American Journal of Preventive Cardiology 9 (2022) 100316

Contents lists available at ScienceDirect

American Journal of Preventive Cardiology

journal homepage: www.journals.elsevier.com/the-american-journal-of-preventive-cardiology

Inflammatory bowel disease and atherosclerotic cardiovascular disease in U.S. adults—A population-level analysis in the national health interview survey

Khurram Nasir[a,b,*,**], Isaac Acquah[a,b,*], Amit K. Dey[c], Tanushree Agrawal[a], Syed Zawahir Hassan[a], Kerri Glassner[d], Bincy Abraham[d], Eamonn M.M. Quigley[d], Ron Blankstein[e], Salim S. Virani[f], Michael J. Blaha[g], Javier Valero-Elizondo[a,b], Miguel Cainzos-Achirica[a,b], Nehal N. Mehta[h]

[a] Division of Cardiovascular Prevention and Wellness, Department of Cardiology, Houston Methodist DeBakey Heart and Vascular Center, Houston, MD, United States
[b] Center for Outcomes Research, Houston Methodist Research Institute, Houston, MD, United States
[c] Department of Medicine, MedStar Union Memorial Hospital, Baltimore, MD, United States
[d] Division of Gastroenterology, Lynda K and David M Underwood Center for Digestive Disorders, Houston Methodist Hospital, Houston, MD, United States
[e] Cardiovascular Imaging Program, Department of Medicine and Radiology, Brigham and Women's Hospital, Boston, MD, United States
[f] Michael E. DeBakey Veterans Affairs Medical Center and Baylor College of Medicine, Houston, MD, United States
[g] Ciccarone Center for Prevention of Cardiovascular Disease, Johns Hopkins University, Baltimore, MD, United States
[h] Section of Inflammation and Cardiometabolic Diseases National Institutes of Health, Bethesda, MD, United States

ARTICLE INFO

Keywords:
Cardiovascular disease
Inflammation
Prevention
Young adults

ABSTRACT

Objectives: To evaluate the association between inflammatory bowel disease (IBD) and atherosclerotic cardiovascular disease (ASCVD) and whether this association is modified by age or sex.

Methods: We conducted a cross-sectional analysis using data from the 2015–2016 National Health Interview Survey (NHIS). The exposure of interest was self-reported IBD. The outcome of interest was prevalent ASCVD, which included a history of angina, myocardial infarction or stroke. We used survey-specific descriptive statistics to obtain weighted national estimates for IBD and ASCVD prevalence. Logistic regression models were used to assess the association between IBD and ASCVD, progressively adjusting for demographics and traditional risk factors. Effect modification by age and sex was evaluated.

Results: Among participants with IBD, the age-adjusted prevalence of ASCVD was 12.0% compared to 6.9% among those without IBD ($p < 0.001$). In multivariable regression analyses IBD was associated with increased odds of having ASCVD, even after adjustment for demographics and traditional risk factors (odds ratio 1.58, 95% CI 1.17–2.13). We found statistically significant interaction by age ($p < 0.001$) whereby those in the younger age strata had the strongest association (fully adjusted odds ratio among 18- to 44-year-olds 3.35, 95% CI 1.75, 6.40) while the association was null in those ≥65 years. Effect modification by sex was not observed.

Conclusion: Our analysis confirms an independent association between IBD and ASCVD in the U.S., particularly among young adults. Further studies are needed to fully establish a causal relationship between IBD and ASCVD, characterize the mechanisms underlying these associations, and identify tailored opportunities for ASCVD prevention in young and middle-aged adults with IBD.

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; ASCVD, atherosclerotic cardiovascular disease; CI, confidence interval; IBD, Inflammatory bowel disease; NHIS, National Health Interview Survey.

