Meta-Analysis

Chrononutrition and metabolic health in children and adolescents: a systematic review and meta-analysis

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Context: *Obesity has emerged as a global health issue for the pediatric population, increasing the need to investigate physiopathological aspects to prevent the appearance of its cardiometabolic complications. Chrononutrition is a field of research in nutritional sciences that investigates the health impact of 3 different dimensions of feeding behavior: regularity of meals, frequency, and timing of food intake.* ***Objective:*** *We carried out a systematic review and meta-analysis to investigate the association between chrononutrition in children and adolescents and the risk of overweight/obesity or a cluster of metabolic abnormalities related to glucose and lipid metabolism, blood pressure, and cardiovascular disease risk.* ***Data Extraction:*** *A literature search was performed using PubMed, EMBASE, and The Cochrane Library for relevant articles published before August 2022.* ***Data Analysis:*** *A total of 64 articles were included in the narrative synthesis (47 cross-sectional and 17 cohort studies), while 16 studies were included in the meta-analysis. Meta-analysis showed that non–daily breakfast consumers (≤6 d/wk) had a higher risk of overweight/obesity (odds ratio [OR], 1.45; 95% confidence interval [CI], 1.08–1.82] compared with daily breakfast eaters (7 d/wk). Similarly, irregular breakfast consumption (only 0-to-3 times/wk) increased the risk of abdominal obesity (waist-to-height ratio ≥ 0.5) compared with regular consumption (5-to-7 times/wk) (OR, 1.38; 95% CI, 1.26–1.49). There was evidence to suggest that a regular frequency of meal consumption (≥4 times/d) is preventive against overweight/obesity development compared with fewer meals (≤3 times/d) (OR, 0.83; 95% CI, 0.70–0.97). In the narrative synthesis, snacking habits showed controversial results, while food timing was the most understudied dimension.* ***Conclusion:*** Overall, our data

https://doi.org/10.1093/nutrit/nuad122

indicate a potential implication of chrononutrition in affecting pediatric metabolic health; however, the evidence of this association is limited and heterogeneous. Further prospective and intervention studies with a consistent approach to categorize the exposure are needed to elucidate the importance of chrononutrition for pediatric metabolic health.

Key words: *abdominal obesity, breakfast habits, children and adolescents, childhood obesity, chrononutrition, meal frequency.*

INTRODUCTION

Over the past decades, obesity, cardiovascular diseases (CVDs) and other noncommunicable diseases have emerged as a global issue, with a very large impact on the health of both adult and pediatric populations. It is known that modern societies often experience an irregular sleep–awake and fasting–feeding cycles, due to social plans, work, and unhealthy habits. This can result in a disturbance of physiological rhythm, set by the hypothalamus, that regulates lipid and glucose metabolism and blood pressure (BP), and can lead to an increased risk of developing type 2 diabetes and CVD.[1]

Recently, the role of chrononutrition on cardiometabolic health has been investigated. Chrononutrition is an emerging field of research involving 3 dimensions of feeding behavior: regularity of energy intake in meals throughout the day, frequency (numbers of meals per day), and timing of food intake (actual time of meals).[1–3] Some authors have studied whether the timing and regularity of food intake could play a significant role in obesity, diabetes, and CVD.[4,5] Despite previously controversial results,[6–8] a recent systematic review and meta-analysis has elucidated the role of regular breakfast consumption on weight and cardiometabolic risk in an adult population.[9] In line with this, the negative impact of breakfast skipping on adiposity was also shown in children and adolescents.[10] Accordingly, another dimension of feeding behavior—namely, later eating rhythm—is under consideration for its impact on overweight and obesity risk in both adults and children.[11,12] Circadian misalignment resulting from impaired chrononutrition can alter leptin concentrations, together with glucose and insulin levels and mean BP.[13,14] Given the potential cardiometabolic health implications closely related to chrononutrition and the limited evidence from studies in children and adolescents, a comprehensive evaluation is needed to explore this association.

The aim of the present study was to conduct a comprehensive systematic review and meta-analysis on the association between chrononutrition in children and adolescents and overweight/obesity (OW/OB) or a cluster of metabolic abnormalities related to glucose and lipid metabolism, BP, or CVD risk.

METHODS

This review was developed in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement and a PRISMA checklist was followed (see Table S1 in the Supporting Information online).[15]

Data sources and search strategies

The literature search was conducted using 3 databases, including MEDLINE/PubMed, EMBASE, and The Cochrane Library. The review was developed and structured according to the PICOS (Population, Intervention/Exposure, Comparisons, Outcomes, and Study design) methodology to define the research question (Table 1):

Population. Studies involving children and/or adolescents, aged 1 to 18 years old were included. Studies conducted on groups of children with pre-existing pathological conditions (eg, type 1 and type 2 diabetes, obesity, polycystic ovary syndrome, attention-deficit/hyperactivity disorder, eating disorders) were excluded.

Intervention/exposure. As noted in the Introduction, chrononutrition involves 3 aspects of feeding behavior (regularity of meals, frequency of meals per day, and timing of food intake). Therefore, at least 1 wrong dimension of eating behavior was considered as the "exposure": irregularity in meal routine (eg, skipping breakfast or fasting during meals); frequency of eating (eg, low number of meals, $\leq$3 times/d, or snacking frequency); and clock time eating (eg, late night eating or meal timing). Studies on Ramadan were excluded due to the frequent lack of relevant comparison groups. Moreover, the characteristics of Muslim fasting are highly different among populations according to cultural habits and local climatic conditions.

Comparisons. The 3 dimensions of adequate eating behavior were considered as comparisons: regular meal routine (eg, daily breakfast consumption [7 days a week]); appropriate meal frequency (eg, $\geq$4 meals/d); and adequate meal timing (eg, diurnal clock time eating).

Table 1 **PICOS criteria for inclusion of studies**

Parameter	Criterion
Population	Children and/or adolescents (1–18 y)
Intervention/exposure	At least 1 of the 3 wrong dimensions of eating behavior (irregularity in meal routine, eg, skipping breakfast or fasting; frequency of eating, eg, low number of meals $\leq$3 times/d or snacking frequency; clock time eating, eg, late-night eating or meal timing)
Control	Adequate dimensions of eating behavior (regular meal routine, eg, daily breakfast consumption [7 days a week]; appropriate meal frequency, eg, $\geq$4 times/d; adequate meal timing, eg, diurnal clock-time eating)
Outcomes	Four different outcomes: A. Overweight and obesity B. Glucose metabolism C. Lipid markers and CVD risk D. Blood pressure
Study design	Observational studies and randomized controlled trials

Abbreviation: CVD, cardiovascular disease.

Outcomes. To investigate the impact of chrononutrition on pediatric metabolic health, 4 lines of outcomes were identified prior to starting the electronic search. The 4 different outcomes were (A) overweight or obesity, (B) glucose metabolism, (C) lipid markers and CVD risk, and (D) BP. Studies on obesity-related outcomes were included if they reported at least 1 of the following: body mass index (BMI), BMI *z* scores or BMI percentiles, waist circumference (WC), waist-to-height ratio (WHtR), and body fat (%). Studies on glucose metabolism were included if they evaluated blood glucose, insulin levels, or homeostasis model assessment (HOMA) index. Similarly for the lipid markers and CVD risk outcome, studies were included if they collected at least 1 of the following: total cholesterol (TC), high-density-lipoprotein (HDL) cholesterol, low-density-lipoprotein (LDL) cholesterol, triglycerides (TGs), as well as overall metabolic syndrome (MetS) risk. Last, studies on BP outcome were included if they collected systolic BP (SBP), diastolic BP (DBP), and related percentiles.

Study design. Observational studies (cohort studies, cross-sectional studies, and case-control studies) and randomized controlled trials were included in the search strategy. Literature reviews, meta-analyses, case-series, and any other type of publication were excluded.

Search strategy

A systematic search of the studies published between 2007 and August 2022 was conducted using 3 electronic databases: The Cochrane Library, Embase, and Pubmed/MEDLINE. The complete search strategy terms are listed in Table 2. Only studies written in English were included in the review. To be eligible, studies had to be original articles conducted in children and/or adolescents (1–18 years).

Identification of relevant studies

The Rayyan reference management software (Rayyan Systems Inc.) package was used to manage all of the records. After duplicates were removed, title and abstract were initially screened independently by 2 pairs of authors in a double-blinded fashion. The first pair of authors were assigned the study selection for outcomes A and D, while the second pair of authors screened articles for the outcomes B and C. Disagreements on the eligibility of articles were resolved by a third author. The third reviewer decided whether the articles should be kept or excluded. The full-text selection of potentially relevant articles was performed independently by the 2 pairs of authors. In addition, reference lists of the selected studies were searched manually to identify further potentially eligible publications. Moreover, selected articles with more than 1 outcome were included in more than 1 category. Reasons for exclusion were recorded and are listed in Fig. 1—namely, wrong exposure, wrong outcome, wrong publication type, wrong population, foreign language, and insufficient/missing data.

Data extraction

Data extraction was performed in parallel by 2 independent authors in a double-blinded fashion. Selected articles were fully analyzed to extract the following information: authors, publication year, country, study design, sample size, sample age, exposure variable assessed and type of assessment, outcome investigated, and details about the method, confounders, and main results.

Quality assessment

Critical appraisal checklists for cross-sectional and cohort studies proposed by the Joanna Briggs Institute were used to assess the methodological validity of the selected studies.[16,17] The checklist for cross-sectional studies included 8 question items, assessing several

Table 2 **Search strategy terms**

	Terms
Exposure	"Snacks" [MeSH] OR "Circadian rhythm" [MeSH] OR "Feeding behavior" [MeSH] OR "Eating habit" OR "Nocturnal eating" OR "Meal routine" OR "Food intake" OR "Meal timing" OR "Chrononutrition" OR "Chronotype" OR "Chronobiology" OR "Breakfast skipping" OR "Meal skipping" OR "Meal frequency" OR "snacking"
Outcomes	
Group A: overweight and obesity	"obesity" OR "high caloric intake" OR "body composition" OR "body weight" OR "excessive weight gain" OR "BMI" OR "overweight" OR "body fat" OR "excessive fat accumulation" OR "adiposity"
Group B: glucose metabolism	"diabetes" OR "glycemia" OR "postprandial state" OR "insulin" OR "fasting blood glucose" OR "fasting blood glucose level" OR "hemoglobin a1c" OR "glycated hemoglobin" OR "homeostasis model assessment" OR "homa index"
Group C: lipid markers and CVD risk	"high density lipoprotein" OR "high density lipoprotein cholesterol" OR "low density lipoprotein" OR "low density lipoprotein cholesterol" OR "cholesterol blood level" OR "cholesterol" OR "triglycerides blood levels" OR "triacylglycerol" OR "metabolic disorder" OR "metabolic syndrome" OR "cardiovascular disease" OR "cardiovascular risk" OR "cardiovascular risk factor"
Group D: blood pressure	"blood pressure" OR "systolic blood pressure" OR "diastolic blood pressure" OR "hypertension" OR "elevated blood pressure" OR "blood pressure monitoring"

domains: population characteristics, exposure, confounders, outcomes, and statistical analysis. For each item, 4 possible responses are provided: yes, no, unclear, or not applicable. Studies that answered at least 4 out of 8 questions with "yes" answers were considered as having acceptable quality to be included in this systematic review.[18] The checklist for cohort studies included 12 question items, also including follow-up to the already reported domains. At least 6 out of 11 questions answered with "yes" answers were considered as having acceptable quality to be included.[18] The synthesis of the risk-of-bias assessment for each study was conducted by applying the Risk-of-bias VISualization (robvis) tool (see Fig. S1 in the Supporting Information online).[19] The quality assessment of the articles excluded to due quality control is reported in Table S2 (see the Supporting Information online).

Statistical analysis

The association between chrononutrition and OW/OB, glucose profile, lipid metabolism and CVD risk, or BP was discussed through narrative synthesis and, only when applicable, was studied by means of meta-analysis. Given the variety of definitions of chrononutrition, studies included in the current review were divided into 4 categories: breakfast consumption, meal frequency, snack frequency, and meal timing. Studies to be included in the meta-analysis needed to fulfill the following criteria:

1. Present data with sufficient detail for the pooled analysis
2. Have a similar definition of the exposure and measurement of the outcome
3. Include odds ratios (ORs) and confidence intervals (CIs)

Meta-analysis was performed when at least 3 articles were available for each subset and a dichotomization of the exposure variable could be identified. Detailed descriptions of exclusion from analysis are presented in Tables S3–S10 (see the Supporting Information online). As a result, only for outcome A "overweight and obesity" were all criteria met and 3 primary meta-analyses were conducted as follows:

1. Non–daily breakfast consumption ($\leq$6 d/wk) vs daily breakfast consumption (7 d/wk; reference category) and association with OW/OB
2. Regular meal frequency ($\geq$4 times/d) vs low number of meals ($\leq$3 times/d; reference category) and association with OW/OB
3. Irregular breakfast consumption (0-to-3 times/wk) vs regular consumption (5-to-7 times/wk; reference category) and association with an abdominal obesity measure (WHtR)

With regard to the outcome OW/OB, studies were included in the meta-analysis if the BMI categorization was based on any of the following definitions: World Health Organization (WHO) *z* scores, the International Obesity Task Force cutoff points of Cole et al,[20] or the Centers for Disease Control and Prevention (CDC) percentiles. For abdominal obesity measures, a WHtR $\geq$0.5 was considered as the abdominal adiposity marker.[21]

Odds ratios and CIs were extracted from the included studies when available. Adjusted ORs were selected over unadjusted ORs, and in case of multiple models of adjustments, the most-adjusted model was chosen.[22] A reference group was identified for each meta-analysis. To ensure consistency across studies, in case of an opposite reference group, both ORs and CIs were appropriately adjusted to change the direction and align with other studies. Both the reciprocal OR and the new CIs for a reversed OR were calculated.[22,23] Articles that included multiple exposure points opposite to the reference group underwent sub-meta-analyses to obtain an overall value relative to the individual

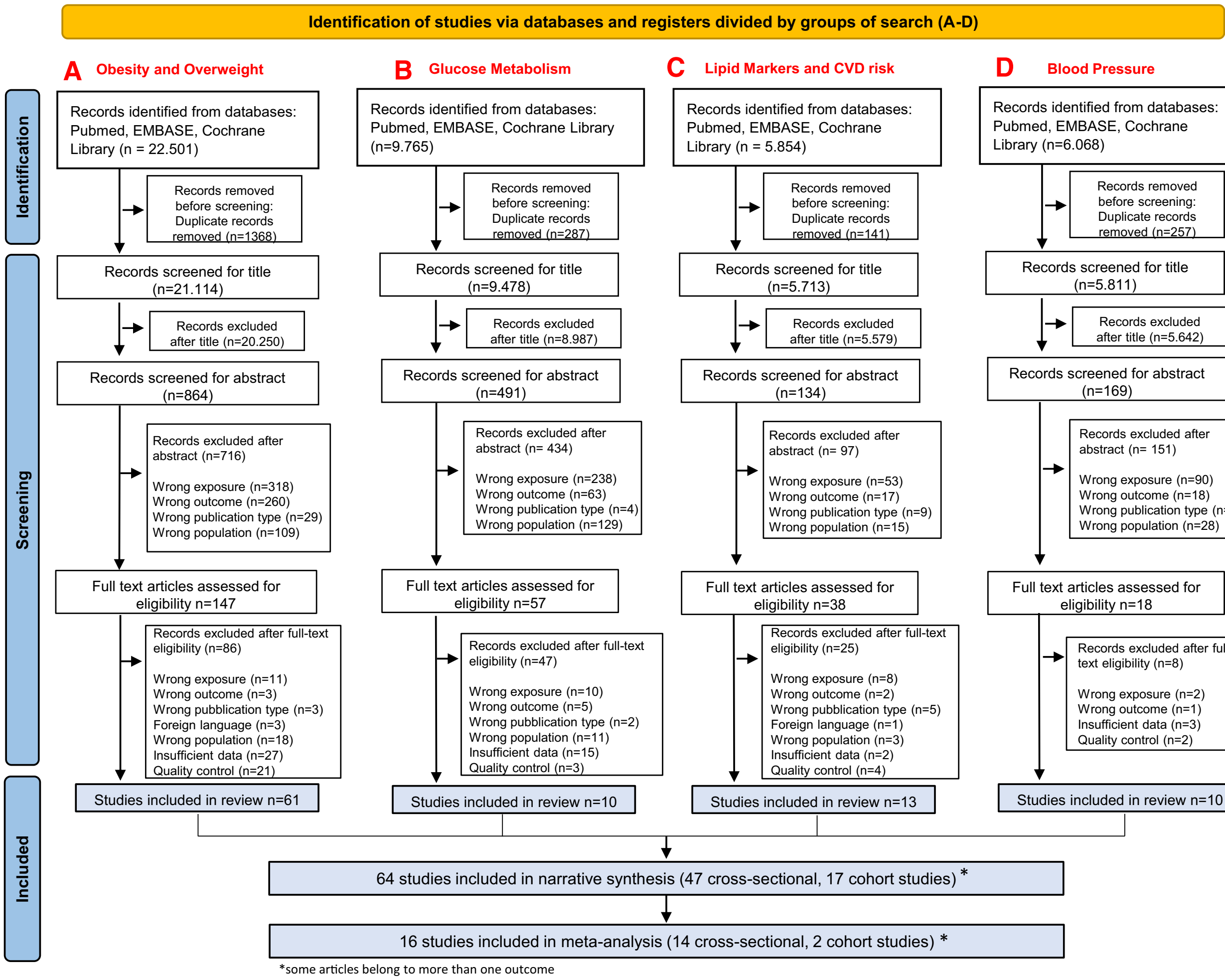

Figure 1 **Flow diagram of the literature search process**. *Abbreviation*: CVD, cardiovascular disease.

study (see Figs. S2 and S3 in the Supporting Information online). The merged OR and CI were then included in the final meta-analysis.

The "Metafor" package from R (R Foundation for Statistical Computing) was used to perform the meta-analyses. After assessing heterogeneity, random-effects models were performed with restricted-maximum-likelihood estimation. Subgroup analysis on sex categories, age group, or different study design were unlikely to be performed due to insufficient data. In case of high heterogeneity, a subanalysis was performed only on European countries to assess the possible bias from other continents.

