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Fruit and vegetable intake and risk of upper respiratory tract infection in pregnant women

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Abstract

Objective: The present study evaluated the association between fruit and vegetable intake and the incidence of upper respiratory tract infection (URTI) during pregnancy.
Design: In a cohort of 1034 North American women, each subject was asked retrospectively about their fruit and vegetable intake during the six months before the pregnancy and their occurrences of URTI during the first half of pregnancy. Multivariable-adjusted hazard ratios (HR) were calculated with Cox proportional hazards models.
Results: The adjusted HR of URTI for women in the highest quartile (median 8·54 servings/d) *v.* the lowest quartile (median 1·91 servings/d) of total fruit and vegetable intake was 0·74 (95 % CI 0·53, 1·05) for the 5-month follow-up period and 0·61 (95 % CI 0·39, 0·97) for the 3-month follow-up period, respectively. A dose-related reduction of URTI risk according to quartile of intake was found in the 3-month (*P* for trend = 0·03) but not the 5-month follow-up. No association was found between either fruit or vegetable intake alone in relation to the 5-month or the 3-month risk of URTI.
Conclusions: Women who consume more fruits and vegetables have a moderate reduction in risk of URTI during pregnancy, and this benefit appears to be derived from both fruits and vegetables instead of either alone.

Keywords
Fruits
Vegetables
Upper respiratory tract infection
Pregnant women
Retrospective cohort

Every year about 25 million people in the USA visit their family doctor with uncomplicated upper respiratory tract infections (URTI)[1], and pregnant women are no exception. As one of the most frequently reported maternal disorders during pregnancy, URTI – ranging from the common cold, generally mild and self-limited, to more severe and even life-threatening pneumonia (complicated URTI) – may adversely affect the fetus in a direct or indirect way. For example, shorter gestational age at delivery and higher rate of preterm birth were found to be related with complicated URTI during pregnancy[2]. Some congenital abnormalities such as anencephaly and cleft lip were also reported to be associated with maternal common colds[3–5].

Eating 5 servings of fruits and vegetables each day is commonly recommended to reduce the susceptibility to URTI[6], and women are advised to eat more fruits and vegetables during pregnancy[7] since fruits and vegetables are rich dietary sources of a variety of nutrients and many biologically active compounds. However, no study has been conducted to evaluate the association between fruit and vegetable intake and URTI incidence during pregnancy. We therefore examined this relationship in a retrospective cohort of pregnant women followed for 5 months since their last menstrual period (LMP).

Methods

Study population

Study women were the mothers who had participated in a case–control study of children with congenital craniofacial malformations, which has been described elsewhere. Briefly, in the previous study, children 3 years of age or younger with idiopathic hemifacial microsomia, facial asymmetry, Goldenhar syndrome or unilateral anotia/microtia were identified from craniofacial centres in twenty-six cities across the USA and Canada from 1996 to 2002. Control children, matched to cases by age at ascertainment, were identified from the cases' paediatricians (or a similar) practice[8,9]. Mothers of cases and controls were interviewed by telephone about demographic and reproductive factors, pregnancy exposures and behaviours. All 1163 mothers (of 279 cases and 884 controls) served as the eligible cohort of pregnant women

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for the current study. No protocol approval was need for this study since the data were derived from an existing data resource, which was approved by the Boston University Institutional Review Board.

Dietary intake assessment

During the retrospective interview, women were administered the National Cancer Institute (NCI)–Block sixty-item FFQ, which is a semi-quantitative FFQ designed to provide estimates of usual and customary dietary intake. Women were instructed to report their average intakes for the 6-month period before they became pregnant. They were read each food item and what constituted a medium serving (e.g. orange juice – a 6 oz glass; broccoli – half a cup) and were asked how often, on average, they consumed it. There were up to nine possible responses, which ranged from never to four or more times per day. Subjects were also able to indicate if their usual serving was smaller or larger than the stated medium serving. This dietary questionnaire contained eight fruit and eight vegetable food items. For each participant, we estimated the total daily servings of both fruits and vegetables, and fruits and vegetables separately[10]. Energy per 100 g of each food item (from the US Department of Agriculture's Nutrient Database for Standard Reference, Release 19[11]) was adjusted for serving size (0·5 for small; 1·0 for medium; 1·5 for large) and multiplied by the number of average daily servings; total average daily energy was the sum across all food items. Women were grouped into equal-sized quartiles based on the distribution of daily fruit and vegetable intake. Quartiles were used to avoid assumptions about the shape of the dose–response relationship.

