HORMONE RESEARCH IN PÆDIATRICS

Horm Res Paediatr 2018;90:358–367 DOI: 10.1159/000496563 Received: September 3, 2018 Accepted: January 3, 2019 Published online: February 8, 2019

# Prediction Models for Early Childhood Obesity: Applicability and Existing Issues

Éadaoin M. Butler<sup>a, b</sup> José G.B. Derraik<sup>a-c</sup> Rachael W. Taylor<sup>a, d</sup>

Wayne S. Cutfield<sup>a, b</sup>

<sup>a</sup> A Better Start – National Science Challenge, New Zealand; <sup>b</sup>Liggins Institute, University of Auckland, Auckland, New Zealand; <sup>c</sup>Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden; <sup>d</sup>Department of Medicine, University of Otago, Dunedin, New Zealand

### Keywords

Children · Intervention · Overweight · Prevention · Risk

### Abstract

Statistical models have been developed for the prediction or diagnosis of a wide range of outcomes. However, to our knowledge, only 7 published studies have reported models to specifically predict overweight and/or obesity in early childhood. These models were developed using known risk factors and vary greatly in terms of their discrimination and predictive capacities. There are currently no established guidelines on what constitutes an acceptable level of risk (i.e., risk threshold) for childhood obesity prediction models, but these should be set following consideration of the consequences of false-positive and false-negative predictions, as well as any relevant clinical guidelines. To date, no studies have examined the impact of using early childhood obesity prediction models as intervention tools. While these are potentially valuable to inform targeted interventions, the heterogeneity of the existing models and the lack of consensus on adequate thresholds limit their usefulness in practice.

© 2019 S. Karger AG, Basel

## KARGER

© 2019 S. Karger AG, Basel

E-Mail karger@karger.com www.karger.com/hrp

### Introduction

Clinical prediction models are becoming increasingly prevalent in the medical literature [1]. These models be can either diagnostic or prognostic. Diagnostic models aim to estimate the likelihood of an individual currently having a disease/illness, whereas prognostic models aim to estimate the risk of an individual experiencing a particular outcome at a specified future time. Clinical prediction models are commonly developed using regression modelling, but other approaches such as machine-learning techniques and decision trees have also been utilized [1–4].

Prediction models exist for a wide variety of health outcomes, such as cardiovascular disease [5], lung cancer [6], acute kidney injury [7], and infertility treatment success [8]. There is an overwhelming number of models for the prediction of specific outcomes, with, for example, more than 350 prediction models developed for cardiovascular disease in the general population [5]. Conversely, very few studies have focused on the prediction of overweight or obesity in early childhood (between 2 and 8 years of age) [9–16], which is the focus of this review.

## Childhood Obesity: Prevalence and Associated Health Risks

The prevalence of childhood obesity increased in every region of the world between 1975 and 2016 [17]. It is now estimated that, worldwide, 41 million children under the age of 5 years are overweight or obese [18]. In New Zealand, one third of 4- to 5-year-olds are overweight or obese [19]. Childhood obesity is associated with both long-term and immediate health risks. In the long term, it is predictive of diabetes risk [20, 21], and it is associated with premature mortality [22] and increased cardiovascular risk [21, 22], predominantly as a result of a substantially greater risk of adult obesity [20, 23-26]. In the short term, childhood overweight and obesity are associated with psychosocial distress [22, 27–29], a lower health-related quality of life [30], and a range of physical comorbidities [29, 31]. For example, even among preschool children (aged 3-6 years), an increase in body mass index (BMI) of 1 kg/m<sup>2</sup> has been associated with increased systolic and diastolic blood pressure [32]. Furthermore, conditions that were previously considered restricted to adults (e.g., type 2 diabetes and sleep apnea) are now being diagnosed more and more frequently in obese youth [23, 29, 31].

### **Treatment versus Prevention**

Prevention, rather than treatment, has been argued to be more successful in reducing childhood obesity [23], as obesity is difficult to reverse once established [23, 33]. Interventions to reduce obesity in adults have mostly focused on lifestyle changes alone, and they have struggled to maintain results 36 months after intervention [34]. Weight loss medication and bariatric surgery are associated with side effects and risks [34, 35]. In addition, as childhood obesity is associated with health risks even in very young children [32], it would be preferable to prevent obesity from occurring in the first place.

There are a number of potentially modifiable risk factors that are known to be associated with early childhood obesity, such as excessive gestational weight gain [36, 37], maternal pre-pregnancy BMI [36–38], maternal smoking during pregnancy [36–38], and rapid infant weight gain [36, 38–40]. However, despite the identification of these potentially modifiable risk factors, reviews of interventions to prevent early childhood obesity have reported inconsistent results [41–44].

## **Early Childhood Obesity Prediction Models**

To our knowledge, 7 studies have been published reporting models for predicting overweight/obesity in young children aged  $\leq 8$  years [9–15]. Two studies reporting the prediction of childhood obesity and/or overweight beyond 8 years of age were excluded [40, 45]. The study by Morandi et al. [13] reported a number of models with the outcome at various ages, and only those falling within our age range criteria were considered. Additionally, we excluded certain models from 2 studies that predicted obesity and/or overweight within approximately 12 months from the time of prediction [11, 15], but their other models were included in this review.

The details of the derived prediction models included in this review are examined in Table 1, while Table 2 outlines the respective validation models. These models are all prognostic, aiming to calculate the risk of an infant or toddler becoming overweight or obese at a future time point. Six of these studies used regression modelling [9, 10, 12–15], while the remaining study used data-mining methods [11]. The models used a variety of modifiable predictors, including maternal prepregnancy BMI [10, 12-15], paternal BMI [10, 12, 13], and maternal smoking during pregnancy [10, 13] (Table 3; online suppl. Table 1; see www.karger.com/doi/10.1159/000496563 for all online suppl. material). Conversely, non-modifiable risk predictors included infant birth weight [10, 12-14], infant weight gain [10, 11], and sex [10–12, 15] (Table 3; online suppl. Table 1). Table 3 outlines the various predictor variables used in the derivation models, as well as their respective OR where available. Additionally, online supplementary Table 1 describes the predictor variables used in each derivation model. In general, the models focused on predictor variables that can be routinely collected in clinical practice, although 3 models also included paternal BMI [10, 12, 13], and that may not be consistently available. While external validation is strongly recommended following development and internal validation of a prediction model [2, 46], this was only done for 3 of the 7 models [13, 15, 47].