The strength of the overall body of evidence for each meta-analysis was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology.[24]

Sensitivity analysis

Sensitivity analyses were carried out to assess the robustness of the meta-analysis results. The main analyses using unadjusted or adjusted ORs were repeated excluding low-quality studies.

RESULTS

Initially, a total of 22 501, 9765, 5854, and 6068 articles published between 2007 and August 2022 were retrieved for outcomes A, B, C, and D, respectively (Fig. 1).

The flowchart of the literature search and exclusion process is shown in Fig. 1. After removal of duplicate records, articles were screened for title in each group. Next, irrelevant articles were discarded based on abstract. Among the reasons for abstract removal were as follows: wrong exposure, wrong outcome, wrong publication type, and wrong population. The remaining 147, 57, 37, and 18 articles in groups A, B, C, and D, respectively, were assessed for full-text eligibility. All studies underwent quality assessment, as described above, and those considered as having overall sufficient methodological quality were included in the narrative synthesis (see Fig. S1 in the Supporting Information online). A total of 64 articles out of 86 were included in the narrative synthesis: 47 studies were cross-sectional and 17 studies were cohort studies. No case-control or randomized controlled trials were found. Some articles evaluated multiple outcomes. Thus, the included articles were divided as follows according to the health outcome under investigation: 61 in the "obesity/overweight" group (A), 10 in the "glucose metabolism" group (B), 13 in the "lipid markers and CVD risk" group (C), and 10 in the "blood pressure" group (D). All of the studies fit into 4 exposures developed from the 3 aspects of chrononutrition dimensions. Sixteen studies were included in the meta-analysis examining the relationship between 2 of the exposures and OW/OB outcome (14 cross-sectional and 2 cohort studies). Two of the studies included examined 2 exposures each.[25,26] The numbers of articles included in the narrative synthesis and meta-analysis by exposure are shown in Fig. 2.

Almost all studies included in the narrative synthesis (95.7%) identified confounding factors and strategies to address them, whereas only 4.7% ($n = 3$) were unadjusted. Socioeconomic factors were considered as potential confounding factors in approximately 70% of the articles, while physical activity was considered in approximately 57% of articles (see Table S11 in the Supporting Information online). With regard to dietary assessment methods, food diaries were collected in only 17% of the studies analyzed (16/94), while self-administered questionaries were the most used procedure (37%), followed by 24-hour recall (16%), researcher-administered questionnaire (12%), validated/standardized questionnaires (12%), and food-frequency questionnaires (6%). Results are presented according to different outcomes.

Association between chrononutrition and obesity/overweight

The association between chrononutrition and obesity or overweight was investigated in 82 studies, of which only 61 had sufficient quality to be included in the final review while 21 were eliminated (see Table S2 in the Supporting Information online).[27–47] The association between the 4 exposures and OW/OB was studied according to BMI, anthropometric measure and index (WC, WHtR), or body fat (%).

Overall, 35 studies evaluated obesity outcome by means of BMI assessment alone, of which 24 were cross-sectional studies[25,48–70] and 11 were prospective studies[71–81] (Table 3[25,48–81]), and 26 articles assessed obesity according to anthropometric measurements or body composition, of which 21 were cross-sectional studies[26,82–101] and 5 were prospective studies[102–106] (Table 4[26,82–106]).

In 3 studies BMI was self-reported,[48,54,72] and in 3 studies BMI was not standardized for sex and age.[53,83,102] The remaining studies classified children as overweight and/or obese (OW/OB) referring to CDC, International Obesity Task Force, or WHO, or using percentiles obtained from sex- and age-specific national growth charts. Among studies evaluating anthropometric parameters, obesity risk has been assessed principally by means of BMI in combination with WC and WHtR in 22 studies. In addition, 1 study evaluated body composition by dual-energy X-ray absorptiometry,[106] while 4 studies used bioelectrical impedance.[88,93,98,99] Moreover, 4 studies evaluated skinfold thickness.[82,88,96,103] The majority of studies collected data from large cohorts of both school-age children and adolescents, while evidence on preschool-age children was reported in 15 studies.[50,51,61,62,65,67,74,77–80,89,91,95,103] Only 1 study examined the effects of feeding time in a cohort of singletons aged 12 to 24 months,[78] while a Japanese longitudinal study evaluated the risk of childhood OW/OB in toddlers who skipped their breakfast using a 10.5-year follow-up.[80]

Regularity of meals and overweight/obesity. Irregularity in meals, especially in breakfast consumption, was the dimension of chrononutrition most investigated.[25,26,49,50,55,56,58,60,63–65,69,73,74,80,83,85–88,90,93,96–98,100,104–106] Three studies investigated longitudinally the increased risk of being overweight and obesity (according to BMI) and the regularity in breakfast consumption,[72,74,80] while only 3 prospective studies evaluated this association in combination with WC,[104] WHtR,[105] or body fat.[106] Using a cohort of 43 663 Japanese toddlers followed until 12 years of age, Okada et al[80] showed that children who skipped breakfast had an increased risk of OW/OB than children who do not skip breakfast. The prevalence of OW/OB according to the International Obesity Task Force criteria decreased as the frequency of breakfast consumption increased. In contrast, this association has not been demonstrated longitudinally in younger children followed from 2 to 5 years of age.[74] With regard to other obesity parameters, Wennberg et al[104] showed that poor breakfast habits in adolescence predicted abdominal obesity in adulthood (defined according to WC). Similarly, Traub et al[105] showed that skipping breakfast in school-age children led to increased changes in WHtR. Interestingly, in the study of Cayres et al,[106] non–skipping breakfast adolescents demonstrated an inverse relationship with absolute changes in body fat (dual-energy X-ray absorptiometry assessment) and this relationship was not mediated by physical activity.

Some studies reported differences between sexes. Particularly, Barrett et al,[60] using a subsample of adolescents ($n = 1894$) belonging to the Healthy Lifestyle in Europe by Nutrition in Adolescence (HELENA) study conducted in 10 European cities, observed that male

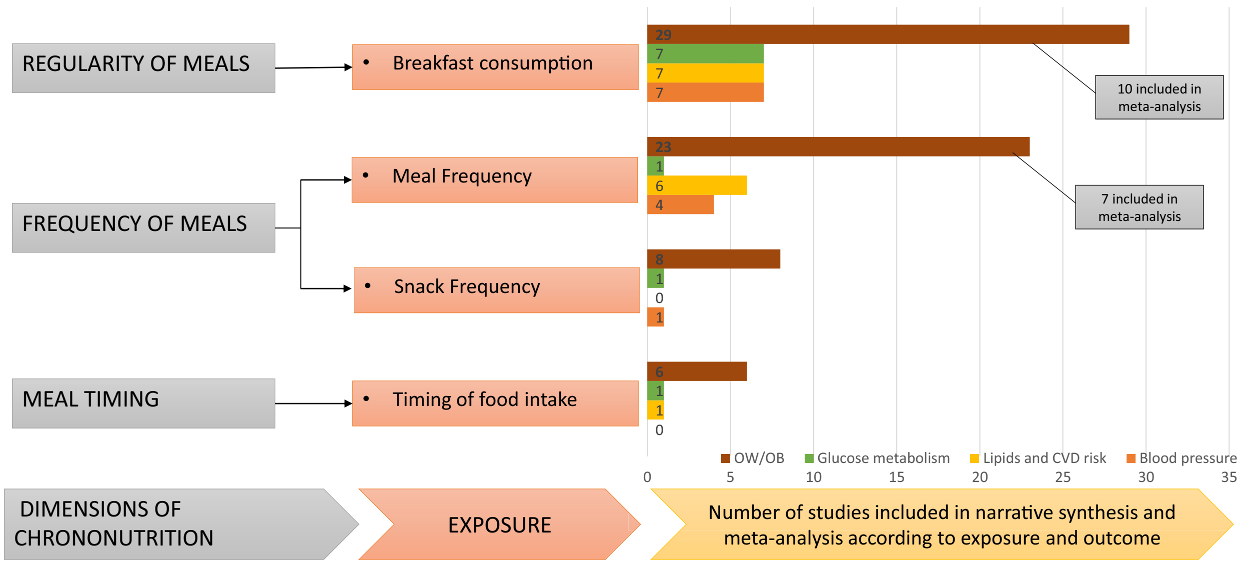

Figure 2 **Studies included in the narrative synthesis and meta-analysis according to exposure and outcome.** *Abbreviations*: CVD, cardiovascular disease; OW/OB, overweight/obesity.

skippers were significantly more likely than non-skippers to have OW/OB (adjusted OR [aOR] = 2.34; 95% CI, 1.40–3.90), but this was not observed among females (aOR = 0.89; 95% CI, 0.59–1.34). Conversely, Aanesen et al[63] showed an association between skipping breakfast and OW/OB only in girls (OR, 1.71; 95% CI, 1.20–2.42) but not in boys, with a slight reduction after adjustments for potential confounders.

The first meta-analysis was based on 8 studies (see Table S3 in the Supporting Information online),[25,26,48,50,55,70,74,100] which compared the odds of OW/OB in non–daily breakfast consumers (≤6 d/wk) vs those who daily consume breakfast (7 d/wk), and yielded a pooled OR of 1.45 (95% CI, 1.08–1.82) (Fig. 3A[25,26,48,50,55,70,74,100]). There was elevated statistical heterogeneity, with an I^2 of 95% ($P < 0.0001$). After exclusion of low-quality studies in sensitivity analysis,[25,74] the pooled OR was 1.39 (95% CI, 1.13–1.65), with an I^2 of 90% ($P < 0.0001$) (Fig. 3B[26,48,50,55,70,100]). Last, a subgroup meta-analysis among European countries was conducted, which yielded nonsignificant results (OR, 1.26; 95% CI, 0.95–1.58) and less heterogeneity (I^2 = 88%; $P < 0.0001$), which, nevertheless, remains high (see Fig. S4 in the Supporting Information online).

A second meta-analysis of 3 studies (see Table S4 in the Supporting information online),[26,87,90] was carried out to assess the odds of abdominal obesity (WHtR ≥ 0.5) for irregular breakfast consumption (defined as 0 to 3 times/wk) compared with regular consumption (defined as 5 to 7 times/wk). The pooled OR of 1.38 (95% CI, 1.26–1.49) demonstrated a significantly higher risk of abdominal adiposity in breakfast skippers compared with regular consumers (Fig. 3C[26,87,90]). Analysis yielded very low heterogeneity (I^2 = 0,04%, P = 0.43).

According to the GRADE system, the certainty of the evidence was very low for both meta-analyses.

Frequency of meals and overweight/obesity. The second dimension that was more investigated was the frequency of meals, classified into 2 different exposures: meal frequency and snack consumption. In total, 23 studies evaluated meal frequency in the narrative synthesis.[25,26,52,54,57,59,66–68,71,75,76,79,82,86,89,91,92,94,95,97,99,102] The majority of cross-sectional studies confirmed a positive relationship existing between lower daily eating frequency and the risk of developing OW/OB, according to BMI. Evidence from longitudinal studies evaluating this exposure was weaker.[71,75,76,79,102] In addition, this association appears to be lacking during the first years of life. In this regard, the prospective study of Taylor et al[79] reported that eating frequency at 2 years was not associated with current or subsequent change in BMI. Similarly, BMI at age 1 year did not predict eating frequency at 2 years of age.[79]

Six studies demonstrated an inverse association between adiposity (evaluated with multiple methods—namely, WC, WHtR, dual-energy X-ray absorptiometry, and skinfold thickness) and eating frequency,[82,84,86,92,102,103] whereas 3 studies did not find any relationship.[91,95,97] In particular, a longitudinal 10-year follow-up cohort study demonstrated greater increases in BMI and WC in females adolescents with lower eating frequency.[102]

Seven studies were included in the third meta-analysis (see Table S5 in the Supporting Information online),[25,52,54,57,67,76,92] which investigated the odds of

Table 3 **Studies included in the qualitative synthesis for outcome A, considering BMI as an overweight/obesity outcome**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
Franko et al, 2008, USA[71]	Longitudinal population-based cohort	At baseline, 1209 Black girls and 1166 White girls (9-10 y)	Meal frequency assessed with 3-d food records (2 weekdays and 1 weekend day) collected annually for visits 1–5 and then again at visits 7, 8, and 10	CDC growth charts: BMI *z* scores	• Participants who ate >3 meals on more days had lower BMI *z* scores (main effect of meal frequency, $P < 0.0001$) • For each additional day of eating 3+ meals (holding constant the other variables in the model), BMI *z* scores were estimated to decrease by 0.05 (95% CI: 0.3–0.6) • The main effect for meal frequency was not significant ($P = 0.20$), but there was a significant race-by-meal frequency interaction ($P = 0.02$). This indicates that, on average, Black girls who ate 3+ meals on more days exhibited a decreased likelihood of overweight; for each additional day consuming 3+ meals, Black girls were 1.23 times (95% CI: 1.05–1.50) less likely to be overweight. • In contrast, there was no effect of meal frequency on overweight for White girls (OR: 1.02; 95% CI: 0.84-1.18)
Timlin et al, 2008, USA[72]	Longitudinal population-based cohort and cross-sectional	2216 middle- and high-school students participating in Project EAT (mean age, 14.9 ± 1.6 y)	Breakfast frequency assessed with a self-reported questionnaire using the question, "During the past week, how many days did you eat breakfast?" Responses included never, 1 to 2 days, 3 to 4 days, 5 to 6 days, and every day	BMI absolute values, based on self-reported weight and height	• Compared with daily breakfast eaters, a higher BMI was observed in those who ate breakfast intermittently or never. Similar associations were observed at time 2. • The inverse associations between breakfast frequency and BMI remained largely independent of all confounding and dietary factors and were similar for boys and girls ($P < 0.10$ for gender × breakfast interaction). • The frequency of eating breakfast was inversely associated with BMI in a dose-response manner ($P < 0.01$).
Croezen et al, 2009, Netherlands[48]	Cross-sectional	Over 35 000 adolescents in grade 2 (13–14 y old) and grade 4 (15–16 y old)	Breakfast skipping assessed with a self-reported questionnaire assessing the frequency of eating breakfast during a week (ranging from 0–7 d/wk)	OW/OB classification: IOTF cutoff criteria for BMI values, from self-reported weight and height	• In grade 2, adjusted ORs for the association with overweight were 2.17 (95% CI: 1.66–2.85) for skipping breakfast. Statistically significant associations with overweight were also found in grade 4.

(continued)

Table 3 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
					• Dose–response relations were found between skipping breakfast and overweight. • Breakfast skipping showed the strongest relation with overweight (OR: 1.68; 95% CI: 1.43–1.97 for grade 2; OR: 1.32; 95% CIL 1.14–1.54 for grade 4) and obesity.
Würbach et al, 2009, Germany[49]	Cross-sectional	2054 schoolchildren and adolescents aged 7-14 y	Validated questionnaire to assess meal patterns during a week: School lunch participation ("daily," "1–4 per week," and "no participation"); breakfast consumption ("2 daily," "1 daily," and "no breakfast"; "2 daily" means early breakfast at home + a late breakfast at school); meal frequencies, ranging from 2 to 5/d	• National growth charts (German): BMI percentiles and *z* scores • OW/OB group classified as >90th percentile	• Greater meal frequency was related to decreasing BMI *z* scores • No significant associations with breakfast consumption
Dubois et al, 2009, Canada[50]	Cross-sectional	1520 preschool children with a mean age of 49 mo and a range from 44 to 56 mo	Breakfast consumption assessed through a standardized eating behavior questionnaire and a 24-h dietary recall. Parents were asked: "Does your child eat breakfast in the morning?" Responses included (1) yes, every morning; (2) regularly, but not every day; (3) only on occasion; and (4) never. Breakfast skippers classified as <7 d/wk.	• CDC growth charts: BMI percentiles • OW/OB classification: IOTF cutoff criteria for BMI values	OR of being overweight at 4 y was double for breakfast skippers compared with those who ate breakfast every day in all models (crude OR: 2.00; 95% CI: 1.20-3.35; aOR: 2.50; 95% CI: 1.45–4.31)
Eng et al, 2009, USA[51]	Cross-sectional	11 072 children and adolescents aged 2-18 y in the National Health and Nutrition Examination Survey (NHANES) 1999–2004	The time and occasion of food consumption through 24-h recalls	CDC growth charts: BMI *z* scores	The proportion of total daily energy consumed in the latter part of the day was associated positively with being classified as overweight in the 6–11-y-old group, but negatively in the overweight 12–18-y-old group.
Toschke et al, 2009, Germany[52]	Cross-sectional	4642 children aged 5-6 y	Meal frequency and breakfast consumption assessed by self-administered parental questionnaire. How many meals per day (breakfast, lunch, tea, dinner, other snacks containing fruit or sandwiches/packed lunch, but	OW/OB classification: IOTF cutoff criteria for BMI values	• Children who regularly consume 4 meals or >5 meals daily have a lower risk of obesity than a reference group (<3 meals/d; aOR: 0.71 [95%CI: 0.50–1.01] and 0.57 [95% CI: 0.37–0.88], respectively)

(continued)

