Artificial Intelligence In Medicine 104 (2020) 101844

Contents lists available at ScienceDirect

Artificial Intelligence In Medicine

journal homepage: www.elsevier.com/locate/artmed

Computerized decision support and machine learning applications for the prevention and treatment of childhood obesity: A systematic review of the literature

Andreas Triantafyllidis[a,*], Eleftheria Polychronidou[a], Anastasios Alexiadis[a], Cleilton Lima Rocha[b], Douglas Nogueira Oliveira[b], Amanda S. da Silva[b], Ananda Lima Freire[b], Crislanio Macedo[b], Igor Farias Sousa[b], Eriko Werbet[b], Elena Arredondo Lillo[c], Henar González Luengo[c], Macarena Torrego Ellacuría[c], Konstantinos Votis[a], Dimitrios Tzovaras[a]

[a] Information Technologies Institute, Centre for Research and Technology Hellas (CERTH), Thessaloniki, Greece

[b] Instituto Atlântico, Fortaleza, Brazil

[c] Innovation Unit, Hospital Clinico San Carlos, Madrid, Spain

ARTICLE INFO

Keywords:
Childhood obesity
Computerized decision support
Machine learning
Digital health
Review

ABSTRACT

Background: Digital health interventions based on tools for Computerized Decision Support (CDS) and Machine Learning (ML), which take advantage of new information, sensing and communication technologies, can play a key role in childhood obesity prevention and treatment.

Objectives: We present a systematic literature review of CDS and ML applications for the prevention and treatment of childhood obesity. The main characteristics and outcomes of studies using CDS and ML are demonstrated, to advance our understanding towards the development of smart and effective interventions for childhood obesity care.

Methods: A search in the bibliographic databases of PubMed and Scopus was performed to identify childhood obesity studies incorporating either CDS interventions, or advanced data analytics through ML algorithms. Ongoing, case, and qualitative studies, along with those not providing specific quantitative outcomes were excluded. The studies incorporating CDS were synthesized according to the intervention's main technology (e.g., mobile app), design type (e.g., randomized controlled trial), number of enrolled participants, target age of children, participants' follow-up duration, primary outcome (e.g., Body Mass Index (BMI)), and main CDS feature(s) and their outcomes (e.g., alerts for caregivers when BMI is high). The studies incorporating ML were synthesized according to the number of subjects included and their age, the ML algorithm(s) used (e.g., logistic regression), as well as their main outcome (e.g., prediction of obesity).

Results: The literature search identified 8 studies incorporating CDS interventions and 9 studies utilizing ML algorithms, which met our eligibility criteria. All studies reported statistically significant interventional or ML model outcomes (e.g., in terms of accuracy). More than half of the interventional studies (n = 5, 63 %) were designed as randomized controlled trials. Half of the interventional studies (n = 4, 50 %) utilized Electronic Health Records (EHRs) and alerts for BMI as means of CDS. From the 9 studies using ML, the highest percentage targeted at the prognosis of obesity (n = 4, 44 %). In the studies incorporating more than one ML algorithms and reporting accuracy, it was shown that decision trees and artificial neural networks can accurately predict childhood obesity.

Conclusions: This review has found that CDS tools can be useful for the self-management or remote medical management of childhood obesity, whereas ML algorithms such as decision trees and artificial neural networks can be helpful for prediction purposes. Further rigorous studies in the area of CDS and ML for childhood obesity care are needed, considering the low number of studies identified in this review, their methodological limitations, and the scarcity of interventional studies incorporating ML algorithms in CDS tools.

* Corresponding author at: Information Technologies Institute, Centre for Research and Technology Hellas, Thessaloniki, 57001, Greece.
E-mail address: atriand@iti.gr (A. Triantafyllidis).

https://doi.org/10.1016/j.artmed.2020.101844
Received 29 August 2019; Received in revised form 9 March 2020; Accepted 12 March 2020

1. Introduction

Childhood obesity is unarguably a major public health challenge, which is associated with adult obesity and the prevalence of many non-communicable diseases such as diabetes, cardiovascular disease, and cancer [1–3]. In this context, the development of interventions which can effectively diagnose, manage, treat, or prevent childhood obesity is of paramount importance.

New computer-assisted information and communication tools can provide useful means to develop smart digital health interventions to fight childhood obesity [4,5]. Data collected through Internet-linked systems (including web sites), electronic health records capturing clinical or demographic information, sensors (such as wearable trackers monitoring parameters such as activity and heart rate) and mobile devices (such as smartphones or tablet computers tracking user behavior), provide the opportunity to generate useful knowledge in regard to a patient's health, behavior, and progress [6]. In this direction, the knowledge generated through the collection, processing, and evaluation of clinical, sensed, behavioral, or demographic data can be used to support the decisions made by caregivers in terms of management, treatment and follow-up interventions, and coach patients where required, so that these are engaged in the monitoring of their condition [7]. In the context of this review, we refer to such computer-based services for caregiver support in decision-making and patient coaching as "Computerized Decision Support" (CDS) [8,9]. The potential of such CDS systems in improving the efficiency and quality of healthcare delivery systems has been reported [10,11], and as a result, their use in clinical practice for the management of many medical conditions such as cardiovascular disease [12], diabetes [13], and lung diseases [14], has risen [15].

Machine learning (ML) [16,17], has recently been shown to be an emerging underlying technology for many CDS systems targeting e.g., patients with diabetes or sepsis [7,18], with potential to revolutionize healthcare delivery [19]. In particular, ML as an algorithmic framework can provide useful insights into data, facilitate inference, and derive knowledge, and thus it has been widely applied for the purpose of prognosis or diagnosis of a disease [19,20].

Despite the unarguable benefits of CDS and ML adoption found in several healthcare applications, literature reviews in the area of CDS and ML for childhood obesity care have been remarkably limited. Related reviews have merely focused on the broader use and effectiveness of specific means for user interaction such as mobile and wireless devices [21], interactive electronic media [22], or health information technology including telephone support and text messaging [6]. Other review studies have a more narrow focus on prediction of childhood obesity through statistical methods [23,24], rather than the application of ML techniques for childhood obesity care [25].

Considering the potential of CDS and ML in deriving useful knowledge, supporting patients and caregivers on their decisions, and improving the healthcare delivery for medical conditions, we wanted to assess their application for the prevention and treatment of childhood obesity. In this direction, we conducted a systematic literature review demonstrating the main characteristics and outcomes of studies adopting CDS and/or ML, with the aim to advance our understanding towards the development of smart and effective interventions for childhood obesity care.

