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Review

Conceptualization and Assessment of 24-H Timing of Eating and Energy Intake: A Methodological Systematic Review of the Chronic Disease Literature

Sydney G O'Connor [1,2,*,†], Lauren E O'Connor [2,3,†], Kelly A Higgins [3,4], Brooke M Bell [5,6], Emily S Krueger [2], Rita Rawal [3], Reiley Hartmuller [2], Jill Reedy [2], Marissa M Shams-White [2]

[1] *Office of Behavioral and Social Sciences Research, National Institutes of Health, Bethesda, MD, United States;* [2] *Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Rockville, MD, United States;* [3] *Food Components and Health Laboratory, Beltsville Human Nutrition Research Center, Agricultural Research Service, United States Department of Agriculture, Beltsville, MD, United States;* [4] *Exponent Inc., Washington, DC, United States;* [5] *Friedman School of Nutrition Science and Policy, Tufts University, Boston, MA, United States;* [6] *Yale School of Public Health, Yale University, New Haven, CT, United States*

A B S T R A C T

Timing of eating (TOE) and energy intake (TOEI) has important implications for chronic disease risk beyond diet quality. The 2020 Dietary Guidelines Advisory Committee recommended developing consistent terminology to address the lack of TOE/TOEI standardization. The primary objective of this methodological systematic review was to characterize the conceptualization and assessment of TOE/TOEI within the chronic disease literature (International Prospective Register of Systematic Reviews registration number: CRD42021236621). Literature searches in Cumulative Index to Nursing and Allied Health Literature (CINAHL) Plus, Embase, PubMed, and Scopus were limited to English language publications from 2000 to August 2022. Eligible studies reported the association between TOE/TOEI and obesity, cardiovascular disease, type 2 diabetes mellitus, cancer, or a related clinical risk factor among adults (≥19 y) in observational and intervention studies. A qualitative synthesis described and compared TOE/TOEI conceptualization, definitions, and assessment methods across studies. Of the 7579 unique publications identified, 259 studies (observational [51.4 %], intervention [47.5 %], or both [1.2 %]) were eligible for inclusion. Key findings indicated that most studies (49.6 %) were conducted in the context of obesity and body weight. TOE/TOEI variables or assigned conditions conceptualized interrelated aspects of time and eating or energy intake in varying ways. Common TOE/TOEI conceptualizations included the following: *1*) timepoint (specific time to represent when intake occurs, such as time of breakfast [74.8 %]); *2*) duration (length of time or interval when intake does/does not occur, such as "eating window" [56.5 %]); *3*) distribution (proportion of daily intake at a given time interval, such as "percentage of energy before noon" [29.8 %]); and *4*) cluster (grouping individuals based on temporal ingestive characteristics [5.0 %]). Assessment, definition, and operationalization of 24-h TOE/TOEI variables varied widely across studies. Observational studies most often used surveys or questionnaires (28.9 %), whereas interventions used virtual or in-person meetings (23.8 %) to assess TOE/TOEI adherence. Overall, the diversity of terminology and methods solidifies the need for standardization to guide future research in chrononutrition and to facilitate inter-study comparisons.

Keywords: chrononutrition, temporal eating patterns, ingestive behavior, meal timing, eating architecture, time-restricted eating, chronic disease

Statement of Significance

In response to the growing interest yet lack of standardization in the developing field of chrononutrition, this systematic review examined how researchers conceptualize, define, and assess timing of eating and timing of energy intake in the chronic disease literature.

Abbreviations: DGAC, Dietary Guidelines Advisory Committee; EI, energy intake; T2DM, type 2 diabetes mellitus; TOE, timing of eating; TOEI, timing of energy intake; TOE/TOEI, timing of eating and timing of energy intake; TRE, time-restricted eating.

* Corresponding author. *E-mail address:* sydney.oconnor@nih.gov (S.G. O'Connor).
† SGO and LEO contributed equally to this work.

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Introduction

There is growing scientific interest in understanding how features of dietary patterns beyond energy, nutrient, or food group intakes impact chronic disease risk [1]. One such feature of interest is chrononutrition, defined as the circadian timing of food intake [2], which considers factors, such as ingestive frequency (the number of ingestive events per unit time), regularity, the distribution of energy intake (EI) or nutrient intake over a period of time, and the timing of the daily eating period [3–5]. Timing of eating or timing of EI within the 24-h d (hereafter referred to as TOE/TOEI), a subcomponent of frequency of eating [6], may represent a distinct dietary pattern feature with important implications for human health. For example, several diet-related chronic diseases, including diabetes [7,8], cardiovascular disease [9,10], and obesity [11,12], have been linked to TOE/TOEI, suggesting that targeting timing as a distinct intervention approach may impact the development and/or the progression of these diseases. In addition, given well-documented challenges with changing and maintaining components of a healthy diet (e.g., energy, added sugars, sodium, or saturated fat restriction), interventions targeting TOE/TOEI have garnered interest because of their relative simplicity [13] and have been demonstrated to be an effective tool to restrict EI and promote weight loss [14]. Recent evidence suggests that there are time-of-day-dependent physiological responses to food intake (e.g., insulin sensitivity and fat oxidation) [3,15]. In addition, differences in dietary intake and diet quality at different times of the day and different days of the week have been well-documented [16–19], although evidence is mixed [20]. There is also a growing understanding of how other 24-h behavioral patterns may covary along with other modifiable risk factors and health behaviors. For example, consumption occurring at certain times of day may be more likely to be accompanied by either sedentary behavior or physical activity, which may in turn impact the amounts, types, and physiological impact of eating [21,22] (e.g., late night, energy-dense snacks on movie night). Similarly, because eating and drinking occasions occur within a broader social and behavioral context, intake at 1 timepoint may influence compensation either by reducing ingestive frequency or decreasing the portion size at subsequent ingestive events [23,24]. TOE/TOEI patterns and other dietary pattern metrics, such as overall diet quality or EI [25,26], are interrelated and also differ by demographic characteristics [6]. However, chrononutrition is an emerging field and there is still uncertainty regarding whether and how TOE/TOEI influence chronic disease outcomes; for example, how does TOE/TOEI interact with diet quality to impact biological processes impacting health, and how can TOE/TOEI be leveraged to improve specific risk or protective factors? More research is needed to determine the unique effects of TOE/TOEI as well as interactions with other dietary features on health.

Because of its infancy as a field of study, there is no consensus or standardization for how TOE/TOEI should best be conceptualized, described, or assessed [1]. The 2020 Dietary Guidelines Advisory Committee (DGAC) highlighted the need for improved strategies of classifying dietary behaviors, including TOE/TOEI, as well as the lack of consistent terminology in this field. Therefore, the objective of this systematic review was to summarize how researchers currently conceptualize, describe, and assess various TOE/TOEI variables or assigned conditions in the chronic disease literature by addressing the following 3 key questions: *1*) How do researchers conceptualize various TOE/TOEI variables or assigned conditions in the chronic disease literature? *2*) How do researchers describe these identified variables or assigned conditions and their conceptualizations? and *3*) What methods do researchers use to assess these variables or assigned conditions?

Methods

The PRISMA checklist was followed for this review [27]. The systematic review protocol was written a priori following the PRISMA Protocol template and registered on PROSPERO in April 2021 (PROSPERO registration number: CRD42021236621). See Table 1 for a list of terms and definitions used for the conduct of this systematic review.

Inclusion and exclusion criteria

Details on the Population, Intervention/Exposure, Comparison, Outcome, and Study Design are outlined in Table 2. Eligibility criteria are described in Table 3. Briefly, a TOE/TOEI variable (assessed in observational studies) or condition (assigned in intervention studies) was defined as one that ascribed a temporal element (e.g., clock time, biological time, or other time anchor) to a within-day eating behavior. Peer-reviewed reports of randomized and nonrandomized intervention studies; observational studies including prospective or retrospective cohorts, cross-sectional, and case-control studies; and protocol papers focused on adult populations (i.e., ≥19 y) that assessed or manipulated an aspect of TOE, TOEI, or TOE/TOEI within the 24-h d and examined that intervention/exposure in relation to a specified chronic disease risk factor or outcome (e.g., obesity, cardiovascular disease, diabetes, or cancer) were included. These study design types were included because they form the basis for most dietary recommendations made in the United States [28,29]. Studies describing TOE/TOEI variables or conditions over a time period longer than ~24 h (e.g., multiday fasting interventions) or that only described TOE/TOEI using socially constructed meal types (e.g., absence or presence of breakfast consumption) without an additional element of timing (e.g., time of breakfast consumption) were excluded.