## Area under the Receiver Operating Characteristic Curve

The area under the receiver operating characteristic curve (AUROC) is a useful indicator of a model's ability to discriminate between those at high risk and those at lower risk of a given outcome [48]. The following are gen-

Table 1	. Summary of published	prediction models for	early childhoo	l overweight or	obesity	derived from	data collected	before 2 years
of age				-				

Study	Validation	Participants	Prediction age	Outcome predicted	Risk threshold and/or model	AUROC <sup>1</sup>	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Levine et al. [9]	none	UK: ALSPAC $(n = 14,000)$ and	infancy	overweight/obesity at 5 years	$0.02^2$ $0.03^2$	unreported unreported	92 79	21 51	6 8	98 98
		Cohort Study			0.04 <sup>2</sup>	unreported	71	61	9	98
		(n = 18,000)			0.05 <sup>2</sup>	unreported	63	72	11	97
					0.10 <sup>2</sup>	unreported	42	91	20	97
					0.20 <sup>2</sup>	unreported	12	98	25	96
Morandi et al. [13]	external (model A only)	Finland: Northern Finland Birth Cohort ( <i>n</i> = 4,032)	at birth	obesity at age 7 years (model A)	0.75 <sup>3</sup>	0.78	72	77	9	99
				overweight/obesity at 7 years (model B)	0.75 <sup>3</sup>	0.67 (0.65–0.69)	45	79	29	88
Robson et al. [14]	internal	US: Latino mother-child	infancy	obesity at 5 years (reduced model)	0.25 <sup>3</sup>	0.82 (0.74-0.89)	96	37	41	95
		pairs ( <i>n</i> = 166)			0.50 <sup>3</sup>	0.82 (0.74–0.89)	80	64	51	88
					0.75 <sup>3</sup>	0.82 (0.74–0.89)	46	84	57	77
					0.90 <sup>3</sup>	0.82 (0.74–0.89)	24	97	79	73
				obesity at 5 years (full model)	0.25 <sup>3</sup>	0.84 (0.77-0.91)	95	35	40	94
					0.50 <sup>3</sup>	0.84 (0.77-0.91)	86	66	54	91
					0.75 <sup>3</sup>	0.84	51	85	61	79
					0.90 <sup>3</sup>	0.84 (0.77–0.91)	30	99	93	76
Santorelli et al. [15]	internal <sup>4</sup>	UK: Born in Bradford birth cohort (n = 1,868)	6±1.5 months	obesity at 2 years	unreported	0.87 (0.83–0.90)	unreported	unreported	unreported	unreported
Steur	internal	The Netherlands: PIAMA birth cohort study	unds: at birth 1	overweight/obesity at 8 years	≥5% <sup>5</sup>	0.78	97	20	16	97
et al. [12]					≥10% <sup>3</sup>	0.78	82	55	23	95
		(n = 1,687)			≥15% <sup>5</sup> ≥20% <sup>5</sup>	0.78	67 50	85	30 35	93 91
Weng et al. [10]	internal and external	UK: Millennium Cohort Study ( <i>n</i> = 13,513)	6–12 months	overweight/obesity at 3 years	Risk score ≥25 <sup>6</sup>	0.72	70	68	38	87
Zhang et al. [11]	none	UK: Wirral child database ( <i>n</i> = 16,523)	6 weeks, 8 months	overweight/obesity at 3 years from data by 6 weeks	unreported <sup>7</sup> unreported <sup>8</sup>	0.82 0.83	11 2	96 100	36 54	84 83
				overweight/obesity	unreported7	0.82	36	92	46	88
				at 3 years from data by 8 months	unreported <sup>8</sup>	0.68	46	73	25	87
				overweight/obesity at 3 years from data by 8 months	unreported9	0.84	12	98	unreported	unreported
					unreported10	0.84	18	97	unreported	unreported
					unreported11	0.84	13	98	unreported	unreported
					unreported12	0.84	10	98	unreported	unreported
					unreported13	0.82	15	96	unreported	unreported
					unreported14	0.68	46	73	unreported	unreported
					unreported15	0.82	36	92	unreported	unreported
					unreported <sup>16</sup>	0.82	36	92	unreported	unreported

AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value.<sup>1</sup> 95% confidence intervals are reported in parentheses (where available).<sup>2</sup> Values represent the predictive value; PPV, positive predictive value.<sup>1</sup> 95% confidence intervals are reported in parentheses (where available).<sup>2</sup> Values represent the prediction joint. <sup>3</sup> Values represent the percentile threshold of obesity risk. <sup>4</sup> Only the results for equation 1 are presented here, as the findings for equation 2 were nearly identical and equation 1 is more clinically useful due to an earlier prediction age. Note that equation 1 was not externally validated due to insufficient numbers. <sup>5</sup> Values represent the estimated risk of overweight at 8 years of age. <sup>6</sup> A risk score algorithm was created with a range of 0–59.<sup>7</sup> Model derived using naïve Bayes.<sup>8</sup> Model derived using support vector machines (SVM).<sup>9</sup> Model derived using decision tree.<sup>10</sup> Model derived using decision rules.<sup>11</sup> Model derived using linear SVM. <sup>16</sup> Model derived using radial basis function SVM. <sup>15</sup> Model derived using Bayesian network.<sup>16</sup> Model derived using naïve Bayesian.

