

Prospective study of dietary patterns and persistent cough with phlegm among Chinese Singaporeans

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ABSTRACT

Rationale: Using principal components analysis to examine dietary patterns complements the evaluation of individual food and nutrient intake in relation to health outcomes, but has not yet been applied to nonmalignant respiratory disease or symptoms. *Objective:* To examine the relation between patterns of dietary intake at baseline and new-onset of persistent cough with phlegm in a population-based cohort of Singapore Chinese. *Methods:* A 165-item validated food frequency questionnaire was administered in-person at baseline in 1993. We identified 623 cases of incident cough with phlegm among 52,325 subjects by telephone interview from 1999 through 2004. We identified two distinct food patterns: a “meat-dim sum” pattern characterized by pork and chicken dim sum foods and noodle dishes, and a “vegetable-fruit-soy” pattern characterized by vegetables, fruit and soyfood items. *Main Results:* The meat-dim sum pattern was positively associated with new-onset cough with phlegm (odds ratio=1.43; 95% confidence interval: 1.08, 1.89; comparing fourth to first quartile, *P* for trend=0.02,), after adjustment for age, gender, total energy intake, smoking, education and non-starch polysaccharide intake, a protective factor for cough with phlegm in this cohort. Weaker associations were seen for more chronic symptoms and for incident asthma. A weak inverse association for the vegetable-fruit-soy pattern disappeared after adjustment for non-starch polysaccharide intake. *Conclusion:* A diet rich in meats, sodium plus refined carbohydrates may increase risk of developing cough with phlegm, independently of the apparent beneficial effects of a diet high in non-starch polysaccharides in this Singapore Chinese cohort.

Key words: Asthma, chronic bronchitis; COPD; diet; signs and symptoms, respiratory.

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INTRODUCTION

Although smoking is the major risk factor, diet contributes to the pathogenesis of nonmalignant lung disease and symptoms (1-3). Dietary nutrients may modulate oxidative stress-induced lung damage among both smokers and nonsmokers, although prospective data are few (4-7). We previously identified reduced risk of cough with phlegm, the symptoms of chronic bronchitis, with higher non-starch polysaccharide intake in a cohort of Chinese Singaporeans (8).

Epidemiologic analyses that focus on individual nutrients and food items in relation to chronic disease, while valuable, have limitations (9). When nutrients of interest correlate strongly, teasing out individual effects can be difficult. Further, the single-nutrient approach cannot capture the complex interactions between individual nutrients, and their correlations with other dietary (10, 11), lifestyle (12, 13), and socio-demographic patterns (14, 15) that may confound associations with health outcomes. Principal components analysis is a dimension-reduction statistical technique that has been used to define dietary patterns in epidemiological studies (16). The high level of intercorrelation of individual nutrients can impede traditional analyses, but aids in the identification of dietary patterns in principal components analysis. Looking beyond individual nutrients or foods to identify overall patterns of diet that reflect actual eating habits can better inform public health dietary recommendations.

Dietary patterns have been associated with cancer (17) and heart disease (18, 19), but have not been studied in relation to nonmalignant respiratory disease or symptoms. Few data address empirically-defined dietary patterns among U.S. Asians (13, 14, 20) or Chinese populations (21). To our knowledge, there are no published data on dietary patterns in a Singaporean Chinese population. The Singaporean Chinese diet differs from Western diets. It

consists primarily of mixed dishes combining Chinese, Malay and Indian influences, is generally high in refined carbohydrates (e.g. noodles and white rice), soyfoods and green leafy vegetables, and uses relatively small quantities of meats, such as fish, chicken and pork. It is common to consume meals outside the home from either food courts or dim sum restaurants, where typical foods include meat-filled dumplings, buns and noodle dishes.

We examined whether dietary patterns are related to risk of cough with phlegm in the Singapore Chinese Health Study. Some of the results of these analyses have been previously reported in the form of an oral presentation at the American Thoracic Society 2005 Conference (22).

METHODS

Study Population

The design of the Singapore Chinese Health Study has been previously described (23). Briefly, the cohort was drawn from men and women, aged 45 to 74 years, who belonged to one of the major dialect groups (Hokkien or Cantonese) of Chinese in Singapore. Between April 1993 and December 1998, 63,257 individuals completed an in-person interview that included questions on diet and smoking. The Institutional Review Boards at the University of Southern California, the National University of Singapore, and the National Institute of Environmental Health Sciences approved this study.

Identification of Respiratory Symptoms

Beginning in July 1999 a follow-up telephone interview was administered that included standardized questions on history of asthma and habitual cough and phlegm production (24). Of the baseline cohort, 52,325 completed the follow-up interview. As of December 31, 2004, 7,722 subjects had died. The average time from baseline to follow-up interview was 5.3 years

(range=2 to 11 years). Incident cases were subjects who reported that they usually have cough with phlegm on arising or during the rest of the day, initiated at least one year after the baseline interview. Subjects were divided into mutually exclusive categories based on cough and/or phlegm, and their incidence or prevalence, with a joint reference category of non-cases (N=46,942) without cough or phlegm. Six hundred and twenty three subjects had incident cough with phlegm, and of those, 380 had both symptoms for three or more months of the year. The remaining 5,383 individuals had either incident cough only (N=549), incident phlegm only (N=1,349), prevalent cough with phlegm (N=727) or discordant incident/prevalent combinations of cough and/or phlegm (N=2,132). Analyses of the 5,383 subjects with these secondary outcomes can be found in the online supplement (Table E1).

