

1 **Online supplementary**

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3 **Appendix 1 – METHODS**

4 **AGE score calculation**

5         There currently lacks a standardized and validated method of estimating AGE consumption. As a result, we adapted a  
6 previously published strategy of approximating AGE intake,<sup>1</sup> albeit in an adolescent population. This strategy utilizes the NHANES  
7 FFQ and assumes consumption of standard portion sizes, as the FFQ does not report portion sizes. Further, as the NHANES FFQ does  
8 not capture detailed cooking methodology, which may affect AGE content particularly for meats,<sup>2</sup> we assumed conventional methods  
9 of cooking, specifically with the use of high, dry heat (roasting, grilling, broiling, frying and searing). Despite these assumptions, our  
10 AGE score may still be used as a reasonable comparison of relative AGE intake across this cohort.

11         Consistent with published methodology, each food item was assigned a multiplication factor based on consumption frequency  
12 (0 if consumption was at most 2-3 times per month, 1 if at most once per week, 2 if twice per week, 3.5 if 3-4 times per week, 5.5 if 5-  
13 6 times per week, 7 for daily and 14 for twice per day) (Figure S2).<sup>1</sup> We then calculated estimated AGE intake per week for each food  
14 item as the product of the multiplication factor and the approximate AGE content of the food item from an existing database.<sup>2</sup> A daily  
15 average AGE intake was calculated from the weekly estimated AGE intake for all food. Finally, this value was standardized by  
16 reported total kilocalorie intake from the 24-hour dietary recall to arrive at an AGE score representing an estimate of the daily average  
17 AGE consumption per participant (Figure S2).<sup>2</sup>

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**19 Explanation of covariates**

20 Poverty to income ratio (PIR) was calculated according to the annual Department of Health and Human Services' poverty  
21 guidelines by dividing family income by a family size-specific poverty threshold with scores ranging from 0 (no income) to 5 ( $\geq 5$   
22 times the federal poverty level).<sup>3,4</sup> BMI percentile was used to classify BMI in accordance with expert committee recommendations  
23 from the American Medical Association,<sup>5</sup> and calculated using the SAS code based on the 2000 Centers for Disease Control and  
24 Prevention growth chart.<sup>6</sup> A self-reported diagnosis of current asthma was defined as an affirmative response to the following  
25 questions: "Has a doctor or other health professional ever told you that you have asthma?" and "Do you still have asthma?" The total  
26 HEI score is a validated measure of overall diet quality and adherence to recommendations from the 2010 Dietary Guidelines for  
27 Americans (DGA).<sup>7</sup> Scores range from 0 to 100 with higher scores representing better adherence. For each participant, the total HEI  
28 score was calculated using the 24-hour dietary recall interview and the recommended HEI scoring algorithms from the National  
29 Institutes of Health.<sup>8</sup>

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**31 Statistical analyses**

32 For the multivariable models, respiratory questions that elicited a numerical or ordinal response were dichotomized, indicating either  
33 presence or absence of the symptom. AGE and meat consumption scores were natural-log-transformed. Pearson's correlation was  
34 conducted between non-survey-weighted AGE and meat consumption scores. Bonferroni correction for multiple testing was applied

35 for the seven secondary outcomes using  $\alpha < 0.007$  for statistical significance. All analyses were conducted using Statistical Analysis  
36 Software (SAS) (version 9.4) and figures were made using R (version 3.5).

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52 **Appendix 2 - RESULTS**

53 **Bonferroni corrections**

54 After Bonferroni correction for the 7 secondary outcomes, higher AGE scores were significantly associated with wheezing  
55 requiring prescription medication use at  $\alpha = 0.007$ , while there were no significantly increased odds of having wheezing or cough  
56 symptoms with higher consumption of any meat at  $\alpha = 0.007$ .

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58 **Interaction by race/ethnicity**

59 When race/ethnicity was defined as non-Hispanic whites, non-Hispanic blacks, Hispanics and others, there was no significant overall  
60 interaction by race/ethnicity ( $p_{\text{int}} = 0.05$ ). However, there was a significant interaction effect ( $p_{\text{int}} = 0.04$ ) when non-Hispanic blacks  
61 were compared with non-Hispanic whites. Stratified analysis showed that only non-Hispanic whites had increased odds of wheezing  
62 with higher AGE intake (OR 1.29; 95% CI 1.02 to 1.63).

