Published in final edited form as:
Diabetes Res Clin Pract. 2010 December ; 90(3): 365–371. doi:10.1016/j.diabres.2010.09.010.

Asthma, Chronic Obstructive Pulmonary Disease, and Type 2 Diabetes in the Women's Health Study

Yiqing Song, MD, ScD[a,*], **Anna Klevak, PhD**[a], **JoAnn E. Manson, MD, DrPH**[a,b], **Julie E. Buring, ScD**[a,b,c], and **Simin Liu, MD, ScD**[a,d,e]

[a] Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States

[b] Department of Epidemiology, Harvard School of Public Health, Boston, MA, United States

[c] Department of Ambulatory Care and Prevention, Harvard Medical School, Boston, MA, United States

[d] Program on Genomics and Nutrition, Department of Epidemiology, UCLA School of Public Health, Los Angeles, CA, United States

[e] Center for Metabolic Disease Prevention, Department of Medicine, David Geffen School of Medicine, UCLA, Los Angeles, CA, United States

Abstract

Background—Chronic airway inflammation in asthma or chronic obstructive pulmonary disease (COPD) may be involved in the pathogenesis of type 2 diabetes; however, prospective data have been limited.

Methods—A prospective cohort of 38,570 women who were aged ≥ 45 years, free of cardiovascular disease and cancer at baseline, and free of diabetes at baseline and in the first 12 month were analyzed. We classified all women into three groups according to the presence and absence of self-reported asthma or COPD (including emphysema, chronic bronchitis, and bronchiectasis).

Results—During a median follow-up of 12.2 years, 2,472 incident type 2 diabetes events were documented. Women who had ever reported asthma or COPD were associated with an increased diabetes risk; the multivariate RRs were 1.37 (95% CI, 1.20–1.57) for women who had asthma alone and 1.38 (95% CI, 1.14–1.67) for COPD without asthmatic symptoms. Furthermore, these associations were not significantly modified by age, smoking status, physical activity, BMI, alcohol intake, hormone replacement therapy, menopausal status or randomized treatment.

Conclusions—Asthma and COPD were individually and independently associated with an increased risk of type 2 diabetes in women, indicating that chronic airway inflammation may contribute to diabetes pathogenesis.

[*]Corresponding author at: Division of Preventive Medicine, Brigham and Women's Hospital, 900 Commonwealth Avenue East, Boston, MA 02215. Tel: 617-278-0913; fax: 617-731-3843; ysong3@rics.bwh.harvard.edu (Y. Song).

Conflict of Interest

The authors declare that they have no conflict of interest.

Keywords

Asthma; COPD; type 2 diabetes; and women

1. Introduction

Asthma and COPD are inflammatory lung disorders associated with significant morbidity and mortality worldwide [1]. Their commonly reported comorbidities include cardiovascular disease, diabetes mellitus, hypertension, osteoporosis, and other chronic medical conditions [2]. Respiratory viral and bacterial infections, tobacco smoking, and pollutants are important factors in triggering a plethora of inflammatory pathways that may mediate the relation of chronic lung diseases and their comorbid diseases [1,2]. Although the inflammatory process in COPD is different from that in asthma in terms of inflammatory cells, mediators, and inflammatory response to therapy [3], there is growing evidence to show a role of several common inflammatory signaling pathways in the pathogenesis of both asthma [4] and COPD [5]. Low-grade inflammation as reflected by elevated levels of many proinflammatory biomarkers such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), C-reactive protein (CRP), and adhesion molecules has been recognized as a major contributor to the development of type 2 diabetes [6,7]. It thus seems reasonable to speculate that elevated circulating levels of certain inflammatory cytokines caused by chronic airway inflammation may also contribute to the development of insulin resistance in the liver, skeletal muscle, and vascular endothelium, ultimately leading to the clinical expression of type 2 diabetes.

In epidemiologic studies, several cross-sectional studies have suggested that lung function impairment was associated with high prevalence of the metabolic syndrome [8] and type 2 diabetes, even after adjusting for adiposity [2]. Several prospective studies have shown inverse associations between lung functions and risk for developing insulin resistance or type 2 diabetes in nondiabetic individuals from diverse populations [9–11]. One recent prospective cohort study from the Nurses' Health Study reported increased risk of type 2 diabetes associated with patients with COPD but not among asthma patients [12]. Although the differences in the diabetes risk between patients with COPD and those with asthma may reflect the different underlying inflammatory processes in asthma and COPD, no other independent studies have confirmed this relationship.