Information sources and search strategy

A biomedical librarian developed the search strategies in consultation with the review team, conducted the search in September 2021, and reran the search in August 2022. The databases searched were CINAHL Plus (EBSCOhost), Embase (Elsevier), PubMed (United States National Library of Medicine), and Scopus (Elsevier). The keywords, phrases, and Medical Subject Headings terms used in the search strategy varied by database; however, each search included terms related to TOE (e.g., "timing of eating," "meal timing," "time restricted eating," and "chronutrition") combined with a term related to chronic diseases or their risk factors (e.g., "cardiovascular disease," "insulin resistance," "body weight," and "metastasis"). The final comprehensive search strategies are in Supplemental File 1. The searches were limited by language (English only); by publication year (2000–August 2022); to human studies only; and included both

TABLE 1
Terms and definitions

Term	Definition
Timing of eating (TOE)	TOE refers to a variable or condition in which the timing of intake (eating vs. not eating) is of interest, without an explicit focus on the distribution of energy intake timing
Timing of energy intake (TOEI)	TOEI refers to a variable or condition in which energy intake (absolute or relative amount of energy) is measured and of interest
Record	Citations identified in the database search that included peer-reviewed articles as well as gray literature, such as abstracts, magazine articles, etc.
Article	An eligible record that was screened as part of the search strategy and included in the qualitative syntheses
Study	The unique framework or design through which the association of TOE/TOEI in relation to relevant outcomes is assessed. There may be multiple "studies" per article (defined above), e.g., if a single article includes both a cross-sectional and a longitudinal analysis, or includes both an observational and an intervention aim, we considered it to include 2 unique studies for the purposes of this systematic review
Study designs	
Observational (OBS)	A study design in which TOE/TOEI is measured and assessed but is not manipulated. Types of OBS studies include cross-sectional, prospective or retrospective cohort, and case-control
Intervention (INT)	A study design in which TOE/TOEI is manipulated and assessed in relation to a relevant health outcome. Types of INT studies include randomized control trials and nonrandomized trials
TOE/TOEI constructs	
Variable	A TOE/TOEI construct assessed in an observational study
Condition	A TOE/TOEI construct that is manipulated or assigned in an intervention study
TOE/TOEI conceptualization	
Duration	A variable or condition in which TOE or TOEI is described or manipulated in terms of its duration, length, or speed; OR by the interval or duration between eating events; OR by the interval between an eating event and another time anchor
Timepoint	A variable or condition in which TOE or TOEI is described as or manipulated to occur at a specific timepoint or within a specific time range/window
Distribution	A variable or condition in which TOE or TOEI is described as or manipulated in terms of the daily or relative distribution or ratio of eating occasions or energy intake
Cluster	A variable in which TOE or TOEI is described holistically as a person-specific temporal eating pattern, encompassing multiple aspects of TOE or TOEI information
Other	A variable or condition in which TOE or TOEI is described or manipulated in a way that does not fit into the 4 specified conceptualizations above
Time anchor	
Clock	A variable or condition defined in relation to clock time or minutes in relation to a specific clock time
Pseudo clock	A variable or condition defined in relation to pseudo clock time without a specified clock equivalent (e.g., nighttime)
Sleep	A variable or condition defined in relation to sleeping or waking time (e.g., interval between waking and first eating occasion)
Biological	A variable or condition defined in relation to a metric of internal biological time (e.g., dim-light melatonin-onset; DLMO)
Other	A variable or condition defined in relation to another specified metric of time, not captured in the above categories

TABLE 2
Population, intervention, comparison, outcome, and study design (PI(E)COS)

Population	Generally healthy (nonclinical population) adults aged 19+ y, males and females, females not pregnant or lactating
Intervention/exposure	Various constructs of timing of eating, meal timing, or time-restricted eating
Comparator	No restrictions based on comparator
Outcome	Outcomes and/or associated risk factors of obesity, cardiovascular disease, diabetes, or cancer
Study design	Observational studies (prospective or retrospective cohorts, cross-sectional, case-control), interventions (randomized, nonrandomized), and protocol papers for these study designs
Research questions	1) How do researchers conceptualize TOE/TOEI in the chronic disease literature? 2) How do researchers describe TOE/TOEI? 3) What methods do investigators use to assess identified TOE/TOEI

Abbreviations: TOE, timing of eating; TOEI, timing of energy intake.

original research and gray literature (e.g., conference abstracts or proceedings, study protocols). Publication year was limited to 2000, because there was very little literature on the topic prior to 2000 (see Figure 1). The reference lists of included studies were not reviewed, because estimating health effects was beyond the scope of this methodology-focused systematic review. EndNote 20 (Clarivate Analytics) was used to collect, manage, and identify duplicate citations.

Screening and data extraction process

Screening and data extraction were completed in the systematic review software, Covidence (Veritas Health Innovations). Pilot screening for both the title/abstract and full-text review phases was conducted with all reviewers, and the eligibility criteria and process in the protocol were updated prior to commencing screening. Two researchers independently screened records at both the title/abstract and full-text phases of

TABLE 3
Eligibility criteria

No.	Criteria	Eligible	Ineligible
1	Publication details	Peer-reviewed, original research, full-text article, English language, published in 2000–August 2022	Nonpeer-reviewed (e.g., gray literature, conference proceeding), not original research (commentary, editorial), or nonfull-text (abstract only) or full text not available, not available in English language, or published before 2000
2	Population	Generally healthy adults and/or individuals at risk of chronic disease[1]; 19+ y; conducted in high development country (HDI ≥0.70)	Animals, cell culture studies, conducted in a low- or middle-development country (HDI <0.70), pediatric (mean age ≤18), pregnant/lactating, fasting for religious purposes, mean BMI >40, clinical population only
3	Study design	RCTs, nonrandomized interventions, observational studies (e.g., cohort, case-control, cross-sectional), and protocol papers for these study types	Reviews, meta-analyses, position statements, case studies/series/reports, qualitative focus group/interview, calibration/methods development studies
4	Outcome	At least 1 of the specified chronic diseases (e.g., obesity, T2DM, CVD, cancer) events, diagnoses, or established clinical risk factors, as described in the data extraction template	None of the specified outcomes present; clinical events or risk factors not listed (e.g., microbiome, ghrelin, thermic effect of food) in the absence of a qualified outcome
5	Exposure	Study describes or manipulates TOE /TOEI in relation to clock, pseudo-clock (terms such as morning, mid-morning, afternoon, without clock equivalent), biological (melatonin, circadian), or sleep/wake time	In the absence of a qualified exposure, study describes or manipulates 1 of the following: timing or distribution of specific aspect of diet (micronutrient, macronutrient, foods); >24 h/multiday eating patterns (e.g., weekly frequency, regularity, irregularity, ADF/5:2 feed/fast interventions); timing defined in relation to exercise/sedentary time
6	Primary objective	Study measures and reports an eligible 24-h TOE/TOEI exposure in relation to an eligible outcome	The association between an eligible 24-h TOE/TOEI variable and outcome is not measured or reported

Abbreviations: ADF, alternate day fasting; CVD, cardiovascular disease; HDI, Human Development Index; RCT, randomized control trial; T2DM, type 2 diabetes mellitus; TOE, timing of eating; TOEI, timing of energy intake.

[1] Eligible studies enrolled participants who are generally healthy and/or at risk for chronic disease, including those with obesity (unless mean BMI >40 kg/m^2), or populations that exclusively consist of individuals at risk of chronic disease because of hypertension, high cholesterol, metabolic syndrome, or prediabetes but that do not exclusively look at change in the inclusion risk factor as indicator of outcome.

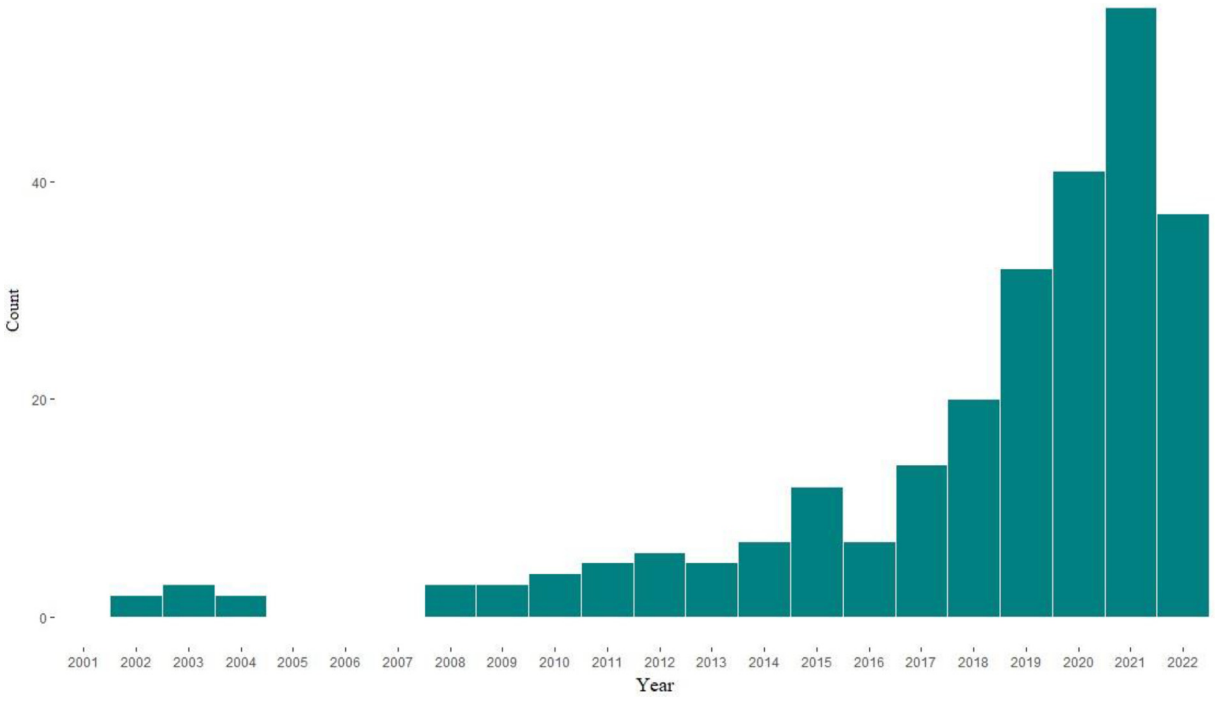

FIGURE 1. Search results by the year of publication.

screening. All discrepancies for both phases were resolved by a third reviewer.