Definition of upper respiratory tract infection

Women were asked 'Did you have any upper respiratory infections, such as a cold, flu or sinusitis' and, if so, 'When did it began and for how long?' For the present study, URTI was defined as the first reported URTI episode that occurred between the LMP and the end of the fifth month after the LMP. Reported occurrences of asthma or allergy were not considered as URTI. Women who reported URTI were also asked whether or not they had had any of a list of symptoms. The start date, duration and symptoms for each episode of URTI were reviewed by hand to determine whether they were a 'probable' or 'possible' URTI. URTI status was determined using the following criteria.

1. Probable URTI: report of typical symptoms of URTI, including nasal stuffiness or congestion, headache, sore throat, cough, achiness and fever, with a duration of no more than 6 weeks.
2. Possible URTI: report of URTI, but either of greater than 6 weeks' duration or with no typical symptoms of URTI.

Statistical analysis

Among the 1163 women, we excluded those with an incomplete FFQ (*n* 88) or those whose estimated energy intake was outside the plausible range of 2510 to 14 644 kJ/d (600 to 3500 kcal/d; *n* 41)[12], leaving 1034 women for analyses. We used Cox proportional hazards models to generate hazard ratios (HR) as estimates of relative risks of URTI. Each eligible woman contributed person-time from her LMP to the onset of the first URTI episode since the LMP or to the end of the fifth gestational month (after which information on URTI was not collected), whichever came first. Within the 5-month period, we recorded a total of 347 URTI episodes with a known start date. An additional 44 URTI episodes with an unknown start date were excluded from Cox proportional hazards model analyses.

As covariables, we categorized each woman's socio-demographic data, including age at pregnancy (13–19, 20–29, 30–45 years), race (white/non-white), BMI (weight in kilograms divided by the square of height in metres, classified as $<18·5$, 18·5–24·9, 25·0–29·9, $\geq 30\,kg/m^2$, unknown), marital status (married, single with partner, single without partner), employment (yes/no), years of education (≤ 12, 13–15, ≥ 16 years) and annual family income ($\leq$\$US 25 000, \$US 25 001–65 000, $>$\$US 65 000, unknown). We also examined lifestyle information, such as multivitamin supplement intake between LMP and the end of the fifth month of pregnancy (never use, 1–2 months' use, ≥ 3 months' use), daily energy intake (2510–6276, 6277–10 460, 10 461–14 644 kJ; corresponding to 600–1500, 1501–2500, 2501–3500 kcal), smoking (never/ever/current) and drinking (never/ever/current). In addition, each woman was asked whether pregnancy was planned (yes/no) and the number of previous live births occurring within 5 years, which was used as a proxy for the number of children in the household (counted as 0, 1, ≥ 2). Based on the month of the LMP we assigned a season for each participant (Mar–May, Jun–Aug, Sep–Nov, Dec–Feb).

All distributions of these covariables were examined according to quartiles of fruit and vegetable intake. Using the lowest quartile as the reference group, we estimated the crude and adjusted hazard ratios and 95 % confidence intervals of URTI for each higher quartile of intake. We also assessed linear relationships by using ordinal rather than indicator variables for quartiles of fruit and vegetable intake. We judged any covariable to be a potential confounder if it changed, by at least 5 %, the coefficient for fruit and vegetable intake and risk of URTI when added to the model. Thus, race and daily energy intake were deemed potential confounders. We repeated these methods with either fruit or vegetable intake alone in relation to the URTI incidence. In addition, maternal age was also controlled as a potential confounder in all multivariate models.

We tested the assumption of proportionality of hazards for the outcome of URTI by adding to the Cox model

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interaction terms of follow-up time with each fruit and vegetable intake indicator variable. The proportional hazards assumption was valid in these data.

Since women may change their diet after they realize they are pregnant, fruit and vegetable intake in the six months before pregnancy might be most relevant in relation to URTI occurrences in the first trimester. Therefore, we also evaluated the associations between intake and the 3-month risk of URTI, using the same methods. There were 188 URTI episodes recorded in the first three months of follow-up.

