDM
Bhargava (2004)[103] *NEJM* South Delhi, India	1526 (58% male)	19%	Mean bwt: 2.85kg (normal)	< 30	Males / Females: 2-yr height: 0.979 (0.891, 1.077) – NS / 1.008 (0.885, 1.148) – NS 2-yr weight: 0.890 (0.672, 1.180) – NS / 0.775 (0.521, 1.150) – NS 2-yr BMI: 0.931 (0.708, 1.225) – NS / 0.668 (0.449, 0.993) Data are ORs (95% CIs) for NIDDM for a 1-unit increase in 2-yr size, adjusted for sex, current age, current BMI & current waist-to-hip ratio.	No association between **infant size** and NIDDM (apart from 2-yr BMI for females – probably due to chance)

Table 5.1D (i). Description and quality assessment of studies included in review of infant size/growth and adult cancer

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Barker (1989)[4] *Lancet* East Herts, UK **Source:** Electronic **Risk of bias:** Medium	Controlled retrospective cohort study of impaired growth in infancy as a risk factor for **lung cancer**. Popn. based but relatively small geog, region (6 health dists). Sample was all births in study region & period traceable on NHSCR.	5654 male births during 1911-30. Mean bwt normal; mean gest. age not given. SES at death given (& infant feeding); no other baseline info or mean age at death. Excl criteria stated but no reasons. 36% FU. Incl Ss had slightly higher weights at birth & 1 year than to those lost to FU – no stat test though. Numbers & reasons for losses given. IHD rates in study region were below national average.	Infancy: size (weight) at 1 year of age measured by local health visitor and recorded on birth register, but no reliability info. Weight measurements rounded to nearest lb or half-lb. No blinding info. Outcome: mortality from **lung cancer**, from death certificate (ICD9 used).	SMRs with tests for trend; Cox PH regression. SES at death & infant feeding considered, but not for the analysis of interest. No direct measure of assoc.
Osmond (1993)[98] *BMJ* East Herts, UK **Source:** Electronic **Risk of bias:** Medium	Extension of **lung cancer** study by Barker (1989)[1] (covering 11 health dists), with a larger cohort of males & a new cohort of females.	5585 females born during 1922-30 and 10141 males born during 1911-30. Mean bwts normal; no gest. age info. SES at death & infant feeding given; no other baseline info or mean age at death (although range given). Excl criteria stated but no reasons. 43% FU (55% for males, 40% for females). Incl. males had slightly higher weights at birth & 1 year than to those lost to FU – no stat test though. No diffs for females. Numbers & reasons for losses given.	As for Barker (1989)[1]	SMRs with tests for trend; Cox PH regression. SES at death & infant feeding considered, but not for the analysis of interest. No direct measure of assoc.
De Stavola (2004)[104] *Am J Epidemiol* Various, UK From expert	Prospective cohort study of assoc. betw. childhood growth and risk of breast cancer. Popn. based; source popn. was a birth cohort covering all of England, Scotland & Wales.	2187 females born during week of March 3-9, 1946. No info on bwt or gest. age. Sampled by SES: original cohort comprised all births to non-manual & agricultural families and 1 in 4 births to manual-worker families. No further baseline info. Excl criteria clearly stated. 86% FU. No info on non-participants, but for the 2187, the probability of a particular childhood m'ment not having been collected was found not to be related to later size or breast cancer diagnosis.	Infancy: size (height & BMI) at age 2, from child health records. Carried out by health visitors during home visits. No info on reliability or rounding. Outcome: **breast cancer morbidity** at ages 36.4 to 53.8yrs, by self-response q'aire and use of NHSCR – no info on reliability of diagnosis data. Also, only 15% of cases were known to be naturally post-menopausal.	Cox proportional-hazards and logistic regression models giving OR for a 1SD increase in 2-yr ht. Multiple imputation procedure used in case of missing data (18.5% of 2187 for 2-yr ht).

Table 5.1D (ii). Summary data extracted from studies included in review of infant size/growth and adult cancer

Details	***Design and Participants***				***Size/growth measurements***	***Main Findings***			***Conclusion***
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (days) (SD*)		Measure of association	Outcome	Statistical significance	
Barker (1989)[4] *Lancet* Herts, UK MEDLINE	5654 males	36%	3.59 (0.59)	--	Wt at age 1 year	Trend in SMRs with wt at age 1 year	Lung cancer (males)	NS*	No association between **infant size** (weight) at 1 yr and lung cancer
Osmond (1993)[98] *BMJ* Herts, UK MEDLINE	10141 males 5585 females	55% 40%	3.54 (--) 3.41 (--)	--	Wt at age 1 year Wt at age 1 year	Trends in SMRs with wt at age 1 year	Lunc cancer (males) Lung cancer (females)	NS NS	No association between **infant size** (weight) at 1 yr and lung cancer
De Stavola (2004)[104] *Am J Epidemiol* Various, UK From expert	2187 female	86%	NG*	NG*		Statistic	OR (95% CI) of breast cancer for 1 SD increase in size/growth	Missing data (% of 2187)	No association between **infant size** and **growth** in height and BMI and breast cancer
						2-yr height 2-yr BMI	1.15 (0.87, 1.51) – NS 1.02 (0.78, 1.33) – NS	18.5 22.0	
						N.B. All analyses used multiple imputation for missing data, so that all 2187 Ss are used. Overall prevalence of breast cancer: 59 cases in 2187 = 2.7%.			

* SD = standard deviation; NG = "not given"; HR = hazard ratio; OR = odds ratio; CI = confidence interval; NS = not significant
† Direction of association between *increased* infant size/growth and risk of later outcome.

Table 5.1E (i). Description and quality assessment of studies included in review of infant size/growth and osteoarthritis

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Aihie Sayer (2003)[105] *Arthritis Rheum.* Various, UK MEDLINE	Retrospective cohort study of assoc. betw. infant size and prevalence of **hand osteoarthritis**. Popn. based – data from a national birth cohort . Target popn. was all members of the cohort still alive & UK resident at time of study.	2986 Ss born in 1946 and participating in the National Survey of Health & Development. Bwt normal; no gest. age info. 49% male; no race info. Mean age at FU was 53yrs. Only incl criteria were singletons & legitimate births. 69% FU. Numbers & reasons for losses to FU given. Stated that SES & bwt of study Ss was representative of the national cohort, but no data given.	Infancy: Wt at 2yrs, measured by community nurses to nearest 0.1kg wearing light clothing; no further info. Outcome: Hand osteoarthritis (OA), ascertained by trained research nurses using well-validated clinical criteria. Reproducibility good. No blinding info.	Mean 2-yr wt for those with & without hand OA at FU. *p*-value for diff given. Results given for each sex separately, but no further consideration for confounders.

Table 5.1E (ii). Summary data extracted from studies included in review of infant size/growth and osteoarthritis

Details	*Design and Participants*				*Main Findings*				*Conclusion*
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (days) (SD*)	Group	Diff in 2yr wt (kg) (OA – No OA)	*p*-value for diff	Prevalence of OA (%)	
Aihie Sayer (2003)[105] *Arthritis Rheum.* Various, UK	2986 (49% male)	69%	3.39 (NG) (Normal)	NG*	Males Females	-0.2 0.0	0.12 (NS) 0.79 (NS)	19% 30%	No association between **infant size** (weight) at 2 years and OA.