** Corresponding author: Division of Cardiovascular Prevention and Wellness, Department of Cardiology, Houston Methodist DeBakey Heart & Vascular Center, 6550 Fannin St Suite 1801, Houston, TX 77030, United States.
E-mail address: knasir@houstonmethodist.org (K. Nasir).
* Drs. Nasir and Acquah contributed equally to this work

https://doi.org/10.1016/j.ajpc.2022.100316
Received 23 September 2021; Received in revised form 31 December 2021; Accepted 15 January 2022

1. Introduction

Atherosclerotic cardiovascular disease (ASCVD) remains a major killer in the U.S [1]. Chronic inflammatory diseases such as rheumatoid arthritis, psoriasis, and systemic lupus erythematosus have been associated with increased risk of ASCVD events, often presenting at premature ages [2–4]. Inflammatory bowel disease (IBD) is a chronic disorder of the gut comprised of ulcerative colitis, Crohn's disease, and IBD unclassified. IBD involves chronic local and systemic inflammation, and multiple studies have suggested a link between IBD and incident ASCVD events [5–7]. Despite this, current American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the primary prevention of ASCVD do not explicitly mention IBD as a risk enhancing factor, while this is the case for other chronic inflammatory conditions.

The U.S. has the highest age-standardized prevalence of IBD in the world (464.5 per 100,000), and the country faces a significant burden of ASCVD [1,8,9]. Despite this, research on the association between IBD and ASCVD has so far been scarce in the U.S., particularly at the national level. In addition, whether a potential association between IBD and ASCVD is modified by age and sex remains poorly defined. A better understanding of the relationship between IBD and ASCVD can have direct implications for ASCVD prevention strategies, which currently are typically directed towards middle-aged and older adults, while IBD is usually diagnosed between the second and fourth decades of life [9].

The aim of our study was thus to characterize the potential association between IBD and ASCVD using data from a nationally representative U.S. population, and to assess whether there is effect modification by age and sex.

2. Materials and methods

We used data from the 2015–2016 National Health Interview Survey (NHIS). The NHIS is a nationwide annual cross-sectional household survey conducted by the Centers for Disease Control and Prevention, providing information on the health of the civilian noninstitutionalized population of the U.S. The sample design, a multistage area probability sampling, adjusts for nonresponse and further allows for national representativeness [10]. The survey consists of four core questionnaires: the household composition, the family core, the sample adult core and the sample child core. Each household selected by the sampling procedure is mailed a letter prior to a visit by an interviewer. One adult per household is randomly selected to complete the sample adult module and to provide detailed information on health status, healthcare service and health behavior. In this study, we used the sample adult file with supplementation of variables from other cores. The response rates for the adult core for 2015 and 2016 were 55.2% and 54.3% respectively [10]. Due to the de-identified nature of NHIS, this study was considered exempt from institutional review board by Houston Methodist Hospital.

The study population consisted of individuals ≥18 years of age. Presence of IBD was self-reported and defined as an affirmative response to the question: "*Have you ever been told by a doctor or other health professional that you had Crohn's disease or ulcerative colitis*?"[11] ASCVD diagnosis was also self-reported, and was defined by an affirmative response to any of the following questions: "*Have you ever been told by a doctor or other health professional that you had … coronary heart disease?", "… angina, also called angina pectoris?", "… a heart attack (also called myocardial infarction)?"*), and/or stroke ("Yes" to the following question: *"Have you ever been told by a doctor or other health professional that you had a stroke?"*) [12,13]. Other data collected in NHIS and used for this study included age (18–44, 45–64 and ≥65), sex (male and female), race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic Asian and Hispanic) and self-reported cardiovascular risk factors (hypertension, diabetes, high cholesterol, current smoking, obesity and insufficient physical activity). Hypertension, diabetes and high cholesterol were ascertained from the questions: "*Have you ever been told by a doctor or other health professional that you had …hypertension?" "…diabetes or sugar diabetes?" "… high cholesterol?*" respectively. Current smoking was ascertained from the question: *Do you now smoke cigarettes every day, some days or not at all*? Obesity was ascertained from self-reported weight and height and defined as a body mass index of ≥30 kg/m^2. Insufficient physical activity was defined as not participating in >150 min per week of moderate-intensity aerobic physical activity, >75 min per week of vigorous-intensity aerobic physical activity, or a total combi-

Table 1
Characteristics of the study population by IBD and ASCVD status, National Health Interview Survey 2015–16.