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69 **Appendix 3 – FIGURES AND TABLES**

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71 **Figure S1. Selection flowchart for study participant inclusion.** Participants were included if they had valid responses to the FFQ  
72 and 24-hour dietary recall interview, and had completed the interview questionnaire on respiratory symptoms. Participants were also  
73 required to provide responses to relevant covariates including age, sex, race/ethnicity, the ratio of family income to poverty, body  
74 mass index percentiles, and asthma status. Children younger than 2 years of age were excluded as the FFQ was conducted amongst  
75 participants at least 2 years of age. Participants with missing responses or the responses “Don’t know” or “Refused” were excluded.  
76 NHANES: National Health and Nutrition Examination Survey; FFQ: Food frequency questionnaire.

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86 **Table S1.** Interview questions included from the NHANES Respiratory Health Questionnaire on respiratory symptoms

Questions	Target population	Range of responses
<i>Primary outcome</i>		
In the past 12 months, have you had wheezing or whistling in your chest?	Both males and females 1-150 years old	Yes No Refused Don't know Missing
<i>Secondary outcomes</i>		
In the past 12 months, how often, on average, has your sleep been disturbed because of wheezing? Would you say this happens...	Both males and females 1-150 years old	Never ≥1 nights per week <1 night/week Refused Don't know Missing
In the past 12 months, has your chest sounded wheezy during or after exercise or physical activity?	Both males and females 1-150 years old	Yes No Refused Don't know Missing
In the past 12 months, how many times have you gone to the doctor's office or the hospital emergency room for one or more of these attacks of wheezing or whistling?	Both males and females 1-150 years old	0-15 ≥20 Refused Don't know Missing
In the past 12 months, have you taken medication, prescribe by a doctor, for wheezing or whistling?	Both males and females 1-150 years old	Yes No Refused Don't know Missing
During the past 12 months, how much did you limit your usual activities due to wheezing or whistling? Would you say...	Both males and females 1-150 years old	Not at all A little

		A fair amount A moderate amount A lot Refused Don't know Missing
During the past 12 months, how many days of work or school did you miss due to wheezing or whistling?	Both males and females 6-69 years old	None 1-7 8-30 ≥31 Refused Don't know Missing
In the past 12 months, have you had a dry cough at night not counting a cough associated with a cold or chest infection lasting 14 days or more?	Both males and females 1-150 years old	Yes No Refused Don't know Missing

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94 **Figure S2. Flow diagram depicting step-wise approach used for each participant in determining a daily AGE score**  
95 **representative of approximate AGE intake (adapted from Saha et al.)<sup>1</sup>**

96 \*Multiplication factors representative of food consumption frequency, adapted from Saha et al.<sup>1</sup>

97 †As the NHANES FFQ does not describe detailed cooking methodology or portion size consumed, exact AGE intake could not be  
98 obtained. Consequently, a unitless AGE value was derived to approximate AGE intake, utilizing a published database of measured  
99 AGE content for various foods.<sup>2</sup> This derived AGE value represents approximate AGE intake per one-time consumption of food item,  
100 assuming standard portion sizes.

101 ‡Total caloric intake for each participant taken from NHANES 24-hour dietary recall interview.

102 FFQ: Food frequency questionnaire

103 AGE: Advanced glycation end-product

104 NHANES: National Health and Nutrition Examination Survey

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111 **Table S2.** Frequency of respiratory symptoms

<b>Respiratory symptoms (over past 1 year)</b>	<b>Weighted % (Crude Frequency: "Yes"/Total) *</b>
Wheezing in chest	13.04 (537/4388)
At least 1 sleep disturbance due to wheezing	7.04 (304/4388)
Wheezing during exercise	6.91 (292/4385)
At least 1 doctor, hospital, or emergency room visit for wheezing	8.17 (325/4388)
Wheezing requiring prescription medication use	9.45 (399/4388)
Limitation of usual activities due to wheezing	5.39 (229/4388)
At least 1 day of school or work missed due to wheezing	4.31 (169/4245)
Dry nocturnal cough	2.63 (124/4386)

112 \*Survey procedures were used to take into account the NHANES survey design and to obtain population weighted estimates for  
113 prevalence.

