Egg Consumption and Risk of Type 2 Diabetes in Men and Women

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</tbody>
</table>
OBJECTIVE — Whereas limited and inconsistent findings have been reported on the relation between dietary cholesterol or egg consumption and fasting glucose, no previous study has examined the association between egg consumption and type 2 diabetes. This project sought to examine the relation between egg intake and the risk of type 2 diabetes in two large prospective cohorts.

RESEARCH DESIGN AND METHODS — In this prospective study, we used data from two completed randomized trials: 20,703 men from the Physicians’ Health Study I (1982–2007) and 36,295 women from the Women’s Health Study (1992–2007). Egg consumption was ascertained using questionnaires, and we used the Cox proportional hazard model to estimate multivariable hazard ratios for type 2 diabetes.

RESULTS — During mean follow-up of 20.0 years in men and 11.7 years in women, 1,921 men and 2,112 women developed type 2 diabetes. Compared with no egg consumption, multivariable adjusted hazard ratios for type 2 diabetes were 1.09 (95% CI 0.87–1.37), 1.09 (0.88–1.34), 1.18 (0.95–1.45), 1.46 (1.14–1.86), and 1.58 (1.25–2.01) for consumption of 0–2, 2–4, 4–6, and ≥7 eggs/week, respectively, in men (P for trend <0.0001). Corresponding multivariable hazard ratios for women were 1.06 (0.92–1.22), 0.97 (0.83–1.12), 1.19 (1.03–1.38), 1.18 (0.88–1.58), and 1.77 (1.28–2.43), respectively (P for trend <0.0001).

CONCLUSIONS — These data suggest that high levels of egg consumption (daily) are associated with an increased risk of type 2 diabetes in men and women. Confirmation of these findings in other populations is warranted.

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Egg intake and type 2 diabetes

low-dose aspirin and vitamin E (WHS) in
the prevention of cardiovascular disease
and cancer. Detailed description of the
PHS I and WHS has been published pre-
viously (16–18). Briefly, a total of 22,071
U.S. male physicians aged ≥40 years at
entry (1982) were randomized using a
2×2 factorial design to aspirin (325 mg
every other day), β-carotene (50 mg every
other day), or their corresponding place-
bos. Similarly, 39,876 female health pro-
fessionals aged ≥49 years at entry (1992–
1995) were randomized to low-dose
aspirin (100 mg on alternate days), vita-
min E (600 IU on alternate days), or their
corresponding placebos. Each participant
gave written informed consent, and the
institutional review board at Brigham and
Women’s Hospital approved both study
protocols. For the present analyses, we
excluded 1,368 men because of prevalent
type 2 diabetes (n = 641), missing data on
egg consumption (n = 365), or missing
data on potential confounders: smoking,
energy intake, BMI, exercise, hyperten-
sion, and fruits and vegetables (n = 362).
Among women, we excluded 3,581 be-
cause of prevalent type 2 diabetes (n = 1,171),
missing data on egg consumption (n = 852),
or missing data on potential con-
founders: BMI, exercise, smoking, energy
intake, fruits and vegetables, nutrients, al-
cohol consumption, and hypertension (n = 1,598). Thus, a final sample of 20,703 men
and 36,295 women was used in the current
analyses.

Egg consumption

Among men, information on egg con-
sumption was self-reported at baseline
using a simple abbreviated semiquan-
titative food-frequency questionnaire. Par-
ticipants were asked to report how often, on
average, they had eaten one egg during
the past year. Possible response categories
included rarely/never,” “1–3/month,” “1/week,”
“2–4/week,” “5–6/week,” “daily,” and
“2+/day.” This information was ob-
tained at baseline and at 24, 48, 72, 96,
and 120 months after randomization.
Among women, information on egg con-
sumption was self-reported using a
131-item validated food-frequency
questionnaire (19) at baseline. Women
were asked to report their average con-
sumption of eggs over the past year. Possible
response categories were “Never or
<1/month,” “1–3/month,” “1/week,” “2–4/
week,” “5–6/week,” “1/day,” “2–3/day,”
“4–5/day,” and “6+/day.” Because very
few subjects consumed one or more eggs
day (7.8% for men and 1.0% for
women), we combined categories of one
der per day and beyond for stable estimates.
The validity of food-frequency question-
naires in similar populations has been
published elsewhere (19,20). The corre-
lation of egg consumption with dietary
cholesterol was 0.61 (P < 0.0001) and
with saturated fat among women was 0.26 (P < 0.0001).