Study	Validation type	Participants	Prediction age	Outcome predicted	Risk threshold/and or model	AUROC	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Morandi et al. [13]	external	US: Project Viva cohort (n = 1,032)	birth	obesity at 7 years	unreported (model A) <sup>1</sup>	0.73 (0.67–0.80)	unreported	unreported	unreported	unreported
Robson et al. [14]	internal	bootstrap with 1,000	infancy	obesity at 5 years	unreported (full model)	0.78	unreported	unreported	unreported	unreported
		samples			unreported (reduced model)	0.76	unreported	unreported	unreported	unreported
Santorelli et al. [15]	internal	bootstrap with 1,000 samples	6±1.5 months <sup>2</sup>	obesity at 2 years	unreported	0.86 (0.82–0.90)	unreported	unreported	unreported	unreported
	unclear <sup>2</sup>	unclear	phone model A:	obesity at 2 years	0.10 <sup>4</sup> (model A)	0.85 (0.81-0.90)	51	94	41	96
			6±1.5 months <sup>3</sup> phone model B: 6±1.5 months <sup>3</sup>	obesity at 2 years	0.20 <sup>4</sup> (model A)	0.85 (0.81-0.90)	70	84	28	97
					0.30 <sup>4</sup> (model A)	0.85	78	74	21	98
					0.10 <sup>4</sup> (model B)	0.86	51	94	41	96
					0.20 <sup>4</sup> (model B)	0.86	71	85	29	97
					0.30 <sup>4</sup> (model B)	(0.82-0.90) (0.82-0.90)	82	75	22	98
Steur et al. [12]	internal	bootstrap with 200 samples	birth	overweight/obesity at 8 years	unreported	0.75	unreported	unreported	unreported	unreported
Weng et al. [10]	internal	UK: Millennium Cohort Study, 20% of the total (n = 13,513)	6–12 months	overweight/obesity at 3 years	risk score ≥25⁵	0.76	77	67	37	89
Redsell et al. [46]	external	UK: 10% sample from	4–12 months rom 2 –	overweight/obesity at 5 years using IOTF	unreported <sup>7</sup>	0.67 (0.62-0.72)	unreported	unreported	unreported	unreported
(validation of Weng		ALSPAC – Children in Focus (CiF) (n = 1,432)		criteria [63] <sup>6</sup>	unreported <sup>8</sup>	0.70 (0.65-0.74)	unreported	unreported	unreported	unreported
et al. [10])					unreported9	0.79	unreported	unreported	unreported	unreported
					$2.5\%^{10}$	0.93	99	5	unreported	unreported
					5% <sup>10</sup>	(0.88-0.98) (0.88-0.98)	90	24	unreported	unreported
					$10\%^{10}$	0.93	53	71	unreported	unreported
					15% <sup>10</sup>	0.93	24	92	unreported	unreported
					20%10	0.93	12	98	unreported	unreported
					25% <sup>10</sup>	(0.00-0.90) 0.93 (0.88-0.98)	4	99	unreported	unreported
					30% <sup>10</sup>	(0.88-0.98) (0.88-0.98)	3	100	unreported	unreported

## **Table 2.** Internal and/or external validations of childhood overweight/obesity prediction models based on data recorded before 2 yearsof age

AUROC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value. <sup>1</sup> Also externally validated on the Veneto cohort (Italy), but the age range is outside the scope of this review (4–12 years). <sup>2</sup> Only the results for equation 1 are presented here, as the findings for equation 2 were nearly identical and equation 1 is more clinically useful due to an earlier prediction age. <sup>3</sup> These are the models used in the phone application Healthy Infant Weight?; it is unclear whether this is a validation model and what population was used in its development. Phone model A consisted of sex, birthweight z score gain from birth, while phone model B also included maternal BMI. <sup>4</sup> Values represent the percentile threshold of obesity risk. <sup>5</sup> A risk score algorithm was created with a range of 0–59.<sup>6</sup> Results were also reported for UK 1990 (Cole et al. [64])-defined overweight. Only the IOTF (International Obesity Task Force) [63] is reported here as results were similar, and the IOTF was considered model. <sup>10</sup> Recalibrated imputed model.

erally accepted interpretations of AUROC values: poor (<0.60), possibly helpful ( $\geq$ 0.60 but <0.70), acceptable ( $\geq$ 0.70 but <0.80), excellent ( $\geq$ 0.80 but <0.90), and outstanding ( $\geq$ 0.90) [48, 49].

None of the models reported here had a poor AUROC, although they did vary considerably (Table 1). The model with the lowest AUROC (i.e., 0.67) predicted overweight/obesity at 7 years, but the authors did not validate it, as they did not deem it clinically useful [13] (Table 1). The highest reported AUROC (i.e., 0.87) was for a model to predict overweight at 2 years based on data gathered at 4.5–6.5 months [15] (Table 1). It is possible that the short time between the prediction age and the outcome age partly explains this high AUROC value. In general, regression models that were supplemented by data on infant weight gain [14, 15] produced higher AUROC values than those that used birth data alone [12, 13], with one exception [10]. These findings suggest that the inclusion

