

# **Is There an Association between Early Overweight and Obesity Status and Utility Based Health-Related Quality of Life in Young Children?**

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## **Abstract**

**Purpose:** Few studies focus on the health-related quality of life (HRQoL) of preschool children with overweight or obesity. This is relevant for evaluation of obesity prevention trials using a quality adjusted life year (QALY) framework. This study examined the association between weight status in the preschool years and HRQoL at age 5 years, using a preference-based instrument.

**Methods:** HRQoL (based on parent proxy version of the Health Utilities Index Mark 3 (HUI3)) and weight status were measured in children born in Australia between 2007 and 2009.

Children's health status was scored across eight attributes of the HUI3 - vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain, and these were used to calculate a multi-attribute utility score. Ordinary Least Squares (OLS), Tobit and two-part regressions were used to model the association between weight status and multi-attribute utility.

**Results:** Of the 368 children for whom weight status and HUI3 data were available, around 40% had overweight/obesity. After adjusting for child's sex, maternal education, marital status and household income, no significant association between weight status in the preschool years and multi-attribute utility scores at 5 years was found.

**Conclusions:** Alternative approaches for capturing the effects of weight status in the preschool years on preference-based HRQoL outcomes should be tested. The application of the QALY framework to economic evaluations of obesity-related interventions in young children should also consider longitudinal effects over the life-course.

## **Introduction**

Overweight and obesity in childhood is a growing public health issue worldwide. Since 1975, the global prevalence of childhood obesity has increased around eight-fold in both girls (0.7% to 5.6%) and boys (0.9% to 7.8%), with the total number of 5 to 19 years old affected by obesity estimated to be 124 million in 2016 [1]. The slow and inconsistent progress towards tackling childhood obesity has prompted further calls for action and highlighted the need for interventions in early childhood [2]. Early childhood is an important period for intervention because excess weight gained during this period may have physical and psychological health impacts [3] and is likely to contribute to risk factors for adverse long-term health outcomes during adulthood [4-6].

As well as the need for interventions that are effective at tackling childhood obesity, there is a need for interventions that are cost-effective, as public health resources are finite and increasingly limited. Cost-effectiveness based decision making provides a framework for maximizing health benefits or broader measures of social welfare given finite resources. To date, there have been relatively few cost-effectiveness analyses conducted for obesity-related preventive or treatment interventions in early childhood [7] and even fewer cost-utility analyses [8]. Furthermore, modelled economic evaluations of obesity-related interventions in childhood generally assume no impact on quality-adjusted life years (QALYs) or other health outcomes until adulthood [9, 10]. Establishing a relationship between weight status and utility based health-related quality of life (HRQoL) in children is therefore relevant for modelled economic evaluations that seek to estimate QALYs gained during childhood as a result of preventive or treatment interventions.

Among school-age children and adolescents, existing evidence suggests an inverted-U-shaped relationship between weight status and HRQoL [11, 12]. However, only a few studies have used

preference-based instruments to measure HRQoL and there is no consensus among them regarding the impact of weight status on HRQoL in children and adolescents. For example, some studies have found statistically significant poorer HRQoL in school-age children and adolescents with overweight or obesity [13-15], while others found no association [16-22]. In studies where 5-year old children have been examined, they were grouped together with older children as a cohort [17, 20] or had already started primary school [19]. This gap in the literature highlights the need for more studies to be undertaken in preschool-age children, which would inform economic evaluations of early childhood obesity preventive or treatment interventions. Our aim in this study was to determine the association between weight status in the preschool years and HRQoL at age 5 years using a preference-based instrument, the Health Utilities Index (HUI).

## **Methods**

### ***Participants***

Participants were 368 children who took part in the Healthy Beginnings Trial (HBT), an obesity prevention intervention in early childhood, and who had HRQoL determined at age 5 years. The details of the research protocol and the main outcomes of the HBT have been reported elsewhere [23-25]. Briefly, 667 first-time mothers were recruited from antenatal clinics at two hospitals located in a socially disadvantaged area of south-western Sydney, Australia, with their infants born between 2007 and 2009. The mothers were eligible if they were aged 16 years or above, were expecting their first child, were between weeks 24 and 34 of pregnancy, were able to speak English and lived in the local area; mothers were excluded if they had a severe medical condition as evaluated by their physicians. A total of 465 families agreed to be involved in the follow-up study, which followed children from their second until their fifth birthday and collected health economic data, including HRQoL data at 5 years [25]. Ethics approval for the trial was obtained

from the Sydney Local Health District Research Ethics Review Committee (X10-0312; and HREC/10/RPAH/546).

