U.S. Department of Veterans Affairs
Public Access Author manuscript
Clin Nutr. Author manuscript; available in PMC 2021 April 01.

Published in final edited form as:
Clin Nutr. 2020 April ; 39(4): 1203–1208. doi:10.1016/j.clnu.2019.05.008.

Fried Food Consumption and Risk of Coronary Artery Disease: The Million Veteran Program

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Abstract

Introduction—Previous studies of the relationship between fried food consumption and coronary artery disease (CAD) have yielded conflicting results. We tested the hypothesis that frequent fried food consumption is associated with a higher risk of incident CAD events in Million Veteran Program (MVP) participants.

Methods—Veterans Health Administration electronic health record data were linked to questionnaires completed at MVP enrollment. Self-reported fried food consumption at baseline was categorized: (<1, 1–3, 4–6 times per week or daily). The outcome of interest was non-fatal myocardial infarction or CAD events. We fitted a Cox regression model adjusting for age, sex, race, education, exercise, smoking and alcohol consumption.

Results—Of 154,663 MVP enrollees with survey data, mean age was 64 years and 90% were men. During a mean follow-up of approximately 3 years, there were 6,725 CAD events. There was a positive linear relationship between frequency of fried food consumption and risk of CAD (p for trend 0.0015). Multivariable adjusted hazard ratios (95% CI) were 1.0 (ref), 1.07 (1.01–1.13), 1.08 (1.01–1.16), and 1.14 (1.03–1.27) across consecutive increasing categories of fried food intake.

Conclusions—In a large national cohort of U.S. Veterans, fried food consumption has a positive, dose-dependent association with CAD.

Frying is a common method of food preparation in the United States both at home and in restaurants and fast food establishments. In addition to altering the taste of foods, the frying

Conflict of interest
None.

process modifies them through polymerization, oxidation, and hydrogenation [1, 2]. The nutritional impact of frying depends on the type of fat or oil used as the frying medium, the food being fried and the duration of frying time, but ultimately results in increased caloric density of the food consumed [3]. Evaluating the potential health impact of this cooking method is critical for public health, given that over a quarter of American adults patronize fast food chains where calorie-dense fried food is regularly available [4, 5]. A growing body of evidence has shown that fried food consumption is associated with chronic health conditions such as type 2 diabetes, heart failure, obesity, and hypertension [6]. Yet, the literature has been mixed regarding the association between fried food intake and coronary artery disease (CAD) [7–12]. Given the immense burden of CAD in the Veteran population, the Million Veteran Program (MVP) is uniquely positioned to address this relationship. Dietary data has been collected via surveys for approximately 300,000 Veterans enrolled in MVP and linkage with electronic heath records (EHR) enables adequate collection of CAD events. The goal of this analysis was to test the hypothesis that frequent fried food consumption is associated with a higher rate of CAD events in Veterans.

Methods

MVP is an observational cohort study and biobank which enrolls patients from the Veterans Health Administration (VHA) healthcare system. Enrollment of Veterans nationwide started in 2011, and participants supplied a blood sample and completed health questionnaires. As of March 2018, approximately 650,000 Veterans have enrolled in MVP. A detailed description of MVP design and methods has been published [13]. Of 291,519 patients who completed the MVP Lifestyle Survey containing nutrition data, 73,547 with prevalent CAD were excluded. After exclusion of patients with incomplete data on demographics, lifestyle factor, and nutrition data, the final sample was comprised of 154,663 Veterans. This study was approved by the Veterans Affairs Central Institutional Review Board, which granted a waiver of informed consent.

Fried food consumption was obtained from the MVP Lifestyle Survey. The two questions used to define fried food intake were: “How often do you eat food that is fried at home (exclude “Pam”-type spray)?” and “How often do you eat fried food away from home (e.g., French fries, fried chicken, fried fish)?” The pre-specified response options for both questions were “Less than once a week”, “1–3 times per week”, “4–6 times per week”, and “Daily”. The responses to these two questions were first transformed into intake per day, then summed and categorized into intake per week to define total weekly fried food intake. The primary outcome of interest was non-fatal myocardial infarction (MI) or CAD events, defined as presence of International Classification of Diseases (ICD) −9 codes 410–414 and ICD-10 codes I20–I25 except I25.2 in the EHR. A secondary, composite CAD outcome included fatal and non-fatal coronary events, coronary angioplasty and coronary revascularization defined by CPT and ICD-9 procedure codes. Date and cause of death was obtained from the National Death Index [14]. Information on age, sex, education, race, weight and height was obtained from the MVP Baseline Survey. The MVP Lifestyle survey collected information on alcohol consumption, dietary habits, smoking, comorbidity, and exercise.

