British Journal of Nutrition (2021), 126, 1355–1363 doi:10.1017/S0007114520005255

Dietary acrylamide intake and risk of women's cancers: a systematic review and meta-analysis of prospective cohort studies

Sanaz Benisi-Kohansal[1], Asma Salari-Moghaddam[1], Zahraalsadat Seyed Rohani[2] and Ahmad Esmaillzadeh[1,3,4]*

[1]*Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran*
[2]*Students' Science and Research Branch, Islamic Azad University, Tehran, Iran*
[3]*Obesity and Eating Habits Research Center, Endocrinology and Metabolism Molecular-Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran*
[4]*Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran*

(Submitted 30 July 2020 – Final revision received 15 December 2020 – Accepted 19 December 2020 – First published online 8 January 2021)

Abstract

This systematic review and meta-analysis was done to review earlier publications on the association between dietary acrylamide intake and risk of breast, endometrial and ovarian cancers. We performed a systematic search in the online databases of PubMed, ISI Web of Science and Scopus for relevant publications up to August 2020. Prospective cohort studies that considered dietary acrylamide as the exposure variable and breast, endometrial or ovarian cancer as the main outcome variable or as one of the outcome variables were included in this systematic review and meta-analysis. A total of fourteen cohort studies were included in the meta-analysis. We found no significant association between dietary acrylamide intake and the risk of breast (relative risk (RR) 0·95; 95 % CI 0·90, 1·01), endometrial (RR 1·03; 95 % CI 0·89, 1·19) and ovarian cancers (RR 1·02; 95 % CI 0·84, 1·24). In addition, we observed no significant association between dietary acrylamide intake and the risk of breast, endometrial and ovarian cancers in different subgroup analyses by smoking status, menopausal status, BMI status and different types of breast cancer. In conclusion, no significant association was found between dietary acrylamide intake and the risk of breast, endometrial and ovarian cancers.

Key words: **Acrylamide: Breast cancer: Endometrial cancer: Ovarian cancer**

Women's cancers including breast, endometrial and ovarian cancers are the most common causes of cancer deaths among women in the world[1–4]. Due to the high prevalence and high mortality rate of these conditions, finding modifiable risk factors is of high priority.

Acrylamide is a neurotoxin in the body, and a carcinogen in experimental animals, that has been reported to have several probable carcinogenic effects on human health by the International Agency for Research on Cancer[5]. Exposure to acrylamide occurs primarily through tobacco smoke, occupational exposure and specifically through diet[6]. According to prior investigations, several heat-treated, carbohydrate-rich foods, such as, French fries, potato chips, bread, breakfast cereals, cookies and coffee, have been reported to contain high levels of acrylamide[7]. Although, in general population, smoking was suggested to be the key source of acrylamide exposure, recent studies have clarified that dietary acrylamide intake plays a significant part in the incidence of various cancers, especially women's cancers. However, such evidence was not provided for all types of women's cancers. For instance, Netherlands Cohort Study data indicated a significant direct linkage between high dietary acrylamide intake and greater odds of postmenopausal endometrial and ovarian cancers, but not breast cancer[8]. Another study from the Investigation into Cancer and Nutrition cohort, however, has demonstrated no noticeable association between increased women's cancers risk and not only dietary acrylamide intake but also other acrylamide biomarkers such as acrylamide adducts to Hb[9–11]. On the other hand, an increased risk of breast cancer was reported among postmenopausal women with higher levels of these adducts in a Danish prospective study[12]. Different reasons might contribute to this inconsistency in the findings. The causality of the observed associations between

Abbreviations: ER, oestrogen receptor; NOS, Newcastle–Ottawa Scale; PR, progesterone receptor; RR, relative risk.

* **Corresponding author:** Ahmad Esmaillzadeh, fax +98 21 88984861, email a-esmaillzadeh@tums.ac.ir

British Journal of Nutrition

acrylamide intake and cancer risk is equivocal, due to observational design of studies. Moreover, the underlying mechanisms through which acrylamide plays a carcinogenic role, including genotoxic pathway[7] and sex hormones modulation[13], are different for each type of cancer.

Given the controversial findings in previous publications and greater cancer risks in humans compared with predicted odds in rodent's studies, this study was done to systematically review earlier publications on the association between dietary acrylamide exposure and women's cancers including breast cancer, endometrial cancer and ovarian cancer and to perform a meta-analysis of relevant prospective studies in this regard.

Methods and materials

The PROSPERO registration no. is CRD42020212620.

Search strategy

A systematic search was carried out in the online databases of PubMed, ISI Web of Science and Scopus for relevant publications up to August 2020. The keywords used in our search strategy were as follows: (acrylamide OR glycidamide) AND ('ovarian cancer' OR 'ovarian neoplasm' OR 'ovarian malignancy' OR 'ovarian carcinoma' OR 'ovarian tumor' OR 'breast cancer' OR 'breast neoplasm' OR 'breast malignancy' OR 'breast carcinoma' OR 'breast tumor' OR 'endometrial cancer' OR 'endometrial neoplasm' OR 'endometrial malignancy' OR 'endometrial carcinoma' OR 'endometrial tumor'). We considered no restriction on time of publication and language. In addition, the reference lists of the relevant papers were also hand-searched to identify further relevant studies. In the search strategy, unpublished studies were excluded. Two reviewers independently screened the output of the search to identify potentially eligible publications (S. B. K. and A. S. M.).