All analyses were performed using the SAS statistical software package version 9·1 (SAS Institute, Cary, NC, USA).

Results

Table 1 shows the medians and ranges for each quartile of total fruit and vegetable intake and for either fruit or vegetable intake alone. The median intake of total fruits and vegetables was 4·62 with a range from 0·07 to 29·04 servings/d for all women. The median intakes of fruit and vegetables alone were 2·33 (range 0–22·51) and 2·01 (range 0–13·46) servings/d, respectively.

Table 2 presents the characteristics of the 1034 pregnant women according to fruit and vegetable intake quartiles. The participants ranged in age from 13 to 45 years; their mean age was 28 years. Generally, women who consumed more fruits and vegetables were older, were more likely to be non-whites (including Hispanic), had higher daily total energy intake, had higher education level (≥16 years), had higher family income (>$US 65 000), were less likely to be single, and reported less smoking and drinking. It should be noted that the distributions for most of the above characteristics did not present a linear trend with increasing quartiles. There was no apparent difference in BMI, employment, number of children aged 5 years or younger, multivitamin intake, planned pregnancy and birth outcome across fruit and vegetable intake quartiles. Moreover, there was no marked relationship between seasonality and quartile of fruit and vegetable intake.

As Table 3 indicates, consumption of fruits and vegetables was inversely associated with the 5-month risk of URTI in pregnancy. Women in the highest quartile of fruit and vegetable intake were 26 % less likely to have URTI, relative to those in the lowest quartile (HR = 0·74, 95 % CI 0·53, 1·05) after controlling for age, race and energy intake. Although there seemed to be a decreasing linear trend in the 5-month risk of URTI according to quartile of fruit and vegetable intake, it was not significant (*P* for trend = 0·11). Neither fruit nor vegetable intake alone was found to be associated with the 5-month risk of URTI.

The patterns observed for total fruit and vegetable intake and either fruit or vegetable intake alone in relation to the 3-month risk of URTI were consistent with those when assessing the 5-month risk of URTI (Table 4). Women in the highest quartile of fruit and vegetable intake had a stronger reduced 3-month risk (adjusted HR = 0·61, 95 % CI 0·39, 0·97) than the 5-month risk of URTI. Moreover, there was a significant decreasing linear trend for the 3-month risk of URTI with consumption of fruits and vegetables (*P* for trend = 0·03).

We conducted two additional sub-analyses. In order to assess the accuracy of URTI, we excluded the twenty-nine women with possible URTI and found that HR were similar for each measure of intake in relation to both the 5-month and 3-month risks of URTI (data not shown). We also restricted the analyses to the subgroup of 780 women with normal infants and found similar risk estimates as those observed for all women (data not shown).

Discussion

Our findings suggest that high consumption of both fruits and vegetables is associated with a moderate reduction in risk of URTI among pregnant women. However, no association was found between either fruit or vegetable intake alone and risk of URTI. For total fruits and vegetables, there was a dose-related decline in URTI incidence according to quartile of their intake, especially in the first three months after the LMP.

To our knowledge, the present study is the first to investigate fruit and vegetable intake in relation to the occurrence of URTI among pregnant women. Frequent intake of fruits and vegetables was reported to be associated with fewer episodes of acute respiratory infections

Table 1 Quartiles of fruit and vegetable intake (servings/d) among North American pregnant women (*n* 1034), 1996–2002

Food group	1st quartile (*n* 259)	2nd quartile (*n* 259)	3rd quartile (*n* 258)	4th quartile (*n* 258)
Fruits and vegetables				
Median	1·91	3·71	5·59	8·54
Range	0·07–2·89	2·90–4·62	4·63–6·70	6·71–29·04
Fruits alone				
Median	0·68	1·80	3·02	5·09
Range	0–1·30	1·31–2·32	2·33–3·86	3·87–22·51
Vegetables alone				
Median	0·73	1·53	2·47	4·00
Range	0–1·11	1·12–2·00	2·01–3·03	3·04–13·46

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Table 2 Characteristics of North American pregnant women (*n* 1034) according to quartile of fruit and vegetable intake, 1996–2002