Baseline characteristics were described using frequencies, means, and standard deviations according to frequency of total fried food consumption. Person-time of follow up was computed as time from MVP Lifestyle Survey completion to the first occurrence of CAD or censoring date, defined as the last patient visit date at a VHA clinic or hospital, through March 2018. We used a Cox-proportional hazard model to estimate the hazard ratios (95% CI) of CAD across categories of fried food intake, using infrequent consumption as the reference group. We built sequential models based on a priori knowledge of major confounders. In addition to the crude model (Model 1), we adjusted for age in Model 2 and age, sex, race, and education in Model 3. The final model (Model 4) adjusted for variables in Model 3 as well as exercise, smoking, and alcohol consumption.

In secondary analyses, we fitted Cox regression models stratified by body mass index (BMI), diabetes status at baseline, and sex. We also performed sub-analyses adjusting for family history of CAD (maternal or paternal history of disease), type of fat used in frying and dietary pattern. Comparison of fried food consumption at home versus away from home was also performed. Categories of each confounder can be found in Table 1.

Assumptions for proportional hazard model were tested using product term of fried food and log-transformed person-time and met ($p < 0.05$). All analyses were performed using SAS version 9.2 (Cary, NC).

Results

Of 154,663 MVP participants, 90% were men and the mean age was 64 years (standard deviation 11.8 years). The majority of the participants consumed fried food less than once per week (45%) and a small proportion consumed fried food daily (5%). Frequent consumers of fried food were mostly non-white, male, and had lower educational attainment and higher proportion of current smokers (Table 1). During a mean follow-up of approximately 3 years, there were 6,725 CAD events (crude incidence rate 15.82 cases per 1,000 person-years) and 6,953 CAD events including deaths (crude incidence rate 16.35 cases per 1,000 person-years). The crude incidence rate of CAD was 14.61, 16.57, 16.82, and 18.28 cases per 1,000 person-years for fried food intake of less than once a week, 1–3 times per week, 4–6 times per week, and daily intake, respectively.

Fried food consumption was associated with a higher risk of CAD. Multivariable adjusted hazard ratios (HRs) (95% confidence interval, CI) were 1.0 (ref), 1.07 (1.01–1.13), 1.08 (1.01–1.16), and 1.14 (1.03–1.27) across consecutive categories of fried food intake controlling for age, sex, race, education, exercise, smoking, and alcohol consumption ($p = 0.0015$, Table 2). There was also evidence of a dose–response relationship between fried food intake and the secondary CAD outcome including fatal events. Multivariable adjusted HRs (95% CI) were 1.0 (ref), 1.07 (1.02, 1.13), 1.09 (1.02, 1.16), and 1.14 (1.03, 1.27) across increasing categories of fried food consumption ($p = 0.0008$, Table 2).

In a secondary analysis, we observed a stronger association between fried food and primary CAD outcome among overweight and obese subjects compared to Veterans with normal BMI (p interaction BMI-by-fried food intake 0.019, Table 3), however the magnitude of effect was similar. We observed an association between fried food consumption and CAD risk among Veterans with type 2 diabetes (p for trend 0.0014), but did not observe a significant association in those without diabetes (Table 4).

The stratified analysis by sex showed a similar dose–response trend which was stronger in females (p interaction sex-by-fried food intake 0.0338). For the highest category of fried foods, HRs (95% CI) were 1.12 (1.01, 1.25) for males and 2.17 (1.20, 3.94) for females. The sub-analysis adjusting for family history of CAD showed slightly attenuated risk in a multivariable adjusted model [HR (95% CI): 1.0 (ref), 1.07 (1.01–1.13), 1.08 (1.01–1.15), and 1.14 (1.03–1.27) (p for trend 0.0020)].