Inclusion criteria

In our meta-analysis, eligible publications were selected in accordance with the following criteria: (1) all prospective cohort studies assessing the association between dietary acrylamide intake and women's cancers including breast, endometrial and ovarian cancers; (2) studies that were of prospective design and (3) those that reported OR, relative risks (RR) or hazard ratios along with the 95 % CI for the relationship between dietary acrylamide intake and breast, endometrial and ovarian cancers.

Data extraction

Study selection and data extraction from each eligible study were carried out independently by two investigators (S. B. K. and A. S. M.), and any disagreements were figured out in consultation with the principal investigator (A. E.). In prospective studies, dietary acrylamide intake was the key exposure variable. Furthermore, the key outcome variable was the incidence of breast, endometrial or ovarian cancers during the follow-up. Any reported hazard ratio or RR for each of these cancers among individuals in the highest category of dietary intake of acrylamide compared with those in the lowest category were extracted. Information from each study was recorded as follows: first authors' last name, year of publication, country of origin, age range at study baseline, cohort size, number of participants with incident breast, endometrial and ovarian cancers, duration of follow-up, methods used for assessing dietary intake of acrylamide and breast, endometrial and ovarian cancers, the maximally adjusted RR or hazard ratios with the corresponding 95 % CI and the study quality score.

Quality assessment of studies

We used the Newcastle–Ottawa Scale (NOS) to evaluate the quality of included studies[14]. Based on this method, a maximum of nine points can be awarded to each prospective study: four for selection, two for comparability and three for assessment of outcomes (nine represented the highest quality). Any discrepancies were resolved by discussion. In the current study, those that had the NOS score of six or more were considered as high-quality publications (Table 1).

Statistical analysis

All reported RR and hazard ratios and their 95 % CI for the risk of breast, endometrial and ovarian cancers were used to calculate log RR and their standard errors. Using a random effects model that incorporates between-study heterogeneity into account, the overall effect size was calculated. Between-study heterogeneity was examined using Cochrane's Q test and I^2. We considered I^2 values of 25, 50, and 75 % as low, moderate, and high, respectively[15]. Subgroup analyses were used to identify possible sources of heterogeneity. The predefined criteria for subgroup analyses were as follows: smoking status (smoker/non-smoker), menopausal status (premenopausal/postmenopausal), different types of breast cancer (oestrogen receptor (ER) positive, progesterone receptor (PR) positive/ER positive, PR negative/ER negative, PR negative (ER+PR+/ER+PR−/ER−PR−)) and BMI status (<25 kg/m^2/≥25 kg/m^2). In these analyses, we used fixed effects models. Sensitivity analysis was used to explore the extent to which inferences might depend on a particular study or group of studies. Publication bias was assessed using Egger's test[16]. Statistical analyses were done in Stata, version 14 (Stata Corp.). Values of P<0·05 were considered statistically significant.

Results

In our initial search, 381 articles were identified. After elimination of duplicates, 244 articles remained. Finally, 222 studies were excluded on the basis of the title and abstract and twenty-two articles remained for further assessment. Another eight publications were further excluded because of the following reasons: two studies were of case–control design[17,18]. In addition, four nested case–control studies that examined the association of adduct levels of acrylamide and the risk of women's cancers were also excluded[9,12,19,20]. Five studies were conducted on the same population[8,21–24]. To avoid including duplicate studies, we included the ones which had longer duration of follow-up[21–23] and excluded two other studies[8,24]. Finally,

Table 1. Main characteristics of studies examining the association between dietary acrylamide intake and the risk of breast, endometrial and ovarian cancers (Relative risk (RR) or hazard ratio (HR) and 95 % confidence intervals)

Author, year (reference)	Country	Age range or mean age (years)	Follow-up duration (years)	Number of cases/ cohort size	Exposure assessment	Outcome assessment	Comparison	RR or HR	95 % CI	Quality score
Breast cancer										
Hogervorst *et al.*, 2019[21]	Netherlands	55–69	20·3	1238/62 573	FFQ	Registries	Q5 *v.* Q1	0·85	0·66, 1·09	7
Kotemori *et al.*, 2018[25]	Japan	45–74	15·4	792/48 910	FFQ	Registries	T3 *v.* T1	0·95	0·79, 1·14	9
Wilson *et al.*, 2010[26]	USA	30–55	26	6301/88 672	FFQ	Medical records	Q5 *v.* Q1	0·95	0·87, 1·03	7
Burley *et al.*, 2010[27]	UK	35–69	11	1084/33 731	FFQ	Registries	Q5 *v.* Q1	1·16	0·88, 1·52	8
Larsson *et al.*, 2009[28]	Sweden	53·6	17·4	2952/61 433	FFQ	Registries	Q4 *v.* Q1	0·91	0·80, 1·02	8
Wilson *et al.*, 2009[29]	USA	25–42	14	1179/90 628	FFQ	Medical records	Q5 *v.* Q1	0·92	0·76, 1·11	8
Mucci *et al.*, 2005[30]	Sweden	39	11	667/43 404	FFQ	Registries	Q5 *v.* Q1	1·19	0·91, 1·55	7
Endometrial cancer										
Kotemori *et al.*, 2018[31]	Japan	45–74	15·5	161/47 185	FFQ	Registries	T3 *v.* T1	0·85	0·54, 1·33	9
Hogervorst *et al.*, 2016[23]	Netherlands	55–69	20·3	393/62 573	FFQ	Registries	Q5 *v.* Q1	1·03	0·71, 1·51	7
Obon-Santacana *et al.*, 2014[10]	10 European countries*	50·2	11	1382/301 113	DQ	Registries and health insurance data	Q5 *v.* Q1	0·98	0·78, 1·25	8
Wilson *et al.*, 2010[26]	USA	30–55	26	484/69 019	FFQ	Medical records	Q5 *v.* Q1	1·41	1·01, 1·97	7
Larsson *et al.*, 2009[32]	Sweden	53·6	17·7	687/61 226	FFQ	Registries	Q4 *v.* Q1	0·96	0·76, 1·21	8
Ovarian cancer										
Kotemori *et al.*, 2018[31]	Japan	45–74	15·6	122/47 185	FFQ	Registries	T3 *v.* T1	0·77	0·49, 1·23	9
Hogervorst *et al.*, 2017[22]	Netherlands	55–69	20·3	373/62 573	FFQ	Registries	Q5 *v.* Q1	1·38	0·95, 1·99	7
Obon-Santacana *et al.*, 2015[11]	10 European countries*	50·7	11	1191/325 006	DQ	Registries and health insurance data	Q5 *v.* Q1	0·97	0·76, 1·23	8
Wilson *et al.*, 2010[26]	USA	30–55	26	416/80 011	FFQ	Medical records	Q5 *v.* Q1	1·25	0·88, 1·77	7
Larsson *et al.*, 2009[33]	Sweden	53·6	17·5	368/61 057	FFQ	Registries	Q4 *v.* Q1	0·86	0·63, 1·16	8

