Supplementary Online Content

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eTable. Characteristics of studies examining the relationship between obesity and clinical outcomes in ill children, grouped by patient condition type

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable. Characteristics of studies examining the relationship between obesity and clinical outcomes in ill children, grouped by patient condition type (n=28)

Cohort Studies (n=24)

Citation/site	Population analyzed	Obesity/overweight definition, prevalence, criteria	Outcomes relevant to review question	Limitations
Critical illness/trauma				
Brown, et al 2006[19] Single center, U.S.	316 trauma pts. admitted to surgical ICU, age 6-19 years	BMI ≥95th percentile for age; 54 obese, 262 non-obese. Reference growth data not specified.	• Mortality not significantly different between obese and non-obese groups (9% vs. 15%, p=.39) • More sepsis (15% vs. 4%, p=.007) and wound infections (26% vs. 8%, p=.03) in obese • Longer but not significant ICU LOS (8±9 vs. 6±6 days, p=.05) and hospital LOS in obese group (18±19 vs. 14±12 days, p=.08)	No controlling for confounders. History of pts. not included. Trauma not clearly defined and may not represent PICU population.
Carroll, et al 2006[43] Single center, U.S.	209 pts. admitted to PICU for status asthmaticus, age 2-18 years	Weight for age >95th percentile; 45 obese, 164 non-obese. CDC 2000 growth data.	• PICU (116±125 vs. 69±57 hrs., p=.02) and hospital (9.8±7 vs. 6.5±3.4 days, p<.01) LOS significantly longer in obese compared to non-obese group • In stepwise multiple regression model, obesity remained a significant predictor of PICU LOS (p=.021), when adjusted for age, baseline & admission asthma severity scores	Limited to pts. admitted with status asthmaticus. No height measurements.
Rana, et al 2009[32] Single center, U.S.	1314/4853 admitted trauma pts. selected with documented height and weight, age 6-20 years	BMI ≥95th percentile; 294 obese, 1020 non-obese. CDC 2000 growth data.	• No difference in mortality between groups (1 death in each) • No difference in wound infections (data not provided) • No difference in LOS (2.6 vs. 2.9 days)	Sample may be biased to pts. with weight concerns. No adjustment for covariates noted.

Citation/site	Population analyzed	Obesity/overweight definition, prevalence, criteria	Outcomes relevant to review question	Limitations
Patel, et al 2010[44] Single center, U.S.	528 pts. admitted with burn injuries, age 0-18 years	BMI ≥95th percentile (2-18 years) or weight for length ≥95th percentile (0-2 years); 92 obese, 436 non-obese. CDC 2000 growth data.	• Median LOS significantly longer in obese compared to non-obese group (9.3 vs. 7.1 days, p=.01) • In stepwise multiple regression model, obese children had a 6.5% longer LOS (p=.03), when adjusted for % body surface area burned, % full thickness burn, and being insured by Medicaid	39% of patients were < 2 years and obesity criteria may not be as interpretable.
Srinivasan, et al 2010[34] Prospective, Multicenter, U.S.	1268 pts. who experienced in hospital CPR events in 167 sites, age <18 years	Weight for length or BMI for age ≥95th percentile; 213 obese, 484 normal weight, 571 underweight. WHO 2006 growth data.	• Obese group had lower rates of survival compared to normal weight group (23% vs. 34%, adj. OR = .62, 95% CI .38-.93), when adjusted for age, gender, facility, and multiple clinical variables in multivariate logistic regression	BMI estimated based on median height/length for age values. Limited to pts. with CPR event may not generalize to all ill children.
Yu, et al 2011[35] Multicenter, China	9966 pts. selected from 31562 cases of H1N1 influenza admitted to hospital, all ages included	BMI for age ≥95th percentile for age 2-17 years; 696 of 3582 cases age 2-17 years were obese. Used both Chinese & CDC growth data.	• Obesity was a significant predictor of ICU admission or death among pts. 2-17 years of age (OR 1.34, 95% CI 1.1-1.63, p=.004), when controlled for age and chronic medical condition	Selection bias inherent to chart abstraction by local physicians. Unclear how individuals not meeting both Chinese & CDC criteria for obesity would be classified.
Goh, et al 2012[24] Single center, U.S.	1146 pts. requiring mechanical ventilation in PICU, age 2-18 years	Weight for age z-score -1.89-1.04 = normal (n=753), 1.05-1.65 = overweight (n=137), 1.66-2.33 = obese (n=76), >2.33 = severely obese (n=64). CDC 2000 growth data.	• Compared to normal weight, neither overweight (adj. OR 1.06, 95% CI .62-1.82, p=.8372), obese (adj. OR .68, 95% CI .31-1.48, p=.3246), nor severely obese (adj. OR 1.02, 95% CI .45-2.34) predicted mortality when adjusted for admission type, trauma status, surgical status, functional status and risk of mortality score	No height measurements. Underweight pts. and patients with tracheostomies excluded.