Subjects reporting asthma were considered to be incident (n=406) if their reported age at onset of asthma on the follow-up questionnaire was later than the age at baseline interview. Among the 406, 35 also reported incident cough with phlegm. We completed validation home visits on 331 of the 406 (81.5%) incident asthmatics where we asked again about their history of asthma, age at onset, current symptoms, and medication use. Among the 331 respondents, 270 (81.6%) subjects confirmed asthma, 52 (15.7%) confirmed asthma but gave age at onset consistent with prevalent asthma and 9 (2.7%) did not confirm asthma. Further details on the asthma validation are in the online supplement.

Identification of Dietary Patterns

At baseline, a 165-item quantitative food frequency questionnaire, developed for and validated in this population, was administered to assess usual diet over the past year (23, 25). Using principal components analysis (16, 26) among the baseline cohort (N=63,257), we identified patterns from the food frequency responses. Extraction of principal components was

followed by orthogonal rotation. The number of components retained for rotation was based primarily on examination of scree plots and factor interpretability, but eigenvalues (>1.0) and percent variance explained were also considered (16).

For each dietary pattern, a component score was computed as a linear composite of the foods with meaningful loading scores (e.g. ≥ 0.30). Scores were calculated by taking the unweighted sum of standardized frequencies of intake for each food associated with the pattern, then dividing them into quartiles based on the distribution of the baseline cohort. Principal components analyses were conducted using the FACTOR PROCEDURE in SAS version 9 (SAS Institute, Cary, NC). Examples of the SAS programming code used have been previously cited (17), and are available online (27).

The sensitivity and reproducibility of the identified dietary patterns were also assessed. These methods can be found in the online supplement.

Statistical Analysis

The following variables were included in all models because these factors were either related both to the outcome and to the dietary patterns, or because there was compelling evidence from the literature for possible confounding (in the case of smoking and environmental tobacco smoke): age at baseline (continuous), gender, dialect group (Hokkien, Cantonese), total energy intake (continuous logarithm), highest education level (no formal education, primary school, secondary school or beyond), energy-adjusted non-starch polysaccharide intake (quartiles) (8), smoking status (never, past, current), amount smoked (never, past, current and ≤ 12 cigarettes, current and 13-22 cigarettes, current and ≥ 23 cigarettes), age at starting smoking (never, past, current and ≥ 20 years, current and 15-19 years, current and ≤ 14 years), and adult ETS exposure at home or work (ever, never). All nutrient data were adjusted for total energy intake using the

residual method (28). Individuals were categorized as never active smokers if they had never smoked at least one cigarette a day for one year or longer. Further information on the evaluation of confounding, including variables evaluated for confounding but not retained, is available in the online supplement.

RESULTS

We identified two distinct dietary patterns from the baseline cohort using principal components analysis: "vegetable-fruit-soy" and "meat-dim sum" patterns. The individual food items and their loading factor values are listed in Table 1. The higher the loading of a given food item the greater the contribution of that food to the pattern. The vegetable-fruit-soy pattern was characterized by vegetable, fruit and soyfood intake; of the 32 foods included in the pattern, 23 were vegetables, five were soyfood items, and four were fruit items. The meat-dim sum pattern contained 31 food items, predominantly chicken, pork, fish, rice and noodle dishes and preserved foods. Eleven of the 19 dim sum or snack items on the questionnaire were included in this pattern. No food or beverage items overlapped between the two patterns.

Distributions for selected baseline sociodemographic and smoking characteristics are presented for the quartiles of each dietary pattern among subjects with follow-up in Table 2. Individuals in the highest quartile of vegetable-fruit-soy scores were less likely to be of the Hokkien dialect group, to smoke, and to lack formal education than those in the lowest quartile. Individuals with the highest meat-dim sum scores were more likely to be younger, male, current smokers and have had formal education compared to the lowest quartile of the meat-dim sum scores. Mean body mass index was similar across all quartiles of both dietary patterns, and body mass index was not correlated with either the vegetable-fruit-soy pattern ($r=0.003$) or the meat-dim sum pattern ($r=0.004$).

We present correlations between each dietary pattern and selected food items, food groups, and nutrients of interest among subjects with follow-up in Table 3. The strongest positive correlations with the vegetable-fruit-soy pattern were for non-starch polysaccharides, vitamin E, total carotenoids, total fruit, vegetables and soyfoods. The strongest positive correlations with the meat-dim sum pattern were for total energy, sodium, total red meat, preserved red meat, preserved fish/shellfish, and fresh eggs. Total dietary fat was similarly correlated with each pattern, but correlations among fat subtypes varied. For example, the omega-3 and omega-6-fatty acids were moderately correlated with the vegetable-fruit-soy pattern, but not with the meat-dim sum pattern, whereas saturated fat intake was moderately associated with the meat-dim sum pattern, but not with the vegetable-fruit-soy pattern.