DQ, dietary questionnaire; T, tertile; Q, quartile or quintile.
* Including: France, the UK, the Netherlands, Germany, Sweden, Denmark, Norway, Italy, Spain and Greece.

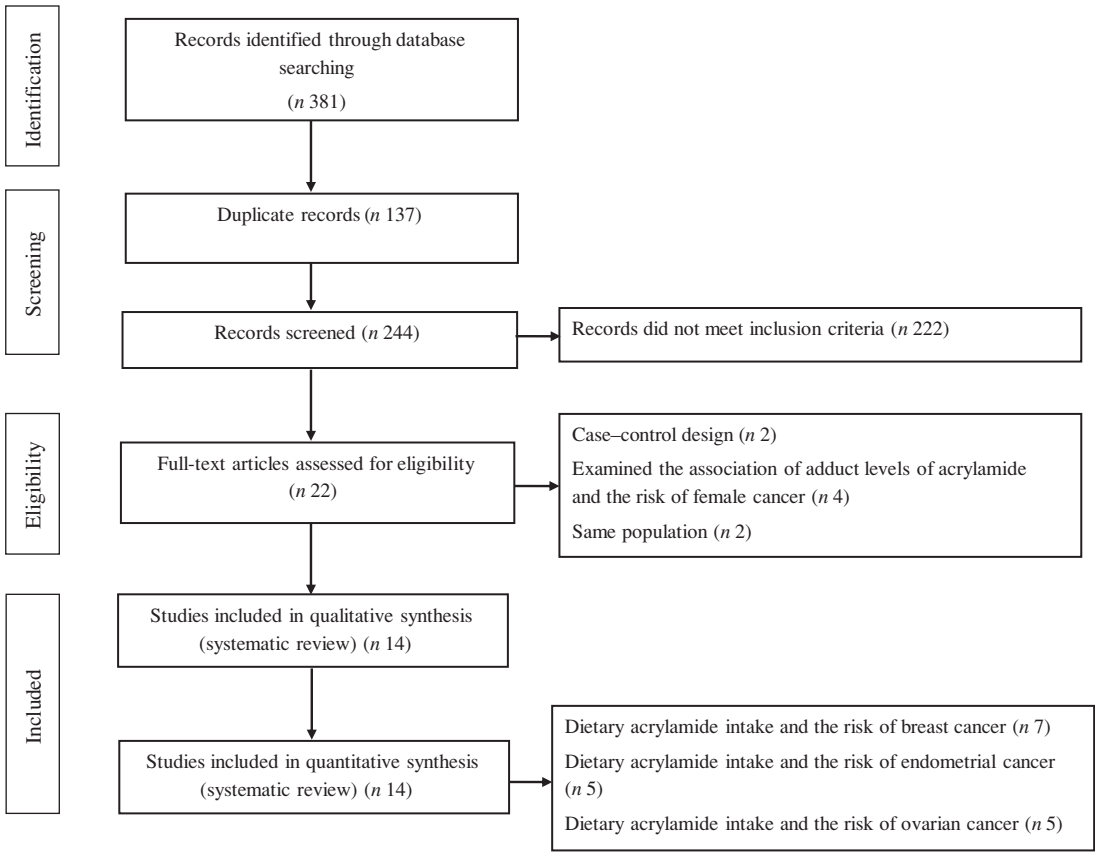

Fig. 1. Flow chart of the study selection process.

fourteen prospective studies were included in this systematic review (Fig. 1).

Results from the systematic review on dietary acrylamide intake and the risk of breast cancer

Seven studies examined dietary acrylamide intake in relation to the risk of breast cancer[21,25–30]. These studies included 429 351 participants aged ≥25 years. The total number of subjects with breast cancer was 14 213 varying from 667 to 6301 between studies. These papers were published between 2005 and 2019; two were from the USA[26,29], two from Sweden[28,30], along with others from the Netherlands[21], Japan[25] and the UK[27]. Duration of follow-up ranged from 11 to 26 years among studies. To assess dietary acrylamide intake, all studies had used FFQ. To examine breast cancer, five studies had used cancer registries[21,25,27,28,30] and two other studies had used medical records[26,29]. Based on the NOS, all included studies were of high quality (Table 1).