Table 5.1F (i). Description and quality assessment of studies included in review of infant size/growth and mental illness

Details (author (pub. year); journal; location; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Barker (1995)[106] *BMJ* Herts, UK MEDLINE	Retrospective cohort study of high rates of infant growth as a risk factor for **suicide**. Popn. based (11 health dists). Sample was all births in study region & period traceable on NHSCR.	5585 females born during 1923-30 and 10141 males born during 1911-30. Bwt normal; no gest. age info. Infant feeding, mean age at death & SES at death given, but no other baseline info. Incl/excl criteria not given, but presumably similar to other Hertfordshire studies. 43% FU (55% for males, 40% for females). Incl. Ss had similar weights at birth & 1 year to those lost to FU – no stat test though. Suicide rate amongst study Ss was less than national average.	Infant size/growth measurement: as for Barker (1989)[1]. Outcome: mortality from **suicide**, from death certificate (ICD9 used). No further info.	SMRs with tests for trend. Infant feeding & SES at death considered in analysis, but not adjusted for. Percentage risk increase given for change in weight gain over the first year.
Thompson (2001)[107] *Br J Psychiatr* Herts, UK MEDLINE	Retrospective cohort study of of assoc. of bwt and wt at 1 yr with prevalence of **depression**. Popn. based (11 health dists). Sample was all Ss who took part in an earlier study on *Helicobacter pylori* infection.	542 males and 340 females born during 1920 and 1930. No bwt or gest. age info. 67% of males and 56% of females were in the lower SES groups (III manual to V) at FU. Mean age at FU was 68yrs. Incl/excl unclear, as Ss were from a previous study. 86% FU (similar for each sex). No info on losses to FU or original source popn.	Infant size/growth measurement: as for Barker (1989)[1]. Outcome: prevalence of depression in late life. 2 well-validated measured used – GDS & GMS†. Administered by trained & supervised nurses; inter-rater reliability validated during study. Blind to birth records; hence presumably to 1yr records too.	ORs with CIs for depression in each of 4 1-yr wt gps. Chi-sq test for trend in ORs given. Adjustment for bwt, presence of CHD & infant feeding. SES related to outcome but not to infant size/growth.

N.B. 'Source' refers to how the paper was encountered. If it was found in a search of electronic databases, the name of the database is given (e.g. MEDLINE, EMBASE). 'Reference list' would mean that the paper was found in the reference list of a paper already included in the review, whilst 'Author' would mean that the paper was brought to our attention through correspondence with an author of a paper already included in the review, and 'Expert' through correspondence with a scientist considered to be an expert in his or her field.

† GDS = Geriatric Depression Scale – see Almeida OP, Almeida SA. Short versions of the Geriatric Depression Scale: a study of their validity for the diagnosis of major depressive episode according to ICD-10 and DSM-IV. *International Geriatric Psychiatry* 1999;**14**:858-65. GMS = Geriatric Mental State B-version – see McWilliam C et al. The Geriatric Mental State Examination as a case-finding instrument in the community. *Br J Psychiatr* 1988;**152**:205-8

Table 5.1F (ii). Summary data extracted from studies included in review of infant size/growth and mental illness

Details	***Design and Participants***				***Main Findings***			***Conclusion***
author (pub. year); journal; location; source	No. of subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (days) (SD*)				
Barker (1995)[106] *BMJ* Herts, UK MEDLINE	10141 males 5585 female	55% 40%	3.54 (NG*) 3.41 (NG*) (Normal)	Not given	Statistic	Males	Females	Males: **Inverse** association with **growth** (wt gain) betw. birth & 1yr; **no assoc**. for females. Overall: **Inverse** association betw. **1-yr size** (wt) & risk of suicide.
					% increase in suicide risk with each kg decrease in wt gain (birth to 1yr)	45% (7%, 98%)	31% (-29%, 142%); NS	
						All subjects		
					SMR in lowest 1-yr weight gp: SMR in highest 1-yr weight gp: Chi-sq for trend (p-value)	61 34 5.3 (p = 0.02)		
Thompson (2001)[107] *Br J Psychiatr* Herts, UK MEDLINE	542 males 340 female	86% 87%	Not given	Not given	ORs for risk of depression for Ss in the highest category for weight at 1 year (> 24.5lb) when compared with those in the lowest category (≤ 20.5lb), adjusted for bwt:			**No association** betw. **1-yr size** (weight) and risk of depression.
					Size measure	OR (95% CI)	p-value for trend	
					Males Females	2.1 (0.8, 5.6) – NS 1.3 (0.3, 5.0) – NS	p=0.10 p=0.65	
					N.B. Analysing just those Ss with CHD (65 males, 37 females) gave similar results, as did adjustment for infant feeding.			

* SD = "standard deviation"; NG = "not given"; NS = "non-significant".
† SPPC = Self-Perception Profile for Children; RCMAS = Revised Children's Manifest Anxiety Scale; MFQ = Mood and Feelings Questionnaire; TRF = Teacher's Report Form; CBC = Child Behaviour Checklist.

Table 5.2A (i). Description and quality assessment of studies included in review of infant size/growth and adult obesity

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
He (1999)[108] *Pediatr Res* Gothenburg, Sweden MEDLINE	Retrospective cohort study using data from birth to 18yrs to assess growth and **obesity**. Popn. based but small geog. region (1 city). Source popn: final-grade school children born in or around Gothenburg.	3650 Ss born during 1972-5 (mostly in 1974). 51% male. No bwt info, but said to be "healthy"; gest. age 37-42wks (normal). No other baseline info. Excl criteria stated but no reasons. 71% FU. Numbers & brief reasons for losses given. Study popn. likely to be representative since 98% of children aged 17-19yrs remain in school, but unclear whether *all* final grade children were included or a selection, e.g. from specific schools – small potential for SES bias.	Infancy: size (BMI) at 1 and 2yrs of age, taken from child health centre notes but no reliability info. No reason to suspect rounding occurred. No blinding info. Outcome: **obesity** at age 18yrs, using weights from school records and height measured by "trained observers"; overweight/obesity defined as BMI ≥ 25kg/m^2.	Cumulative percentages of subjects obese at 18yrs in relation to their BMI values in infancy being above certain cut-off points (>6kg/m^2, >7, ... >23). No p-values, direct size-of-effect measures or adjustment for confounders.
Whitaker (1997)[109] *NEJM* **Washington State, USA** MEDLINE	Retrospective cohort study assessing relationship betw. **obesity** in infancy and in young adulthood. Not popn. based; source popn was members of a single US health co-operative.	854 Ss born during 1965-70 at the health co-operative. 36% male (use of healthcare services in young adulthood is an incl. criterion, & authors state women more likely to do this). No bwt or gest. age info. 94% non-Hispanic white; 93% married mothers. Incl/excl criteria fairly clear. 64% FU. No info on losses to FU. SES profile of health co-operative members likely to be middle-class whites – selection bias likely.	Infancy: size (BMI) betw. 1 & 2yrs, taken from health co-operative records but no reliability info. "Obese" = above 85th percentile; "very obese" = above 95th, using NHANES. No rounding info, but categorisation used. Outcome: **obesity**, defined as average BMI betw. 21 & 29yrs ≥ 27.8kg/m^2 for men and ≥ 27.3kg/m^2 for women; data from outpatient visits to health co-operative.	Logistic regression giving ORs for obesity in adulthood by whether "not obese", "obese" or "very obese" in infancy. Parental obesity considered, but nothing else.
Rolland-Cachera (1987)[110] *Ann Hum Biol.* Various, France MEDLINE	Uses data from a longitudinal cohort study of growth and **obesity** in healthy children begun in 1953. Precise setting unclear.	164 subjects selected from a larger study with m'ments beyond 16yrs. 52% male. No further baseline info. 49% FU. States that no stat. diff. betw. proportions of lean, medium & fat subjects at 1yr in the present study and in the original cohort of 334, and that BMI did not differ significantly at any age betw. study Ss and those lost.	Infancy: size (BMI) at 1yr; no info on data source. "Fat" (obese) defined as BMI over 75th centile using a ref. popn. of 8695 Ss – no further info. Outcome: **obesity** at 21yrs; no info on data source. Obesity defined as BMI over 75th centile using same ref. popn. Resulting BMI cut-off values were 23.4 kg/m^2 for males and 22.3kg/m^2 for women.	Percentages of Ss following different paths of adiposity ("lean", "medium" and "fat") between 1yr and 21yrs. Raw figures also given, from which ORs and relative risks can be calculated. No consideration of confounders.