			• No association between log transformed LOS and weight categories (p=.8431) among survivors	
Citation/site	**Population analyzed**	**Obesity/overweight definition, prevalence, criteria**	**Outcomes relevant to review question**	**Limitations**
Kraft, et al 2012[36] Single center, U.S.	592 pts. admitted with burns to >30% total body surface area, mean age 8.9 years	BMI $\geq$95th percentile = morbidly obese (n=144), 90th-95th = obese (n=83), 85th-90th = overweight (n=50), <85th = normal (n=315). CDC 2000 growth data.	• Neither mortality nor survival analysis (p=.442) was significantly different among groups • No significant difference in sepsis, infections, or LOS between normal weight group and $\geq$85th percentile group	No regression analysis performed to account for associations or covariates. Sample size may be too small to detect differences with more widely accepted obesity cutoff (>95th percentile)
Cancer/HSCT				
Lange, et al 2005[29] Multicenter, international	768 pts. with AML on international cooperative group trial (CCG-2961), age 1-20 years	BMI (or weight/length for age 1-2 years) $\geq$95th percentile = overweight (n=114), 11-94th percentile = middleweight (n=570), $\leq$10th percentile = underweight (n=84). CDC 2000 growth data.	• Overweight group had higher death rate than middleweight group (17% vs. 5%, p=.001) • Overweight pts. were less likely to survive (HR 1.88, 95% CI 1.25-2.83, p=.002) and had greater treatment related mortality (HR 3.49, 95% CI 1.99-6.1, p<.001) than middleweight pts. when adjusted for age, race, WBC count, cytogenetics, and HSCT	Incomplete data excluded 462 pts. from multivariate analysis. Remaining pts. might have overrepresented any factor. Admission weight does not account for changes during treatment.
Baillargeon, et al 2006[17] Multicenter, Texas	322 mostly Hispanic pts. with ALL, age 2-18 years	BMI $\geq$95th percentile = obese (15.2%), 85th-95th = overweight (10.9%), <85th = normal (73.9%). CDC 2000 growth data.	• Obese pts. had significantly decreased overall survival compared to non-obese by unadjusted log-rank test (p=.04) • When adjusted for sex, age, WBC and ethnicity, obesity was not associated with overall survival (HR 1.40, 95% CI .69-2.87)	Underweight pts. not separated out – could potentially reduce survival of non-obese group. Also did not examine overweight and obese as a group, effects likely limited by small sample.
Hijiya, et al 2006[26] Single center, U.S.	621 pts. with newly diagnosed ALL, age 1-18.8 years	BMI or weight/length: $\geq$95th percentile = overweight (n=55), 85-95th percentile = risk of overweight (n=64), 10-	• Overall survival did not differ among groups by log-rank test (p=.533) • In Cox proportional hazards	Single measure of BMI may not reflect important subsequent changes related to treatment. Low incidence of overweight in

		85th percentile = normal (n=400), ≤10th percentile = underweight (n=102). CDC 2000 growth data.	models adjusted for age, sex, WBC count, genetic subtypes, and protocol, BMI was not an independent predictor of survival (data not reported)	sample.
Citation/site	**Population analyzed**	**Obesity/overweight definition, prevalence, criteria**	**Outcomes relevant to review question**	**Limitations**
Bulley, et al 2007[20] Single center, Canada	325 pts. for first myeloablative allogeneic HSCT, age 2-19.4 years	BMI >95th percentile = overweight (n=54), >10th and <95th percentile = middleweight (n=234), ≤10th percentile = underweight (n=37). CDC 2000 growth data.	• Overweight group had lower 5 year survival (46.6±7.3% vs. 59.5±3.2%, p=.02) and greater treatment-related mortality (39.3±7.3% vs. 22.2±2.7%, p=.01) than non-overweight. • In Cox proportional hazards model, overweight was a significant predictor of death from any cause (HR 1.7, 95% CI 1.1-2.6, p=.02) and treatment-related mortality (HR 1.9, 95% CI 1.2-3.3, p=.01).	Not able to adjust for all comorbidities due to lack of data. Covariates included in model not specified. Small sample.
Fernandez, et al 2009[23] Multicenter, international	1532 pts. with favorable histology Wilms tumor on National Wilms Tumor Study Group protocol, grouped by < 2 years of age (n=493) and ≥ 2 years of age (n=1039)	BMI percentile (≥2 years) or weight for age percentile (<2 years), categorized into 5 groups: <5%ile, 5-9.9%ile, 10-89.9%ile (normal), 90-94.9%ile, ≥95%ile; 75 pts. < 2 years and 137 pts. ≥ 2 years were ≥ 90th percentile. CDC 2000 growth data.	• In Cox proportional hazards model adjusted for stage and treatment group, no significant difference in event free survival among weight categories (p=.16) and event free survival in patients < 2 years of age • Similarly, no significant difference in event free survival among weight categories and event free survival (p=.71) in patients ≥ 2 years of age	Single diagnosis and treatment protocol with presumed but not reported, wide age distribution in ≥2 years group. >82% event free survival in all groups reduced power to detect significant predictors. Relapse and death = 1 outcome, therefore may not be able to determine independent association with mortality