Ascertainment of incident type 2
diabetes

Type 2 diabetes was ascertained by self-
report on annual follow-up question-
naires in both men and women. Follow-up and ascertainment of type 2 diabetes cases were completed in March
2007. Because all men were physicians,
self-report was deemed sufficient. Among
the female health professionals, self-
reports of type 2 diabetes were validated
using American Diabetes Association cri-
tera, for which additional information
was obtained using telephone interviews,
supplemental questionnaires, or review of
medical records from treating physicians
(21,22). Overall, the positive predictive
value for type 2 diabetes validation was
91% (21).

Other variables

Demographic data were collected at base-
line. In addition, information on prevalence
of hypertension, hypercholesterolemia,
family history of diabetes (WHS only),
smoking, exercise, and alcohol consump-
tion was obtained using telephone interviews,
supplemental questionnaires, or review of
medical records from treating physicians
(21,22). Overall, the positive predictive
value for type 2 diabetes validation was
91% (21).

Statistical analyses

We classified each subject according to the
following categories of egg consump-
tion per week: 0, <1, 1, 2–4, 5–6, and
≥7. We computed person-time of fol-
low-up from baseline until the first occur-
rence of J) type 2 diabetes, 2) death, or 3)
censoring date, the date of receipt of the
last follow-up questionnaire (March
2007). Within each egg-consumption
group, we calculated the incidence rate
of type 2 diabetes by dividing the number of
cases by the corresponding person-time.
We used Cox proportional hazard models
to compute multivariable adjusted hazard
ratios (HRs) with corresponding 95% CIs
using subjects in the lowest category of
egg consumption as the reference group.
The initial model adjusted for age, whereas the multivariable model con-
trolled for age (continuous), BMI (<25,
25–29, ≥30 kg/m²), smoking (never,
former, and current smokers), alcohol
consumption (0, 1–3 drinks/month, 1–6
drinks/week, ≥1 drinks/day), physical
activity (vigorous exercise <0, <1, 1–3, ≥4
times per week in men and quintiles of
kilocalories per week expended in leis-
ure-time physical activity in women),
and history of hypercholesterolemia and
hypertension. Because detailed informa-
tion on diet and family history was avail-
able for women, the multivariable model
in women also adjusted for family history
of diabetes, energy intake (quintiles), in-
take of fruits and vegetables (quintiles),
red meat consumption (<0.5, 0.5–0.9,
and ≥1 serving/day), and intake of poly-
unsaturated fats (quintiles), saturated fats
(quintiles), and trans fats (quintiles).
To examine whether the relation between egg
and diabetes was mediated by dietary cho-
lesterol, we evaluated the risk of diabetes
associated with dietary cholesterol and also
included dietary cholesterol in the multiva-
rable model in women. A similar approach
was used for saturated fat. A P value for lin-
ear trend was obtained by fitting a continu-
ous variable that assigned the median egg
consumption in each egg category in a Cox
regression model.