2. Methodology

We searched the bibliographic databases of PubMed and Scopus to identify recent studies published over a 10-year period (2008–2018), which incorporated CDS within a digital health intervention or used ML, for the purposes of prevention or treatment of childhood obesity. The inclusion criteria for study selection were the following: a) the study should be conducted with children or adolescents till the age of 18 years, either in an interventional research setting or retrospectively, b) CDS features within a computer-assisted technology (such as mobile apps, web sites, or other electronic health tools) or ML algorithms/models used should be described, c) quantitative outcomes of the study should be presented, and d) the paper describing the study, must have been written in English. Ongoing studies, case reports, surveys or reviews, qualitative studies, studies describing protocols, and all studies conducted before 2008 were excluded from the review.

A search within the title, abstract, and keywords of the manuscripts was performed using the following terms: *"decision support" OR "coaching" OR "machine learning" OR "data mining" OR "artificial intelligence" AND "obesity" AND ("child" OR "children" OR "childhood" OR "adolescent" OR "adolescence")*. Besides using the term "machine learning", we used the generic search term "artificial intelligence", which is the broader concept for ML applications, and the term "data mining", which is relevant to ML, since it refers to the pattern extraction from data by combining methods from computational statistics and ML [26]. Three reviewers (AT, CLR, DNO) independently reviewed and selected the papers, to avoid making errors or including biased results in the selection process. The reviewers first screened all the abstracts of the found articles and assessed their eligibility according to the inclusion and exclusion criteria. Moreover, the reviewers selected the final papers for inclusion after reading the full manuscripts of the eligible articles.

We used the Effective Public Health Practice Project (EPHPP) tool to assess the methodological quality of the studies conducted in an interventional research setting, because EPHPP has been found to be reliable [27]. The studies incorporating CDS were synthesized according to the intervention's main technology (e.g., mobile app), design type (e.g., randomized controlled trial), number of enrolled participants, target age of children (including adolescents), participants' follow-up duration, primary outcome (e.g., Body Mass Index (BMI)), and main CDS feature(s) and their outcomes (e.g., notifications for caregivers when BMI is high). The studies using ML were synthesized according to the number of subjects included and their age, the ML algorithm(s) that has been used (e.g., logistic regression), as well as their main outcome (e.g., prediction of obesity). The systematic review was conducted following the PRISMA guidelines [28]. We have included a completed PRISMA checklist as Supplementary Material.

3. Results

3.1. Literature search outcomes

We performed the search in the widely-used electronic databases of PubMed and Scopus in July 2018, with 278 results being returned in total (72 results from PubMed and 206 results from Scopus) (Fig. 1). The retrieved records were imported into the Zotero© bibliography management software [29], and 65 duplicates were removed. The abstracts of the remaining 213 articles were screened according to our inclusion and exclusion criteria, from which we identified 28 eligible articles. The reviewers read the full-text of those 28 manuscripts, and agreed to include 17 eligible manuscripts, from which 8 described the outcome of CDS interventions [30–37], and 9 described outcomes of ML techniques [38–46]. 11 studies were excluded because they did not present any quantitative outcome related either to CDS or ML [47–50], did not focus on CDS, but instead described the generic use of SMS or email [51–53], did not include important details such as the number of participants and the duration of the study [54], and three studies reported additional outcomes of an intervention already included in the review [55–57].

3.2. Quality assessment

The 8 studies reporting CDS interventions were assessed according to the EPHPP criteria for selection bias, design, confounders, blinding, data collection, and drop-outs. The methodological quality was found

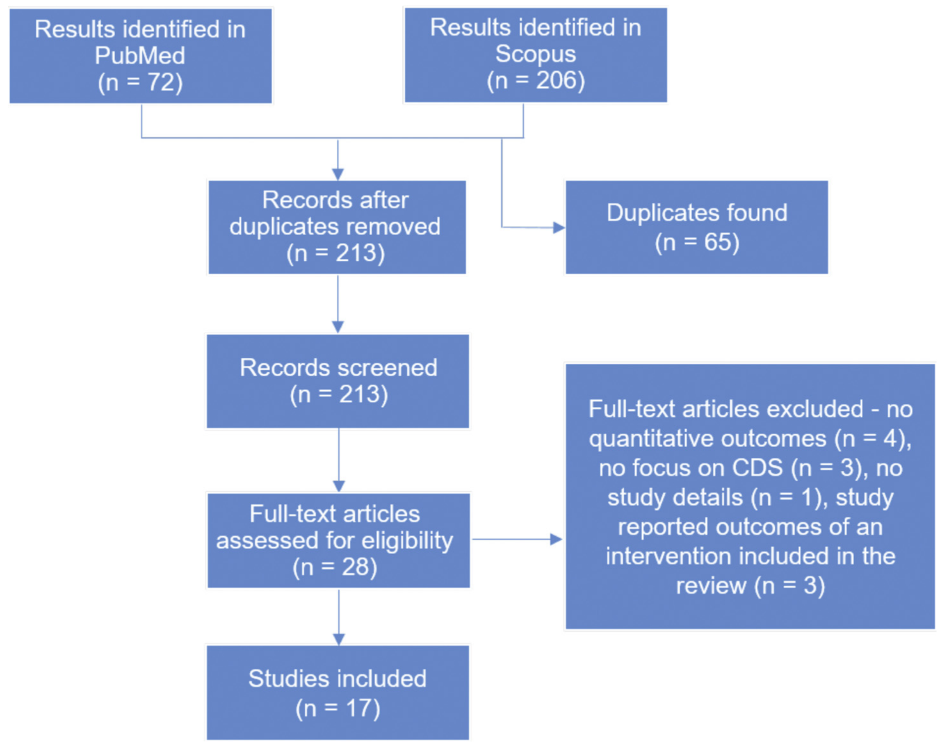

Fig. 1. PRISMA flow diagram for study inclusion.

Table 1
Quality assessment (W: Weak, M: Moderate, S: Strong) of included studies reporting CDS interventions based on the EPHPP criteria (SB: Selection bias, SD: Study design, CF: Confounders, BL: Blinding, DC: Data collection methods, WD: Withdrawals and dropouts).

Study	EPHPP Criteria						Global Rating
	SB	SD	CF	BL	DC	WD	
Gance-Cleveland et al. [30]	M	S	W	M	M	W	W
Shaikh et al. [31]	W	S	S	M	S	W	W
Staiano et al. [32]	M	S	S	S	W	S	M
Taveras et al. [33]	W	S	M	S	S	S	M
Taveras et al. [34]	W	S	S	W	S	S	W
Taveras et al. [35]	M	M	M	W	S	W	W
Tripicchio et al. [36]	W	M	M	W	W	M	W
Yacef et al. [37]	W	M	W	W	W	W	W

to be weak for most studies [30,31,34–37] (n = 6, 75 %), mainly due to participants' selection bias caused because of a low participation rate (therefore the chance of participants being representative of the population is small), lack of blinding caused because of making participants aware of the research question (thereby increasing the chance of reporting bias), and high study drop-out rates (or absence of their reporting) (Table 1). Two studies (25 %) were found to be of moderate quality [32,33]. In total, five studies [30–34] (63 %) were designed as randomized controlled trials. Taveras et al. used a quasi-experimental design [35], Tripicchio et al. utilized a cohort study [36], and Yacef et al. employed a pre-post pilot study [37].