Level	Predictors	Study	Notes/comment	OR (95% CI)
Maternal	age (years) education English proficiency ethnicity gestational weight gain (%) occupation parity	Robson et al. [14] Levine et al. [9] Robson et al. [14] Santorelli et al. [15] Morandi et al. [13] Morandi et al. [13] Robson et al. [14]	nonuniversity vs. university no vs. yes South Asian ethnicity vs. white British ranked employment categories 1–4 first child vs. later children	$\begin{array}{c} 0.90 \ (0.82-0.99)^1 \\ 0.92 \ (0.83-1.26)^2 \\ \text{unreported} \\ 1.73 \ (0.60-5.00)^1 \\ 1.80 \ (1.05-3.11)^3 \\ 1.02 \ (1.01-1.03)^4 \\ 0.50 \ (0.31-0.79)^5 \\ 0.61 \ (0.23-1.62)^2 \end{array}$
	prepregnancy BMI (kg/m²) smoking during pregnancy	Morandi et al. [13] Robson et al. [14] Steur et al. [12] Santorelli et al. [15] Weng et al. [10] Morandi et al. [13] Weng et al. [10]	18.5 to <25 kg/m <sup>2</sup> (reference: <18.5) 25 to <30 kg/m <sup>2</sup> (reference: <18.5) ≥30 kg/m <sup>2</sup> (reference: <18.5) yes vs. no yes vs. no yes vs. no	$\begin{array}{c} 1.13 \ (1.08-1.17)^5 \\ 1.13 \ (1.10-1.16)^4 \\ 1.11 \ (1.02-1.20)^1 \\ 1.12 \ (1.02-1.22)^2 \\ \text{unreported} \\ 1.05 \ (1.00-1.09)^3 \\ 1.76 \ (1.21-2.56) \\ 2.35 \ (1.60-3.47) \\ 2.98 \ (1.98-4.47) \\ 1.84 \ (1.20-2.81)^5 \\ 1.28 \ (1.05-1.57)^4 \\ 1.33 \ (1.15-1.55) \end{array}$
Paternal	BMI (kg/m <sup>2</sup> )	Morandi et al. [13] Steur et al. [12] Weng et al. [10]	18.5 to <25 kg/m <sup>2</sup> (reference: <18.5) 25 to <30 kg/m <sup>2</sup> (reference: <18.5) ≥30 kg/m <sup>2</sup> (reference: <18.5)	1.19 (1.13–1.27) <sup>5</sup> 1.11 (1.08–1.15) <sup>4</sup> unreported 1.09 (0.55–2.15) 1.57 (0.79–3.10) 1.98 (1.00–3.96)
Family	household smoking household members ( <i>n</i> ) parental obesity	Steur et al. [12] Morandi et al. [13] Levine et al. [9]	yes vs. no	unreported 0.73 (0.63–0.84) <sup>5</sup> 0.88 (0.84–0.93) <sup>4</sup> unreported
Birth	birth weight (kg) birth weight >4 kg birth weight <i>z</i> score	Morandi et al. [13] Steur et al. [12] Weng et al. [10] Levine et al. [9] Robson et al. [14] Santorelli et al. [15] Zhang et al. [11]	2.93 to <3.24 kg (reference: <2.93 kg) 3.24 to <3.49 kg (reference: <2.93 kg) 3.49 to <3.81 kg (reference: <2.93 kg) ≥3.81 kg (reference: <2.93 kg)	2.12 $(1.48-3.04)^5$ 1.45 $(1.22-1.73)^4$ unreported 1.08 $(0.87-1.33)$ 1.24 $(1.01-1.51)$ 1.44 $(1.18-1.75)$ 1.63 $(1.33-1.98)$ unreported 4.02 $(2.01-8.03)^1$ 5.47 $(2.47-12.1)^2$ 2.09 $(1.59-2.75)^3$ unreported <sup>6,7</sup>
	ethnicity gestational age <37 weeks time of gestation sex	Levine et al. [9] Santorelli et al. [15] Zhang et al. [11] Robson et al. [14] Steur et al. [12] Weng et al. [10] Zhang et al. [11]	male vs. female female vs. male female vs. male	unreported $0.26 (0.07-0.96)^3$ unreported <sup>7</sup> $1.76 (0.67-4.60)^2$ unreported 1.15 (1.02-1.29) unreported <sup>6,7</sup>

### Table 3 (continued)

Level	Predictors	Study	Notes/comment	OR (95% CI)
Infancy	BMI height <i>z</i> score length <i>z</i> score rapid weight gain weight gain <i>z</i> score	Zhang et al. [11] Zhang et al. [11] Zhang et al. [11] Weng et al. [10] Robson et al. [14] Santorelli et al. [15] Levine et al. [9] Zhang et al. [11]	∆ <i>z</i> score ≥0.67 vs. <0.67	unreported <sup>6, 7</sup> unreported <sup>6</sup> unreported <sup>6, 7</sup> 4.15 (3.64-4.73) $3.15 (1.82-5.46)^1$ $3.85 (2.04-7.28)^2$ $4.45 (3.28-6.04)^3$ unreported unreported <sup>6, 7</sup>
Other	age at introduction of solids breastfeeding hospital delivery	Robson et al. [14] Robson et al. [14] Weng et al. [10] Steur et al. [12]	>6 vs <6 months exclusive vs. not exclusive breastfeeding exclusive vs. not exclusive breastfeeding any breastfeeding vs. no breastfeeding no breastfeeding vs. any breastfeeding hospital vs. home delivery	0.50 (0.18–1.37) <sup>2</sup> 0.47 (0.19–1.15) <sup>1</sup> 0.48 (0.18–1.26) <sup>2</sup> 0.72 (0.27–1.94) <sup>2</sup> 1.25 (1.09–1.42) unreported

BMI, body mass index; OR, odds ratio. <sup>1</sup> Robson et al.'s reduced model. <sup>2</sup> Robson et al.'s full model. <sup>3</sup> Santorelli et al. developed 3 models, i.e., one for use at 6±1.5 months (equation 1), a second for use at 9±1.5 months (equation 2), and the third for use at 12±1.5 months (equation 3). Only equation 1 is reported here, as results for equation 1 and equation 2 were very similar, and equation 1 was considered clinically more useful because of the earlier prediction age. Equation 3 is not reported because a prediction age of approximately 12 months before the outcome was not considered clinically helpful. <sup>4</sup> Morandi et al.'s model with overweight and/or obesity as the outcome. <sup>5</sup> Morandi et al.'s model with obesity as the outcome. <sup>6</sup> Models developed from data before 6 weeks or 8 months of age, using support vector machines (SVM) or naive Bayes. <sup>7</sup> Models developed from data before 8 months of age, using decision tree, association rules, logistic regression, neural network, linear SVM, radial basis function SVM, naive Bayesian, or Bayesian network.

of infancy weight gain could increase a model's discriminative ability. However, this would occur at the cost of delaying the model prediction and consequently any intervention, which might affect potential success.

### Sensitivity, Specificity, and Risk Thresholds

Sensitivity and specificity are key determinants of a model's predictive ability. Sensitivity refers to a model's ability to correctly predict the individuals who either have or will develop the outcome of interest [1]. Specificity refers to a model's ability to correctly rule out the individuals who do not have or will not develop the condition of interest [1]. The ideal model would produce 100% sensitivity and 100% specificity, but this is considered to be unrealistic [48].