Results from the systematic review on dietary acrylamide intake and the risk of endometrial cancer

Five studies examined dietary acrylamide intake in relation to the risk of endometrial cancer[10,23,26,31,32]. These studies included 541 116 participants aged ≥30 years. The total number of subjects with endometrial cancer was 3107 varying from 161 to 1382 between studies. These papers were published between 2009 and 2018, one each from Japan[31], the Netherlands[23], the USA[26], Sweden[32] and Europe[10]. Follow-up duration ranged from 11 to 26 years. For dietary acrylamide intake assessment, all studies had used FFQ, except one study that had used a validated country-specific dietary questionnaire[10]. For endometrial cancer assessment, three studies had used cancer registries[23,31,32], one had used medical records[26] and another one had used cancer registries and health insurance data[10]. Based on the NOS, all included studies were of high quality (Table 1).

Results from the systematic review on dietary acrylamide intake and the risk of ovarian cancer

Five studies examined the association between dietary acrylamide intake and the risk of ovarian cancer as the main outcome[11,22,26,31,33]. These studies included 575 832 participants aged ≥30 years. The total number of subjects with ovarian cancer was 2470 varying from 122 to 1191 between studies. These papers were published between 2009 and 2018, one each from the Japan[31], the Netherlands[22], the USA[26], Sweden[33] and Europe[11]. Duration of follow-up ranged from 11 to 26 years. For dietary acrylamide intake assessment, all studies had used FFQ, except one study that had used a validated country-specific dietary questionnaire[11]. To assess ovarian cancer, three studies had used cancer registries[22,31,33], one study had used medical records[26] and one had used cancer registries and health insurance data[11]. Based on the NOS, all included studies were of high quality (Table 1).

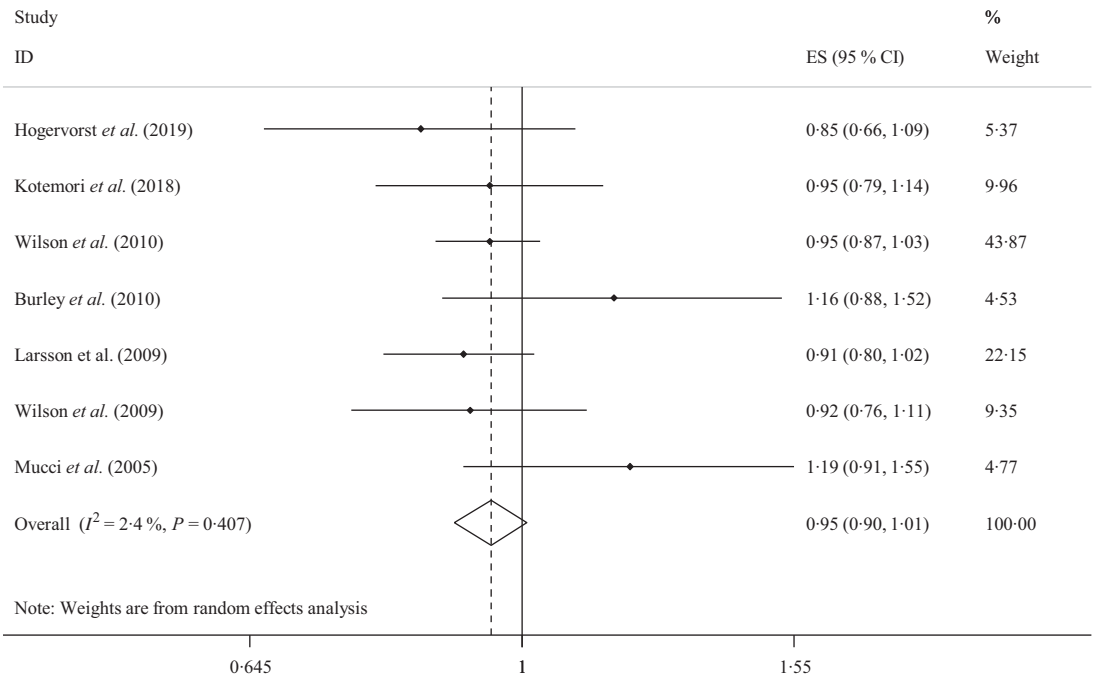

Fig. 2. Forest plot of studies that examined the association between dietary acrylamide intake and the risk of breast cancer using a highest *v.* lowest analysis. ES, effect size.

Meta-analysis on dietary acrylamide intake and the risk of breast cancer

Combining seven effect sizes from seven studies[21,25–30], we found no significant association between dietary acrylamide intake and the risk of breast cancer (RR 0·95; 95 % CI 0·90, 1·01) (Fig. 2). We found no significant between-study heterogeneity ($I^2 = 2{\cdot}4$ %, $P_{heterogeneity} = 0{\cdot}40$). A sensitivity analysis showed that no particular study significantly affected the summary effects. In addition, we observed no evidence of publication bias using Egger's test ($P = 0{\cdot}36$).

In the subgroup analysis, we observed no significant association between dietary acrylamide intake and the risk of breast cancer by smoking status (smoker/non-smoker), menopausal status (premenopausal/postmenopausal), type of breast cancer (ER+PR+/ER+PR−/ER−PR−) and BMI status (BMI < 25 kg/m^2/≥25 kg/m^2) (Table 2).

