Barts Health NHS Trust

TRUST CLINICAL GUIDELINE

DOSING OF ANAESTHETIC AND ANALGESIC DRUGS IN THE OBESE PAEDIATRIC POPULATION (OVER 2 YEARS OLD)

FOR THEATRE USE ONLY

APPROVING COMMITTEE(S)			
VERSION NUMBER	1	Date approved:	
EFFECTIVE FROM			
DISTRIBUTION	Paediatric Anaesthetic Consultants, Paediatric Pain Service		
RELATED DOCUMENTS	N/A		
STANDARDS	N/A		
OWNER	BH Paediatric Guidelines Group		
RESPONSIBLE LEAD CLINICIAN, AND FURTHER INFORMATION	Barry Clifton, Katherine Russell, Mohammed Abou Daya		
SUPERCEDED DOCUMENTS	N/A		
KEY CHANGES FROM PREVIOUS VERSION	N/A		
REVIEW DUE	October 2025		
KEYWORDS	Obesity, obese, anaesthetic(s), anaesthesia, paediatric obesity, analgesia		
INTRANET LOCATION(S)	http:// [file location]		

CONSULTATION	*Barts Health*	Drugs and Therapeutics Committee, Pharmacy clinical Leadership Committee
	External Partner(s)	N/A

SCOPE OF APPLICATION AND EXEMPTIONS	All Trust clinical staff, without exemption. Other staff, students and contractors working within the Trust (for information)

Background

According to Public Health England, 1 in 5 children leaving primary school in England are obese, with prevalence highest in the most deprived groups (1). Data from 2015 suggested 31% of children in Tower Hamlets were living below the national poverty line, which equated to the highest in the UK (2). This, alongside a fast growing, young population (3), makes childhood obesity a significant problem in the community.

In Tower Hamlets, 43% of residents were born outside of the UK and over 2/3 belonging to minority ethnic groups (3). Ethnicity is a known independent risk factor for obesity according to research by Public Health England (4). From 2011 census data, amongst 10-11 year olds, the percentage that were overweight within the White British group was 32%, compared to the Bangladeshi group at 44% and Black African group at 46% (5).

Links between deprivation and obesity are well documented; in the UK, obesity in 10-11 year olds was 27% in the most deprived areas, and just 13% in the least deprived areas (6). In Tower Hamlets 20.8% of children of reception age are overweight or obese. By year 6, 42.1% of children are overweight or obese (for comparison, London 37.7%) (7). Tower Hamlets has the fifth highest proportion of obese 10 to 11 year olds in London and the sixth highest in the country (8).

A survey from 2009 looking at health and lifestyle in the Tower Hamlets population found a high intake of fast food takeaways and low intake of the recommended amounts of fruit and vegetables per day, amongst 16 year olds (9). Research by the City of London University found an estimate of 41.8 fast food outlets per secondary school in Tower Hamlets (10). The School Food Trust used this index in 2008, with an average of 23 outlets per school overall, and an urban average of 25 outlets per school (11). This research all points towards a growing population which is vulnerable to childhood obesity.

Traditionally, children are dosed according to their body-weight or age, as a surrogate of 'normal' size and function (12). However, body composition and physiological changes in obesity can affect drug pharmacokinetics and the distribution of drugs into tissues (12, 13). It is therefore important to consider the consequences of these changes as failure to adjust doses appropriately in patients who are obese may result in therapeutic failure or drug-related toxicity (14,15).

How to define obesity in childhood

Defining obesity in childhood is more complex than in adults as children grow at different rates at different times. In children over 2 years old, BMI can be used: weight (kg) / height $(m)^2$. This figure then has to be referenced on a BMI centile chart (16) using data from the 'UK WHO' (for children aged 2-4 years)(17) and 'UK90' (for children over 4 years)(18) reference sets. After plotting the child's age and calculated BMI, their centile can be determined.