RESULTS — The mean ± SD age at
randomization was 53.5 ± 9.4 years
(range 39.7–85.9) in the PHS I and
54.5 ± 7.0 years (38.7–89.9) in the
A total of 1,921 new cases of type 2 diabetes were documented in men during a mean follow-up of 20.0 years. Among women, 2,112 new cases of type 2 diabetes occurred during a mean follow-up of 11.7 years. From the lowest to the highest category of egg consumption, crude incidence rates of diabetes were 35.8, 41.3, 42.7, 46.8, 62.4, and 67.0 cases per 10,000 person-years in the PHS I. A similar increase in rates of type 2 diabetes with egg consumption was observed in women, with corresponding crude incidence rates of 39.6, 45.8, 43.3, 64.8, 76.8, and 112.7 cases per 10,000 person-years, respectively. Whereas consumption of up to one egg per week was generally not associated with an increased risk of type 2 diabetes in either sex in multivariate analyses, more frequent consumption of eggs was associated with an increased risk of type 2 diabetes (Table 2). Compared with subjects who did not report egg consumption, intake of seven or more eggs per week was associated with a 58% increased risk of type 2 diabetes in men and a 77% increased risk of type 2 diabetes in women after adjustment for potential confounders (Table 2). Updating egg consumption using time-dependent Cox regression (PHS I) yielded a stronger relation between egg consumption and incidence of type 2 diabetes in men with HRs of 1.23, 1.40 (1.10–1.77), 1.77 (1.39–2.26), and 1.99 (1.23–3.23), from the lowest to the highest category of egg consumption, respec- tively, using a multivariable model as