The most common cooking oil used for frying at home was vegetable oil (72%) followed by butter (28%) and margarine (17%). Very few used vegetable shortening (4.6%) or lard (1%) to fry foods. When we restricted fried food intake to those that used vegetable oil as means for frying foods multivariable HR (95% CI) were 1.0 (ref), 1.08 (1.01–1.15), 1.08 (0.99–1.16), 1.18 (1.05–1.33) for the primary CAD outcome. Corresponding values for butter were 1.0 (ref), 1.21 (1.09–1.35), 1.03 (0.90–1.18) and 0.99 (0.80–1.24). We performed adjustment for servings per day of fish, fruits and vegetables which did not impact the magnitude of our findings: multivariable adjusted hazard ratios (95% confidence interval, CI) were 1.0 (ref), 1.07 (1.01–1.13), 1.08 (1.01–1.15), and 1.14 (1.03–1.27) for increasing levels of fried food consumption (p for trend 0.0026).

Almost 20% of Veterans consumed fried food only at home, 17% only away from home and 18% consumed fried food both at home and away from home. The remaining Veterans consumed fried food infrequently, less than once per week. The magnitude of CAD risk for the primary outcome was similar across settings with multivariable HRs (95% CI) 1.0 (ref) for infrequent consumers, 1.09 (1.02–1.16) at home only, 1.06 (0.99–1.14) away from home only and 1.10 (1.03–1.17) at home and away from home (Table 5).

Discussion

In this prospective cohort, we found that baseline fried food consumption is associated with higher CAD risk among Veterans in a dose dependent manner. The risk of CAD was present after adjustment for demographic characteristics and lifestyle factors and we observed effect modification of the fried food-CAD relation by BMI.

Our results are comparable to a prospective study performed by Cahill and colleagues in the Nurses' Health Study (NHS) and the Health Professionals Follow-Up Study (HPFS) [7]. The pooled results combining data from both cohorts showed a positive association between fried food consumption and CAD (p for trend 0.04) using fried food intake of <1/week, the fully adjusted model yielded HRs of 1.03 (95% CI: 0.97, 1.09) for consumption 1–3 times per week, 1.13 (95% CI: 1.04, 1.22) for consumption 4–6 times per week, and 1.08 (95% CI: 0.95, 1.24) for daily fried food consumption. While Cahill and colleagues did not observe a dose–response relationship, the hazard ratios observed were similar to our findings. The same survey questions ascertaining fried food intake were used in NHS, HPFS and MVP, with nearly identical patterns of daily total fried food consumption across the three cohorts.

The cohort size and number of CAD events in Cahill's analysis were comparable to our Veteran population (5778 events in a pooled cohort of 111,631 compared to 6725 events observed in 154,663 MVP participants). Our studies differed greatly by percentage of women included in analysis (37% compared to 10% in MVP) and average follow-up time (23 years compared to 3 years in MVP). However, our stratified analysis comparing the association of fried food consumption with CAD by sex showed a similar trend that was slightly stronger in females. The MVP cohort is more diverse than the NHS and HPFS cohorts, which are 95% white, compared to 72% in MVP.

Several case–control studies also found a positive association between fried food consumption and CAD. The INTERHEART study of 5761 cases and 10,646 controls from 52 countries found a 13% higher risk of CAD [odds ratio = 1.13 (95% CI: 1.02–1.25)] comparing the highest to the lowest tertile of fried foods (p for trend <0.0001) [8]. Mean fried food intake per day across all nations in the INTERHEART study was 0.16 (standard deviation 0.31), about once per week, which was comparable to the MVP cohort. A study in India of 165 cases and 199 controls showed increased risk of CAD with deep fried food consumption in cases (average intake 15.2 g/day compared to 1.0 g/day for controls, p for trend <0.01) [9].