The data extraction form was developed in Covidence, and each extraction item was accompanied by detailed instructions and trainings to ensure consistency in extraction. The data extraction form and process were pilot tested by all researchers prior to starting to ensure usability and to identify any additional extraction criteria. The data were extracted from each included publication by 2 researchers independently, and a third researcher reconciled discrepancies. The exception was free-text items that

required researchers to extract text directly from the publication, which was not extracted in duplicate; instead, 1 researcher extracted the data and a second researcher reviewed and checked the extracted data for accuracy. The data extraction template is included in Supplemental File 2. Article authors were not contacted for additional information, because the aim was to characterize the reporting of TOE/TOEI methods in existing literature using the information presented in peer-reviewed publications, as in methodological systematic reviews by Wingrove et al. [30] and Leech et al. [31].

A series of study characteristics were extracted from included articles. Characteristics were extracted to document the key elements of the study (e.g., TOE/TOEI variable information), capture key study design characteristics (e.g., primary chronic disease context and population special characteristics), and other relevant measures that are collected from populations within this body of literature (e.g., other biological or behavioral outcomes examined). The following study characteristics were extracted from each included article: *1*) journal name, *2*) PubMed ID, *3*) country, *4*) purpose statement or aim of study, *5*) trial or cohort name (if relevant), *6*) cycle year for trial or cohort (if relevant), *7*) study population characteristics (e.g., exclusively individuals with overweight or obesity), *8*) case population description (for case-control studies), *9*) population special characteristic (e.g., night shift workers), *10*) population age, *11*) total number of participants, *12*) primary chronic disease context [e.g., obesity, type 2 diabetes mellitus (T2DM)], *13*) cancer type (if cancer outcome), *14*) eligible health outcomes examined (e.g., BMI [kg/m^2], blood pressure), *15*) other biological or behavioral outcomes examined (e.g., energetics, physical activity), *16*) study design, and *17*) relevant limitations noted in discussion on TOE/TOEI measurement/assessment (see Supplemental File 2 for details). Given the methodological focus of this systematic review, quantitative results from health outcome data were not extracted, which is consistent with other methodological reviews on dietary patterns research methodology [30–32].

The TOE/TOEI methods data that were extracted differed slightly by study design. For observational studies, 1 researcher (SGO) extracted the following data: *1*) TOE/TOEI variable, conceptualization, and time anchor; *2*) eating/fasting definitions; *3*) weekend compared with weekday description; *4*) TOE/TOEI variable names, definitions/descriptions, operationalization, method of assessment, and details when available; *5*) number of timepoints from which TOE/TOEI variables or conditions were assessed; *6*) number of days TOE/TOEI was assessed at each timepoint; *7*) reporting timeframe, if habitual diet was selected; *8*) follow-up time; *9*) covariates used in analyses; and *10*) any additional relevant information. For intervention studies, 1 researcher (LEO) extracted the following data: *1*) TOE/TOEI condition name, conceptualization, and time anchor; *2*) eating/fasting definitions; *3*) weekend compared with weekday description; *4*) whether the intervention was a crossover study; *5*) intervention duration; *6*) TOE/TOEI intervention name, description, and mode of administration; *7*) adherence tool, description, frequency of assessment, and number of days at each assessment; *8*) how adherence to the intervention was defined, and any dietary manipulations in addition to the TOE/TOEI intervention; *9*) dietary control or comparison across interventions; and *10*) any additional relevant information. A second researcher (BMB or KAH) reviewed and checked the selection for both intervention and observational studies to ensure continuity across approaches. All discrepancies were resolved by either SGO (for observational studies) or LEO (for interventions).

Assessment of reporting quality in included studies

The team created a tool to assess the clarity and transparency of methodological reporting in included studies (Supplemental File 3). A series of reporting characteristics were identified, and each study was evaluated on the basis of whether these characteristics were reported within the manuscript. The transparency of methods reported in the manuscripts was rated and not the quality of the study designs or tools used in the studies themselves, because of the volume of articles identified, the broad range of designs and tools used within this sample of articles, and the lack of consensus in the field regarding the best way to assess various TOE/TOEI variables or conditions [6].

Data analysis and synthesis

Data were analyzed and synthesized, and results were organized to address each of the following 3 questions posed in this review: *1*) How do researchers conceptualize TOE/TOEI in the chronic disease literature? *2*) How do researchers describe TOE/TOEI? and *3*) What methods do investigators use to assess identified TOE/TOEI? A measure of effect between TOE/TOEI variables or conditions and health outcomes was not assessed for this methodological review, because the focus was how TOE/TOEI was conceptualized, described, and assessed in the context of chronic disease research. Data were managed and qualitatively synthesized using Microsoft Excel and SAS Software (version 9.4; SAS). Figures were created using Microsoft Excel, R (Version 4.2.1; R Core Team, 2022), RStudio (Version 2022.07.1+554; Rstudio Team, 2022), and SAS. Means and frequencies were calculated for study-level and variable/condition-level characteristics. Stacked bar charts were created to display combinations of TOE/TOEI characteristics within a given variable or condition. Heatmaps were created to depict the frequency of publication by country and the co-occurrence of study and variable or condition characteristics.

Results

The PRISMA flow diagram is displayed in Figure 2. The literature search results included 12,887 records, of which 5362 were duplicates. Of these, 6695 records were excluded at title/abstract screening and 561 were excluded at full-text screening. A total of 259 records, hereafter referred to as "articles" because all were from peer-reviewed journals, were included in the qualitative synthesis, representing 136 unique observational and 126 unique intervention studies (3 articles included both an eligible observational and intervention study and thus were double counted). The number of eligible articles published per year increased from 2000 to 2022, particularly since 2015 (Figure 1). The majority of data were collected in the United States (30.9 %), followed by Australia (7.3 %), Japan (7.3 %),

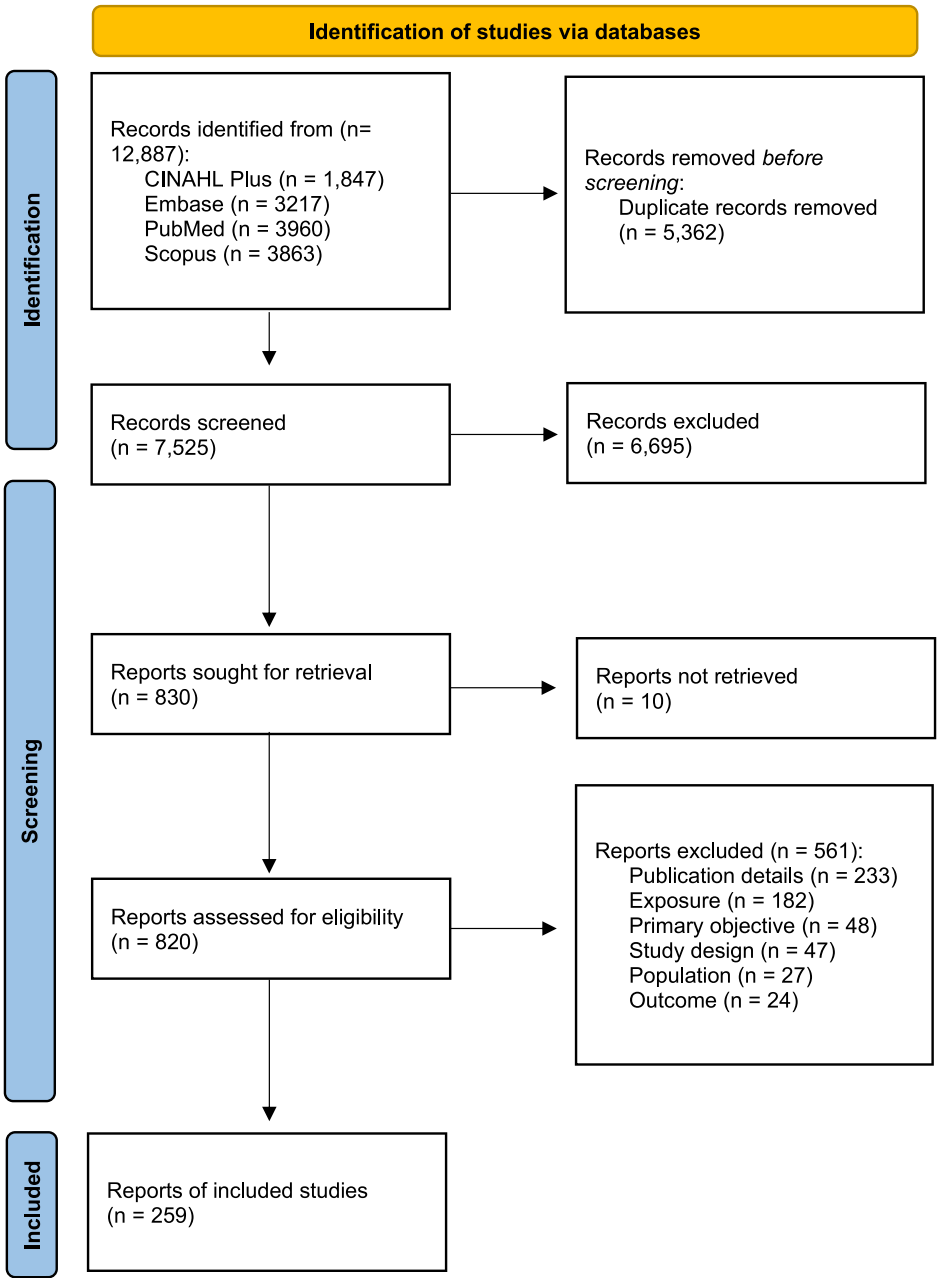

FIGURE 2. PRISMA diagram.
*Some articles included more than 1 study, and thus, some articles were double counted as observational and interventional studies.

and Spain (6.2 %) (Figure 3). The full list of excluded records at full-text screening and reasons for exclusions are listed in Supplemental File 4 and the full list of the included articles is included in Supplemental File 5.

