Review

Association between Breakfast Skipping and Body Weight – a Systematic Review and Meta-Analysis of Observational Longitudinal Studies

Julia Wicherski [1], Sabrina Schlesinger [2] and Florian Fischer [3,4,*]

1 School of Public Health, Bielefeld University, Bielefeld, Germany; julia.wicherski@bfarm.de
2 Institute for Biometry and Epidemiology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University, Düsseldorf, Germany; sabrina.schlesinger@ddz.de
3 Institute of Public Health, Charité – Universitätsmedizin Berlin, Berlin, Germany; florian.fischer1@charite.de
4 Institute of Gerontological Health Services and Nursing Research, Ravensburg-Weingarten University of Applied Sciences, Weingarten, Germany; florian.fischer@rwu.de
* Correspondence: florian.fischer1@charite.de; Tel.: +49(0)751-501-9441

Abstract: Globally, increasing rates of obesity are one of the most important health issues. The association between breakfast skipping and body weight is contradictory between cross-sectional and interventional studies. The systematic review and meta-analyses aim to summarize this association based on observational longitudinal studies. We included prospective studies on breakfast skipping and overweight/obesity or weight change in adults. Literature was searched until September 2020 in PubMed and Web of Science. Summary RRs with a 95% CI were estimated in pairwise meta-analyses by applying a random-effects model. In total, 9 studies were included in the systematic review and 6 of them were included in the meta-analyses. The meta-analysis indicated an 13% increased RR for overweight/obesity when breakfast was skipped on ≥ 3 days per week compared to ≤ 2 days per week (95% CI: 1.06, 1.21, n=3 studies). The meta-analysis on weight change displays a 21% increased RR for weight gain for breakfast skippers compared to breakfast eaters (95% CI: 1.05, 1.40, n=2 studies). The meta-analysis on BMI change displayed no difference between breakfast skipping and eating (RR=1.02, 95% CI: 0.99, 1.05, n=2 studies). This study provides low meta-evidence for an increased risk for overweight/obesity and weight gain for breakfast skipping.

Keywords: breakfast skipping; overweight; obesity; weight gain; BMI change; systematic review; meta-analysis; observational longitudinal studies

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1. Introduction

Nowadays, the world is experiencing an obesity epidemic. In 2016, 39% of adults were overweight and 13% were obese, worldwide. Thus, obesity's prevalence is threefold higher than in 1975 [1] and it is still rising. For example, the prognosis for the United Kingdom (UK) estimates that a share of 60% of men and 50% of women will be obese by 2050 [2]. Globally, this rapid increase of overweight and obesity is one of the most important health issues [3,4].

Obesity is a major contributor to the global burden of disease through its deuteropathies of serious non-communicable diseases (NCDs) [5]. Psychological, pulmonary, orthopaedical, cardiovascular, metabolic, reproductive, and oncological diseases are attributable to obesity [6–11]. Therefore, obesity may cause premature death. It contributed to 4 million deaths what is equal to a share of 7.1% of all-cause mortality in 2015, worldwide [5]. Furthermore, there is a huge economic and social burden of obesity. Total health costs and drug costs increase with increasing body mass, which is proportionally beyond their standard values. Obesity correlates to a low socioeconomic status, as well [12–18].

The underlying pathological process of obesity is the increase of both the total number and size of fat cells which leads to a heightened accumulation of fat cells for one's body size [6,19]. Overweight is defined as elevated body fat accumulation while obesity defines the situation of excessed body fat mass [1,20,21]. The most common used measurements to assess the human body size are anthropometric measures (e.g. body mass index [BMI] or waist-hip ratio [WHR]) and measures of body composition (e.g. bioelectrical impedance analysis [BIA] or dual-energy x-ray absorptiometry [DEXA]). However, there are far more methods to assess human's body weight status [22–26].

The etiology of obesity is multifactorial, but the fundamental determinant is the positive energy balance. The latter is mostly determined by a high energy intake through inappropriate nutrition and a low energy expenditure through physical inactivity [20,21]. Breakfast is usually the meal eaten after the longest period with an empty stomach [27] and it has the potential to decrease the risk of weight gain due to several metabolic mechanisms [28]. Additionally, international recommendations on breakfast are agreed in their statement that a daily breakfast consumption is advisable for providing a sufficient intake of macro- and micronutrients, maintaining body weight, and improving cognitive functions [29–33]. By contrast, breakfast skipping is associated with elevated plasma lipoproteins and fasting glucose [17,33], and insufficient intakes of micronutrients [34].

Considering the huge medical, financial, and social burden of obesity, this study aims to examine whether breakfast skipping is associated with adult's body weight. Existing systematic reviews and meta-analyses of this topic examined the target groups of children and adolescents in all study designs [35–47], but for adults only in cross-sectional [48–50] and interventional study designs [51–58]. Interventional studies comprise the highest level of evidence but are limited to comparably young and healthy participants analyzed in small sample sizes under laboratory conditions. For that reason, this systematic review and meta-analysis is based on primary studies using observational longitudinal study designs, to gain further evidence with high external validity.

2. Materials and Methods

A systematic review and subsequently meta-analyses were conducted. The study was planned and conducted in accordance to the "Meta-analysis Of Observational Studies in Epidemiology" (MOOSE) standards [59]. The systematic literature search, the screening of identified literature, data extraction and quality assessment have been carried independently out by two reviewers (JW, FF). There have been no discrepancies in judgements between the two independent reviewers.

2.1 Search Strategy

According to the PICO framework, the population of interest was all adults aged 18 years or older, worldwide. The exposure of interest was breakfast skipping. This was compared to breakfast eating in regarding the occurrence of overweight or obesity or weight gain, respectively. The literature review was conducted in PubMed and Web of Science and included all literature related to the topic published until September 2020.

Studies included were from observational longitudinal study design and had specified effect estimates expressed as risk ratios (RRs) such as odds ratios, hazard ratios, or relative risk, respectively. These RRs are reported with the corresponding 95% confidence interval (95% CI). Alternatively, instead of RRs, the included studies reported a coefficient with the corresponding 95% CI, in case regression models contained a linear term such like continuous variables for breakfast frequency and/or BMI. Participants of included studies were aged ≥ 18 years. The outcome was measured through BMI, WC, WHR, WHtR, BF%, or weight change (gain or loss). The included studies were published/peer-reviewed articles in English or German language. Studies were excluded if the study was an interventional study, a cross-sectional study, case studies or case reports. Likewise, studies were excluded if they did not have specified effect estimates expressed as RRs or coefficients. Participants of excluded studies were aged < 18 years (e.g. children, adolescents) or were pregnant.

