Effects of Kimchi on human health
A protocol of systematic review of controlled clinical trials
Myung-Sunny Kim, PhDab, Hye Jeong Yang, PhDa, Soon-Hee Kim, PhDa, Hye Won Lee, PhDc, Myeong Soo Lee, PhDde,

Abstract
Background: Kimchi, a traditional, fermented Korean food that is consumed daily, has been recognized as a health food due to its beneficial effects on human health. The aim of this overview is to critically evaluate all clinical trials of the use of Kimchi in the treatment of any condition or symptom.

Methods and analysis: Eight databases will be searched from inception until March 2018. We will include all prospective trials, including randomized controlled trials (RCTs), non-RCTs, and uncontrolled trials. The methodological quality of the trials will be assessed using Cochrane risk of bias (ROB) assessment tool and ROB in nonrandomized studies-I for RCTs and non-RCTs, respectively.

Ethics and dissemination: Ethical approval will not be required, given that this protocol is for a systematic review. The full systematic review will be published in a peer-reviewed journal. The review will also be disseminated electronically and in print. Updates of the review will be conducted to inform and guide health care practice and policy.

Trial registration number: PROSPERO 2018 CRD42018087375

Abbreviations: RCT = randomized controlled trial, ROB = risk of bias.

Keywords: ethnic food, fermented vegetable, health care, Kimchi

1. Introduction
Kimchi, a traditional, fermented Korean food that is consumed daily, has been recognized as a health food due to its beneficial effects on human health. As it is fermented with various vegetable ingredients and seasonings, it is abundant in dietary fiber, vitamins, lactic acid bacteria, minerals, and other active compounds that are present either in Kimchi ingredients such as cabbage, garlic, ginger, and red pepper powder[1,2] or in fermented products in general.

Scientific studies have shown that the biological compounds of Kimchi stimulate immune function and reduce pro-oxidants, free radicals, certain cancers, cardiovascular disease (CVD), metabolic syndrome risks, and aging, as reviewed.[3-8]

Several studies have evaluated the potential benefits to human health, and accumulating data on human Kimchi consumption has shown that Kimchi consumption lowers lipids and the atherogenic index in plasma[9-11]; it also changes the composition as well as count of intestinal microflora[12,13] and increases iron levels.[14]

Since a systematic review of these topics is not available, we access evidence of the beneficial effects of Kimchi consumption on human health. The aim of this overview is to critically evaluate all clinical trials of the use of Kimchi in the treatment of any condition or symptom.

2. Methods
2.1. Study registration
This protocol of review has been registered on PROSPERO 2018 CRD42018087375 (http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018087375).

2.2. Criteria for considering studies for this review

2.2.1. Types of studies. All prospective trials will be included. We will include randomized controlled trials (RCTs) and non-RCTs. We will exclude uncontrolled trials, case series, case studies, and retrospective clinical trials.

2.2.2. Type of participants. We will include trials with healthy persons and persons with any health condition. We will also include trials with participants regardless of age or sex, including children, adults, and the elderly.
2.2.3. Type of interventions. We will include all types of Kimchi, traditional fermented Korean food that is consumed daily, regardless of vegetable ingredients, origin of region, production date, and presence or absence of water.

2.2.4. Type of outcome measures. The primary outcome will be related to the target conditions. We will use the timing and effect measures as the value of the end of treatment. Secondary outcomes will be quality of life and adverse events.

2.3. Search methods for the identification of studies 2.3.1. Data searches. The following databases will be searched for content dated up to March 2018: MEDLINE, Embase, and the Cochrane Library, as well as Korean databases (Oriental Medicine Advanced Searching Integrated System, the National Digital Science Library, DBpia, the Research Information Service System, and the Korean Studies Information Service System). Relevant journals include Preventive Nutrition and Food Science, and Food Industry and Nutrition Conference will be hand-searched as gray literature for proceedings from the Korean Society of Food Science and Nutrition. The references in all identified articles will also be searched.

2.3.2. Search strategies. The search strategy will use the key words [“Kimchi” OR “Kim Chi” OR “fermented vegetable”] AND [“clinical trial”] and will be principally based on the individual database-specific structure.

2.4. Selection of studies Two authors (MSK and HJY) will select articles to include by checking article titles and abstracts. These authors will review hard copies of relevant publications to determine their inclusion. Any disagreement will be resolved through discussion and, if necessary, will use a 3rd reviewer (MSL).

2.5. Data extraction and management Three authors will participate in the data extraction (MSK, SHK, and HWL). Information regarding study design, population, symptom types, and interventions and outcomes will be extracted from the studies. Disagreements will be resolved by discussion between the authors.

2.6. Risk of bias assessment The quality of each study will be assessed on the basis of the study design; to this end, risk of bias (ROB) assessment is used for RCTs.[13] Domains including sequence generation, allocation concealment, blinding of participants, blinding of outcome assessors, incomplete outcome data, selective reporting, and other biases will be assessed, and ROB for each domain will be decided as being low, high, or unclear based on the Cochrane collaboration guideline.