Reporting quality

The quality of study reporting is described in Table 4. All observational studies provided a description of the frequency of TOE/TOEI assessment, and most (71 %) described the number of observations per measurement timepoint. The majority of intervention studies (92 %) described the assessment tool or approach, whereas fewer than half (44 %) described whether or how weekend and weekday differences were considered in the assessment or analysis of TOE/TOEI. Most observational and intervention studies reported the measurement tool or approach (98 % and 92 %, respectively); however, definitions of eating and fasting were not well reported for either study design (61 % and 55 %, respectively).

Study characteristics

Overall characteristics for the 136 observational and 126 intervention studies are displayed in Table 5. Observational studies ranged in sample size from 11–50 to 50,001+ participants, with the most commonly reported sample size (25.7 %) falling into 1001–5000 participants; intervention studies ranged in size from ≤10 to 101–500, and most often (65.1 %) included

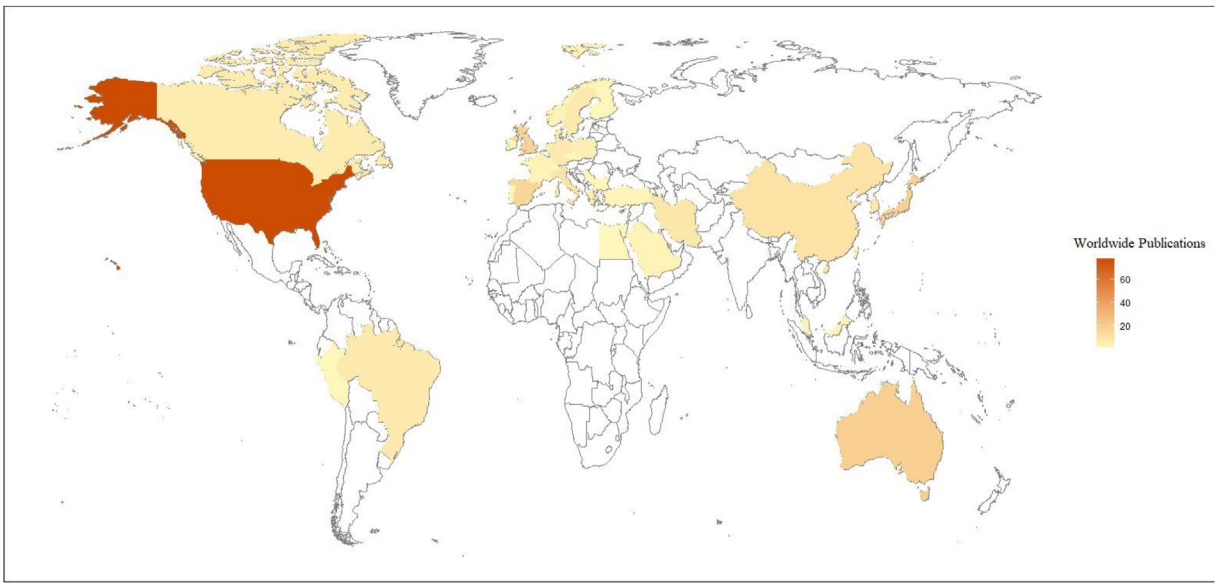

FIGURE 3. Included articles by country.

TABLE 4
Study reporting quality rating

Did the authors describe...	Observational (n = 136)			Intervention (n = 126)		
	Yes	*No*	*%Yes*	*Yes*	*No*	*%Yes*
Frequency of measurement timepoints	136	0	100 %	74	15	83 %[1]
Number of observations per measurement timepoint	97	39	71 %	53	36	60 %[1]
The measurement tool or approach	133	3	98 %	116	10	92 %
Consideration of weekend and weekday differences in assessment or analysis	82	54	60 %	55	71	44 %
Definition of eating and/or fasting	83	53	61 %	69	57	55 %

[1] Does not include n = 37 laboratory-based studies using direct observation for which these criteria were not applicable.

11–50 participants. The majority (80.1 %) of observational studies were cross-sectional and the majority (67.5 %) of intervention studies were randomized controlled trials. Most studies enrolled adults aged between 18 and 59 y (96.9 %) and examined TOE/TOEI in relation to body weight or another indicator of body composition (80.9 %). The least common chronic disease context studied across study designs was cancer (3.8 %, of which all instances were observational studies) (Figure 4). Observational studies most often (47.1 %) did not control for any other aspects of diet quality when examining the association of TOE/TOEI on chronic disease risk factors or outcomes; among studies that did control for dietary covariates, 33.1 % controlled for EI, whereas a small number controlled for dietary quality (11.0 %) or intake of specific nutrients (3.7 %). For intervention studies, 40.5 % were crossover design, 32.5 % were in-laboratory under direct observation, and 16.6 % provided some or all foods and beverages to participants. Almost half of intervention studies (42.5 %) had participants self-select dietary intake, 17.5 % of studies prescribed energy restriction in addition to TOE/TOEI, and 39.7 % prescribed certain foods or dietary patterns in addition to TOE/TOEI.

How do researchers conceptualize TOE/TOEI?

Timepoint and duration were the only TOE/TOEI conceptualizations that were used for both observational and intervention studies, with timepoint being the most common (Figure 5A). Cluster variables were only utilized in cross-sectional observational studies. Compared with observational variables, intervention conditions were more frequently classified as having multiple conceptualizations (Figure 5A), particularly duration + timepoint, a combination commonly used to describe time-restricted eating (TRE) studies. Anthropometrics were the most common outcome assessed across TOE/TOEI conceptualizations for both observational (Figure 5B) and intervention studies (Figure 5C). Timepoint was most commonly examined in relation to anthropometrics, T2DM, and cardiovascular disease outcomes/risk factors in both study designs.

Among the 136 observational studies, 490 eligible TOE/TOEI variables were extracted. There were 263 total conditions across all the articles, but only 220 were TOE/TOEI related (i.e., nontimed controls were excluded from the analyses). The most common TOE/TOEI conceptualization for observational variables was timepoint (n = 233), followed by duration

TABLE 5
Characteristics of included studies

	Observational (n = 136)		Intervention (n = 126)		Total (n = 262)	
	n	%	n	%	n	%
Study design[1]						
Observational: Cohort	22	16.2 %	—	—	22	16.2 %
Observational: Case-control	7	5.1 %	—	—	7	5.1 %
Observational: Cross-sectional	109	80.1 %	—	—	109	80.1 %
Intervention: Randomized	—	—	85	67.5 %	85	67.5 %
Intervention: Nonrandomized	—	—	41	32.5 %	41	32.5 %
Number of participants						
≤10	0	0.0 %	17	13.5 %	17	6.5 %
11–50	9	6.6 %	82	65.1 %	91	34.7 %
51–100	14	10.3 %	16	12.7 %	30	11.5 %
101–500	32	23.5 %	9	7.1 %	41	15.6 %
501–1000	18	13.2 %	0	0.0 %	18	6.9 %
1001–5000	35	25.7 %	0	0.0 %	35	13.4 %
5001–10,000	5	3.7 %	0	0.0 %	5	1.9 %
10,001–50,000	21	15.4 %	0	0.0 %	21	8.0 %
50,001+	2	1.5 %	0	0.0 %	2	0.8 %
Not specified	0	0.0 %	2	1.6 %	2	0.8 %
Age of participants[1]						
Adults (18–59 y)	131	96.3 %	123	97.6 %	254	96.9 %
Older adults (60+ y)	70	51.5 %	23	18.3 %	93	35.5 %
Primary chronic disease context						
Obesity	83	61.0 %	47	37.3 %	130	49.6 %
T2DM	7	5.1 %	22	17.5 %	29	11.1 %
CVD	8	5.9 %	6	4.8 %	14	5.3 %
Cancer	10	7.4 %	0	0.0 %	10	3.8 %
Multiple	23	16.9 %	47	37.3 %	70	26.7 %
Other[2]	5	3.7 %	4	3.2 %	9	3.4 %
Study population characteristics[1]						
Generally healthy population	117	86.0 %	67	53.2 %	184	70.2 %
Exclusively individuals with overweight or obesity	17	12.5 %	58	46.0 %	75	28.6 %
Exclusively individuals with metabolic syndrome	0	0.0 %	2	1.6 %	2	0.8 %
Exclusively individuals with prediabetes	1	0.7 %	4	3.2 %	5	1.9 %
Exclusively individuals with hypertension	1	0.7 %	0	0.0 %	1	0.4 %
Individuals with disease or other characteristic (for case/control studies)	11	8.1 %	0	0.0 %	11	4.2 %
Clinical outcomes assessed[1]						
Body weight or composition	121	89.0 %	91	72.2 %	212	80.9 %
T2DM diagnosis or risk factor	48	35.3 %	99	78.6 %	147	56.1 %
CVD outcome or risk factor	6	4.4 %	0	0.0 %	6	2.3 %
Stroke (ischemic or hemorrhagic)	3	2.2 %	0	0.0 %	3	1.1 %
Blood pressure or vascular function	32	23.5 %	35	27.8 %	67	25.6 %
Blood lipids or lipoproteins	34	25.0 %	73	57.9 %	107	40.8 %
Inflammatory markers	7	5.1 %	20	15.9 %	27	10.3 %
Oxidative stress	1	0.7 %	5	4.0 %	6	2.3 %
Cancer diagnosis or established clinical risk factor for cancer	11	8.09 %	0	0	11	4.2 %

n = 259 records, 3 records have both observational (OBS) and intervention (INT) components, so columns add up to n = 262.
All extracted variables are described and further defined within the data extraction template in the Supplemental Materials.
Abbreviations: CVD, cardiovascular disease; T2DM, type 2 diabetes mellitus.
[1] *N*s may add to more than the column total; some studies (n = 6) also included participants <19 y.
[2] List of other primary chronic disease contexts: chronic kidney disease (CKD), gastroesophageal reflux disease (GERD), underweight, lower-extremity functioning, and chronotype and sleep during COVID-19 [from observational studies]; athletic performance [from intervention studies].