We therefore prospectively examined the association of asthma and COPD with risk of type 2 diabetes in a large cohort of women with over 12 years of follow-up. In addition, we investigated whether the associations would vary for the presence of asthma and/or COPD when examined separately and whether they would differ according to levels of potential factors, including age, BMI, smoking status, physical activity, alcohol intake, postmenopausal hormone use, and menopausal status.

2. Subjects and Methods

2.1. Study Population

The Women's Health Study (WHS) was a randomized, double-blind, placebo-controlled trial designed to evaluate the balance of benefits and risks of low-dose aspirin and vitamin E in the primary prevention of cardiovascular disease (CVD) and cancer [13]. As described previously, participants provided detailed information on behavioral, lifestyle, and demographic risk factors at baseline [14]. In total, 39,876 female health professionals aged ≥ 45 years who were free of coronary heart disease (CHD), stroke, and cancer (except for non-melanoma skin cancer) have been followed up. We excluded individuals with self-reported

diabetes at baseline and the first 12 months, which left 38,570 women for the analysis. All participants in the WHS provided written informed consent and the study protocol was approved by the institutional review board of the Brigham and Women's Hospital (Boston, Mass).

2.2. Data collection

On the baseline questionnaire, we collected detailed information on demographics, medical history, and lifestyle factors [14]. In the enrollment questionnaire and annually thereafter, participants provided information on lifestyle exposures including cigarette smoking status, physical activity, total intakes of beer, wine, and liquor, use of multivitamin, use of postmenopausal hormone therapy, and menopausal status. Moreover, participants reported their medical history characteristics such as age, height, weight, history of type 2 diabetes, and family history of diabetes in first-degree relatives. Total calorie intake and dietary intakes were assessed using a 131-item semiquantitative food frequency questionnaire at baseline [14].

2.3. Ascertainment of asthma and COPD

During the follow-up, all participants were specifically asked about a physician diagnosis of asthma and other chronic obstructive lung disease (i.e. COPD, including emphysema, chronic bronchitis, and bronchiectasis) and the date of diagnosis of these diseases. Although we lacked detailed information on lung function to confirm all self-reported COPD cases, our study population is a cohort of U.S. female health professionals, who are likely to report more accurate diagnostic information of clinical diseases than a general population. Among 38,570 women participants free of prior CVD, cancer, or diabetes, we identified 6,322 women (16.4% of the total participants), who had developed asthma, COPD or both. Of them, there were 1,808 women (4.7% of the total participants) with COPD, 1,733 (4.5 %) of the participants with COPD without any asthma, and 3,368 (8.7 %) women, who had reported asthma or asthmatic symptoms only.

2.4. Ascertainment of incident type 2 diabetes

Details regarding ascertainment of incident type 2 diabetes in our cohorts have been reported previously [6,15]. After excluding those with diabetes at baseline, all participants were asked annually whether and when they had been diagnosed with diabetes since baseline. Using the diagnostic criteria by the American Diabetes Association [16], all self-reported cases of type 2 diabetes were confirmed by a supplemental questionnaire. In populations of health professionals such as WHS, self-reported diabetes diagnosis yields high validity in identifying true cases. As confirmation, a small validation study (n=473) was conducted, where self-reported diabetes in WHS was validated via physician-led telephone interviews, supplementary questionnaires, and medical record reviews, all yielding positive predictive values >91% [6,15].