Meta-analysis on dietary acrylamide intake and the risk of endometrial cancer

Combining five effect sizes from five studies[10,23,26,31,32], we found no significant association between dietary acrylamide intake and the risk of endometrial cancer (RR 1·03; 95 % CI 0·89, 1·19) (Fig. 3). We found no significant between-study heterogeneity ($I^2 = 13{\cdot}2$ %, $P_{heterogeneity} = 0{\cdot}33$). A sensitivity analysis showed that no particular study significantly affected the summary effects. In addition, we observed no evidence of publication bias using Egger's test ($P = 0{\cdot}80$).

In the subgroup analysis, we observed no significant association between dietary acrylamide intake and the risk of endometrial cancer by smoking status (smoker/non-smoker), menopausal status (premenopausal/postmenopausal), and BMI status (BMI < 25 kg/m^2/≥25 kg/m^2) (Table 2).

Meta-analysis on dietary acrylamide intake and the risk of ovarian cancer

Combining the five effect sizes[8,11,26,31,33], no significant association was observed between dietary acrylamide intake and the risk of ovarian cancer (RR 1·02; 95 % CI 0·84, 1·24) (Fig. 4). Results showed no significant between-study heterogeneity ($I^2 = 40{\cdot}0$ %, $P_{heterogeneity} = 0{\cdot}15$). We observed no evidence of publication bias (Egger's test = 0·86).

In the subgroup analysis, we observed no significant association between dietary acrylamide intake and the risk of ovarian cancer by smoking status (smoker/non-smoker), menopausal status (premenopausal/postmenopausal), and BMI status (BMI < 25 kg/m^2/≥25 kg/m^2) (Table 2).

Discussion

Findings from this systematic review and meta-analysis on fourteen prospective cohort studies revealed no significant association between dietary acrylamide intake and the risk of breast, endometrial and ovarian cancers. In addition, no significant association was observed in different subgroup analyses including smoking status, menopausal status, BMI status and different types of breast cancer.

The association between acrylamide intake, a probable human carcinogen, and the risk of cancer has been debated for many years. In this systematic review and meta-analysis, we summarised findings from earlier publications on the

British Journal of Nutrition

Table 2. Subgroup analysis for dietary acrylamide intake and the risk of breast, endometrial and ovarian cancers (Relative risk (RR) or hazard ratio (HR) and 95 % confidence intervals)

Variables	Number of effect sizes	I^2 (%)	RR or HR	95 % CI	$P_{between}$
Breast cancer					
Smoking status					0·90
Smoker	2	0·0	0·94	0·58, 1·52	
Non-smoker	5	0·0	0·92	0·83, 1·00	
Menopausal status					0·44
Premenopausal	4	38·5	1·00	0·88, 1·14	
Postmenopausal	3	0·0	0·94	0·87, 1·03	
Type of breast cancer					0·27
ER+PR+	4	0·0	0·98	0·89, 1·08	
ER+PR−	2	0·0	1·09	0·89, 1·33	
ER−PR−	4	0·0	0·88	0·74, 1·04	
BMI					0·58
<25 kg/m^2	2	0·0	0·93	0·83, 1·03	
≥25 kg/m^2	2	0·0	0·97	0·87, 1·08	
Endometrial cancer					
Smoking status					0·24
Smoker	3	0·0	0·91	0·68, 1·23	
Non-smoker	5	8·9	1·12	0·93, 1·35	
Menopausal status					0·49
Premenopausal	3	66·2	0·88	0·59, 1·32	
Postmenopausal	3	46·4	1·03	0·83, 1·28	
BMI					0·91
<25 kg/m^2	3	79·1	1·03	0·79, 1·36	
≥25 kg/m^2	3	36·9	1·01	0·79, 1·29	
Ovarian cancer					
Smoking status					0·20
Smoker	1	–	0·23	0·02, 3·39	
Non-smoker	3	63·9	1·24	0·92, 1·66	
Menopausal status					0·65
Premenopausal	2	41·2	1·21	0·66, 2·22	
Postmenopausal	2	0·0	1·03	0·74, 1·43	
BMI					0·08
<25 kg/m^2	2	78·0	1·31	0·91, 1·88	
≥25 kg/m^2	2	0·0	0·78	0·49, 1·24	

ER, oestrogen receptor; PR, progesterone receptor.