The Royal College of Paediatrics and Child Health define the 91^{st} centile as overweight, 98^{th} centile as very overweight/ obese and the 99.6^{th} centile as severely obese (16). For the purposes of this project, we will be using the 98^{th} centile as our definition of obese and therefore appropriate for dose adjustments. There is limited information to assist with decision making regarding dosing of anaesthetic drugs on the obese paediatric population, with most guidance being extrapolated from adult studies. The threshold of 98^{th} centile has been chosen as we consider this group to gain the greatest benefit. We encourage clinicians to consider adjusting dosing for all overweight patients (above 91st centile).

The impact of drug dosing in obese children

Obesity demonstrates important alterations in physiology such as changes in tissue composition, increased circulating blood volume and cardiac output, altered regional flow distribution, and impaired liver and kidney function (19). All of these physiologic alterations can affect pharmacokinetic (PK) parameters including drug absorption, volume of distribution, metabolism, and elimination (20). Furthermore, physiochemical properties of a drug, such as lipid solubility or relative protein binding, might have differential effects on drug PK in obese versus non-obese children (19).

To account for these physiologic and pharmacologic factors, it may be necessary to adjust weight-based dosing for certain drugs using various metrics of body size, such as Ideal Body Weight (IBW) or Adjusted Body Weight (AjBW) (21). Ideal body weight can be calculated in many different ways; given we are using BMI to determine obesity, we have decided to use the reverse BMI equation to calculate IBW. The AjBW approach uses the IBW of the child and adds a specific cofactor, which is the fraction of excess weight gain between IBW and total body weight (TBW), accounting for excess fluid in adipose tissue (14).

Table 1: Common measures of weight used when dosing medicines in childhood obesity

Size Descriptor (kg)	Measurement/ Calculation
Total Body Weight (TBW)	Weight in kg (no adjustment necessary)
Body Mass Index (BMI)	TBW(kg)/ (Height in m)^2
Ideal Body Weight (IBW)[a]	BMI_{50} x Height (m)^2
Adjusted Body Weight (AdjBW)[b]	IBW + Adjustment Factor (0.35) x (TBW-IBW)

[a] BMI_{50} represents the 50th centiles of a BMI at the 50th centile for a patient's height, age and gender
[b] Adjustment factor varies in the literature. Neonatal and Paediatric Pharmacist Group (NPPG) recommends using an adjustment factor of 0.35 as a pragmatic solution to calculating adjusted body weight in children living with obesity (21).

The most appropriate size descriptor has been recommended in table 2, to inform dosing of certain drugs. This is derived from the limited clinical data in children and evidence from adult obesity studies.

The implications of childhood obesity in the perioperative period

The initial findings of the PEACHY study has demonstrated an over representation of obese children within the paediatric surgical population, with 14% of children requiring surgery in 102 UK hospitals defined as overweight or obese (22). We know obese adult patients are at risk of complications under anaesthesia due to difficult airways, obstructive sleep apnoea, hypertension, diabetes and venous thromboembolic disease (23). There is little evidence at present to confirm similar pathophysiology in children, though the same factors may play a role in this population.

Signposting for GP review

Overweight and obese children should be signposted by the anaesthetist or surgeon to see their GP for advice and support +/- investigation of possible complications. Height and weight should be recorded on CRS. Obesity should be coded as a diagnosis on CRS.

Barts Health NHS
NHS Trust

Quick Reference Guide:
Dosing of anaesthetic drugs in obese children over 2 years old

Step 1

Identify the obese child

Measure the child's **height** and **weight**

Use the NHS BMI calculator (https://www.nhs.uk/live-well/healthy-weight/bmi-calculator/) (24) to determine whether the child is **above the 98th centile for BMI** ('very overweight'/ 'obese'). If so, proceed to step 2, 3 & 4.