The choice of where to set the model's risk threshold (i.e., the level of risk at or above which an individual will be classified as having an outcome) will impact on the sensitivity and specificity levels produced by the model [1]. Some models (e.g., the Framingham risk prediction tool for cardiovascular disease) use thresholds that are

similar guidelines for the prediction of early childhood obesity [16]. Indeed, some researchers have reported their results at a variety of risk thresholds without any discussion as to the most appropriate one to use [16]. In this context, the model reported by Robson et al. [14] illustrates the impact of varying risk thresholds can have on sensitivity and specificity. At the 25th percentile risk threshold, their model produced 95% sensitivity and 35% specificity, while at the 90th percentile the sensitivity was 30% and the specificity 99% [14]. Decision curve analysis, relative utility curves, and net benefits are methods for determining both risk thresholds and the clinical usefulness of prediction models [51-53]. However, to date, none of these methods have been utilized in the development or evaluation of early childhood obesity prediction models.

supported by clinical guidelines [50], but there are no

Importantly, the characteristics of the proposed intervention and the prevalence of obesity in the target population should also influence the choice of risk threshold. A model that gives a high sensitivity but a low specificity will potentially identify most, if not all, infants likely to develop obesity, but it will also mistak-

enly identify lots of infants as being at risk when they are not (i.e., a high false-positive rate). Such a scenario may be considered acceptable for early childhood obesity interventions that encourage healthy lifestyle behaviors that would not be physically harmful to participants, such as breastfeeding, which is widely accepted as beneficial for the health of infants and mothers alike [16, 54]. On the other hand, such models (i.e., with a high sensitivity and a low specificity) would generally be no different from non-targeted community-wide interventions, yet parents may experience avoidable stigmatization if they are unnecessarily invited to participate in an intervention based on the assumption that their infant will become an obese child. When interviewed about the use of interventions resulting from early childhood obesity risk prediction models, parents were receptive to the concept, but also expressed fears of judgement and concerns about feeling upset, ashamed, and guilty [55]. However, a pilot study of lifestyle counselling to prevent early childhood obesity showed that the intervention was generally acceptable [56], suggesting that any anxiety may be a function of the initial prediction rather than the intervention itself.

Conversely, while a model that produces a low sensitivity and a high specificity will be unlikely to misclassify infants as being at risk of obesity, it will likely fail to identify a large number of infants who will eventually become obese children. This would mean that, although fewer families are at risk of unnecessary stigmatization, more infants would potentially go on to experience known physical and psychosocial obesity comorbidities, including psychological distress due to weight-related stigmatization [20–22, 27–32].

The availability of resources for intervention should also influence the choice of risk threshold. If resources are scarce, a higher risk threshold may be preferable, thereby ensuring that those at a greater risk of developing obesity are prioritized. Alternatively, a low-cost and easily resourced intervention may warrant a lower risk threshold [16]. Lastly, the prevalence of obesity in the target population should also be considered when setting the risk threshold. For populations with a high prevalence of obesity, prediction models would be more useful to identify those at the highest level of obesity risk. On the other hand, in populations where the prevalence of obesity is low, prediction models would likely be more useful, aiming to identify infants across a wider range of the obesity risk spectrum.

## **Practical Applications and Implications**

Prediction models are primarily developed to improve healthcare-related decision making and therefore patient health [57]. In the case of early childhood obesity models, their purpose is to predict an infant's likelihood of being obese by a specified future point that is still early in the individual's life so that preventative measures can be taken to maximize long-term health benefits. As prediction models invariably have a less-than-perfect performance (i.e., sensitivity and specificity levels below 100%), Moons et al. [57] suggested that only impact analysis studies can truly determine their true clinical value. Such studies are generally developed using a comparative intervention approach to assess health outcomes obtained by using the prediction model versus not using it (i.e., standard care) [2]. Although all early childhood obesity prediction models display a less-than-perfect performance, as of yet, none have been subjected to an impact analysis study.

Nonetheless, 2 models have been developed into tools for use by clinicians or parents [16]. Firstly, Santorelli et al. [15] developed their model into a smartphone application called "Healthy Infant Weight?". The application allowed parents to obtain their baby's risk of obesity at 2 years by entering their baby's sex, birthweight, and weight change between birth and 6, 9, or 12 months. Adding maternal BMI was optional but, as can be seen in Table 2, this made little difference to the sensitivity or specificity of the model [15]. Unfortunately, this mobile application was withdrawn due to funding issues [Santorelli, pers. commun.] and no research has been published regarding any outcomes achieved through its use [16].

The second tool is the Proactive Assessment of Obesity Risk during Infancy (ProAsk) [58], which was developed using the prediction model derived by Weng et al. [10] and later externally validated by Redsell et al. [47]. It should be noted that the name of the tool is somewhat misleading given that it does not actually predict the risk of obesity in particular, but instead the risk of overweight. It is also unclear what outcome age was used by ProAsk, although the development and validation models used ages 3 and 5 years, respectively [10, 47, 58]. ProAsk was designed to be used on tablets and adopted the following predictors: birth weight and length, infant's current weight, maternal and paternal weight, maternal smoking during pregnancy, and breastfeeding. The tool also incorporated a therapeutic wheel of suggested behavioral changes to reduce the infant's risk [58]. A feasibility study into the use of ProAsk by UK public health nurses with parents of infants aged 3 months produced disappointing

results: the recruitment target was not achieved and attrition rates were high [58]. There were also methodological issues identified, such as public health nurses not fully adhering to the study protocols. On a positive note, 8 out of 12 parents interviewed at follow-up found ProAsk to be engaging. However, on balance, the researchers concluded that it would require significant additional resources for the delivery of ProAsk to be a feasible part of the public health nurses' role [58].

Both of the above mentioned practical applications of early childhood obesity prediction models utilized digital technology. The relentless increase in worldwide smartphone ownership rates [59] makes them attractive tools for delivering public health interventions. A review of 23 studies on mobile phone applications aimed at changing health behaviors found that 19 reported statistically significant improvements in the behavior of interest [60]. Applications that were more effective utilized behavior change theory, were user friendly, had personalized features or feedback, and had involvement of health professionals [60]. These findings were echoed by Litterbach et al. [61], who found that participant engagement with their infant feeding application was increased by tailored content, user friendliness, and credible information sources. Breastfeeding mothers reported more confidence to continue breastfeeding, while formula-feeding mothers reported more confidence to feed in response to infant hunger cues [61]. These findings suggest that there may be potential for mobile phone applications based on early childhood obesity prediction models (such as Healthy Infant Weight? [15]) to be successfully implemented. However, it should also be noted that sole reliance on smartphone applications for early childhood obesity interventions may further alienate populations that are already traditionally difficult to engage. Worldwide, people with lower incomes and less education report less smartphone ownership and Internet access [59].