Table 5.2A (i) (continued). Description and quality assessment of studies included in review of infant size/growth and (adult) obesity

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Guo (1994)[111] *Am J Clin Nutr*. Various, USA MEDLINE	Uses data from 4 different longitudinal cohort studies begun in the USA from 1928 onwards, to study the predictive value of childhood BMI for adult obesity. Settings vary, but mostly popn. or school based.	555 subjects born betw. 1929 and 1960 participating in one of 4 larger studies. 50% male; all were white. No further baseline info. %FU unknown, but incl/excl criteria fairly clear. No non-participant info, but Ss were "not selected with regard to factors known to be associated with obesity". Said to be a wide range of SES, but no data or further info.	Infancy: size (BMI) for every year from 1 to 18yrs (only 1 & 2yrs relevant though). M'ment procedures "closely similar" to those recommended by a reference manual, and reliability is "excellent". BMI percentiles by age & sex calculated using NHANES. Outcome: obesity at 35yrs, defined as average BMI betw. 30 & 39yrs > 28kg/m^2 for men and > 26kg/m^2 for women. Measured in same way as in infancy.	Logistic regression giving ORs for overweight in adulthood by a higher BMI percentile in infancy compared to a lower one (50^{th}, 75^{th} and 90^{th} percentiles used). Tables presented separately for each sex, but no consideration of confounders.
Eriksson (2003)[112] *Int J Obesity* Helsinki, Finland MEDLINE	Retrospective cohort study examining the relation of adult obesity to infant BMI. Source popn. was all births in a single university hospital who were still resident in Finland in 1971.	4515 Ss born during 1933-44 in Helsinki Univ. Hospital. 47% male. Mean bwt normal; no gest. age info. 63% of fathers were labourers. No incl/excl criteria other than ability to trace records – clearly stated. 64% FU (respondents to q'aire). No info on non-participants.	Infancy: serial m'ments of ht & wt from birth to 7yrs, from child welfare clinic records. Size (BMI) at 6mo used in analysis of interest. No rounding or blinding info. Outcome: adult obesity, defined as maximum lifetime BMI ≥30kg/m^2. Data self-reported by q'aire, but authors state that in a previous study, self-reports by same cohort correlated well with actual m'ments.	Incidence (percentage) of adult obesity in each of 4 BMI categories at 6mo, with 95% CIs. Also, charts of ht, wt & BMI z-scores for Ss who became obese compared to whole cohort.
Mossberg (1989)[113] *Lancet* Stockholm, Sweden MEDLINE	Longitudinal cohort study following up obese children into adulthood. Hospital based; source popn. was all Ss admitted for obesity to children's hospitals in a single city.	27 Ss with onset of diffuse obesity before age 2yrs, born during 1927-47, from a larger study gp of 504 Ss. Baseline info such as mean age at admission, food intake and family history of obesity given for the whole 504 Ss but not for the subgroup of interest. Of the 27, 52% had FU info at puberty, and 67% had in adulthood. No non-participant info.	Infancy: size (wt-for-ht SD score) at admission; no further info but presumably measured in hospital. Reference popn. was a Swedish cohort; little info given. Outcome: wt-for-ht SD score, using similar ref. popn. and derived from FU info obtained by self-response questionnaire every 10yrs. Likely to be prone to misreporting (e.g. about weight or eating habits).	Not much of relevance to the review. Weight-for-height SD scores allow comparison with reference popn. in infancy and at FU, but no analysis at all. No consideration of confounders.
Charney (1976)[114] *NEJM* Rochester, USA Reference list	Retrospective cohort study assessing the relationship betw. obesity in infancy and in adulthood. Not popn. based; source popn. was the records of 3 selected physicians in the Rochester area. Target popn was infants following one of 3 specific growth patterns.	366 Ss born during 1945-55 with infant records at one of 3 physicians & with specific growth patterns – selection bias likely, & authors in fact state that Ss were "not necessarily representative of those seen by paediatricians" due to selection. All bwts >2270g; no gest. age info. No sex, race or any other baseline info. Incl/excl criteria fairly clear. 90% FU of stated target popn (130 Ss for each of the 3 growth patterns), but no info on overall size of potential sample. Losses to FU due to refusals & "medical reasons"; no further info.	Infancy: size (ht & wt) at 3 & 6mo, taken from physicians' records – no further info. Classified into 'heavy' (wt percentile >90% at 3 & 6mo), 'average' (25-75%) & 'light' (<10%). Stuart's growth charts used*. Rounding not stated but considered possible. Outcome: obesity at 20-30yrs, defined as wt ≥20% above median for ht & age. Wt & ht self-reported, but corrected using measurements of a subset of 50 Ss taken at physicians' clinics.	Contingency tables of 'heavy', 'average' & 'light' infants and 'underweight', 'normal', 'overweight' & 'obese' adults, from which ORs or RRs can be derived. Also tables controlling for bwt, infant ht & parental overweight.

See footnote at the end of Table B1.

Table 5.2A (i) (continued). Description and quality assessment of studies included in review of infant size/growth and adult obesity

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Stettler (2003)[115] *Am J Clin Nutr* Philadelphia, USA From expert	Retrospective analysis of a prospective cohort following Ss from birth to 20yrs. Source popn was p'pants in a previous study on blood pressure, but those data were from a single city hospital contributing to a larger national perinatal project.	300 Ss born during 1959-66 to mothers receiving prenatal care at Pennsylvania Hospital & enrolled in the perinatal project. All Ss were Afr-Am; 54% male. Mean bwt & gest. age normal. Other baseline info given, incl. birth order, size at FU, & maternal BMI & educ. 67% FU of Ss in previous study, or 8% of originally eligible Ss. No sig diffs from Ss in previous study other than less likely to have rapid infant wt gain. Compared to originally eligible Ss, study Ss had older mothers with higher average educ, & less likely to have rapid infant wt gain.	Infancy: growth (wt from birth to 4mo). 'Rapid' growth defined as increase in wt-for-age z-score ≥1 SD above mean betw. birth & 4mo. [data source not given] Outcome: obesity at 20yrs, defined as BMI ≥30kg/m^2. Also, 'overwt-overfat' defined as BMI ≥25kg/m^2 with sum of triceps and subscapular skinfold thicknesses ≥85th centile, using CDC growth charts. [data source not given]	Logistic regression giving ORs and 95% CIs for risk of obesity or overwt-overfat at 20yrs by presence of rapid infant weight gain. Adjustment for bwt, maternal size, maternal educ and others, but not infant feeding.
Garn (1985)[116] *Am J Dis Child* Tecumseh, USA Reference list	Longitudinal cohort study of the tracking of obesity from infancy into adulthood. Source popn. was participants in a small town community health survey.	135 Ss entering into the survey at age 1 or 2yrs during 1959-60. 39% male. No bwt or gest. age info. All of Scottish-Irish & German descent; no SES info. No incl/excl criteria, %FU or info on size of original cohort. The relatively small scale, small geographical area setting and lack of info at baseline and on source popn. increase the risk of bias.	Infancy: obesity at 1 & 2yrs, defined using both subscapular and triceps skinfolds. Measured according to standard methods, but no info on observers. Classified into 'lean' (<15th percentile for age & sex), 'medium' (15-85th) or 'obese' (>85th) using a reference population. Outcome: obesity at 21-22yrs, defined & measured as for infancy.	Cell counts in each category ('lean', 'medium' & 'obese') in infancy, and percentages of Ss remaining in the same category at outcome (20yrs later). No consideration of confounders.
Tienboon (2002)[117] *Asia Pac J Clin Nutr* New South Wales, Australia MEDLINE	Prospective cohort study of size and obesity going from infancy to adolescence. Popn. based; source popn. was all children in a single district with relevant size data in infancy & adolescence.	83 subjects born in Geelong district, NSW, in the second half of 1972. 48% male. Mean bwts normal, & not sig. diff. from general popn. for either sex. No other baseline info. Incl/excl not explicit, other than that certain size m'ments required. 7% FU. No info on losses to FU other than data not available, which with such a low %FU is a serious flaw.	Infancy: size (BMI) at 1yr, obtained from infant welfare records but no reliability info. Overweight defined as BMI >1 SD from group mean for age. No reason to suspect rounding occurred. No blinding info. Outcome: obesity at 15yrs. Wt & ht measured by single observer; good info on instruments, methods & ethical procedure. Overweight defined in same way as in infancy.	Percentages of Ss following different paths of adiposity ("underwt", "normal" and "overwt") between 1yr and 15yrs. Raw figures also given, from which ORs and relative risks can be calculated. No consideration of confounders.