3.3. Type, outcomes, and actors of CDS interventions

The CDS interventions (Table 2) were of different types and as such they were grouped together as follows: a) half of the interventions (n = 4, 50 %) used Electronic Health Records (EHRs) for the clinical management of childhood obesity via alerts based on the Body Mass Index (BMI) [31,33–35], b) a couple of interventions (n = 2, 25 %) used a tablet app for goal-setting and videoconferences held between a trained health coach and the family [36], or educational purposes [37], c) one intervention (n = 1, 13 %) used a web site for family and health providers, in which measurements and lifestyle information could be compared to recommendations based on clinical guidelines [30], and d) one intervention (n = 1, 13 %) used exergames and video-chat in a gaming console to build child's self-efficacy for weight loss and encourage health behavior change [32]. Wearable trackers to monitor physical activity (e.g., steps) were used in only 2 interventions (25 %) [32,37].

The primary outcome for most interventional studies (n = 5, 63 %) was change in BMI [32–36]. Other outcomes included the adherence to clinical guidelines (n = 2, 25 %) [30,31], and physical activity (n = 1, 13 %) [37]. All studies reported significantly positive (statistically significant) interventional outcomes. Most studies (n = 6, 75 %) targeted children up to 13 years old, while a couple of studies (n = 2, 25 %) included children aged from 2 to 18 years.

The primary actors of the interventions also varied; 2 interventions (25 %) targeted specifically the support of health professionals towards their adherence to clinical guidelines (e.g., in obesity diagnosis) [30,31], while 3 interventions (38 %) targeted both clinicians (pediatricians) and families (e.g., to coach and motivate them) [33–35]. In addition, 2 interventions (25 %) involved children, their families and a fitness coach (for health behavior change) [32,36], and 1 intervention (13 %) aimed only at children and their education [37]. The average number of enrolled participants in the studies was 925 (range 33–5493), and the average follow-up duration was 276 days (range 30–730).

3.4. Engagement and satisfaction with CDS interventions

The engagement of the different actors in the CDS interventions varied. In the study by Gance-Cleveland et al. [30], targeting adherence of health professionals with clinical guidelines, it was reported that the 17 training modules for the use of the CDS intervention were completed by only 11 % of the providers participating, and 64 % completed at least 75 % of the modules. Concerning the studies targeting both

Table 2
Characteristics of included studies for CDS interventions (MT: Main technological form, SD: Study design, NP: Number of enrolled participants, TA: Target age, FU: Follow-up duration, PO: Primary outcome, SO: Significantly positive outcome reported, CD: Computerized decision support feature, CO: Computerized decision support outcome).

	MT	SD	NP	TA	FU	PO	SO	CD	CO
Gance-Cleveland et al. [30]	Web site	RCT	33	5-12	180	Adherence to guidelines by health professionals	Yes	Comparison of measurements and patient lifestyle information with clinical guidelines	Growth chart, risk factors, recommendations for care providers
Shaikh et al. [31]	EHR	RCT	432	2-18	270	Adherence to guidelines by health professionals	Yes	Alert BMI ≥ 85th percentile	Diagnosis of overweight/obesity, follow-up visits, counseling
Staiano et al. [32]	Exergames and wearable tracker	RCT	46	10-12	180	BMI	Yes	Encouragement through gameplay and coaching videoconference sessions	Building the child self-efficacy and social support for physical activity
Taveras et al. [33]	EHR	RCT	549	6-12.9	365	BMI and quality of care	Yes	Alert BMI ≥ 95th percentile	Notification for pediatrician with links for education, parent educational materials, documentation, referral (weight-management program), and order placement (laboratory study)
Taveras et al. [34]	EHR	RCT	721	2-12	365	BMI	Yes	Alert BMI ≥ 85th percentile	Clinical decision support tools for pediatric weight management, parent educational materials, a Neighborhood Resource Guide, and monthly text messages
Taveras et al. [35]	EHR	Quasi-experimental study	5493	2-12	730	BMI	Yes (for 1 out of 2 intervention sites)	Alert BMI ≥ 85th percentile	Notification for pediatrician with links for education, documentation, referral (weight-management program), and order placement (laboratory study)
Tripicchio et al. [36]	Tablet app	Cohort study	64	2-18	84	BMI	Yes (for cohort with skype coaching sessions)	Goal-setting, motivational feedback, and coaching video-conference sessions	Health behavior change
Yacef et al. [37]	Tablet app and wearable tracker	Pilot study	59	10-12	30	Physical activity	Yes	User interfaces for education	Rewards and encouragement

clinicians and families, it was reported that 67.8 % of the participating parents completed the required telephone calls, text message/email program with a health coach [33], and 65 % completed their visits [34]. The high-fidelity participants showed the greatest improvements in BMI in those studies. In the study by Staiano et al. [32], adherence to exergaming sessions (completed vs. expected minutes per week) was 94.4 % for children, and reached 92.7 % in video-chats with a fitness coach for children and their families. In the study by Trippichio et al. [36], the intervention group of children and their families which had at least one video-chat with a health coach, used the fitness app for goal-setting, for an average of 38.7 min per week (significantly better than the 20.5 min per week of the group without video-chats), and it was significantly associated with BMI reduction. No outcomes related to the engagement of study participants with the intervention were provided in the studies by Shaikh et al. [31], Taveras et al. [35], and Yacef et al. [37].

In all studies reporting satisfaction with or acceptance of the CDS intervention, this was deemed to be high. More specifically, satisfaction of health professionals with the training on the use of the CDS system was high in the study by Gance-Cleveland et al. [30], with overall satisfaction means ranging from 3.76 to 3.2 in a 4-point Likert scale. In the studies by Taveras et al. [33,34] which employed similar design, parents in the CDS + coaching intervention who were provided with educational material and additional individualized family coaching, showed an increased satisfaction compared to the CDS intervention without individualized family coaching (increase from 46.9 % to 81.3 % in [33] and from 48 % to 63 % in [34]). In the study by Staiano et al. [32], the majority of children found the exergaming acceptable and enjoyable. In the study by Tripicchio et al. [35], parents participating in the intervention group which was provided with both video-chats with a health coach and a fitness app, found the intervention as helpful to reach their own health goals.