(n = 108), distribution (n = 75), and cluster (n = 11) (Figure 6A). Timepoint variables often examined the time at which a specific meal was consumed (e.g., lunch time EI [33]; dinner EI [34]); or whether or not eating or EI occurred within a specific window of time (e.g., night EI, defined as 20:30–04:59 [35]). Less frequently, observational variables were described using >1 TOE/TOEI conceptualization, such as distribution + timepoint (n = 55), cluster + duration (n = 2), or cluster + timepoint (n = 1). The distribution + timepoint variables were largely describing the absolute or relative amount of energy or meals consumed within a certain time window or time range, or conversely, the time of day at which a certain percentage of energy or meals were consumed. For example, 1 study examined EI, proportion of daily EI, and hourly EI across 5 clock time-defined time windows, from "morning" to "night" [36], and another study created 3 variables to denote the clock time at which the participant reached 25 %, 50 %, and 75 % of their total daily EI [37]. Of 126 intervention studies, there were 220 time-related conditions administered (Figure 6B). The most common time conceptualization used to describe the assigned conditions was

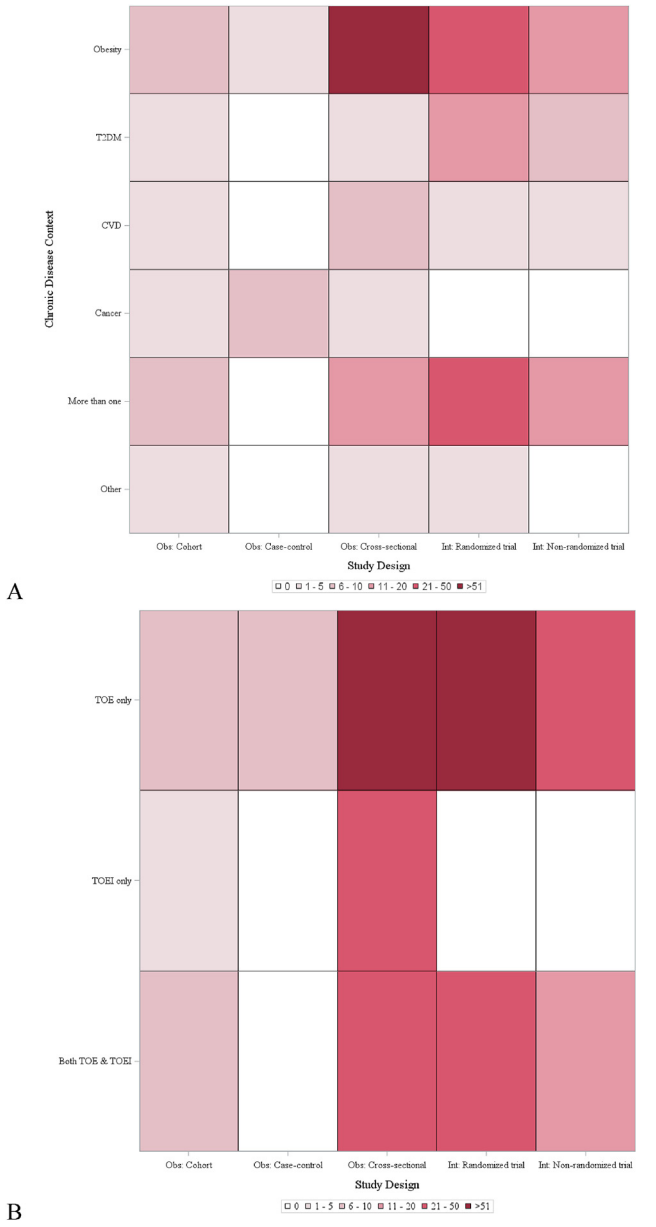

FIGURE 4. Heatmaps depicting the frequency of co-occurrence of study characteristics.
Panel (A) depicts the frequency of primary chronic disease contexts by study design. Panel (B) depicts the co-occurrence of TOE type by study design. All interventions that manipulated TOE by default manipulated TOEI (n = 262 studies). TOE, timing of eating; TOEI, timing of energy intake.

timepoint (n = 176), followed by duration (n = 139) and distribution (n = 65). Almost all distribution intervention conditions examined the effects of EI distribution across the 24-h day. For example, EI distributed predominantly in the morning compared with evening (45 %, 35 %, 20 % compared with 20 %, 35 %, 45 % of EI at breakfast, lunch, and dinner, respectively) [38]. Many intervention conditions were described using >1 TOE/TOEI conceptualization: duration + timepoint (n = 77), duration + distribution (n = 65), distribution + timepoint (n = 29), and 20 intervention conditions incorporated all 3 conceptualizations. The duration + timepoint intervention conditions were largely TRE studies that asked participants to consume food over a certain duration that was also anchored by a timepoint (e.g., an 8-h eating window in which participants ate ad libitum from 10:00 to 18:00 and fasted from 18:00 to 10:00) [39]. This is in contrast to TRE interventions that asked participants to adhere to an eating window duration but allowed them to self-select the timepoint (considered as duration-only interventions) [40].

How do researchers describe TOE/TOEI?

The TOE/TOEI variables or conditions used in both study designs are presented in Figure 6. For both observational and intervention studies, the most common time anchor was clock time (n = 372 and 209, respectively), followed by sleep time (n = 53 and 26), pseudo clock time (n = 36 and 5), and biological time (n = 2 and 15). Twenty-three observational studies and 27 intervention studies used >1 time anchor to describe the variables or condition. The most common combination of conceptualization and time anchor was a timepoint and clock time (n = 193 and 171); an example of this is the variable "breakfast time," defined as the "average clock time of participant-defined breakfast meal" [33]. Sleep time was most often used as an anchor in the context of a duration variable for observational studies (n = 32); an example of this is the variable "sleep end-first meal," defined as the "duration... between sleep offset and the first meal" [41] (Table 6; Figure 6A).

In observational studies, there were varying degrees of specificity in defining eating and fasting. Many studies (n = 34) using survey-based assessments of TOE asked participants to self-report on habitual eating timing, but the term "eating" was not further defined in the majority of these studies (n = 26). For example, 1 study surveyed "getting up at night to eat" without further clarification about what constituted "eating" or "night" [12]. Studies that used 24-h dietary recalls or similar approaches to assess EI over a 24-h period employed varying degrees of specificity in defining and operationalizing when eating had occurred; in 1 study the "information on types and amounts of food and beverages consumed at each eating occasion [EO]" was used without further thresholds for how no/low-energy foods or beverages were treated [42], whereas in another study, "EO was defined as any occasion at which food or drink was ingested and provided a minimum energy content of 210 kJ (50 kcal) and was separated in time from the surrounding EOs by 15 min" [43]. Definitions of fasting (e.g., the noneating portion of a TRE study) varied across studies that included an intervention component. Most studies (n = 30), namely TRE studies, allowed no/low-energy beverages, such as coffee or tea with no additions, or diet sodas or sparkling waters [11], whereas others prohibited beverages that contained caffeine or low-calorie sweeteners as they may influence metabolism. This is in contrast to other studies (n = 20) that only allowed water during the fasting period/window [44]. One study allowed water and 1–2 "very low-calorie" drinks and foods (mints and gum) that contained <4 kcal/serving [7]. Definitions of "eating" were less common and largely based on the intake of any caloric foods or beverages. One study defined the eating window as the

