Supplementary Online Content


**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)

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<tr>
<th>Citation/site</th>
<th>Population analyzed</th>
<th>Obesity/overweight definition, prevalence, criteria</th>
<th>Outcomes relevant to review question</th>
<th>Limitations</th>
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<td><strong>Critical illness/trauma</strong></td>
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</table>
| Brown, et al 2006<sup>19</sup> | 316 trauma pts. admitted to surgical ICU, age 6-19 years | BMI >95<sup>th</sup> 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<sup>43</sup> | 209 pts. admitted to PICU for status asthmaticus, age 2-18 years | Weight for age >95<sup>th</sup> 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<sup>32</sup> | 1314/4853 admitted trauma pts. selected with documented height and weight, age 6-20 years | BMI >95<sup>th</sup> 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. |
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| Patel, et al 2010<sup>44</sup> Single center, U.S. | 528 pts. admitted with burn injuries, age 0-18 years | BMI ≥95th percentile (2-18 years) or weight for length ≥95<sup>th</sup> 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. |
<p>| Srinivasan, et al 2010&lt;sup&gt;34&lt;/sup&gt; Prospective, Multicenter, U.S. | 1268 pts. who experienced in hospital CPR events in 167 sites, age &lt;18 years | Weight for length or BMI for age ≥95&lt;sup&gt;th&lt;/sup&gt; 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&lt;sup&gt;35&lt;/sup&gt; Multicenter, China | 9966 pts. selected from 31562 cases of H1N1 influenza admitted to hospital, all ages included | BMI for age ≥95&lt;sup&gt;th&lt;/sup&gt; percentile for age 2-17 years; 696 of 3582 cases age 2-17 years were obese. Used both Chinese &amp; 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 &amp; CDC criteria for obesity would be classified. |
| Goh, et al 2012&lt;sup&gt;24&lt;/sup&gt; 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), &gt;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. |</p>
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<td>Kraft, et al 2012&lt;sup&gt;36&lt;/sup&gt;</td>
<td>592 pts. admitted with burns to &gt;30% total body surface area, mean age 8.9 years</td>
<td>BMI &gt;95th percentile = morbidly obese (n=144), 90th-95th = obese (n=83), 85th-90th = overweight (n=50), &lt;85th = normal (n=315). CDC 2000 growth data.</td>
<td>Neither mortality nor survival analysis (p=.442) was significantly different among groups</td>
<td>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 (&gt;95th percentile)</td>
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<td>Cancer/HSCT</td>
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<td>Lange, et al 2005&lt;sup&gt;29&lt;/sup&gt;</td>
<td>768 pts. with AML on international cooperative group trial (CCG-2961), age 1-20 years</td>
<td>BMI (or weight/length for age 1-2 years) &gt;95th percentile = overweight (n=114), 11-94th percentile = middleweight (n=570), ≤10th percentile = underweight (n=84). CDC 2000 growth data.</td>
<td>Overweight group had higher death rate than middleweight group (17% vs. 5%, p=.001)</td>
<td>Incomplete data excluded 462 pts. from multivariate analysis. Remaining pts. might have overrepresented any factor. Admission weight does not account for changes during treatment.</td>
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<td>Baillargeon, et al 2006&lt;sup&gt;17&lt;/sup&gt;</td>
<td>322 mostly Hispanic pts. with ALL, age 2-18 years</td>
<td>BMI &gt;95th percentile = obese (15.2%), 85th-95th = overweight (10.9%), &lt;85th = normal (73.9%). CDC 2000 growth data.</td>
<td>Obese pts. had significantly decreased overall survival compared to non-obese by unadjusted log-rank test (p=.04)</td>
<td>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.</td>
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<td>Hijiya, et al 2006&lt;sup&gt;26&lt;/sup&gt;</td>
<td>621 pts. with newly diagnosed ALL, age 1-18.8 years</td>
<td>BMI or weight/length: &gt;95th percentile = overweight (n=55), 85-95th percentile = risk of overweight (n=64), 10-</td>
<td>Overall survival did not differ among groups by log-rank test (p=.533)</td>
<td>Single measure of BMI may not reflect important subsequent changes related to treatment. Low incidence of overweight in</td>
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| Bulley, et al 2007<sup>20</sup> Single center, Canada | 325 pts. for first myeloablative allogeneic HSCT, age 2-19.4 years | BMI >95th percentile = overweight (n=54), >10<sup>th</sup> and <95<sup>th</sup> percentile = middleweight (n=234), ≤10<sup>th</sup> 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<sup>23</sup> 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 ≥ 90<sup>th</sup> 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 201111

**Multicenter**

- **Population analyzed**: 200 pts. with malignancies for unrelated cord blood transplants, age 2.07-17.9 years
- **BMI definition**: 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.
- **Outcomes relevant to review question**:
  - 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

**Limitations**

- Small sample, not generalizable to other settings/treatments.
- Categorized overweight and obese separately.