The following query was used for PubMed: "((((((breakfast* OR "breakfast skipping" OR "breakfast frequency" OR "breakfast omission" OR "breakfast"[Mesh] OR ((breakfast* AND (skipp* OR frequen*

OR omit* OR omis* OR consum*))) AND ("body weight"[Mesh] OR "overweight"[Mesh] OR "obesity"[Mesh] OR "body weights and measures"[Mesh] OR "body weight" OR "body fat" OR "body mass" OR *weight OR obes* OR adipos* OR "BMI" OR "WHR" OR "WC" OR "WHtR" OR waist OR circumference OR "body size" OR "body fat distribution"[Mesh]) AND (cohort* OR "cohort studies"[Mesh] OR "case control studies"[Mesh] OR "OR" OR "RR" OR "HR" OR retrospective OR prospective OR observational OR "longitudinal studies"[Mesh] OR "follow-up studies"[Mesh] OR "Observational Studies as Topic"[Mesh] OR "Observational Study"[Publication Type])))))))".

For Web of Science, the following query was utilized: "((TI=(breakfast*) AND TI=(skipp* OR omi* OR freq* OR eat*) OR (TI=("breakfast skipping" OR "breakfast omission" OR "breakfast frequency") OR TS=("breakfast skipping" OR "breakfast omission" OR "breakfast frequency"))) AND (TI=(*weight OR obes* OR adipos* OR fat OR mass OR "body weight" OR "body fat" OR "body mass") OR TS=(*weight OR obes* OR adipos* OR fat OR mass OR "body weight" OR "body fat" OR "body mass")))". Figure 1 illustrates the flowchart of this procedure of literature screening.

2.2 Data Extraction and Quality Assessment of Included Studies

Information on first author's surname, year of publication, country, study's name, design and follow-up period, number of participants in total, number of cases, distribution of sex and mean age, exposure's and outcome's definitions and measurements, specified effect estimates expressed as RRs or coefficients with the corresponding 95% CI, and adjusted covariables were extracted from each study and included in the qualitative and quantitative syntheses.

The risk of bias in included studies was assessed by applying the "Risk Of Bias In Non-randomized Studies of Interventions" (ROBINS-I) tool [60] on each study (Supplementary Appendix, Table S2). Along with the risk of bias due to confounding, age, sex, education or socioeconomic status, smoking, alcohol, physical activity and total energy intake (TEI) were established in accordance with the literature [27,29,35,61–76] as important covariables because of their confounding nature of being associated with breakfast and body weight. Moreover, the quality of evidence of the conducted meta-analyses was assessed by using the "Nutrition Grading of Recommendations Assessment, Development and Evaluation" (NutriGRADE) approach [77] (Supplementary Appendix, Table S3).

2.3 Statistical Analysis

Pairwise meta-analyses were conducted by comparing skipping breakfast on ≥ 3 days per week to≤ 2 days per week and skipping breakfast to eating breakfast without detailed category definition, respectively. The first meta-analysis for breakfast skipping focused on the occurrence of overweight (defined as BMI ≥ 25 kg/m^2) and/or obesity (defined as BMI ≥ 30 kg/m^2). The second meta-analysis for breakfast skipping versus eating breakfast focused on average weight gain defined as changes (from baseline to ≥ 5% BMI value or ≥ 5 kg body weight) in kilograms of body weight. The third meta-analysis for breakfast skipping versus eating focused on changes in BMI (change in kg/m^2).

A random-effects model was applied, because it assumed a normal distribution of the true effect and that the heterogeneity within and between the studies is caused by unexpected effects rather than residual effects [78,79]. At first, the natural logarithm of each risk estimate expressed as a risk ratio (logRR) for overweight/obesity and weight change, respectively, was calculated. Subsequently, the logRR for each included study was weighted and pooled accordingly to the variance-based method of DerSimonian and Laird [80], which considers the variability within and between the studies. In scope of the third meta-analysis, beta regression coefficients were transformed to RRs before the logRRs were calculated.

We used the I^2 test to evaluate the heterogeneity. I^2 is a measure of inconsistency which describes the variability between the studies included in the meta-analysis due to heterogeneity rather than chance [81]. According to Cochrane recommendation [82], analysis should include ≥ 10 studies to check for publication bias. Since there are merely 3 and 2 studies included in the meta-analyses, funnel plots and the Egger's test were not applied. Checking for missing studies by applying trim and fill analysis was not practicable, as well. The meta-analyses were conducted by using metan package in Stata version 16.1.

3. Results

3.1 Identified Literature and Characteristics of Included Studies

Overall, 3,294 records were obtained through database screening and additional 23 records were identified due to searching in reference lists. In scope of the inclusion criteria, 2,952 records were excluded. Out of 180 remained articles, 171 were excluded after the full-text screening. Most excluded studies had no observational longitudinal study design (n = 68), or their exposure was not matching with the corresponding inclusion criterion (n = 30). Further studies were excluded because they were published in other languages than English or German (n = 22), or either their outcome (n = 21) or both their exposure and outcome was not matching with the corresponding inclusion criterion (n = 15). Furthermore, participants were < 18 years or pregnant in 9 studies, another 4 studies specified no effect estimates or other effect estimates than required, and 2 studies were excluded because there was no full text available and their authors were not reached. Figure 1 exemplifies the literature screening process in a PRIMA flowchart.