Step 2

Calculate Ideal Body Weight

Find BMI for 50th centile (BMI_{50}) according to the child's age and gender using the table below, then calculate:

Ideal body weight = BMI_{50} x Height (m)2

Age	BMI $_{50}$ for girls	BMI $_{50}$ for boys
2	15.7	16
2.5	15.5	15.8
3	15.4	15.6
3.5	15.3	15.4
4	15.7	15.8
4.5	15.6	16.3
5	15.5	15.5
5.5	15.5	15.5
6	15.5	15.5
6.5	15.6	15.5
7	15.7	15.6
7.5	15.8	15.6
8	16	15.7
8.5	16.2	15.9
9	16.4	16
9.5	16.4	16.2
10	16.9	16.4
10.5	17.2	16.6
11	17.5	16.9
11.5	17.8	17.2
12	18.1	17.4
12.5	18.4	17.7
13	18.8	18
13.5	19.1	18.4
14	19.4	18.7
14.5	19.7	19
15	20	19.3
15.5	20.2	19.6
16	20.4	19.9

Barts Health NHS
NHS Trust

Step 3

Calculate Adjusted Body Weight

Adjusted body weight =
Ideal Body Weight + 0.35 X (Total body weight – Ideal Body Weight)

The Neonatal and Paediatric Pharmacist Group (NPPG) recommend using a standard adjustment factor of 0.35 to calculate AdjBW for those drugs where it is required.

Step 4

Calculate drug doses required as listed on the following pages

Table 2:

Recommended dose calculations, by drug

Drug	Weight to calculate dose	Dose	References
Induction agents/ Pre-medications			
Propofol	Ideal Body Weight Titrate to response	2-3mg/kg IV for induction	26, 27, 28
Fentanyl	Adjusted Body Weight	1-2mcg/kg IV for intraoperative analgesia dosing	21
Midazolam	Total body weight (loading)	0.5mg/kg PO for pre-medication (max dose 20mg)	21, 26, 29
Analgesia			
Morphine	Ideal Body Weight	0.1-0.2mg/kg IV for intraoperative analgesia 0.1-0.4mg/kg PO 3 hourly for post-operative analgesia (as 'Oramorph') (max single dose 20mg)	21, 27, 28, 30
Paracetamol	Adjusted Body Weight	15mg/kg 6 hourly IV or PO (Max single dose: 1g)	21, 31, 32
Ibuprofen	Adjusted Body Weight	Maintenance dose: 7.5 mg/kg PO 6 hourly (max single dose 400mg) If >12 years and >40 kg: 400 mg 8hly (Max daily dose 1.2g daily)	21, 31, 32
Diclofenac	Ideal body weight	1mg/kg IV 12 hourly (Max single dose 75mg) 1mg/kg PO 8 hourly (Max daily dose 150mg)	**
Muscle Relaxants			
Atracurium	Ideal Body Weight	0.5mg/kg IV	26, 27, 33
Rocuronium	Ideal Body Weight	0.6mg/kg IV	26, 27, 33
Suxamethonium	Total Body Weight	1-2mg/kg IV	26, 27, 28, 30

Drug	Weight to calculate dose	Dose	References
Local Anaesthetics			
Lignocaine	Total Body Weight (loading dose)	3mg/kg without adrenaline (for local infiltration)	26, 32, 34
Levobupivacaine	Ideal Body Weight	2mg/kg (for local infiltration)	33
Antibiotics			
Penicillins	Total Body Weight	Co-amoxiclav 30mg/kg IV (Max single dose 1.2g)	21
Amikacin	Adjusted Body Weight	15mg/kg IV 24 hourly	21, 32
Anti-emetics			
Ondansetron	Total Body Weight	0.1mg/kg IV/ PO (max 4mg) 8 hourly	21
Dexamethasone	Total Body Weight	0.1-0.2mg/kg IV	21
Cyclizine	Total Body Weight	1mg/kg IV/ PO (max 50mg) 8 hourly	**
Reversal Agents			
Neostigmine with glycopyrrolate (0.5/2.5mg/ml)	Adjusted Body weight	0.02ml/kg IV (max 0.5/2.5mg = max 1ml)	26, 30, 32 (Neostigmine)
Sugammadex	Total Body Weight	Routine reversal 2mg/kg IV	27, 35, 36
Anticholinergics			
Atropine	Total Body Weight	20mcg/kg (max 600mcg) IV *Larger doses may be used in emergencies	32

*This list is not exhaustive and absence does not imply that no dose adjustment is needed in children who are obese. The table above provides recommendations and does not intend to replace clinical judgement. Please contact your pharmacist if you need support with any other drugs.