	1st quartile (*n* 259)		2nd quartile (*n* 259)		3rd quartile (*n* 258)		4th quartile (*n* 258)	
	n	%	*n*	%	*n*	%	*n*	%
Age (years)								
13–19	25	9·6	18	6·9	22	8·5	21	8·1
20–29	140	54·1	125	48·3	106	41·1	114	44·2
30–45	94	36·3	116	44·8	130	50·4	123	47·7
Race								
White	194	74·9	178	68·7	160	62·0	132	51·2
Non-white	65	25·1	81	31·3	98	38·0	126	48·8
BMI (kg/m^2)								
<18·5	16	6·2	10	3·9	11	4·3	10	3·9
18·5–24·9	149	57·5	154	59·5	166	64·3	164	63·6
25·0–29·9	50	19·3	55	21·2	46	17·8	50	19·4
≥30	37	14·3	34	13·1	25	9·7	25	9·7
Unknown	7	2·7	6	2·3	10	3·9	9	3·5
Employment*								
Yes	172	66·4	179	69·4	167	64·7	156	60·5
No	87	33·6	79	30·6	91	35·3	102	39·5
Marital status*								
Married	179	69·1	190	73·6	200	77·5	181	70·2
Single with partner	42	16·2	40	15·5	37	14·3	53	20·5
Single	38	14·7	28	10·9	21	8·1	24	9·3
Education (years)								
≤12	114	44·0	87	33·6	97	37·6	114	44·2
13–15	71	27·4	53	20·5	65	25·2	51	19·8
≥16	74	28·6	119	45·9	96	37·2	93	36·0
Family income* ($US)								
≤25 000	77	29·7	48	18·5	60	23·4	74	28·7
25 001–65 000	102	39·4	106	40·9	94	36·6	74	28·7
>65 000	62	23·9	86	33·2	78	30·4	79	30·6
Unknown	18	7·0	19	7·3	25	9·7	31	12·0
Number of children†								
0	143	55·2	142	54·8	139	53·9	141	54·6
1	93	35·9	95	36·7	92	35·7	92	35·7
≥2	23	8·9	22	8·5	27	10·5	25	9·7
Planned pregnancy*								
Yes	131	50·6	143	55·4	140	54·3	148	57·4
No	128	49·4	115	44·6	118	45·7	110	42·6
Birth outcome								
Non-malformed infant	192	74·1	205	79·2	185	71·7	198	76·7
Malformed infant	67	25·9	54	20·8	73	28·3	60	23·3
Multivitamin intake								
Never use	24	9·3	18	7·0	16	6·2	29	11·2
1–2 months' use	35	13·5	26	10·0	23	8·9	29	11·2
≥3 months' use	200	77·2	215	83·0	219	84·9	200	77·5
Daily energy intake (kJ)‡								
2510–6276	161	62·2	101	39·0	71	27·5	28	10·9
6277–10 460	92	35·5	141	54·4	151	58·5	160	62·0
10 461–14 644	6	2·3	17	6·6	36	14·0	70	27·1
Smoking								
Never	158	61·0	185	71·4	203	78·7	200	77·5
Ever	30	11·6	36	13·9	23	8·9	27	10·5
Current	71	27·4	38	14·7	32	12·4	31	12·0
Drinking								
Never	101	39·0	95	36·7	111	43·0	135	52·3
Ever	34	13·1	31	12·0	32	12·4	33	12·8
Current	124	47·9	133	51·4	115	44·6	90	34·9
Season§								
Mar–May	67	25·9	52	20·1	60	23·3	64	24·8
Jun–Aug	61	23·6	72	27·8	57	22·1	66	25·6
Sep–Nov	71	27·4	65	25·1	74	28·7	69	26·7
Dec–Feb	60	23·2	70	27·0	67	26·0	59	22·9

*One missing value.
†Children aged ≤5 years.
‡Corresponding to 600–1500, 1501–2500, 2501–3500 kcal.
§At the last menstrual period.