Table 3 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
			not sweets, crisps, or related products) does your child consume? Possible answers: 1/2/3/4/5/>5 and "do not know."		• Any additional meal decreases the OR for obesity to 0.72 (95% CI: 0.58–0.90), which remained significant also after adjustments
Lehto et al, 2010, Finland[53]	Cross-sectional	656 schoolchildren and adolescents, aged 9-11 y	Meals regularity assessed with a WHO Health Behavior of School-aged Children (HBSC) study questionnaire asking breakfast/school lunch/dinner consumption in 5 school days (regular meal patterns comprises usual consumption of breakfast, school lunch, and/or dinner during all 5 d)	BMI absolute value	• Irregular consumption of breakfast was associated with a higher BMI in all the statistical models. • The regularity of school lunch, dinner or family dinner was not associated with the children's BMI. • Irregular meal patterns were associated with a higher BMI in all statistical models.
Vik et al, 2010, Norway[54]	Cross-sectional	2870 students (mean age 15.5 y)	Number of meals eaten the day before assessed with a self-reported questionnaire (yes and no responses, giving a scale ranging from zero to 4 meals/d)	OW/OB classification: IOTF cutoff criteria for BMI values from self-reported weight and height	• The proportion being overweight related to number of meals eaten were: 10% (0–1 meals), 18% (2 meals), 14% (3 meals), and 10% (4 meals), $P < 0.001$. • ORs for being overweight were 0.8 (95% CI: 0.3–1.9), 1.8 (95% CI: 1.2–2.7), and 1.6 (95% CI: 1.2–2.3), respectively, for eating 0–1, 2, and 3 meals vs 4 meals. • Eating 4 meals/d was significantly negatively related to being overweight
Veltsista et al, 2010, Finland and Greece[55]	Cross-sectional	6468 16-y-old Finnish adolescents and 2842 17- and 18-y-old Greek adolescents	Breakfast consumption assessed with a self-reported questionnaire assessing the frequency of eating breakfast during the previous year (daily, 1–3 times/wk, 1–3 times/mo, and never/rarely)	OW/OB classification: IOTF cutoff criteria for BMI values	• Among boys, daily breakfast consumption was inversely associated with weight status in both cohorts ($P < 0.001$ for Greeks and Finns), but no association was found among girls. • The odds of overweight/obesity were 40% lower in Finnish and 30% lower in Greek boys who had a daily breakfast compared with those who did not. Among girls, no significant associations were found.
Sandercock et al, 2010, United Kingdom[56]	Cross-sectional	4326 adolescents aged 10–16 y	School-day breakfast habits assessed by a single question: "On how many school days per week do you normally eat breakfast at home," with numerical responses	• National growth charts (UK): BMI *z* scores • OW/OB classification: IOTF cutoff criteria for BMI values	• Participants who sometimes ate breakfast were more likely to be obese than those who always did ($P < 0.05$). • Compared with boys who always ate breakfast, boys who sometimes ate breakfast were more likely to be obese ($P = 0.002$). There was a trend towards

(continued)

Table 3 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
					an increased likelihood of obesity in boys who never did so ($P = 0.18$). • Girls who never ate breakfast were nearly twice as likely to be obese compared with those who always did.
Tin et al, 2011, China[73]	Longitudinal population-based cohort and cross-sectional	68 606 primary-school children (mean age = 9.85 y)	Breakfast consumption assessed using a questionnaire ("I usually have breakfast at. . ."). Children who chose "home," "fast food stall/cafeteria/restaurant," or "some other places" in response were classified as "breakfast eaters" and those who chose "no breakfast at all" as "breakfast skippers."	OW/OB classification: IOTF cutoff criteria for BMI values	• Breakfast skippers had a higher mean BMI than did eaters both at baseline and at follow-up ($P < 0.001$). • Compared with breakfast eaters, breakfast skippers experienced a larger mean BMI increase over 2 y ($P < 0.001$) and this association was stronger among lunch skippers than eaters (P for interaction = 0.04).
Antonogeorgos et al, 2012, Greece[57]	Cross-sectional	700 adolescents aged 10-12 y	Meal frequency and breakfast consumption assessed with a semi-quantitative FFQ included in the PANACEA survey	OW/OB classification: IOTF cutoff criteria for BMI values	Children who consumed >3 meals per day and also consumed breakfast daily, were 2 times less likely to be overweight or obese.
Coppinger et al, 2012, United Kingdom[66]	Cross-sectional	264 adolescents aged 10–13 y	Self-report measures of dietary intake via 3-d food/drink diaries (Friday to Sunday). An eating frequency chart was created for each participant.	National growth charts (UK): BMI *z* scores	• Breakfast consumers had significantly lower BMI *z* scores compare with irregular breakfast consumers (0.18 vs 0.57; $P = 0.036$) • In multiple linear regression, there was no association between BMI *z* score, eating frequency, and breakfast consumption
Küpers et al, 2014, Netherlands[74]	Longitudinal population-based cohort	1488 children examined at age 2 y and 13 666 children at 5 y	Breakfast frequency assessed with a questionnaire answered by parents about breakfast consumption classified as "eating breakfast daily" (7 times/wk) or "not eating breakfast daily" (<7 times/wk)	• National growth charts (Dutch): BMI *z* scores • OW/OB classification: IOTF cutoff criteria for BMI values	• At 2 y, 8.3% of children were overweight and 3.0% did not eat breakfast daily. At 5 y, 13.2% children were overweight and 5.3% did not eat breakfast daily. • No association between skipping breakfast and overweight, either at age 2 (OR: 1.85; 95% CI: 0.61–5.64) or at age 5 (OR: 0.46; 95% CI: 0.19–1.11).
Evans et al, 2014, USA[75]	Longitudinal population-based cohort	155 schoolchildren and adolescents aged 9–15 y in the Daily D Study	Eating frequency assessed using 2 nonconsecutive weekday 24-h dietary recalls during the 3-mo study period. First collected in-person, the second by phone 3–21 d after the first recall.	CDC growth charts: BMI *z* scores (changes baseline vs 6 mo vs 1 y)	• Cross-sectional analysis at baseline suggests that BMI *z* score was 0.23 units lower for each additional reported eating occasion (regression coefficient = −0.23; 95% CI: −0.44, −0.07). • From baseline to 6 mo, BMI *z* score increased by 0.03 units for each

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Table 3 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
					additional reported eating occasion (regression coefficient = 0.03; 95% CI: 0.01, 0.05). • This relationship was no longer statistically significant at 1 y (regression coefficient = 0.01; 95% CI: −0.01, 0.03).
Stea et al, 2015, Norway[76]	Longitudinal population-based cohort	428 children and adolescents examined at age 9–10 y and 12–13 y	Meal frequency and regularity during the last 6 mo assessed with a retrospective modified validated FFQ. Parents reported habitual consumption of main meals (breakfast, lunch, dinner and evening meal); meal frequencies registered with 8 response alternatives ranging from "never/rarely" to "daily"	OW/OB classification: IOTF cutoff criteria for BMI values	• The number of children eating 4 main meals per day (regular meal frequency) decreased from the fourth grade (47%) to the seventh grade (38%). • Those who ate regular meals in the fourth grade but not in the seventh grade had higher odds of being overweight in the seventh grade after adjusting for gender, maternal education, and physical activity.
Wünstel et al, 2015, Poland[70]	Cross-sectional	1700 adolescents aged 13-18.9 y, with analysis carried out in 3 age groups: 13-14.9, 15-16.9, and 17-18.9 y	Breakfast consumption assessed with a validated Block questionnaire. The categories of consumption were expressed as regular consumption (every day), irregular consumption (1–6 times/wk) and hardly ever (<1 time/wk)	OW/OB classification: IOTF cutoff criteria for BMI values	In the youngest group (13–14.9 y), there is a higher chance of being overweight among adolescents less frequently eating breakfast than among adolescents regularly consuming breakfast
Saikia et al, 2016, India[25]	Cross-sectional	752 adolescents aged 10–14 y	Dietary habits assessed with a self-administered questionnaire on food frequency (breakfast eating frequency, meal frequency, number of extra snacks, excluding morning tea and evening snacks), per week	WHO growth reference data: BMI *z* scores; OW/OB group classified as ≥ +2 *z* scores	• 18.2% overweight/obese adolescents had less than 3 meals/. • Normal-weight adolescents (57.6%) were found to have their meals more regularly than overweight and obese adolescents (44.6%). • 14.9% of OW/OB adolescents skipped breakfast for >3 d/wk in comparison to 4% of normal-weight adolescents. • In OW/OB adolescents, 17.4% were having ≥3 snacks/d as compared to 7.1% of normal-weight adolescents. • 62.0% of normal-weight adolescents did not have any extra snacks.
Taillie et al, 2016, China[77]	Longitudinal population-based cohort	964 children and adolescents whose age was 2–13 y in 2006 (2–6 compared with 7–13 y of age)	Snacking frequency assessed with 3 consecutive 24-h dietary recalls	• WHO growth reference data: BMI *z* scores • OW/OB classification: IOTF cutoff criteria for BMI values	• In children who were underweight at baseline, snacking in the top tertiles was associated with increases in BMI *z* scores from 2006 to 2011 (+1.2 and +1.1 BMI *z*-score units for ages 2–6 and 7–13 y, respectively; $P < 0.05$).

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Table 3 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
					• In overweight/obese 2- to 6-y-old children at baseline, being in the lowest snacking tertile was associated with declines in BMI *z* score (23.3), whereas in overweight 7- to 13-y-old children, being in the top tertile of snacking was associated with the greatest decline in BMI *z* score (22.1) ($P < 0.05$).
Cheng et al, 2016, Japan[78]	Longitudinal population-based cohort	349 singletons examined from 12 to 24 mo of age	Feeding time assessed with a validated multi-pass 24-h recall (5 steps) to record food intakes and feeding times on the previous day	WHO growth reference data: BMI *z* scores	Compared with predominantly day-time feeding, predominantly night-time feeding was associated with a higher BMI *z*-score gain from 12 to 24 mo of age (adjusted $\beta = 0.38$; 95% CI: 0.11, 0.65; $P = 0.006$) and increased risk of becoming overweight at 24 mo of age (adjusted OR: 2.78; 95% CI: 1.11, 6.97; $P = 0.029$)
Coulthard and Pot, 2016, United Kingdom[58]	Cross-sectional	768 children aged 4–10 y and 852 adolescents aged 11–18 y belonging to the UK's National Diet and Nutrition Survey Rolling Programme (2008–2012)	Dietary assessment (the timing of the evening meal) through a 4-d estimated (unweighed) food diary. The food diary included time period in which the food was eaten (the diary was pre-structured into 7 different time periods).	• National growth charts (UK): BMI percentiles • OW/OB classification: OW >85th and OB >95th percentile	There was no association between evening meal timing and risk of obesity or risk of overweight and obesity combined in either the 4–10-y age group (obesity: OR, 1.43; 95% CI, 0.49–4.13; OW/OB combined: OR, 1.33; 95% CI: 0.53–3.33) or the 11–18-y age group (obesity: OR, 0.50; 95% CI, 0.24–1.02; OW/OB combined: OR, 0.83; 95% CI, 0.50–1.38), split by sex or as combined.
Silva et al, 2017, Brazil[59]	Cross-sectional	708 children and adolescents aged 7-14 y	Meal frequency assessed with a structured questionnaire reporting usual frequency of meals (breakfast, morning snack, lunch, afternoon snack, dinner, and evening snack) categorized according to the mean value as risk (<4 meals) and no risk (≥4 meals)	WHO growth reference data: BMI *z* scores	In the age range of 10–14 y, individuals with fewer meals showed a higher chance of having elevated BMI (PR = 1.33; 95% CI: 1.02–1.74; $P = 0.032$).
Taylor et al, 2017, New Zealand[79]	Longitudinal population-based cohort and cross-sectional	371 children aged 1–3.5 y in the Prevention of Overweight in Infancy (POI) Study	Eating frequency at 2 y of age calculated from a feeding diary completed over the course of 2 full days. The mean total number of eating occasions per day was calculated as the average	WHO growth standards: BMI *z* scores	• Eating frequency at 2 y was not associated with current (difference in BMI *z* score per additional eating occasion: −0.02 [95% CI: −0.10, 0.05]) or subsequent change (0.02 [−0.03, 0.06]) in BMI.

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Table 3 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
			from meals and snacks combined across the 2 days.		• Similarly, BMI at age 1 y did not predict eating frequency at 2 y of age (difference in eating frequency per additional BMI *z*-score unit: −0.03; 95% CI: −0.19, 0.13).
Liu et al, 2017, China[67]	Longitudinal population-based cohort and cross-sectional	42 531 children aged 4-5 y old participating in Jiaxing Birth Cohort (JBC) study	Eating frequency collected through a questionnaire at in-person interviews by trained nurses/doctors during the clinic visit	WHO growth standards: BMI *z* scores	Children with meal/snack frequency ≥6 times/d (compared with 3 times/d) were associated with 0.12 (95% CI: 0.03, 0.2) higher BMI *z* score, and this association was significant only in boys, not girls.
Okada et al, 2018, Japan[80]	Longitudinal population-based cohort	42 663 children aged 1.5 y in the "Longitudinal Survey of Newborns in the 21st Century–Japan" followed until 12 y of age	Breakfast skipping evaluated through 12 surveys (corresponding to the children's age from 2.5 to 12 y), whereas breakfast skipping is classified as a binary variable (yes or no)	OW/OB classification: IOTF cutoff criteria for BMI values	Compared with children who did not skip breakfast, children who skipped breakfast had 18–116% increased risk of OW/OB; the multivariable ORs were 1.18 (95% CI: 1.05–1.32) and 2.16 (95% CI: 1.55–2.99), respectively.
Tee Siong et al, 2018, Malaysia[69]	Cross-sectional	5332 children and adolescents aged 6-12 y and 3000 adolescents aged 13-17 y	Breakfast consumption assessed with a self-reported questionnaire. For children aged 6 to 9 y, the questionnaires were answered by their parents. Breakfast frequency was categorized into 3 groups—namely, breakfast skippers (0–2 d/wk), irregular breakfast eaters (3–4 d/wk), and regular breakfast eaters (5–7 d/wk).	WHO growth reference data: BMI *z* scores	Compared with regular breakfast eaters, primary school boys who skipped breakfast were 1.71 times (95% CI = 1.26–2.32, $P = 0.001$) more likely to be overweight/obese, while the risk was lower in primary school girls (OR = 1.36, 95% CI = 1.02–1.81; $P = 0.039$) and secondary school girls (OR = 1.38, 95% CI = 1.01–1.90; $P = 0.044$).
Barrett et al, 2018, Europe[60]	Cross-sectional	1894 adolescents aged 12-17 y in the Healthy Lifestyle in Europe by Nutrition in Adolescence (HELENA) study population	Breakfast consumption assessed with two 24-h dietary recalls and "Food Choices and Preferences Questionnaire" (question: "I often skip breakfast"). Scoring system went from 1 "strongly disagree" to 7 "strongly agree". Classification was 5–7 scores "skippers," 1–3 scores "non-breakfast skippers," and 4 score excluded.	OW/OB classification: IOTF cutoff criteria for BMI values	Male skippers were significantly more likely than non-skippers to be overweight/obese (aOR = 2.34; 95% CI, 1.40–3.90), but this was not observed among females (aOR = 0.89; 95% CI, 0.59–1.34].
Kachurak et al, 2018, USA[61]	Cross-sectional	54 669 children aged 1 to 5 y in the 2005 to 2014 National Health and Nutrition Examination Survey (NHANES)	Snacking assessed by two 24-h dietary recalls. Two main occasion-based definitions of snacking were used: (1) only those occasions identified by the	• <2 y, WHO growth standards: weight-for-length percentiles; OW classified as ≥97.7th percentile	• Among children <2 y of age, snacking more frequently than recommended by AAP was significantly associated with increased odds of OW/OB

(continued)

Table 3 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
			caregiver as a snack and (2) snack occasions plus all other foods/beverages consumed between meals as given by "beverage" and "extended consumption" occasion labels. Each of these definitions (snacks, beverages, and extended consumption) were evaluated with and without occasion of trivial energy consumption (<5 kcal). The AAP recommendations were considered as the reference group (2–3 small snacks daily for toddlers and 2 snacks daily for preschool-aged children).	• >2 y, CDC growth charts: BMI *z* scores. OW classified as ≥85th percentile	($P < 0.01$), particularly when excluding <5-kcal occasions. • Among children 2 to 5 y old, odds of OW/OB did not differ between children who snacked within recommendations versus more frequently than recommended, regardless of the snacking definition used. • When taking into account all EOs between meals (including <5-kcal occasions), children 2 to 5 y old who snacked infrequently (0-1 times daily) were less likely to have OW/OB compared with children who snacked within recommendations ($P < 0.05$).
Charvet, 2018, USA[62]	Cross-sectional	197 children aged 3-4.9 y participating in the Broward County Special Supplementation Nutrition Program for Women, Infants, and Children (WIC)	Frequency of snacks and meals assessed with a previously validated researcher-administered questionnaire	• CDC growth charts: BMI percentiles • OW/OB classification: OW ≥85th and OB ≥95th percentile	• There was no significant correlation between the number of EOs or SF and the prevalence of overweight or obesity, but a trend in which the prevalence of overweight and obesity decreased as the number of EOs per day increased. • Similarly a marginally significant trend was found for more frequently consumed nutrient-poor snacks and a higher prevalence of OW/OB.
Vilela et al, 2019, Portugal[68]	Cross-sectional	517 children aged 3–9 y participating in the "National Food, Nutrition and Physical Activity Survey of the Portuguese population, 2015–2016"	Dietary intake (snacking and eating frequency) estimated as the mean of 2 nonconsecutive days of food diaries, followed by face-to-face interviews	WHO growth reference data: BMI *z* scores	• Having <3 snacks/d was positively associated with being overweight/obese (OR = 1.98; 95% CI: 1.00–3.90), compared with having ≥3 snacks/d. • A higher eating frequency, maintaining the same energy intake, seems to contribute to a healthy body weight in children.
Vilela et al, 2019, Portugal[81]	Longitudinal population-based cohort	1961 children 4 y of age from the population-based birth cohort Generation XXI	Three-day food diary (2 weekdays and 1 weekend day) to assess time-of-day energy and macronutrient intake at 4 y of age and the effect on weight status at 7 y of age. Identification of 3 patterns: "Mid-afternoon"; "Lunch&Dinner"; "Lunch&Evening" according to energy intake distribution.	WHO growth reference data: BMI *z* scores	After adjustment, higher scores in the pattern "Mid-afternoon" (OR = 1.18, 95% CI = 1.05–1.34) and "Lunch&Evening" (OR = 1.19, 95% CI = 1.05–1.34) for energy intake at 4 y were associated with a higher odds of being overweight/obese at 7 y (model 1).