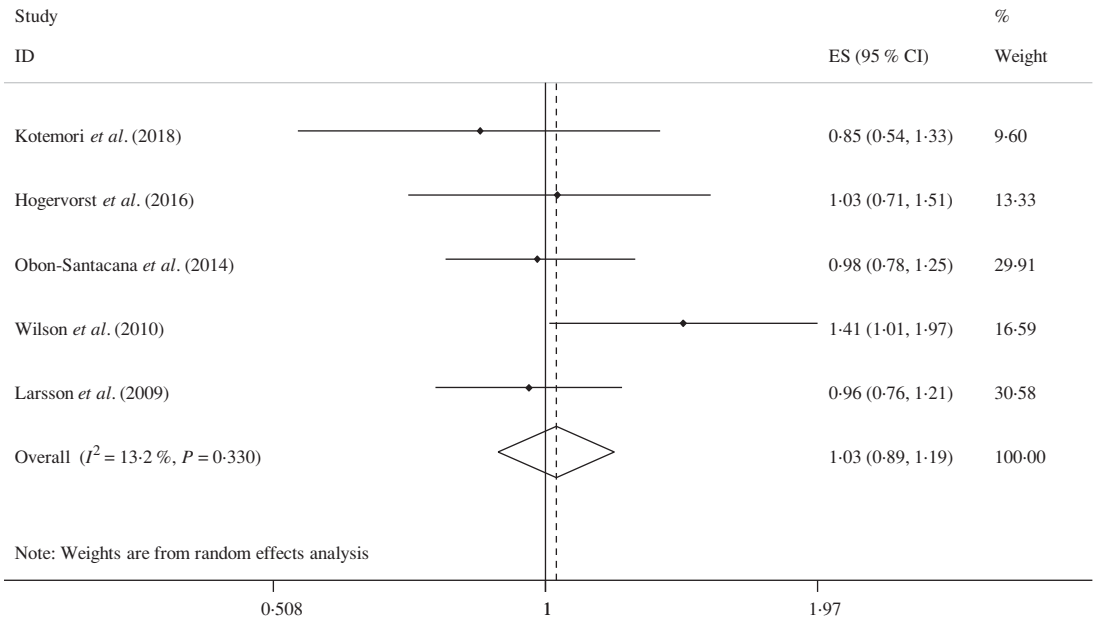

Fig. 3. Forest plot of studies that examined the association between dietary acrylamide intake and the risk of endometrial cancer using a highest *v.* lowest analysis. ES, effect size.

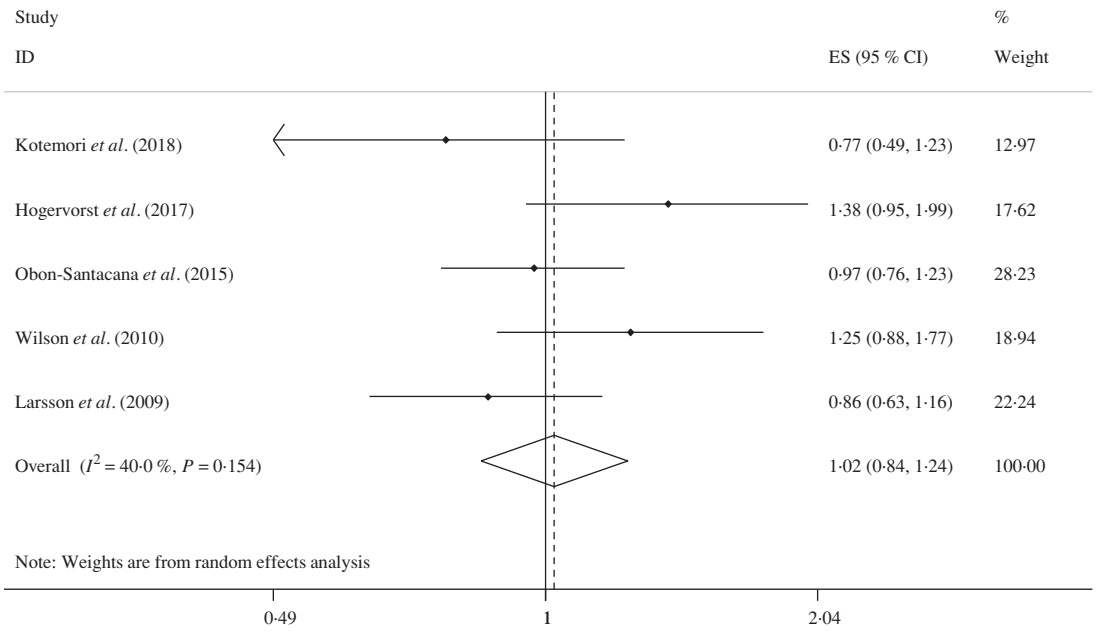

Fig. 4. Forest plot of studies that examined the association between dietary acrylamide intake and the risk of ovarian cancer using a highest *v.* lowest analysis. ES, effect size.

association between dietary acrylamide intake and the risk of breast, endometrial and ovarian cancers. In the body, acrylamide is metabolised to glycidamide, which is a DNA-reactive epoxide[34]. Both acrylamide and glycidamide can interact with Hb to construct Hb–acrylamide adducts and Hb–glycidamide adducts, respectively. These metabolites are considered as relevant biomarkers of internal exposure, which represent one's exposure over the lifespan[9]. Several studies have examined the association between acrylamide–Hb adduct levels in relation to the risk of cancer. Nested case–control studies found no significant association between Hb adduct levels of acrylamide and the risk of ovarian cancer[9,19]. Another nested case–control study revealed a significant positive association between acrylamide–Hb adduct levels and the risk of ER+ breast cancer[12]. In addition, no significant association was observed between biomarkers of acrylamide exposure and the risk of endometrial cancer[20]. Due to limited number of studies on the association between acrylamide–Hb adduct levels and the risk of women's cancers, we did not perform meta-analysis in this regard. Given these findings, it seems that acrylamide does not contribute to the risk of breast, endometrial and ovarian cancers. Further studies are needed to reach a definite conclusion.

In the subgroup analysis by menopausal status, we found no significant association between dietary acrylamide intake and risk of women's cancers. Pedersen *et al.* reported a statistically non-significant increased risk of ER+, PR+ and joint-receptor positive breast cancer in postmenopausal women[24]. Another study found no significant interaction between acrylamide intake and menopausal status and risk of breast, ovarian and endometrial cancers[26]. Hormonal mechanisms might be involved in the association of acrylamide and risk of women's cancers. Further studies are required in this field to elucidate this association more precisely.

The association between dietary acrylamide intake and the risk of women's cancers has been examined in earlier meta-analyses[35,36]. Nevertheless, these previous meta-analyses have included prospective cohort studies published before 2014. In comparison with the previous meta-analyses, our study included fourteen prospective cohort studies, including the additional six studies that were not included in previous ones[11,21–23,25,31]. Thus, despite some overlap in the data included in our study and the previous meta-analyses, we believe that the present study is more comprehensive than previous ones in terms of the data contributing to the summary estimates. In addition, we performed several subgroup analyses based on menopausal status, smoking status, BMI status and different types of breast cancer, which may better clarify the association between dietary acrylamide intake and risk of women's cancers.