3.5. Applications of machine learning: algorithms, features, and outcomes

The highest percentage of the 9 studies using ML algorithms (Table 3) targeted the prediction of obesity (n = 4, 44 %) [38,41,42,46], while a couple of studies targeted the diagnosis (or pre-diagnosis) of obesity itself (n = 2, 22 %) [43,44]. Moreover, the remaining studies explored the classification of physical activity [39], the correlation between proximity to a supermarket and obesity treatment [40], and patterns that describe the increase in BMI [45]. As a matter of fact, all studies reported statistically significant results. The average number of study participants was 49,431 range 16–419299) and the children ages varied (from 1 to 18 years old), with one study targeting specifically pre-school children aged from 1 to 6 years old [43].

Most studies using ML algorithms sought to solve classification problems (n = 7, 78 %) [38,39,41–44,46], while a couple of studies dealt with regression problems (n = 2, 22 %) [40,45]. The most used ML algorithm in those studies was decision trees (C4.5, ID3, and improved decision trees) (n = 4, 44 %) [38,42,44,46], followed by the application of Artificial Neural Networks (ANNs) (n = 3, 33 %) [39,44,46] and logistic regression (n = 3, 33 %) [41,44,46], random forests (n = 2, 22 %) [38,44], and linear regression (n = 2, 22 %) [40,45].

Features (i.e., prognostic factors) for predicting obesity were found to be overweight before the age of two [38], having a TV in the bedroom [41], increased consumption (3–5 times/week) of soft drinks, delicatessen meat, sweets, fried and junk food while not eating enough fish and seafood (less than 2 times/week) [42], and increased consumption (more than 1 time/day) of soft drinks or using computer often (more than 3 h/day) [46]. The ML models in the studies for obesity prediction were mainly based on data acquired through questions such as demographic and clinical history questions [38], screen exposure questions [41], diet questions and sociodemographic data [42], as well as diet and physical activity behavior questions [46].

Table 3
Characteristics of included ML studies (NP: Number of participants, TA: Target age, ML: Machine learning algorithm used along with reported % accuracy, FE: Features used, MO: Machine learning outcome. In column ML, the best performing algorithms where applicable, are found in bold.

	NP	TA	ML (% accuracy or other used performance metric/effect size)	FE	MO
Dugan et al. [38]	7519	2-10	**RandomTree** (84 % **accuracy**), **random forests (86 % accuracy)**, J48 (C4.5) decision tree (79% accuracy), **ID3 decision tree (85 % accuracy)**, Naive Bayes (65% accuracy), and BayesNet (63% accuracy)	Demographic and clinical history questions	Prediction of obesity
Fergus et al. [39]	16	10-11	Multilayer perceptron (Artificial Neural Network - ANN) (96 % accuracy)	Accelerometer data, direct observations, and BMI	Classification of physical activity (drawing, free play, jogging, and walking)
Fiechtner et al. [40]	498	6-12	Linear regression & alert BMI≥95th percentile (BMI z-score decreased by 0.05 units (95 % CI = −0.01, −0.10) for every mile home closer to large supermarket	BMI, distance of home to supermarket, diet, fruit, vegetable intake	Association of proximity to supermarket with the effect of an obesity intervention
Hendrix et al. [41]	11141	2-11	Generalized linear mixed effects regression (P = 0.01 for having TV in the bedroom, P = 0.54 for watching TV/computer for > 2 hours/day)	Screen exposure questions	Prediction of obesity
Lazarou et al. [42]	634	9-13	C4.5 decision tree (risk of obesity of 75 % when children consume frequently fried food, delicatessen meat, sweets and junk food, soft drinks and do not consume enough fish)	Diet questions, sociodemographic data	Prediction (risk) of obesity
Lingren et al. [43]	428	1-6	Support vector machines, Naive Bayes, **patient vectors based on ICD-9 diagnosis codes (rule-based algorithm) (positive predictive value of 0.895 and 0.770 in 2 data-sets)**	Electronic health records (demographic and clinical data, clinical notes)	Detection of severe obesity excluding potential secondary obesity (diagnosis)
Rios-Julian et al. [44]	221	6-13	J48 (C4.5) decision tree (94.57 % accuracy), **logistic model trees (98.19% accuracy)**, **multilayer perceptron (ANN) (98.19 % accuracy)**, random forests (95.48% accuracy), **simple logistic regression (98.19 % accuracy)**	Anthropometric data	Overweight-obesity screening (pre-diagnosis)
YoussefAgha et al. [45]	419299	2-18	Linear regression (mean trends for obesity (R^2 = 0.513) and overweight (R^2 = 0.72) had increasing slopes of 0.189 and 0.227, respectively)	BMI	Patterns based on increased BMI over time
Zheng et al. [46]	5127	14-18	Binary logistic regression (56 % accuracy), Improved Decision Tree (IDT) (80 % accuracy), **weighted k-nearest Neighbor (KNN) (89 % accuracy)**, **ANN (84 % accuracy)**	Diet questions, physical activity questions, sleep duration	Prediction of obesity

In the study by Lingren et al. [43], the focus was to define a high precision phenotype for the diagnosis of childhood obesity. This was made possible through a feature set for machine learning which employed the Unified Medical Language System (UMLS) concept unique identifiers, ICD-9 codes, and RxNorm codes captured in EHRs. In another study aiming at obesity diagnosis by Rios-Julian et al. [44], it was found that a feature set including anthropometric variables other than skinfold thickness, could be utilized to diagnose overweight/obese children in the State of Guerrero, Mexico. The tested models in the above-mentioned studies for obesity diagnosis/pre-diagnosis were based on data acquired through EHRs (e.g., unstructured clinical notes and demographic data) [43], as well as anthropometric data such as skinfold thickness, BMI, and waist circumference [44].

The study by Fergus et al. [39], focused on the classification of physical activity (drawing, free play, jogging, and walking), which was achieved accurately through applying ANNs using the mean hand and mean waist accelerometer count using the validated ActiGraph device [58], along with direct observation values (each child's activity was coded every 10-s by a trained observer).

The study by Fiechtner et al. [40], showed that living closer to a supermarket is associated with improvements in fruit/vegetable intake and weight status. The linear model which was built in this study used data based on the BMI, the distance of home to supermarket, as well as diet, fruit, and vegetable intake captured through a valid food frequency questionnaire [59].

The study by YoussefAgha et al. [45], identified a dominant pattern flaw from overweight to obese for elementary school children in Pennsylvania counties, based on their BMI and its change over time. Both means trend and linear regression slope for children through grade 12, showed that the rate of obesity steeply increased from 2005 to 2009.