### Barker, et al 201118

**Multicenter, international**

- **Population analyzed**: 1281 pts. from CIBMTR registry with aplastic anemia for allogeneic HSCT, age 2-19 years
- **BMI definition**: 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.
- **Outcomes relevant to review question**:
  - 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)

**Limitations**

- 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 201142

**Multicenter**

- **Population analyzed**: 498 pts. with osteosarcoma on group trial (COG INT-0133 legacy trial), age 3.7-30 years
- **BMI definition**: High BMI = >95th percentile (n=43), middle BMI = 11-94th percentile (n=382), low BMI = <10th percentile (n=73). CDC 2000 growth data.
- **Outcomes relevant to review question**:
  - Patients with high BMI did not have significantly higher risk of wound infection compared to middle weight (OR 3.5, p=.18)

**Limitations**

- 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 201237

**Single center, Australia**

- **Population analyzed**: 113 children for autologous or allogeneic HSCT, interquartile ranges 3.2-15.1
- **BMI definition**: Ideal weight calculated from weight percentile matched to height percentile. Overweight = >110% of ideal weight (n=41), ideal weight = 90-
- **Outcomes relevant to review question**:
  - 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 &

**Limitations**

- Small sample size, follow-up time varied from ~3 to 11 years.
- Did not consider cause of death among subjects.
<table>
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<tr>
<th>Elective Surgeries</th>
<th>years</th>
<th>110% (n=57), underweight = &lt;90% (n=15). CDC 2000 growth data.</th>
<th>year of HSCT. No significant difference in mortality between underweight and ideal weight.</th>
</tr>
</thead>
</table>
| Nafiu, et al 2009⁴¹ | 2170 pts. for adenotonsillectomy, 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. |

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<td>Garey, et al 2010&lt;sup&gt;39&lt;/sup&gt;</td>
<td>312 pts. for laparoscopic cholecystectomy, age 0-20 years</td>
<td>BMI &gt;95&lt;sup&gt;th&lt;/sup&gt; percentile = obese (n=97), 85&lt;sup&gt;th&lt;/sup&gt;-95&lt;sup&gt;th&lt;/sup&gt; percentile = overweight (n=65), &lt;85&lt;sup&gt;th&lt;/sup&gt; percentile = normal (n=150). CDC 2000 growth data.</td>
<td>• 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)</td>
<td>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.</td>
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<td>Solid organ transplants</td>
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<td>Hanevold, et al 2005&lt;sup&gt;25&lt;/sup&gt;</td>
<td>6658 kidney transplant recipients at 126 centers in North America, age 2-17 years</td>
<td>BMI &gt;95&lt;sup&gt;th&lt;/sup&gt; percentile; 649 obese, 6009 non-obese. CDC 2000 growth data.</td>
<td>• Overall mortality not significantly different between obese (5.5%) and non-obese (5.8%)</td>
<td>Unable to investigate several pre-transplant contributors to outcomes, e.g. hypertension, time on dialysis, and steroid treatment.</td>
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<td>Rossano, et al 2007&lt;sup&gt;33&lt;/sup&gt;</td>
<td>105 heart transplant recipients, 1 year after transplant, age 2-20 years</td>
<td>BMI &gt;95&lt;sup&gt;th&lt;/sup&gt; percentile = overweight (n=8), 5-94&lt;sup&gt;th&lt;/sup&gt; percentile = normal (n=75), &lt;5&lt;sup&gt;th&lt;/sup&gt; percentile = underweight (n=22). CDC 2000 growth data.</td>
<td>• 92 (88%) pts. survived to 1 year post-transplant</td>
<td>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.</td>
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| Kaufman, et al 2008<sup>28</sup> Single center, U.S. | 180 pts. listed for heart transplant, age 0-21 years | >120% IBW and/or ≥95<sup>th</sup> percentile BMI or weight/length = obese (n=22), <90% IBW and/or <5<sup>th</sup> 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<sup>27</sup> Multicenter, international (13 countries) | 2333 heart transplant recipients from International Society of Heart and Lung Transplant registry, age 2-18 years | BMI ≥95<sup>th</sup> percentile = obese (n=195), 5-95<sup>th</sup> percentile = normal (n=1592), <5<sup>th</sup> 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. |
<p>| Dick, et al 2010&lt;sup&gt;22&lt;/sup&gt; 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 &lt; 2 years of age infrequently used to classify obesity. Most of sample was under 5 years and 30% |  |</p>
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<tr>
<th>Citation/Type</th>
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| Linam, et al 2009 | 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 >95<sup>th</sup> 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 | 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 >95<sup>th</sup> percentile = obese; BMI 5-84<sup>th</sup> percentile = normal, BMI 85-94<sup>th</sup> percentile = overweight, BMI >95<sup>th</sup> percentile = obese, BMI 5-84<sup>th</sup> percentile = normal, BMI <5<sup>th</sup> percentile = underweight; 236 obese in study cohort, 236 in verification cohort. CDC 2000 growth data. | • Obesity had a significant independent effect on events - death, induction failure & 2<sup>nd</sup> 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 | Convenience sample of 361 pts. hospitalized with H1N1 influenza with measured or estimated height and calculated BMI, 233 deaths | BMI 85-94<sup>th</sup> percentile = overweight, BMI >95<sup>th</sup> percentile = obese, BMI 5-84<sup>th</sup> percentile = normal, BMI <5<sup>th</sup> 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.

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<td>Fung, et al 2010⁵⁸</td>
<td>49 consecutive obese pts., mean age 9.33 years (SD 2.98) for tonsillectomy and/or adenoidectomy for sleep-disordered breathing, age &amp; gender pair-matched to 49 non-obese controls, mean age 9.19 years (SD 3.04)</td>
<td>BMI &gt;95th percentile = obese, 90-95th percentile = overweight. BMI &lt;85th percentile = non-obese. Reference growth data not specified.</td>
<td>• 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&lt;.001)</td>
<td>No control for asthma (more prevalent in obese, p=.05) or other comorbidities.</td>
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</tbody>
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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.