Table 5.2A (i) (continued). Description and quality assessment of studies included in review of infant size/growth and adult obesity

Details (author (pub. year); journal; country; source)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Monteiro (2003)[118] *Int J Obes Relat Metab Disord* Pelotas, Brazil From expert.	Uses data from a large prospective birth cohort study to look at growth and obesity. Almost popn. based – source popn. was all hospital births in a single city, but non-hospital births accounted for less than 1% of total.	1041 Ss born in Pelotas, Brazil in 1982. 52% were male. 86% had bwt 2.5 to 4.0kg; 95% had gest. age ≥ 37wks. No further baseline info. Incl. criteria not explicit, but low risk of bias. 27% random sample of original birth cohort taken at FU; 1041 represents 68% of this sample, but 18% of whole cohort. Traced Ss at FU compared to original birth cohort; no diffs for sex or mat educ, but a smaller propn. of Ss from low-income families were traced.	Infancy: size (wt-for-age, ht-for-age & wt-for-ht z-scores, using NCHS reference) at 2yrs (mean age 20mo); growth from birth to 2yrs using change in z-scores. M'ments obtained during visits to families by members of research team, but no info on how many people, equipment, reliability etc. Outcome: overweight at 14-16yrs, defined as BMI ≥ 85th percentile for sex and age, using NHANES. Obesity defined as overweight plus 2 skinfolds at ≥ 90th percentile, again using NHANES. Wt & ht measurements carried out by researchers.	Poisson regression giving prevalence ratios (i.e. relative risks) for obesity in adolescence associated with a 1 unit change in infancy z-scores for size and growth. Raw figures also given, from which ORs can be calculated. SES, mother's BMI and infant feeding all adjusted for, along with many other variables.
Heald (1965)[119] *J Pediatrics* Washington DC & Massachusetts, USA Reference list	Case-control study of infant size & growth amongst obese & non-obese adolescents. Source popn. of cases was a summer camp for obese girls; controls from a nearby summer camp & private school.	158 cases from a summer camp for obese girls; 94 controls, 14 from a neighbouring camp & 80 from a private school in Washington DC. All Ss were white female Americans. Mean bwt normal; no gest. age info. SES probably high in both gps due to attendance at private camps & schools, but no data given. No info on size of source popn, %FU or non-participants, although states that 18 controls excluded as "probably overwt" using wt-for-ht. Lack of rigorous definition of cases & controls or efforts to ensure similarity on all other vars gives a high risk of bias.	Infancy: Size (wt & ht) at 6mo & 1yr; also growth in wt & ht betw. all combinations of birth, 6mo & 1yr. Data from medical records supplied by parents; no further info. Outcome: Obesity at mean age 15yrs, defined by attendance at camp. Controls seemingly defined only by non-attendance & not being obviously overweight (mean age 14yrs).	Mean values for infant size or growth given for cases & controls, with SDs and t-tests for differences. No consideration for confounders.

Table 5.2A (ii). Summary data extracted from studies included in review of infant size/growth and adult obesity

Details	*Design and Participants*			*Size of effect measure (odds ratio unless otherwise stated)*					
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Birthweight & gestation info	Exposure	Outcome	Other info		OR (95% CI)	Summary of trend
He (1999)[108] *Pediatr Res* Gothenburg, Sweden	3650 (51% male)	71	All full-term (37-42 wks)	BMI >18kg/m^2 (both sexes) at 1 or 2yrs	BMI ≥ 25kg/m^2 (both sexes) at 18yrs (Unadjusted OR)	1yr: 2yrs:	Males: Females: Both: Males: Females: Both:	1.62 (1.10, 2.38) 2.31 (1.57, 3.41) 1.93 (1.47, 2.54) 3.00 (2.03, 4.43) 2.90 (1.95, 4.31) 2.92 (2.22, 3.86)	Positive association between **infant size** and obesity at 18 years
Whitaker (1997)[109] *NEJM* Washington State, USA	854 (36% male)	64	None given	BMI >85th percentile (obese) or >95th (very obese) at 1-2yrs	BMI ≥ 27.8kg/m^2 (men) or ≥ 27.3kg/m^2 (women) at 25yrs	Unadjusted: Obese or very obese Very obese Adj. for parental obesity: Obese or very obese		 1.3 (0.7, 2.5) - NS 2.0 (0.7, 5.7) - NS 1.3 (0.6, 3.0) – NS	No association between **infant size** and obesity at 25 years
Rolland-Cachera (1987)[110] *Ann Hum Biol.* , France	164 (52% male)	49	None given	BMI >75th centile at 1yr	BMI >75th centile: >23.4 kg/m^2 (men) or >22.3kg/m^2 (women) at 21yrs	Unadjusted		2.76 (1.32, 5.77)	Positive association between **infant size** and obesity at 21 years
Guo (1994)[111] *Am J Clin Nutr.* Various, USA	555 (50% male)	Unknown	None given	BMI at 75th percentile compared with at 50th %ile	BMI >28kg/m^2 (men) or >26kg/m^2 (women) at 35yrs (Unadjusted OR)	1yr: 2yrs:	Males: Females: Males: Females:	1.48 (0.99, 2.21) – NS 1.54 (1.01, 2.35) 1.63 (1.04, 2.54) 1.51 (0.96, 2.38) – NS	Inconclusive evidence of an association between **infant size** and obesity at 35 years
Eriksson (2003)[112] *Int J Obesity* Helsinki, Finland MEDLINE	2135 males 2380 female	64	Birthweight (mean, SD) 3.46 (0.50) 3.33 (0.46)	BMI at 6mo	Maximum lifetime BMI ≥ 30kg/m^2	Males: Lowest 6-mo gp (< 16.3 kg/m^2) Highest 6-mo gp (> 18.0 kg/m^2) Females: Lowest 6-mo gp (< 16.3 kg/m^2) Highest 6-mo gp (> 18.0 kg/m^2)		Cumulative incidence: 28.6 (24.1, 33.1) 44.1 (40.0, 48.5) p for trend < 0.0001 27.5 (23.8, 31.3) 36.8 (32.0, 41.7) p for trend = 0.001	Positive association, for both sexes between **infant size** and lifetime risk of obesity
Mossberg (1989)[113] *Lancet* Stockholm, Sweden	27 (no sex info)	52 (in late childhood) 67 (in adulthood)	None	All overweight in infancy	Wt-for-ht SD scores compared to reference popn.	Admission Late childhood Adulthood (40-50yrs)		SD scores, NOT ORs: +2.3 (0.31) +1.8 (0.46) +0.2 (0.28)	Inconclusive evidence of an assoc btwn **infant size** and obesity in adulthood
Charney (1976)[114] *NEJM* Rochester, USA Reference list	366 (no sex info)	90	All birthweights >2270g	Weight percentile >90% at 3 & 6mo	Weight ≥20% above median for height & age at 20-30yrs	Unadjusted (n=366) Neither parent overwt (n=225) At least 1 parent overwt (n=110) Combined (n=335)		1.63 (1.14, 2.33) 1.81 (0.96, 3.44) - NS 3.37 (1.69, 6.70) 2.51 (2.25, 2.80)	Positive assoc between **infant size** and obesity at 20-30 years; stronger if parents are also overweight.