**Due to the lack of evidence, the paediatric pharmacist, Mohammed Abou Daya, has chosen the most appropriate size descriptor for diclofenac and cyclizine. This is based on the pharmacokinetic profile of the drugs, specifically, the volume of distribution and clearance.

Implementation of our guideline

Steps 2-4 above will be built into an automated excel spreadsheet to improve ease and accuracy of calculations as well as encourage use.

The clinician will need to perform step 1 independently to determine whether the child is appropriate for dose adjustments.

Barts Health NHS
NHS Trust

Table 3: BMI_{50} for ages 2-16 years

Girls

Age (years)	2	2.5	3	3.5	4	4.5	5	5.5	6	6.5	7	7.5	8	8.5	9	9.5	10	10.5	11	11.5	12	12.5	13	13.5	14	14.5	15	15.5	16
BMI_{50}	15.7	15.5	15.4	15.3	15.7	15.6	15.5	15.5	15.5	15.6	15.7	15.8	16	16.2	16.4	16.4	16.9	17.2	17.5	17.8	18.1	18.4	18.8	19.1	19.4	19.7	20	20.2	20.4

Boys

Age (years)	2	2.5	3	3.5	4	4.5	5	5.5	6	6.5	7	7.5	8	8.5	9	9.5	10	10.5	11	11.5	12	12.5	13	13.5	14	14.5	15	15.5	16
BMI_{50}	16	15.8	15.6	15.4	15.8	16.3	15.5	15.5	15.5	15.5	15.6	15.6	15.7	15.9	16	16.2	16.4	16.6	16.9	17.2	17.4	17.7	18	18.4	18.7	19	19.3	19.6	19.9