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121 **Figure S3. Heat map showing Pearson's correlation co-efficients between advanced glycation end-product (AGE) and**  
122 **meat consumption scores.** Any non-seafood meat is defined as the total consumption frequencies of red meat, processed meat  
123 and poultry. Any meat includes the consumption frequencies of red meat, processed meat, poultry and seafood. All correlations  
124 were statistically significant at  $p < 0.0001$ .

**Table S3.** Survey-design-adjusted multivariable logistic regression of associations between meat consumption frequencies and respiratory symptoms

<b>Respiratory outcomes (over past 1 year)</b>	<b>Odds Ratio</b>	<b>95% Confidence Interval</b>	<b>p value</b>
<b>Red meat</b>			
Wheezing in chest	1.20	0.68-2.12	0.52
At least 1 sleep disturbance due to wheezing	1.89	0.96-3.72	0.07
Wheezing during exercise	1.40	0.67-2.93	0.37
At least 1 doctor, hospital, or emergency room visit for wheezing	1.19	0.53-2.66	0.67
<b>Wheezing requiring prescription medication use</b>	<b>1.92</b>	<b>1.03-3.57</b>	<b>0.04</b>
Limitation of usual activities due to wheezing	1.27	0.68-2.41	0.45
At least 1 day of school or work missed due to wheezing	1.43	0.43-4.78	0.56
Dry nocturnal cough	1.59	0.58-4.39	0.37
<b>Poultry</b>			
Wheezing in chest	1.34	0.81-2.23	0.25
<b>At least 1 sleep disturbance due to wheezing</b>	<b>1.94</b>	<b>1.11-3.40</b>	<b>0.02</b>
Wheezing during exercise	1.64	0.84-3.21	0.15
At least 1 doctor, hospital, or emergency room visit for wheezing	1.05	0.50-2.24	0.89
<b>Wheezing requiring prescription medication use</b>	<b>1.86</b>	<b>1.09-3.19</b>	<b>0.02</b>
Limitation of usual activities due to wheezing	1.48	0.78-2.80	0.23
At least 1 day of school or work missed due to wheezing	0.86	0.41-1.80	0.69
Dry nocturnal cough	1.26	0.63-2.49	0.51
<b>Processed meat</b>			
Wheezing in chest	1.13	0.77-1.66	0.53
<b>At least 1 sleep disturbance due to wheezing</b>	<b>1.82</b>	<b>1.05-3.17</b>	<b>0.03</b>
Wheezing during exercise	1.05	0.55-2.03	0.88
At least 1 doctor, hospital, or emergency room visit for wheezing	0.89	0.50-1.73	0.73
<b>Wheezing requiring prescription medication use</b>	1.66	0.94-2.94	0.08
Limitation of usual activities due to wheezing	1.42	0.70-2.89	0.33
At least 1 day of school or work missed due to wheezing	1.16	0.53-2.53	0.71
Dry nocturnal cough	1.27	0.83-1.93	0.27
<b>Any non-seafood meat</b>			
Wheezing in chest	1.25	0.70-2.25	0.45
<b>At least 1 sleep disturbance due to wheezing</b>	<b>2.32</b>	<b>1.11-4.82</b>	<b>0.02</b>
Wheezing during exercise	1.41	0.60-3.30	0.43
At least 1 doctor, hospital, or emergency room visit for wheezing	1.01	0.39-2.64	0.99

<b>Wheezing requiring prescription medication use</b>	<b>2.23</b>	<b>1.10-4.54</b>	<b>0.03</b>
Limitation of usual activities due to wheezing	1.53	0.67-3.51	0.32
At least 1 day of school or work missed due to wheezing	1.15	0.36-3.63	0.82
Dry nocturnal cough	1.52	0.70-3.30	0.29
<b>Seafood</b>			
Wheezing in chest	1.17	0.72-1.89	0.53
At least 1 sleep disturbance due to wheezing	1.82	0.83-3.99	0.13
Wheezing during exercise	1.09	0.65-1.84	0.75
At least 1 doctor, hospital, or emergency room visit for wheezing	1.13	0.51-2.55	0.76
Wheezing requiring prescription medication use	1.46	0.71-3.02	0.30
Limitation of usual activities due to wheezing	1.11	0.60-2.06	0.75
At least 1 day of school or work missed due to wheezing	1.54	0.77-3.06	0.22
Dry nocturnal cough	1.08	0.63-1.85	0.78

## Appendix - References

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