In studies comparing two or more ML algorithms, one study for obesity prediction in children up to 10 years of age, showed that the ID3 decision tree algorithm, RandomTree, and random forests had similar performance in terms of accuracy, which had been superior than the performance of J48 (C4.5) decision tree, Naïve Bayes, and BayesNet [38]. Another study for obesity prediction in adolescents found that the weighted k-nearest Neighbor (KNN) and ANNs had better accuracy than binary logistic regression and Improved Decision Tree (IDT) [46]. Finally, in a study for overweight-obesity screening in children up to 13 years of age, it was shown that ANNs, logistic model trees and simple logistic regression had better performance in terms of accuracy than J48 (C4.5) decision tree and random forests [44].

4. Discussion

4.1. Principal findings

This review examined the current state of CDS and ML as applied in recent studies of childhood obesity. The main outcome of the review is that CDS interventions based on technologies such as the EHRs or mobile apps have been found to be useful for the children and their caregivers. In this context, children could be able to enhance their self-efficacy and decrease their weight through personal encouragement for health behavior change, goal-setting and education, whereas health professionals could be empowered to be adherent to clinical guidelines mainly through the reception of computerized alerts for BMI. Furthermore, ML techniques have been proven to derive useful knowledge from large amounts of data containing demographic, clinical, and behavioral information, thereby helping caregivers to predict or diagnose childhood obesity. Our review shows variety in the use of study designs, tools, methods and generation of outcomes for childhood obesity prevention and treatment. However, the methodological limitations of included studies in the area of CDS (as identified through our quality assessment), along with the overall small number of identified studies and small number of study participants in some cases [30,39,44], do not allow to generate any strong evidence on the effectiveness of CDS and ML for childhood obesity care.

Whereas CDS was found to be useful for the self-management [32,36,37] or the remote medical management [30,31,33–35] of childhood obesity mainly through the employment of tools such as mobile apps and EHRs, and CDS features such as motivational feedback and BMI alerts, ML techniques were found to be particularly useful for the prediction of obesity [38,41,42,46]. However, all studies for ML have been retrospective. We found no CDS interventions incorporating ML algorithms in a clinical research setting. This might suggest that there is potential for new and original research in making ML more useful in clinical practice, through CDS tools based on ML algorithms, which can be used by children and their caregivers in their daily routine [60]. The development of such tools and their systematic evaluation in interventional healthcare settings within well-designed longitudinal clinical studies which address issues of bias and drop-outs as identified in this review, would then be an important step towards data-driven clinical decision making, improved self-management, and preventive care.

Considering the outcomes of methodologically sound studies (according to our quality assessment) with CDS interventions [32,33], it appears that exergames could play a key role for the encouragement of children to change their health behaviour (e.g., improve their level of fitness), and fight obesity. This finding is in-line with other reviews [61,62], although there have also been studies which have shown unclear benefits of exergames [63,64]. Therefore, the design of exergames and their integration with CDS features such as video-chat and motivational feedback [32], should be carefully considered, since this could bring added benefits in terms of child engagement and health outcomes. Furthermore, the use of EHRs by clinicians and the reception of computer-based alerts based on the BMI [33] could improve the quality of the delivered care, and contribute to the optimal management of childhood obesity. Information captured in EHRs or other digital health tools could be enriched with objective data (e.g., steps or minutes of moderate-to-vigorous physical activity) provided by wearable trackers, a feature which was missing from most interventions in this review.

Our review also revealed that the engagement of both health professionals [30] and families [33,34] with CDS interventions was not often high. Considering the dose-effect relationship in interventions, strategies to improve engagement of caregivers and therefore decrease the possibility of study drop-outs (a methodological limitation of several studies included in this review) and increase the chance of bringing better health outcomes, can be particularly important. In this direction, the communication of health professionals with families and children, e.g., through coaching sessions in the form of video-chats for personal education and encouragement, has been regarded as extremely helpful [35]. Furthermore, the satisfaction of caregivers when such coaching sessions are present, is deemed to be high [33,34,36].

ML was shown to provide useful data insights for diagnosis of childhood obesity, classification of physical activity for childhood obesity care, obesity treatment based on proximity to supermarkets, increasing BMI patterns, and more dominantly childhood obesity prediction. For example, the features used to predict childhood obesity in the different studies were found to be many (e.g., being overweight before the age of two, drinking a lot of soft drinks daily, etc.), and further research is needed to verify their importance as prognostic factors. Nevertheless, these outcomes show the virtue of ML in preventive care, considering the wide availability of enormous amounts of data in clinical settings [65].

In studies incorporating more than one ML algorithm and reporting accuracy, it was shown that decision trees and random forests based on demographic and clinical history data [38], as well as KNN and ANNs based on questions for diet and physical activity [46], could accurately predict childhood obesity. This suggests that both models which can be interpreted by health professionals, such as decision trees, and models which cannot be easily interpreted, such as ANNs, could be effective.

Furthermore, ANNs were found to be more accurate than logistic regression for prediction of obesity [46]. In studies for other purposes, e.g., for obesity-overweight screening [44], in which however the low number of subjects should be noticed, logistic regression was found to be an effective technique.

4.2. Limitations

We translated the research objective of the review into related generic search terms and did not use keywords related to specific CDS tools or ML algorithms, which nevertheless might have resulted in an inadvertent omission of studies adopting some form of CDS (e.g., EHRs) or ML (e.g., linear regression). Certain studies may have been overlooked due to not meeting our search word criteria or lack of indexing in searched databases, resulting to a limited final sample of included articles (n = 17), and limiting the generalizability of the findings of this review. As with all systematic reviews, and despite following the PRISMA guidelines and incorporating three reviewers for the screening of the literature, the possibility of publication bias (e.g., inevitable omission of unpublished studies with null findings) should also be acknowledged. The search was restricted to only two online databases, i.e., Pubmed and Scopus. However, these databases are two of the most largely-used in the world [66], which index journals and articles from all disciplines related to the review, i.e., medicine, engineering, and computer science. An exploration of the grey-literature was not conducted. A meta-analysis was also not possible due to the fact that the included studies were heterogeneous in terms of design, target population and primary outcomes. To the authors' knowledge there is no available a reliable tool for the quality assessment of studies incorporating ML, and as a result, the quality of the studies that have been found in this area could not be systematically assessed. In this light, the handling of missing values and the use of valid data sources should be noticed. Although most ML studies described handling of missing values, e.g., through removing records based on specified criteria [39,40,42,43,45], a few studies did not provide such a description [38,44]. Furthermore, the validity of the data processed (e.g., through the use of valid questionnaires [40]) in some cases was not clearly reported [44], or could be questionable, as for example in [46], where children were asked for their height and weight to calculate the BMI.

