

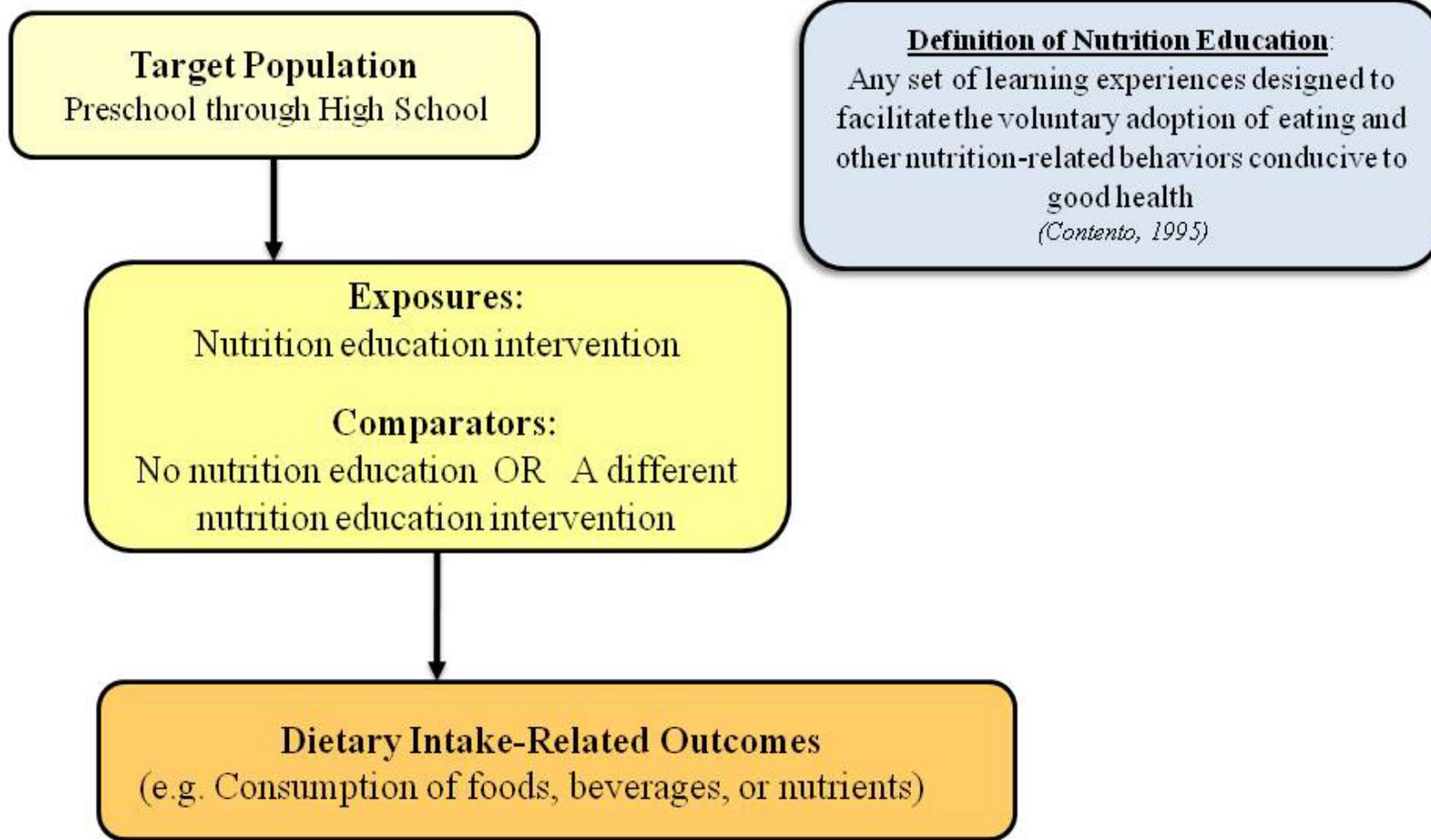
1 Appendices

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Appendix A: Analytical Framework



1 **Appendix B: Research Design and Implementation Checklist for**
 2 **Primary Research Articles**

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 4 Each study the included in a NEL systematic review receives a quality rating of positive, neutral,
 5 or negative, based upon a predefined scoring system. The appraisal of study quality is a critical
 6 component of the systematic review methodology because in a highly transparent manner, it
 7 indicates the relevance (external validity/generalizability) and validity of each study’s results.

8 The Research Design and Implementation Checklist: Primary Research includes ten validity
 9 questions based on the AHRQ domains for research studies. Sub-questions are listed under each
 10 validity question that identify important aspects of sound study design and execution relevant to
 11 each domain. Some sub-questions also identify how the domain applies in specific research
 12 designs.

Relevance Questions	
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition and public health practice?
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)
If the answers to all of the above relevance questions are “Yes,” the report is eligible for designation with a plus (+) on the Evidence Research Design and Implementation Worksheet, depending on answers to the following validity questions.	
Validity Questions	
1.	Was the research question clearly stated? 1.1 Was the specific intervention(s) or procedure (independent variable(s)) identified? 1.2 Was the outcome(s) (dependent variable(s)) clearly indicated? 1.3 Were the target population and setting specified?
2.	Was the selection of study subjects/patients free from bias? 2.1 Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study? 2.2 Were criteria applied equally to all study groups? 2.3 Were health, demographics, and other characteristics of subjects described? 2.4 Were the subjects/patients a representative sample of the relevant population?
3.	Were study groups comparable? 3.1 Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT) 3.2 Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline? 3.3 Were concurrent controls used? (Concurrent preferred over historical controls.) 3.4 If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis? 3.5 If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.) 3.6 If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., “gold standard”)?
4.	Was method of handling withdrawals described? 4.1 Were follow-up methods described and the same for all groups? 4.2 Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)