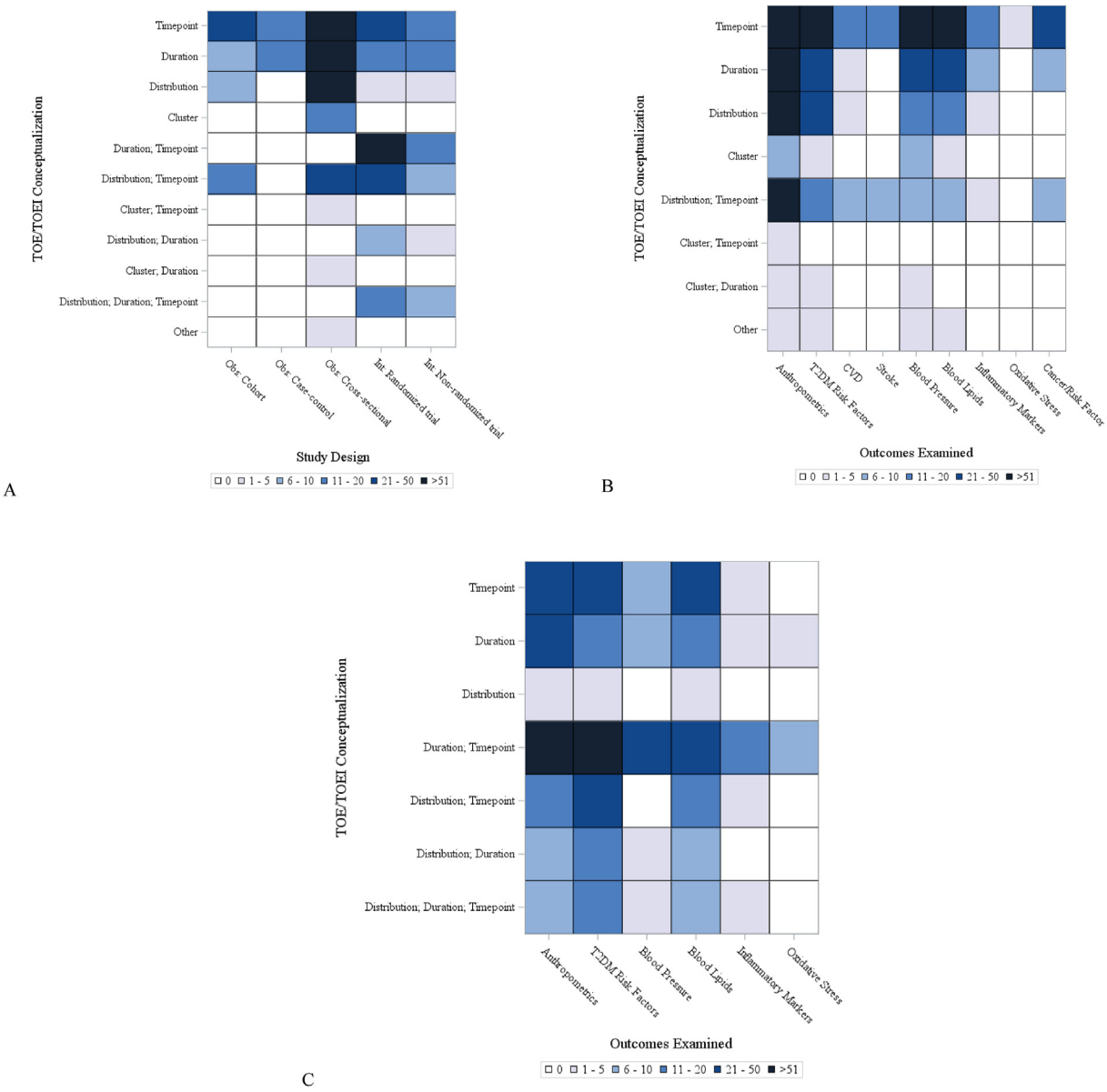

FIGURE 5. Heatmaps depicting the co-occurrence of characteristics for TOE/TOEI constructs.
Panel (A) depicts the frequency of co-occurrence of TOE/TOEI constructs by study design. Panel (B) depicts the frequency of co-occurrence of TOE/TOEI conceptualizations by chronic disease risk factors examined in observational variables only (n = 490 variables). Panel (C) depicts the frequency of co-occurrence of TOE/TOEI conceptualizations by chronic disease risk factors examined in intervention conditions only (n = 220 conditions). TOE, timing of eating; TOEI, timing of energy intake.

time interval when 95 % (2.5–97.5 percentile) of all energy-containing ingestive events occurred [8].

What methods do researchers use to assess TOE/TOEI?

In observational studies, the tools most commonly used to assess TOE/TOEI were surveys or questionnaires (28.9 %) about habitual intake assessed at 1 timepoint (Table 7). A small percentage of studies (<5 %) used assessment methods developed specifically to assess the timing of ingestive events, such as meal timing grids [9,45,46] or time-use methodology [47–49], although the validity of these tools was rarely described. Twenty-two studies used "Other" tools to assess TOE/TOEI, including face-to-face interview [10], combined ecologic momentary assessment (EMA), actigraphy for passive assessment of ingestive occasions (e.g., bite detection) [50–52]. Most intervention studies employed >1 tool to assess adherence to TOE/TOEI conditions, with virtual or in-person check-ins with study staff or dietitians as the most common (23.8 %) (Table 8). Almost 20 % of adherence tools were administered daily, mostly as daily food records/diaries/logs, intake timing logs, or prompts from a smartphone application. Continuous glucose monitors were used as objective measures of TOE/TOEI in 2 intervention studies to corroborate adherence to prescribed eating and fasting windows. Few time-specific tools used previously described methods or approaches; many studies simply instructed participants to log the time of each ingestive occasion using diaries. Adherence measures were not described for 10 intervention studies. Researchers described the parameters used to deem participants as adherent to the intervention condition for 40 (31.7 %)

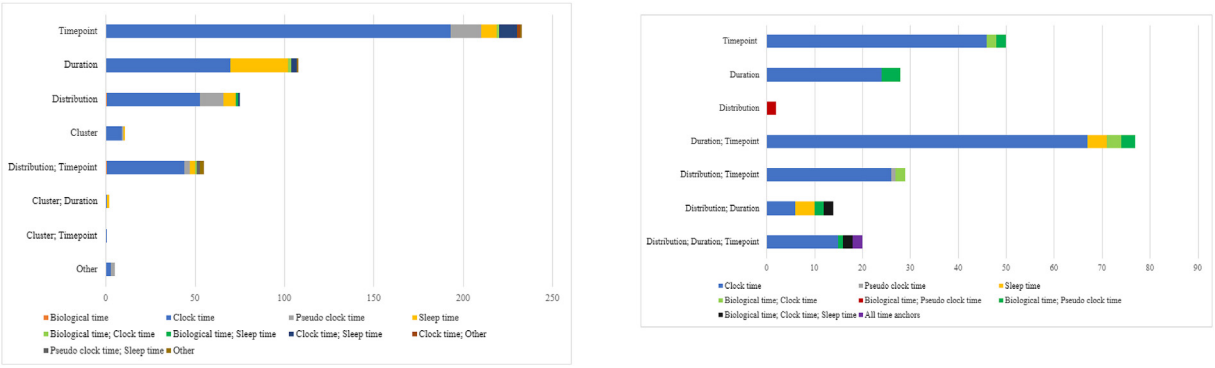

FIGURE 6. Stacked bar graph of combinations of TOE/TOEI conceptualizations and time anchors by study design. TOE, timing of eating; TOEI, timing of energy intake.

studies. These parameters differed across intervention studies. For example, some researchers allowed 15- [8], 30- [53], or 60-min [54] buffer periods to count a participant adherent to their prescribed eating or fasting window.

Discussion

The goal of this systematic review was to summarize how researchers currently conceptualize, describe, and assess various TOE/TOEI variables or assigned conditions in the chronic disease literature. A comprehensive understanding of the conceptualization, description, and assessment of TOE/TOEI in the current chronic disease literature is crucial for taking stock of methodological commonalities and disparities, and for highlighting areas for improvement in the standardized reporting of chrononutrition information; together, these findings can help to strengthen this body of literature by providing researchers with an overview of methodological approaches, as well as opportunities for improvement in study design and reporting. This review was conducted in response to the recommended future research directions described in the 2020 DGAC report for frequency of eating [6]. Between 2000 and July 2022, a total of 259 articles were identified that examined TOE/TOEI in relation to an eligible chronic disease risk factor or outcome, representing 136 unique observational and 126 unique intervention studies. Most often, studies were conducted in the context of obesity and body weight, highlighting the relevance of TOE/TOEI as a potential risk factor for obesity or a strategy for weight loss and/or maintenance. Among this body of literature, a wide range of tools were used to assess TOE/TOEI across a broad range of populations and settings. The tools varied in the specificity of what may be assessed, from habitual patterns of intake timing within a population over a certain period of time to detailed information on EI by an individual participant over repeated days. In addition, even when similar assessment methods were used, there was a wide variation in how the data were operationalized to represent unique TOE/TOEI variables or conditions that were then examined in relation to chronic disease outcomes. Results quantitatively describe the wide variability in variables or conditions and methods used in chrononutrition research, highlighting the need for a standardized research framework and lexicon to ease evidence synthesis for future research and dietary guidance related to TOE/TOEI.

There is a need within the field of nutrition to better understand the limitations and values of diverse dietary assessment methods [55], and this applies to the methods used in the growing field of chrononutrition. Despite this need, there was a notable lack of transparency and/or precision in methods reporting from studies that investigated TOE/TOEI in the chronic disease context. The lack of transparency is not specific to TOE/TOEI research, but it is rather ubiquitous in nutrition research more generally [56,57]. Many studies included in this systematic review lacked details on how eating was defined and what constituted an eating event. Researchers make many decisions during the study design and analysis (e.g., whether to consider beverage-only intake occasions as EOs in the context of a 24-h dietary recall dataset, how to handle distinct intake occasions that occur in close time proximity). These decisions were not often reported in the included studies, hindering interpretability and reproducibility of the study. Not defining these terms compounds the measurement error associated with self-reported dietary intake data, such as asking participants to report on their "habitual meal times" without defining what constitutes a meal (e.g., whether a meal includes breakfast, lunch, and dinner only, or also includes snacks or beverage-only snacks). The 2020 DGAC defined an ingestive event to include preloads, meals or snacks, food or beverage, and energy yielding or nonenergy yielding [29], yet many of the included studies did not define ingestive events and the ones that did define eating or fasting implemented a range of definitions. Some exemplar studies [43] included detailed definitions of eating and fasting, but a standardized definition and reporting practice recommendations are still needed.