References

(1) Public Health England. *Obesity Profile.* Available from: https://fingertips.phe.org.uk/profile/national-child-measurement-programme [Accessed 18th October 2021]
(2) Tower Hamlets Council. *Borough Statistics, Child Poverty in Tower Hamlets.* Available from: https://www.towerhamlets.gov.uk/Documents/Borough_statistics/Income_poverty_and_welfare/2015_Child_Poverty_Briefing.pdf [Accessed 18th October 2021]
(3) Tower Hamlets Council. *Borough Profile 2018, 2. Population.* Available from: https://www.towerhamlets.gov.uk/Documents/Borough_statistics/Research-briefings/Population_2_BP2018.pdf [Accessed 18th October 2021]
(4) Public Health England. *Research and analysis: Differences in childhood obesity by ethnic group.* Available from: https://www.gov.uk/government/publications/differences-in-child-obesity-by-ethnic-group/differences-in-child-obesity-by-ethnic-group [Accessed 18th October 2021]
(5) Public Health England. National Child Measurement Programme. *Overweight Children*. Available from: https://www.ethnicity-facts-figures.service.gov.uk/health/diet-and-exercise/overweight-children/latest [Accessed 18th October 2021]
(6) Rachel Batterham. Royal College of Physicians. *Health Inequality and Obesity.* Available from: https://www.rcplondon.ac.uk/news/health-inequalities-and-obesity [Accessed 18th October 2021]
(7) Somen Banerjee. Tower Hamlets Council. Health and Adults Scrutiny Sub-Committee. *Addressing Childhood Obesity in Tower Hamlets*. Available from: 3 [Accessed 18th October 2021]
(8) Tower Hamlets Council. *Healthy lifestyle, children and young people.* Available from: https://www.towerhamlets.gov.uk/lgnl/health__social_care/public_health/healthy_lifestyle,_children.aspx [Accessed 18th October 2021]
(9) Ipsos MORI. Tower Hamlets Primary Care Trust. *Health and Lifestyle Research.* Available from: https://www.towerhamlets.gov.uk/Documents/Borough_statistics/Health_and_social_care/Tower-Hamlets-Health&Lifestyle1.pdf [Accessed 18th October 2021]
(10) Caraher, M., Lloyd, S., Madelin, T. The "School Foodshed": schools and fast-food outlets in a London borough. British Food Journal [internet]. 2014: 116(3), pp. 472-493. Available from: https://openaccess.city.ac.uk/id/eprint/3392/1/The%20School%20Foodshed.pdf
(11) School Food Trust. *Junk Food Temptation Towns Index*. 2008
(12) Mulla H, Johnson TN. Dosing dilemmas in obese children. Arch Dis Child Educ Pract Ed. [Internet]. 2010; 95 (4): 112-117. Available from: https://pubmed.ncbi.nlm.nih.gov/20585055/
(13) Kendrick JG, Carr RR, Ensom MH. Pediatric Obesity: Pharmacokinetics and implications for drug dosing. Clin Ther. [Internet].2015; 37(9): 1897-923. Available from: https://pubmed.ncbi.nlm.nih.gov/26361823/
(14) Callaghan LC. Prescribing in paediatric obesity: methods to improve dosing safety in weight-based dose calculations. Arch Dis Child Educ Pract Ed. [Internet]. 2018; 103(5):274-277. Available from: https://pubmed.ncbi.nlm.nih.gov/29374622/
(15) Bourne K, Russel H. *Drug Dose Adjustments in Obese Patients. Hospital Guideline.* Sheffield Children's NHS Foundation Trust. June 2014, reviewed April 2017.
(16) Royal College of Paediatrics and Child Health. *Body Mass Index 2-20 years*. 2013. Available from: https://www.rcpch.ac.uk/sites/default/files/2018-03/boys_and_girls_bmi_chart.pdf
(17) Wright C, Williams, A.F, Elliman D, Bedford H, Birks E, Butler G et al. Using the new UK-WHO growth charts. *BMJ. [Internet.]* 2010; 340: c1140. Available from: https://www.bmj.com/content/340/bmj.c1140.long
(18) Cole T.J, Freeman J.V, Preece M.A. Body mass index reference curves for the UK, 1990. *Archives of Disease in Childhood. [Internet.]* 1995;73:25-29. Available from: https://adc.bmj.com/content/73/1/25.short
(19) Harskamp-van Ginkel M.W, Hill K.D, Becker K.C, Testoni D, Cohen-Wolkowiez M, Gonzalez D, Drug Dosing and Pharmacokinetics in Children With Obesity: A Systematic Review. JAMA Pediatr. [Internet]. 2015 Jul;169(7):678-85. Available from: https://pubmed.ncbi.nlm.nih.gov/25961828/
(20) Jain R, Chung SM, Jain L, et al. Implications of obesity for drug therapy: limitations and challenges. Clin Pharmacol Ther. [Internet] 2011; 90(1):77–89. Available from: https://pubmed.ncbi.nlm.nih.gov/21633345/
(21) Specialist Pharmacy Service. UK Medicines Information (UKMi) pharmacists with input from the Neonatal and Paediatric Pharmacists Group (NPPG) for NHS healthcare professionals. *How should medicines be dose in children who are obese*. 2021. Available from: https://www.sps.nhs.uk/articles/how-should-medicines-be-dosed-in-children-who-are-obese/ [Accessed 18th October 2021]
(22) Burton Z, Lewis R, Bennett T, McLernon D.J, Paediatric Anaesthesia Trainee Research Network, Engelhardt T, Brooks P.B, Edwards M.R. Prevalence of PErioperAtive CHildhood obesitY in children undergoing general anaesthesia in the UK: a prospective, multicentre, observational cohort study. Br J Anaesth. [Internet]. 2021. Available from: https://www.bjanaesthesia.org/article/S0007-0912(21)00548-1/pdf