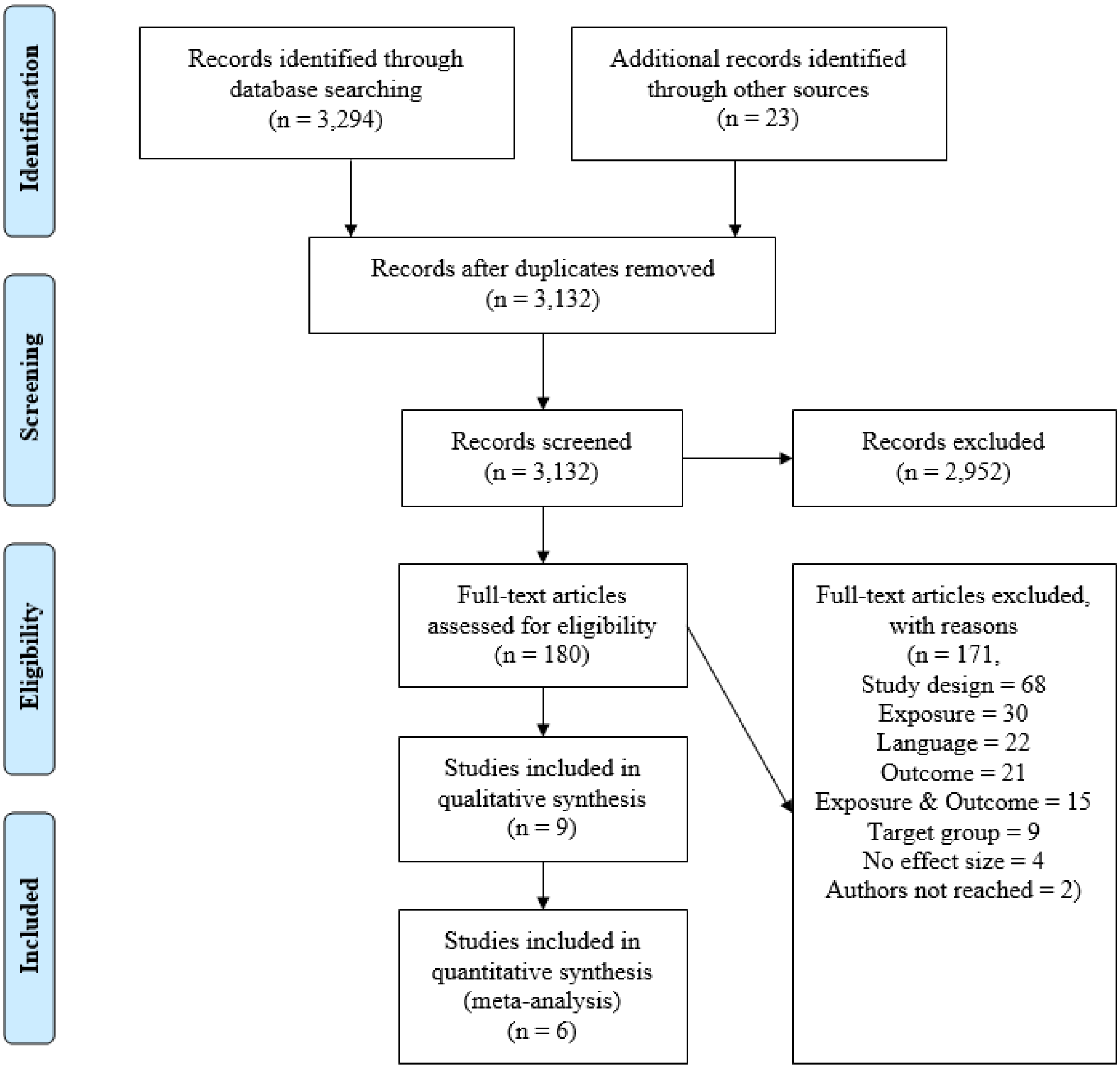

Figure 1. PRISMA flowchart [83] of the literature screening on the association between breakfast skipping and body weight

Consequently, 9 studies were included in the qualitative synthesis. As a result of this synthesis, 3 studies were not comparable in a meta-analysis due to their too different exposure or outcome categories, respectively. Accordingly, Guinter et al. [84] used the breakfast eating category of 3-4 days per week as reference and compared to 0, 1-2, 5-6, and 7 days per week. Due to this reference category, it was not practicable to pool this study result with the results of Hurst and Fukuda [32], Kito et al. [33] and Odegaard et al. [85]. In view of linear models, Nooyens et al. [86] and Smith et al. [34] were not comparable, because of their very different exposure categories: continuous breakfast frequency 0-7 days per week versus dichotomous met/not met breakfast guideline. Lastly, 6 studies were included in the quantitative synthesis consisting of 2 meta-analyses (see Figure 1). In accordance with this screening process, Table S1 in the Supplementary Appendix lists the studies excluded sorted by exclusion criteria.

The characteristics of the 9 studies included in the review are shown in Table 1. The studies were published between 2005 and 2020. They were conducted in Japan (n = 3), the USA (n = 4), Canada (n = 1), the Netherlands (n = 1) and Australia (n = 1). All 9 studies had an observational longitudinal study design and their follow-up duration ranged from 5 years to 18 years. Out of 9 studies, 3 studies were retrospective cohort studies [31–33] while the other 5 studies were prospective cohort studies [34,84–88]. In 4 studies, only male participants were involved in their analyses [31,33,86,88]. Guinter et al. [84] involved only female participants. The remaining 4 studies included both genders but proportionally, females were more represented in 3 out of these 4 studies [34,85,87]. The mean age of the participants ranged from 21.5 years to 58 years. Odegaard et al. [85], Smith et al. [34] and Nooyens et al. [86] recruited among citizens of their analyzed regions, whereby the latter study only included male citizens. Kahleova et al. [87] recruited within the Adventist church members, while van der Heijden et al. [88] enlisted male health professionals. Hurst and Fukuda [32] and Kito et al. [33] used health insurance data, whereby the latter study enlisted only male participants. Guinter et al. [84] recruited 'healthy' sisters of women diagnosed with breast cancer (healthy in the way of not having a cancer diagnosis, too).

The categorization of the exposure of breakfast skipping varied between the studies. Hurst and Fukuda [32], Kito et al. [33], and Odegaard et al. [85] defined breakfast as skipped when participants were skipping on ≥ 3 days per week, while Goto et al. [31] defined breakfast as skipped already when participants skipped breakfast on ≥ 2 days per week. Moreover, Kahleova et al. [87], Smith et al. [34] and van der Heijden et al. [88] defined breakfast as skipped or eaten without any specification of days per week. Nooyens et al. [86] used a continuous exposure variable defined as breakfast skipped on 0 days to 7 days per week, while Guinter et al. [84]used breakfast eating frequency categories like eating breakfast on 0, 1-2, 3-4, 5-6, and 7 days per week. Concerning the exposure measurement, only 5 studies used a validated tool [33,34,84–86] (see Table 2). With regard to the underlying definition of breakfast, most studies [31–33,84,86,88] reported no definition. The study by Odegaard et al. [85] reported that they did not have an explicit definition of breakfast. By contrast, Kahleova et al. [87] defined breakfast as "a meal eaten between 05:00 and 11:00", whereas Smith et al. [34] defined breakfast skipping as "not eating a snack, small meal or large meal between 6:00 and 9:00 am".

In view of the outcome, 6 studies used the BMI as their measure for body weight [31–33,84,85,87]. Out of them, Hurst and Fukuda [32], Kito et al. [33], Odegaard et al. [85], and Guinter et al. [84] used a BMI cut-off to define participants body weight as overweight or obese, respectively. Accordingly, overweight was defined as a BMI ≥ 25kg/m² in Hurst and Fukuda [32], Kito et al. [33] and Guinter et al. [84]. Obesity was defined as a BMI ≥ 30kg/m² in Odegaard et al. [85] and Guinter et al. [84]. On the other hand, Goto et al. [31], Kahleova et al. [87] and Hurst and Fukuda [32] analyzed changes in BMI values over different periods. Nooyens et al. [86], Smith et al. [34], van der Heijden et al. [88] and Guinter et al. [84] investigated the outcome of weight change by analyzing changes in kilograms of body weight over different periods. Moreover, 3 studies used the WC as an outcome measure for overweight or weight change, as well [32,85,86]. Other measures of body weight (i.e. WHtR or WHR or BF%) were not utilized in the included studies. Except for Guinter et al. [84], they utilized the measures WC and WHR, but only for cross-sectional outcomes, not for incident outcome measurement, unfortunately.