Pine, et al 2011[31] Multicenter	200 pts. with malignancies for unrelated cord blood transplants, age 2.07-17.9 years	BMI >95th percentile = obese (n=39), BMI 85-95th percentile = overweight (n=35), BMI 5-85th percentile = normal (n=117), BMI <5th percentile = underweight (n=9). CDC 2000 growth data.	• No significant association between treatment-related mortality and overweight (HR 1.32, 95% CI .63-2.75, p=.46) or obese (HR 1.54, 95% CI .71-3.34, p=.27) with regression modeling controlling for other risk factors • No significant association between overall survival and overweight (HR 1.16, 95% CI .65-2.07, p=.626) or obese (HR 1.54, 95% CI .85-2.78, p=.155) with Cox proportional hazards model	Small sample, not generalizable to other settings/treatments. Categorized overweight and obese separately.
Citation/site	**Population analyzed**	**Obesity/overweight definition, prevalence, criteria**	**Outcomes relevant to review question**	**Limitations**
Barker, et al 2011[18] Multicenter, international	1281 pts. from CIBMTR registry with aplastic anemia for allogeneic HSCT, age 2-19 years	BMI >95th percentile = overweight (n=143), 76th-95th percentile = at risk for overweight (n=306), 25th-75th percentile = normal (n=527), 5th-<25th percentile = at risk for underweight (n=196), <5th percentile = underweight (n=109). CDC 2000 growth data.	• Adjusted for race, ethnicity, region, donor type, HLA matching, conditioning regimen, performance score & years post-transplant, overweight pts. had a significantly higher risk of death compared with normal weight pts. (RR 1.71, 95% CI 1.24-2.35, p<.01)	Defined population of aplastic anemia and HSCT not generalizable to wider HSCT/oncology community. Did not account for infections, except as cause of death.
Hingorani, et al 2011[42] Multicenter	498 pts. with osteosarcoma on group trial (COG INT-0133 legacy trial), age 3.7-30 years	High BMI = >95th percentile (n=43), middle BMI = 11-94th percentile (n=382), low BMI = <10th percentile (n=73). CDC 2000 growth data.	• Patients with high BMI did not have significantly higher risk of wound infection compared to middle weight (OR 3.5, p=.18)	Sample size small for incidence of wound complication rate - only 3 pts. had wound infections (7%). Adults included could skew results. No adjustment for covariates.
White, et al 2012[37] Single center, Australia	113 children for autologous or allogeneic HSCT, interquartile ranges 3.2-15.1	Ideal weight calculated from weight percentile matched to height percentile. Overweight = >110% of ideal weight (n=41), ideal weight = 90-	• Overweight associated with higher mortality than ideal weight (HR 1.91, 95% CI 1.1-3.31, p=0.02), when adjusted for age, sex, donor source, conditioning therapy &	Small sample size, follow-up time varied from ~3 to 11 years. Did not consider cause of death among subjects.

	years	110% (n=57), underweight = <90% (n=15). CDC 2000 growth data.	year of HSCT. No significant difference in mortality between underweight and ideal weight.	
Elective Surgeries				
Nafiu, et al 2009[41] Single center, U.S.	2170 pts. for adenotonsill-ectomy, age 3-18 years	BMI >95th percentile = obese , BMI >85th and <95th percentile = overweight , BMI <85th percentile = normal; 456 overweight/obese, 1714 healthy weight. CDC 2000 growth data.	• Overweight/obese pts. were more likely to be admitted to hospital than healthy weight (29.2% vs. 18.7%, p<.001) • BMI was significantly correlated with length of stay (r=.141, p<.001) and was a significant independent predictor of admission (p=.009) by multiple logistic regression	Defined population with overall short length of stay not generalizable to wider population.