The development of tools such as ProAsk [58], which was designed to be used by health professionals on handheld devices, may serve to increase engagement with difficult-to-reach populations as they are easily portable. Indeed, despite the overall disappointing results, 33% of the participants recruited by the ProAsk study were from areas of increased social deprivation. In addition, Salvy et al. [62] identified the US home visitation program for atrisk families as an ideal opportunity for interventions to prevent early childhood obesity, as these programs are already engaging with high-risk families in the home environment where the obesity-promoting behaviors are likely to occur. Thus, it may be that future research could

Prediction Models for Early Childhood Obesity

learn from the methodological issues identified in the ProAsk feasibility study [58] and successfully utilize risk prediction models for early childhood obesity prevention in the home setting. However, without any kind of impact analysis study, it is not possible to determine the true clinical value of any early childhood obesity risk prediction model, irrespectively of the use or not of digital technology. This may not be possible until clinically relevant risk thresholds and sensitivity and specificity levels have been agreed upon for early childhood obesity prediction [16].

The rationale for obesity prediction models is to identify young children at risk of obesity for whom targeted interventions can be implemented. In addition, these prediction models could be even more useful if they contained modifiable factors that relate to the preconception and pregnancy phases. This means that early interventions could be put in place to improve the outcome for children born from subsequent pregnancies within a given family. Further, the focus of interventions could also be extended to young women who may become pregnant, to ensure the best possible weight-related outcomes for their offspring. Healthcare professionals communicating the risk of early childhood obesity to families may need specific training regarding the discussion of a potentially distressing topic, and the provision of accurate information about lifestyle changes that can reduce the risk.

### Conclusions

To date, 7 studies have been published reporting early childhood obesity prediction models [9-15]. The AUROC, sensitivity, and specificity produced by the models varied greatly, as did the risk thresholds applied to them. Risk thresholds in particular should be defined after careful weighing of the consequences of false-positive versus false-negative predictions in the context of existing (if any) clinically relevant guidelines [16]. Although there are no such guidelines for obesity prediction, methods to assist with the identification of appropriate risk thresholds do exist. However, these have not been utilized in the development of any of the previously published models for the prediction of early childhood obesity. Impact analysis studies of these models are currently absent from the literature, even though 2 models have been developed into tools to be used by parents and healthcare providers [15, 58]. In this context, digital technology may be a promising avenue for the practical application of obesity prediction models. Considering that many of the variables found to be important in published models are

modifiable, they could be useful tools to inform targeted interventions. Nonetheless, it is essential that clinically relevant risk thresholds be determined for early childhood obesity prediction.

### **Disclosure Statement**

The authors have no financial or nonfinancial conflicts of interests to disclose that may be relevant to this work. The funders had no role in the study design, data collection and analysis, the decision to publish, or the preparation of this paper.

### References

- 1 Steyerberg EW. Clinical prediction models a practical approach to development, validation, and updating. New York: Springer; 2009.
- 2 Moons KG, Altman DG, Reitsma JB, Ioannidis JP, Macaskill P, Steyerberg EW, et al. Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD): explanation and elaboration. Ann Intern Med. 2015 Jan;162(1): W1-73.
- 3 Cook NR. Statistical evaluation of prognostic versus diagnostic models: beyond the ROC curve. Clin Chem. 2008 Jan;54(1):17–23.
- 4 Hendriksen JM, Geersing GJ, Moons KG, de Groot JA. Diagnostic and prognostic prediction models. J Thromb Haemost. 2013 Jun; 11(Suppl 1):129–41.
- 5 Damen JA, Hooft L, Schuit E, Debray TP, Collins GS, Tzoulaki I, et al. Prediction models for cardiovascular disease risk in the general population: systematic review. BMJ. 2016 May;353:i2416.
- 6 Gray EP, Teare MD, Stevens J, Archer R. Risk prediction models for lung cancer: A systematic review. Clin Lung Cancer. 2016 Mar; 17(2):95–106.
- 7 Wilson T, Quan S, Cheema K, Zarnke K, Quinn R, de Koning L, et al. Risk prediction models for acute kidney injury following major noncardiac surgery: systematic review. Nephrol Dial Transplant. 2016 Feb;31(2): 231–40.
- 8 Zarinara A, Zeraati H, Kamali K, Mohammad K, Shahnazari P, Akhondi MM. Models predicting success of infertility treatment: A systematic review. J Reprod Infertil. 2016 Apr-Jun;17(2):68–81.
- 9 Levine RS, Dahly DL, Rudolf MC. Identifying infants at risk of becoming obese: can we and should we? Public Health. 2012 Feb;126(2): 123–8.
- 10 Weng SF, Redsell SA, Nathan D, Swift JA, Yang M, Glazebrook C. Estimating overweight risk in childhood from predictors duringinfancy. Pediatrics. 2013 Aug;132(2):e414– 21.
- 11 Zhang S, Tjortjis C, Zeng X, Qiao H, Buchan I, Keane J. Comparing data mining methods with logistic regression in childhood obesity prediction. Inf Syst Front. 2009;11(4):449–60.
- 12 Steur M, Smit HA, Schipper CM, Scholtens S, Kerkhof M, de Jongste JC, et al. Predicting the risk of newborn children to become over-

weight later in childhood: the PIAMA birth cohort study. Int J Pediatr Obes. 2011 Jun;6(2-2):e170–8.