In view of the outcome measurement, in 7 out of 9 studies the outcome values were measured by trained stuff [31,33,34,84–87]. In 3 out of these 6 studies, self-reported information on weight and height were collected, additionally [34,84,87]. Guinter et al. [84] measured by trained stuff only at baseline and collected self-reported weight at baseline and follow-up. By contrast, van der Heijden et al. [88] used only self-reported weight values. Within the study of Hurst and Fukuda [32] it was not clear whether BMI and WC values were measured or self-reported (see Table 1).

In addition to Table 1, Table 2 displays the adjusted confounders of the included studies. Only in 2 studies [84,85] analyses were adjusted for all the important confounders (see Table 2).

3.2 Association between Breakfast Skipping and Body Weight

Regarding the analyzed association between breakfast skipping and body weight, all 9 studies showed an increased relative risk regarding overweight/obesity. Within this, 7 out of 9 studies reported that skipping breakfast were associated with weight gain [31–34,85,87,88]. Nooyens et al. [86] described that with increasing frequency of breakfast eating, weight was gained. Guinter et al. [84] described that eating breakfast rarely (i.e. 0 or 1-2 d/wk) and eating breakfast often (i.e. 5-6 or 7 d/wk) decreased the risk for 5-year incident weight gain, compared to having an inconsequent breakfast eating frequency (i.e. eating breakfast on 3-4 d/wk). Focusing the 7 studies with the inverse associations, 4 studies described that eating breakfast decreased the relative risk of overweight, obesity, gain of weight, BMI, or WC, respectively [32,85,87,88]. The other 3 studies described the same inverse correlation, but the other way around. Breakfast skipping increased the relative risk for overweight, obesity, gain of weight, BMI, or WC, respectively [31,33,34] (see Table 1).

In scope of increased BMI values, Guinter et al. [84] reported a 1,35 times higher relative risk for incident 5-year BMI ≥ 25 kg/m² for women who ate breakfast on 3 to 4 days per week than women who ate breakfast on 0 days per week (i.e. 1/PR = 1/0.74 = 1.35). But on the other hand, the same analysis displayed a 12% decreased risk for incident 5-year BMI ≥ 25 kg/m² for women who ate breakfast on 7 days per week, compared to women who ate breakfast on 3 to 4 days per week (i.e. PR = 0.88). Similar directions were observed for 5-year incident BMI ≥ 30 kg/m² within this analysis of The Sisters Study (see Table 1).

In view of weight change, The Sisters Study [84] displayed no association between breakfast eating frequency categories and 5-year incident ≥ 5 kg weight gain. Nooyens et al. [86] found no linear association between breakfast skipping and weight change, whereas Smith et al. [34] reported an increase in body weight when breakfast was skipped. Accordingly, people who did not meet the guidelines on breakfast (i.e. they skipped breakfast), gained in general 1.5 kg weight over a period of 5 years compared to people who met the guidelines on breakfast (i.e. they ate breakfast) [34].

Regarding measurements of abdominal obesity, WC was used in some included studies. Results of the Doetinchem Cohort Study displayed that the WC of Dutch men increased about 0.10 cm for each day on which breakfast was skipped [86]. In the study by Hurst and Fukuda [32] there was no linear association between breakfast skipping and WC change. In contradiction to these 2 studies, results of the CARDIA study showed that the hazard ratio for abdominal obesity was 0.84 (95% CI: 0.70; 0.99) when breakfast was consumed on 4 to 6 days per week, and 0.78 (95% CI: 0.66; 0.91) when breakfast was consumed on 7 days per week. Both compared to participants who consumed breakfast on ≤ 3 days per week [85].

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Table 1. Characteristics of the included studies

Authors (Year)	Country	Study design & follow-up period	Participants		Exposure vs. Comparison, Measurement	Outcome, Measurement	Results
			N total N cases*	Sex** Age***			estimated effect sizes (95%CI LL; UL****)
Goto et al. (2008)	Japan	retrospective, check-up data, 2000-2007	4,634 598	100% 21.5	Skipping ≥ 2 vs. ≤ 1 d/wk+, self-administered questionnaire	> 5% increased BMI, weight & height measurement	OR[a] = 1.34 (1.12; 1.62)
Guinter et al. (2020)	USA, Puerto Rico	Sisters Study, prospective cohort, 2003-2015	46,037 2,797, 2,383, 6,807	0% 55.3	Eating 3-4 d/wk+ vs. 0, 1-2 ,5-6, 7 d/wk+, FFQ	5-year incident BMI ≥ 25 kg/m², ≥ 30 kg/m², ≥ 5 kg weight gain, weight & height measurement & self-reported weight	5-yr incident BMI ≥ 25kg/m²: 0 d/wk+ PR[b] = 0.74 (0.62; 0.89), 1-2 d/wk+ PR[b] = 0.91 (0.78; 1.07), 5-6 d/wk+ PR[b] = 0.97 (0.85; 1.09), 7 d/wk+ PR[b] = 0.88 (0.78; 0.99) 5-yr incident BMI ≥ 30kg/m²: 0 d/wk+ PR[b] = 0.72 (0.59; 0.87), 1-2 d/wk+ PR[b] = 0.75 (0.62; 0.89), 5-6 d/wk+ PR[b] = 0.91 (0.80; 1.04), 7 d/wk+ PR[b] = 0.79 (0.70; 0.90) 5-yr incident ≥ 5 kg weight gain: 0 d/wk+ PR[b] = 1.00 (0.90; 1.11), 1-2 d/wk+ PR[b] = 0.98 (0.89; 1.08), 5-6 d/wk+ PR[b] = 0.99 (0.92; 1.06), 7 d/wk+ PR[b] = 0.97 (0.91; 1.04)

* participants, in which the analyzed outcome occurred ǀ ** male sex in percentage ǀ *** mean age in years ǀ **** 95% confidence interval: lower limit – upper limit ǀ + days per week ǀ ++ information not given ǀ a odds ratio ǀ b prevalence ratio ǀ c hazard ratio ǀ # referring to the 2010 Dietary Guidelines for Americans: eating a nutrient-dent breakfast vs. not eating breakfast [35]