### Table 1—Baseline characteristics of 20,703 men and 36,295 women according to egg consumption

<table>
<thead>
<tr>
<th>Eggs per week</th>
<th>0</th>
<th>&lt;1</th>
<th>1</th>
<th>2–4</th>
<th>5–6</th>
<th>≥7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>1,430</td>
<td>3,025</td>
<td>6,466</td>
<td>6,792</td>
<td>1,378</td>
<td>1,612</td>
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<tr>
<td>Age (years)</td>
<td>53.1 ± 9.2</td>
<td>52.8 ± 9.3</td>
<td>53.2 ± 9.3</td>
<td>53.4 ± 9.4</td>
<td>53.8 ± 9.3</td>
<td>56.4 ± 10.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.1 ± 2.7</td>
<td>24.6 ± 2.6</td>
<td>24.7 ± 2.7</td>
<td>24.9 ± 2.7</td>
<td>25.1 ± 2.9</td>
<td>24.9 ± 3.1</td>
</tr>
<tr>
<td>Fruits and vegetables per week</td>
<td>15.2 ± 8.4</td>
<td>14.1 ± 7.4</td>
<td>14.8 ± 7.1</td>
<td>15.3 ± 6.9</td>
<td>15.8 ± 7.4</td>
<td>17.0 ± 8.5</td>
</tr>
<tr>
<td>Whole milk</td>
<td>16.7</td>
<td>31.1</td>
<td>37.1</td>
<td>42.8</td>
<td>50.9</td>
<td>54.2</td>
</tr>
<tr>
<td>Skim milk</td>
<td>60.8</td>
<td>61.9</td>
<td>67.7</td>
<td>65.9</td>
<td>61.4</td>
<td>53.5</td>
</tr>
<tr>
<td>Nut intake*</td>
<td>72.2</td>
<td>77.9</td>
<td>80.4</td>
<td>81.8</td>
<td>82.7</td>
<td>77.8</td>
</tr>
<tr>
<td>Breakfast cereal</td>
<td>60.7</td>
<td>62.1</td>
<td>74.2</td>
<td>77.7</td>
<td>74.2</td>
<td>58.9</td>
</tr>
<tr>
<td>Smoking</td>
<td>6.4</td>
<td>8.8</td>
<td>9.8</td>
<td>12.0</td>
<td>14.6</td>
<td>16.8</td>
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<tr>
<td>Never smokers</td>
<td>56.9</td>
<td>51.0</td>
<td>51.1</td>
<td>48.6</td>
<td>46.9</td>
<td>41.6</td>
</tr>
<tr>
<td>Exercise</td>
<td>84.4</td>
<td>86.2</td>
<td>87.4</td>
<td>87.6</td>
<td>87.4</td>
<td>84.9</td>
</tr>
<tr>
<td>Current drinkers of ≥1 per day</td>
<td>21.5</td>
<td>23.3</td>
<td>23.9</td>
<td>25.8</td>
<td>26.4</td>
<td>30.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>22.8</td>
<td>20.3</td>
<td>22.8</td>
<td>22.9</td>
<td>24.7</td>
<td>26.2</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>14.6</td>
<td>12.9</td>
<td>12.0</td>
<td>11.1</td>
<td>10.4</td>
<td>10.4</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>6,381</td>
<td>10,758</td>
<td>9,222</td>
<td>8,921</td>
<td>647</td>
<td>366</td>
</tr>
<tr>
<td>Age (years)</td>
<td>55.2 ± 7.2</td>
<td>54.3 ± 7.0</td>
<td>54.4 ± 6.9</td>
<td>54.5 ± 7.0</td>
<td>54.6 ± 7.0</td>
<td>55.1 ± 7.2</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.3 ± 4.6</td>
<td>25.7 ± 4.8</td>
<td>25.8 ± 4.8</td>
<td>26.6 ± 5.2</td>
<td>27.4 ± 6.0</td>
<td>26.9 ± 6.0</td>
</tr>
<tr>
<td>Fruits and vegetables per week</td>
<td>6.2 ± 3.6</td>
<td>5.7 ± 3.2</td>
<td>6.0 ± 3.1</td>
<td>6.3 ± 3.1</td>
<td>6.4 ± 3.5</td>
<td>6.4 ± 3.8</td>
</tr>
<tr>
<td>Red meat (servings/day)</td>
<td>0.45 ± 0.45</td>
<td>0.62 ± 0.46</td>
<td>0.75 ± 0.49</td>
<td>0.93 ± 0.59</td>
<td>1.15 ± 0.76</td>
<td>1.26 ± 0.83</td>
</tr>
<tr>
<td>Energy intake (kcal/day)</td>
<td>1,547 ± 506</td>
<td>1,614 ± 498</td>
<td>1,758 ± 503</td>
<td>1,925 ± 530</td>
<td>2,043 ± 585</td>
<td>2,072 ± 605</td>
</tr>
<tr>
<td>Exercise (kcal/week)</td>
<td>1,078 ± 1,282</td>
<td>931 ± 1,172</td>
<td>911 ± 1,145</td>
<td>882 ± 1,104</td>
<td>833 ± 1,073</td>
<td>800 ± 1,040</td>
</tr>
<tr>
<td>Dietary cholesterol (g/day)†</td>
<td>0.17 ± 0.06</td>
<td>0.20 ± 0.05</td>
<td>0.22 ± 0.05</td>
<td>0.28 ± 0.05</td>
<td>0.35 ± 0.07</td>
<td>0.44 ± 0.15</td>
</tr>
<tr>
<td>Trans fat (g/day)†</td>
<td>1.95 ± 1.11</td>
<td>2.28 ± 1.08</td>
<td>2.35 ± 1.01</td>
<td>2.40 ± 1.00</td>
<td>2.55 ± 1.11</td>
<td>2.41 ± 0.98</td>
</tr>
<tr>
<td>Polyunsaturated fat (g/day)†</td>
<td>10.6 ± 3.2</td>
<td>11.0 ± 2.9</td>
<td>11.2 ± 2.7</td>
<td>11.4 ± 2.7</td>
<td>11.8 ± 2.8</td>
<td>11.9 ± 3.1</td>
</tr>
<tr>
<td>Saturated fat (g/day)†</td>
<td>17.3 ± 5.2</td>
<td>19.4 ± 4.7</td>
<td>20.0 ± 4.40</td>
<td>20.9 ± 4.4</td>
<td>22.4 ± 4.8</td>
<td>23.1 ± 5.5</td>
</tr>
<tr>
<td>Smoking</td>
<td>10.8</td>
<td>12.1</td>
<td>11.8</td>
<td>15.3</td>
<td>19.8</td>
<td>23.5</td>
</tr>
<tr>
<td>Current drinkers of ≥1 per day</td>
<td>10.2</td>
<td>9.8</td>
<td>10.8</td>
<td>11.5</td>
<td>10.5</td>
<td>10.4</td>
</tr>
<tr>
<td>Hypertension</td>
<td>24.7</td>
<td>23.6</td>
<td>23.4</td>
<td>26.6</td>
<td>29.5</td>
<td>27.1</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>38.0</td>
<td>28.9</td>
<td>26.4</td>
<td>25.3</td>
<td>26.1</td>
<td>19.1</td>
</tr>
<tr>
<td>Family history of diabetes</td>
<td>24.6</td>
<td>24.2</td>
<td>24.1</td>
<td>25.9</td>
<td>27.5</td>
<td>23.5</td>
</tr>
</tbody>
</table>