5. Conclusion

Our review showed that the CDS interventions can be useful in self-management of childhood obesity, e.g., through personal encouragement to reduce weight, as well as its remote medical management, e.g., through clinician adherence to medical guidelines. Furthermore, the use of ML techniques in the area of childhood obesity such as decision trees and ANNs, seems to have brought new data insights, especially in terms of prediction of obesity. Considering the small number of identified studies in this review and their methodological limitations, further evidence of the clinical effectiveness of CDS and ML for childhood obesity care is needed. Despite their promise, ML techniques have not been found to be part of CDS tools in this review. In this direction, the integration of ML algorithms into electronic tools such as mobile devices and EHRs, for personal or population-based clinical decision-making, can be explored by researchers towards the development of smart and impactful digital health interventions.

Authors' contributions

Author AT was responsible for the study conduction; Authors AT, CLR, DNO reviewed the literature and assessed the quality of the included studies; AT synthesized the literature according to the described methodology; ALF reviewed the synthesis results; AT wrote a first draft of the manuscript and all other authors contributed to the final version. All authors have read and agreed to the paper being submitted as it is.

What was already known on the topic?

- Digital health interventions based on tools for Computerized Decision Support (CDS) and Machine Learning (ML) have shown potential in improving the efficiency and quality of healthcare delivery systems.

What this study added to our knowledge?

- CDS interventions based on technologies such as the Electronic Health Records (EHRs) or mobile apps have been found to be useful for the children and their caregivers, towards fighting childhood obesity.
- ML techniques have been proven to derive useful knowledge from large amounts of data containing demographic, clinical, and behavioral information, thereby helping caregivers to predict or diagnose childhood obesity.
- The integration of ML algorithms into electronic tools such as EHRs, emerges as the rational next step towards the development of smart and impactful digital health interventions.
- Further rigorous studies are needed to provide evidence of the clinical effectiveness of CDS and ML for childhood obesity care.

Summary points

;1;

Declaration of Competing Interest

The authors of this manuscript declare no conflicts of interest.

Acknowledgements

The study was supported by the European Union's HORIZON 2020 Programme (2014-2020), under ID n° 777082, and from the Brazilian Ministry of Science, Technology and Innovation through Rede Nacional de Ensino e Pesquisa (RNP) under Ocariot.

References

[1] Simmonds M, Burch J, Llewellyn A, Griffiths C, Yang H, Owen C, et al. The use of measures of obesity in childhood for predicting obesity and the development of obesity-related diseases in adulthood: a systematic review and meta-analysis. Health Technol Assess (Rockv) 2015;19:1–336. https://doi.org/10.3310/hta19430.

[2] Shields M, Tremblay MS, Connor Gorber S, Janssen I. Abdominal obesity and cardiovascular disease risk factors within body mass index categories. Health Rep 2012;23:7–15 (Accessed 24 August 2018). http://www.ncbi.nlm.nih.gov/pubmed/22866535.

[3] Vucenik I, Stains JP. Obesity and cancer risk: evidence, mechanisms, and recommendations. Ann N Y Acad Sci 2012;1271:37–43. https://doi.org/10.1111/j.1749-6632.2012.06750.x.

[4] Lau PWC, Lau EY, Wong DP, Ransdell L. A systematic review of information and communication technology-based interventions for promoting physical activity behavior change in children and adolescents. J Med Internet Res 2011;13. https://doi.org/10.2196/jmir.1533.

[5] Tate EB, Spruijt-Metz D, O'Reilly G, Jordan-Marsh M, Gotsis M, Pentz MA, et al. mHealth approaches to child obesity prevention: successes, unique challenges, and next directions. Transl Behav Med 2013;3:406–15. https://doi.org/10.1007/s13142-013-0222-3.

[6] Smith AJ, Skow A, Bodurtha J, Kinra S. Health information technology in screening and treatment of child obesity: a systematic review. Pediatrics 2013;131:e894–902. https://doi.org/10.1542/peds.2012-2011.

[7] Donsa K, Spat S, Beck P, Pieber TR, Holzinger A. Towards personalization of diabetes therapy using computerized decision support and machine learning: some open problems and challenges. Cham: Springer; 2015. p. 237–60. https://doi.org/10.1007/978-3-319-16226-3_10.

[8] Triantafyllidis A, Filos D, Claes J, Buys R, Cornelissen V, Kouidi E, et al. Computerised decision support in physical activity interventions: a systematic literature review. Int J Med Inform 2018;111:7–16. https://doi.org/10.1016/j.ijmedinf.2017.12.012.

[9] Ben-Zvi T. Measuring the perceived effectiveness of decision support systems and their impact on performance. Decis Support Syst 2012;54. https://doi.org/10.1016/j.dss.2012.05.033.

[10] Moja L, Kwag KH, Lytras T, Bertizzolo L, Brandt L, Pecoraro V, et al. Effectiveness of computerized decision support systems linked to electronic health records: a systematic review and meta-analysis. Am J Publ Health 2014;104:e12–22. https://doi.org/10.2105/AJPH.2014.302164.

[11] Roshanov PS, Fernandes N, Wilczynski JM, Hemens BJ, You JJ, Handler SM, et al. Features of effective computerised clinical decision support systems: meta-regression of 162 randomised trials. BMJ 2013;346:f657. https://doi.org/10.1136/BMJ.F657.