Table 1. *continued*

Authors (Year)	Country	Study design & follow-up period	Participants		Exposure vs. Comparison, Measurement	Outcome, Measurement	Results
			N total N cases*	Sex** Age***			estimated effect sizes (95%CI LL; UL****)
Hurst & Fukuda (2018)	Japan	secondary analysis of insurance & health check-up data, 2008-2013	59,717 20671	66% 47.4	Skipping ≤ 2 vs. ≥ 3 d/wk+, Health check-up question	BMI ≥ 25 kg/m², BMI & WC change, BMI & WC data from check-up	BMI ≥ 25kg/m²: OR[a] = 0.92 (0.87; 0.97) BMI change (in kg/m²): β = 0.00 (-0.03; 0.04) WC change (in cm): β = 0.03 (-0.11; 0.16)
Kahleova et al. (2017)	North America Canada	AHS-2, prospective cohort, 2002-2010	50,660 n.g.++	36% 58	Eating vs. skipping, Hospital History Form	BMI change/year, weight & height measurement & self-report	BMI change (in kg/m²): β = -0.03 (-0.04; -0.01)
Kito et al. (2019)	Japan	retrospective cohort, 2008/09-2012	45,524 5,093	100% 34	Skipping ≥ 3 vs. ≤ 2 d/wk+, Health check-up question	BMI ≥ 25 kg/m², weight & height measurement	OR[a] = 1.18 (1.04; 1.33)

* participants, in which the analyzed outcome occurred ǀ ** male sex in percentage ǀ *** mean age in years ǀ **** 95% confidence interval: lower limit – upper limit ǀ + days per week ǀ ++ information not given ǀ a odds ratio ǀ b prevalence ratio ǀ c hazard ratio ǀ # referring to the 2010 Dietary Guidelines for Americans: eating a nutrient-dent breakfast vs. not eating breakfast [35]

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Table 1. *continued*

Authors (Year)	Country	Study design & follow-up period	Participants		Exposure vs. Comparison, Measurement	Outcome, Measurement	Results
			N total N cases*	Sex** Age***			estimated effect sizes (95%CI LL; UL****)
Nooyens et al. (2005)	the Nether-lands	Doetinchem Cohort Study, prospective, 1987-2002	288 n.g.++	100% 54.9	Eating 0–7 d/wk+ Dutch version of EPIC FFQ	Weight & WC change/year, weight, height & WC measurement	Weight change (in kg): β = 0.04 (n.g.++) WC change (in cm): β = 0.10 (n.g.++)
Odegaard et al. (2013)	USA	CARDIA Study, prospective cohort, 1992/93-2011	3,598 972 WC 783 BMI	44% 32.1	Eating ≤ 3 vs. 4–6, 7 d/wk+, interviewer-administered CARDIA DHQ	BMI ≥ 30 kg/m², WC > 88 cm for women & > 102 cm for men, weight, height & WC measurement	BMI ≥ 30 kg/m²: 4-6 d/wk+ HRc = 0.75 (0.62; 0.90), 7 d/wk+ HRc = 0.57 (0.47; 0.68) WC > 88 or 120 cm: 4-6 d/wk+ HRc = 0.84 (0.70; 0.99), 7 d/wk+ HRc = 0.78 (0.66; 0.91)
Smith et al. (2017)	Australia	CDAH Study, prospective cohort, baseline 2002/04-2011	1,155 410	43% 31.5	Met guidelines# consistently vs. met not, postal questionnaire	5-year weight change, weight & height measurement & self-report	5-yr weight change (in kg): β = 1.5 (0.5; 2.8)
Van der Heijden et al. (2007)	USA	HPFS, prospective cohort, 1992-2002	20,064 5,857	100% 57.3	Eating vs. skipping, semi-quantitative FFQ	≥ 5 kg weight gain, self-reported weight	HRc = 0.87 (0.82; 0.93)

* participants, in which the analyzed outcome occurred | ** male sex in percentage | *** mean age in years | **** 95% confidence interval: lower limit – upper limit | + days per week | ++ information not given | a odds ratio | b prevalence ratio | c hazard ratio | # referring to the 2010 Dietary Guidelines for Americans: eating a nutrient-dent breakfast vs. not eating breakfast [35]

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Table 2. Adjusted confounders in included studies

	Adjustment for important variables								Adjustment for other variables
Authors	**age**	**sex**	**education**	**smoking**	**physical activity**	**alcohol**	**TEI**	**all 7**	
Goto et al.					◎	◎			fatty food, living alone
Guinter et al.	◎	◎	◎	◎	◎	◎	◎	◎	race/ethnicity, Healthy Eating Index 2015, weight loss dieting, average sleep hours, perceived level of stress
Hurst & Fukuda	◎	◎							baseline BMI, obesity status, antidiabetic medication
Kahleova et al.	◎	◎	◎	◎	◎		◎		ethnicity, dietary pattern, marital status, sleep, tv watching, high blood pressure medication
Kito et al.	◎			◎	◎				BMI, eating speed, late-night meals/ snacking, drinking, sleep, interactions
Nooyens et al.	◎			◎	◎				retirement, type of job, diet, sugared soft drinks, fiber density, interactions
Odegaard et al.	◎	◎	◎	◎	◎	◎	◎	◎	race, fast food, dietary quality, meal frequency, baseline BMI and WC
Smith et al.	◎	◎	◎	◎					baseline weight, time to follow-up, meal pattern, weekday of follow-up
Van der Heijden et al.	◎			◎	◎	◎			baseline BMI, marital status, weightlifting

3.2.1 Association between Breakfast Skipping and Overweight/Obesity

The meta-analysis on breakfast skipping on ≥ 3 days compared to ≤ 2 days per week and the occurrence of overweight/obesity comprised 3 studies, involving 26,547 cases among 108,839 participants (Figure 2).

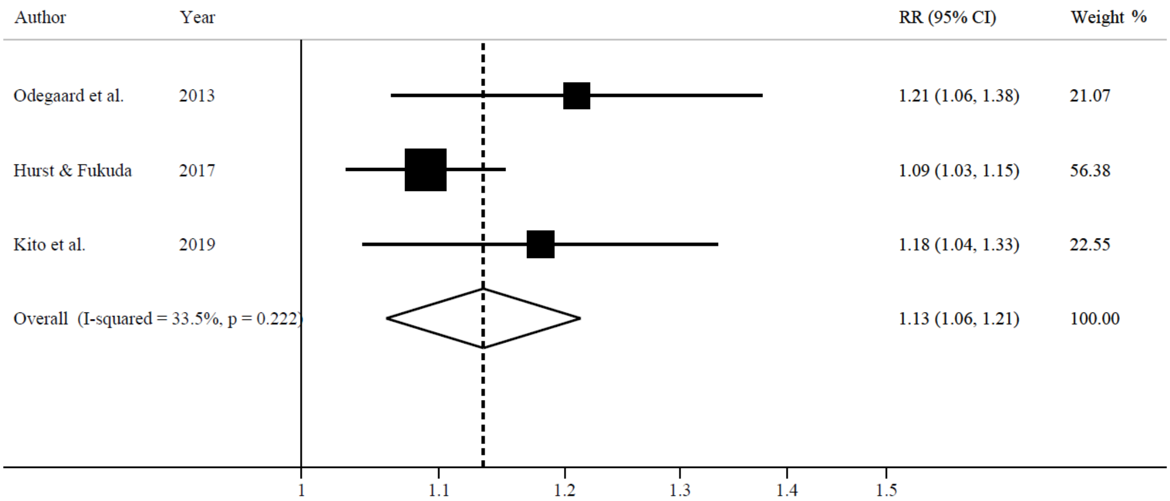

Figure 2. Forest plot for breakfast skipping ≥ 3 versus ≤ 2 days per week and overweight/obesity by using random-effects meta-analysis