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Table 3 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
Aanesen et al, 2020, Iceland[63]	Cross-sectional	4752 first-grade children aged 5.6 to 7.4 y who participated in the annual health examination in Iceland during 2016 and 2017	Breakfast skipping was measured by asking "Have you eaten breakfast today?" with binary responses (yes/no). Skipping breakfast was assessed as not eating breakfast on the day of the assessment.	OW/OB classification: IOTF cutoff criteria for BMI values	• No evidence emerged to support an association between skipping breakfast and OW/OB in boys, regardless of coming from the unadjusted (OR: 1.08; 95% CI: 0.68–1.72) or adjusted analysis (OR: 1.02; 95% CI: 0.63–1.63). • Girls who skipped breakfast were significantly more likely to have OW/OB than girls who had eaten breakfast (unadjusted OR: 1.71; 95% CI: 1.20–2.42). Adding potential confounders reduced only slightly the OR to 1.66.
Champilomati et al, 2020, Greece[64]	Cross-sectional	1728 adolescents aged 10–12 y	Breakfast consumption assessed through self-administered, anonymous questionnaires and categorized in the following categories: (1) never/almost never, (2) 1–2 times/wk, (3) 3–4 times/wk, (4) 5–6 times/wk, (5) every day	OW/OB classification: IOTF cutoff criteria for BMI values	The frequency of breakfast consumption was not associated with childhood OW/OB, including after adjustments.
Guimarães et al, 2021, Brazil[65]	Cross-sectional	463 children aged 24 to 59 mo	Breakfast consumption assessed with interviews conducted by parents previously trained through a standardized questionnaire asking the frequency of breakfast consumption during a week (every day, 3–6 d/wk, 1–2 d/wk, rarely or never). Breakfast skippers were defined as those who eat breakfast <7 d/wk.	WHO growth standards: BMI *z* scores; OW/OB group classified as $\geq +2$ *z* scores	• The prevalence of OW/OB decreased as the frequency of breakfast consumption increased ($P = 0.035$). • A relationship between skipping breakfast and children with OW/OB was not observed when performing the multivariate regression.

Abbreviations: AAP, American Academy of Pediatrics; aOR, adjusted odds ratio; BMI, body mass index; CDC, Centers for Disease Control and Prevention; CI, confidence interval; EO, eating occasion; FFQ, food-frequency questionnaire; IOTF, International Obesity Task Force; OR, odds ratio; OW/OB, overweight/obesity; SF, snacking frequency; PANACEA, Physical Activity, Nutrition and Allergies in Children Exposed in Athens; WHO, World Health Organization.

Table 4 **Studies included in the qualitative synthesis for outcome A, considering anthropometric measurements and body composition as the obesity outcome**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
Zerva et al, 2007, Greece[82]	Cross-sectional	151 schoolchildren and adolescents aged 9-11 y	Dietary intake assessed with 3-d food records. Eating frequency was calculated for each child as the mean daily number of eating episodes (including all meals and snacks). Youth were categorized in tertiles according to the daily number of eating episodes.	BMI; skinfolds tricipital, bicipital, subscapular, supra-iliac; trunk to extremity ratio (TER), an index of body fat distribution; % body fat was estimated from triceps and subscapular skinfolds from which fat mass and fat-free mass were calculated	• The number of eating episodes was inversely associated ($P < 0.05$) with the sum of skinfolds ($r = -0.17$) and % body fat ($r = -0.18$) after controlling for age and sex. • Frequent eaters presented lower total ($P < 0.05$) and central adiposity ($P < 0.01$) compared with the infrequent eaters.
Smith et al, 2010, Australia[83]	Longitudinal cross-sectional	6559 children and adolescents aged 9-15 y and a follow-up of 2184 adults aged 26-36 y	Skipping breakfast assessed with a self-reported questionnaire reporting usual breakfast consumption (yes/no response); meal patterns chart reporting data for the previous day, modified FFQ regarding the previous 12 mo, and a food-habits questionnaire in adulthood (classification in 4 groups: skipped breakfast in neither childhood nor adulthood/skipped breakfast only in childhood/skipped breakfast only in adulthood/skipped breakfast in both childhood and adulthood)	BMI; OW/OB classification: IOTF cutoff criteria for BMI values; WC	• Compared with participants who reported eating breakfast at both time points, those who skipped breakfast at both time points had, on average, a 4.7-cm greater WC. • Similar associations were observed for BMI. • No significant differences in anthropometric measurements were observed between those who reported skipping breakfast only in childhood or only in adulthood and those who ate breakfast at both time points.
Keast et al, 2010, USA[84]	Cross-sectional	5811 adolescents aged 12–18 y	Snacking frequency assessed with a 24-h recalls (0, 1, 2, 3, or 4 snacks/d)	BMI according to CDC growth charts; WC according to reference percentiles for age and sex	• The prevalence of OW/OB and of abdominal obesity decreased with increased snacking frequency ($P < 0.01$ for trends across snack consumption groups). • OR (95% CI) for overweight or obesity and for abdominal obesity ranged from 0.63 (0.48-0.85) to 0.40 (0.29-0.57) and from 0.61 (0.43-0.86) to 0.36 (0.21-0.63) for 2 to $\geq$ 4 snacks/d, respectively.
Deshmukh-Taskar et al, 2010, USA[85]	Cross-sectional	4320 children aged 9-13 y and 5339 adolescents aged 14-18 y in NHANES 1999–2006	Breakfast consumption assessed through 24-h dietary recall. No food or beverage consumption, excluding water, classified as breakfast skippers. RTE group ate ready-to-eat cereals at a breakfast meal occasion (regardless of other foods or beverages consumed at that meal occasion), and other breakfast	BMI *z* score according to CDC growth charts; obesity classified as >95th percentile; WC	• In children/adolescents, breakfast skippers had higher BMI *z* scores ($P < 0.05$) and a higher WC ($P < 0.05$) than RTE cereal and other breakfast consumers. • The prevalence of obesity was higher in breakfast skippers than RTE cereal consumers ($P < 0.05$) in children/adolescents and was higher in other breakfast consumers than RTE cereal

(continued)

Table 4 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
			consumers were defined as those who consumed other foods or beverages at the breakfast meal.		consumers only in adolescents ($P < 0.05$).
Ritchie, 2012, USA[102]	Longitudinal population-based cohort	2379 female participants from ages 9–10 to 19–20 y recruited in the 10-y National Heart, Lung, and Blood Institute Growth and Health Study (NGHS) in 1987	Eating frequency (number of meals, number of snacks, and total number of eating episodes [meals+snacks]) investigated by 3-d food record consisting of 2 weekdays and 1 weekend day, regularly review by trained and certified nutritionists	BMI absolute value; WC	• Among White girls, lower initial snack and total eating frequencies were related to greater 10-y increases in BMI ($P = 0.023$ and 0.012, respectively) and WC ($P = 0.030$ and 0.015, respectively). • Among Black girls, lower initial meal and snack frequencies were related to greater increases in BMI ($P = 0.004$ and 0.022, respectively) and WC ($P = 0.052$ and 0.005, respectively). In addition, among Black girls, lower initial total eating frequency was related to greater increases in WC ($P = 0.010$).
Jääskeläinen et al, 2013, Finland[86]	Cross-sectional	3066 boys and 3181 girls aged 16 y in the Northern Finland Birth Cohort 1986 (NFBC1986)	Assessment of meal patterns through self-reported questionnaire including 5-item questions with dichotomous responses (yes/no). The data were categorized as follows: 5 meals/d including breakfast (regular meal pattern), <4 meals/d including breakfast (semi-regular meal pattern), and <4 meals/d not including breakfast (breakfast skippers).	BMI; OW/OB classification: IOTF cutoff criteria for BMI values; WC	• The regular 5-meal-a-day pattern including breakfast was significantly associated with a decreased risk of OW/OB in both genders (OR [95% CI] for boys: 0.41 [0.29-0.58]; girls: 0.63 [0.45-0.89]) and abdominal obesity in boys compared with the breakfast skipping pattern (ie ≤4 meals/d without breakfast; OR: 0.32; 95% CI: 0.16-0.63). • The regular 5-meal-a-day pattern was associated with reduced risks of OW/OB and abdominal obesity among boys and girls. • Compared with the breakfast skippers (reference group), the reductions in the risk of OW/OB among the adolescents who ate 5 meals per day were 61% in boys and 43% in girls, while those in the risk of abdominal obesity were 73% in boys and 44% in girls.
Shafiee et al, 2013, Iran[87]	Cross-sectional	5625 adolescents aged 10-18 y	Breakfast consumption assessed with a Likert scale questionnaire (none, 1-2 d, 3-6 d, every day) categorized as 0-2 d/wk (Seldom); 3-5 d/wk (Often); 6-7 d/wk (Regular)	BMI absolute value; WC	• The average of BMI was higher in the "seldom breakfast eater" group (P for trend < 0.001). • "Seldom breakfast eaters" were found to have an increased risk of abdominal obesity from 39% to 58% in all models

(continued)

Table 4 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
					compared with the usual breakfast eater. • In the multivariate model, "seldom breakfast eaters" had a significantly higher risk of general obesity (OR: 1.47; 95% CI: 1.20-1.82), abdominal obesity (OR: 1.39; 95% CI: 1.04-1.86), and MetS (OR: 1.96; 95% CI: 1.18-3.27).
Donin et al, 2014, United Kingdom[88]	Cross-sectional	4116 schoolchildren and adolescents aged 9-10 y	Breakfast consumption assessed with a self-administered questionnaire assessing usual breakfast consumption (every day, most days, some days, or not usually)	BMI; skinfolds tricipital, bicipital, subscapular, supra-iliac; body composition through bioelectrical impedance	Fat mass index and sum of skinfolds were all lower among children who reported eating breakfast every day and showed evidence of graded and statistically significant associations across the breakfast frequency groups ($P < 0.0001$).
Shroff et al, 2014, Colombia[103]	Longitudinal population-based cohort	975 children and adolescents aged 5–12 y	At recruitment in 2006, trained dietitians administered an FFQ to mothers. The snacking pattern was characterized by intakes of high-energy, low-nutrient-density foods.	BMI *z* scores according to WHO reference data; triceps and subscapular skinfold thicknesses	• Children in the highest quartile of adherence to the snacking pattern had a 0.09-kg/m^2 per year higher BMI gain than children in the lowest quartile (P for trend = 0.05). • A similar association was observed for mean change in subscapular: triceps skinfold thickness ratio ($P = 0.03$).
Murakami et al, 2014, United Kingdom[89]	Cross-sectional	818 children aged 4–10 y and 818 adolescents aged 11–18 y	Dietary intake assessed using a 7-d weighed dietary record. Eating occasions were defined as any occasion when any food or drink was consumed.	National growth charts (UK): BMI *z* scores; WC and WHtR for subjects >11 y	• EF was found to be positively associated with BMI *z* score in adolescents ($P = 0.004$), but not in children • No associations between EF and WHtR
Wennberg et al, 2015, Sweden[104]	Longitudinal population-based cohort	889 adolescents aged 16 y with a 27-y follow-up up to 43 y	Breakfast skipping assessed with a self-reported questionnaire answered at age 16 y ("What did you have for breakfast this morning?"). The group "Poor breakfast habits" was defined as those reporting not eating anything or only drinking or eating something sweet.	WC (central obesity defined according to the International Diabetes Federation)	• Poor breakfast habits in adolescence predicted MetS in adulthood (OR= 1.68; 95% CI: 1.01-2.78). • Of the MetS components, poor breakfast habits in adolescence predicted central obesity in adulthood (OR = 1.71; 95% CI: 1.00-2.92).
Ahadi et al, 2015, Iran[90]	Cross-sectional	13 486 children and adolescents aged 6-18 y	Breakfast frequency assessed by self-reported questionnaire defining participants as skippers (eating breakfast 0-2 d/wk), semi-skippers (eating breakfast 3-4 d/wk), and non-skippers (eating breakfast 5-7 d/wk)	BMI percentile according to WHO reference data; WC	Skipping breakfast was associated with a greater risk of abdominal obesity (OR: 1.35; 95% CI: 1.18-1.53), overweight (OR: 1.16; 95% CI: 1.01-1.34), and general obesity (OR: 1.61; 95% CI: 1.39-1.89).

(continued)

Table 4 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
Murakami and Livingstone, 2015, United Kingdom[91]	Cross-sectional	818 children aged 4–10 y and 818 adolescents aged 11-18 y in the UK National Diet and Nutrition Survey	Dietary intake (eating frequency, variability in eating frequency) assessed using a 7-d weighed dietary record. For all dietary variables, mean daily values over 7 d were used in the analysis.	National growth charts (UK): BMI *z* scores; WC and WHtR for subjects >11 y	There were no associations between EF variability and BMI *z* score and WHtR.
Kelishadi et al, 2016, Iran[92]	Cross-sectional	14 880 children and adolescents aged 6-18 y	Eating frequency assessed with a parent-reported questionnaire answering the sum of the daily consumption frequency of main meals and snacks (between 1 and 9), categorized into 4 groups as EF $\leq$ 3, EF = 4, EF = 5, and EF $\geq$ 6 according to its distribution.	BMI percentile according to WHO reference data; WC, hip circumferences, waist-to-hip ratio (WHR), and WHtR	• Anthropometric indices, such as weight (45.95 vs 39.66 kg), WC (68.75 vs 65.56 cm), and BMI (19.61 vs 18.17 kg/m^2), were higher among those who had an EF of $\leq$3 compared to students with an EF $\geq$ 6 (all *P* values < 0.001). • The likelihood of being abdominally obese was higher among boys who had an EF $\leq$ 3 (22.01%) compared with their counterparts with an EF $\geq$ 6 (18.30%) ($P = 0.030$). • A significant association was observed between EF and obesity; students who reported an EF of 4 (OR: 0.67; CI: 0.57-0.79), 5 (OR: 0.74; CI: 0.62-0.87), and 6 (OR: 0.54; CI: 0.44-0.65) had a lower likelihood of being obese compared with those who had an EF $\leq$ 3. • The odds of central obesity had a significant inverse association with EF; having an EF of 4 (OR: 0.82; CI: 0.71-0.94), 5 (OR: 0.86; CI: 0.74-0.99), and $\geq$6 (OR: 0.73; CI: 0.63-0.85) decreased the OR of abdominal adiposity.
Marlatt et al, 2016, USA[93]	Cross-sectional	367 adolescents aged 11-18 y	Breakfast consumption assessed with a self-reported validated questionnaire including average number of days/week that breakfast was consumed.	BMI percentiles according to CDC growth charts, body composition through bioelectrical impedance	Breakfast consumption was significantly associated with lower BMI and body fat ($P < 0.05$).
Murakami and Livingstone, 2016, United Kingdom[94]	Cross-sectional	4346 children aged 6–11 y and 6338 adolescents aged 12–19 y participating in the NHANES 2003–2012	EF, MF, and SF assessed with two 24-h dietary recalls. Eating occasions were defined as any occasion when any food or drink was consumed.	BMI percentiles according to CDC growth charts; WC and WC percentiles according to NHANES III to assess abdominal obesity	Higher SF and EF, but not MF, were associated with higher risks of overweight and abdominal obesity in children, whereas associations varied in adolescents, depending on the definition of meals and snacks.

(continued)

Table 4 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
Murakami and Livingstone, 2016, United Kingdom[95]	Cross-sectional	818 children aged 4–10 y and 818 adolescents aged 11–18 y in the National Diet and Nutrition Survey (NDNS)	Eating occasions assessed with 7-d weighed dietary record. Definition of meals or snacks on the basis of contribution to energy intake (≥15% or <15%) or clock time	National growth charts (UK): BMI *z* scores; WC and WHtR for subjects >11 y	All measures of MF and SF showed no association with adiposity measures.
Traub et al, 2018, Germany[105]	Cohort	1733 children aged 7.08 ± 0.6 y	Skipping breakfast assessed with a self-administered validated questionnaire of the German KiGGS survey. Breakfast consumption assessed on a 4-point Likert scale (answers dichotomized as "Never and rarely" versus "often and always").	National growth charts (German): BMI percentiles; WHtR	Skipping breakfast led to increased changes in WHtR ($P = 0.007$), weight ($P < 0.001$) and BMI measures ($P = 0.027$).
Cayres et al, 2018, Brazil[106]	Longitudinal population-based cohort	86 adolescents aged 11–14 y	Breakfast intake assessed with face-to-face interviews conducted at the baseline and the follow-up time points, accounting for the number of days with breakfast consumption in a typical week (variable ranging from zero to 7 d)	BMI; percentage whole BF and TF were estimated using a densitometry scanner	• At baseline, adolescents who consumed breakfast regularly presented with lower BMI ($P = 0.032$), TF ($P = 0.019$), and BF ($P = 0.012$) than their counterparts. • After 12 mo of follow-up, TF (3.5%; 95% CI: 6.9-0.2) and BF (2.3%; 95% CI: 3.9-0.7) of adolescents who had consumed breakfast regularly decreased more than adolescents who did not. • Adolescents stratified as non-skipping breakfast demonstrated an inverse relationship with absolute changes in BF ($r = -0.274$; 95% CI: 0.498-0.051); however, this relationship was not mediated by physical activity.
Sila et al, 2019, Croatia[96]	Cross-sectional	802 adolescents aged 15-16 y	Breakfast consumption assessed with a multi-pass 24-h recall (5 steps) asking about breakfast consumption (defined as the intake of foods or beverages before 10:00, containing a minimum of 250 kcal) and number of eating occasions	BMI; OW/OB classification: IOTF cutoff criteria for BMI values; skinfolds tricipital, bicipital, subscapular, suprailiac; assessment of the the sum of 4 skinfolds (S4SF)	• Participants who consumed breakfast had significantly lower body fat % ($P = 0.011$ for boys; $P < 0.001$ for girls) compared with breakfast nonconsumers. • Breakfast consumption was negatively associated with adiposity only in the boys at the highest tertile of physical activity ($P = 0.04$).