[12] Triantafyllidis A, Filos D, Buys R, Claes J, Cornelissen V, Kouidi E, et al. Computerized decision support for beneficial home-based exercise rehabilitation in patients with cardiovascular disease. Comput Methods Programs Biomed 2018;162:1–10. https://doi.org/10.1016/j.cmpb.2018.04.030.
[13] Lim S, Kang SM, Kim KM, Moon JH, Choi SH, Hwang H, et al. Multifactorial intervention in diabetes care using real-time monitoring and tailored feedback in type 2 diabetes. Acta Diabetol 2016;53:189–98. https://doi.org/10.1007/s00592-015-0754-8.
[14] Song B, Becker M, Gietzelt M, Haux R, Kohlmann M, Schulze M, et al. Feasibility study of a sensor-based autonomous load control exercise training system for COPD patients. J Med Syst 2015;39:150. https://doi.org/10.1007/s10916-014-0150-x.
[15] Martínez-Pérez B, de la Torre-Díez I, López-Coronado M, Sainz-de-Abajo B, Robles M, García-Gómez JM. Mobile clinical decision support systems and applications: a literature and commercial review. J Med Syst 2014;38:4. https://doi.org/10.1007/s10916-013-0004-y.
[16] Cruz JA, Wishart DS. Applications of machine learning in cancer prediction and prognosis. Cancer Inform 2006;2. https://doi.org/10.1177/117693510600200030. 117693510600200.
[17] Mirzaei G, Adeli A, Adeli H. Imaging and machine learning techniques for diagnosis of Alzheimer's disease. Rev Neurosci 2016;27:857–70. https://doi.org/10.1515/revneuro-2016-0029.
[18] Gultepe E, Green JP, Nguyen H, Adams J, Albertson T, Tagkopoulos I. From vital signs to clinical outcomes for patients with sepsis: a machine learning basis for a clinical decision support system. J Am Med Inform Assoc 2014;21:315–25. https://doi.org/10.1136/amiajnl-2013-001815.
[19] Obermeyer Z, Emanuel EJ. Predicting the future - big data, machine learning, and clinical medicine. N Engl J Med 2016;375:1216–9. https://doi.org/10.1056/NEJMp1606181.
[20] Salvatore C, Cerasa A, Battista P, Gilardi MC, Quattrone A, Castiglioni I. Magnetic resonance imaging biomarkers for the early diagnosis of Alzheimer's disease: a machine learning approach. Front Neurosci 2015;9:307. https://doi.org/10.3389/fnins.2015.00307.
[21] Turner T, Spruijt-Metz D, Wen CKF, Hingle MD. Prevention and treatment of pediatric obesity using mobile and wireless technologies: a systematic review. Pediatr Obes 2015;10:403–9. https://doi.org/10.1111/ijpo.12002.
[22] Nguyen B, Kornman KP, Baur LA. A review of electronic interventions for prevention and treatment of overweight and obesity in young people. Obes Rev 2011;12:e298–314. https://doi.org/10.1111/j.1467-789X.2010.00830.x.
[23] Butler ÉM, Derraik JGB, Taylor RW, Cutfield WS. Prediction models for early childhood obesity: applicability and existing issues. Horm Res Paediatr 2018;90:358–67. https://doi.org/10.1159/000496563.
[24] Ziauddeen N, Roderick PJ, Macklon NS, Alwan NA. Predicting childhood overweight and obesity using maternal and early life risk factors: a systematic review. Obes Rev 2018;19:302–12. https://doi.org/10.1111/obr.12640.
[25] Witten I, Frank E, Hall M, Pal C. Data mining: practical machine learning tools and techniques. 2016.
[26] Hastie T, Tibshirani R, Friedman J. The elements of statistical learning. New York, New York, NY: Springer; 2009. https://doi.org/10.1007/978-0-387-84858-7.
[27] Armijo-Olivo S, Stiles CR, Hagen NA, Biondo PD, Cummings GG. Assessment of study quality for systematic reviews: a comparison of the cochrane collaboration risk of bias tool and the effective public health practice project quality assessment tool: methodological research. J Eval Clin Pract 2012;18:12–8. https://doi.org/10.1111/j.1365-2753.2010.01516.x.
[28] Moher D, Liberati A, Tetzlaff J, Altman DG, Group TP. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:1–6. https://doi.org/10.1371/journal.pmed.1000097.
[29] Ahmed KKM, Al Dhubaib BE. Zotero: a bibliographic assistant to researcher. J Pharmacol Pharmacother 2011;2:303–5. https://doi.org/10.4103/0976-500X.85940.
[30] Gance-Cleveland B, Aldrich H, Schmiege S, Tyler K. Virtual obesity collaborative with and without decision-support technology. Int J Qual Health Care 2016;28:316–23. https://doi.org/10.1093/intqhc/mzw029.
[31] Shaikh U, Berrong J, Nettiksimmons J, Byrd RS. Impact of electronic health record clinical decision support on the management of pediatric obesity. Am J Med Qual 2015;30:72–80. https://doi.org/10.1177/1062860613517926.
[32] Staiano AE, Beyl RA, Guan W, Hendrick CA, Hsia DS, Newton RLJ. Home-based exergaming among children with overweight and obesity: a randomized clinical trial. Pediatr Obes 2018;13:724–33. https://doi.org/10.1111/ijpo.12438.
[33] Taveras EM, Marshall R, Kleinman KP, Gillman MW, Hacker K, Horan CM, et al. Comparative effectiveness of childhood obesity interventions in pediatric primary care: a cluster-randomized clinical trial. JAMA Pediatr 2015;169:535–42. https://doi.org/10.1001/jamapediatrics.2015.0182.
[34] Taveras EM, Marshall R, Sharifi M, Avalon E, Fiechtner L, Horan C, et al. Comparative effectiveness of clinical-community childhood obesity interventions: a randomized clinical trial. JAMA Pediatr 2017;171:e171325. https://doi.org/10.1001/jamapediatrics.2017.1325.
[35] Taveras EM, Perkins M, Anand S, Woo Baidal JA, Nelson CC, Kamdar N, et al. Clinical effectiveness of the Massachusetts childhood obesity research demonstration initiative among low-income children. Obesity 2017;25:1159–66. https://doi.org/10.1002/oby.21866.
[36] Tripicchio GL, Ammerman AS, Neshteruk C, Faith MS, Dean K, Befort C, et al. Technology components as adjuncts to family-based pediatric obesity treatment in low-income minority youth. Child Obes 2017;13:433–42. https://doi.org/10.1089/chi.2017.0021.
[37] Yacef K, Caillaud C, Galy O. Supporting learning activities with wearable devices to develop life-long skills in a health education app. Lect Notes Comput Sci (Including Subser Lect Notes Artif Intell Lect Notes Bioinform) 2018;10948:394–8. https://doi.org/10.1007/978-3-319-93846-2_74. LNAI.
[38] Dugan TM, Mukhopadhyay S, Carroll A, Downs S. Machine learning techniques for prediction of early childhood obesity. Appl Clin Inform 2015;6:506–20. https://doi.org/10.4338/ACI-2015-03-RA-0036.
[39] Fergus P, Hussain A, Hearty J, Fairclough S, Boddy L, Mackintosh KA, et al. A machine learning approach to measure and monitor physical activity in children to help fight overweight and obesity. Lect Notes Comput Sci (Including Subser Lect Notes Artif Intell Lect Notes Bioinform) 2015;9226:676–88. https://doi.org/10.1007/978-3-319-22186-1_67.
[40] Fiechtner L, Kleinman K, Melly SJ, Sharifi M, Marshall R, Block J, et al. Effects of proximity to supermarkets on a randomized trial studying interventions for obesity. Am J Publ Health 2016;106:557–62. https://doi.org/10.2105/AJPH.2015.302986.
[41] Hendrix KS, Carroll AE, Downs SM. Screen exposure and body mass index status in 2- to 11-year-old children. Clin Pediatr (Phila) 2014;53:593–600. https://doi.org/10.1177/0009922814526973.
[42] Lazarou C, Karaolis M, Matalas A-L, Panagiotakos DB. Dietary patterns analysis using data mining method. An application to data from the CYKIDS study. Comput Methods Programs Biomed 2012;108:706–14. https://doi.org/10.1016/j.cmpb.2011.12.011.
[43] Lingren T, Thaker V, Brady C, Namjou B, Kennebeck S, Bickel J, et al. Developing an algorithm to detect early childhood obesity in two tertiary pediatric medical centers. Appl Clin Inform 2016;7:693–706. https://doi.org/10.4338/ACI-2016-01-RA-0015.
[44] Ríos-Julián N, Alarcón-Paredes A, Alonso GA, Hernández-Rosales D, Guzmán-Guzmán IP. Feasibility of a screening tool for obesity diagnosis in Mexican children from a vulnerable community of Me'Phaa ethnicity in the State of Guerrero, Mexico. Pan Am. Heal. Care Exch. PAHCE. 2017. https://doi.org/10.1109/GMEPE-PAHCE.2017.7972105.
[45] YoussefAgha AH, Lohrmann DK, Jayawardene WP. Use of data mining to reveal body mass index (BMI): patterns among Pennsylvania schoolchildren, pre-k to grade 12. J Sch Health 2013;83:85–92. https://doi.org/10.1111/josh.12002.
[46] Zheng Z, Ruggiero K. Using machine learning to predict obesity in high school students. Proc. - 2017 IEEE Int. Conf. Bioinforma. Biomed. BIBM 2017 2017:2132–8. https://doi.org/10.1109/BIBM.2017.8217988.
[47] Polacsek M, Orr J, O'Brien LM, Rogers VW, Fanburg J, Gortmaker SL. Sustainability of key Maine Youth Overweight Collaborative improvements: a follow-up study. Child Obes 2014;10:326–33. https://doi.org/10.1089/chi.2014.0036.
[48] Yoong SL, Williams CM, Finch M, Wyse R, Jones J, Freund M, et al. Childcare service centers' preferences and intentions to use a web-based program to implement healthy eating and physical activity policies and practices: a cross-sectional study. J Med Internet Res 2015;17. https://doi.org/10.2196/jmir.3639.
[49] Wiechmann P, Lora K, Branscum P, Fu J. Identifying discriminative attributes to gain insights regarding child obesity in hispanic preschoolers using machine learning techniques. 2017 IEEE 29th Int. Conf. Tools with Artif. Intell. 2017. p. 11–5. https://doi.org/10.1109/ICTAI.2017.00014.
[50] Schmiege SJ, Gance-Cleveland B, Gilbert L, Aldrich H, Gilbert KC, Barton A. Identifying patterns of obesity risk behavior to improve pediatric primary care. J Spec Pediatr Nurs 2016;21:18–28. https://doi.org/10.1111/jspn.12131.
[51] Nguyen B, Shrewsbury VA, O'Connor J, Lau C, Steinbeck KS, Hill AJ, et al. A process evaluation of an adolescent weight management intervention: findings and recommendations. Health Promot Int 2015;30:201–12. https://doi.org/10.1093/heapro/dau110.
[52] Nguyen B, Shrewsbury VA, O'Connor J, Steinbeck KS, Hill AJ, Shah S, et al. Two-year outcomes of an adjunctive telephone coaching and electronic contact intervention for adolescent weight-loss maintenance: the Loozit randomized controlled trial. Int J Obes 2013;37:468–72. https://doi.org/10.1038/ijo.2012.74.
[53] Kornman KP, Shrewsbury VA, Chou AC, Nguyen B, Lee A, O'Connor J, et al. Electronic therapeutic contact for adolescent weight management: the Loozit ® study. Telemed e-Health 2010;16:678–85. https://doi.org/10.1089/tmj.2009.0180.
[54] Abdullah FS, Manan NSA, Ahmad A, Wafa SW, Shahril MR, Zulaily N, et al. Data mining techniques for classification of childhood obesity among year 6 school children. Adv Intell Syst Comput AISC 2017;549:465–74. https://doi.org/10.1007/978-3-319-51281-5_47.
[55] Price S, Ferisin S, Sharifi M, Steinberg D, Bennett G, Wolin KY, et al. Development and implementation of an interactive text messaging campaign to support behavior change in a childhood obesity randomized controlled trial. J Health Commun 2015;20:843–50. https://doi.org/10.1080/10810730.2015.1018582.
[56] Gance-Cleveland B, Ford LC, Aldrich H, Oetzel KB, Cook P, Schmiege S, et al. Technology to support motivational interviewing. J Pediatr Nurs 2017;35:120–8. https://doi.org/10.1016/j.pedn.2017.03.014.
[57] Taveras EM, Marshall R, Horan CM, Gillman MW, Hacker K, Kleinman KP, et al. Improving children's obesity-related health care quality: process outcomes of a cluster-randomized controlled trial. Obesity (Silver Spring) 2014;22:27–31. https://doi.org/10.1002/oby.20612.
[58] Dyrstad SM, Hansen BH, Holme IM, Anderssen SA. Comparison of self-reported versus accelerometer-measured physical activity. Med Sci Sports Exerc 2014;46:99–106. https://doi.org/10.1249/MSS.0b013e3182a0595f.
[59] Blum RE, Wei EK, Rockett HR, Langeliers JD, Leppert J, Gardner JD, et al. Validation of a food frequency questionnaire in Native American and Caucasian children 1 to 5 years of age. Matern Child Health J 1999;3:167–72. https://doi.org/10.1023/A:1022350023163.
[60] Triantafyllidis AK, Tsanas A. Applications of machine learning in real-life digital health interventions: review of the literature. J Med Internet Res 2019;21:e12286. https://doi.org/10.2196/12286.
[61] Pakarinen A, Parisod H, Smed J, Salanterä S. Health game interventions to enhance