The pooled effect estimate expressed as a summary risk ratio (RR) for the occurrence of overweight/obesity is 1.13 (95% CI: 1.06, 1.21; I^2 = 33.5%, p heterogeneity = 0.222; n = 3 studies). Accordingly, participants who skipped breakfast on ≥ 3 days per week have a relative increased risk of 13% to become overweight/obese compared to participants who skipped breakfast on ≤ 2 days per week. In view of the inconsistency of this meta-analysis, there is 33.5% variability between the included studies due to heterogeneity.

3.2.2 Association between Breakfast Skipping and Weight Gain

The meta-analysis on the association between breakfast skipping compared to breakfast eating and weight gain comprised 2 studies, involving 6,455 cases among 24,698 male participants (Figure 3).

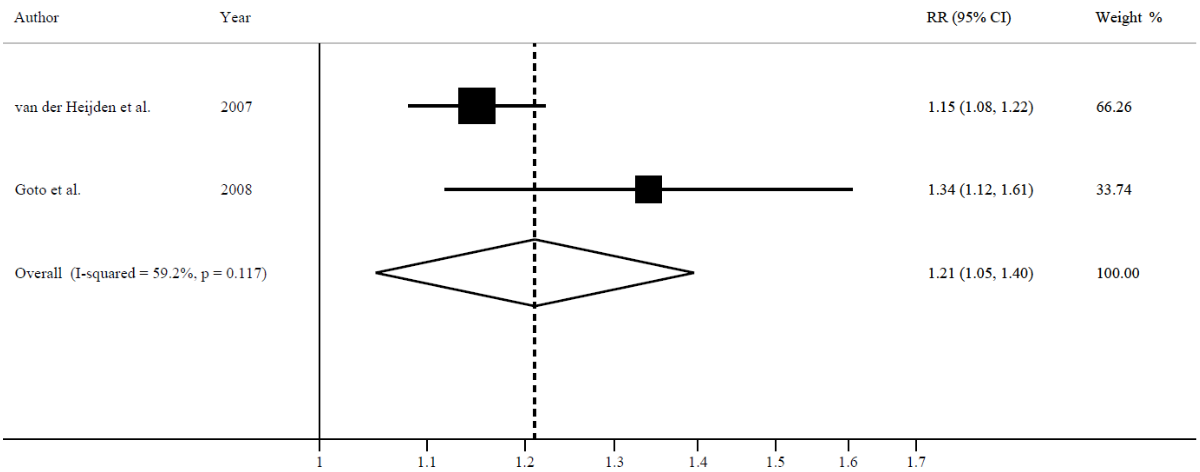

Figure 3. Forest plot for breakfast skipping versus breakfast eating and weight gain by using random-effects meta-analysis

The summary RR is 1.21 (95% CI: 1.05, 1.40; I^2 = 59.2%, p heterogeneity = 0.117; n = 2 studies). Accordingly, men who skipped breakfast had an increased relative risk of 21% to gain weight compared to participants who eat breakfast. In view of the inconsistency of this meta-analysis, there is 59.2% variability between the included studies due to heterogeneity.

3.2.3 Association between Breakfast Skipping and BMI Change

The meta-analysis on the association between breakfast skipping compared to breakfast eating and BMI change comprised 2 studies, involving 108,413 participants (Figure 4).

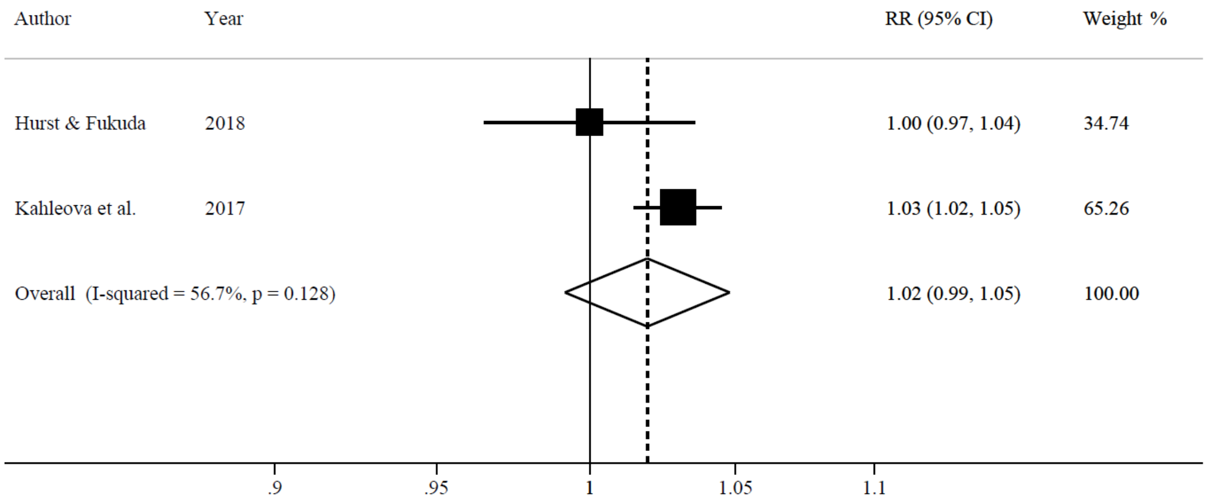

Figure 4. Forest plot for breakfast skipping versus breakfast eating and BMI change by using random-effects meta-analysis

The summary RR is 1.02 (95% CI: 0.99, 1.05; I^2 = 56.7%, p heterogeneity = 0.128; n = 2 studies). It seems like breakfast skippers had a slightly elevated relative risk for an increasing BMI. But precision of this estimate is low and there is no association in BMI change between breakfast skipping and eating. In view of the inconsistency of this meta-analysis, there is 56.7% variability between the included studies due to heterogeneity.

3.5 Quality of Included Studies

To assess the risk of bias in the included studies, ROBINS-I tool was applied on each study. In accordance, only 2 study was judged with a moderate risk of bias [84,85], other 6 studies had a serious risk of bias [31,33,34,86–88], and 1 study was assigned with a critical risk of bias [32] (see Table S2 in Supplementary Appendix). To assess the quality of evidence of the 3 conducted meta-analysis, NutriGRADE was used. In accordance, the first and second meta-analysis were assigned with a low scored meta-evidence while the third meta-analysis was assigned with a very low scored meta-evidence. Table S3 (Supplementary Appendix) gives an overview about the assessed domains and points achieved each domain and meta-analysis.