- 13 Morandi A, Meyre D, Lobbens S, Kleinman K, Kaakinen M, Rifas-Shiman SL, et al. Estimation of newborn risk for child or adolescent obesity: lessons from longitudinal birth cohorts. PLoS One. 2012;7(11):e49919.
- 14 Robson JO, Verstraete SG, Shiboski S, Heyman MB, Wojcicki JM: A risk score for childhood obesity in an urban Latino cohort. J Pediatr 2016;172:29-34.e1.
- 15 Santorelli G, Petherick ES, Wright J, Wilson B, Samiei H, Cameron N, et al. Developing prediction equations and a mobile phone application to identify infants at risk of obesity. PLoS One. 2013 Aug;8(8):e71183.
- 16 Butler EM, Derraik JGB, Taylor RW, Cutfield WS. Childhood obesity: how long should we wait to predict weight? J Pediatr Endocrinol Metab. 2018 Apr;31(5):497–501.
- 17 Abarca-Gómez L, Abdeen ZA, Hamid ZA, Abu-Rmeileh NM, Acosta-Cazares B, Acuin C, et al.; NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in bodymass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128-9 million children, adolescents, and adults. Lancet. 2017 Dec;390(10113):2627– 42.
- 18 UNICEF, World Health Organization, World Bank Group: Joint child malnutrition estimates: levels and trends. Geneva: WHO;2017.
- 19 Shackleton N, Milne BJ, Audas R, Derraik JGB, Zhu T, Taylor RW, et al. Improving rates of overweight, obesity and extreme obesity in New Zealand 4-year-old children in 2010-2016. Pediatr Obes. 2018 Dec;13(12): 766–77.
- 20 Liang Y, Hou D, Zhao X, Wang L, Hu Y, Liu J, et al. Childhood obesity affects adult metabolic syndrome and diabetes. Endocrine. 2015 Sep;50(1):87–92.
- 21 Juonala M, Magnussen CG, Berenson GS, Venn A, Burns TL, Sabin MA, et al. Childhood adiposity, adult adiposity, and cardiovascular risk factors. N Engl J Med. 2011 Nov; 365(20):1876–85.
- 22 Reilly JJ, Kelly J. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. Int J Obes. 2011 Jul;35(7):891–8.

- 23 Pandita A, Sharma D, Pandita D, Pawar S, Tariq M, Kaul A. Childhood obesity: prevention is better than cure. Diabetes Metab Syndr Obes. 2016 Mar;9:83–9.
- 24 Singh AS, Mulder C, Twisk JW, van Mechelen W, Chinapaw MJ. Tracking of childhood overweight into adulthood: a systematic review of the literature. Obes Rev. 2008 Sep; 9(5):474–88.
- 25 Guo SS, Wu W, Chumlea WC, Roche AF. Predicting overweight and obesity in adulthood from body mass index values in childhood and adolescence. Am J Clin Nutr. 2002 Sep; 76(3):653–8.
- 26 Deshmukh-Taskar P, Nicklas TA, Morales M, Yang SJ, Zakeri I, Berenson GS. Tracking of overweight status from childhood to young adulthood: the Bogalusa Heart Study. Eur J Clin Nutr. 2006 Jan;60(1):48–57.
- 27 Gibson LY, Allen KL, Davis E, Blair E, Zubrick SR, Byrne SM. The psychosocial burden of childhood overweight and obesity: evidence for persisting difficulties in boys and girls. Eur J Pediatr. 2017 Jul;176(7):925–33.
- 28 Rankin J, Matthews L, Cobley S, Han A, Sanders R, Wiltshire HD, et al. Psychological consequences of childhood obesity: psychiatric comorbidity and prevention. Adolesc Health Med Ther. 2016 Nov;7:125–46.
- 29 Kumar S, Kelly AS. Review of childhood obesity: from epidemiology, etiology, and comorbidities to clinical assessment and treatment. Mayo Clin Proc. 2017 Feb;92(2):251–65.
- 30 Anderson YC, Wynter LE, Treves KF, Grant CC, Stewart JM, Cave TL, et al. Assessment of health-related quality of life and psychological well-being of children and adolescents with obesity enrolled in a New Zealand communitybased intervention programme: an observationalstudy. BMJ Open. 2017 Aug;7(8):e015776.
- 31 Anderson YC, Wynter LE, Treves KF, Grant CC, Stewart JM, Cave TL, et al. Prevalence of comorbidities in obese New Zealand children and adolescents at enrolment in a community-based obesity programme. J Paediatr Child Health. 2016 Dec;52(12):1099–105.
- 32 Gopinath B, Baur LA, Garnett S, Pfund N, Burlutsky G, Mitchell P. Body mass index and waist circumference are associated with blood pressure in preschool-aged children. Ann Epidemiol. 2011 May;21(5):351–7.
- 33 Proietto J. Why is treating obesity so difficult? Justification for the role of bariatric surgery. Med J Aust. 2011 Aug;195(3):144–6.

- 34 Dombrowski SU, Knittle K, Avenell A, Araújo-Soares V, Sniehotta FF. Long term maintenance of weight loss with non-surgical interventions in obese adults: systematic review and meta-analyses of randomised controlled trials. BMJ. 2014 May;348:g2646.
- 35 Roqué i Figuls M, Martínez García L, Martinez-Zapata MJ, Pacheco R, Mauricio D, Bonfill Cosp X. Interventions for treating overweight or obesity in adults: an overview of systematic reviews. Cochrane Database Syst Rev. 2013;(8):CDC010665.
- 36 Woo Baidal JA, Locks LM, Cheng ER, Blake-Lamb TL, Perkins ME, Taveras EM. Risk factors for childhood obesity in the first 1,000 days: A systematic review. Am J Prev Med. 2016 Jun;50(6):761–79.
- 37 Robinson SM, Crozier SR, Harvey NC, Barton BD, Law CM, Godfrey KM, et al. Modifiable early-life risk factors for childhood adiposity and overweight: an analysis of their combined impact and potential for prevention. Am J Clin Nutr. 2015 Feb;101(2):368–75.
- 38 Weng SF, Redsell SA, Swift JA, Yang M, Glazebrook CP. Systematic review and metaanalyses of risk factors for childhood overweight identifiable during infancy. Arch Dis Child. 2012 Dec;97(12):1019–26.
- 39 Zheng M, Lamb KE, Grimes C, Laws R, Bolton K, Ong KK, et al. Rapid weight gain during infancy and subsequent adiposity: a systematic review and meta-analysis of evidence. Obes Rev. 2018 Mar;19(3):321–32.
- 40 Druet C, Stettler N, Sharp S, Simmons RK, Cooper C, Smith GD, et al. Prediction of childhood obesity by infancy weight gain: an individual-level meta-analysis. Paediatr Perinat Epidemiol. 2012 Jan;26(1):19–26.
- 41 Blake-Lamb TL, Locks LM, Perkins ME, Woo Baidal JA, Cheng ER, Taveras EM. Interventions for childhood obesity in the first 1,000 days a systematic review. Am J Prev Med. 2016 Jun;50(6):780–9.
- 42 Patro-Gołąb B, Zalewski BM, Kołodziej M, Kouwenhoven S, Poston L, Godfrey KM, et al. Nutritional interventions or exposures in infants and children aged up to 3 years and their effects on subsequent risk of overweight, obesity and body fat: a systematic review of systematic reviews. Obes Rev. 2016 Dec;17(12): 1245–57.
- 43 Matvienko-Sikar K, Toomey E, Delaney L, Harrington J, Byrne M, Kearney PM; Choosing Healthy Eating for Infant Health (CHEr-