Socio-demographic characteristics such as maternal age, country of birth, marital status, education and employment status, and household questions on income and language spoken at home were collected at baseline, using standard questions from the New South Wales Population Health Survey [26]. As there were no significant differences in preference-based HRQoL outcomes by treatment allocation (Mann-Whitney test  $p > 0.05$ ), we pooled the data in this analysis and used information for all children in the trial for whom the HUI was completed at age 5 years and for whom information on height and weight was available between age 2 and 5 years.

### ***Weight status measurement***

Height and weight were measured by a research assistant during home visits as part of HBT, when children were 2, 3.5 and 5 years old. A portable stadiometer with a vertical blackboard and movable headboard was used to measure height while a digital scale (TI1582136K; <http://www.wedderburn.com.au>) was used to measure weight [25]. The height and weight measurements were converted into BMI-for-age z-scores at 2, 3.5 and 5 years old using the World Health Organization (WHO) software, AnthroPlus [27]. Mean values of the three BMI-for-age z-score readings were then used to determine overall weight status in the preschool years. By incorporating BMI-for-age z-scores across three distinct ages, we were able to capture a holistic perspective of weight status in children during their early years of life, specifically before they start school. We followed the WHO criteria to classify weight status in childhood: underweight ( $< -2$  standard deviations (SD)), healthy weight ( $-2$  to  $1$  SD), overweight ( $> 1$  to  $2$  SD) and obese ( $> 2$  SD) [28].

### ***Health-related quality of life measurement***

HRQoL of children was measured using the Health Utilities Index with the Mark 3 scoring algorithm (HUI3) [29], a generic measure of health status that has been widely used in HRQoL studies related to children and adolescents [30, 31]. The HUI3 was selected because it allows utility measurement in children aged as young as 5 years of age [32], which is one of the ages that our participants have recorded BMI z-scores. The HUI3 measures HRQoL across eight attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain. Function within each HUI3 attribute is graded on a five- or six-point scale corresponding to the level of severity, ranging from normal function (level 1) to severe impairment (level 5 or 6). Due to the young age of our participants, we administered the parent proxy version of the HUI3 questionnaire through face-to-face interviews conducted by research assistants, which is the recommended format for children aged between 5 and 8 years [32]. Responses to the questionnaire were converted into single-attribute utility scores, ranging from 0 (worst level) to 1 (best level), for each attribute using established utility functions [33]. Multi-attribute utility scores which represent children's overall health status across all attributes were also calculated, using a scoring algorithm based on preferences derived from a general population sample [33]. The multi-attribute utility scores were expressed on an interval scale ranging from -0.36 (representing the health state with the lowest level of function for all attributes) to 1.00 (representing the health state with the highest level of function for all attributes). Missing data within the individual HUI attributes was, on average, less than 3% and thus mean imputation [34, 35] was used to impute missing attribute scores.

### ***Statistical analysis***

Child and family characteristics were described using summary statistics, across weight status categories. The underweight category included only one observation and therefore was excluded from our analysis. For each of the eight attributes of the HUI3, we determined the proportion of children with suboptimal levels of function (defined as below level 1 function) across weight status groups (healthy weight, overweight and obesity). The Pearson's Chi-square test for equality of proportions was used to determine whether the differences in suboptimal function between weight status groups were statistically significant.