(continued)

Table 4 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
Wadoloska et al, 2019, Poland[26]	Cross-sectional	1566 adolescents aged 11–13 y	Meal frequency, breakfast consumption (number of days/week), and school meal consumption (number of days/week) assessed with a questionnaire; breakfast skipping classified as 4–7 times/wk (frequent skipping), 1–3 times/week (skipping a few times a week), and 0 times/week (never skipping; ie, every day consumption); school meal skipping classified as 3-5 times/wk (frequent skipping), 1–2 times/week (skipping a few times a week), and 0 times/week (never skipping; ie, every school day consumption)	WC; WHtR; OW/OB classification: IOTF cutoff criteria for BMI values; BMI-for-age $>$25 kg/m^2 as a general adiposity marker; WHtR $>$0.5 as a central adiposity marker	• Frequent breakfast skippers were more likely to be overweight/obese (OR: 1.89; 95% CI: 1.38-2.58) and centrally obese (OR: 1.63; 95% CI: 1.09-2.44), while less likely to fall in the thinness category (OR: 0.52; 95% CI: 0.29-0.94), in comparison to never-skippers. • Breakfast skippers and school-meal skippers a few times a week were more likely to be overweight/obese (OR: 1.37; 95% CI: 1.06-1.78) in comparison to never skippers.
Suhadi et al, 2020, Indonesia[97]	Cross-sectional	768 adolescents aged 14-18 y	Eating behaviors assessed with a frequency of meals ($\leq$3 or $>$3 times/d), daily breakfast (always/frequent and rare/never), frequency of snacks ($\leq$3 and $>$3 times/d) collected from a face-to-face written interview	BMI percentiles according to CDC growth charts; WC	• Subjects who consumed breakfast tended to have lower BMI ($P = 0.006$). • Female subjects with routine breakfast had better BMI ($P < 0.001$) and lower WC ($P = 0.02$). • Snack frequency did not affect the cardiometabolic risk parameters ($P > 0.05$).
Jeans et al, 2020, USA[98]	Cross-sectional	671 low-income, Hispanic schoolchildren aged 9 y	Breakfast consumption assessed through two 24-h dietary recalls. Subjects were classified as (1) "skippers," having no breakfast EO on either recall day; (2) "intermittent," having a breakfast EO on only 1 recall day; and (3) "regular," having a breakfast EO on both recall days.	BMI percentiles according to CDC growth charts; WC; total body fat (%) assessed with bioelectrical impedance	There were no significant relationships between breakfast consumption groups and adiposity.
Martínez-Lozano et al, 2020, Spain[99]	Cross-sectional	397 schoolchildren and adolescents aged 8-12 y from the Obesity, Nutrigenetics, Timing, and Mediterranean Junior study	Late eating assessed with a 7-d dietary record including food timing, completed daily by children with their parents' help. Children were divided into early-dinner eaters (EDE) and late-dinner eaters (LDE) according to the median of the dinner time, 21:07. An age-appropriate Spanish version of the Munich Chronotype Questionnaire (MCTQ) was used to define the chronotype.	BMI *z* score according to WHO growth reference data; WC; total body fat assessed with bioelectrical impedance	• Late dinner eaters (LDE) had higher BMI and WC than EDE and accounted for a higher proportion of overweight/obese children than early eaters ($P < 0.05$) (OR = 2.1; 95%CI: 1.33-3.31). • Associations between LDE and BMI remained significant when adjusted for objective sleep duration ($P = 0.019$) and the same trend was obtained when adjusted for time in bed ($P = 0.055$).

(continued)

Table 4 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
					• When standardizing by sex, these associations remained significant only in girls. • No significant associations were found between intraindividual variation variables (of dinner timing and midpoint of food intake) and BMI *z* scores.
de Souza et al, 2021, Brazil[100]	Cross-sectional	36 956 adolescents aged 12-17 y	Skipping breakfast assessed with a self-administered questionnaire reporting usual breakfast consumption ("I don't have breakfast," "I have breakfast sometimes/almost every day/every day"). Breakfast skipping considered as "I don't have breakfast," "I have breakfast sometimes/almost every day."	• BMI *z* score according to WHO growth reference data; excess body weight classified as: BMI *z* score $\geq$1 • WC $\geq$90th percentile for 12-16 y or $\geq$90 cm for boys and $\geq$80 cm for girls $\geq$16 y old	A higher prevalence of excess body weight (PR = 1.30; 95% CI: 1.18–1.43) and central obesity, both considering WC (PR = 1.27; 95% CI: 1.01–1.61) and WHtR (PR = 1.32; 95% CI: 1.13-1.54), was found in adolescents who skipped breakfast.
Martínez-Lozano et al, 2021, Spain[101]	Cross-sectional	432 children and adolescents aged 8-12 y	Individual chronotype assessed by Cosinor's analysis as an objective biomarker of the individual chronotype. An age-appropriate Spanish version of the Munich Chronotype Questionnaire (MCTQ) was used to subjectively determine individual chronotype; food timing assessed with a 7-d dietary record.	BMI absolute value; WC	• Evening-types had a significantly higher BMI. • A delay of 1 h in the chronotype was related to a 0.56 increase in BMI ($P = 0.036$).

Abbreviations: BF, body fat; BMI, body mass index; CDC, Centers for Disease Control and Prevention; CI, confidence interval; EF, eating frequency; EO, eating occasion; FFQ, food-frequency questionnaire; IAAT, intra-abdominal adipose tissue; IOTF, International Obesity Task Force; KiGGS survey, German Health Interview and Examination Survey for Children and Adolescents; MetS, metabolic syndrome; MF, meal frequency; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio; OW/OB, overweight/obesity; PR, prevalence ratio; RTE, ready-to-eat; SAAT, subcutaneous abdominal adipose tissue; SF, snack frequency; TF, trunk fat; WC, waist circumference; WHO, World Health Organization; WHtR, waist:height ratio.

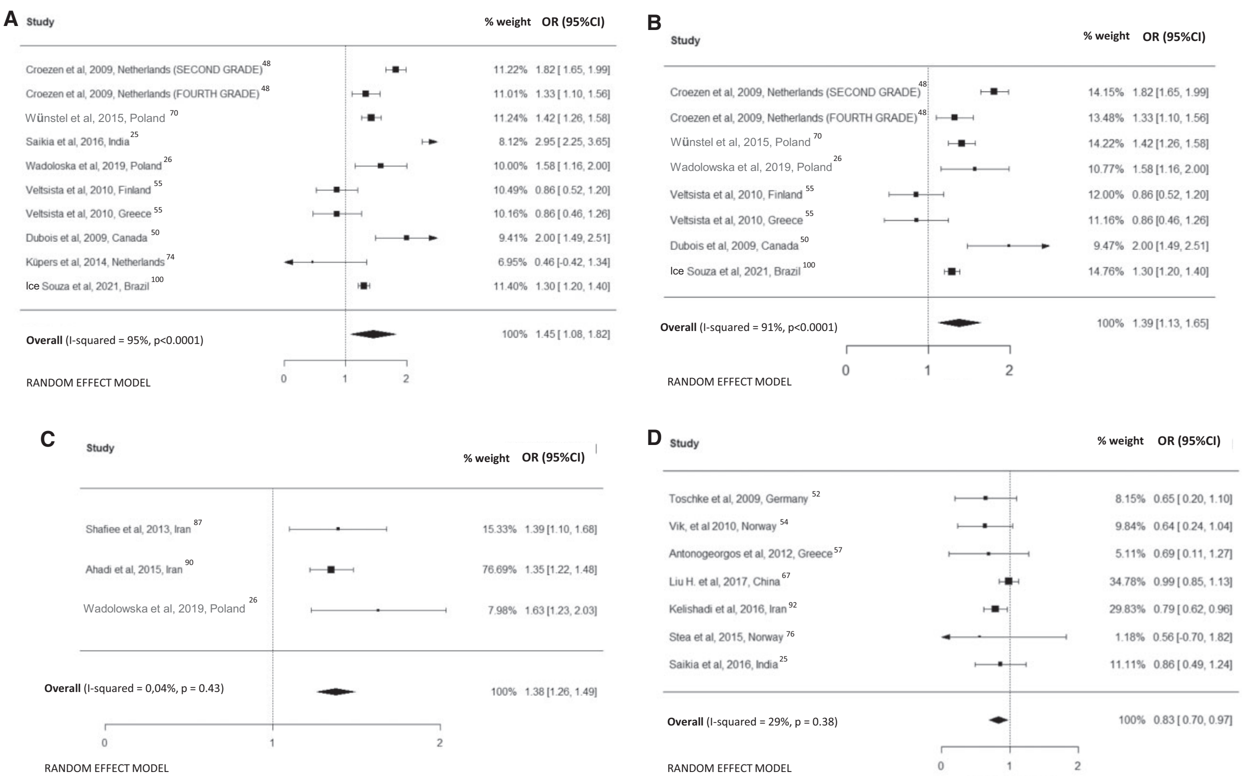

Figure 3 **Meta-analyses of (A) the relationship between breakfast consumption (non-daily breakfast consumers ≤6 d/wk vs daily breakfast consumers 7 d/wk) and overweight/obesity (8 unique studies); (B) the relationship between breakfast consumption (non-daily breakfast consumers ≤6 d/wk vs daily breakfast consumers 7 d/wk) and overweight/obesity (sensitivity analysis, 6 unique studies); (C) the relationship between breakfast consumption (irregular consumption, defined as 0 to 3 times/wk, vs regular consumption, defined as 5 to 7 times/wk), and abdominal obesity (3 unique studies); and (D) the relationship between meal frequency (≥4 times/d vs ≤3 times/d) and overweight/obesity (7 unique studies).** *Abbreviations*: CI, confidence interval; OR, odds ratio

OW/OB for regular frequency of meals (defined as ≥4 times/d) vs a low number of meals (≤3 times/d). The pooled OR was 0.83 (95% CI, 0.70–0.97), and yielded low heterogeneity (I^2 = 29%, $P > 0.38$) (Fig. 3D[25,52,54,57,67,76,92]). These results demonstrated that children with higher meal frequency have a lower risk of OW/OB, compared with those with a low meal frequency. According to the GRADE system, the certainty of the evidence was very low.

Conflicting data have emerged regarding the association between snacking frequency and obesity, which was evaluated in 8 studies.[25,61,62,68,77,84,94,103] There is no consensus on the definition of "snack"; some referred to a snack as any food or drink outside of the 3 main meals.[77] Using this definition, after longitudinal analysis, it was observed that, in normal-weight children, snacking was not associated with changes over time in WHO BMI *z* score. However, in underweight children, snacking was associated with increases in BMI *z* score (+1.2 and +1.1 BMI *z*-score units for ages 2–6 and 7–13, respectively; $P < 0.05$), while, in overweight children, snacking was associated with larger declines in BMI *z* score ($P < 0.05$). Similarly, Vilela et al,[68] using the same definition of snack, showed that having fewer than 3 snacks per day was positively associated with being overweight/obese according to WHO criteria (OR = 1.98; 95% CI, 1.00–3.90), compared with having 3 or more snacks per day. The authors concluded that a higher eating frequency, maintaining the same energy intake, seems to contribute to a healthy body weight in children.

Kachurak et al[61] used 2 main definitions of snacking: (1) occasions identified by the caregiver as a snack and (2) snack occasions plus all other food/beverage consumption between meals. Independently from the definition used, the authors observed that snacking frequency and weight status (according to WHO criteria) were positively associated among US children younger than 2 years old. Snacking more frequently than recommendations (2 small snacks according to the American Academy of Pediatrics) was significantly associated with increased odds of OW/OB among children younger than 2 years but not in children aged 2 to 5 years. Keast et al[84] showed that the prevalence of

OW/OB (according to BMI) and of abdominal obesity (assessed as WC) decreased with increased snacking frequency and with increased percentage of energy from snacks. In particular, a decrease in the OR of abdominal obesity in the "≥4 snacks/day" group compared with snack consumers who ate 2 snacks per day (OR = 0.36; 95% CI, 0.21–0.63 vs OR = 0.61; 95% CI, 0.43–0.86) proved that they were less likely than non-snackers to have abdominal obesity. However, the quality of snacks provided to children may be crucial in influencing body weight status. Notably, Charvet et al[62] assigned snack foods to different snack quality scores (from nutrient-poor snacks to nutritious snack items). They showed a nonsignificant trend in which the under/normal-weight children had a higher frequency of intake of the more nutritious snack items when compared with the overweight/obese children ($P = 0.090$). Similarly, in the study of Shroff et al,[103] the snacking pattern was characterized by intakes of high-energy, low-nutrient-dense foods (especially soda intake). Children in the highest quartile of snack consumption showed a greater BMI gain and a higher increase in truncal adiposity per year (assessed as subscapular to triceps skinfold thickness ratio) compared with children in the lowest quartile (P-trend < 0.05).[103] Overall, the synthesis of results into a meta-analysis was not possible due to inconsistent exposures (see Tables S6 and S7 in the Supporting Information online).

Food timing and overweight/obesity. Only 6 studies assessed the relationship between OW/OB risk and food timing.[51,58,78,81,99,101] Eng et al[51] examined the timing of energy intake and body weight status according to the CDC BMI-for-age growth charts among 2–18-year-old US children. The authors concluded that the proportion of total daily energy consumed in the latter part of the day was positively associated with being classified as overweight in the 6–11-year-olds, but negatively in the overweight 12–18-year-olds. These results could be explained by differences in eating frequencies (meals and snacking) and different dietary habits between the 2 groups.

To confirm this association, a recent prospective cohort study evaluated the effect of time-of-day energy and macronutrient intake at 4 years of age on the weight status at 7 years of age being defined as obese/overweight according to WHO z scores.[81] At 4 years of age, the patterns "Mid-afternoon," characterized by high loadings of energy intakes in the mid-afternoon (OR = 1.18; 95% CI, 1.05–1.34), and "Lunch&Evening," defined as higher energy intake at lunch and supper but lower energy intake at dinner (OR = 1.19; 95% CI, 1.05–1.34), were associated with a higher odds of being overweight/obese at 7 years. Interestingly, circadian feeding patterns exert an impact on BMI status from early life, as reported in the longitudinal study on singletons from 12 to 24 months of age. The authors showed that predominantly night-time feeding was associated with a higher BMI z-score gain (WHO Child Growth Standards) from 12 to 24 months of age compared with predominantly day-time feeding ($P = 0.006$), with an increased risk also of becoming overweight at 24 months of age (aOR, 2.78; 95% CI, 1.11–6.97).[78] Two studies classified children into 2 different chronotypes (evening types and morning types) on the basis of collection of actigraphy rhythms and administration of the Munich chronotype questionnaire.[99,101] Interestingly, a delay of 1 hour in chronotype was related to a 0.56 increase in BMI ($P = 0.036$), which may be explained by several obesogenic behaviors, including insufficient sleep, less physical activity during the day, and late eating.[101] Moreover, children aged 8–12 years identified as late dinner eaters according to dinner timing showed significantly higher BMI z score (WHO growth charts), WC, and inflammatory markers, such as interleukin 6 (IL-6; 1.6-fold) and C-reactive protein (CRP; 1.4-fold), than early dinner eaters.[99] Overall, the subsets of studies focusing on meal timing were too few and heterogeneous to conduct a meta-analysis (see Tables S6 and S7 in the Supporting Information online).

Association between chrononutrition and glucose metabolism

The association between chrononutrition and glucose metabolism was evaluated in 13 studies, 3 of which were considered as not having acceptable quality to be included in this systematic review.[40,47,107] This collection includes 9 cross-sectional studies[83,86–88,93,98,100,101,108] and 1 cohort study[109] (Table 5[83,86–88,93,98,100,101,108,109]).

With regard to the exposure variable, breakfast and/or skipping breakfast habits were assessed in 7 studies,[83,87,88,93,98,100,109] the frequency of meals and/or snack consumption was evaluated in 2 studies,[86,108] while only 1 study analyzed chronotype and timing of food intake.[101]

Half of the studies collected data from large cohorts of school-aged children and adolescents,[83,88, 98,99,109] while 5 studies focused on the subgroup of adolescents.[86,87,93,100,108]

Glucose metabolism was evaluated mainly by fasting blood samples; however, the collection of blood samples without fasting was considered a confounder and negatively affected the quality assessment.[101] All studies evaluated glycemia as the main outcome,[83,86–88,93,98,100,101,108,109] 4 studies analyzed glycated hemoglobin (HbA1c),[88,98,100,109] and 8 studies evaluated insulin concentration.[83,88,93,98,100,101,108,109] In addition, the HOMA index was evaluated in 4

Table 5 **Studies included in the qualitative synthesis for outcome B, "glucose metabolism"**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
Smith et al, 2010, Australia[83]	Longitudinal cross-sectional	6559 children and adolescents 9-15 y old and 2184 adults at the follow up (26-36 y of age)	• Skipping breakfast assessed in childhood by self-questionnaire, and in adulthood by a meal patterns chart, an FFQ, and a food-habits questionnaire • Classification in 4 groups: skipped breakfast in neither childhood nor adulthood, skipped breakfast only in childhood, skipped breakfast only in adulthood, and skipped breakfast in both childhood and adulthood	Fasting blood samples (glucose and insulin concentrations). Calculation of HOMA index as [fasting insulin/6.945] × [fasting glucose/22.5][110]	• Participants who skip breakfast in both childhood and adulthood have a significantly higher fasting insulin (mean difference: 2.02 mU/L; 95% CI: 0.75, 3.29 mU/L) and HOMA index (mean difference: 0.47 mU/L; 95% CI: 0.16, 0.79 mU/L) than those who eat breakfast at both time points. • Fasting glucose is slightly higher in those who skip breakfast in adulthood than in those who eat breakfast. The difference was only statistically significant in those who skipped breakfast only in adulthood.
Sesè et al, 2012, Spain[108]	Cross-sectional	826 adolescents aged 13-16 y	Evaluation of the frequency of snacks and meals by means of the Frequency Choice Questionnaire (FCQ), which includes time of snack consumption (eg, in the morning, in the afternoon, after school), frequency of consumption (never, sometimes, and often)	Calculation of HOMA index as [fasting insulin/6.945] × [fasting glucose/22.5][110]	• "Skipping breakfast often" is associated with a higher HOMA index in males "moderately agreeing" ($P < 0.05$) than those who are "strongly disagreeing." • "Snack events regularly throughout the weekend day" is associated with a higher HOMA index ($P < 0.05$) in females. • HOMA index is higher ($P < 0.01$) in females who "do not eat regularly a snack in the morning on school day."
Jääskeläinen et al, 2012, Finland[86]	Cross-sectional	6247 adolescents aged 16 y old	Meal frequencies and breakfast consumption assessed by means of 5-item self-administered questionnaires using the question "Do you usually have the following meals (breakfast, lunch, snack, dinner, evening snack) on weekdays?" (yes/no). Groups were categorized as follows: 5 meals/d including breakfast (regular meal pattern), ≤4 meals/d including breakfast (semi-regular meal pattern), and	Fasting blood samples (glucose concentration)	No significant difference in fasting blood sugar was found between the groups.