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Table 3 Five-month risk of upper respiratory tract infection by fruit and vegetable intake in North American pregnant women (*n* 1034), 1996–2002

Food group	Crude HR	95 % CI	Adjusted HR*	95 % CI*	*P* for trend
Fruits and vegetables					
1st quartile	1·00	ref	1·00	ref	0·11
2nd quartile	0·91	0·68, 1·21	0·90	0·67, 1·21	
3rd quartile	0·88	0·66, 1·18	0·89	0·65, 1·21	
4th quartile	0·73	0·54, 0·99	0·74	0·53, 1·05	
Fruits alone					
1st quartile	1·00	ref	1·00	ref	0·18
2nd quartile	1·02	0·77, 1·36	1·03	0·77, 1·38	
3rd quartile	0·82	0·61, 1·11	0·83	0·61, 1·13	
4th quartile	0·80	0·60, 1·09	0·85	0·60, 1·20	
Vegetables alone					
1st quartile	1·00	ref	1·00	ref	0·33
2nd quartile	1·12	0·82, 1·51	1·11	0·81, 1·51	
3rd quartile	1·13	0·84, 1·52	1·15	0·84, 1·58	
4th quartile	1·10	0·81, 1·49	1·17	0·84, 1·64	

HR, hazard ratio; ref, referent category.
*For fruit and vegetables, adjusted for age, race and energy intake; for fruit alone, adjusted for age, race, energy and vegetable intakes; for vegetables alone, adjusted for age, race, energy and fruit intakes.

Table 4 Three-month risk of upper respiratory tract infection by fruit and vegetable intake in North American pregnant women (*n* 1034), 1996–2002

Food group	Crude HR	95 % CI	Adjusted HR*	95 % CI*	*P* for trend
Fruits and vegetables					
1st quartile	1·00	ref	1·00	ref	0·03
2nd quartile	0·77	0·52, 1·12	0·76	0·52, 1·13	
3rd quartile	0·68	0·46, 1·01	0·68	0·44, 1·03	
4th quartile	0·62	0·41, 0·93	0·61	0·39, 0·97	
Fruits alone					
1st quartile	1·00	ref	1·00	ref	0·27
2nd quartile	0·93	0·64, 1·37	0·97	0·66, 1·44	
3rd quartile	0·71	0·47, 1·07	0·76	0·49, 1·17	
4th quartile	0·77	0·52, 1·15	0·84	0·53, 1·33	
Vegetables alone					
1st quartile	1·00	ref	1·00	ref	0·78
2nd quartile	0·97	0·66, 1·44	0·97	0·65, 1·46	
3rd quartile	0·81	0·54, 1·22	0·84	0·55, 1·30	
4th quartile	0·93	0·62, 1·38	0·98	0·63, 1·52	

HR, hazard ratio; ref, referent category.
*For fruit and vegetables, adjusted for age, race and energy intake; for fruit alone, adjusted for age, race, energy and vegetable intakes; for vegetables alone, adjusted for age, race, energy and fruit intakes.

in the Australian general population[13] and with a lower incidence of influenza-like symptoms in Japanese children[14]. Whole fruits and vegetables provide a natural balance of multiple nutrients and bioactive compounds which may improve host immune function against exogenous bacterial or viral invasion in a complementary, combined or synergistic manner[15] that could account for the protective effect observed from high consumption of both fruits and vegetables in our study.

There are numerous studies, including clinical trials, on single nutrients such as vitamin C and Zn in relation to the common cold. However, none has been found to effectively prevent the common cold, although the combination of vitamin C and Zn may reduce the duration of URTI[16]. Two large population-based studies also reported no association between vitamin C, vitamin E, β-carotene or Zn and risk of common cold[17,18], but both of them estimated intake based on diet and use of supplements. Since accurate estimation of nutrients depends on multiple factors, such as the precision of the nutrient assignments and the exact nature of the quantification method for each food item[19], rather than food item or food group measurement, investigation of single nutrient exposure is more likely to suffer from misclassification bias. We evaluated collected information on dietary intake of fruits and vegetables as a whole food and thus avoided that potential bias to the extent possible.

There are several possible explanations why the observed reduction in URTI risk was confined to fruit and vegetables combined and not either type of food alone. One possibility could be that consumption levels of either fruits or vegetables were too low for a protective effect against URTI in pregnancy. Pregnant women, whose bodies are in special physiological period involving enormous hormonal, circulatory and mechanical alterations, may require more fruits and vegetables than

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usual. In the current study, the median consumption of overall fruits and vegetables in the highest quartile of intake was 8·54 servings/d compared with 5·09 servings of fruits and 4·00 servings of vegetables daily. While these levels are higher than the recommended daily minimum of 2 servings for fruit and 4 servings for vegetables for pregnant women[7], they may be insufficient for some outcomes, such as effective immunity.