In animal studies, a positive dose–response relationship has been shown between acrylamide exposure and cancer in several organs[37], especially in hormone-sensitive organs such as the uterus and the mammary gland[38,39]. However, epidemiological studies on the association between dietary acrylamide intake and risk of breast, endometrial and ovarian cancers are scarce. In addition, most of these studies did not find any significant association. Lack of association between dietary acrylamide intake and risk of breast, endometrial and ovarian cancers in epidemiological studies may be due to low levels of acrylamide from foods[28].

Several potential mechanisms may explain the association of dietary acrylamide intake with the risk of cancer. Acrylamide conversion to glycidamide, a DNA-reactive epoxide, is one of the hypothesised mechanisms for the carcinogenic effects of acrylamide[7]. Some epidemiological studies showed a positive association between dietary acrylamide intake and the risk of hormone-related cancers including ER+ breast, endometrial and

British Journal of Nutrition

ovarian cancers[8,12], which may suggest another pathway for the carcinogenic effects of acrylamide. Another proposed mechanism for acrylamide carcinogenicity is that acrylamide may modulate sex hormone systems[13], which can in turn explain carcinogenicity effects of acrylamide for ER+ and PR+ breast cancer.

The current study has some strengths. Our study included fourteen prospective cohort studies with a large sample size which can provide sufficient power to detect the associations between dietary acrylamide intake and the risk of breast, endometrial and ovarian cancers. This study was conducted on prospective cohort studies in which minimising the possibility of recall or selection bias occurs in case–control studies. In addition, we did several subgroup analyses by smoking status, menopausal status, BMI status and type of breast cancer to assess the relationship between dietary acrylamide intake and the risk of women's cancers. However, some points need to be considered when interpreting our findings. In all included studies, the dietary acrylamide intake was assessed by questionnaires. Therefore, self-reported dietary acrylamide intake through questionnaires might inevitably result in measurement error and misclassification of study participants. In addition, large variations in acrylamide levels among different foods due to different processing methods might influence our results. Acrylamide formation is affected by several factors such as cooking temperature and duration of temperature that could have contributed to the variability of total acrylamide intake. However, we did not consider these variables in our study due to lack of data. Finally, the current study includes studies that enrolled subjects from different countries with different dietary habits and racial factors, which may be associated with different risks for cancer.

Conclusion

In conclusion, we observed no significant association between dietary acrylamide intake and the risk of breast, endometrial and ovarian cancers.

Acknowledgements

This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

S. B. K., A. S. M. and A. E. contributed to the conception, design, data extraction, statistical analyses, data interpretation and manuscript drafting. Z. S. R. contributed to the data interpretation and manuscript drafting. All authors contributed to the approval of the final version of the manuscript and agreed for all aspects of the work.

None of the authors had any conflicts of interest.

References

1. Harbeck N & Gnant M (2017) Breast cancer. *Lancet* **389**, 1134–1150.
2. Rojas K & Stuckey A (2016) Breast cancer epidemiology and risk factors. *Clin Obstetr Gynecol* **59**, 651–672.
3. Lortet-Tieulent J, Ferlay J, Bray F, *et al.* (2018) International patterns and trends in endometrial cancer incidence, 1978–2013. *J Natl Cancer Inst* **110**, 354–361.
4. Roett MA & Evans P (2009) Ovarian cancer: an overview. *Am Family Phys* **80**, 609–616.
5. International Agency for Research on Cancer (1994) *International Agency for Research on Cancer: Some Industrial Chemicals*. Lyon, France: International Agency for Research on Cancer.
6. Lipworth L, Sonderman JS, Tarone RE, *et al.* (2012) Review of epidemiologic studies of dietary acrylamide intake and the risk of cancer. *Eur J Cancer Prevent* **21**, 375–386.
7. Dybing E, Farmer PB, Andersen M, *et al.* (2005) Human exposure and internal dose assessments of acrylamide in food. *Food Chem Toxicol* **43**, 365–410.
8. Hogervorst JG, Schouten LJ, Konings EJ, *et al.* (2007) A prospective study of dietary acrylamide intake and the risk of endometrial, ovarian, and breast cancer. *Cancer Epidemiol Biomark Prevent* **16**, 2304–2313.
9. Obon-Santacana M, Lujan-Barroso L, Travis RC, *et al.* (2016) Acrylamide and glycidamide hemoglobin adducts and epithelial ovarian cancer: a nested case–control study in nonsmoking postmenopausal women from the EPIC cohort. *Cancer Epidemiol Biomark Prevent* **25**, 127–134.
10. Obon-Santacana M, Kaaks R, Slimani N, *et al.* (2014) Dietary intake of acrylamide and endometrial cancer risk in the European Prospective Investigation into Cancer and Nutrition cohort. *Br J Cancer* **111**, 987–997.
11. Obon-Santacana M, Peeters PH, Freisling H, *et al.* (2015) Dietary intake of acrylamide and epithelial ovarian cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. *Cancer Epidemiol Biomark Prevent* **24**, 291–297.
12. Olesen PT, Olsen A, Frandsen H, *et al.* (2008) Acrylamide exposure and incidence of breast cancer among postmenopausal women in the Danish Diet, Cancer and Health Study. *Int J Cancer* **122**, 2094–2100.
13. Besaratinia A & Pfeifer GP (2007) A review of mechanisms of acrylamide carcinogenicity. *Carcinogenesis* **28**, 519–528.
14. Wells GA, Shea B, O'Connell D, *et al.* (2009) *The Newcastle–Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses*. The Ottawa Hospital Research Institute. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
15. Higgins JP, Thompson SG, Deeks JJ, *et al.* (2003) Measuring inconsistency in meta-analyses. *BMJ* **327**, 557–560.
16. Egger M, Davey Smith G, Schneider M, *et al.* (1997) Bias in meta-analysis detected by a simple, graphical test. *BMJ* **315**, 629–634.
17. Pelucchi C, Galeone C, Levi F, *et al.* (2006) Dietary acrylamide and human cancer. *Int J Cancer* **118**, 467–471.
18. Pelucchi C, Galeone C, Negri E, *et al.* (2016) Dietary acrylamide and the risk of endometrial cancer: an Italian case–control study. *Nutr Cancer* **68**, 187–192.
19. Xie J, Terry KL, Poole EM, *et al.* (2013) Acrylamide hemoglobin adduct levels and ovarian cancer risk: a nested case–control study. *Cancer Epidemiol Biomark Prevent* **22**, 653–660.
20. Obón-Santacana M, Freisling H, Peeters PH, *et al.* (2016) Acrylamide and glycidamide hemoglobin adduct levels and endometrial cancer risk: a nested case–control study in nonsmoking postmenopausal women from the EPIC cohort. *Int J Cancer* **138**, 1129–1138.
21. Hogervorst JGF, van den Brandt PA, Godschalk RWL, *et al.* (2019) Interaction between dietary acrylamide intake and genetic variants for estrogen receptor-positive breast cancer risk. *Eur J Nutr* **58**, 1033–1045.
22. Hogervorst JGF, van den Brandt PA, Godschalk RWL, *et al.* (2017) Interactions between dietary acrylamide intake