	<p>4.3 Were all enrolled subjects/patients (in the original sample) accounted for?</p> <p>4.4 Were reasons for withdrawals similar across groups?</p> <p>4.5 If diagnostic test, was decision to perform reference test not dependent on results of test under study?</p>
5.	<p>Was blinding used to prevent introduction of bias?</p> <p>5.1 In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?</p> <p>5.2 Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)</p> <p>5.3 In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?</p> <p>5.4 In case control study, was case definition explicit and case ascertainment not influenced by exposure status?</p> <p>5.5 In diagnostic study, were test results blinded to patient history and other test results?</p>
6.	<p>Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?</p> <p>6.1 In RCT or other intervention trial, were protocols described for all regimens studied?</p> <p>6.2 In observational study, were interventions, study settings, and clinicians/provider described?</p> <p>6.3 Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?</p> <p>6.4 Was the amount of exposure and, if relevant, subject/patient compliance measured?</p> <p>6.5 Were co-interventions (e.g., ancillary treatments, other therapies) described?</p> <p>6.6 Were extra or unplanned treatments described?</p> <p>6.7 Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?</p> <p>6.8 In diagnostic study, were details of test administration and replication sufficient?</p>
7.	<p>Were outcomes clearly defined and the measurements valid and reliable?</p> <p>7.1 Were primary and secondary endpoints described and relevant to the question?</p> <p>7.2 Were nutrition measures appropriate to question and outcomes of concern?</p> <p>7.3 Was the period of follow-up long enough for important outcome(s) to occur?</p> <p>7.4 Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?</p> <p>7.5 Was the measurement of effect at an appropriate level of precision?</p> <p>7.6 Were other factors accounted for (measured) that could affect outcomes?</p> <p>7.7 Were the measurements conducted consistently across groups?</p>
8.	<p>Was the statistical analysis appropriate for the study design and type of outcome indicators?</p> <p>8.1 Were statistical analyses adequately described and the results reported appropriately?</p> <p>8.2 Were correct statistical tests used and assumptions of test not violated?</p> <p>8.3 Were statistics reported with levels of significance and/or confidence intervals?</p> <p>8.4 Was “intent to treat” analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?</p> <p>8.5 Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?</p> <p>8.6 Was clinical significance as well as statistical significance reported?</p> <p>8.7 If negative findings, was a power calculation reported to address type 2 error?</p>
9.	<p>Are conclusions supported by results with biases and limitations taken into consideration?</p> <p>9.1 Is there a discussion of findings?</p> <p>9.2 Are biases and study limitations identified and discussed?</p>
10.	<p>Is bias due to study’s funding or sponsorship unlikely?</p> <p>10.1 Were sources of funding and investigators’ affiliations described?</p> <p>10.2 Was the study free from apparent conflict of interest?</p>
<p>MINUS/NEGATIVE If most (six or more) of the answers to the above validity questions are “No,” the report should be designated with a minus (-) symbol on the Evidence Research Design and Implementation Worksheet.</p>	
<p>NEUTRAL If the answers to validity criteria questions 2, 3, 6, and 7 do not indicate that the study is exceptionally strong, the report should be designated with a neutral (∅) symbol on the Evidence Research Design Worksheet.</p>	
<p>PLUS/POSITIVE If most of the answers to the above validity questions are “Yes” (including criteria 2, 3, 6, 7 and at least one additional “Yes”), the report should be designated with a plus symbol (+) on the Evidence Research Design Worksheet.</p>	

1 Appendix C: Conclusion Statement Grading Criteria

Conclusion Statement Grading Criteria					
Criteria for judging the strength of the body of evidence supporting the Conclusion Statement					
Elements	I: Strong	II: Moderate	III: Limited	IV: Expert Opinion Only	V: No Evidence Available
Quality <ul style="list-style-type: none"> Scientific rigor and validity Consider study design and execution 	Studies of strong design Free from design flaws, bias, and execution problems	Studies of strong design with minor methodological concerns OR only studies of weaker study design for question	Studies of weak design for answering the question OR inconclusive findings due to design flaws, bias, or execution problems	No studies available Conclusion based on usual practice, expert consensus, clinical experience, opinion, or extrapolation from basic research	No evidence that pertains to question being addressed
Consistency Of findings across studies	Findings generally consistent in direction and size of effect or degree of association, and statistical significance with minor very exceptions	Inconsistency among results of studies with strong design, OR consistency with minor exceptions across studies of weaker design	Unexplained inconsistency among results from different studies, OR single study unconfirmed by other studies	Conclusion supported solely by statements of informed nutrition or medical commentators	NA
Quantity <ul style="list-style-type: none"> Number of studies Number of subjects in studies 	One large study with a diverse population or several good quality studies Large number of subjects studied Studies with negative results have sufficiently large sample size for adequate statistical power	Several studies by independent investigators Doubts about adequacy of sample size to avoid Type I and Type II error	Limited number of studies Low number of subjects studied and/or inadequate sample size within studies	Unsubstantiated by published research studies	Relevant studies have not been done
Impact <ul style="list-style-type: none"> Importance of studied outcomes Magnitude of effect 	Studied outcome relates directly to the question Size of effect is clinically meaningful Significant (statistical) difference is large	Some doubt about the statistical or clinical significance of the effect	Studied outcome is an intermediate outcome or surrogate for the true outcome of interest OR size of effect is small or lacks statistical and/or clinical significance	Objective data unavailable	Indicates area for future research
Generalizability To population of interest	Studied population, intervention and outcomes are free from serious doubts about generalizability	Minor doubts about generalizability	Serious doubts about generalizability due to narrow or different study population, intervention or outcomes studied	Generalizability limited to scope of experience	NA