Overwhelmingly, included studies used clock time to define and describe TOE/TOEI. However, other time anchors were also used, such as sleep/wake time and proxy indicators for internal biological time. Although all individuals living within a time zone share a common clock time, the degree to which an individual's internal time and the degree of synchronization (i.e., phase angle) of internal to clock time may vary greatly [58]. Thus, considering each individual's eating patterns in relation to their unique circadian phase, as well as in relation to other health behaviors (e.g., physical activity patterns) [59,60], may yield more precise insights into the interplay of TOE/TOEI with biological processes [61] and disease risks [4]. Studies that defined TOE/TOEI as simply as socially defined meals (e.g., "breakfast" is a meal typically consumed in the morning) were excluded; however, studies that described eating using a "pseudo clock time," such as "late-morning" with no specific clock time were included. Some studies used a dual approach, defining variables

TABLE 6
Examples of combinations of characteristics for TOE/TOEI variables and conditions

TOE vs. TOEI	Conceptualization	Time anchor	Observational study variable examples	Intervention study condition examples
TOE	Timepoint	Clock	Breakfast time: average clock time of participant-defined breakfast meal	Early eating: eating lunch at 13:00 after 8:00 breakfast, and before 20:00 dinner
		Pseudo clock	Afternoon meal: regular intake of an afternoon meal (meal between lunch and dinner), also called "merienda"	N/A
		Sleep	Late night dinner: eating dinner within 2 h before bedtime ≥3 times/wk	N/A
		Biological	N/A[1]	N/A
	Duration	Clock	Daily eating interval: the total time period of daily eating, calculated as the time between the first and last eating occasion during a 24-h period	Time-restricted 8-h feeding: self-selected 16-h fasting/8-h feeding windows. Participants did not have similar meal times to avoid disruptions to their individual circadian rhythm on the basis of normative sleep/wake and feeding cycles
		Pseudo clock	N/A	N/A
		Sleep	Sleep end-first meal: duration (hours:minutes) between sleep offset and the first meal	N/A
		Biological	Last meal-DLMO: duration between dim-light-melatonin-onset (DLMO) and the average clock time of the last meal	N/A
	Distribution	Clock	Hourly percentage of eating events: percentage of all eating events in 1-h bin, calculated as eating events at each hour divided by the total eating events; also referred to as eating architecture	N/A
		Pseudo clock	N/A	N/A
		Sleep	N/A	N/A
		Biological	N/A	N/A
	Cluster	Clock time	Temporal eating patterns: latent class analysis (LCA) used to identify distinct temporal eating patterns, based on whether or not an eating event occurred in each hour of the day	N/A
		Pseudo clock	N/A	N/A
		Sleep	Meal-to-sleep interval: we applied LCA to determine classes (subcategories of each domain) of the meal-to-sleep interval dietary practice, using the lunch, dinner, and last snack-to bed indicators; A 1-class model was applied, then the number of latent classes was increased to determine the most parsimonious model	N/A
		Biological	N/A	N/A
TOEI[2]	Timepoint	Clock	Night energy intake: total calories consumed during 20:30–04:59	N/A
		Pseudo clock		N/A
		Sleep	Energy intake in the late afternoon-early evening: percentage of total daily energy intake consumed in the late afternoon-early evening (from midpoint of the waking period until 2 h before bedtime)	N/A
		Biological	Timing of the latest daily calories: average timing of the latest daily caloric event, defined relative to clock hour and relative to the timing of DLMO	N/A
	Duration	Clock	N/A	N/A
		Pseudo clock	N/A	N/A
		Sleep	Caloric intake relative to sleep onset time	N/A
		Biological	Caloric midpoint-DLMO: duration between the average clock time of midpoint of caloric intake and DLMO	N/A
	Distribution	Clock	Nighttime energy intake ratio (ER %): ER % was calculated as each individual's energy intake during the nighttime (21:00–03:00) divided by the total energy intake over 24 h	N/A
		Pseudo clock	Proportion of total calories in morning meals: proportion of total energy intake (% kcal) in the morning (breakfast + morning snacks)	N/A
		Sleep		N/A

(*continued on next page*)

TABLE 6 (*continued*)

TOE vs. TOEI	Conceptualization	Time anchor	Observational study variable examples	Intervention study condition examples
			Early energy eaters: participants who consumed ≥60 % of their energy during the first half of awake time; nonearly energy eaters were defined as those who consumed <60 % of their energy during the first half of their time awake	
		Biological	Caloric intake across circadian phase: percentage of daily caloric intake consumed across circadian time, defined using each participant's DLMO; 0 Degrees = 23:17 on average in the study population	N/A
	Cluster	Clock	Temporal dietary pattern (TDP): absolute energy intake at each hour of the day was used to divide population into clusters representing similar TDPs	N/A
		Pseudo clock	Time-of-day energy intake patterns: time-of-day energy intake patterns were determined using LCA; latent classes of time-of-day energy intake patterns were identified on the basis of the categorization of proportion of total energy intake from Morning eating occasion (EO), Noon EO, and Evening EO	N/A
		Sleep	N/A	N/A
		Biological	N/A	N/A

Abbreviations: TOE, timing of eating; TOEI, timing of energy intake.
[1] N/A indicates that there were 0 instances of the specific combination in the dataset.
[2] TOEI was not relevant to intervention studies.

with 2 (or more) time anchors. For example, Rangaraj et al. [37] examined the timing of meals using both participant-defined "morning" and "evening" windows, as well as identifying the exact clock time at which certain proportions of daily intake occurred. McHill et al. [33] also examined differences in using dim-light-melatonin-onset compared with clock time. Defining the time anchor in multiple ways, potentially by following the framework developed in Table 1, may ease cross-comparison of studies.

Although several studies were designed to answer a similar research question, the variables or conditions were often assessed or operationalized differently. This may be because of limitations of assessment methodology or other factors such as cultural differences in the timing of meals. Several studies sought to understand the interplay of TOE and TOEI by combining multiple dietary assessment methods. Some studies used 2 tools to separately capture habitual TOE (e.g., a survey of usual timing) and TOEI (e.g., single-day 24-h dietary recall), combining this information to estimate habitual TOE/TOEI. However, there was often a lack of clarity in describing what information was drawn from what tool, and whether these tools were specifically validated for time. Importantly, many of the tools used to assess TOE/TOEI are based on self-reported data, which is prone to measurement error and intraindividual variability [62]. Common tools used in the included studies to assess TOE/TOEI were 24-h recalls or food records. These tools commonly ask the time of each ingestive event but are validated for energy, nutrients, and food intake only. This type of variable (time) likely suffers from the terminal digit-bias, as commonly described for blood pressure readings [63], but this is understudied. Furthermore, it is unknown how close to "truth" is needed: e.g., if self-reported intake is off by 10- compared with 30-min deviation, would this yield a biologically relevant difference that should be accounted for in the measurement? The lack of validated time-specific assessment methods is a limitation, and investigation is needed to understand the accuracy of retrofitting traditional dietary assessment tools for TOE/TOEI.

Several recent studies have sought to evaluate the reliability and validity of deriving TOE/TOEI from assessment tools originally validated to measure other aspects of a diet. Peterson et al. [64] evaluated the reliability of single and repeated 24-h dietary recalls for estimating several "meal timing parameters." They found that that a single 24-h recall produced "poor" reliability for "overnight fasting duration" and moderate reliability with three 24-h recalls, with reliability varying across studies and differing by key characteristics, such as sex and day of the week. Similarly, Hartman et al. [65] assessed the relative validity and 1-y reproducibility of a 24-h grid approach administered twice, 1 y apart, to assess TOE as compared with 6 unannounced 24-h recalls; this study found that the reproducibility of the 24-h grid was ≥0.5 for most TOE variables, and that relative validity compared with 24-h recalls was the highest for weekday reporting and for "hour of first eating occasion." However, as noted above, the accuracy with which the timing of meals is reported on 24-h recalls to serve as "truth" in these comparisons is unclear. These newer validation studies suggest that, as with estimating habitual EI [66] or dietary quality, there may be a minimum number of assessment days required for a valid or reliable estimate. In the sample of studies included in this review, the majority of observational and intervention studies assessed TOE/TOEI for fewer than 3 d, indicating that future studies may be strengthened by leveraging a longer assessment period or repeated measurements.

Recommendations for future studies

The current findings point to several considerations and recommendations for future observational and intervention studies proposing to examine TOE/TOEI in the context of chronic disease. First, the field would greatly benefit from greater transparency in reporting aspects of TOE/TOEI conceptualization, description, and assessment. Researchers should include in their

TABLE 7
TOE/TOEI assessment tools, frequency, and intensity for observational studies

Eating assessment tool	*n*	%
Survey or questionnaire	39	28.9 %
Daily	0	0.0 %
One timepoint[1]		
Habitual	35	25.9 %
More than one timepoint	0	0.0 %
Other/unspecified food record, food log, or food diary[2]	26	19.3 %
Daily	5	3.7 %
One timepoint[3]		
1 d	1	0.7 %
>1 d	17	12.6 %
More than one timepoint		
1 d	0	0.0 %
>1 d	2	1.5 %
Other/unspecified interviewer-administered 24-h dietary recall	15	11.1 %
Daily	0	0.0 %
One timepoint		
1 d	8	5.9 %
>1 d	5	3.7 %
More than one timepoint		
1 d	1	0.7 %
>1 d	1	0.7 %
AMPM (UDSA) interviewer-administered 24-h dietary recall	11	8.1 %
Daily	0	0.0 %
One timepoint		
1 d	7	5.2 %
>1 d	3	2.2 %
More than one timepoint		
1 d	1	0.7 %
>1 d	0	0.0 %
Smartphone application	7	5.2 %
Daily	3	2.2 %
One timepoint		
1 d	0	0.0 %
>1 d	4	3.0 %
Multiple tools	4	3.0 %
Automated Self-Administered 24 h (ASA-24) dietary recall or record	3	2.2 %
Daily	0	0.0 %
One timepoint	0	0.0 %
More than one timepoint		
1 d	2	1.5 %
>1 d	1	0.7 %
Meal timing grid[4]	3	2.2 %
Daily	0	0.0 %
One timepoint		
1 d	1	0.7 %
>1 d	0	0.0 %
More than one timepoint		
Habitual	1	0.7 %
Time-use methods	3	2.2 %
Daily	0	0.0 %
One timepoint		
1 d	3	2.2 %
>1 d	0	0.0 %
More than one timepoint	0	0.0 %
NDSR/NCC interviewer-administered 24-h dietary RECALL	2	1.5 %
Daily	0	0.0 %
One timepoint		
1 d	1	0.7 %
>1 d	1	0.7 %
More than one timepoint	0	0.0 %
Other	22	16.3 %
Daily	2	1.5 %
One timepoint[5]		
1 d	2	1.5 %
>1 d	6	4.4 %
Habitual	6	4.4 %
More than one timepoint		
1 d	2	1.5 %
>1 d	3	2.2 %

"Daily" indicates that a study administered the tool consecutively for 4 or more days. The tool type in $N = 1$ study was not described, and thus was omitted from the table (table shows $N = 135$ of $N = 136$ studies). Abbreviations: AMPM, automated multiple-pass method; NCC, Nutrition Coordinating Center; NDSR, Nutrition Data System for Research; TOE, timing of eating; TOEI, timing of energy intake.