2.5. Statistical Analysis

Participants with a prior history of CHD, stroke, cancer, or diabetes in the first 12 months were excluded from analysis. To minimize potential time-varying confounding effect, we took into account the information from all follow-up questionnaires on covariates and pre-existing chronic lung disease status and incident diabetes. For each women, we calculated person-years of follow-up from the date of return of the earliest questionnaire to date of first diabetes diagnosis, death, or to the last questionnaire received, whichever came first. Participants were divided into three groups according to the presence of asthma and/or COPD, asthma alone, or COPD alone without asthmatic symptoms, respectively, and were compared to women without asthma and/or COPD. We used time-varying Cox proportional

hazards models to estimate the rate ratios (described as relative risks, RRs) and 95% confidence interval (CI) of incident type 2 diabetes for women with chronic lung diseases versus those without. Using information from all follow-up questionnaire, our Cox proportional hazard models with time-varying covariates accounted for time-varying changes in covariates and the presence of chronic lung diseases over the follow-up period.

The first model was adjusted for age and randomized treatment assignment (vitamin E and aspirin). The second model additionally controlled for BMI The first multivariable model (multivariable model 1) further adjusted for smoking (never, past, and current smokers [<25 cigarettes/day and ≥25 cigarettes/day]), physical activity (METs, quintiles), alcohol intake (rarely/never, 1–3 drinks/month, 1–6 drinks/week, and ≥1 drink/day), postmenopausal hormone use (never, past, and current), family history of diabetes (yes/no), history of hypertension (yes/no), and high cholesterol (yes/no); The second multivariate-adjusted model (multivariable model 2) included the variables in model 1, with the addition of dietary factors including total calorie intake (continuous), intakes of trans fatty acids, polyunsaturated fat, glycemic load, and caffeine intake (all categorized as quintiles). The same analytic approach as above was used for women with asthma alone, or women with COPD alone without asthmatic symptoms.

Furthermore, we used prespecified stratified analysis to assess the potential effect modifications by age (39–50, 51–56, >56 years), BMI (<25, 25–29.9, and ≥30), current smoking status (yes or no), alcohol intake (rarely/never, 1–3 drinks/month, 1–6 drinks/week, and ≥1 drink/day), physical activity (< 600 Kcal and ≥600 Kcal), postmenopausal hormone use (never and current users), menopausal status (premenopausal or postmenopausal status), and randomized treatment of aspirin and vitamin E (yes or no). The log likelihood ratio test was used to test the significance of the interactions by comparing models with and without the interaction terms.

All statistical analyses were conducted using SAS (version 9.1; SAS Institute Inc., Cary, NC). All reported *P* values were two-tailed.

3. Results

3.1. Characteristics of women with and without chronic lung diseases

The prevalence of patients with COPD or asthma was 16.4% (n=6,322) among all participants. There were 1,808 women with COPD without asthmatic component, among whom, 32.7 % were never smokers, 32.6% were past smokers, and 35.7% were current smokers. The prevalence of patients with asthma alone (n=3,368) was 8.73%, among whom, 52.6 % were never smokers, 38.9% were past smokers, and 8.5% were current smokers.

Overall, women with self-reported asthma or COPD were older and heavier, were less likely to drink alcohol and exercise, and were more likely to smoke cigarettes and take postmenopausal hormones than those without (Table 1). Women with these chronic lung diseases also had a higher likelihood of having a family history of diabetes, history of hypertension, or history of hyperlipidemia than those without.

3.2. Associations between asthma, COPD, and risk of type 2 diabetes

During a median of 12.2 years of follow-up (441,496 person-years), we identified 2,472 incident cases of type 2 diabetes. Table 2 displays the association between COPD with and without asthma and risk of type 2 diabetes. In the age and randomized treatment-adjusted model, the presence of asthma and/or COPD was associated with a 1.75-fold increased risk of type 2 diabetes as compared with those without (Table 2). After additional adjustment for BMI, the positive association was attenuated but persisted; the multivariate-adjusted RR was

1.49 (95% CI, 1.34–1.64) for women with these chronic lung diseases compared with those without. The excess risk of type 2 diabetes remained significant even after further controlling for other traditional diabetes risk factors including physical activity, cigarette smoking, alcohol intake, postmenopausal hormone use, family history of diabetes, history of hypertension, and history of hypercholesterolemia (Multivariate-adjusted Model 1) or dietary factors (Model 2). After excluding those with asthmatic symptoms, women with COPD alone also had a higher risk of type 2 diabetes than those with neither COPD nor asthma (multivariate-adjusted RR, 1.38; 95% CI, 1.14–1.67). Similarly, patients with preexisting asthma alone were at substantially higher risk of type 2 diabetes than those in the same control group (the multivariate-adjusted RR, 1.37; 95% CI, 1.20–1.57).