We employed several multivariable estimators to model the association between weight status and multi-attribute utility scores. Ordinary least squares (OLS) and Tobit regressions were used, where the latter accounts for the distribution of utility data, bounded at 1.0 [36]. To increase the rigour of our analysis, a two-part regression model was also estimated. The first part of the model was a logistic regression, where the dependent variable is a binary indicator for perfect health/less than perfect health. The second part used a generalized linear model (GLM) with gamma distribution to test for differences in utility score across weight status categories for those with less than perfect health. Based on information in a systematic review of HRQoL in children and adolescents affected by obesity [12], we identified several potentially important demographic factors as controlling covariates. These were child sex, maternal education and marital status, and household income. Our primary analysis was based on a measure of average weight status based on assessments at three time points (i.e. 2, 3.5 and 5 years). As a sensitivity analysis, we also repeated the estimation of OLS, Tobit and two-part models using child weight status based on BMI-for-age z-scores at 5 years of age only. All analyses were conducted in Stata v14.2 [37].

## **Results**

### ***Study participants***

Of the 497 participants who completed HBT phase 1 [23], 465 agreed to be involved in the follow-up study [24]. A further 96 (19.3%) were lost to follow-up during the course of the study [25], leaving a total of 369 participants for this study. After excluding one participant in the underweight category, weight status and health utility data were analysed for 368 participants. Approximately 31% of participants were overweight and 8% had obesity (Table 1). Table 1 shows the child, maternal and household characteristics of the study participants.

### ***Single-attribute HUI3 utility values***

The mean single-attribute utility values for the eight HUI3 attributes were generally similar across children with healthy weight, overweight and obesity status (Table 2). Figure 1 shows the proportion of children with suboptimal function for each attribute, stratified by weight status group. For most attributes, the proportion of children with suboptimal function was very low. With the exception of ambulation, none of the differences in suboptimal function between the three weight groups were statistically significant (Chi-squared test  $p > 0.05$ ).

### ***Multi-attribute HUI3 utility values***

The proportion of children scoring less than perfect health as determined by the HUI3 multi-attribute utility function was 33%, 31% and 30% in children with healthy weight, overweight and obesity, respectively. Table 3 shows the results of the OLS and Tobit regressions that modelled the association between weight status in preschool years and multi-attribute utility values at age 5. After adjusting for child sex, maternal education, marital status and household income, there was no significant effect of child overweight or obesity status on utility based HRQoL – even after accounting for the distribution of the utility data. With the exception of mother's marital



status, none of the demographic factors was independently associated with the overall multi-attribute utility score at age 5 years. Both the OLS and Tobit regressions found significantly lower utility based HRQoL for children of mothers who were not married or in de facto relationships.

Similar to the OLS and Tobit models, the adjusted two-part model showed no significant association between weight status in the preschool years and multi-attribute HUI3 utility scores at age 5 years (Table 4). Additionally, the GLM indicated no significant effect of weight status on multi-attribute utility scores for children with less than perfect health. For the sensitivity analysis, we re-estimated the OLS, Tobit and two-part models using a sample that defined child weight status based on BMI-for-age z-score readings at 5 years of age only (Tables S1 and S2 in Online Resource). The results from the models using only one measure of weight status were consistent with those models using child weight status based on the average of the three BMI-for-age z-scores during the preschool years, i.e. there was no significant association between weight status on utility based HRQoL.

## **Discussion**

To the best of our knowledge, this is the first study to investigate the association between weight status measured across the preschool years and preference-based HRQoL outcomes in children. We found no statistically significant association between weight status (defined as either mean weight status between the ages of 2 and 5 years or weight status at five years of age) and preference-based HRQoL outcomes. Analysis of single-attribute utility scores revealed that for most individual HUI3 attributes, there were also non-significant differences between children with healthy weight, overweight or obesity.

Our study findings are consistent with those from published studies administering preference-based HRQoL instruments in slightly older children. Canaway & Frew [18] interview-administered two pediatric preference-based utility instruments, the Child Health Utility 9D (CHU-9D) and the EuroQol 5D-Youth (EQ-5D-Y) to UK children aged six to seven years, and found no statistically significant associations between weight status and preference-based HRQoL outcomes. In a further study, Frew et al. [19] interview administered the CHU-9D to UK children with a mean age of 6.3 years and found relatively weak (i.e. in the expected direction of effect but not statistically significant) associations between weight status and preference-based HRQoL outcomes. Our results are also consistent with the non-significant findings of published studies using the HUI to examine associations between weight status and preference-based HRQoL outcomes in older children or adolescents [16, 17].