	No IBD				IBD			
	Total	ASCVD	No ASCVD	*p*-value	Total	ASCVD	No ASCVD	*p*-value
Sample (N)	65,659	6360	59,299		951	165	786	
Weighted sample	240,345,699	19,217,346 (8.0)	221,128,360 (92.0)		3121,394	500,280 (16.0)	2621,114 (84.0)	
Age Category				<0.001				<0.001
18–44	26,618 (46.6)	408 (8.6)	26,210 (49.9)		254 (30.4)	16 (9.8)	238 (34.4)	
45–64	22,089 (34.1)	1972 (34.1)	20,117 (34.1)		405 (44.7)	73 (49.4)	332 (43.8)	
≥65	16,952 (19.3)	3980 (57.3)	12,972 (16.0)		292 (24.9)	76 (40.7)	216 (21.9)	
Sex				<0.001				0.57
Male	29,696 (48.3)	3322 (55.8)	26,374 (47.7)		330 (39.1)	64 (41.6)	266 (38.6)	
Female	35,963 (51.7)	3038 (44.2)	32,925 (52.3)		621 (60.9)	101 (58.4)	520 (61.4)	
Race/ethnicity				<0.001				0.13
Non-Hispanic White	43,649 (65.8)	4635 (73.9)	39,014 (65.1)		751 (76.9)	133 (82.5)	618 (75.9)	
Non-Hispanic Black	8191 (12.4)	868 (12.4)	7323 (12.3)		66 (5.9)	10 (3.3)	56 (6.4)	
Non-Hispanic Asian	3604 (6.0)	169 (3.0)	3435 (6.2)		25 (3.3)	3 (5.9)	22 (3.8)	
Hispanic	9289 (15.9)	591 (10.7)	8698 (16.3)		96 (13.8)	15 (13.6)	81 (13.9)	
Cardiovascular risk factors								
Hypertension	22,921 (30.9)	4700 (72.5)	18,221 (27.3)	<0.001	450 (45.6)	130 (79.3)	320 (39.1)	<0.001
Diabetes	7012 (9.6)	1935 (31.6)	5077 (7.8)	<0.001	129 (14.9)	39 (28.1)	90 (12.4)	<0.001
High cholesterol	19,388 (27.1)	4176 (66.2)	15,212 (23.7)	<0.001	372 (38.8)	107 (66.6)	265 (33.5)	<0.001
Smoking	10,577 (15.3)	1174 (18.3)	9403 (15.0)	<0.001	182 (17.9)	46 (29.6)	136 (15.7)	0.002
Obesity	21,548 (32.4)	2503 (39.9)	19,045 (31.8)	<0.001	326 (33.6)	69 (38.9)	257 (32.6)	0.24
Insufficient physical activity	32,758 (49.4)	4463 (69.1)	28,295 (47.7)	<0.001	533 (58.3)	117 (71.8)	416 (55.8)	0.003
Cardiovascular risk profile				<0.001				<0.001
Optimal	30,980 (52.7)	803 (14.5)	30,177 (56.0)		337 (38.9)	18 (12.1)	319 (43.7)	
Average	24,458 (36.9)	2978 (49.5)	21,480 (35.9)		414 (44.8)	76 (52.9)	338 (43.3)	
Poor	7457 (10.3)	2172 (36.0)	5245 (8.2)		154 (16.3)	57 (34.9)	97 (12.9)	

Results are presented as number (weighted%).
Abbreviations: ASCVD, atherosclerotic cardiovascular disease; IBD, inflammatory bowel disease.