When further stratified by potential effect modifiers such as age, cigarette smoking, BMI, alcohol intake, physical activity, hormone replacement therapy, menopausal status, randomized treatment assignment of aspirin and vitamin E (Table 3), the positive associations of asthma and/or COPD with type 2 diabetes were not substantially altered. Although the magnitude of the RRs and their 95% CIs varied in different subgroups, we found no evidence for any significant interactions (all P values for interactions >0.05).

4. Discussion

In this large prospective study of middle-aged and older US women followed over 12 years, we found that patients with pre-existing asthma and/or COPD had a higher risk of developing subsequent type 2 diabetes than those without. The positive associations between these chronic lung diseases and type 2 diabetes were independent of cigarette smoking and other diabetes risk factors and also persisted after excluding all COPD cases with asthmatic symptoms. We further investigated any potential modifiers and found no evidence that the association differed by smoking status and other risk factors.

Previous prospective studies have consistently shown the inverse associations between lung functions and risk for developing insulin resistance or type 2 diabetes in nondiabetic individuals [9–11], indicating that nonspecific chronic inflammation associated with pulmonary disorders may play a role in the development of type 2 diabetes. However, prospective data on the link of chronic lung disease to type 2 diabetes are relatively limited. In our study, we focused on COPD, including emphysema, chronic bronchitis, and bronchiectasis, which may reflect a chronic inflammatory state. Our study estimated that the presence of COPD was associated with an approximately 1.50-fold increased risk of type 2 diabetes. The association was unchanged when we excluded all cases with asthmatic symptoms. This finding is supported by a previous prospective study in the Nurses' Health Study (NHS) with 8 years of follow-up, which found a similar association [12]. In the NHS, Rana et al. reported that patients with COPD were at an approximately 1.8-fold increased risk of type 2 diabetes relative to those without COPD [12]. Our similar findings strongly support the hypothesis linking chronic airway inflammation to type 2 diabetes.

We found that the presence of asthma alone was independently associated with a 1.50-fold increased risk of type 2 diabetes whereas the NHS found no such a significant association between asthma and type 2 diabetes [12]. It has been speculated that differences in the inflammatory cells and cytokine profile between COPD and asthma might explain why COPD, but not asthma, is associated with increased risk of type 2 diabetes. However, there is a lack of experimental or observational evidence to support the notion. Existing differences in our follow-up duration, demographic characteristics and lifestyle variables could explain the different results for asthma.

We investigated several other population subgroups of women with asthma and/or COPD in order to determine if the association was modified by those prespecified factors including cigarette smoking, BMI, age, physical activity, alcohol intake, postmenopausal hormone use, and menopausal status. Overall, there were similar trends for positive associations between these chronic lung diseases and type 2 diabetes in all subgroups. Although the associations tended to be weaker among women with lower BMI (<25 kg/m^2), higher alcohol intake (≥1 drink/day), high levels of physical activity (≥600 Kcal), or cigarette smoking, the interactions were not significant and the numbers of diabetes cases were small. Thus, different RRs with varying CIs in subgroups could be caused due to small sample sizes. Of note, cigarette smoking is a strong factor for COPD but a moderate risk factor for type 2 diabetes. Smoking status could be both a confounder and effect modifier for the observed association. Our study did not find significant effect modification by cigarette smoking status. Systemic inflammation and oxidative stress has been implicated to be involved in the adverse consequences of cigarette smoking, but it seems plausible that chronic inflammation elicited by smoking could attenuate the observed association between chronic airway inflammation and type 2 diabetes.