Another possible explanation is that either fruit or vegetable intake alone does not provide an optimal protection against URTI unless they are consumed together. Although fruits and vegetables share some common essential nutrients, they vary greatly for many nutrients, such as more vitamin C in fruit but more carotenoids and folate in vegetables. The newly released Food Guide Pyramid underscores the importance of a healthy diet including a variety of both fruits and vegetables for pregnant women[20], not just one or two of them, taking into account the potential complementary effects between them.

The NCI–Block sixty-item FFQ has been widely used in many large, multifaceted epidemiological studies and national surveys. The accuracy and comprehensiveness of this questionnaire have been well documented and validated[21,22]. Median daily servings for each quartile of fruit and vegetable intake in our study were very close to the reported intake in American women from the National Institutes of Health–AARP Diet and Health Study[23], except for a slightly higher median daily serving in the fourth quartile in our study (8·5 *v.* 7·3 servings/d). Also, to improve accuracy of the FFQ data, we excluded women with total energy intake beyond plausible ranges. Women were interviewed on average 8 months, but up to 36 months, after delivery, which means they were asked to recall pre-pregnancy dietary intake that was on average 20 months, but as many as 48 months, earlier. Hence, the accuracy of exposure measurement depended on recall of diet and the assumption that these women changed little in their main dietary habits, a challenge for all self-reports of diet[19]. As an indirect validation assessment, we conducted a sub-analysis of those women who were interviewed within 1 year of their pregnancy to see if the finding remained when the recall interval was shorter and presumably more reliable. We found no material difference in risk estimates for this subgroup.

Misclassification of exposure may also exist because the data collected on dietary intake may not represent the most relevant time frame for URTI occurrence in pregnancy. For example, if women who rarely ate fruits and vegetables before pregnancy changed their diet to include more fruits and vegetables once they realized they were pregnant, the diet information collected during the six months prior to the LMP would not provide an accurate assessment and misclassification would attenuate the association between fruit and vegetable intake and URTI incidence. When we shortened the follow-up period from the first five lunar months to the first three months, a stronger decreased risk of URTI was observed for women in the highest quartile of fruit and vegetable intake, suggesting that such misclassification may indeed be present. In addition, the stronger HR for the more recent follow-up period lends some credence to the fruit and vegetable–URTI association.

To ensure the accuracy of self-reported URTI, all symptoms and duration for each URTI episode were reviewed by hand. When we analysed these data based on probable URTI we found similar results with all URTI, providing reassurance that self-reported URTI were satisfactory. Despite this, there is undoubtedly misreporting of URTI because other conditions, such as allergies, have URTI-like symptoms. Furthermore, our study population comprised mothers both with non-malformed and malformed children in which URTI were reported by more mothers in the latter group. We could not exclude the possibility that mothers with malformed children over-reported or mothers of non-malformed children under-reported URTI episodes. However, after we restricted our study subjects to mothers with non-malformed children, there was little change in the relationship between fruit and vegetable intake and risk of URTI.

In the current study we collected information on numerous covariables, such as socio-economic, lifestyle and seasonal variables, to control for potential confounders. We did not, however, put all of them in the multivariate model because a majority of covariables had even distributions over quartiles of fruit and vegetable intake. More importantly, they did not change the association between fruit and vegetable intake and URTI incidence by more than 5 %. Residual confounding is possible by other covariables not included in models or those we did not collect, such as physical activity. It is noteworthy that of all covariables we examined, only race was significantly associated with URTI incidence: white women had an increased risk of URTI. They also ate fewer fruits and vegetables, causing slight confounding of HR.

In conclusion, our results suggest that high intake of fruits and vegetables might moderately reduce URTI risk among pregnant women. It appears that these beneficial effects are dependent on intake of both fruits and vegetables, instead of either alone. If diets enriched with fruits and vegetables truly have a preventive or protective effect against URTI in pregnant women, the public health implications may be considerable given that URTI as well as treatments for URTI symptoms may affect fetal development[5,9,24]. However, the limitations discussed above make it necessary to replicate our findings through studies specially designed to address this question.

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