We assessed risk of cough with phlegm by quartiles of component scores of each dietary pattern (Table 4). Cough with phlegm was associated with the meat-dim sum pattern, with a statistically significant trend by quartile. There was a weak inverse association with the vegetable-fruit-soy pattern. The association with the meat-dim sum patterns was attenuated and lost statistical significance when restricted to the smaller number of subjects with more chronic symptoms. The positive association between cough and phlegm and the meat-dim sum pattern is independent of our previously reported inverse association with non-starch polysaccharides (8). This was expected given the weak correlation between these two dietary factors ($r = -0.09$). In contrast, the weak inverse association with the vegetable-fruit-soy pattern was eliminated by adjusting for the more highly correlated ($r = 0.49$) non-starch polysaccharide intake. The adjusted odds ratios for the fourth versus first quartiles of non-starch polysaccharide intake were not appreciably altered by inclusion of the meat-dim sum pattern in the model (OR=0.61; 95% CI:0.48, 0.79 with meat-dim sum pattern, versus OR=0.59; 95% CI:0.47, 0.76 without).

The association between the meat-dim sum pattern and cough with phlegm was similar in nonsmokers (OR = 1.41; 95% CI: 0.96, 2.05 for fourth compared to first quartile; *P* for trend = 0.05) and ever smokers (OR = 1.56; 95% CI: 1.01, 2.40 for fourth compared to first quartile; *P* for trend = 0.2). The associations between each dietary pattern and cough with phlegm did not vary appreciably by gender, dialect group (Hokkien, Cantonese), age (at the median), body mass index (< 25, ≥25), or education (no formal education, primary school, secondary or greater) (data not shown).

To better understand the association between cough with phlegm and the meat-dim sum pattern we explored individual foods, food groups and nutrients that were highly correlated with the pattern. Of the five individual foods with the highest loading factors [siew mai, other steamed snack, gravy noodle, chicken rice, otar otar (spiced fish paste), Table 1], only siew mai had a statistically significant positive association with the symptoms (OR = 1.34; 95% CI: 1.01, 1.77, comparing ≥2.5 servings per month versus none), but this was attenuated (OR = 1.23; 95% CI: 0.92, 1.66) when included in the same model with the meat-dim sum pattern. The odds ratio was unchanged for the meat-dim sum pattern (OR = 1.38; 95% CI: 1.05, 1.84). When we examined food groups and nutrients highly correlated with the meat-dim sum pattern, statistically significant positive association were seen in individual models for preserved red meat (OR = 1.40; 95% CI: 1.07, 1.84), preserved fish and shellfish (OR = 1.38; 95% CI: 1.06, 1.79), and sodium (OR = 1.36; 95% CI: 1.06, 1.75), comparing fourth to first quartile of intake and adjusting for age, gender, dialect, smoking, the meat-dim sum pattern and non-starch polysaccharide intake. When sodium intake, preserved fish and shellfish and preserved red meat were included in the same model with the dietary pattern, all were attenuated and only preserved

red meat retained statistical significance (OR = 1.33; 95% CI: 1.01, 1.75 for the top relative to the bottom quartile).

Although our primary focus was on incident cough with phlegm, which was previously associated with non-starch polysaccharide intake in this cohort, we also examined other outcomes. For both “all reported” and “confirmed” incident asthma, subjects in the upper three quartiles of the meat-dim pattern were at non-statistically significantly increased risk without a trend (Table 5). There was no association with the vegetable-fruit-soy pattern, after adjustment for non-starch polysaccharide intake. Although numbers become small on stratification among confirmed asthma, there were similar findings for the fourth relative to the first quartile among nonsmokers (OR=1.23; 95% CI: 0.74, 2.05) and among ever smokers (OR=1.43; 95% CI: 0.65, 3.14).

We also examined incident cough without phlegm, incident phlegm without cough, as well as prevalent cough with phlegm (see online supplement Table E1). The meat-dim sum pattern was more weakly associated with prevalent than with incident cough and phlegm, and the vegetable-fruit-soy pattern was weakly inversely associated with incident phlegm alone.

DISCUSSION

To our knowledge, this is the first report of analyses of dietary patterns in relation to nonmalignant respiratory disease or symptoms. We identified two distinct dietary patterns in a large cohort of adult Chinese Singaporeans. The highest quartile of the meat-dim sum pattern was associated with 1.4-fold increase in risk of cough with phlegm. The association reported for meat-dim sum pattern was not attributed to individual foods that were the major contributors to the pattern. However, we cannot exclude the possibility that this pattern may be due in part to correlated individual nutrients, such as sodium, or food groups, such as preserved meats or fish.

Our previously reported inverse association between non-starch polysaccharide intake and cough with phlegm (8) was not changed by adjustment for the meat-dim sum pattern. The vegetable-fruit-soy pattern was not associated with risk of cough and phlegm when adjusted for non-starch polysaccharide intake.

There are similarities between the newly identified dietary patterns in our Chinese Singaporean population-based cohort and those previously identified in U.S. populations. For example, in various U.S. populations, two primary patterns have been consistently described (29-31), the "Western" pattern, characterized by red and processed meats, sweets and desserts, French fries, refined grains, and the "prudent" pattern, characterized by fruits, vegetables, legumes, fish, poultry and whole grains (32). The meat-dim sum pattern, identified in our cohort, is also characterized by red meat intake, preserved foods, such as red meat and eggs, and rice and noodle-based dishes and desserts. Deep-fried foods are also common dim sum items. However, the U.S. prudent pattern and the Singaporean vegetable-fruit-soy pattern have fewer similarities, in that there is no contribution of fish, poultry or whole grains to the Singapore pattern, and vegetables contribute more than fruits. Whole grain intake is exceedingly rare in Singapore, as indicated in a study of food availability and sources of fiber intake (33).