Table 5.2A (ii) (continued). Summary data extracted from studies included in review of infant size/growth and adult obesity

Details	***Design and Participants***			***Size of effect measure (relative risk unless otherwise stated)***				
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Birthweight (kg) & gestation (wks)	Exposure	Outcome	Other info	RR (95% CI)	Summary of trend
Stettler (2003)[115] *Am J Clin Nutr* Philadelphia, USA From expert	300 (54% male)	67	Both median (25^{th} to 75^{th} percentile): Bwt: 3.12 (2.44 to 4.00) GA: 40 (37 to 41)	Increase in wt-for-age z-score ≥1 SD above mean from birth to 4mo	BMI ≥30kg/m^2 at 20yrs	Unadjusted: Adjusted for maternal size & educ, bwt, sex and others:	Odds ratios: 2.73 (1.20, 6.23) 5.22 (1.55, 17.6)	Positive association between **infant growth** and obesity at 20 years
Garn (1985)[116] *Am J Dis Child* Tecumseh, USA Reference list	135 (39% male)	NG	No info given	At 1 or 2yrs: Triceps skinfold >85^{th} percentile for age & sex Subscapular skinfold; same definition.	Same, at 21 or 22yrs	Percentage of obese infants that remained obese 20 years later, with p-value for deviation from chance figure of 15% (using Binomial test): 1yr – 21yrs 2yrs – 22yrs 1yr – 21yrs 2yrs – 22yrs	 33.3% (p=0.21 – NS) 18.2% (p=0.77 – NS) 33.3% (p=0.21 – NS) 20.0% (p=0.66 – NS)	Evidence of a positive assoc. between **infant size** (skinfold thickness) and obesity at 21-22 years , but not statistically significant
Tienboon (2002)[117] *Asia Pac J Clin Nutr* New South Wales, Australia	83 (48% male)	7	Birthweight (mean, SD): Males: 3.52 (0.56) Females: 3.38 (0.53)	BMI >1 SD from group mean at 1yr	BMI >1 SD from group mean at 15yrs	Unadjusted	2.03 (0.469, 8.82) – NS	No association between **infant size** and obesity at 15 years
Monteiro (2003)[118] *Int J Obes Relat Metab Disord* Pelotas, Brazil	1041 (52% male)	68	86% had birthweights between 2500g and 4000g. 95% had gestational ages ≥37wks	Wt-for-ht SD score at 2yrs ('rapid growth': >0.67 z-score change 0-2yrs)	BMI ≥ 85th percentile at 14-16yrs	Unadjusted OR (cut-off +1SD at 2yrs) OR for 1 unit z-score increase in wt-for-ht SD (adjusted) OR for rapid infant growth y/n (adjusted)	3.54 (2.53, 4.96) 1.35 (1.53, 1.73) 1.66 (1.20, 2.31)	Positive association between rapid **infant growth** and obesity at 14-16 years
Heald (1965)[119] *J Pediatrics* Washington DC & Massachusetts, USA Reference list	158 cases 94 controls (all female)	NG	7.044 +/-1.2 lb 7.188 +/-0.9 lb (not sig diff)	Measurement 6mo weight (lb) 6mo height (in) 1yr weight (lb) 1yr height (in) 0-6mo wt gain (lb) 0-6mo ht gain (in) 0-1yr wt gain (lb) 0-1yr ht gain (in) 6-12mo wt gain (lb) 6-12mo ht gain (in)	Cases – controls +0.515 (p=0.245; NS) +0.314 (p=0.356; NS) +1.446 (p=0.009) +0.540 (p=0.174; NS) +0.540 (p=0.174; NS) +0.565 (p=0.206; NS) +1.586 (p=0.003) +0.558 (p=0.262; NS) +0.842 (p=0.144; NS) +0.035 (p=0.904; NS)	Cases & controls defined for outcome (obesity) at mean age 15yrs		Positive assoc. for **infant size** (weight) in 1st year), but not height or weight after 1yr.

Table 5.3A (i): Description and quality assessment of studies included in review of infant size/growth and non-health-related quality of life

Details (author (pub. year); journal; country)	*Design & Setting*	*Participants*	*Measurement*	*Analysis and Confounding*
Barker (2004)[120] Unpublished Helsinki, Finland From author	Retrospective cohort study investigating assoc. betw. infant growth and **income**, **educational achievement** and **occupation** in adulthood. Set in a single city univ. hosp. Sample was all survivors with relevant records.	4630 male births during 1933-44. No baseline info given, but cohort is same as that for Eriksson (2001) – mean bwt & gest. age normal; all male. No clear incl/excl criteria. FU varies with outcome from 63% to 77%. No comparison of study Ss and those excluded/lost to FU. Eriksson (2001) states that child welfare clinic attendance is voluntary, and source hosp. accounts for only 60% of total births in the city – potential for selection bias; however, SES dist. appears similar to that of Helsinki as a whole.	Infancy: size (height) at 1 yr of age, from city child welfare clinic records. Weight measurements rounded to nearest 0.5kg; height to nearest 0.5cm. Growth in height betw. birth & 1yr. Outcome: personal taxable income and occupation, taken from the 1990 census. Achieved level of education (classified as 'low/medium' or 'high') – no further info but presumably taken from school records.	Percentages reaching 'high' level of education and becoming labourers, plus mean taxable income, given within 6 ht gps at 1yr. P-values for trend given. Regression analysis for mean income by growth in ht from birth to 1yr, controlling for father's occupation. Parental education not considered as a confounder.

Table 5.3A (ii): Summary data extracted from studies included in review of infant size/growth and non-health-related quality of life

Details	*Design and Participants*				*Main Findings*				
author (pub. year); journal; location; source	No. of Subjects	% FU of target pop[n].	Mean bwt (kg) (SD*)	Mean gest (wks) (SD*)	General Description				Conclusion
Barker (2004)[120] Unpublished Helsinki, Finland From author	4630	84	3.46 (0.49) (from Eriksson (2001)	280 (11) (from Eriksson (2001)	Statistic	Personal taxable income in 1990 (£)	Reached 'high' level of educ (%)	Became labourer (%)	**Positive** assoc. betw. **infant size & growth** and adult **income**. Infant **size** also has **positive** assoc. with **high educational achievement** & **inverse** assoc. with proportion becoming labourers.
					Number of men (% FU of 5510)	3939 (71%)	4252 (77%)	3480 (63%)	
					Lowest 1-yr ht category (≤ 72cm)	15,370	9	44	
					Highest 1-yr ht category (>80cm)	22,270	22	20	
					Test for trend	$p < 0.0001$	$p = 0.001$	$p < 0.0001$	
					Also: Correlation betw. 1-yr height and income: 0.09 (p<0.0001) % increase in income assoc. with 2cm increase in 1-yr ht (controlling for father's occupation): 3.5% (1.6%, 5.4%) Trends for all outcomes similarly strong regardless of SES at birth.				