In contrast, other studies did not find a clear association between fried food consumption and CAD. A prospective study in Spain of 40,757 individuals followed for 11 years on average did not find an association between fried food and coronary heart disease [HR: 1.08 (95% CI: 0.82, 1.43) comparing the highest quartile of fried food consumption to the lowest (p for trend 0.74) [10]]. This study had a low rate of events (606 CAD cases) compared to the NHS, HPFS, and MVP cohorts. The authors suggest that their results could be impacted by the type of frying oil used in Spain (primarily olive oil) and this may have contributed to the null result. Kabagambe and colleagues performed a case–control study in Costa Rica of 485 MI cases and 508 controls [11] and looked at the risk of MI across quintiles for energy from various saturated fats. They reported an odds ratio for a 1% increase in energy intake from total saturated fat of 1.12 (95% CI: 1.03–1.21) and an odds ratio of 1.03 (95% CI: 0.99–1.06) for total fat. The authors noted that fried food consumption was common in the population under study in Costa Rica and the reference group consumed 4.57 servings per day while the remaining quintiles of intake were 6.00, 6.62, 7.78 and 9.75 servings per day, respectively.

Recently, a follow-up study by Hu and colleagues was performed in the Costa Rican population, drawing from the cohort used by Kabagambe [12]. The follow-up study assessed fried food intake both at home and away from home, whereas the initial study looked at only fried food consumption in the home. The results of the Hu study found a positive association between fried food consumption outside of the home and CAD, with odds ratios of 1.02 (95% CI: 0.86–1.21) for fried food intake of 1–3 times per week, 1.26 (95% CI: 0.81–1.95) for 4–6 times per week, and 1.58 (95% CI: 1.08–2.30) for daily fried food intake, using <1 time per week as the reference. This study used a larger sample size than the previous analysis and matched controls (2,154 cases and 2,154 controls). Similar to Kabagambe's analysis, they did not find an association between fried food intake at home and CAD. The authors suggest that cooking practices at home may explain this difference. Our results showed an increased risk of CAD across all settings of fried food consumption.

Few studies have assessed effect measure modification of fried food-CAD relation by adiposity. Studies by Cahill and Hu [7, 12] did not find a significant interaction between BMI and fried food intake, while other studies adjusted for BMI in their analyses [8, 10]. There have been several studies showing an association between fried food consumption and being overweight [6]. Increased BMI itself is a risk factor for CAD and thus likely in the causal pathway of the fried food and CAD association.

There is evidence for a positive relationship between fried food consumption and diabetes [6, 7]. Diabetes is likely on the causal pathway between fried food consumption and CAD, given that diabetics are at higher risk for cardiovascular disease. Several studies adjusted for diabetes in their analysis of the fried food-CAD relationship 9 10 11 12 and one study excluded diabetics given concern of differential intake reporting [8]. Our results suggest that limiting fried food intake could lower the risk of CAD in diabetics.

In addition to diabetes and obesity, there is also evidence in the literature showing a positive association between other known CAD risk factors including decreased HDL cholesterol and hypertension [6, 15, 16]. Given the evidence that risk factors on the causal pathway for CAD are associated with increased fried food intake, this supports the fried food-CAD association found in our analysis.

There are several limitations to our analysis. First, we relied on respondents to provide an unbiased recollection of their dietary habits to define their intake of fried foods. Their recollection may have varied based on the amount of fried food consumed, which could lead to a differential misclassification of exposure. Second, the type of fat, method used for frying, and the type of food fried were not available. The impact of the frying process on the nutritional quality of food depends on the methods and oils used. For example, lipid oxidation has been shown to be decreased when frying in olive oil [17], but we were unable to determine the impact of olive oil use on CAD in our cohort. Third, we were not able to adjust for nutrients as they are not yet available in MVP. Fourth, outcome ascertainment was based on billing codes and mean follow-up was 3 years, which leaves little time between exposure and development of CAD. On the other hand, this could be perceived as a strength in that results are less susceptible to change in fried food consumption habits over longer period. Because ICD codes from the VA EHR were used for outcome ascertainment, non-VA CAD events may not be captured if the Veteran did not return to the VA for care after the event. We would expect this to bias our results toward the null and that the true association between fried food and CAD may be greater than our observed results. Fifth, this was a predominantly male cohort which limits generalizability to women. Finally, this is an observational study and subject to residual and unmeasured confounding.

Our findings provide evidence for a dose-dependent association between fried food consumption and CAD incidence. The MVP cohort provides an ethnically diverse sample of Veterans from across the nation with sufficient events for analysis. The prospective collection of CAD events and ascertainment of exposure data before CAD minimizes bias that could be present in case–control studies. Use of MVP survey questions enables adjustment for lifestyle factors such as education, smoking and alcohol intake that are difficult to ascertain from the EHR alone. It is also the largest prospective study of the relationship between fried food and CAD to date and the results are consistent with the second largest prospective cohort study [7]. While a randomized controlled trial is needed to confirm these results, this may not be feasible given the evidence of cardiovascular disease risk related to fried food consumption.