Citation/site	Population analyzed	Obesity/overweight definition, prevalence, criteria	Outcomes relevant to review question	Limitations
Garey, et al 2010[39] Single center, U.S.	312 pts. for laparoscopic cholecystect-omy, age 0-20 years	BMI >95th percentile = obese (n=97), 85th-95th percentile = overweight (n=65), <85th percentile = normal (n=150). CDC 2000 growth data.	• Mean LOS in days not significantly different among normal (1.6±1.2), overweight (1.7±1.5, p=.7 vs. normal), and obese pts. (1.3±.8, p=.072 vs. normal)	Small sample size with only 9 complications reported. Sample biased and reduced by removal of pts. with associated conditions for length of stay outcome only. No analysis of covariates.
Solid organ transplants				
Hanevold, et al 2005[25] Multicenter, U.S., Mexico, and Canada	6658 kidney transplant recipients at 126 centers in North America, age 2-17 years	BMI >95th percentile; 649 obese, 6009 non-obese. CDC 2000 growth data.	• Overall mortality not significantly different between obese (5.5%) and non-obese (5.8%) • Significantly higher risk of death in obese children age 6-12 years than non-obese (living donors adjusted RR 3.65, 95% CI 1.46-9.11, p=.005; cadaver donors adjusted HR 2.94, 95% CI 1.53-5.63, p=.001)	Unable to investigate several pre-transplant contributors to outcomes, e.g. hypertension, time on dialysis, and steroid treatment.
Rossano, et al 2007[33] Single center, U.S.	105 heart transplant recipients, 1 year after transplant, age 2-20 years	BMI ≥95th percentile = overweight (n=8), 5-94th percentile = normal (n=75), <5th percentile = underweight (n=22). CDC 2000 growth data.	• 92 (88%) pts. survived to 1 year post-transplant • No difference in survival between overweight and normal weight pts. (log-rank p=0.5) • Time to hospitalization for infection not different among weight categories (4.4 years for overweight, 7.4 years for normal weight; p=NS)	Small sample may be unable to detect clinically important outcomes. 19 year accrual period likely includes different treatments. Significant BMI change at 1 year but data not provided.

Citation/site	Population analyzed	Obesity/overweight definition, prevalence, criteria	Outcomes relevant to review question	Limitations
Kaufman, et al 2008[28] Single center, U.S.	180 pts. listed for heart transplant, age 0-21 years	>120% IBW and/or ≥95th percentile BMI or weight/length = obese (n=22), <90% IBW and/or <5th percentile BMI or weight/length = wasted (n=66), all others normal (n=92). CDC 2000 growth data.	• Using %IBW assessment, obesity, compared to normal weight, was a significant predictor for survival by Cox regression analysis controlling for age and diagnosis (HR 3.82, 95% CI 1.81-8.06, p<.001) • No difference in infections among groups (data not reported) • Obese pts. had longer LOS (131.4±91 days, p=.043) than normal (86.6±67 days) and wasted (78.9±11 days) groups, accounting for pre-transplant wait time	Unclear how or if inconsistent results of weight assessment was resolved. Small sample. Post-transplant morbidity analysis reported but no data provided.
Kaufman, et al 2009[27] Multicenter, international (13 countries)	2333 heart transplant recipients from International Society of Heart and Lung Transplant registry, age 2-18 years	BMI >95th percentile = obese (n=195), 5-95th percentile = normal (n=1592), <5th percentile = wasted (n=546). CDC 2000 growth data.	• No significant differences in survival between obese and normal at 1 year (OR 1.33, 95% CI .7-2.5, p=.56) and constant phase (mean follow-up time 4.03±3 years; HR .85, 95% CI .59-1.22, p=.38), adjusted for age, diagnosis, sex, ventilator status, rejection, hospitalizations, diabetes, malignancy, and hypertension • No significant differences in infections among weight groups (p=.54) • No significant differences in LOS (p=.92)	Low incidence of obesity in pediatric end stage heart disease. Some missing covariate data may alter results.
Dick, et al 2010[22] Multicenter, U.S.	7942 liver transplant recipients from UNOS database,	BMI z-score +3 = obese (n=654), +2 = overweight (n=1332), 0 = normal (n=4851), -2 = thinness	• Mortality after 5 years was significantly higher in obese pts. than normal when controlled for era of transplant and region in	BMI z-score for < 2 years of age infrequently used to classify obesity. Most of sample was under 5 years and 30%

	age 0-18 years	(n=563), -3 = severe thinness (n=542). WHO 2006 growth data.	multivariate Cox proportional hazards model (RR 1.5, p=.05).	under 1 year. Unclear how scores between cutoffs classified.