Table C: Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

3.1A: SIDS studies

First author	*Question and risk of bias*															*Reviewers' judgment*	*Association†*
	1. Case definition	**2. Infancy m'ments**	**3. Outcome m'ments**	**4. Control selection**	**5. Rounding**	**6. Setting & popn.**	**7. Blinding**	**8. Analysis**	**9a & b Response rate**		**10. Represen-tativeness**	**11a & b Sample size**		**12. Confoun-ding**	**Overall total***		
									cases	**controls**		**cases**	**controls**				
Williams **(1990)**[15]	Medium	Medium	Low	Medium	Medium	Low	Medium	Medium	High	Medium	Medium	Medium	Medium	Medium	+1	Medium	Inconclusive
Brooks[16]	Low	Medium	Low	Low	Low	Low	Medium	Medium	Medium	Low	Low	High	Medium	Low	+7	Low	No assoc.
Williams (1996)[17]	Low	Medium	Low	Low	Low	Low	Medium	Medium	High	Medium	Medium	Medium	Low	Medium	+5	Low	Inconclusive
Peterson[18]	Medium	High	Medium	High	Low	Medium	Medium	Medium	Medium	Medium	High	Medium	Medium	High	-3	Medium	Inconclusive
Jorgensen[19]	Low	Low	Low	Low	Low	Medium	Medium	Medium	Low	Medium	Medium	Medium	Medium	Medium	+6	Low	No assoc.
Blair[20]	Low	Medium	Low	Low	Low	Low	Medium	Low	High	Medium	Medium	Medium	Low	Low	+7	Low	Negative
Naeye[21]	Medium	Medium	Medium	Medium	Low	Medium	Medium	High	High	High	Medium	Medium	Medium	High	-3	Medium	Inconclusive
Froggatt[22]	Medium	High	Medium	High	Low	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium	High	-2	Medium	Inconclusive

† Direction of association between *increased* infant size/growth and risk of later outcome.

3.1B: Childhood cancer studies

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Partici-pants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Suminoe[23]	Medium	Medium	Medium	Medium	Low	High	Medium	High	Medium	Medium	Medium	-1	Medium	All cancer: no assoc. Neuroblastoma: positive.

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

3.1C: Respiratory disease studies

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Partic-ip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Victora[24]	Low	Medium	Medium	Medium	Low	High	Medium	High	Medium	Medium	Low	+1	Medium	Inconclusive
Yoon[25]	Low	Medium	Medium	Medium	Medium	Low	Medium	Medium	Medium	Low	Low	+4	Low	Inverse

First author	*Question and risk of bias*															*Reviewers' judgment*	*Association†*
	1. Case definition	**2. Infancy m'ments**	**3. Outcome m'ments**	**4. Control selection**	**5. Rounding**	**6. Setting & popn.**	**7. Blinding**	**8. Analysis**	**9a & b Response rate**		**10. Represen-tativeness**	**11a & b Sample size**		**12. Confoun-ding**	**Overall total***		
									cases	**controls**		**cases**	**controls**				
Fonseca[26]	Low	Medium	Low	Low	Medium	Medium	Medium	Low	Low	Low	Low	Medium	Medium	Low	+8	Low	Inverse

3.1D: Autism studies

First author	*Question and risk of bias*											*Reviewers' judgment*	*Association†*
	1. Design	**2. Partic-ip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Courchesne[27]	High	Medium	Medium	Low	Low	High	Low	High	High	Medium	High	-2	High	Positive

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status 3.2A: Childhood obesity studies

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Stettler (2002a)[28]	Medium	Low	Medium	Medium	Low	Medium	Medium	High	Medium	Low	Low	+3	Medium	Positive
Poskitt (1977)[29]	Medium	Medium	Low	Low	Low	High	Medium	High	High	Medium	Medium	0	Medium	Positive
Stettler (2002b)[30]	Medium	Low	Medium	Low	Low	Low	Medium	High	Medium	Low	Low	+5	Low	Positive
Mellbin[31]	Low	Medium	Medium	Medium	Low	High	Medium	Medium	High	Medium	Medium	0	Medium	Inconclusive
Eid[32]	Medium	Medium	Medium	Medium	Medium	Medium	Medium	High	Medium	Medium	Medium	-1	Medium	No association
Asher[38]	High	High	High	Medium	Medium	High	Medium	High	High	Medium	Medium	-6	High	Inconclusive
Mei[34]	Low	Low	Medium	Medium	Medium	Medium	Medium	Medium	High	Medium	Low	+2	Medium	Positive
Johnston[35]	Medium	High	Medium	Medium	Medium	High	Medium	Medium	High	Medium	Medium	-3	High	Positive

First author	*Question and risk of bias*														*Reviewers' judgment*	*Association†*
	1. Case definition	**2. Infancy m'ments**	**3. Outcome m'ments**	**4. Control selection**	**5. Rounding**	**6. Setting & popn.**	**7. Blind-ing**	**8. Analy-sis**	**9a & b Response rate**		**10. Represen-tativeness**	**11a & b Sample size**		**12. Confoun-ding**	**Overall total***	
									Cases	**controls**		**Cases**	**controls**			
Wilkinson[36]	Low	Medium	Medium	Low	Medium	Low	Medium	Medium	High	Medium	High	High	High	Medium	-1	Medium	No association

* Numbers represent an estimate of the overall risk of bias, totalling the risk for each question defined as –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk. † Direction of association between infant size/growth and risk of later obesity, so "Positive" means that increased size/growth is associated with a greater risk of later obesity.

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

3.3A: Studies of HC and cognitive development

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Koller[39]	Medium	Low	Medium	Medium	Low	High	Medium	Medium	High	Medium	Medium	0	Medium	Positive
Ford[40]	Medium	Low	Medium	Medium	Low	High	Medium	Low	Medium	Low	High	+2	Medium	Inconclusive
Fisch[41]	Low	Medium	Medium	Medium	Low	High	Medium	Medium	Medium	Low	Low	+3	Medium	HC: +ve. Wt & ht: inconclusive.
Fernandez-Carrocera[42]	Medium	Low	Low	Medium	Low	High	Medium	Medium	Medium	Low	Medium	+3	Medium	Inconclusive
Pryor[43]	Medium	Medium	Medium	Medium	Low	High	Medium	Medium	Medium	Low	High	0	Medium	SGA: Positive AGA: No assoc.
Camp[44]	Medium	Medium	Medium	High	Low	High	Low	Medium	High	Low	High	-1	Medium	Initial fix: +ve Resp dec: No assoc
Nelson[45]	Medium	Medium	Medium	Medium	Medium	Medium	Medium	High	High	High	Low	-2	High	Positive
Lasky[46]	Low	High	Low	Low	Low	Low	Medium	High	High	Low	Medium	+3	Medium	Positive
Lucas[47]	Medium	High	Medium	Medium	Low	High	Medium	High	High	Medium	Medium	-3	High	Positive
Ernhart[48]	High	High	High	Low	Low	Low	Medium	High	High	Medium	Medium	-2	High	Positive
Stathis[49]	Medium	Medium	Medium	Medium	Low	Medium	Medium	High	Low	Low	High	0	Medium	Positive

* Numbers represent an estimate of the overall risk of bias, totalling the risk for each question defined as –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk. Thus a positive score represents a lower risk of bias than a negative score.

† Direction of association between *increased* infant size/growth and risk of later outcome.

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

3.3A: Studies of HC and cognitive development (continued)

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Hack[50]	Medium	Low	Medium	Medium	Low	Medium	Medium	High	High	Low	Medium	0	Medium	Size: +ve Growth: no assoc.
Ong[51]	Medium	Low	Medium	Low	Low	Medium	Low	High	Low	Low	Medium	+5	Low	Positive (VLBW only)
Gale[52]	Medium	Low	Low	Low	Low	Low	Medium	High	Low	Low	Medium	+6	Low	Positive (size and growth)
Bendersky[53]	Medium	Low	Low	Low	Low	Medium	Low	High	High	Low	Medium	+4	Medium	Positive
Hack (1991)[54]	Medium	Low	Medium	Medium	Low	Medium	Medium	Medium	Low	Low	Medium	+4	Low	Positive

* Numbers represent an estimate of the overall risk of bias, totalling the risk for each question defined as –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk. Thus a positive score represents a lower risk of bias than a negative score.
† Direction of association between *increased* infant size/growth and risk of later outcome.