Prior literature on empirically-derived dietary patterns and lung disease or symptoms are sparse. In a prospective study of dietary patterns and lung cancer in men in the Netherlands, a modest positive association was seen for a dietary pattern characterized by pork, processed meat and potatoes, and weak inverse associations were observed for two dietary patterns characterized by vegetable intake (34). However, dietary patterns identified in U.S. populations have been associated with biologic markers for systemic inflammation (35), increased insulin (29, 36), and carcinogen metabolism (20) that may be relevant for lung disease and symptoms.

Our finding that a dietary pattern characterized by meat and starchy food intake is related to respiratory symptoms in Singapore Chinese is novel. This pattern is notable for the number of starch laden dishes that had high loading for the pattern, particularly the noodle and rice dishes. These starchy items have a high glycemic index and thus may increase insulin resistance over time. Given that both hyperglycemia and chronic obstructive pulmonary disease, which is frequently associated with cough and phlegm, are related to impaired lung function (37, 38), oxidative stress (39, 40), and inflammation (41, 42), it is possible that they may share pathophysiologic mechanisms (43).

The meat-dim sum pattern is also highly correlated with dietary sodium. Many popular Chinese dim sum dishes are high in sodium (44). The major sources of added sodium in the diet in our population are from sauces and condiments and soups, rather than table salt (45). Sodium from these sources were captured in our food frequency questionnaire (23). Although findings from principle component analyses do not allow for drawing conclusions about single nutrient-disease associations, there is some evidence that dietary sodium has effects on asthma and airway hyperreactivity [reviewed in (1)]. Relevant to our study, symptoms of bronchitis (46) have also been reported to be affected by sodium intake.

In addition to sodium, preserved meat and preserved fish/shellfish were also highly correlated with the meat-dim sum pattern as well as with each other ($r \geq 0.33$). Preserved meat and fish are high in sodium but also contain other compounds, such as nitrosamines, that may be relevant. It is difficult to tease out the individual effects of these correlated foods; modeling these foods and the pattern together attenuates all of them. The meat-dim sum pattern offers the advantage of summarizing the effects of these correlated foods.

An alternative explanation for the positive association between cough with phlegm and the meat-dim sum pattern is confounding by lifestyle and socioeconomic factors (47-51). We addressed this, to the extent possible, by evaluating confounding by detailed smoking variables, environmental tobacco smoke, occupation, education, body mass index and dialect group. Positive associations were similar in men and women, in lean and overweight individuals, and in more and less educated individuals. Of note, the association with the meat-dim sum pattern was present both in nonsmokers and smokers, suggesting that it is not due to residual confounding by smoking.

The other dietary pattern in this population, characterized by vegetable, fruit and soyfood intake, was more weakly associated with cough and phlegm and this association disappeared after adjustment for non-starch polysaccharide intake, with which it is highly correlated. The weak association between symptoms and this dietary pattern is not unexpected because vegetables, the major contributor to the pattern, are not related to cough and phlegm in these (7) or other data (1, 2). In contrast, the inverse association with non-starch polysaccharides in our data appears to be driven by fruits and to a lesser degree, soyfoods (7).

The odds ratio for the meat-dim sum pattern was attenuated and lost statistical significance when restricted to the smaller number of subjects with more chronic symptoms. This is similar to what we observed in some previous dietary analyses in this cohort (8). In addition to the reduced power with a smaller sample size, it is possible that diet, which may change over time, has a greater impact on recently occurring symptoms, rather than longer term symptoms. Lastly, long-term symptoms could lead to dietary changes, obscuring etiologic associations.

Limitations of principal components analysis include the subjective nature of determining the number of patterns, labeling the patterns, and interpreting these patterns (52). Reduced rank regression has been suggested to be superior to principal components analysis (53). However, this was not an option for our analyses, because reduced rank regression requires "a priori" knowledge of dietary factors associated with the outcome of interest. Because there is no clear picture of the underlying biologic mechanism or a set of dietary guidelines for preventing chronic lung disease, as there is for cardiovascular disease (54), we chose to use an "a posteriori" method.

We entered individual foods and beverages, without grouping them, into the principal components analysis. One rationale for grouping foods prior to conducting principal components analysis has been to limit influences of within-person variability in individual food intake (55). However, we conducted sensitivity analyses and found a high degree of internal consistency and reproducibility with our patterns. Another reason we chose to assess individual foods and beverages is that a large proportion of items in our questionnaire are mixed dishes (23), which do not lend themselves to a priori grouping. This is in contrast to dietary questionnaires commonly used in the U.S. in which the vast majority of questionnaire items are single foods.