Clearly, more evidence is required on the association between weight status and HRQoL across child and adolescent populations, and across different settings. Generation of this evidence using preference-based instruments will mean that the information can then be used to inform evidence around the cost-utility of preventive or treatment interventions targeted at preschool children. While there are a number of studies that have reported health utility values for children with overweight and obesity [13-22], this is the first study to investigate the association between weight status during preschool years and preference-based HRQoL outcomes at 5 years, the youngest age recommended for use with the HUI instrument [32]. Given the limited published evidence regarding pediatric health-related utilities, our study makes a useful contribution by providing further evidence of a non-significant association between weight status and preference-based HRQoL outcomes in preschool children.

The strengths of our study are that we had three repeated measures of preschool children's BMI using measured (not self-reported) height and weight, which was assessed by trained research assistants using standard measurement techniques. We used a standard HRQoL instrument, the HUI3 and our analysis included both single-attribute and multi-attribute utility scores calculated from established algorithms. Our rigorous statistical analysis used three different estimators to investigate any association between weight status and HRQoL utility scores. These methods have accounted for the distribution of utility scores and controlled for important sociodemographic factors. Additionally, we duplicated all these analyses using only cross-sectional data on weight status and utility based HRQoL at 5 years.

Our findings suggest that young children may not experience any decrement in preference-based HRQoL outcomes associated with their weight status, but there are some limitations of this study that may have influenced this outcome. First, our study is limited by a small sample that may not be representative of the general preschool population and, therefore, generalizability may be limited. Second, the lack of statistically significant associations may reflect a lack of sensitivity of the HUI3 to changes in health status at the lower end of the age range for which the HUI3 is recommended for use [32]. A recently published systematic review and meta-analysis found a relatively wide range of utility values published in the literature for childhood obesity, using different preference-based instruments (including the HUI3) [38]. The meta-analysis also reported statistically significant mean utility differences between healthy weight, overweight and obese status. However, these differences were small, ranging from 0.011 to 0.025. We cannot therefore discount the possibility that the HUI3 may not be sensitive enough to detect weight status-related effects during the early stages of childhood. This possible limitation of the HUI3 is

also reinforced by the fact that other studies using non-preference-based instruments have found significant associations between weight status and HRQoL in young or preschool children [12, 39]. Measuring health state utilities for children and adolescents is an emerging field of research [40], and there is growing recognition of the complexities of collecting reliable information in very young children. These complexities include parental-proxy bias and the degree of accuracy to which multi-attribute utility instruments such as the HUI3 can capture physical, social, psychological and cognitive experiences of young children [41]. A final limitation is that the tariff values for utility weights derived for the HUI3 were elicited from the Canadian adult population, with widespread acceptance that adult preferences for health states may differ markedly from those of children or adolescents [40-42].

While our analyses found no association between weight status in preschool children and HUI3 utility scores, further research should be conducted using other instruments and in different settings [40]. Moreover, it has been hypothesized that decrements in HRQoL due to overweight and obesity are more likely to be experienced by older children and adolescents, rather than preschool children [18]. Acknowledging and capturing these potential longer-term effects will ensure that the cost-utility of obesity interventions targeted at preschool-age children incorporates more evidence on health-related impacts during the child and adolescent life-course. In turn, incorporation of potential long-term QALY effects should ensure that cost-utility is measured over a longer-term time horizon consistent with broader cost-effectiveness based decision making.

## **Conclusion**

There is increasing worldwide recognition of the importance of obesity prevention in the early years of life, and therefore for the need to establish the effectiveness and cost-effectiveness of preventive or treatment interventions targeting childhood obesity. This study presents the first analysis of the association between weight status measured during the preschool years and preference-based HRQoL outcomes. Although no statistically significant association was found between weight status of preschoolers and HRQoL outcomes at age 5 years, further research is required to expand the evidence base both within this age group and across the childhood years, in order to inform cost-utility estimates for obesity interventions targeted at young children.

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## **COMPLIANCE WITH ETHICAL STANDARDS**

**Conflict of interest:** The authors declare that they have no conflict of interest.

**Ethical approval:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Sydney Local Health District Research Ethics Review Committee (X10-0312; and HREC/10/RPAH/546).