(continued)

Table 5 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
			≤4 meals/d not including breakfast (breakfast skippers).		
Shafiee et al, 2013, Iran[87]	Cross-sectional	5625 adolescents aged 10-18 y	Frequency of consumption of breakfast into 3 categories: "regular breakfast eater" (6-7 d/wk), "often breakfast eater" (3-5 d/wk), and "seldom breakfast eater" (0-2 d/wk). Data collected from the third survey of the CASPIAN-V study (2009-2010)	Fasting blood samples (glucose concentration)	No significant difference in fasting blood sugar was found among the breakfast consumption groups.
Donin et al, 2014, United Kingdom[88]	Cross-sectional	4116 children and adolescents aged 9-10 y	Breakfast consumption assessed by means of self-administered questionnaire. Groups of breakfast consumption: breakfast daily, most days, some days, and not usually.	Fasting blood samples (glucose, insulin and HbA1c concentrations)	Children who do not usually eat breakfast have higher fasting insulin, insulin resistance (HOMA index), and glucose ($P < 0.0001$) as well as HbA1c ($P = 0.001$) than those who have breakfast daily. These values persist even after adjustment for adiposity.
Marlatt et al, 2015, USA[93]	Cross-sectional	367 adolescents aged 11-18 y	Breakfast assessed by means of self-reported validated questionnaire, expressed as average number of days/weeks that breakfast was consumed.	Fasting blood samples (glucose and insulin concentrations); calculation of HOMA index as [fasting insulin/6.945] × [fasting glucose/22.5][110]	More frequent breakfast consumption was significantly associated with lower insulin, HOMA-IR, and MetS cluster score ($P < 0.05$).
Martínez-Lozano et al, 2020, Spain[101]	Cross-sectional	432 adolescents 8–12 y	Chronotype assessed objectively by actigraphy (recording 7-d rhythms of wrist temperature–physical activity–body position [TAP]) and subjectively (Munich-chronotype self-reported questionnaire). Food timing was collected by means of 7-d food diaries.	Collection of saliva samples (glucose and insulin concentrations)	• Evening-type children had increased physical activity in the evening, higher body temperature during the day, which suggests an increase in sleepiness, less depth of sleep, lower day–night contrast and more irregular habits. • Evening-type was associated with higher metabolic risk markers such as glucose and insulin levels ($P < 0.05$).
Jeans et al, 2020, USA[98]	Cross-sectional	671 students (mean age: 9 y)	Breakfast consumption, assessed via two 24-h dietary recalls. Breakfast consumption groups defined as (1) skippers, having no breakfast on both recalls; (2) intermittent, having a breakfast	Fasting blood samples (glucose, insulin, and HbA1c concentrations)	There were no significant relationships between breakfast consumption groups and metabolic parameters.

(continued)

Table 5 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
			only on one; and (3) regular, having a breakfast on both.		
de Souza et al, 2021, Brazil[100]	Cross-sectional	36956 adolescents aged 12-17 y	Skipping breakfast assessed by means of self-administered questionnaire. Breakfast skipping estimated from the combination of the categories: "I don't have breakfast," "I have breakfast sometimes," and "I have breakfast almost every day."	Fasting blood samples (glucose, insulin, and HbA1c concentrations)	Breakfast skippers, ranging from having no breakfast to having breakfast almost every day, have significantly higher HbA1c ($P = 0.012$) and insulin levels ($P < 0.001$) than those who consume breakfast every day. In addition, glucose level is higher ($P = 0.062$) among breakfast skippers than breakfast consumers.
Jeans et al, 2022, USA[109]	Longitudinal study (secondary analysis from an RCT)	1417 children and adolescents aged 7-12 y	Breakfast consumption through a validated survey at baseline and post-intervention. To the question "How many school days a week do you usually eat breakfast?," the subjects answered: 0–5 (0 = none, 1 = 1 school day, 2 = 2 school days, 3 = 3 school days, 4 = 4 school days, 5 = 5 school days). To the question "How many weekend days each week do you typically eat breakfast?," the subjects answered: 0–2 (0 = none, 1 = 1 weekend day, 2 = 2 weekend days).	Fasting blood samples (glucose, insulin, and HbA1c concentrations); calculation of HOMA index as: fasting glucose in mmol/L $\times$ fasting insulin in μU/mL/22.5[110]	• Breakfast increasers (those who increased $\geq +2$ d/wk the number of breakfast occasions) had lower fasting insulin ($P = 0.01$) and HOMA index ($P = 0.006$) than breakfast decreasers (those who reduced breakfast ≤ -2 d/wk) • Moreover, for every 1-d increase in breakfast consumption, there was a decrease in fasting insulin ($\beta = -0.44$; $P = 0.003$), HOMA index ($\beta = -0.11$; $P = 0.002$) and HbA1c ($\beta = -0.01$; 0.003).

Abbreviations: CASPIAN-V Study, Child and Adolescent Surveillance and Prevention of Adult Non-communicable diseases Study; CI, confidence interval; FFQ, food-frequency questionnaire; HbA1c, glycated hemoglobin; HOMA/HOMA-IR, homeostasis model assessment of insulin resistance; RCT, randomized controlled trial.

studies,[83,93,108,109] using the formula reported in the literature.[110]

With regard to breakfast consumption, all of the studies reported associations between at least 1 marker of glycemic control (glucose and/or HbA1c) and breakfast habits,[88,100,109] with the exception of 2 studies.[83,93] In addition, regular breakfast consumption was associated with lower insulin resistance, both in terms of reduced insulin concentration and/or HOMA index.[83,88,93,100,109] Particularly in the longitudinal study of Jeans et al,[109] the impact of breakfast frequency was evaluated among children aged 7–12 years. Children who increased the number of breakfast occasions ($\geq +2$ d/wk) had lower fasting insulin ($P = 0.01$) and HOMA-IR ($P = 0.006$) than breakfast decreasers (those who reduced breakfast to ≤ -2 d/wk). Moreover, every 1-day increase in breakfast consumption decreased fasting insulin by 0.44 μIU/mL, HOMA-IR by 0.11, and HbA1c by 0.01% ($P \leq 0.03$).

Only 1 study evaluated the impact of meal frequency on glucose metabolism, and no significant differences were found by comparing different meal patterns (5 meals vs $\leq$4 meals/d with or without breakfast).[86] Conflicting results have been reported regarding snack consumption. Sesé et al[108] found a higher HOMA index both among females eating regular snacks throughout the weekend days ($P < 0.05$) and among females not regularly eating a snack in the morning on school days ($P < 0.001$). However, the authors did not define the type of snack consumed to allow for conclusions.

Chronotype and food timing were only evaluated by Martínez-Lozano et al,[101] as already reported. Children were divided into morning types and evening types; interestingly, evening-type features included increased physical activity in the evening and higher body temperature during the day, which suggests an increase in sleepiness, less deep sleep, lower day–night contrast, and more irregular habits. Evening-type eating was associated with higher glucose and insulin in saliva samples.

Association between chrononutrition and lipid markers and cardiovascular disease risk

The association between chrononutrition and lipid markers or CVD risk was assessed originally in 17 studies, 4 of which were considered as not having acceptable quality to be included in this systematic review.[40,46,47,107] The final 13 articles comprised only those with a cross-sectional design,[59,83,86–89,91,93,98,100,101,111] apart from 1 prospective study[104] (Table 6[59,83,86–89,91,93,98,100,101,104,111]). With regard to the exposure variable, 7 studies assessed as the main outcome breakfast habits and/or skipping breakfast,[83,87,88,93,98,100,104] 6 studies evaluated meal frequencies or eating occasions,[59,86,89,91,101,111] while only 1 study assessed chronotype and food timing.[101] The majority of studies collected data from large cohorts of both school-aged children and adolescents, whereas evidence on preschool-age children (3-to-5 year-old children) was reported only in 1 study.[111] Five articles focused on the subgroup of adolescents.[86,91,93,100,104] CVD risk was assessed principally by means of fasting blood samples (HDL cholesterol, TC, TGs, and indirect assessment of LDL cholesterol); in addition, 1 study evaluated apolipoprotein A1 and B.[111] The collection of blood samples without fasting was considered as a confounder and negatively affected the quality assessment.[101,111] Last, CVD risk profile was investigated by means of heterogeneous MetS scores, such as the International Diabetes Federation consensus definition,[86,104] Adult Treatment Panel III criteria modified for the pediatric age group,[87,93] or according to other previous literature.[83]

With regard to breakfast consumption, all studies reported an association between at least 1 lipid marker (TC, TGs, or LDL cholesterol) and breakfast habits, with the exception of Jeans et al.[98] Conflicting results were reported for HDL-cholesterol levels.[87,88,93,98,104] In some cases, breakfast skipping showed a positive association with MetS scores.[83,87,93,104] Shafiee et al[87] showed that "seldom breakfast eaters" had a significantly higher risk of MetS (OR, 1.96; 95% CI, 1.18– 3.27); in line with these finding, Marlatt et al[93] reported that more frequent breakfast consumption was associated with lower MetS cluster score ($P < 0.05$). Interestingly, in the prospective study of Wennberg et al,[104] poor breakfast habits at age 16 years were associated with higher odds of MetS at age 43 years (aOR = 1.68; 95% CI, 1.01–2.78). In the longitudinal cross-sectional study of Smith et al,[83] breakfast skippers at both time points (childhood and adulthood) had significantly higher TGs, TC, LDL cholesterol, and MetS scores than those who ate breakfast at both time points.

There was no consensus on the definition of regular number of eating occasions or meals. Jääskeläinen et al[86] considered a regular meal pattern to be 5 meals per day, and the latter was associated with a reduced risk of hypertriglyceridemia (aOR, 0.48; 95% CI, 0.26–0.89) and low HDL cholesterol (OR, 0.65; 95% CI, 0.47–0.90) among boys. According to Murakami et al,[89,91] the number of eating occasions was inversely associated with TC and LDL cholesterol in children (4–10 years) but not in adolescents, while Silva et al[59] found the pattern "<4 meals" to be associated with a higher prevalence of increased LDL cholesterol among both children aged 5 to 9 years (prevalence ratio = 1.48; 95% CI, 1.02–2.13; $P = 0.037$) and adolescents aged 10 to 14 years

Table 6 **Studies included in the qualitative synthesis for outcome C, "lipid markers and CVD risk"**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
Smith et al, 2010, Australia[83]	Longitudinal cross-sectional	6559 children and adolescents 9-15 y old and 2184 adults at the follow up (26-36 y of age)	Skipping breakfast assessed in childhood by self-questionnaire, and in adulthood by a meal patterns chart, an FFQ, and a food-habits questionnaire. Classification in 4 groups: skipped breakfast in neither childhood nor adulthood, skipped breakfast only in childhood, skipped breakfast only in adulthood, and skipped breakfast in both childhood and adulthood.	• Fasting blood samples (HDL, TC, TG, and indirect assessment of LDL) • A continuous MetS score was created by using a previous method described in literature[112]	• Participants who skipped breakfast at both time points had significantly higher TG, TC, LDL, and MetS scores than did those who ate breakfast at both time points • No differences were observed between those who skipped breakfast only in childhood and those who ate breakfast at both time points • A higher proportion of participants who skipped breakfast at both time points were classified as having high LDL cholesterol (neither, 7.5%; child only, 5.8%; as an adult, 8.6%; both, 18.3%; $P = 0.037$)
Jääskeläinen et al, 2012, Finland[86]	Cross-sectional	6247 adolescents 16 y old	Meal frequencies and breakfast consumption assessed by means of 5-item self-administered questionnaires using the question "Do you usually have the following meals (breakfast, lunch, snack, dinner, evening snack) on weekdays?" (yes/no). Groups were categorised as follows: 5 meals/d including breakfast (regular meal pattern), ≤4 meals/d including breakfast (semi-regular meal pattern), and ≤4 meals/d not including breakfast (breakfast skippers).	• Fasting blood samples (HDL, LDL, TC, TG) • MetS defined according to pediatric definition of the International Diabetes Federation (IDF)	• Five-meal-a-day pattern was associated with reduced risk of hypertriglyceridemia (adjusted OR: 0.48; 95% CI: 0.26, 0.89) and low HDL (OR: 0.65; 95% CI: 0.47, 0.90) among boys compared with "breakfast skippers" pattern • Meal skipping combined with regular breakfast was associated with lower risks of hypertriglyceridemia (OR: 0.53; 95% CI: 0.31, 0.90) among boys compared with the "breakfast skippers" pattern
Persaud et al, 2013, Canada[111]	Cross-sectional	1856 children aged 3–5 y	Number of meals assessed by means of subscales of the NutriSTEP questionnaire. Responses range in score from 0 (no risk) to 4 (risk), an increased score indicates increased nutrition risk.	Blood samples (lipid profile apolipoproteins A1 and B)	• Eating behaviors subscore was significantly associated with non-HDL ($P = 0.03$) • For each unit increase in the eating behavior subscore there is an increase of 0.02 mmol/L in non-HDL (95% CI: 0.002 to 0.05) • Eating behaviors subscore was significantly associated with LDL ($\beta = 0.02$; 95% CI: 0.002-0.05)

(continued)

Table 6 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
					and apolipoprotein B ($\beta = 0.01$; 95% CI: 0.002-0.01)
Shafiee et al, 2013, Iran[87]	Cross-sectional	5625 children aged 10-18 y	Frequency of consumption of breakfast into 3 categories: "regular breakfast eater" (6-7 d/wk), "often breakfast eater" (3-5 d/wk), and "seldom breakfast eater" (0-2 d/wk). Data collected from the third survey of the CASPIAN-V study (2009-2010).	• Fasting blood samples (HDL, LDL, TC, TG) • MetS defined as ≥3 of the Adult Treatment Panel III criteria modified for the pediatric age group	• TG and LDL were significantly higher and HDL was significantly lower in the "seldom breakfast eater" group than in the "usual breakfast eater" group (P for trend < 0.05) • "Seldom breakfast eater" had the highest prevalence of subjects with elevated TG (9.8%; $P = 0.02$) and elevated LDL (7.7%; $P = 0.02$) vs the other 2 groups • "Seldom breakfast eaters" were significantly more likely to present MetS than those having breakfast ($P = 0.05$) • "Seldom breakfast eaters" had a significantly higher risk of elevated TG (OR: 1.41; 95% CI: 1.03-1.93) and MetS (OR: 1.96; 95% CI: 1.18-3.27)
Donin et al, 2014, United Kingdom[88]	Cross-sectional	4116 schoolchildren aged 9-10 y	Breakfast consumption assessed by means of self-administered questionnaire. Groups of breakfast consumption: breakfast daily, most days, some days, and not usually.	Fasting blood samples (HDL, TC, TG, and indirect assessment of LDL)	• TG and C-reactive protein were all lower and HDL higher among children who reported eating breakfast every day and showed evidence of graded and statistically significant associations across the breakfast frequency groups (also after adjustments). After adjustment for adiposity (third model with sum of skinfolds and fat mass index), they were no longer statistically significant. • Blood lipids showed no difference across the different breakfast contents.
Murakami and Livingstone, 2014, United Kingdom[89]	Cross-sectional	818 children and adolescents aged 4-18 y	Eating frequencies assessed by means of 7-d weighed dietary record	• Anthropometric parameters including WHtR • Fasting blood samples (HDL, TC, TG, and indirect assessment of LDL)	• EF was inversely associated with TC ($P < 0.01$) and LDL ($P < 0.04$) in children (4–10 y)

(continued)

Table 6 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
					• No associations between EF and metabolic risk factors in adolescents (10-18 y)
Murakami and Livingstone, 2015, United Kingdom[91]	Cross-sectional	2479 both children 4-10 y old and adolescents 11-18 y old	Eating frequencies assessed by means of 7-d weighed dietary record	• Anthropometric parameters including WHtR • Fasting blood samples (HDL, TC, TG, and indirect assessment of LDL)	• In both children and adolescents, after adjustment (model 1), variability in EF was not associated with any metabolic risk factors examined. • With further adjustment, larger variability in EF was associated with higher TC and LDL concentrations in children (both $P < 0.03$) but not in adolescents. • There were no associations between EF variability and other metabolic risk factors examined in both groups.
Wennberg et al, 2015, Sweden[104]	Longitudinal population-based cohort	889 16-y-old adolescents with 27-y follow-up (43 y)	Breakfast skipping assessed by means of questionnaire ("What did you have for breakfast this morning?"). The group "Poor breakfast habits" was defined as those reporting not eating anything or only drinking or eating something sweet.	• Anthropometric parameters including WC • Collection of blood samples (HDL, TG) • MetS defined according to the International Diabetes Federation (IDF)	• For components of MetS at age 43 y, adolescents with poor breakfast habits had a higher prevalence of high TG levels • Poor breakfast habits at age 16 y were associated with higher odds of MetS at age 43 y in every model (model 3 adjusted OR = 1.68; 95% CI: 1.01, 2.78) • Poor breakfast habits were significantly associated with TG levels at 43 y in the crude model and model 1, but not in subsequent models (model 1–adjusted OR = 1.83; 95% CI: 1.11, 2.99) • No associations for HDL levels
Marlatt et al, 2016, USA[93]	Cross-sectional	367 adolescents aged 11-18 y	Breakfast consumption (as average number of days per week) assessed by means of self-reported validated questionnaire.	• Fasting blood samples (HDL, LDL, TG) • Assessment of MetS cluster score using modified Adult Treatment Panel III criteria	• More frequent breakfast consumption was significantly associated with lower MetS cluster score ($P < 0.05$) • No significant association for HDL
Silva et al, 2016, Brazil[59]	Cross-sectional	708 children and adolescents aged 7-14 y	Frequency of meals assessed by means of a structured questionnaire. Frequency of meals	• Fasting blood samples (HDL, LDL, TC, TG)	• In children (5-9 y) the pattern "<4 meals" was associated with a higher prevalence of

(continued)

Table 6 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
			categorized according to the mean value as risk (<4 meals) and no risk (≥4 meals).	• LDL levels ≥100 mg/dL were considered as risk factors	increased LDL (PR = 1.48; 95% CI: 1.02-2.13; $P = 0.037$) • Also among adolescents (10-14 y), the same pattern was directly associated with increased LDL levels (PR = 1.33; 95% CI: 1.00-1.75; $P = 0.042$)
Jeans et al, 2020, USA[98]	Cross-sectional	671 students (mean age: 9 y)	Breakfast consumption, assessed via two 24-h dietary recalls, categorized into different groups (BCG) defined as: (1) skippers, having no breakfast on both recalls; (2) intermittent, having a breakfast only on one; and (3) regular, having a breakfast on both.	Fasting blood samples (HDL, LDL, TC, TG)	There were no significant relationships between breakfast consumption groups and metabolic parameters
Martínez-Lozano et al, 2020, Spain[101]	Cross-sectional	432 children and adolescents aged 8–12 y	Chronotype assessed objectively by actigraphy (recording 7-d rhythms of wrist temperature–physical activity–body position [TAP]) and subjectively (Munich-chronotype self-reported questionnaire). Food timing of meals collected by means of 7-d food diaries.	Collection of blood samples (TC and TG)	• Evening-type children had increased physical activity in the evening, higher body temperature during the day, which suggests an increase in sleepiness, less depth of sleep, lower day–night contrast, and more irregular habits • Evening-type was associated with higher metabolic risk markers such as cholesterol and TG levels ($P < 0.05$); this association persisted after adjustment • Mean values of TG were significantly higher in evening-chronotype children compared with morning-chronotype children ($P = 0.003$)
de Souza et al, 2021, Brazil[100]	Cross-sectional	36 956 adolescents aged 12-17 y	Skipping breakfast assessed by means of self-administered questionnaire. Breakfast skipping was estimated from the combination of the categories: "I don't have breakfast," "I have breakfast sometimes," and "I have breakfast almost every day."	• Anthropometric parameters including WHtR and WC • Fasting blood samples (HDL, TC, TG, and indirect assessment of LDL)	• Significant association, after adjustment, between breakfast skipping and TC • Adolescents who skipped breakfast had 14% higher prevalence of high TC than those who had breakfast every day

Abbreviations: CASPIAN-V Study, Child and Adolescent Surveillance and Prevention of Adult Non-communicable diseases Study; CI, confidence interval; CVD, cardiovascular disease; EF, eating frequency; FFQ, food-frequency questionnaire; HDL, high-density-lipoprotein cholesterol; LDL, low-density-lipoprotein cholesterol; MetS, metabolic syndrome; OR, odds ratio; PR, Prevalence Ratio; TC, total cholesterol, TG, triglycerides; WC, waist circumference; WHtR, waist:height ratio.