The mechanisms by which asthma and COPD may increase a woman's risk of type 2 diabetes are not fully understood. The most plausible explanation is that these diseases may share a common inflammatory basis with type 2 diabetes. Asthma and COPD are inflammatory lung disorders involving multiple inflammatory pathways [1,2]. For example, the nuclear factor-κB (NF-κB) signaling pathway may play a central role in the pathogenesis of both asthma and chronic obstructive pulmonary disease (COPD) [1]. NF-κB is transcription factor that induces the expression of a variety of pro-inflammatory genes, including IL-6, TNF-α, and adhesion molecules. Elevated circulating levels of these inflammatory cytokines have been associated with the development of prediabetic insulin resistance and the progression into overt type 2 diabetes [6,17,18]. The etiology of type 2 diabetes is complex and multifactorial involving multiple genetic and environmental factors. The associations of asthma and COPD with type 2 diabetes appeared to be robust, indicating that a common inflammation pathway might exist and largely reflect the underlying proinflammatory mechanisms for both diseases.

The strengths of our study include the prospective study design, large sample size, high follow-up rate, long follow-up duration, and the updated assessment of lifestyle variables and chronic disease status at baseline and during the follow-up. Several limitations, however, warrant consideration. First, our study did not collect detailed data on physician diagnosis of chronic lung diseases and clinical lung function testing, which cannot allow us to confirm all self-reported diagnosis of asthma and COPD. We acknowledge that our cases of asthma and COPD might have been misclassified using questionnaires. However, such misclassification should lead to an underestimate of the true association between chronic lung disease and diabetes, rather than to produce spurious associations. It is noteworthy that our study population is a cohort of U.S. female health professionals, who are likely to report more accurate diagnostic information than a general population. Second, medication use, especially corticosteroid use, could have, at least partially, accounted for our results, and we lacked detailed information on dose and duration. Third, our observed associations might be explained by residual confounding due to uncontrolled factors. Our findings, however, seemed robust after adjustment for traditional diabetes risk factors including those that may potentially influence inflammatory status. Fourth, the lack of information on lung function or specific inflammatory biomarkers at baseline did not allow for quantifying the relation between impaired lung function or inflammatory states and risk of type 2 diabetes. Finally, because our study population included solely female health professionals who were mostly white, results from the present study may not be generalizable to men or to other ethnic groups.

In conclusion, in a large prospective study of middle-aged and older US women followed over 12 years, we found that women with pre-existing asthma or COPD had a higher risk of developing type 2 diabetes, independently of traditional diabetes risk factors including cigarette smoking. Our findings support the hypothesis that chronic airway inflammation may increase the risk of type 2 diabetes through underlying proinflammatory mechanisms. Our study provides clear information on the relation of asthma and COPD with their comorbid diabetes mellitus, indicating the importance of increasing awareness and promotion of diabetes risk reduction for patients with these chronic lung diseases. Future evidence-based preventive strategies should be developed and implemented to improve the overall health burden in adults with asthma and/or COPD who are also at high risk for other chronic comorbidities.

Acknowledgments

We are indebted to the 39,876 dedicated and committed participants of the Women's Health Study. We also acknowledge the contributions of the entire staff of the Women's Health Study. The Women's Health Study was supported by research grants DK066401, HL 043851, HL 080467, and CA 047988 from the National Institutes of Health, Bethesda, MD. Dr. Song is supported by a grant (K01-DK078846) from the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institutes of Health, Bethesda, MD.

Grant Support: the Women's Health Study was supported by research grants DK066401, HL 043851, HL 080467, and CA 047988 from the National Institutes of Health, Bethesda, MD. Dr. Song is supported by a grant (K01-DK078846) from the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institutes of Health, Bethesda, MD.