IsH) study team: effects of healthcare professional delivered early feeding interventions on feeding practices and dietary intake – a systematic review. Appetite. 2018 Apr;123: 56–71.

- 44 Redsell SA, Edmonds B, Swift JA, Siriwardena AN, Weng S, Nathan D, et al. Systematic review of randomised controlled trials of interventions that aim to reduce the risk, either directly or indirectly, of overweight and obesity in infancy and early childhood. Matern Child Nutr. 2016 Jan;12(1):24–38.
- 45 Dugan TM, Mukhopadhyay S, Carroll A, Downs S. Machine learning techniques for prediction of early childhood obesity. Appl Clin Inform. 2015 Aug;6(3):506–20.
- 46 Ivanescu AE, Li P, George B, Brown AW, Keith SW, Raju D, et al. The importance of prediction model validation and assessment in obesity and nutrition research. Int J Obes. 2016 Jun;40(6):887–94.
- 47 Redsell SA, Weng S, Swift JA, Nathan D, Glazebrook C. Validation, optimal threshold determination, and clinical utility of the infant risk of overweight checklist for early prevention of child overweight. Child Obes. 2016 Jun;12(3):202–9.
- 48 Alba AC, Agoritsas T, Walsh M, Hanna S, Iorio A, Devereaux PJ, et al. Discrimination and calibration of clinical prediction models: Users' guides to the medical literature. JAMA. 2017 Oct;318(14):1377–84.
- 49 Hosmer DW, Lemeshow S, Sturdivant RX. Applied logistic regression. 3rd ed. Wiley: Hoboken; 2013.
- 50 Marma AK, Lloyd-Jones DM. Systematic examination of the updated Framingham heart study general cardiovascular risk profile. Circulation. 2009 Aug;120(5):384–90.
- 51 Vickers AJ, Elkin EB. Decision curve analysis: a novel method for evaluating prediction models. Med Decis Making. 2006 Nov-Dec; 26(6):565–74.
- 52 Baker SG, Cook NR, Vickers A, Kramer BS. Using relative utility curves to evaluate risk prediction. J R Stat Soc Ser A Stat Soc. 2009 Oct;172(4):729–48.
- 53 Vickers AJ, Van Calster B, Steyerberg EW. Net benefit approaches to the evaluation of prediction models, molecular markers, and diagnostic tests. BMJ. 2016 Jan;352:i6.
- 54 Victora CG, Bahl R, Barros AJ, França GV, Horton S, Krasevec J, et al.; Lancet Breastfeeding Series Group. Breastfeeding in the 21st

century: epidemiology, mechanisms, and lifelong effect. Lancet. 2016 Jan;387(10017):475–90.

- 55 Bentley F, Swift JA, Cook R, Redsell SA. "I would rather be told than not know" - A qualitative study exploring parental views on identifying the future risk of childhood overweight and obesity during infancy. BMC Public Health. 2017 Aug;17(1):684.
- 56 McKee MD, Maher S, Deen D, Blank AE. Counseling to prevent obesity among preschool children: acceptability of a pilot urban primary care intervention. Ann Fam Med. 2010 May-Jun;8(3):249–55.
- 57 Moons KG, Altman DG, Vergouwe Y, Royston P. Prognosis and prognostic research: application and impact of prognostic models in clinical practice. BMJ. 2009 Jun; 338(2):b606.
- 58 Redsell SA, Rose J, Weng S, Ablewhite J, Swift JA, Siriwardena AN, et al. Digital technology to facilitate Proactive Assessment of Obesity Risk during Infancy (ProAsk): a feasibility study. BMJ Open. 2017 Sep;7(9):e017694.
- 59 Poushter J. Smartphone ownership and internet usage continues to climb in emerging economies. Pew Research Center [Internet]. 2016 Feb. Available from: http://www.pewglobal.org/2016/02/22/smartphone-ownership-and-internet-usage-continues-to-climb-in-emerging-economies/.
- 60 Zhao J, Freeman B, Li M. Can mobile phone apps influence people's health behavior change? An evidence review. J Med Internet Res. 2016 Oct;18(11):e287.
- 61 Litterbach EK, Russell CG, Taki S, Denney-Wilson E, Campbell KJ, Laws RA. Factors influencing engagement and behavioral determinants of infant feeding in an mhealth program: qualitative evaluation of the growing healthy program. JMIR Mhealth Uhealth. 2017 Dec;5(12):e196.
- 62 Salvy SJ, de la Haye K, Galama T, Goran MI. Home visitation programs: an untapped opportunity for the delivery of early childhood obesity prevention. Obes Rev. 2017 Feb;18(2): 149–63.
- 63 Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ. 2000 May;320(7244): 1240–3.
- 64 Cole TJ, Freeman JV, Preece MA. Body mass index reference curves for the UK, 1990. Arch Dis Child. 1995 Jul;73(1):25–9.