4. Discussion

All 9 studies included in the review reported a statistically significant association between breakfast skipping and overweight/obesity or weight gain. Moreover, 8 out of 9 studies displayed that breakfast skipping increased the relative risk for overweight/obesity or weight gain, respectively, compared to breakfast eating. The meta-analyses provided a low meta-evidence but showed an increased relative risk for overweight/obesity or weight gain, respectively, when breakfast is skipped. Skipping breakfast on ≥ 3 days per week increased the risk to become overweight/obese about 13% (95% CI: 6%, 21%) compared to skipping breakfast on ≤ 2 days per week. Also, skipping breakfast increased the risk for weight gain about 21% (95% CI: 5%, 40%) compared to eating breakfast. The third meta-analysis provided very low meta-evidence and showed no association between breakfast skipping and changes in BMI.

These results coincide with recent systematic reviews and meta-analyses on studies with a cross-sectional design. The relative risk for overweight/obesity was increased about 75% (95% CI: 57%, 95%) for breakfast skippers compared to breakfast eaters analyzed in the meta-analysis on cross-sectional studies from Asian and Pacific countries [89]. In contrast, results of meta-analyses on studies with interventional design reported an association between breakfast skipping and body weight concerning weight loss in breakfast skippers [58,90]. In accordance, the recent meta-analysis by Bonnet et al. [58] reported a weighted mean difference of -0.54 kg (95% CI: -1.05 kg, -0.03 kg) in body weight when breakfast was skipped in trials conducted in the UK and USA with a follow-up time between 4 and 16 weeks.

In addition, breakfast skipping is part of several intermittent fasting programs [91–93]. One intermittent fasting way is the time-restricted feeding whereby the individual fasts for 16 to 20 hours per day and eats only in the residual 4 to 8 hours per day, mainly in the evening. This fasting program is called "20:4" or "16:8", respectively [91,92,94,95]. Systematic reviews on intermittent fasting programs [91,92] suggest that body weight reduction is possible. This association is stronger in interventional and randomized controlled studies than in observational studies [91,92]. Those results stand against the findings of the present review and meta-analyses and might be reasoned due to the different study designs and outcome measurements.

Randomized controlled trials are considered the gold standard study design, they are conducted under laboratory conditions, provide good internal validity, and are labeled with the highest level of evidence. Typically, their outcome measurements are more trustworthy than outcome measurements in observational study designs. In view of overweight and obesity, trials utilized body composition values (e.g. fat mass and fat free mass) by using DEXA or BIA, respectively [58,90,96] whereas observational longitudinal studies utilized BMI or weight change in kilograms by using a tapeline and scale [31–34,84–88]. But trials like Sievert et al. [90] or Bonnet et al. [58] are limited to small sample size (i.e. < 500 people included in meta-analysis) and short observation intervals (i.e. between 2 and 16 weeks). By contrast, our meta-analyses on cohort studies contained ≥ 100,000 participants (outcome overweight/obesity) and nearly 25,000 participants (outcome weight change), respectively. Furthermore, those observational longitudinal studies followed-up its study population between 5 and 18 years [31–34,84–88]. The main advantage of observational longitudinal studies is that they are able to picture out real-world conditions. Their results provide better external validity and are more transferable on underlying general population than results of trials, tendentially. A last difference to take into account is the fact that the analyzed population in 5 out of 7 trials included in the meta-analysis by Bonnet et al. [58] (or 5 out of 10 trials included in Sievert et al. [90]) is overweight/obese, and its population is younger with a mean age of 35 years.

The physiological principles of intermittent fasting are interesting in view of weight changes. Metabolism's conversion of receiving energy from the glycogen storages of the body starts 12 hours after the last ingestion. A few days later, up to 90% of energy supply stems from the adipose tissue. This has the clinical effect of losing the visceral fat. With losing this fat, the body weight and the metabolic health risk decreased, but levels of the hormone leptin increased. The latter causes ravenous appetite [93]. People who skipped breakfast are more likely to crave for high caloric food than for low caloric food [97]. In accordance with this, it is discussed whether breakfast's satiating effect takes influence on the TEI and whether breakfast eating or skipping increase the TEI. Some studies reported a lower TEI in breakfast eaters compared to skippers [98–100], while other studies reported a higher TEI [36,66,70,90,101].

Breakfast is only one of several determinants on body weight, and even in scope of breakfast itself, there are different factors influencing the body weight status through nutritional physiological processes. For instance, breakfast's time of the day (e.g. before 10 a.m.), time spend on it (e.g. at least 20 minutes), its energy intake (e.g. containing 25% of TEI) and its composition (e.g. wholegrain-based, fiber-rich) are associated with the body weight status due to the release of gut hormones and the effect of satiety [57]. Exemplary, the analysis by Deshmukh-Taskar et al. [35]suggest ready-to-eat cereals as the best kind of breakfast for losing and maintaining body weight. This difference between the type of breakfast and the body weight status was also seen in further studies [36,102]. Additionally, the analysis by Kent et al. [103] displays that the larger the breakfast proportion size, the lower the BMI of men. The observed relationship was even more pronounced in vegetarian men compared to their non-vegetarian counterparts [103]. This opens a new aspect which should be considered when looking at the relationship between breakfast skipping and body weight.

Since nourishments of European, American, and Asian breakfasts are not well comparable [36, 92, 94], one needs to consider that the current meta-analyses pooled breakfasts from countries with different breakfast types. Therefore, this analysis is limited to the extent that the examined results are most likely not transferable to the context of an individual country.

Furthermore, breakfast is an indicator of general health-promoting lifestyle and behavior: Breakfast skippers are more likely to be smokers compared to breakfast eaters [29,35,69,71–73,75,104]. With a decreasing number of days on which breakfast is consumed per week the likelihood to be a smoker increased [71]. Likewise, breakfast skipping is associated with a higher alcohol consumption [29,35,69,104]. Breakfast skippers drank on average 20.5 grams alcohol per day, whereas breakfast eaters drank averagely 11.9 or 8.6 grams alcohol per day, respectively. Ready-to-eat cereal breakfast consumers drank less alcohol than consumers of other types of breakfast [104]. As well, breakfast skippers are more likely to be physical inactive than breakfast eaters [29,65,66,69,71–73,104]. Moreover, breakfast skipping is correlated to a lessened quality of sleep [71–73]. Furthermore, breakfast skippers are more likely to have deficits in macro- and micronutrients intake [36,66,100,101,104,105]. In addition, breakfast skippers consumed the highest content of added and free sugar [66]. Lastly, breakfast skippers are more likely to have lower scores of general health perceptions, vitality, social functioning, emotional role, mental health, and the total score of health status compared to breakfast eaters [69]. Therefore, these factors should be adjusted as it was done in some of the included studies.