References

1. Edwards MR, Bartlett NW, Clarke D, Birrell M, Belvisi M, Johnston SL. Targeting the NF-kappaB pathway in asthma and chronic obstructive pulmonary disease. Pharmacol Ther 2009;121:1–13. [PubMed: 18950657]
2. Chatila WM, Thomashow BM, Minai OA, Criner GJ, Make BJ. Comorbidities in chronic obstructive pulmonary disease. Proc Am Thorac Soc 2008;5:549–555. [PubMed: 18453370]
3. Barnes PJ. Mechanisms in COPD: differences from asthma. Chest 2000;117:10S–14S. [PubMed: 10673467]
4. Hart LA, Krishnan VL, Adcock IM, Barnes PJ, Chung KF. Activation and localization of transcription factor, nuclear factor-kappaB, in asthma. Am J Respir Crit Care Med 1998;158:1585–1592. [PubMed: 9817712]
5. Di Stefano A, Caramori G, Oates T, Capelli A, Lusuardi M, Gnemmi I, Ioli F, Chung KF, Donner CF, Barnes PJ, Adcock IM. Increased expression of nuclear factor-kappaB in bronchial biopsies from smokers and patients with COPD. Eur Respir J 2002;20:556–563. [PubMed: 12358328]
6. Liu S, Tinker L, Song Y, Rifai N, Bonds DE, Cook NR, Heiss G, Howard BV, Hotamisligil GS, Hu FB, Kuller LH, Manson JE. A prospective study of inflammatory cytokines and diabetes mellitus in a multiethnic cohort of postmenopausal women. Arch Intern Med 2007;167:1676–1685. [PubMed: 17698692]
7. Song Y, Manson JE, Tinker L, Rifai N, Cook NR, Hu FB, Hotamisligil GS, Ridker PM, Rodriguez BL, Margolis KL, Oberman A, Liu S. Circulating levels of endothelial adhesion molecules and risk of diabetes in an ethnically diverse cohort of women. Diabetes 2007;56:1898–1904. [PubMed: 17389327]
8. Leone N, Courbon D, Thomas F, Bean K, Jego B, Leynaert B, Guize L, Zureik M. Lung function impairment and metabolic syndrome: the critical role of abdominal obesity. Am J Respir Crit Care Med 2009;179:509–516. [PubMed: 19136371]
9. Ford ES, Mannino DM. Prospective association between lung function and the incidence of diabetes: findings from the National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. Diabetes Care 2004;27:2966–2970. [PubMed: 15562215]

10. Lazarus R, Sparrow D, Weiss ST. Baseline ventilatory function predicts the development of higher levels of fasting insulin and fasting insulin resistance index: the Normative Aging Study. Eur Respir J 1998;12:641–645. [PubMed: 9762793]
11. Yeh HC, Punjabi NM, Wang NY, Pankow JS, Duncan BB, Brancati FL. Vital capacity as a predictor of incident type 2 diabetes: the Atherosclerosis Risk in Communities study. Diabetes Care 2005;28:1472–1479. [PubMed: 15920070]
12. Rana JS, Mittleman MA, Sheikh J, Hu FB, Manson JE, Colditz GA, Speizer FE, Barr RG, Camargo CA Jr. Chronic obstructive pulmonary disease, asthma, and risk of type 2 diabetes in women. Diabetes Care 2004;27:2478–2484. [PubMed: 15451919]
13. Buring JE, Hennekens CH. The Women's Health Study: summary of the study design. J Myocard Ischemia 1992;4:27–29.
14. Rexrode KM, Lee IM, Cook NR, Hennekens CH, Buring JE. Baseline characteristics of participants in the Women's Health Study. J Womens Health Gend Based Med 2000;9:19–27. [PubMed: 10718501]
15. Song Y, Manson JE, Buring JE, Liu S. A prospective study of red meat consumption and type 2 diabetes in middle-aged and elderly women: the women's health study. Diabetes Care 2004;27:2108–2115. [PubMed: 15333470]
16. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 1997;20:1183–1197. [PubMed: 9203460]
17. Pradhan AD, Cook NR, Buring JE, Manson JE, Ridker PM. C-reactive protein is independently associated with fasting insulin in nondiabetic women. Arterioscler Thromb Vasc Biol 2003;23:650–655. [PubMed: 12692007]
18. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA 2001;286:327–334. [PubMed: 11466099]

Diabetes Res Clin Pract. Author manuscript; available in PMC 2011 December 1.