In this first study of dietary patterns in relation to nonmalignant respiratory disease or symptoms, we identified two primary dietary patterns in the Chinese Singaporean population. One of the patterns, characterized by meat intake, meat-containing noodle, rice and savory mixed dishes was associated with an increased risk of developing cough with phlegm. The positive association with the meat-dim sum pattern was independent of non-starch polysaccharide intake, which we previously identified as a protective factor for cough with phlegm in this cohort. The other pattern, characterized by vegetable, fruit and soyfood intake was not independently

associated with cough and phlegm after adjustment for non-starch polysaccharide intake. Although reducing cigarette smoke exposure remains the most important preventative measure for respiratory disease, these data suggest that there may be deleterious dietary patterns independent of smoking. For the Singapore population, dietary recommendations based on our analysis of dietary patterns might include consuming fewer dim sum meals or choosing more healthful dim sum items, with lower glycemic index, saturated fat and sodium content. Although studies in other populations would be required, consuming foods with lower glycemic index, saturated fat and sodium content may also be a healthful modification to Western diets.

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Table 1 Factor loadings for foods associated with each dietary pattern: Singapore Chinese Health Study

Vegetable-Fruit-Soy			Meat-Dim sum		
Food item	Food type*	Loading factor (x100)	Food item	Food type*	Loading factor (x100)
Cauliflower	V	55	Siew mai	DS, M	46
Broccoli	V	50	Other steamed snack	DS, M	44
Carrots	V	49	Gravy noodle	M, St	43
Green beans/peas	V	48	Chicken rice	M, St	42
Other plain tofu in soups, mixed dishes or alone	S	46	Otar otar (spiced fish paste)	DS	41
Tung goo	V	43	Pork satay	M	40
Tomatoes	V	43	Chicken, mutton curry	M	39
Corn	V	43	Glutinous rice dumpling	DS, St	39
Yin choy, po choy	V	43	Steamed meat bao	DS, M	39
Kai lan	V	42	Popiah	DS, M	38
Head lettuce, Chinese lettuce	V	42	Ngor hiang	DS, M	38
Gum jum, dried fungus	V	42	Chinese rojak	DS, V	37
Tou gay, tai tau nga	V	41	Puffs, such as curry or bean	DS, V	37
Pak choy, siew pak choy	V	41	Chicken satay	M	37
Choi sum	V	41	Roasted duck or goose	M	37
White potatoes	V	40	Coconut rice dishes	St	36
Other tau kwa	S	40	Roti prata	St	36
Fu kua, mo qua	V	39	Other pig organs	M	36
Watercress	V	39	Preserved eggs	O	35

Table 1 (continued)

Vegetable-Fruit-Soy			Meat-Dim sum		
Food item	Food type *	Loading factor (x100)	Food item	Food type *	Loading factor (x100)
Head cabbage, wong nga pak	V	38	Deep fried chicken	M	35
Celery	V	37	Coconut desserts	DS	34
Foojook vegetarian meats	S	36	Other flavored rice, such as duck or char siew	St	34
Kai choi	V	36	Curry rice	St	34
Apple	F	35	Deep-fried snack, such as jian dui, fried prawn or fish ball, etc.	DS	33
Cucumber	V	34	Dry noodle dish, such as fishball, chicken or wanton mee	M, St	33
Yong tau foo	S	33	Belly pork	M	33
Other tau pok in soups, mixed dishes or alone	S	33	Lup chong	M	33
Other dark green leaves	V	32	Other fried noodle	St	32
Papaya	F	31	Luncheon meat	M	31
Pear	F	31	Fried rice	St	30
Honeydew	F	31	Squid	M	30
Gee choi	V	30			
% variance explained		7.3			7.2
Coefficient alpha		0.81			0.76

*V=vegetable, S=soyfood, F=fruit, M=meat dish (includes fish/shellfish), DS=dim sum/snack

dish, St=high starch item (e.g. rice dish, noodle dish, bread), O=other

Table 2 Sociodemographic and smoking characteristics by dietary pattern quartiles in the Singapore Chinese Health Study

	Vegetable-fruit-soy pattern quartiles				Meat-dim sum pattern quartiles			
	1 (low)	2	3	4 (high)	1 (low)	2	3	4 (high)
Mean age, years	56.8	55.9	55.4	55.1	58.1	56.3	55.1	53.8
Hokkien, %	56.5	52.2	49.4	48.3	53.7	51.7	50.5	50.5
Female, %	54.4	58.5	58.7	58.4	71.1	62.2	54.3	42.4
Smoking status, %								
Never	64.7	72.7	74.3	75.6	79.9	74.1	70.1	63.1
Past	11.1	10.0	10.1	10.5	8.9	10.0	11.1	11.8
Current	24.2	17.4	15.6	13.9	11.2	15.9	18.8	25.1
Age at starting to smoke (% of current smokers)								
≥ 20 years	44.1	43.9	45.6	46.2	46.9	45.2	45.9	42.7
15-19	37.0	37.3	36.5	36.2	33.1	36.2	36.2	39.3
≤ 14 years	19.0	18.9	17.9	17.6	20.0	18.6	17.9	18.1

Table 2 (continued)

Years smoked (% of								
current smokers)								
<40 years	58.1	59.3	62.0	63.8	48.6	55.6	62.1	67.3
≥40 years	41.9	40.7	38.0	36.2	51.4	44.4	37.9	32.7
Cigarettes smoked per								
day (% of current								
smokers)								
≤12	38.0	42.5	41.9	45.2	53.2	47.0	39.4	34.0
13-22	42.3	41.8	41.5	39.0	36.9	39.0	43.4	43.3
≥23	19.7	15.7	16.7	15.9	10.0	14.0	17.2	22.7
Adult environmental								
tobacco smoke								
exposure,* %								
None	17.5	17.9	17.8	19.3	21.2	18.2	17.5	15.7
Home and/or work	82.5	82.1	82.2	80.7	78.8	81.8	82.5	84.3

Table 2 (continued)

Education level, %								
No formal	32.2	27.0	23.2	20.6	36.0	28.2	22.4	16.5
Primary school	44.7	44.7	45.2	44.0	42.4	44.6	46.2	45.5
Secondary/vocational/ university	23.1	28.3	31.6	35.4	21.6	27.3	31.5	38.1
Body mass index - mean kg/m ²	23.1	23.2	23.1	23.2	23.1	23.2	23.2	23.2

*Environmental tobacco smoke exposure when 18 years or older.