[1] Includes $N = 4$ with NS number of assessment days.
[2] Includes $N = 2$ weighted food records.
[3] Includes $N = 1$ with NS number of assessment days.
[4] Includes $N = 1$ with NS number of assessment days.
[5] Includes $N = 1$ with NS number of assessment days.

manuscripts detailed information on the specific tool used to assess TOE/TOEI, whether it was validated for this purpose specifically, the frequency and intensity with which it was administered, and how the resultant data were used to define and operationalize the relevant TOE/TOEI variables or conditions. Future studies should consider including the elements described in the study reporting rating tool to facilitate transparency and cross-study comparison [67,68]. A standardized research framework and lexicon for TOE/TOEI research in the chronic disease context is essential for expanding the evidence base for the role of TOE/TOEI on health outcomes, as well as for facilitating evidence synthesis.

In addition, there is a need to critically evaluate the methodologies available for assessing TOE/TOEI and to promote the use of time-specific tools instead of relying on tools that were not developed to accurately record time (i.e., retrofitting old methods to new concepts). Very few studies leveraged ambulatory assessment methods (e.g., sensors, EMA) for TOE/TOEI, which may be particularly useful and appropriate for capturing TOE in the context of daily life [69–71]. Although some tools have been developed and validated specifically to assess TOE in the context of the 24-h day [65,72], many studies relied on single-item retrospective surveys to assess habitual TOE/TOEI. Still, others leveraged assessment tools that capture detailed time-stamp information, yet have not been fully validated for capturing this information. The validation of such existing tools (e.g., ASA24, AMPM 24-h dietary recall) for TOE/TOEI would provide a benefit to the field of chrononutrition; it would also provide the added benefit of enabling researchers to integrate the what with the when. By allowing the concurrent assessment of not just timing, but dietary quality, EI, and macronutrient

TABLE 8
TOE/TOEI adherence tools, frequency, and intensity for interventions

Adherence tool	*n*	%
Virtual or in-person meeting with staff or Registered Dietitian[1]	**48**	**23.8 %**
Daily	1	0.5 %
Once		
1 d	2	1.0 %
>1 d	0	0.0 %
More than once[2]		
1 d	32	15.8 %
>1 d	2	1.0 %
Unspecified food record, diary, or log[3]	**41**	**20.3 %**
Daily[4]	8	4.0 %
Once		
1 d[5]	2	1.0 %
>1 d	1	0.5 %
More than once[6]		
1 d	0	0.0 %
>1 d[7]	20	9.9 %
Direct observation (laboratory-based study)	**37**	**18.3 %**
Intake timing log[8]	**19**	**9.4 %**
Daily	14	6.9 %
Once		
1 d	0	0.0 %
>1 d	0	0.0 %
More than once		
1 d	1	0.5 %
>1 d	1	0.5 %
Smartphone application	**18**	**8.9 %**
Daily	10	5.0 %
Once		
1 d	0	0.0 %
>1 d	0	0.0 %
More than once		
1 d	3	1.5 %
>1 d	5	2.5 %
Body weight measured or reported	**13**	**6.4 %**
Daily	1	0.5 %
Once		
1 d	0	0.0 %
>1 d	0	0.0 %
More than once		
1 d	11	5.4 %
>1 d	1	0.5 %
24-h recall	**8**	**4.0 %**
Daily	0	0.0 %
Once		
1 d	2	1.0 %
>1 d	0	0.0 %
More than once		
1 d	3	1.5 %
>1 d	3	1.5 %
Survey or questionnaire[9]	**8**	**4.0 %**
Daily	1	0.5 %
Once[9]	1	0.5 %
More than once[9]	5	2.5 %
Smartphone application[9]	**4**	**2.0 %**
Daily	3	1.5 %
Once	0	0.0 %
More than once	0	0.0 %
Biomarker[9]	**4**	**2.0 %**
Daily[10]	1	0.5 %
Once		
1 d	1	0.5 %
>1 d	0	0.0 %
More than once	0	0.0 %
1 d	0	0.0 %
>1 d[10]	1	0.5 %
Food weigh backs[9]	**2**	**1.0 %**
Daily	0	0.0 %
Once	0	0.0 %
1 d	0	0.0 %
>1 d	0	0.0 %
More than once		
1 d	1	0.5 %
>1 d	0	0.0 %

Ten studies did not report measures of adherence and are omitted from the total count ($n = 116$ of 126). Some details were not further specified, as denoted in footnotes; hence, percentages may not add ≤100 %.
[1] NS = 9.
[2] NS = 2.
[3] NS = 6.
[4] Includes 2 weighted food records.
[5] Includes 1 weighted food record.
[6] NS = 4.
[7] Includes 6 weighted food records.
[8] NS = 3.
[9] NS = 1.
[10] Includes study that used continuous glucose monitoring for adherence measures.

distribution within the 24-h day in a standardized and accessible platform, these tools could help provide new insights into how TOE/TOEI relates to other aspects of diet and health [73]. Furthermore, culture plays a strong influence on daily time-use patterns, including dimensions of TOE/TOEI, such as the temporal pattens of TOE/TOEI within the 24-h day and the amount of time devoted to eating [74]; future studies should examine the relative influence of TOE/TOEI, diet quality, and other cultural factors on health outcomes, as well as the unique role of culture on TOE/TOEI patterns. Of note, many of the challenges identified within the TOE/TOEI literature are challenges present across the field of nutrition and dietary assessment, providing further support for holding nutrition research to higher methodological and reporting standards [67,68].

The current study also yields some practical implications. For TOE/TOEI research to effectively inform the development of broader guidelines (e.g., the Dietary Guidelines for Americans), it is clear that a more developed and systematic body of evidence is needed. For example, there is a great diversity of definitions and conceptualizations for a single TOE/TOEI variable or condition. This lack of unity across studies may hinder the broader research community's ability to interpret and synthesize results such that recommendations may be derived. In addition, health professionals who would like to recommend TOE/TOEI strategies to their patients may face similar challenges. For example, it may be challenging for health professionals to provide specific guidance for TRE because of the large variability in how TRE is defined (e.g., 6- compared with 10-h window of eating), anchored (e.g., starting 2 h after awakening compared with starting at noon), and contextualized (e.g., only water during fasting window compared with low-calorie foods allowed during fasting window).

Strengths and limitations

This systematic review examined a large number of eligible studies and followed both the PRISMA [27] and AMSTAR 2

criteria [75], as appropriate, for high-quality method reporting. This qualitative synthesis provides an overview of the methods used to conceptualize, describe, and assess TOE/TOEI across a diverse range of study designs and settings, laying the groundwork for future standardization efforts. This review also has some limitations that may limit the generalizability of our systematic review to populations and settings beyond those that were considered. Only studies published in 2000 or later were included, and earlier studies were not considered; in particular, given publication trends there may be some literature in the past year that was not eligible for inclusions in this review, and synthesis of these studies should be a priority for future research. There may be a language bias because only studies published in English were assessed. Furthermore, studies that were conducted among youth age $\leq$18 y, which may have used different assessment tools or TOE/TOEI variables or conditions unique to a younger population, were not included. Finally, studies that defined TOE/TOEI using only socially defined meal labels (e.g., studies examining the frequency of "breakfast" intake, without any additional temporal information or definition for when breakfast intake occurs) were excluded. Although these studies were excluded because they did not meet the criteria for an eligible exposure, this type of study represents a large body of literature on meal timing that may provide additional insights into methods and survey tools used.

Conclusion

This systematic review provides the foundation for a standardized research framework and lexicon for TOE, TOEI, and chrononutrition research to help facilitate evidence synthesis on this topic for consideration in future dietary guidance. Results demonstrate the burgeoning body of research examining TOE/TOEI in relation to chronic disease risk factors and outcomes; illustrates the disparate methods and approaches used to characterize TOE/TOEI within the literature; and highlights future research priorities of tool validation, transparency of reporting, and a critical examination of additional factors (i.e., cultural) to be considered when assessing TOE/TOEI in various populations.

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Author contributions

The authors' responsibilities were as follows – SGO, LEO: designed research, conducted research, analyzed data, wrote paper, and had primary responsibility for the final content; KAH: conducted research and analyzed data; BMB, ESK, RR, RH: conducted research; JR: designed research; MMS-W: designed research, conducted research, and wrote paper; and all authors: read and approved the final manuscript.

Conflict of interest

KAH is employed by Exponent Inc. (August 2023–present; 2019–2021); serves as the President of the Washington, DC section of the Institute of Food Technologists; and has a close relative employed by a consumer-packaged goods company. All other authors report no conflicts of interest.

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Disclaimer

The opinions expressed in this article are the authors' own and do not reflect the view of the National Institutes of Health, the Department of Health and Human Services, the Department of Agricultulure, or the United States government.

Data availability

The data extraction template and cleaned final data are included in the Supplementary Materials.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.advnut.2024.100178.

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