Data are mean ± SD or %. *Nut consumption assessed 1 year after randomization. †Energy adjusted.

WHS. Among egg consumers, the median egg consumption was approximately one egg per week in men and women. Table 1 presents baseline characteristics of the study participants. Frequent consumption of eggs was associated with higher BMI, higher proportion of current smoking, higher prevalence of hypertension, and lower prevalence of hypercholesterolemia. In addition, frequent consumption of eggs was associated with older age and more alcohol consumption in men and higher energy intake, as well as intakes of saturated and trans fatty acids, and dietary cholesterol in women.

Djoussé and Associates
Egg intake and type 2 diabetes

Table 2—HR (95% CI) of type 2 diabetes according to egg consumption in men and women

<table>
<thead>
<tr>
<th>Egg intake per week</th>
<th>n</th>
<th>Age adjusted</th>
<th>Model 1*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>0</td>
<td>104</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>&lt;1</td>
<td>254</td>
<td>1.16 (0.92–1.45)</td>
<td>1.09 (0.87–1.37)</td>
</tr>
<tr>
<td>1</td>
<td>560</td>
<td>1.19 (0.96–1.46)</td>
<td>1.09 (0.88–1.34)</td>
</tr>
<tr>
<td>2–4</td>
<td>637</td>
<td>1.30 (1.06–1.61)</td>
<td>1.18 (0.95–1.45)</td>
</tr>
<tr>
<td>5–6</td>
<td>169</td>
<td>1.73 (1.36–2.21)</td>
<td>1.46 (1.14–1.86)</td>
</tr>
<tr>
<td>≥7</td>
<td>197</td>
<td>1.82 (1.44–2.31)</td>
<td>1.58 (1.25–2.01)</td>
</tr>
</tbody>
</table>

P for trend <0.0001

Men Women

<table>
<thead>
<tr>
<th>Egg intake per week</th>
<th>n</th>
<th>Age adjusted</th>
<th>Model 1†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>0</td>
<td>104</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>&lt;1</td>
<td>254</td>
<td>1.16 (1.01–1.34)</td>
<td>1.06 (0.92–1.22)</td>
</tr>
<tr>
<td>1</td>
<td>576</td>
<td>1.10 (0.95–1.27)</td>
<td>0.97 (0.83–1.12)</td>
</tr>
<tr>
<td>2–4</td>
<td>470</td>
<td>1.65 (1.44–1.89)</td>
<td>1.19 (1.03–1.38)</td>
</tr>
<tr>
<td>5–6</td>
<td>669</td>
<td>1.97 (1.48–2.63)</td>
<td>1.18 (0.88–1.58)</td>
</tr>
<tr>
<td>≥7</td>
<td>46</td>
<td>2.88 (2.11–3.94)</td>
<td>1.77 (1.28–2.43)</td>
</tr>
</tbody>
</table>