Table 3 Spearman correlation coefficients between food and energy-adjusted nutrient intake and dietary patterns: Singapore Chinese Health Study

	Vegetable-fruit-soy pattern	Meat-dim sum pattern
Total energy, kcal	0.43	0.56
Nutrients (daily intake)*		
Non-starch polysaccharides, g	0.49	-0.11
Vitamin C, mg [†]	0.41	-0.06
Vitamin E, mg [†]	0.60	0.07
Total carotenoids, µg [†]	0.59	-0.04
Total isoflavones, mg	0.35	0.04
Total fat, g	0.32	0.33
Saturated fat, g	0.17	0.36
Omega-3 fatty acid, g	0.31	0.04
Omega-6-fatty acid, g	0.30	0.09
Carbohydrate, g	-0.21	-0.32
Sodium, mg	0.05	0.41
Cholesterol, mg	-0.04	0.37
Nitrosamine, µg	-0.27	-0.14
Foods (median daily intake), g		
Total fruit	0.50	0.18
Total vegetables	0.83	0.27
Soyfoods	0.55	0.32
Total red meat	0.18	0.65
Preserved red meat	0.18	0.61
Total fish and shellfish	0.34	0.35
Preserved fish and shellfish	0.24	0.46
Fresh eggs	0.16	0.46

*Nutrient values are adjusted for energy intake.

[†]Nutrient intake from food sources.

Table 4 Odds ratios by quartile of dietary pattern intake in relation to incident cough with phlegm: The Singapore Chinese Health Study

	No cough or phlegm N=46,942	All cases of incident cough with phlegm N=623	Base adjusted model OR (95% CI)*	Plus non-starch polysaccharide intake OR (95% CI)†	Cases with symptoms for ≥3 months per year N=380	Base adjusted model OR (95% CI)*	Plus non-starch polysaccharide intake OR (95% CI)†
Dietary pattern							
Meat-dim sum							
Quartile 1	12,026	117	1.0 (ref.)	1.0 (ref.)	81	1.0 (ref.)	1.0 (ref.)
Quartile 2	11,855	150	1.25 (0.98, 1.60)	1.22 (0.95, 1.56)	96	1.18 (0.87, 1.59)	1.15 (0.85, 1.55)
Quartile 3	11,624	162	1.35 (1.05, 1.74)	1.29 (1.00, 1.67)	96	1.18 (0.86, 1.62)	1.13 (0.82, 1.55)
Quartile 4	11,437	194	1.53 (1.16, 2.01)	1.43 (1.08, 1.89)	107	1.25 (0.88, 1.78)	1.18 (0.83, 1.67)
<i>P</i> for trend‡			0.01	0.02		0.3	0.5
Vegetable-fruit-soy							
Quartile 1	11,635	185	1.0 (ref.)	1.0 (ref.)	108	1.0 (ref.)	1.0 (ref.)
Quartile 2	11,759	163	0.96 (0.77, 1.19)	1.05 (0.85, 1.32)	103	1.09 (0.83, 1.44)	1.21 (0.91, 1.60)
Quartile 3	11,748	137	0.81 (0.64, 1.02)	0.96 (0.75, 1.22)	79	0.86 (0.64, 1.17)	1.04 (0.75, 1.43)
Quartile 4	11,800	138	0.79 (0.62, 1.02)	1.07 (0.81, 1.41)	90	1.00 (0.73, 1.37)	1.38 (0.96, 1.96)
<i>P</i> for trend‡			0.04	0.8		0.7	0.1

*Models are adjusted for age, total energy intake, dialect group, gender, smoking status (never, former, current), age at starting to smoke (≥20, 15-19, ≤14 years), cigarettes per day (≤12, 13-22, ≥23), adult ETS (none, home and/or work), and education (no formal education, primary, secondary/vocational/university).

†Models are adjusted for all factors listed above, in addition to energy-adjusted daily non-starch polysaccharide intake (quartiles).

‡The linear trend tests for diet-disease associations were based on median values within each quartile.