Note: All cohort studies were retrospective unless specified prospective (n=1).

Case-Control Studies (n=4)

Citation/type	Populations analyzed	Obesity definition and prevalence	Outcomes relevant to review question	Limitations
Linam, et al 2009[40] Retrospective Single center, U.S.	44 cases (age 6-22.1 years) of posterior spinal fusion with surgical site infection (SSI), matched 1:3 by date of surgery to 132 controls (age 1.2-27.2 years) without SSI	BMI >95th percentile, 15 obese cases, 18 obese controls. CDC 2000 growth data.	• Obesity was a significant risk factor for SSI (OR 3.5, 95% CI 1.5-8.3, p=.004) • In multivariate regression model, obesity remained a significant independent risk factor for SSI (adjusted OR 3.1, 95% CI 1.1-9.1, p=.039)	Single center, small sample of cases, defined population may not be generalizable to other situations. Did not examine length of stay as possible confounder.
Butturini, et al 2007[21] Retrospective Multicenter, international	Pts. with ALL in 6 Children's Cancer Group studies: 4260 pts. enrolled 1988-1995 (study cohort), 1733 pts. with high risk ALL on single protocol, 1996-2002 (verification cohort), all age 2-20 years	BMI ≥95th percentile = obese; 343 obese in study cohort, 236 in verification cohort. CDC 2000 growth data.	• Obesity had a significant independent effect on events - death, induction failure & 2nd cancer - when adjusted for age, WBC count, race and bone marrow response at day 7 (adjusted HR 1.36, 95% CI 1.04-1.77, p=.021) • In a subgroup of pts. ≥ 10 years of age, obesity predicted poorer outcome (adjusted HR for events 1.5, 95% CI 1.1-2.1, p=.009) • Similar subgroup results in verification cohort (adjusted HR 1.42, 95% CI 1.03-1.96, p=.032)	With one time measure of BMI, unable to assess impact of changes in obesity following diagnosis, or etiology of obesity at time of diagnosis. Multivariate events could skew relationship of mortality.
Morgan, et al 2010[30] Retrospective Multicenter, U.S.	Convenience sample of 361 pts. hospitalized with H1N1 influenza with measured or estimated height and calculated BMI, 233 deaths	BMI 85-94th percentile = overweight, BMI ≥95th percentile = obese, BMI 5-84th percentile = normal, BMI <5th percentile = underweight; 23 overweight and 41 obese of	• No significant association between BMI category and death among children 2-19 years; overweight and underweight categories not separately defined for deaths	Selection bias, no weight and height data on deaths – reports of obesity only. 27% of children had BMI category estimated due to lack of height data.

	reported to CDC with H1N1 and complete data, compared with NHANES data 2003-6; age ≥2 years	161 hospitalized pts. age 2-19 years; 3 obese of 31 deaths age 2-19 years; 15.5% overweight and 16.4% obese in NHANES data. CDC 2000 growth data.	(OR .5, p=.81)	Classified chronic medical conditions may be less relevant to pediatric conditions. Sample size small for pediatric cases.
Citation/site	**Population analyzed**	**Obesity/overweight definition, prevalence, criteria**	**Outcomes relevant to review question**	**Limitations**
Fung, et al 2010[38] Prospective Single center, Canada	49 consecutive obese pts., mean age 9.33 years (SD 2.98) for tonsillectomy and/or adenoidectomy for sleep-disordered breathing, age & gender pair-matched to 49 non-obese controls, mean age 9.19 years (SD 3.04)	BMI ≥95th percentile = obese, 90-95th percentile = overweight. BMI <85th percentile = non-obese. Reference growth data not specified.	• Obese pts. had significantly longer mean time in hospital than non-obese pts. (18 vs. 8 hrs.; mean difference 10 hrs., 95% CI 2.01-17.99, p<.001)	No control for asthma (more prevalent in obese, p=.05) or other comorbidities.

LOS = length of stay, PICU = pediatric intensive care unit, CDC = Centers for Disease Control, OR = odds ratio, RR = relative risk, HR = hazard ratio, AML = acute myelogenous leukemia, ALL = acute lymphoblastic leukemia, HSCT = hematopoietic stem cell transplantation.