P for trend <0.0001

n = cases of type 2 diabetes. *Adjusted for age (continuous), BMI (<25, 25–29.9, and ≥30 kg/m²), smoking (never, former, and current smokers), alcohol consumption (0, 1–3 drinks/month, 1–6 drinks/week, and ≥1 drink/day), vigorous exercise (0, <1, 1–3, and ≥4 times per week), and history of hypercholesterolemia and hypertension. †Adjusted for age (continuous), BMI (<25, 25–29.9, and ≥30 kg/m²), smoking (never, former, and current smokers), alcohol consumption (0, 1–3 drinks/month, 1–6 drinks/week, and ≥1 drink/day), exercise (quintiles of kilocalories per week), red meat intake (<0.5, 0.5–0.9, and ≥1 servings/day), quintiles of energy intake, fruits and vegetables, saturated fatty acids, trans fatty acids, polyunsaturated fatty acids, family history of diabetes, and history of hypercholesterolemia and hypertension.

above (this was not done for women due to lack of updated information on egg consumption). Lastly, exclusion of subjects with follow-up time <2 years in either cohort did not alter the results (P for trend <0.0001 in men and 0.0001 in women).

Dietary cholesterol was positively associated with the risk of diabetes (multivariable adjusted HR 1.00 [reference], 0.94 [95% CI 0.80–1.11], 1.03 [0.88–1.21], 1.07 [0.91–1.25], and 1.28 [1.10–1.50], from the lowest to the highest quintile of dietary cholesterol, respectively (P for trend <0.0001). Additional adjustment for dietary cholesterol in women attenuated the point estimates in the multivariable model with corresponding HRs of 1.00 (reference), 0.91 [0.80–1.01], 0.94 [0.80–1.10], 0.97 [0.90–1.27], 0.99 [0.73–1.37], and 1.09 [1.06–1.09], respectively (P for trend = 0.10). However, saturated fat was not associated with type 2 diabetes (multivariable adjusted HR 1.0, 1.03 [0.87–1.21], 1.00 [0.84–1.19], 1.00 [0.84–1.20], and 1.10 [0.92–1.33], from the lowest to the highest quintile of energy-adjusted saturated fat, respectively). Additional control for saturated fat did not alter the results (e.g., HR of 1.78 [1.30–2.45] without and 1.77 [1.28–2.43] with additional control for saturated fat, comparing the highest with the lowest egg consumption categories). Imputing missing data did not change the findings (online appendix Table A1, available at http://dx.doi.org/10.2337/dc08-1277).

In a secondary analysis stratified by prevalent hypercholesterolemia at baseline (Table 3), similar patterns were observed in subjects of either sex with and without hypercholesterolemia (P for interaction 0.37 for men and 0.13 for women). Similar relations were observed between egg consumption and type 2 diabetes when data were stratified by low energy from carbohydrate (P for linear trend = 0.0004 for low energy from carbohydrate and 0.12 for high energy from carbohydrate) in women only (data were not available to estimate carbohydrate intake in men), and these findings were not altered when restricted to overweight or obese subjects (online appendix Table A2).

CONCLUSIONS — In this large prospective study, we have demonstrated that daily consumption of at least one egg is associated with an increased risk of type 2 diabetes in both men and women, independently of traditional risk factors for type 2 diabetes. Furthermore, the observed association between egg consumption and incident type 2 diabetes was not modified by prevalent hypercholesterolemia in either sex.

To the best of our knowledge, this is the first study to examine prospectively

Table 3—Hazard ratios of diabetes according to prevalent hypercholesterolemia and egg consumption

<table>
<thead>
<tr>
<th>Egg consumption per week</th>
<th>Normal cholesterol</th>
<th>High or treated cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>1</td>
<td>1.03 (0.80–1.31)</td>
<td>1.28 (0.84–1.94)</td>
</tr>
<tr>
<td>2–4</td>
<td>1.16 (0.92–1.48)</td>
<td>1.19 (0.79–1.81)</td>
</tr>
<tr>
<td>5–6</td>
<td>1.34 (1.01–1.79)</td>
<td>1.78 (1.11–2.87)</td>
</tr>
<tr>
<td>≥7</td>
<td>1.47 (1.11–1.94)</td>
<td>1.96 (1.23–3.12)</td>
</tr>
</tbody>
</table>