(23) Association of Anaesthetists of Great Britain and Ireland. Peri-operative management of the obese surgical patient 2015. Anaesthesia. [Internet]. 2015. 70; 859–876. Available from: http://onlinelibrary.wiley.com/enhanced/doi/10.1111/anae.13101/
(24) NHS. BMI Health Weight Calculator. [Internet].2018. Available from: https://www.nhs.uk/live-well/healthy-weight/bmi-calculator/. [Accessed 18th October 2021]
(25) Royal College of Paediatrics and Child Health, Department of Health. Body mass index 2-20 years. [Internet]. 2013. Available from: https://www.rcpch.ac.uk/sites/default/files/2018-03/boys_and_girls_bmi_chart.pdf (Accessed on 12th November 2021]
(26) Chidambaran V, Tewari A, Mahmoud M. Anesthetic and pharmacologic considerations in perioperative care of obese children. J. Clin. Anesth.[Internet] 2018. 45: 39-50. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0952818017310899
(27) Mortensen A, Lenz K, Abildstrøm H, Lauritsen T.L.B. Anesthetizing the obese child. Paediatr Anaesth. [Internet]. 2011. 21; (6); 623-629. Available from: https://onlinelibrary.wiley.com/doi/epdf/10.1111/j.1460-9592.2011.03559.x
(28) Brzenski A, Dontukurthy S, Raman V. T. Challenges of pediatric obesity in perioperative care. Int. Anesthesiol Clin. [Internet] 2020. 58; (3); 9-13. Available from: https://journals.lww.com/anesthesiaclinics/Citation/2020/05830/Challenges_of_pediatric_obesity_in_perioperative.2.aspx
(29) Kyler, K, Wagner J, Hosey-Cojocari C, Watt K, Shakhnovich V. Drug Dose Selection in Pediatric Obesity: Available Information for the Most Commonly Prescribed Drugs to Children. Paediatr drugs. [Internet] 2019, 21(5): 357–369. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7681556/
(30) Burke C.N, Voepel- Lewis T, Wagner W, Lau I, Baldock A, Malviya S et al. A retrospective description of anesthetic medication dosing in overweight and obese children. Paediatr. Anaesth. [Internet]. 2014. 24;(8); 857-862. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/pan.12396
(31) Guidelines for treating acute pain in paediatric inpatients. Acute Paediatric Pain Service February 2018. Barts Health NHS Trust.
(32) Ross EL, Heizer J, Mixon MA, et al. Development of recommendations for dosing of commonly prescribed medications in critically ill obese children. Am J Health Syst Pharm. [Internet] 2015; 72(7): 542-56. Available from: https://academic.oup.com/ajhp/article-abstract/72/7/542/5111678?redirectedFrom=fulltext
(33) Joint Formulary Committee. *British National Formulary* (online) London: BMJ Group and Pharmaceutical Press. Available from: https://bnfc.nice.org.uk. [Accessed 18th October 2021]
(34) Reid TD, Sanjay P, Woodward A. Local anesthetic hernia repair in overweight and obese patients. World J Surg. [Internet]. 2009; 33(1):138-41. Available from: https://pubmed.ncbi.nlm.nih.gov/18841412/
(35) Bridion®. (Sugammadex) Merck Sharp and Dohme Ltd. Summary of Product Characteristics. [Internet]. Available from www.medicines.org.uk. [Accessed on 5th November 2021]
(36) United Kingdom Clinical Pharmacy Association, Critical Care Group. Drug dosing in extremes of body weight in critically ill patients, 1st edition. [Internet]. September 2013. Available from https://www.scottishintensivecare.org.uk/uploads/2014-07-24-19-55-33-Drugdosingatextremesofbod-45662.pdf. [Accessed on 5th November 2021]