Consumption of fried foods is associated with a higher risk of CAD and our evidence suggests that the relationship is dose-dependent.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We are grateful to the MVP participants and staff. This publication does not represent the views of the Department of Veterans Affairs or the United States Government.

Sources of funding

This research is based on data from the Million Veteran Program, Veterans Health Administration Office of Research and Development, and was supported by award MVP#000. This research was also supported by the VA Merit Award I01 BX003340-01. This publication does not represent the views of the Department of Veterans Affairs or the U.S. government.

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Table 1:

Baseline Characteristics by Frequency of Fried Food Consumption

		Frequency of Total Fried Food Consumption			
		<1 time per week	**1–3 times per week**	**4–6 times per week**	**Daily**
		n = 69,617	**n = 50,314**	**n = 26,623**	**n = 8,109**
Age, years		64.1 ± 12.0	64.5 ± 12.0	64.1 ± 11.5	63.9 ± 11.3
Male (%)		86.9	91.9	94.0	95.1
Race (%)	Black	10.6	11.6	14.0	15.9
	White	85.2	84.6	81.8	78.7
	Other	4.2	3.8	4.2	5.4
BMI, kg/m^2		28.6 ± 5.3	29.3 ± 5.5	29.7 ± 5.6	29.9 ± 6.1
Alcohol Use (%)	Never	7.9	7.3	7.7	8.4
	Former	37.6	39.4	40.3	45.0
	Current	54.6	53.4	52.0	46.6
Education Status (%)	Less than high school	2.2	2.6	3.0	4.5
	High school diploma/ GED	17.1	20.8	22.7	26.4
	> High school	80.7	76.6	74.3	69.1
Exercise (%)	<1 time/week	37.8	42.5	44.8	48.7
	1 time/week	12.9	14.3	14.6	13.2
	2–4 times/week	32.3	29.7	28.3	24.0
	5+ times/week	17.0	13.4	12.3	14.0
Smoking Status (%)	Never	31.4	28.6	28.1	27.4
	Former	52.4	52.5	52.1	50.4
	Current	16.2	18.9	19.8	22.2
Diabetes at baseline		23.6	27.1	28.8	30.6
Fish, servings/day		0.2 ± 0.3	0.2 ± 0.2	0.2 ± 0.3	0.2 ± 0.4
Vegetables, servings/day		1.4 ± 1.7	1.2 ± 1.5	1.2 ± 1.6	1.4 ± 2.4
Fruit, servings/day		1.7 ± 1.8	1.5 ± 1.6	1.4 ± 1.6	1.5 ± 2.1
Type of Fried Food Consumption	Infrequent (less than once per week)	100	0	0	0
	At Home Only	0	51.2	12.6	15.6
	Away from Home Only	0	48.8	6.1	3.5
	At Home and Away from Home	0	0	81.3	80.8

Values are mean ± standard deviation or %. **BMI**: Body mass index.

Table 2:

Hazard Ratios (95% CI) for CAD According to Frequency of Fried Food Intake among Veterans

	Total Fried Food Consumption				
	<1 time per week	**1–3 times per week**	**4–6 times per week**	**Daily**	**p - trend**
Primary CAD Outcome					
Cases/PY	2,812/192,405	2,277/137,456	1,229/73,075	407/22,259	-
IR	14.61	16.57	16.82	18.28	-
Model 1	ref	1.13 (1.07, 1.20)	1.15 (1.08, 1.23)	1.25 (1.13, 1.39)	<0.0001
Model 2	ref	1.13 (1.06, 1.19)	1.16 (1.09, 1.24)	1.28 (1.15, 1.41)	<0.0001
Model 3	ref	1.10 (1.04, 1.16)	1.12 (1.04, 1.19)	1.21 (1.09, 1.34)	<0.0001
Model 4	ref	1.07 (1.01, 1.13)	1.08 (1.01, 1.16)	1.14 (1.03, 1.27)	0.0015
Secondary CAD Outcome					
Cases/PY	2,902/192,394	2,354/137,447	1,275/73,069	422/22,253	-
IR	15.08	17.13	17.45	18.96	-
Model 1	ref	1.13 (1.07, 1.20)	1.16 (1.08, 1.24)	1.26 (1.13, 1.39)	<0.0001
Model 2	ref	1.13 (1.07, 1.19)	1.17 (1.09, 1.25)	1.28 (1.16, 1.42)	<0.0001
Model 3	ref	1.10 (1.04, 1.16)	1.12 (1.05, 1.20)	1.21 (1.09, 1.34)	<0.0001
Model 4	ref	1.07 (1.02, 1.13)	1.09 (1.02, 1.16)	1.14 (1.03, 1.27)	0.0008