P for trend <0.0001

Women

<table>
<thead>
<tr>
<th>Normal cholesterol</th>
<th>High or treated cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.11 (0.91–1.37)</td>
<td>1.02 (0.83–1.25)</td>
</tr>
<tr>
<td>1.00 (0.80–1.24)</td>
<td>0.98 (0.79–1.22)</td>
</tr>
<tr>
<td>1.26 (1.02–1.55)</td>
<td>1.14 (0.92–1.42)</td>
</tr>
<tr>
<td>0.88 (0.57–1.36)</td>
<td>1.68 (1.13–2.51)</td>
</tr>
<tr>
<td>1.84 (1.24–2.75)</td>
<td>1.72 (0.98–3.02)</td>
</tr>
</tbody>
</table>

P for trend 0.0045 0.0028

*Adjusted for age (continuous), BMI (<25, 25–29.9, and ≥30 kg/m²), smoking (never, former, and current smokers), alcohol consumption (none, 1–3 drinks/month, 1–6 drinks/week, and ≥1 drink/day), vigorous exercise (0, <1, 1–3, and ≥4 times per week), and history of hypertension. †Adjusted for age (continuous), BMI (<25, 25–29.9, and ≥30 kg/m²), smoking (never, former, and current smokers), alcohol consumption (none, 1–3 drinks/month, 1–6 drinks/week, and ≥1 drink/day), exercise (quintiles of kilocalories per week), red meat intake (<0.5, 0.5–0.9, and ≥1 servings/day), quintiles of energy intake, fruits and vegetables, saturated fatty acids, trans fatty acids, polyunsaturated fatty acids, family history of diabetes, and history of hypertension.
the association between egg consumption and incident type 2 diabetes in a large population of men and women. Before the current study, limited and inconsistent data (mainly from animal models) have been reported in the literature on the effects of eggs or dietary cholesterol on glucose metabolism. In an animal experiment, a diet rich in fat was shown to induce hyperglycemia and hyperinsulinemia (8). Furthermore, Adamopoulos et al. (9) demonstrated that a diet enriched with egg yolk resulted in elevated plasma glucose compared with a control diet in male Wistar albino rats.

Data from the Zutphen Study (10) showed a positive association between egg consumption or dietary cholesterol and fasting glucose. These animal studies and data from the Zutphen Study are consistent with our findings. In contrast, in a randomized trial of 28 overweight or obese subjects on a carbohydrate-restricted diet, consumption of three eggs per day had no effects on fasting glucose compared with no egg consumption (11). Because the positive associations described above were observed in studies without restricted consumption of carbohydrates, it is possible that the hyperglycemic effect of frequent egg consumption might only occur with a diet rich in carbohydrates. However, our secondary data analysis provided no evidence for such a hypothesis in that we observed similar increased risk of type 2 diabetes with consumption of one or more eggs per day in women with low or high energy intake from carbohydrate. Further restriction to women with BMI ≥25 kg/m², to mimic the above trial of 28 overweight or obese subjects on restricted carbohydrate diet (11), did not alter these findings. Under the premise that our observed findings were driven by dietary cholesterol contained in eggs, one possible explanation for the inconsistency in reported data on the association between egg consumption and glucose metabolism could be the large variability of individual response to dietary cholesterol (14,15,23). Whereas dietary cholesterol has been shown to increase plasma cholesterol in hyperresponders (2,12,24), no effect was documented among hyper responders (12–14). Second, the lack of an effect of egg consumption on fasting glucose among obese or overweight subjects in the only human randomized trial (11) may imply differential physiological effects of eggs in lean versus overweight or obese subjects. However, the lack of repeated data on fasting glucose in men and women in the present study prevented us from further exploring the relation between adiposity, egg consumption, and fasting glucose.