Table 5 Odds ratios by quartile of dietary pattern intake in relation to incident asthma: The Singapore Chinese Health Study

	No asthma*	Incident asthma reported on follow-up questionnaire	Base adjusted model	Plus non-starch polysaccharide intake	Incident asthma confirmed during validation questionnaire	Base adjusted model	Plus non-starch polysaccharide intake
	45,104	406	OR (95% CI) [†]	OR (95% CI) [‡]	270 [§]	OR (95% CI) [†]	OR (95% CI) [‡]
Dietary pattern							
Meat-dim sum							
Quartile 1	11,599	91	1.0 (ref.)	1.0 (ref.)	57	1.0 (ref.)	1.0 (ref.)
Quartile 2	11,374	113	1.32 (0.99, 1.75)	1.29 (0.97, 1.71)	76	1.39 (0.98, 1.97)	1.37 (0.96, 1.94)
Quartile 3	11,179	106	1.31 (0.97, 1.77)	1.27 (0.94, 1.71)	71	1.36 (0.93, 1.97)	1.33 (0.91, 1.93)
Quartile 4	10,952	96	1.25 (0.89, 1.77)	1.19 (0.84, 1.68)	66	1.32 (0.86, 2.01)	1.28 (0.84, 1.95)
<i>P</i> for trend			0.4	0.6		0.4	0.5
Vegetable-fruit-soy							
Quartile 1	11,203	117	1.0 (ref.)	1.0 (ref.)	72	1.0 (ref.)	1.0 (ref.)
Quartile 2	11,291	119	1.10 (0.85, 1.44)	1.19 (0.91, 1.55)	86	1.28 (0.93, 1.77)	1.34 (0.97, 1.86)
Quartile 3	11,289	87	0.83 (0.62, 1.11)	0.94 (0.69, 1.28)	51	0.78 (0.53, 1.13)	0.84 (0.57, 1.25)
Quartile 4	11,321	83	0.81 (0.59, 1.11)	1.00 (0.70, 1.43)	61	0.95 (0.65, 1.40)	1.09 (0.71, 1.68)
<i>P</i> for trend			0.08	0.7		0.4	0.8

*These individuals reported no history of asthma, cough or phlegm.

[†]Models are adjusted for age, total energy intake, dialect group, gender, smoking status (never, former, current), age at starting to smoke (≥ 20 , 15-19, ≤ 14 years), cigarettes per day (≤ 12 , 13-22, ≥ 23), adult ETS (none, home and/or work), and education (no formal education, primary, secondary/vocational/university).

[‡]Models are adjusted for all factors listed above, in addition to energy-adjusted daily non-starch polysaccharide intake (quartiles).

[§]Of 406 self-reported asthmatics, 331 responded to a validation questionnaire – 270 confirmed incident asthma, 52 confirmed asthma but not incident timing, 9 did not confirm asthma.

^{||} The linear trend tests for diet-disease associations were based on median values within each quartile.

ON-LINE SUPPLEMENT DATA

Prospective study of dietary patterns and persistent cough with phlegm among Chinese
Singaporeans

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METHODS SUPPLEMENT

Identification of Dietary Patterns

At baseline, a 165-item quantitative food frequency questionnaire, developed for and validated in this population, was administered to assess usual diet over the past year (E1, 2). Using principal components analysis (E3, 4) among the baseline cohort (N=63,257), we identified patterns from the food frequency responses of 147 food items and 18 beverages. Frequency of consumption for each item was converted to units of servings per month. Extraction of principal components was followed by orthogonal rotation. The number of components retained for rotation was based primarily on examination of scree plots and factor interpretability, but eigenvalues (>1.0) and percent variance explained were also considered (E3). As an additional assessment of the robustness of the patterns identified, we used oblique rather than orthogonal rotation, but the same patterns emerged. Factors were given descriptive labels based on our interpretation of the underlying dietary construct represented by each factor.

A component score was calculated for each dietary pattern and for each individual to represent the individual's level of intake for the pattern. The score for each pattern was computed as a linear composite of the foods with meaningful loadings for that pattern. Only foods with loading scores ≥ 0.30 were retained in the final patterns. Cronbach's coefficient alpha was calculated for all foods, then each food was removed one by one. If the removal of a food resulted in a higher coefficient alpha value, then that food was removed from the final pattern (E3). Scores were calculated by taking the unweighted sum of standardized frequencies of intake for each food associated with the pattern, then divided into quartiles based on the distribution of the baseline cohort. Principal components analyses were conducted using the

FACTOR PROCEDURE in SAS version 9 (SAS Institute, Cary, NC). Examples of the SAS programming code used have been previously cited (E5), and are available online (E6).

To assess the sensitivity of these final patterns to variation in the cutpoint for the loading scores, we also identified patterns identified using a less conservative cutpoint of ≥ 0.20 . This less conservative cutpoint resulted in the inclusion of a larger number of foods for each identified pattern, and in a lower coefficient alpha for one of the patterns. We decided to use the more conservative cutpoint in the final analysis, because the internal consistency was greater and the pattern was more clearly interpretable (e.g. food lists were mutually exclusive), two primary goals of principal components analysis.

To confirm reproducibility of the patterns identified, we repeated the principal components analysis among individuals in two randomly split samples of approximately equal size. The patterns identified were similar across split samples and also similar to those identified in the entire sample. Cronbach's coefficient alpha (E3) was used to evaluate internal consistency for each component retained from each split sample. For example, food items that were retained in a component identified from the first split sample, but not in the second split sample, were added to the component identified in the second split sample. If the change in the coefficient alpha was considerable between the original component and the component with the additional food item, then the food was determined to be important and included in the final dietary pattern. The opposite was also assessed, for example, if the removal of a food from the component of one sample considerably changed the alpha statistic, then it was retained in the final pattern. There were few foods that differed between the dietary patterns from each sample (correlation coefficient values >0.98), and when these foods were either added or removed from the corresponding split sample pattern, the coefficient alpha values were nearly unchanged (data not

shown). Therefore, we present results based on dietary patterns identified from the entire sample.