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

3.3B: Studies of failure-to-thrive and cognitive development

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Skuse[55]	Low	Low	Low	Medium	Low	Medium	Medium	Low	Medium	Low	High	+5	Low	Positive
Boddy[56]	Medium	Low	Medium	Low	Low	Medium	Medium	Medium	Medium	Low	High	+3	Medium	No assoc.
Corbett[57]	Medium	High	Medium	Low	Low	High	Low	Medium	High	Low	High	0	Medium	Inconclusive
Drewett[58]	Low	Low	Medium	Low	Low	Low	Low	Medium	Low	Low	Medium	+8	Low	No assoc.
Drotar (1985)(10042}	Medium	Medium	Medium	Low	Low	Medium	Medium	Medium	Medium	Low	High	+2	Medium	Positive
Drotar (1988)[60]	Medium	Medium	Medium	Medium	Low	Medium	Low	High	Medium	Low	High	+1	Medium	Inconclusive
Mackner (1997)[61]	Medium	Medium	Medium	Medium	Low	Medium	Medium	High	Medium	Medium	Medium	0	Medium	Inconclusive
Mackner (2003)[62]	Medium	Medium	Medium	Low	Low	Low	Low	Medium	Medium	Medium	Medium	+4	Medium	Positive
Kerr[63]	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium	0	Medium	No assoc.
Kelleher[64]	Medium	Low	Medium	Medium	Low	Medium	Low	High	Medium	Medium	Medium	+2	Medium	IQ: Positive Behaviour: No assoc.

* Numbers represent an estimate of the overall risk of bias, totalling the risk for each question defined as –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk. Thus a positive score represents a lower risk of bias than a negative score.

† Direction of association between increased infant size/growth and improved later development, so "Positive" means that presence of FTT is associated with poorer development.

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

3.3B: Studies of failure-to-thrive and cognitive development (continued)

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Roundin g**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Singer[65]	Medium	Medium	Medium	Medium	Low	High	Medium	Medium	Medium	Medium	High	-1	Medium	IQ: Positive Visual recog: No assoc.
Glaser[66]	Medium	Medium	Medium	Medium	Medium	High	Medium	Medium	High	High	High	-4	High	Inconclusive
Reif[67]	Medium	Medium	Medium	High	Low	High	Medium	Medium	High	Medium	Medium	-2	Medium	Inconclusive
Field[68]	Medium	Medium	Medium	Medium	Medium	Medium	Medium	High	Medium	Medium	High	-2	High	Inconclusive
Hack (1982)[69]	Medium	Low	Medium	Medium	Low	Medium	Medium	Low	Medium	Medium	Medium	+3	Medium	AGA: Positive SGA: Inconclusive
Mitchell[70]	Medium	Low	Medium	Low	Medium	Medium	Low	Medium	High	Medium	High	+1	Medium	No assoc.
Tudehope[71]	Medium	Medium	Medium	Medium	Low	High	Medium	High	High	Medium	Medium	-2	High	AGA: Positive SGA: Inconclusive
Abramson[72]	Medium	Low	Medium	Low	Low	High	Medium	Medium	High	Medium	High	0	Medium	Overall: no assoc. (some diffs for subscales)
Dykman[73]	High	Medium	Medium	Medium	Low	High	Medium	High	High	Medium	High	-4	High	Inconclusive

* Numbers represent an estimate of the overall risk of bias, totalling the risk for each question defined as –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk. Thus a positive score represents a lower risk of bias than a negative score.

† Direction of association between increased infant size/growth and improved later development, so "Positive" means that presence of FTT is associated with poorer development.

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

3.3C: Studies of weight or height and cognitive development

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Berkman[74]	Low	Medium	Medium	Low	Medium	Medium	Low	High	Medium	Low	Medium	+3	Medium	Positive
Monckeberg[75]	Medium	Medium	High	Medium	Low	High	Medium	High	Medium	Medium	Medium	-2	High	Positive
Paine[76]	Medium	Medium	Low	Low	Low	Medium	Low	High	High	Medium	High	+1	Medium	SGA: Positive AGA: No assoc.
Gherpelli[77]	Medium	Low	Medium	Low	Medium	High	Medium	High	High	Medium	High	-2	Medium	Positive
Ross[78]	Medium	Low	Medium	Low	Medium	Medium	Low	Medium	Medium	Medium	High	+2	Medium	Positive
Rose[79]	Medium	Low	Low	Low	Medium	Low	Low	Low	Low	Medium	Medium	+7	Low	Positive
Corbett[103]	Low	Medium	Medium	Medium	Medium	Medium	Medium	High	Medium	Low	Low	+2	Medium	Inconclusive
Whaley[81]	Medium	Medium	Medium	Low	Low	Medium	Medium	Medium	Medium	Medium	Medium	+2	Medium	Inconclusive
Latal-Hajnal[82]	Medium	Low	Medium	Low	Low	Medium	Low	Low	Medium	Low	Medium	+6	Low	Inconclusive
Upadhyay[83]	Medium	High	Medium	Medium	Medium	Medium	Medium	High	High	Medium	Medium	-3	High	No assoc.

* Numbers represent an estimate of the overall risk of bias, totalling the risk for each question defined as –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk. Thus a positive score represents a lower risk of bias than a negative score.

† Direction of association between increased infant size/growth and improved later development, so "Positive" means that presence of FTT is associated with poorer development.

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

3.3D: Motor development studies

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Astbury[38]	Medium	Medium	Medium	Low	Low	High	Medium	Low	Medium	Medium	Medium	+2	Medium	Positive
Connors[84]	Medium	Low	Medium	Medium	Low	Medium	Low	Medium	Medium	Low	Medium	+4	Medium	Inconclusive
Jaffe[85]	Low	Medium	Medium	Low	Medium	High	Medium	Low	Low	Medium	Medium	+3	Medium	Inverse
Kohlhauser[86]	Medium	Low	Medium	Medium	Low	Medium	Medium	Medium	Medium	Medium	High	+1	Medium	Positive
Whaley[81]	Medium	Medium	Medium	Low	Low	Medium	Medium	Low	Medium	Medium	Medium	+3	Medium	Inconclusive
Latal-Hajnal[82]	Medium	Low	Medium	Low	Low	Medium	Low	Low	Medium	Low	Medium	+6	Low	Positive
Tenovuo[37]	Low	Medium	Medium	Medium	Medium	High	Medium	Medium	Medium	Medium	Medium	0	Medium	Positive
Hack (1991)[54]	Medium	Low	Medium	Medium	Low	Medium	Medium	Medium	Low	Low	Medium	+4	Low	No assoc.
Simon[87]	Medium	Medium	Medium	Low	Medium	High	Low	Medium	Medium	Medium	High	0	Medium	Positive

* Overall score, assigning for each question –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk.
† Direction of association between *increased* infant size/growth and risk of later outcome.