physical activity self-efficacy of children: a quantitative systematic review. J Adv Nurs 2017;73:794–811. https://doi.org/10.1111/jan.13160.

[62] Lamboglia CMGF, da Silva VTBL, de Vasconcelos Filho JE, Pinheiro MHNP, da S. Munguba MC, Silva Júnior FVI, et al. Exergaming as a strategic tool in the fight against childhood obesity: a systematic review. J Obes 2013;2013:438364. https://doi.org/10.1155/2013/438364.

[63] Peng W, Crouse JC, Lin J-H. Using active video games for physical activity promotion. Health Educ Behav 2013;40:171–92. https://doi.org/10.1177/1090198112444956.

[64] LeBlanc AG, Chaput J-P, McFarlane A, Colley RC, Thivel D, Biddle SJH, et al. Active video games and health indicators in children and youth: a systematic review. PLoS One 2013;8:e65351. https://doi.org/10.1371/journal.pone.0065351.

[65] Murdoch TB, Detsky AS. The inevitable application of big data to health care. JAMA 2013;309:1351. https://doi.org/10.1001/jama.2013.393.

[66] Falagas ME, Pitsouni EI, Malietzis GA, Pappas G. Comparison of PubMed, scopus, web of science, and google scholar: strengths and weaknesses. FASEB J 2008;22:338–42. https://doi.org/10.1096/fj.07-9492lsf.