Identification of Asthma

Subjects reporting asthma were considered to be incident (n=406) if their reported age at onset of asthma on the follow-up questionnaire was later than the age at baseline interview. Among the 406, 35 also reported incident cough with phlegm. We completed validation home visits on 331 of the 406 (81.5%) incident asthmatics where we asked again about their history of asthma and the presence and duration of symptoms and use of medications. Interviewers recorded the names of all medications on hand for asthma and asked when had been last used. We considered a subject to have confirmed incident asthma if, at the validation visit, they reported asthma symptoms or current use of asthma medications and age at onset of asthma consistent with incident status relative to the baseline questionnaire. Among the 331 respondents, 270 (81.6%) confirmed incident asthma, 52 confirmed asthma but gave age at onset consistent with prevalent asthma (15.7%) and 9 did not confirm asthma (2.7%). We conducted analyses two ways – using all 406 incident asthmatics based on the follow-up interview and using only the 270 confirmed incident asthmatics.

Description of Additional Covariates Assessed for Confounding

Several factors were considered for inclusion in the final adjusted models, but not retained. A separate variable for years smoked was not necessary in the final model, because both age at interview and age at start of smoking were included. We evaluated several variables for ETS exposure throughout the life course including living with smokers in the home as a child (and number of smokers), living with smokers during adulthood in the past or currently (with number of smokers), and working with smokers (with number of smokers). A single variable for

adult ETS was retained in the final model although neither this ETS variable or the other ETS variables were confounders. Detailed information on ETS exposure in this study has been previously described (E7). We also evaluated whether changes in smoking status from baseline to follow-up interview altered the association. The vast majority of subjects (84.4%) had no change in smoking status. Addition of categorical terms for change in smoking status from baseline to follow-up (categories: no change, stopped smoking, reduced amount of smoking, increased amount of smoking, began smoking) did not materially alter any associations and so were not included in final models. Other variables that were not retained in final models because they did not appreciably alter the odds ratios for the dietary patterns include saturated fat intake, body mass index, highest education level (no formal education, primary school, more than primary school) and longest held occupation (8 categories).

Table E1 Odds ratios by quartile of dietary pattern intake in relation to cough and/or phlegm outcomes other than incident cough with phlegm: The Singapore Chinese Health Study

	Non-cases	Incident cough only		Incident phlegm only		All prevalent cough with phlegm		Miscellaneous cough and/or phlegm*	
	N=46,942	N=549	OR (95% CI) [†]	N=1,349	OR (95% CI) [†]	N=727	OR (95% CI) [†]	N=2,132	OR (95% CI) [†]
Dietary pattern									
Meat-dim sum									
Quartile 1	12,026	125	1.0 (ref.)	300	1.0 (ref.)	132	1.0 (ref.)	381	1.0 (ref.)
Quartile 2	11,855	144	1.12 (0.88, 1.43)	306	0.96 (0.81, 1.13)	161	1.07 (0.84, 1.35)	464	1.06 (0.92, 1.22)
Quartile 3	11,624	143	1.11 (0.86, 1.43)	350	1.07 (0.91, 1.26)	200	1.23 (0.98, 1.56)	600	1.25 (1.09, 1.44)
Quartile 4	11,437	137	1.02 (0.76, 1.36)	393	1.12 (0.93, 1.35)	234	1.24 (0.96, 1.61)	687	1.22 (1.05, 1.42)
<i>P</i> for trend [‡]			0.8		0.1		0.09		0.01

Table E1 (continued)

	Non-cases	Incident cough only	Incident phlegm only	All prevalent cough with phlegm	Miscellaneous cough and/or phlegm*				
	N=46,942	N=549	OR (95% CI) [†]	N=1,349	OR (95% CI) [†]				
				N=727	OR (95% CI) [†]				
					N=2,132				
					OR (95% CI) [†]				
Vegetable-fruit-soy									
Quartile 1	11,635	140	1.0 (ref.)	373	1.0 (ref.)	218	1.0 (ref.)	530	1.0 (ref.)
Quartile 2	11,759	155	1.10 (0.87, 1.40)	349	0.97 (0.83, 1.13)	177	0.95 (0.77, 1.17)	476	0.92 (0.81, 1.05)
Quartile 3	11,748	127	0.88 (0.68, 1.15)	337	0.92 (0.78, 1.09)	164	0.93 (0.74, 1.16)	567	1.08 (0.95, 1.24)
Quartile 4	11,800	127	0.85 (0.63, 1.15)	290	0.77 (0.64, 0.94)	168	1.02 (0.79, 1.33)	559	1.05 (0.90, 1.23)
<i>P</i> for trend [‡]			0.1		0.01		0.8		0.3

*The miscellaneous group includes the remaining discordant combinations of incident and prevalent cough and/or phlegm.

[†]Models are adjusted for age, total energy intake, dialect group, gender, smoking status (never, former, current), age at starting to smoke (≥ 20 , 15-19, ≤ 14 years), cigarettes per day (≤ 12 , 13-22, ≥ 23), adult ETS (none, home and/or work), education (no formal education, primary, secondary/vocational/university), and energy-adjusted daily non-starch polysaccharide intake (quartiles).

[‡]The linear trend tests for diet-disease associations were based on median values within each quartile.

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