**Informed consent:** Informed consent was obtained from all individual participants included in the study.

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**Table 1** - Characteristics of the study population

|                         | Participants (n=368) |    |
|-------------------------|----------------------|----|
|                         | N                    | %  |
| Child sex               |                      |    |
| Male                    | 186                  | 49 |
| Female                  | 182                  | 51 |
| Child weight status*    |                      |    |
| Healthy weight          | 224                  | 61 |
| Overweight              | 114                  | 31 |
| Obese                   | 30                   | 8  |
| Mother's education      |                      |    |
| Primary                 | 46                   | 13 |
| HSC/TAFE                | 207                  | 56 |
| University              | 114                  | 31 |
| Mother's marital status |                      |    |
| Never married           | 26                   | 7  |
| Married/De-facto        | 342                  | 93 |
| Annual household income |                      |    |
| <\$40,000               | 82                   | 22 |
| \$40,000 to <\$80,000   | 113                  | 31 |
| ≥\$80,000               | 173                  | 47 |

\* Weight status in preschool years determined from mean of BMI-for-age z-scores collected at 2, 3.5 and 5 years.

*Abbreviations:* HSC, high school certificate; TAFE, technical and further education.

**Table 2** - Single-attribute and multi-attribute utility values, using the HUI3 by weight status\*; mean (standard deviation)

|                           | Healthy weight<br>(n=224) | Overweight<br>(n=114) | Obese<br>(n=30) |
|---------------------------|---------------------------|-----------------------|-----------------|
| Single-attribute          |                           |                       |                 |
| Vision                    | 0.996 (0.04)              | 0.999 (0.01)          | 1.000 (0.00)    |
| Hearing                   | 1.000 (0.00)              | 0.999 (0.01)          | 1.000 (0.00)    |
| Speech                    | 0.985 (0.06)              | 0.964 (0.12)          | 0.955 (0.19)    |
| Ambulation                | 1.000 (0.00)              | 1.000 (0.00)          | 0.994 (0.03)    |
| Dexterity                 | 0.999 (0.01)              | 1.000 (0.00)          | 1.000 (0.00)    |
| Emotion                   | 0.998 (0.01)              | 0.996 (0.02)          | 0.994 (0.02)    |
| Cognition                 | 0.959 (0.09)              | 0.972 (0.07)          | 0.973 (0.07)    |
| Pain                      | 0.997 (0.02)              | 0.995 (0.05)          | 1.000 (0.00)    |
| Multi-attribute (overall) | 0.956 (0.08)              | 0.956 (0.09)          | 0.952 (0.10)    |

\* Weight status in preschool years determined from mean of BMI-for-age z-scores collected at 2, 3.5 and 5 years.

*Abbreviations:* HUI3, Health Utilities Index Mark 3.

**Table 3** - OLS and Tobit regressions of association between weight status\* and multi-attribute HUI3 utility scores, after controlling for socio-demographic characteristics

|                         | OLS regression |                         |              | Tobit regression |                         |              |
|-------------------------|----------------|-------------------------|--------------|------------------|-------------------------|--------------|
|                         | Coeff.         | 95% CI                  | P-value      | Coeff.           | 95% CI                  | P-value      |
| Child weight status     |                |                         |              |                  |                         |              |
| Healthy weight          | (ref)          |                         |              |                  |                         |              |
| Overweight              | -0.001         | (-0.020, 0.018)         | 0.885        | 0.004            | (-0.050, 0.060)         | 0.873        |
| Obese                   | -0.008         | (-0.048, 0.032)         | 0.681        | -0.012           | (-0.105, 0.080)         | 0.792        |
| Child sex               |                |                         |              |                  |                         |              |
| Male                    | 0.001          | (-0.015, 0.018)         | 0.870        | 0.016            | (-0.034, 0.065)         | 0.528        |
| Female                  | (ref)          |                         |              | (ref)            |                         |              |
| Mother's education      |                |                         |              |                  |                         |              |
| Primary                 | 0.007          | (-0.027, 0.042)         | 0.678        | -0.008           | (-0.096, 0.080)         | 0.854        |
| HSC/TAFE                | 0.001          | (-0.021, 0.023)         | 0.915        | -0.003           | (-0.060, 0.054)         | 0.924        |
| University              | (ref)          |                         |              | (ref)            |                         |              |
| Marital status          |                |                         |              |                  |                         |              |
| Never married           | <b>-0.073</b>  | <b>(-0.143, -0.003)</b> | <b>0.041</b> | <b>-0.137</b>    | <b>(-0.234, -0.041)</b> | <b>0.005</b> |
| Married/De-facto        | (ref)          |                         |              |                  |                         |              |
| Annual household income |                |                         |              |                  |                         |              |
| <\$40,000               | 0.007          | (-0.019, 0.033)         | 0.586        | 0.006            | (-0.089, 0.027)         | 0.870        |
| \$40,000 to <\$80,000   | -0.011         | (-0.032, 0.010)         | 0.304        | -0.031           | (-0.089, 0.027)         | 0.298        |
| ≥\$80,000               | (ref)          |                         |              | (ref)            |                         |              |