Table 1

Baseline characteristics of 38,570 participants in the Women's Health Study

Characteristic	Group 1	Group 2	Group 3	*P* value [a]	
	COPD alone (excluding asthma)	Asthma alone (without COPD)	Neither COPD nor Asthma	Group 1 vs. Group 3	Group 2 vs. Group 3
N (numbers of participants)	1,808	3,368	32,248		
Age (years)	57.8	53.8	55.0	<0.0001	<0.0001
BMI (kg/m^2)	26.1	27.0	25.7	0.008	<0.0001
Physical Activity (METs, kcal/week)	825.2	998.4	986.4	<0.0001	<0.0001
Alcohol Intake					
Never/rarely	48.9	45.5	43.7	<0.0001	0.05
1 to 3 drinks/month	12.8	13.8	13.2	0.65	0.28
1 to 6 drinks/week	26.8	31.4	32.7	<0.0001	0.12
≥1 drinks/day	11.6	9.3	10.4	0.13	0.04
Cigarette Smoking, %					
Never smoker	31.9	52.6	52.6	<0.0001	0.99
Past smoker	32.7	38.9	35.6	0.01	0.0002
Current smoker (<15 cigarettes/day)	8.2	3.8	4.7	<0.0001	0.02
Current smoker (≥15 cigarettes/day)	27.2	4.7	7.0	<0.0001	<0.0001
Postmenopausal Hormone Use (%)					
Never users	39.5	37.4	42.8	0.006	<0.0001
Past users	15.0	9.6	10.4	<0.0001	0.18
Current users	45.5	53.0	46.8	0.27	<0.0001
Menopausal Status					
Premenopausal	12.0	24.2	23.1	<0.0001	0.14
Menopausal	74.3	59.4	64.1	<0.0001	<0.0001
Family history of diabetes (%)	27.8	26.4	24.4	0.0013	0.01
History of hypertension (%)	37.7	35.1	30.8	<0.0001	<0.0001
History of hyperlipidemia (%)	38.8	34.5	33.7	<0.0001	0.38
Total calorie (kcal/day)	1708.5	1744.6	1723.5	0.26	0.03

[a] Crude comparisons using t-test for continuous variables and chi-square test for categorical variables.

Diabetes Res Clin Pract. Author manuscript; available in PMC 2011 December 1.

Table 2

Relative risks (95% CI) of type 2 diabetes according to asthma and/or COPD in the Women's Health Study

	Neither asthma nor COPD	Asthma alone (without COPD)	COPD alone (without asthma)	Asthma and/or COPD
Person-years (cases sum)	12,535	2,237	1,088	4,158
Incident diabetes (n)	1,850	332	166	622
Age-adjusted [a]	1.00	1.70 (1.50 – 1.93)	1.74 (1.45 – 2.08)	1.75 (1.59 – 1.93)
Age- and BMI- adjusted [b]	1.00	1.43 (1.25 – 1.63)	1.61 (1.34 – 1.93)	1.49 (1.34 – 1.64)
Multivariate model 1 [c]	1.00	1.37 (1.20 – 1.57)	1.38 (1.14 – 1.67)	1.38 (1.24 – 1.53)
Multivariate model 2 [d]	1.00	1.36 (1.19 – 1.57)	1.33 (1.09 – 1.63)	1.36 (1.22 – 1.51)

[a] Adjusted for age (continuous), and randomized treatment assignment (vitamin E and aspirin) in the Women's Health Study;

[b] Adjusted for age, randomized treatment assignment, and body mass index (< 25, 25 – 30, >= 30);

[c] Multivariate model 1: additionally adjusted for physical activity (METs, quartiles), smoking (never, past, current smoker [<15 cigarettes/day], and current smoker [>=15 cigarettes/day]), alcohol intake (never/rarely, 1 to 3 drinks/mon, 1to 6 drinks/wk, and >=1 drink/day), Postmenopausal hormone use (never, past, and current), family history of diabetes (yes/no), history of hypertension (yes/no), and history of hypercholesterolemia (yes/no).

[d] Multivariate model 2: model 1 with additional adjustment for total calorie intake (continuous) and dietary factors (including trans fatty acid intake, polyunsaturated fat intake, glycemic load, and caffeine intake in quintiles).