Model 1: Crude; **Model 2**: Age-adjusted; **Model 3**: Adjusted for age, sex, race, and education; **Model 4**: Adjustments for Model 3 and exercise, smoking and alcohol consumption. **CAD**: Coronary artery disease. **CI**: Confidence interval. **IR**: Crude incidence rate per 1,000 person-years. **PY**: Person-years.

Table 3:

Hazard Ratios (95% CI) for Primary CAD Outcome Stratified by Baseline BMI

	Total Fried Food Consumption				
	<1 time per week	**1–3 times per week**	**4–6 times per week**	**Daily**	**p - trend**
BMI < 25 (n=32,184)					
Cases/PY	559/44,426	391/26,390	212/12,740	72/4,164	-
IR	12.58	14.82	16.64	17.29	-
Model 4	ref	1.05 (0.92, 1.19)	1.15 (0.98, 1.35)	1.14 (0.89, 1.47)	0.073
BMI ≥ 25 (n=122,479)					
Cases/PY	2,253/147,979	1,886/111,066	1,017/60,334	335/18,094	-
IR	15.23	16.98	16.86	18.51	-
Model 4	ref	1.07 (1.00, 1.13)	1.05 (0.98, 1.13)	1.12 (1.00, 1.26)	0.025

Model 4 adjusted for age, sex, race, education, exercise, smoking and alcohol consumption. p for interaction BMI*fried food = 0.019. **BMI**: Body mass index. **CAD**: Coronary artery disease. **CI**: Confidence interval. **IR**: Crude incidence rate per 1,000 person-years. **PY**: Person-years.

Table 4:

Hazard Ratios (95% CI) for Primary CAD Outcome Stratified by Diabetes Status

	Total Fried Food Consumption				
	<1 time per week	**1–3 times per week**	**4–6 times per week**	**Daily**	**p - trend**
No Diabetes (n=114,456)					
Cases/PY	1,856/146,584	1,359/99,768	713/51,889	226/15,415	-
IR	12.66	13.62	13.74	14.66	-
Model 4	ref	1.01 (0.94, 1.08)	1.02 (0.93, 1.11)	1.06 (0.92, 1.22)	0.47
Diabetes (n=40,207)					
Cases/PY	956/45,821	918/37,688	516/21,185	181/6,843	-
IR	20.86	24.36	24.36	26.45	-
Model 4	ref	1.15 (1.05, 1.26)	1.15 (1.03, 1.28)	1.21 (1.03, 1.42)	0.0014

Model 4 adjusted for age, sex, race, education, exercise, smoking and alcohol consumption. p for interaction diabetes*fried food=0.0559. **CAD**: Coronary artery disease. **CI**: Confidence interval. **IR**: Crude incidence rate per 1,000 person-years. **PY**: Person-years.

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Table 5:

Hazard Ratios (95% CI) for Primary CAD Outcome Comparing Fried Food Consumption at Home and Away from Home

	Fried Food Consumption			
	<1 time per week	**At Home Only**	**Away from Home Only**	**At Home and Away from Home**
Cases/PY	2,812/192,405	1,527/83,772	1,077/71,607	1,309/77,410
IR	14.61	18.23	15.04	16.91
Model 4	ref	1.09 (1.02, 1.16)	1.06 (0.99, 1.14)	1.10 (1.03, 1.17)

Model 4 adjusted for age, sex, race, education, exercise, smoking and alcohol consumption. **CAD**: Coronary artery disease. **CI**: Confidence interval. **IR**: Crude incidence rate per 1,000 person-years. **PY**: Person-years.