(prevalence ratio = 1.33; 95% CI, 1.00–1.75; $P = 0.042$). In line with previous data, although with different categorization of eating occasions, another study reported a significant association between eating behavior and LDL cholesterol.[111]

Only Martínez-Lozano et al[101] studied the association between CVD risk and chronotype/food timing in children, as previously reported. Overall, evening-type features were associated with higher metabolic risk markers such as TC and TG levels ($P < 0.05$); in fact, evening-type children had higher mean TG values compared with morning-type children ($P = 0.003$).

Association between chrononutrition and blood pressure

The associations between chrononutrition and BP in children were originally investigated in 12 studies, but after quality assessment, 2 of them were not considered acceptable to be included in this systematic review.[46,47] Of the 10 studies, 9 were cross-sectional[86–90,92,93,97,98] and only 1 study was prospective[104] (Table 7[86–90,92,93,97,98,104]). The majority of studies enrolled a large cohort of both school-aged children and adolescents, and 5 studies focused only on adolescents.[86,87,93,97,104] With regard to the exposure variable, the main outcome investigated was breakfast consumption[87,88,90,93,97,98,104]; however, 4 studies also evaluated meal frequency[86,89,92,97] and 1 study also evaluated snack consumption.[97]

Blood pressure was measured with a manual or automated sphygmomanometer; none of the studies included 24-hour ambulatory BP monitoring to assess the outcome. Generally, 2 or 3 measures were collected, and the mean value was considered. Only a few studies defined hypertension in children using percentiles,[86,87,90,92,97] and this was considered in the quality assessment.

With regard to breakfast consumption, 2 studies showed lower SBP levels in regular breakfast consumers (P for trend < 0.01 and <0.02 in Shafiee et al[87] and Donin et al,[88] respectively) compared with breakfast skippers. Shafiee et al did not find differences in elevated BP prevalence among groups (defined as BP ≥90th percentile for age, sex, and height),[87] while in Donin et al, the evidence of higher SBP was no longer statistically significant after adjustments.[88] Jääskeläinen et al[86] and Suhadi et al[97] found a significant association between regular breakfast consumption and BP exclusively in girls. The first showed a lower risk of hypertension only in crude analysis (OR, 0.60; 95% CI, 0.37–0.96), while the association was no longer significant after adjustments. Suhadi et al found lower DBP levels among girls only ($P = 0.004$). The only longitudinal study reported that adolescents with poor breakfast habits at age 16 years had significantly higher BP levels at 43 years in the crude model (OR, 1.66; 95% CI, 1.06–2.58) but not in subsequent analysis adjusted for confounders.[104] The other studies did not find this significant association.[90,93,98]

With regard to meal frequency, in the study of Murakami et al,[89] eating frequency was inversely associated with DBP levels ($P < 0.04$) when considering the subgroup of children identified as reliable study participants. In overall analysis, there was no significant association between BP and eating frequency. By evaluating a specific number of eating occasions, Kelishadi and colleagues[92] found that subjects with an eating frequency of 3 or fewer times per day were more likely to have higher DBP and SBP compared with those with an eating frequency of 6 or more times daily ($P < 0.001$), regardless of gender. Moreover, in crude analysis, lower odds of elevated BP (defined as values ≥90th percentile for age, sex, and height) were observed among those who had a higher eating frequency (5 or ≥6 a day) than those with fewer eating episodes (≤3 a day); however, associations were no longer significant after further adjustment for covariates. On the contrary, Suhadi et al[97] did not find significant associations between meal frequency, or snack frequency, and BP in children. On the other hand, no study assessed the impact of food timing and chronotype on BP outcome.

DISCUSSION

Main findings

To our knowledge, this is the first systematic review to investigate the association between chrononutrition in children and adolescents and OW/OB or a cluster of metabolic abnormalities related to glucose and lipid metabolism, BP, or CVD risk. The results of the present review suggest that children/adolescents who do not eat breakfast daily are more likely to be overweight or obese compared with those who daily consume it. However, these results require cautious interpretation due to the high heterogeneity in meta-analysis. In addition, statistical evidence of a higher risk of abdominal obesity (defined as WHtR ≥0.5) with irregular breakfast consumption (0 to 3 d/wk) compared with regular breakfast habits (5 to 7 d/wk) in children/adolescents was found, although these homogeneous results were drawn from a small number of studies ($n = 3$). More convincingly, the present review demonstrates the preventive role against OW/OB of a higher meal frequency (≥4 times/d) with respect to a lower consumption of meals (≤3 times/d). Nevertheless, considering the majority of cross-sectional studies and the limited number of cohort studies, the overall certainty of the evidence was low according to the GRADE rating scale.

Table 7 **Studies included in the qualitative synthesis for outcome D, "blood pressure"**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
Jääskeläinen et al, 2013, Finland[86]	Cross-sectional	6247 adolescents, 16 y old	Meal frequencies and breakfast consumption assessed by means of 5-item self-administered questionnaires on meal patterns. Classified into 2 groups according to meal consumption: 5 meals/d including breakfast (regular meal pattern) or ≤4 meals/d (meal skipping); the latter including both regular breakfast eaters (semi-regular meal pattern) and breakfast skippers (breakfast skipping).	Blood pressure was measured using an oscillometric pressure meter and the mean of 2 subsequent measures was taken. Elevated BP has been diagnosed with SBP ≥130 mmHg or DBP ≥85 mmHg.	• The semi-regular meal patter (ie, meal- skipping combined with regular breakfast) was associated with a lower risk of hypertension in girls (OR: 0.60; 95% CI: 0.37-0.96) compared with the "breakfast skippers" pattern • In adjusted analysis for early-life factors, this finding remained significant (OR: 0.55; 95% CI: 0.33-0.93), although, in adjusted analysis for adolescents' factors, the association was no longer significant (OR: 0.65; 95% CI: 0.37-1.13)
Shafiee et al, 2013, Iran[87]	Cross-sectional	5625 adolescents aged 10-18 y	Breakfast skipping assessed through parental questionnaire about the weekly frequency of breakfast consumed at home. Seldom breakfast eaters have breakfast ≤2 times/wk, while regular breakfast eaters have breakfast ≥6 times/wk.	Blood pressure was measured using sphygmomanometer 2 times and the mean of 2 subsequent measures was considered. Elevated BP—either SBP or DBP—at or above the 90th percentile for age, sex, and height.	• SBP was significantly higher in the "seldom breakfast eater" group than in the "usual breakfast eater" group (P for trend < 0.01) • No significant difference in elevated BP prevalence among groups ($P = 0.09$)
Donin et al, 2014, United Kingdom[88]	Cross-sectional	4116 schoolchildren aged 9-10 y	Breakfast consumption assessed by means of self-administered questionnaire. Groups of breakfast consumption were breakfast daily, most days, some days, and not usually.	Blood pressure was measured twice with a professional sphygmomanometer.	• SBP was lower among children who reported eating breakfast every day (P for trend = 0.02), while results did not show significant differences in DBP among groups ($P = 0.28$) • However, after adjustments for socioeconomic status and sum of skinfolds and fat mass index, the evidence of higher SBP among breakfast consumers was no longer statistically significant ($P = 0.25$)
Murakami and Livingstone, 2014, United Kingdom[89]	Cross-sectional	1636 children in total ($n = 818$ children aged 4-10 y and $n = 818$ adolescents aged 11-18 y)	Eating frequency (EF) derived from the 7-d dietary records kept by children's parents or children themselves. Eating occasions were defined as any occasion when any food or	Blood pressure was measured using the Dinamap 8100 oscillometric monitor 3 times. The measurement is the mean between the second and third measurements taken.	• Higher EF was not associated with all metabolic risk factors examined, including BP. In fact, associations of EF with SBP and DBP in both children and adolescents had P values >0.05.

(continued)

Table 7 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
			drink was consumed, both in and out of home. Subjects were identified as acceptable reporters (AR), underreporters, or overreporters of EI based on their ratio of EI to EER.		• In analysis in which only AR children were included ($n = 636$), EF was inversely associated with DBP ($P < 0.04$).
Wennberg et al, 2015, Sweden[104]	Longitudinal population-based cohort	889 16-y-old adolescents with 27-y follow-up (43 y)	Breakfast skipping at 16 y was assessed by means of a questionnaire ("What did you have for breakfast this morning?"). The group "Poor breakfast habits" was defined as those reporting not eating anything or only drinking or eating something sweet.	Blood pressure in 43-y-old participants was measured with a standard sphygmomanometer and the average value of 2 subsequent measures was taken.	In separate analysis of components of metabolic syndrome, adolescents with poor breakfast habits at age of 16 y have significantly higher BP levels at 43 y in the crude model (OR: 1.66; 95% CI: 1.06-2.58), but not in subsequent analysis adjusted for cofounders.
Ahadi et al, 2015, Iran[90]	Cross-sectional	13 486 children aged 6-18 y	Breakfast skipping assessed orally by trained interviewers. Breakfast skippers have breakfast ≤2 d/wk; semi-skippers, 3-4 d/wk; and non-skippers, ≥5 d/wk.	Blood pressure was measured using sphygmomanometer and the average value of 2 subsequent measures was considered. BP was categorized into 3 groups: normal pressure (<90th percentile), prehypertension (>90th percentile), and hypertension (>95th percentile).	• Blood pressure did not differ significantly between breakfast eaters and breakfast skippers ($P = 0.1$) • Breakfast consumption did not affect the risk of elevated BP
Marlatt et al, 2016, USA[93]	Cross-sectional	367 adolescents aged 11-18 y	Breakfast consumption assessed by means of self-reported validated questionnaire, expressed as average number of days/week that breakfast was consumed.	Seated BP was measured 3 times with a sphygmomanometer and the values averaged.	Elevated BP was not associated with breakfast consumption
Kelishadi et al, 2016, Iran[92]	Cross-sectional	14 880 children and adolescents, aged 6-18 y	Eating frequency (EF) categorized into four groups as EF ≤ 3, EF = 4, EF = 5, and EF ≥ 6, according to parental report about the consumption frequency of meals and snacks.	Blood pressure was measured using a sphygmomanometer 2 times within 5 min and the average was considered as the actual value. Diagnosis of elevated BP in children was based on the 90th percentile of the distribution of SBP and/or DBP according to gender, age, and height.	• Subjects with EF ≤ 3 were more likely to have higher DBP and SBP compared with those who had EF ≥ 6 daily ($P < 0.001$), regardless of gender. • Subjects with EF ≤ 3 were more likely to have higher DBP compared with those who had EF ≥ 6 daily ($P < 0.001$). • In crude analysis, lower odds of elevated BP were observed among those who had higher EF (EF = 5/≥6) than those with

(continued)

Table 7 **Continued**

Reference	Study design	Population	Exposure variable and assessment	Outcome and methods	Main results
					fewer eating episodes (EF $\leq$ 3) (EF = 5: OR, 0.68; 95% CI, 0.49-0.94; EF $\geq$ 6: OR, 0.69; 95% CI, 0.51-0.95); however, associations were no longer significant after further adjustment for potential covariates.
Jeans et al, 2020, USA[98]	Cross-sectional	671 students (mean age: 9 y)	Breakfast consumption, assessed via two 24-h dietary recalls. Breakfast consumption groups (BCGs) defined as: skippers, having no breakfast on both recalls; intermittent, having a breakfast only on 1 recall; and regular, having breakfast on both recalls.	Blood pressure was measured via an automated monitor.	No significant relationship was found between BCG and BP.
Suhadi et al, 2020, Indonesia[97]	Cross-sectional	768 adolescents aged 14-18 y old	Eating behaviors were collected from a face-to-face written interview. In particular. frequency of meals ($\leq$3 or $>$3 times/d), breakfast consumption (always/frequent and rare/never), and snack frequency ($\leq$3 and $>$3 times/d) were assessed.	Blood pressure was measured with a professional sphygmomanometer and heart rate was also collected. Blood pressure was considered normal ($<$90th percentile), prehypertension (90–$<$95th percentile), stage I hypertension (95th percentile to $<$stage II threshold), and stage II hypertension (99th percentile plus 5 mmHg). Meanwhile, SBP/DBP was also classified by normal absolute BP $<$120/$<$80 mmHg according to the 2017 ACC/AHA hypertension guideline, and the heart rate threshold was $<$100 times/min.	• Female subjects with routine breakfast had lower DBP ($P = 0.004$) • SBP was not significantly associated with snack or meal frequency and breakfast consumption • Heart rate was not affected by snack or meal frequency or breakfast consumption

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Assocation; BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; EER, estimated energy requirement; EI, energy intake; OR, odds ratio; SBP, systolic blood pressure.

Apart from overweight and obesity parameters, it was not possible to conduct a synthesis of the results for other clusters of metabolic alterations. This systematic review shows that the current documented evidence regarding the association between chrononutrition and metabolic parameters in children and adolescents is limited and heterogeneous. Data on chrononutrition in the pediatric age group are fragmented, as no study has evaluated chrononutrition as a whole dimension comprising multiple aspects of feeding behavior (regularity of meals, frequency, and timing).

Regularity in meals: breakfast consumption

This systematic review confirms with more recent data and strengthens the evidence previously reported on breakfast consumption in the pediatric age group.[10,113–115] Overall, irregularity in meal consumption, particularly breakfast skipping, was the dimension of chrononutrition most studied in the present review. Meta-analyses showed that non–daily breakfast consumption ($\leq$6 d/wk) or irregularity in breakfast habits (consumption 0–3 times/wk) were associated with a higher risk of OW/OB or abdominal obesity (WHtR $\geq$ 0.5) compared with daily and regular breakfast consumption, respectively. In the narrative synthesis, regular breakfast consumption was associated with glycemic control and lowering of at least 1 lipid marker (TC, TGs, LDL cholesterol). Moreover, in some studies, breakfast skipping showed a positive association with MetS scores. The positive effects were reported not only for regular breakfast habits but also in the case of changes in one's habits. For example, increasing the number of breakfast occasions was associated with lower fasting insulin and HOMA-IR values.[109] With regard to the association with HDL-cholesterol values and BP, results lacked consistent associations.

According to the European Society of Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN), skipping breakfast may be a useful predictor of the risk of OW/OB, even if the mechanism of excess weight may be because of a higher energy intake during the following hours in children who skipped breakfast.[116] Skipping breakfast is associated with obesity, possibly because of its role in energy balance and dietary regulation. People who skipped breakfast experience a longer period of fasting and a modification in the release of appetite regulation hormones. According to authors, a morning meal can influence satiety and glucose-regulatory hormones—namely PYY—which, in turn, impact appetite throughout the day.[114,117] Hence, breakfast skippers are more likely to crave high-caloric foods than low-caloric alternatives,[118] and the consequent effects on daily energy intake have been discussed.[114,118]

Eating habits seem to be closely connected to individual chronotype. Individuals with "early" and "neutral" chronotypes show, as a common trait, regular breakfast consumption, while people with late chronotypes usually skip breakfast.[119–122] According to authors, evening-chronotype individuals show a delay in the circadian rhythm and in the release of appetite-regulating peptides, which, in turn, results in reduced hunger stimulation in the morning.[123] Sleep patterns are another important issue associated with breakfast habits. In fact, late chronotypes usually go to sleep late and wake up later during the day, which can lead to the tendency to skip breakfast.[119,120] In children, the morning chronotype is prevalent, with a shift toward eveningness during puberty; thus, strategies to counteract circadian misalignment are of great interest.[115]

Authors have speculated that eating at the "wrong" time of the day, particularly skipping meals such as breakfast, desynchronize circadian rhythms, with impacts on metabolic health.[113,121,124] Misalignment of behavioral and circadian cycles induced adverse metabolic consequences. Evidence from randomized controlled trials on healthy individuals showed that regular daily breakfast eaters maintained a more stable glucose response during the afternoon and evening compared with breakfast skippers.[125,126] Authors have reported breakfast skipping as being also detrimental for insulin sensitivity.[13,126,127] More interestingly, the potential implication of breakfast skipping has been broadened to include clock-controlled gene expression. Results suggest that breakfast consumption is of high relevance for preserving clock gene activity and the correlated postprandial glycemic response in both healthy individuals and patients with diabetes.[128]

However, few authors have looked further into the role of breakfast consumption focusing on its nutritional composition. Previously, authors have reported ready-to-eat cereal as the most frequent food consumed at breakfast and its consumption was associated with a healthier diet; nevertheless, it might be refined with added sugars.[129] In line with this, a recent longitudinal multicenter study from 5 European countries referred to breakfast quality as an important issue. In fact, among all of the eating occasions, breakfast was characterized by the largest consumption of high-sugar-content products.[130] In a recent systematic review of randomized controlled trials, Ricotti et al[115] showed that interventions aimed at increasing breakfast consumption in children and adolescents are effective strategies for improving nutrition education and quality. However, data are scarce regarding the impact of breakfast quality on pediatric metabolic health.