Table 3

Relative risks (95% CI) of type 2 diabetes with asthma and/or COPD in subgroups stratified by age, BMI, smoking, alcohol intake, physical activity, use of hormones, menopausal status, and randomized treatment groups in the Women's Health \study

	Asthma alone (without COPD)		COPD alone (without asthma)		Asthma and/or COPD	
	RR (95% CI)	P value	RR (95% CI)	P value	RR (95% CI)	P value
Age, years						
< 50	1.22 (0.96–1.54)	0.098	2.20 (1.59–3.06)	<0.0001	1.42 (1.18–1.71)	0.0002
51 to 56	1.35 (1.05–1.74)	0.019	1.42 (0.96–2.09)	0.077	1.37 (1.12–1.67)	0.002
≥ 57	1.56 (1.25–1.95)	0.0001	1.10 (0.82–1.48)	0.52	1.39 (1.18–1.64)	<0.0001
BMI, kg/m^2						
< 25	1.45 (0.89–2.35)	0.14	1.49 (0.84–2.64)	0.18	1.38 (0.97–1.96)	0.08
25 to 30	1.58 (1.20–2.07)	0.001	1.60 (1.13–2.26)	0.008	1.60 (1.31–1.95)	<0.0001
≥ 30	1.29 (1.09–1.52)	0.003	1.35 (1.05–1.73)	0.02	1.32 (1.16–1.50)	<0.0001
Current Smoker						
No	1.38 (1.20–1.58)	<0.0001	1.43 (1.15–1.76)	0.001	1.40 (1.25–1.56)	<0.0001
Yes	1.26 (0.70–2.26)	0.44	1.47 (0.93–2.31)	0.097	1.37 (0.99–1.91)	0.06
Alcohol Intake						
Never/rarely	1.35 (1.13–1.60)	0.0008	1.41 (1.11–1.80)	0.006	1.37 (1.20–1.56)	<0.0001
1 to 3 drinks/month	1.21 (0.83–1.77)	0.32	1.02 (0.57–1.84)	0.94	1.09 (0.80–1.48)	0.58
1 to 6 drinks/week	1.64 (1.24–2.17)	0.0005	1.66 (1.11–2.49)	0.01	1.74 (1.41–2.16)	<0.0001
≥ 1 drink/day	1.04 (0.47–2.27)	0.93	2.05 (0.87—4.83)	0.10	1.35 (0.79–2.29)	0.27
Physical Activity						
< 600 Kcal	1.39 (1.17–1.67)	0.0002	1.49 (1.17–1.89)	0.0006	1.40 (1.22–1.60)	<0.0001
≥ 600 Kcal	1.31 (1.06–1.62)	0.011	1.30 (0.95–1.79)	0.10	1.37 (1.16–1.61)	0.0002
Hormone replacement therapy						
Never	1.31 (1.00–1.71)	0.052	1.41 (0.99–2.00)	0.05	1.35 (1.11–1.65)	0.003
Current	1.36 (1.11–1.67)	0.003	1.66 (1.23–2.24)	0.0009	1.48 (1.27–1.74)	<0.0001
Menopausal status						
Premenopausal	1.21 (0.66–2.24)	0.54	1.19 (0.29–4.90)	0.81	1.44 (0.89–2.35)	0.14
Postmenopausal	1.38 (1.19–1.61)	<0.0001	1.42 (1.15–1.74)	0.001	1.41 (1.25–1.58)	<0.0001
Aspirin randomized treatment						

	Asthma alone (without COPD)		COPD alone (without asthma)		Asthma and/or COPD	
	RR (95% CI)	**P value**	**RR (95% CI)**	**P value**	**RR (95% CI)**	**P value**
Yes	1.26 (1.03–1.54)	0.023	1.54 (1.19–1.99)	0.001	1.33 (1.14–1.54)	0.0002
No	1.47 (1.22–1.77)	<0.0001	1.30 (0.97–1.73)	0.075	1.45 (1.26–1.68)	<0.0001
Vitamin E randomized treatment						
Yes	1.37 (1.13–1.67)	0.0013	1.21 (0.90–1.63)	0.20	1.37 (1.18–1.59)	<0.0001
No	1.36 (1.13–1.65)	0.0015	1.63 (1.26–2.09)	0.0002	1.42 (1.23–1.64)	<0.0001

[a]Multivariate model adjusted for age, randomized treatment assignment (vitamin E and aspirin), BMI, physical activity(METs, quartiles), smoking (current smoker or non-current smoker), alcohol intake (never/rarely, 1 to 3 drinks/mon, 1to 6 drinks/wk, and >=1 drink/day), postmenopausal hormone use (never, past, and current), family history of diabetes (yes/no), history of hypertension (yes/no), and history of hypercholesterolemia (yes/no).