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

4.1A: Insulin dependent diabetes mellitus studies

First author	*Question and risk of bias*															*Reviewers' judgment*	*Association†*
	1. Case definition	**2. Infancy m'ments**	**3. Outcome m'ments**	**4. Control selection**	**5. Rounding**	**6. Setting & popn.**	**7. Blind-ing**	**8. Analy-sis**	**9a & b Response rate**		**10. Representativeness**	**11a & b Sample size**		**12. Confoun-ding**	**Overall total***		
									Cases	**controls**		**Cases**	**controls**				
Johansson[89]	Medium	Medium	Medium	Low	Medium	Medium	Medium	Medium	Low	Medium	Medium	Medium	Medium	Medium	+2	Medium	Inverse (mostly due to females)
Hypponen (1999)[90]	Medium	Medium	Medium	Low	Low	Low	Medium	Low	High	High	High	Medium	Medium	Low	+2	Medium	Inverse
Hypponen (2000)[91]	Low	Medium	Medium	Low	Low	Low	Medium	Low	Medium	Medium	Medium	Medium	Medium	Medium	+5	Low	Inverse
Baum[92]	Medium	Medium	Medium	Medium	Low	High	Medium	Medium	High	Medium	High	High	High	High	-5	High	Inconclusive
DiLiberti[93]	Medium	Low	Medium	Medium	Low	Medium	Medium	Medium	Low	Medium	Medium	Medium	Low	Medium	+4	Medium	Positive (mostly due to males)
Ramachan-dran[94]	Medium	Medium	Medium	High	Low	Medium	Medium	High	High	High	Medium	High	Medium	High	-4	High	Inconclusive
Bruining[95]	Medium	Medium	Medium	High	Medium	Low	Medium	Medium	High	Medium	High	High	Medium	High	-4	High	Inverse

4.1B: Mental illness studies

First author	*Question and risk of bias*											*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***	
Drewett[96]	Low	Medium	Medium	Medium	Low	Medium	Medium	High	Medium	Low	Medium	+2	Medium	No association

* Number in parentheses represents the overall score, assigning for each question –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk.
† Direction of association between *increased* infant size/growth and risk of later outcome.

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

5.1A: IHD studies

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Barker (1989)[4]	Low	Low	Medium	Low	Medium	High	Medium	High	Medium	Low	Low	+3	Medium	Negative
Eriksson[5]	Medium	Medium	Medium	Medium	High	High	Medium	Medium	High	Low	Low	-1	Medium	Negative
Fall[97]	Low	Low	Medium	Low	Medium	Medium	Medium	High	Medium	Low	Medium	+3	Medium	Negative
Osmond[98]	Low	Medium	Medium	Low	Medium	High	Medium	High	Medium	Low	Low	+2	Medium	Negative
Forsen[99]	Medium	Low	Medium	Medium	Medium	High	Medium	Medium	Medium	Low	Low	+2	Medium	No assoc.

5.1B: Cerebrovascular disease studies

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Martyn (1996)[100]	Low	Medium	Medium	Low	Medium	High	Medium	High	High	Low	Low	+1	Medium	Inverse

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

5.1C: NIDDM studies

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Hales[101]	Medium	Medium	Medium	Low	Medium	High	Low	High	High	High	Medium	-2	Medium	Inconclusive (Positive?)
Eriksson[102]	Medium	Medium	Medium	High	Medium	High	Medium	Medium	Medium	Medium	Low	-1	Medium	No association
Bhargava[103]	Low	Low	Medium	Low	Low	Low	Medium	High	Medium	Low	Low	+6	Low	No assocation

* Numbers represent an estimate of the overall risk of bias, totalling the risk for each question defined as –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk. Thus a positive score represents a lower risk of bias than a negative score.
† Direction of association between *increased* infant size/growth and risk of later outcome.

5.1D: Adult cancer studies

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Barker (lung)[4]	Low	Low	Medium	Low	Medium	High	Medium	High	Medium	Low	Low	+3	Medium	No assoc.
Osmond (lung)[98]	Low	Medium	Medium	Low	Medium	High	Medium	High	Medium	Low	Low	+2	Medium	No assoc.
De Stavola[104]	Medium	High	Medium	Medium	Medium	High	Medium	Medium	High	Low	Low	-1	Medium	No assoc.

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

5.1E: Osteoarthritis studies

First author	*Question and risk of bias*												*Reviewers' judgement*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Aihie Sayer (2003)[105]	Low	Medium	Medium	Low	Medium	High	Medium	High	Medium	Medium	Low	+1	Medium	No association

* Number in parentheses represents the overall score, assigning for each question –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk.
† Direction of association between *increased* infant size/growth and risk of later outcome.

5.1F: Mental illness studies

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Barker (1995)[106]	Low	Medium	Medium	Low	Medium	Medium	Medium	High	Medium	Low	Low	+3	Medium	Inverse
Thompson[107]	Medium	Medium	Medium	Low	Medium	Low	Low	Medium	High	Low	Medium	+3	Medium	No association

* Number in parentheses represents the overall score, assigning for each question –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk.
† Direction of association between *increased* infant size/growth and risk of later outcome.

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

5.2A: Adult obesity studies

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Partici-pants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
He[108]	Low	Medium	Medium	Low	Low	High	Medium	Medium	Medium	Medium	Low	+3	Medium	Positive
Whitaker[109]	Medium	Medium	Medium	Medium	Low	High	Medium	High	High	Low	Medium	-1	Medium	No assoc.
Rolland-Cachera[110]	Low	Medium	Medium	Medium	Low	High	Medium	High	Low	Medium	Medium	+1	Medium	Positive
Guo[111]	Medium	Medium	Medium	Medium	Medium	High	Medium	Medium	High	Low	Medium	-1	Medium	Inconclusive
Eriksson[112]	Medium	Low	Medium	Medium	Low	High	Medium	High	High	Medium	Low	0	Medium	Positive
Mossberg[113]	Medium	Medium	Medium	High	Low	High	Medium	High	High	High	High	-5	High	Inconclusive
Charney[1141]	High	High	Medium	Medium	Medium	Medium	Medium	Medium	Medium/ High??	Medium	Medium	-2/-3?	High?	Positive
Stettler (2003)[115]	Medium	Low	Medium	Medium	Low	Low	Medium	High	High	Low	Medium	+2	Medium	Positive
Garn[116]	Low	Medium	Medium	Medium	Medium	High	Medium	Medium	Medium	Medium	Medium	0	Medium	Inconclusive
Tienboon[117]	Medium	Medium	Medium	Low	Low	High	Medium	High	High	Medium	Medium	-1	Medium	No assoc.
Monteiro[118]	Low	Low	Medium	Low	Low	Low	Medium	Medium	Medium	Low	Low	+7	Low	Positive

* Numbers represent an estimate of the overall risk of bias, totalling the risk for each question defined as –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk. Thus a positive score represents a lower risk of bias than a negative score.

† Direction of association between *increased* infant size/growth and risk of later outcome.

Table C (continued): Summary of scoring results in terms of risk of bias (low, medium or high) of all studies included in review of infant growth status

5.2A: Adult obesity studies (continued)

First author	*Question and risk of bias*															*Reviewers' judgment*	*Association†*
	1. Case definition	**2. Infancy m'ments**	**3. Outcome m'ments**	**4. Control selection**	**5. Rounding**	**6. Setting & popn.**	**7. Blind-ing**	**8. Analy-sis**	**9a & b Response rate**		**10. Represen tativenes s**	**11a & b Sample size**		**12. Confoun-ding**	**Overall total***		
									Cases	**controls**		**Cases**	**control s**				
Heald[119]	High	Medium	High	Medium	Low	High	Medium	Medium	Medium	Medium	Medium	Medium	High	High	-4	High	Positive

* Numbers represent an estimate of the overall risk of bias, totalling the risk for each question defined as –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk. **Thus a positive score represents a lower risk of bias than a negative score.**
† Direction of association between increased infant size/growth and risk of later obesity.

5.3A: Non-health-related quality of life studies

First author	*Question and risk of bias*												*Reviewers' judgment*	*Association†*
	1. Design	**2. Particip-ants**	**3. Infancy m'ments**	**4. Outcome m'ments**	**5. Rounding**	**6. Confoun-ding**	**7. Blinding**	**8. % FU**	**9. Non-par-ticipants**	**10. Analysis**	**11. Sample size**	**Overall total***		
Barker[120]	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium	High	Low	Low	+1	Medium	Positive

* Numbers represent an estimate of the overall risk of bias, totalling the risk for each question defined as –1 for a "high" risk of bias, 0 for a "medium" risk, and +1 for a "low" risk. Thus a positive score represents a lower risk of bias than a negative score.
† Direction of association between *increased* infant size/growth and risk of later outcome.