\* Weight status in preschool years determined from mean of BMI-for-age z-scores collected at 2, 3.5 and 5 years.  
*Abbreviations:* OLS, ordinary least squares; HUI3, Health Utilities Index Mark 3; HSC, high school certificate; TAFE, technical and further education.

**Table 4** - Two-part model of association between weight status in the preschool years\* and multi-attribute HUI3 utility scores

|                         | Logistic regression<br>(First part) |                |         | Generalized linear model<br>(Second part) |                         |              |
|-------------------------|-------------------------------------|----------------|---------|---|-------------------------|--------------|
|                         | Odds ratio                          | 95% CI         | p-value | Coeff.                                    | 95% CI                  | p-value      |
| Child weight status     |                                     |                |         |   |                         |              |
| Healthy weight          | (ref)                               |                |         |   |                         |              |
| Overweight              | 0.927                               | (0.567, 1.518) | 0.764   | -0.008                                    | (-0.055, 0.039)         | 0.732        |
| Obese                   | 0.986                               | (0.424, 2.297) | 0.975   | -0.043                                    | (-0.124, 0.038)         | 0.299        |
| Child sex               |                                     |                |         |   |                         |              |
| Male                    | 0.807                               | (0.517, 1.261) | 0.347   | -0.014                                    | (-0.057, 0.028)         | 0.506        |
| Female                  | (ref)                               |                |         | (ref)                                     |                         |              |
| Mother's education      |                                     |                |         |   |                         |              |
| Primary                 | 1.296                               | (0.583, 2.880) | 0.525   | 0.036                                     | (-0.036, 0.107)         | 0.330        |
| HSC/TAFE                | 1.068                               | (0.637, 1.791) | 0.803   | 0.009                                     | (-0.041, 0.059)         | 0.714        |
| University              | (ref)                               |                |         | (ref)                                     |                         |              |
| Mother's marital status |                                     |                |         |   |                         |              |
| Never married           | 2.253                               | (0.921, 5.508) | 0.075   | <b>-0.123</b>                             | <b>(-0.200, -0.047)</b> | <b>0.001</b> |
| Married/De-facto        | (ref)                               |                |         | (ref)                                     |                         |              |
| Annual household income |                                     |                |         |   |                         |              |
| <\$40,000               | 1.086                               | (0.567, 2.081) | 0.804   | 0.046                                     | (-0.017, 0.110)         | 0.152        |
| \$40,000 to <\$80,000   | 1.271                               | (0.750, 2.153) | 0.372   | -0.011                                    | (-0.062, 0.039)         | 0.654        |
| ≥\$80,000               | (ref)                               |                |         | (ref)                                     |                         |              |

\* Weight status in preschool years determined from mean of BMI-for-age z-scores collected at 2, 3.5 and 5 years.  
*Abbreviations:* OLS, ordinary least squares; HUI3, Health Utilities Index Mark 3; HSC, high school certificate; TAFE, technical and further education.

## Figure Legends

**Fig 1** Percentage of children with healthy, overweight and obesity scoring less than full health in each of the single attributes of the HUI3. White = healthy weight; grey=overweight; black = obesity. Pearson's Chi-square test for equality of proportions and p values shown.