The ROB of non-RCTs will be assessed using the ROB in nonrandomized studies-I tools.[14] This tool evaluates bias from confounding, selection of participation, classification of intervention, deviation from intended intervention, missing data, measurement of outcome, and selection of the reported results. Each domain will be rated as having low, severe, critical, or unclear ROB.

2.7. Data synthesis We will conduct a meta-analysis if enough studies for each symptom are identified: risk ratio (RR) for dichotomous outcomes and mean difference (MD) for continuous outcomes will be assumed to be used as summary estimates. Considering the expected clinical heterogeneity of types of Kimchi, a random effect model will be adopted for the meta-analysis. We will use the I² statistic for quantifying inconsistencies across the included studies.[15] A result 50% cut off point would represent substantial heterogeneity. If heterogeneity is observed, subgroup analyses will be conducted according to type of Kimchi, type of control intervention (eg, Western medicine, no treatment, or usual care). We will use GRADEpro GDT software (https://gradepro.org/) to create a summary of findings table.

If more than 10 studies are available, we will conduct funnel plot for publication bias and small study effects using Egger method.[17] Funnel plot asymmetry is certainly not same as publication bias. We will attempt to distinguish the possible reasons for the asymmetry, therefore, included poor methodological quality and true heterogeneity of studies.

If there are not enough RCTs for meta-analysis, we will conduct a narrative review based on the research designs. We will summarize the study characteristics and effectiveness of Kimchi based on the individual results of the included studies.

2.8. Ethics and dissemination

Ethical approval is not required, given that this protocol is for a systematic review. The findings of this review will be disseminated widely through peer-reviewed publications and conference presentations.

3. Discussion

No systematic review of these clinical studies has been conducted yet. The completed review will provide a summary of the current state of evidence and will be useful to researchers, food and nutrition policymakers, and food companies, as well as to patients and consumers.

Author contributions

Conceptualization: M.-S. Kim, M.S. Lee.
Data curation: M.-S. Kim.
Formal analysis: M.-S. Kim, H.J.Y. Yang.
Funding acquisition: M.-S. Kim, M.S. Lee.
Methodology: M.S. Lee.
Supervision: M.S. Lee.
Validation: S.-H. Kim, H.W. Lee.
Writing – original draft: M.-S. Kim, M.S. Lee.
Writing – review & editing: H.J.Y. Yang, S.-H. Kim, H.W. Lee.

References

[1] Cheigh HS, Park KY. Biochemical, microbiological, and nutritional aspects of Kimchi (Korean fermented vegetable products). Crit Rev Food Sci Nutr 1994;34:175–203.
[2] Kim GR, Park NY, Lee SH. Fermentation and quality characteristics of Kimchi prepared using various types of maesil. Korean J Food Preserv 2010;17:214–22.
[3] Cho EJ, Choi JS, Kim SH, et al. In vitro anticancer effect of active compounds from Chinese cabbage Kimchi. J Korean Ass Cancer Prev 2004;9:94–103.
[4] Kim EK, An S-Y, Lee M-S, et al. Fermented kimchi reduces body weight and improves metabolic parameters in overweight and obese patients. Nutr Res 2011;31:436–43.
[5] Kim MJ, Kim GR. In vitro evaluation of cholesterol reduction by lactic acid bacteria extracted from Kimchi. Korean J Culinary Res 2006;12:259–68.
[6] Kong C-S, Bahn Y-E, Kim B-K, et al. Antiproliferative effect of chitosan-added Kimchi in HT-29 human colon carcinoma cells. J Med Food 2010;13:6–12.

[7] Ryu BM, Ryu SH, Lee YS, et al. Effect of different kimchi diets on oxidation and photooxidation in liver and skin of hairless mice. J Korean Soc Food Sci Nutr 2004;33:291–8.

[8] Song YO. The functional properties of Kimchi for the health benefits. Food Ind Nutr 2004;9:27–33.

[9] Baek YH, Kwak JR, Kim SJ, et al. Effect of Kimchi supplementation and/or exercise training on body composition and plasma lipids in obese middle school girls. J Koran Soc Food Sci Nutr 2001;30:906–12.

[10] Choi SH, Kwon MJ, Kim MJ, et al. Effects of water-soluble and water-insoluble fractions of Kimchi on the alteration of plasma lipids and fibrinolytic activity in middle-aged healthy subjects. J Food Sci Nutr 2006;11:218–23.

[11] Choi SH, Kim HJ, Kwon MJ, et al. The effect of Kimchi pill supplementation on plasma lipid concentration in healthy people. J Koran Soc Food Sci Nutr 2001;30:913–20.

[12] HKJ, Jung KO, Lee HS, Hwnag IK, et al. Effects of Kimchi on stomach and colon health of Helicobacter pylori-infected volunteers. J Food Sci Nutr 2004;9:161–6.

[13] Lee KE, Choi UH, Ji GE. Effect of Kimchi intake on the composition of human large intestinal bacteria. Korean J Food Technol 1996;28:981–6.

[14] Oh YJ, Hwnag IJ. Effects of Kimchi consumption on roen status in adults male volunteers. Korean J Nutr 1997;30:1188–94.

[15] Higgins JPT, Altman DG, Sterne JAC. Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green, S, editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011): The Cochrane Collaboration.

[16] Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355.

[17] Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–34.