Moreover, there are socioeconomic and demographic differences in characteristics of breakfast skippers compared to breakfast eaters [29,35,66,71,72,74,75,104,106]. People affected by poverty are most likely to skip breakfast [35,104], whereas people affiliated by the highest socioeconomic status are most likely to consume cereals for breakfast [66,74]. As well, being married seems to increase the likelihood of breakfast consumption [71,74,104]. Breakfast skippers tend to be of younger age, so the likelihood of breakfast consumption increased with increasing age [29,35,66,74,75,107]. Likewise, the literature shows a sex gradient: men are more likely to skip breakfast than women [29,35,106]. Lastly, there are differences between ethnicities displayed in the literature. Breakfast skippers are more likely to be of Non-Hispanic black ethnicity and less likely to be of Non-Hispanic white ethnicity than breakfast eaters [70,104].

With regard to the behavioral, demographic and socioeconomic factors which are associated with breakfast skipping, most of them are also associated with overweight/obesity and may, therefore, lead to confounding: People with overweight/obesity are more often physical inactive compared to normal weight people [68,108–110]. An unhealthy diet is also seen more likely in people with overweight/obesity than in people with normal weight [63,68]. Additionally, BMI decreased in people who smoked compared to non-smokers [63]. Overweight/obese people are more likely to have a lower socioeconomic status and/or have a lower educational level [67,111]. Another study [110] reports an increased BMI with increasing economic status in both, women and men. With increasing age, the likelihood of overweight/obesity increased, too [62]. The sex gradient indicates that women are more likely to be overweight/obese, globally [112]. Moreover, overweight's/obesity's prevalence is positive linear related to the income level of a country. The higher a country's income level, the higher the prevalence [112]. Besides income-depending differences in overweight's/obesity's prevalence, a variety in fat distribution regarding the ethnicities could take influence [7].

4.1 Limitations

The described issue of too less studies included in the meta-analyses, is the main limitation of this study: it is likely leading to a publication bias and a small study effect but it was not practicable to check for this with only 3 or 2 included studies. With regard to this, an overestimation of the true effect size is likely [78]. Due to this, this study is not able to estimate the range with appropriate precision in which the true effect is located. This is also visible when looking at the reported 95% CIs which are relatively broad. Furthermore, no sensitivity analysis was possible, so we are not able to say whether (and if to what extent) the reported results are robust for variations [78]. As well, information on differences in this association depending on composition, quantity, and quality of breakfast cannot be displayed. Brikou et al. [113] report that the definitions of breakfast and the classifications of being a breakfast skipper/eater vary highly. As most studies did not report a definition of breakfast or used different definitions of breakfast, a misclassification bias must be considered. Leading the fact that this meta-analysis comprised not a sufficient number of studies to stratify for study's quality or measurement methods, we were not able to provide suggestions on their influence of the analyzed association.

In scope of significance testing, it is to notice that the larger the analyzed sample size, the higher the likelihood for statistically significant results (and rejecting H0). The present meta-analyses contained a large sample (approx. 100,000 and 25,000) but very small number of included studies (i.e. 3 and 2) and showed small or moderate effect sizes (i.e. RR = 1.02, 1.13 and 1.21). Therefore, a false negative effect (i.e. beta error) should be taken into account, as well [114].

Furthermore, the study with the comparably lowest risk of bias (i.e. moderate risk) [85] received the smallest weighting (i.e. 21.07%) for the meta-analysis on overweight/obesity. On the contrary, the study with the comparably highest risk of bias (i.e. critical risk) [32] received the largest weighting (i.e. 56.38%) within the same meta-analysis. Additionally, the provided meta-evidence is low leveled for both meta-analyses.

The measurement methods of breakfast skipping behavior were different between the included studies. Only 1 out of 9 studies used an interview-based assessment while the residual 8 studies used a questionnaire-based assessment of breakfast skipping. This should be taken into account, because the meta-analysis by Horikawa et al. [89] implied that interview-based assessment of breakfast skipping is stronger associated with overweight/obesity than questionnaire-based assessment of breakfast skipping. Therefore, it is suggested that the results of this thesis are limited in their precision. Another limiting factor is confounding in the included studies. Only 2 out of 9 studies adjusted for all 7 important variables [84,85]. Because most studies did not adjust their analyses for these important covariables, confounding due to missing adjustment, and a residual confounding must be considered.

4.2 Strengths and Further Research Needs

On the other hand, to the authors' best knowledge, this is the first meta-analysis on the association between breakfast skipping and body weight examined in observational longitudinal studies of adults, worldwide. Moreover, the association was still present and precisely estimated (null value not included in the 95% CI). Furthermore, the results of these meta-analyses are strengthened due to the observational longitudinal nature of the included cohort studies. They represent the real-world conditions of the association between breakfast skipping and body weight. Cohort studies avoid recall bias and decrease the potential for the selection bias [114].

Considering the reported results of previous and current research, there are still open questions left and new questions accrued which implies a further need for research. In general, there is a need for a clear and consistent definition of breakfast eating and breakfast skipping. Breakfast behavior is mostly not part of a validated measurement tool when looking at the included studies of this analysis. It could be an aim in future research to develop a validated measurement tool for breakfast eating and breakfast skipping.

Moreover, this review displayed a lack of studies conducted in European and African countries compared to the number of studies from the USA and Japan. In addition, future observational studies should consider other measurement methods for body weight/body composition than only BMI. Randomized controlled trials already used these specific outcome measurement methods but analyzed only short-term changes in body weight. Large observational longitudinal studies equipped with those outcome measurement methods would comprise the advantage to answer the question whether breakfast is a relevant setscrew in lifestyle to consider in body weight management to avoid overweight-related deuteropathies whereas long-term randomized trials would be helpful to examine the association itself with high evidence but with less transferability into lifestyle. Lastly, both designs - trials and cohorts - are important to examine the association between exposure and outcome at first and picture out this association under real and heterogenic life conditions subsequently. For another comparison, there is a need for studies with observational longitudinal design on the association between intermittent fasting and body weight to compare those results with the results of breakfast skipping/eating and body weight.

5. Conclusions

In conclusion, evidence from observational studies indicates that in real-world settings breakfast skipping might lead to weight gain and onset of overweight and obesity. However, the findings rely on very few studies and needs to be interpreted with caution. Further observational longitudinal studies on this topic are needed, which use a clear and consistent definition of breakfast eating and breakfast skipping. In addition, future studies should focus on further anthropometric measures besides BMI and consider potential confounders.

Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1, Supplementary Appendix: Table S1. Studies excluded by reason; Table S2. Risk of bias in included studies according to ROBINS-I; Table S3. Quality of evidence of meta-analyses referring to NutriGRADE.

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