Overall, the observed increased risk of type 2 diabetes with daily consumption of eggs in the current study raises the possibility of undesirable health effects with high rates of egg consumption and may help explain previously reported increased risk of CHD that was restricted to individuals with type 2 diabetes in the Health Professional Follow-up Study (6), the Nurses’ Health Study (6), and in our earlier publication from the PHS I showing an increased risk of mortality (and suggesting increased risk of CHD and stroke) with frequent egg consumption by subjects with prevalent type 2 diabetes (7). It is possible that frequent egg consumption may potentiate the risk of cardiovascular disease by inducing impaired glucose metabolism and insulin resistance. Future investigations into underlying physiological mechanisms are warranted.

Besides dietary cholesterol, eggs contain other important nutrients that have been shown to increase (i.e., saturated fat and cholesterol [4,5,25]) or decrease (i.e., polyunsaturated fat [4]) the risk of type 2 diabetes. It is possible that the individual contribution from each of these components as derived not just from eggs but also from other foods may play a role in determining the net effect of egg consumption. Unfortunately, as noted above, we did not have repeated data on fasting glucose, fasting insulin, and other biomarkers of glucose metabolism in either cohort to comprehensively examine possible physiological mechanisms by which egg consumption might influence the risk of type 2 diabetes in our cohort. However, in women, where we had data on dietary cholesterol, there was attenuation of the association after additional adjustment for dietary cholesterol. This suggests that the observed relation between egg intake and diabetes may be partially explained by the cholesterol content of eggs. In contrast, saturated fat was not associated with type 2 diabetes, and adjustment for this did not attenuate the results.

Additional limitations of the present study include the observational nature of the study design in which residual confounding or unmeasured confounding could partly or completely explain our results. In addition, because egg consumption was self-reported, we cannot exclude reporting bias in the present study. However, because information on egg consumption was collected before the occurrence of type 2 diabetes, such reporting bias is more likely to be nondifferential and thus bias the results toward the null. We did not collect information on whether participants consumed egg yolk (rich in cholesterol) to further examine the contribution of dietary cholesterol from eggs on type 2 diabetes risk in this study. In addition, we had limited dietary data for men to further assess the interplay of eggs and other foods, energy, and nutrients with the risk of type 2 diabetes. The generalizability of our finding is limited as both PHS I and WHS consist of homogeneous groups (male physicians and female health professionals, respectively) with the possibility that their behaviors may differ from those of the general population. Furthermore, over 90% of the study participants were Caucasian. Given the self-report nature of type 2 diabetes, we cannot exclude misclassification of the outcome in these data, especially in the WHS where not all participants were physicians, as was the case in the PHS. However, in the WHS, we had a 91% positive predictive value in a validation study of self-reported type 2 diabetes using American Diabetes Association criteria, for which data were attained by telephone interview, supplemental questionnaire, or review of medical records from treating physicians (21).

Moreover, egg consumption was collected before the diagnosis of diabetes; thus, it is likely that any misclassification of diabetes would be nondifferential and bias the results toward the null. Nevertheless, the large sample size, the long duration of follow-up, the repeated and standardized methods for data collection in both cohorts, and the robustness of the findings in sensitivity analyses are major strengths of this study.

In conclusion, our data are consistent with possible detrimental effects of daily consumption of eggs on the risk of type 2 diabetes in both men and women. Because the median egg consumption in this population (one egg per week for men and women) fell within a range not associated with an increased risk of type 2 diabetes, dietary advice to reduce egg consumption may target individuals who consume one or more eggs per day if these findings are confirmed in other studies. Given the societal burden of type 2 diabetes, confirmation of these findings in other populations and exploration of pos-
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sible underlying biological mechanisms are warranted.

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No potential conflicts of interest relevant to this article were reported.

References