British Journal of Nutrition

and genes for ovarian cancer risk. *Eur J Epidemiol* **32**, 431–441.
23. Hogervorst JG, van den Brandt PA, Godschalk RW, *et al.* (2016) The influence of single nucleotide polymorphisms on the association between dietary acrylamide intake and endometrial cancer risk. *Sci Rep* **6**, 34902.
24. Pedersen GS, Hogervorst JG, Schouten LJ, *et al.* (2010) Dietary acrylamide intake and estrogen and progesterone receptor-defined postmenopausal breast cancer risk. *Breast Cancer Res Treat* **122**, 199–210.
25. Kotemori A, Ishihara J, Zha L, *et al.* (2018) Dietary acrylamide intake and risk of breast cancer: The Japan Public Health Center-based Prospective Study. *Cancer Sci* **109**, 843–853.
26. Wilson KM, Mucci LA, Rosner BA, *et al.* (2010) A prospective study on dietary acrylamide intake and the risk for breast, endometrial, and ovarian cancers. *Cancer Epidemiol Biomark. Prevent* **19**, 2503–2515.
27. Burley VJ, Greenwood DC, Hepworth SJ, *et al.* (2010) Dietary acrylamide intake and risk of breast cancer in the UK Women's Cohort. *Br J Cancer* **103**, 1749–1754.
28. Larsson SC, Akesson A & Wolk A (2009) Long-term dietary acrylamide intake and breast cancer risk in a prospective cohort of Swedish women. *Am J Epidemiol* **169**, 376–381.
29. Wilson KM, Mucci LA, Cho E, *et al.* (2009) Dietary acrylamide intake and risk of premenopausal breast cancer. *Am J Epidemiol* **169**, 954–961.
30. Mucci LA, Sandin S, Balter K, *et al.* (2005) Acrylamide intake and breast cancer risk in Swedish women. *JAMA* **293**, 1326–1327.
31. Kotemori A, Ishihara J, Zha L, *et al.* (2018) Dietary acrylamide intake and the risk of endometrial or ovarian cancers in Japanese women. *Cancer Sci* **109**, 3316–3325.
32. Larsson SC, Hakansson N, Akesson A, *et al.* (2009) Long-term dietary acrylamide intake and risk of endometrial cancer in a prospective cohort of Swedish women. *Int J Cancer* **124**, 1196–1199.
33. Larsson SC, Akesson A & Wolk A (2009) Long-term dietary acrylamide intake and risk of epithelial ovarian cancer in a prospective cohort of Swedish women. *Cancer Epidemiol Biomark Prevent* **18**, 994–997.
34. Zödl B, Schmid D, Wassler G, *et al.* (2007) Intestinal transport and metabolism of acrylamide. *Toxicology* **232**, 99–108.
35. Je Y (2015) Dietary acrylamide intake and risk of endometrial cancer in prospective cohort studies. *Arch Gynecol Obstetr* **291**, 1395–1401.
36. Pelucchi C, Bosetti C, Galeone C, *et al.* (2015) Dietary acrylamide and cancer risk: an updated meta-analysis. *Int J Cancer* **136**, 2912–2922.
37. Rice JM (2005) The carcinogenicity of acrylamide. *Mutat Res* **580**, 3–20.
38. Johnson KA, Gorzinski SJ, Bodner KM, *et al.* (1986) Chronic toxicity and oncogenicity study on acrylamide incorporated in the drinking water of Fischer 344 rats. *Toxicol Appl Pharmacol* **85**, 154–168.
39. Friedman MA, Dulak LH & Stedham MA (1995) A lifetime oncogenicity study in rats with acrylamide. *Fundam Appl Toxicol* **27**, 95–105.

British Journal of Nutrition