Eating breakfast regularly was described as a marker of health, but collinearity with potential confounding factors has to be addressed. In fact, the observed beneficial effects of consuming breakfast might only reflect a healthy lifestyle per se—for example, breakfast skippers are more likely to be physically inactive than breakfast eaters[118] and showed lower adherence to the Mediterranean diet.[131] Overall, breakfast consumption is an indicator of a general health-promoting lifestyle and behaviors.

Meal and snacking frequency

A higher eating frequency, maintaining the same energy intake, seems to contribute to a healthy cardiometabolic state in children and adolescents.[68] In particular, a large number of the studies analyzed confirmed the positive relationship that exists between lower daily eating frequency and the higher risk of developing OW/OB. In the narrative synthesis, a negative correlation between the number of eating occasions per day and TC, LDL cholesterol, and TGs has been reported, while a positive association with HDL cholesterol has been documented. Moreover, one can speculate about the possibility of an inverse relationship between eating frequency and DBP and SBP levels in children, although results were contrasting. No relationship has been documented between the number of eating occasions and glucose metabolism. Several pathways might explain the association between a lower eating frequency and an unfavorable cardiometabolic state. Theoretically, there is a direct relationship between eating frequency and metabolism activation with increasing satiety and improvement in glucose and insulin metabolism.[132,133] In a randomized crossover trial involving normal-weight women, meal regularity was associated with a greater thermic effect of food and lower glucose response, with a favorable effect on metabolic health.[134] Additionally, eating frequency seems to be positively associated with levels of physical activity and with an improved composition of snacks and breakfast, in terms of fruit and vegetables, fats, fiber, and carbohydrates, in healthy-weight children aged 9–10 years.[135] Conflicting, and sometimes contradictory, findings have been reported on the associations of eating frequency with metabolic risk factors by varying age groups. Authors reported a positive association between eating frequency and BMI z score (but not with WHtR) in adolescents but not in children.[89] The explanation could lie in the strong association that exists between eating frequency and energy intake, which has also been observed in adults.[136–138] Previous studies have shown that children are generally good energy compensators, although this ability declines with age,[139] which might explain the positive association in adolescents but the null association in children. However, there are differences in eating frequencies (meals and snacking) and dietary habits across different ages. In fact, young children spend a large part of their day in school with structured meal and snack times. It is only when children are in junior high school and high school that they can purchase food more freely at will and may opt not to eat at all during the morning and early afternoon but focus their consumption patterns to the latter part of the day,[51] with a consequent increase in the risk of becoming overweight/obese.

In parallel, a small variation in eating frequency was associated with lower TC and LDL cholesterol in children but not in adolescents,[91] which agrees with previous results reported in intervention trials involving both lean and obese adults.[133, 140] Lower TC and LDL-cholesterol levels in individuals with a regular eating frequency might be a consequence of a lower insulin stimulus to hydroxyl-methyl-glutaryl Co-A reductase, one of the rate-limiting enzymes in cholesterol synthesis, or enhancement of reverse cholesterol transport.[141] It is not clear why this association has been documented only in children but not in adolescents. However, it might be related to the higher mean values and variations in blood lipids in children or to inaccurate dietary information provided by adolescents.[89]

Snacking frequency is relevant for weight status, particularly among young children. The relationship existing between snacking and cardiometabolic risk is influenced by the amount of snack consumed and the quality or type of snack. Snack quality is a matter of concern since snack foods are enriched in fats and energy dense and the unregulated consumption of snack foods could increase energy intake beyond the needs for energy expenditure and promote weight gain and an altered lipid profile. Although the influence of snacking on weight status seems to be clear, it is not possible to establish if there is reverse causality of overweight or obesity status in children and a higher frequency of snack consumption. Certainly, it has been observed that children with greater weight have higher levels of appetitive traits that facilitate excessive intake of energy-dense snacks in the absence of hunger.[142] These traits may increase the susceptibility of some children to become obese.[143,144] However, experimental and longitudinal studies are necessary to evaluate if there is a causal relationship between snacking, child appetite, and weight outcomes. However, the regular intake of snacks may be a strategy to manage weight by the replacement of fats with carbohydrates. Furthermore, regular snack consumption seems to improve diet quality[145–147] and to increase the consumption of fruit, whole grains, and fiber,[145,146] favoring satiety and therefore reducing risk of obesity. Notably, like eating frequency, snacking was also associated with increased physical activity, which compensates for the calories introduced with snacks.[148,149]

Overall, defining the optimal frequency of meals and snacks for promoting healthy growth in pediatric subjects is challenging. According to ESPGHAN recommendations for the prevention of OW/OB, children up to the age of 12 years are encouraged to eat at least 5 meals per day, including a midmorning and a midafternoon snack.[116] Whether eating 6 or more meals per day provides an additional contribution remains to be elucidated, as do the recommendation for older children.[116] Further research is needed to understand whether other dimensions (eg, quality, time of day) or patterns of eating may influence the cardiometabolic state in children and adolescents. One of the limitations in comparing studies on eating frequency/snacking is the lack of consensus on the definition of regular number of eating occasions or meals. Furthermore, many studies that limited their discussion to meals and snacks were underreported.[150] Nevertheless, the exclusion of snacks from the diet might underestimate the overall energy and macronutrient intakes, especially for very young children in whom snacks contribute a large portion of total daily energy intake.[151,152]

Meal timing

Studies on meal timing in children are scarce and a consensus does not exist on the correct time of day for main meals to reduce the risk of obesity and its related complications in the pediatric population. Despite the small numbers of articles evaluating this dimension of chrononutrition, it has been postulated that eating late in the evening is associated with a greater risk of poor cardiometabolic health,[153] with an unfavorable impact on weight status and lipid profile. No studies have evaluated the relationship that exists between time of food intake and BP, while 1 study observed high levels of insulin and glucose in salivary samples of late dinner eaters. However, a recent meta-analysis found a low quality of evidence between OW/OB in those who ate later in the evening compared with those who ate earlier, with a pooled OR of 1.04 (95% CI, 0.68– 1.61).[12] This is a matter of concern considering that unhealthy dietary habits, such as late-time eating, established in early childhood tend to persist to older age and may thus adversely affect long-term health.[154] In adults, late eating, defined as a delayed timing in the main meal or the last meal consumption, was recently shown to be associated with hyperglycemia,[155] impaired glucose tolerance,[156] and increased risk of poor cardiometabolic health.[157]

Different factors could be implicated in these complex relationships. Energy homeostasis is influenced by circadian rhythms of wakefulness and sleep. The circadian misalignment, caused by eating and sleeping more than 12 hours out of the habitual time phase, leads to altered leptin release, increased glucose and insulin levels, and appetite and energy imbalance.[13,14] Eating late in the evening might influence sleep patterns[158] and promote late bedtimes,[159,160] causing sleep deprivation and a consequent increase in ghrelin secretion and an inhibition in leptin secretion, responsible for greater energy intake.[161] Additionally, under conditions of sleep deprivation, late-type individuals can extend the time available to eat and consume meal or snacks at a later time, which may be associated with less satiety.[162]

It is reasonable to suggest that late eating behavior could influence the circadian rhythm of cortisol release, reducing the amplitude of its daily pattern. Cortisol, also known as the stress hormone, follows a circadian rhythm, with a peak in the morning. It is an indicator of the internal clock, regulating energy and metabolic processes,[163] but also behavioral and environmental factors.[164] Daily lower amplitude values of cortisol may be a marker of circadian system alterations in children who eat late at night.[165,166] In fact, late-dinner-eating children might fail to achieve the peak of cortisol in the morning and the intake of breakfast takes place in an earlier circadian phase for these children,[5] altering the appetite and the possibility to consume an adequate energy intake.[167] The reduction in appetite in the morning and evening is also responsible for a misalignment in circadian rhythm, altering hunger and appetite relative to clock time.[168,169] Late eating may lead to an uncoupling of these biological clocks,[170] inducing metabolic imbalances in children.[156,170] This suggests that there is an internal stimulus on the time to eat meals during the day.[171] In addition, different chronotypes influence the body's metabolic response.[172–174] Last, it has been reported that the fasting period during the night induces both fat metabolism and the metabolic switch between glucose and fat oxidation.[175,176]

Considering the close association between obesity and late eating and simultaneously the high rate of proinflammatory cytokine release in obese individuals, a possible role of inflammatory markers in generating a dysmetabolic state in individuals who eat dinner late has been suggested. Although Martínez-Lozano et al[99] found higher levels of CRP and IL-6 in late eaters than in early eaters, these results have no explanation in terms of cardiovascular risk. In fact, high levels of CRP have been reported in association with MetS in children, but it is not yet clear if its levels might be correlated with cardiovascular complications.

Finally, cultural and geographic differences may have a role in generating contrasting results.[177,178] Examining children and adolescents aged 2–18 years, Eng et al[51] documented that late eating was associated with obesity in the entire age group. Conversely, Coulthard et al[58] did not find any connection between eating after 20:00 and the risk of obesity in UK children. The reason could rely in the different cutoff used to define late eating. In particular, Martínez-Lozano et al[99] considered the median values of time of dinner, identifying late dinner eating for children who ate late dinner at 21:00, 1 hour later than the time set by Coulthard et al. Certainly, the geographical area of the world influences the time clock. To overcome this issue, a median clock time should be considered for each population analyzed, with the aim to obtain more generalized and comparable results.

Limitations and strengths

In the present review, no intervention studies or trials were found for any of the outcomes considered. Approximately 80% had a cross-sectional design, while the remaining were longitudinal population-based cohort studies. As a result, it is not possible to establish a causal relationship between the exposure and the outcome analyzed. Overall, the strength of the evidence was low due to the observational design of all included studies, with the majority of them having a cross-sectional design.

Among the limitations of the present review, it was not possible to conduct the meta-analysis for all of the exposure variables and the related outcomes. In fact, not all of the studies were eligible to be included, due to insufficient data or the impossibility of being categorized according to the selection criteria for the meta-analysis. Another limit was the high heterogeneity observed for the meta-analysis related to daily breakfast consumption and OW/OB in children. Despite the strict criteria applied for eligibility of studies in the data synthesis, high heterogeneity, driven by an inconsistent definition of the category "breakfast consumption," was observed. Moreover, heterogeneity could also be attributed to variability in age, type of adjustments across studies, and type of cohorts, which were extrapolated from wide population studies from several geographical areas. Overweight/obesity assessments varied across studies, and they would be more comparable if only 1 generally accepted international criteria for OW/OB was applied, such as International Obesity Task Force or WHO cutoffs.

In addition, methodological differences between studies might explain the results, particularly the broad variety of methods of dietary assessment. Most studies were performed using 24-hour dietary recalls and questionnaires, which are subjective and dependent on the memory and motivation of study participants or their parents. To assess the exposure, some of the studies used qualitative and unspecific categories (usually, often, etc) and others studied the frequency of consumption (1–2 times/wk or day, 3–4 times/wk or day, etc), making comparisons among the studies difficult. Sometimes the dietary history was collected with validated semiquantitative or qualitative methods (food diaries, validated questionnaires for pediatric age). However, nutritional assessment is always challenging, with varying degrees of reliability, and needs careful handling. In addition, the lack of universal and accepted definitions of breakfast skipping, number of eating occasions, snack consumption, or timing of eating limits the comparisons between the studies. To overcome this issue, it might be reasonable to refer to a standardized definition of meals and eating occasions to better analyze data. For this purpose, the American Heart Association recently proposed the definition of breakfast as "the first meal of the day breaking the fast after the long period of sleep". It consists of food or drink of at least 1 food group eaten within 2 to 3 hours of waking. Instead, the term "other meals" has been defined as any consumption occasion that provides more than 15% of the total energy intake, while the term "snack" has been assigned to all eating occasions providing less than 15% of total energy intake.[153]

Nevertheless, this review also has some strengths. The main strength of the present review is the inclusion of all of the dimensions of chrononutrition. This is the first study carrying out a comprehensive analysis of the association between regularity of meals, frequency of meals per day, or timing of food intake and cardiometabolic factors in children and adolescents. The comprehensive and extensive research of the literature enabled us to well explore the association between the exposure variables and outcomes. Moreover, a methodological quality assessment was performed, which allows the inclusion only of studies considered as having acceptable quality. In fact, approximately 12% of studies analyzed were removed because they did not meet the established cutoff of quality. Generally, the advantage of observational longitudinal studies resides in their ability to portray real-world conditions and more transferable results compared with clinical trials. Last, to ensure consistency across studies included in the meta-analysis, a specific category of exposure was strictly selected (eg, daily vs non–daily breakfast consumption, $\leq$3 vs $\geq$4 meals).

CONCLUSION

Studies currently available on chrononutrition and metabolic health status are fragmented, probably due to methodological limitations. Overall, the results of the present review suggest a potential implication of chrononutrition in affecting pediatric metabolic health; however,

Table 8 **Recommendation for future research on chrononutrition**

Recommendations for future research
1. Standardization of the categories "breakfast skipping," "snack frequency," and "time of eating"
2. Going beyond the single exposure of 1 dimension of chrononutrition and exploring the joint impact of multiple exposures
3. Proposal of a nutritional assessment method that evaluates chrononutrition comprehensively (eg, rest hours, time of food consumption, length of fasting period)
4. Definition of a pediatric score to classify children according to their chronotype
5. Intervention studies or trials evaluating the relationship between the 3 dimensions of chrononutrition and cardiometabolic risk factors

the evidence of the association was mainly limited to breakfast consumption and meal frequency. A positive association between overweight and obesity risk was observed for non-daily and irregular breakfast consumption, and also a potential preventive role of a higher meal frequency, even though our findings showed very low quality of evidence due to the observational design of the included studies. In the narrative synthesis, the association between the number of snacking occasions showed controversial results, while food timing was the most understudied dimension of chrononutrition. The study of chrononutrition in the promotion of a healthy cardiometabolic state in the pediatric population deserves more attention. The definition of a pediatric score to classify children according to their chronotype is a valuable strategy to accomplish our knowledge on feeding behavior health impacts (Table 8). Further well-designed prospective and intervention studies addressing the limitations reported in the present review are required to clearly define the association between chrononutrition and pediatric metabolic health.

Acknowledgments

Author contributions. All authors meet full criteria for authorship, and each author participated in the reading and approval of the final manuscript; their respective roles in the submitted work are as follows—G.F.: project administration, investigation, and resources; writing original draft; review and Editing; S.S.: investigation and resources, writing original draft, participated in the manuscript review process; C.R.N.: investigation and resources, writing original draft, participated in the manuscript review process; H.A.: formal analysis, critical revision of the manuscript; M.E.-M.: data administration, review and editing; M.C.P.: investigation and resources, writing original draft, participated in the manuscript review process; A.L.M.: investigation and resources, writing original draft, participated in the manuscript review process; C.M.: methodology, review, and editing; F.C.: methodology, supervision and conceptualization, critical revision of the manuscript; C.C.: methodology, review, and editing; G.Z.. supervision and conceptualization, critical revision of the manuscript; E.V.: methodology, review and editing, supervision and conceptualization.

Funding. No external funding was received to support this work.

Declaration of interest. The authors have no relevant interests to declare.

Supporting Information

The following Supporting Information is available through the online version of this article at the publisher's website.

Figure S1 **Quality assessment of studies included in narrative synthesis**

Figure S2 **Sub-meta-analyses for the exposure breakfast consumption in overweight/obesity outcome**

Figure S3 **Sub-meta-analyses for the exposure meal frequency in overweight/obesity outcome**

Figure S4 **Subgroup meta-analysis among European countries for the relationship overweight/obesity and breakfast consumption**

Table S1 **PRISMA 2020 checklist (template available at** http://www.prisma-statement.org/PRISMAStatement/Checklist.aspx)

Table S2 **Quality assessment of articles excluded from the systematic review**

Table S3 **Reasons for exclusion from the meta-analysis evaluating the effect of "breakfast consumption" on the outcome of overweight/obesity (group A) defined according to BMI**

Table S4 **Reason for exclusion from the meta-analysis evaluating the effect of "breakfast consumption" on the outcome of overweight/obesity (group A) defined according to anthropometric parameters and body composition**

Table S5 **Reason for exclusion from the meta-analysis evaluating the effect of "meal frequency" on the outcome of overweight/obesity (group A) defined according to BMI**

Table S6 **Reason for exclusion from the meta-analysis evaluating the effect of "snack frequency" or** "meal timing" on the outcome of overweight/obesity (group A) defined according to BMI

Table S7 Reason for exclusion from the meta-analysis evaluating the effect of "meal frequency," "snack frequency," and "meal timing" on the outcome of overweight/obesity (group A) defined according to anthropometric parameters and body composition

Table S8 Reason for exclusion from the meta-analysis evaluating the effect of "breakfast consumption," "meal frequency," "snack frequency," and "meal timing" on the outcome glucose metabolism (group B)

Table S9 Reason for exclusion from the meta-analysis evaluating the effect of "breakfast consumption," "meal frequency," and "meal timing" on the outcome lipids and CVD risk (group C)

Table S10 Reason for exclusion from the meta-analysis evaluating the effect of "breakfast consumption," "meal frequency," and "meal timing" on the outcome blood pressure (group D)

Table S11 List of adjustments according to articles

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