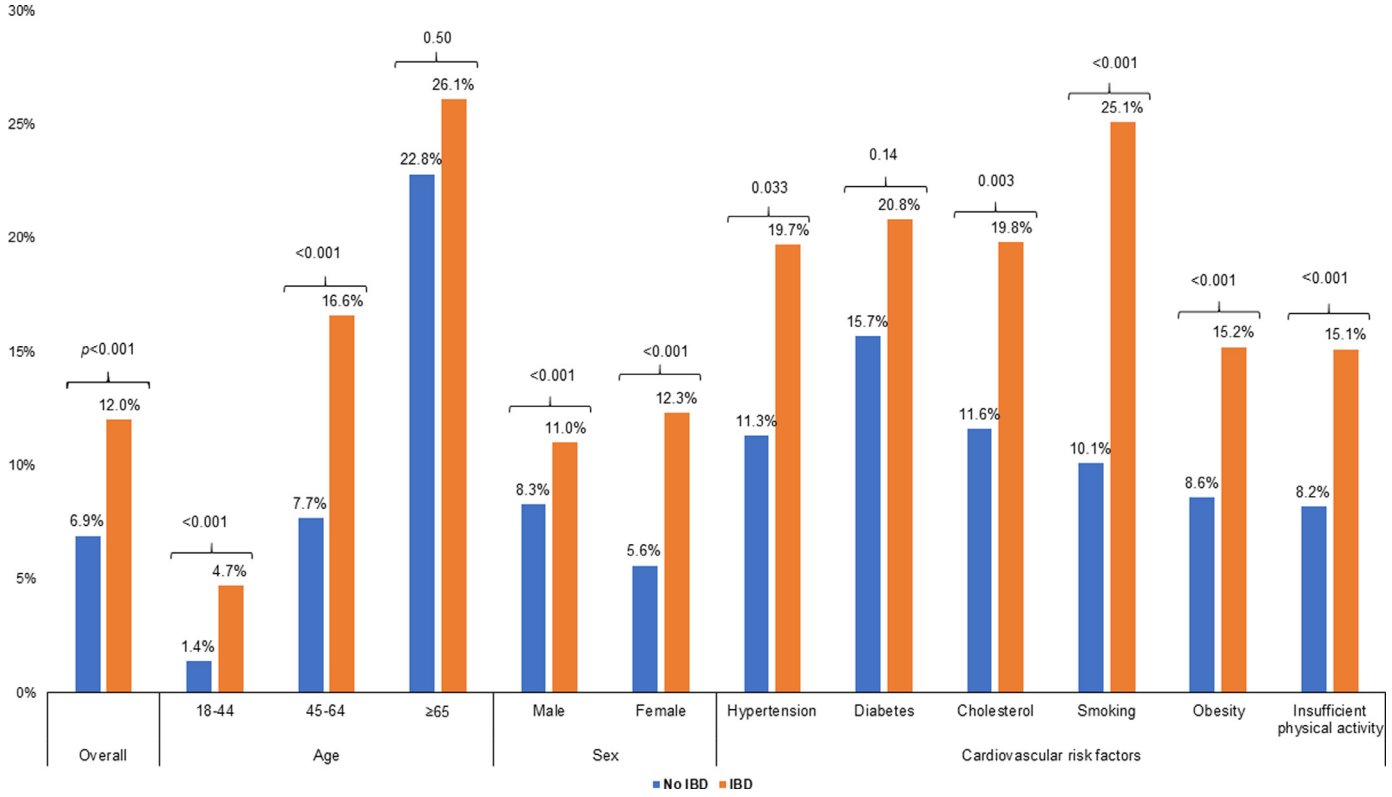

Fig. 1. Age-adjusted prevalence of ASCVD by IBD status, overall and by age, sex and cardiovascular risk factors.
Abbreviations: ASCVD, atherosclerotic cardiovascular disease; IBD, inflammatory bowel disease.

nation of ≥150 min per week of moderate/vigorous-intensity aerobic physical activity. Consistent with other studies, we defined optimal, average, and poor cardiovascular risk factor profiles as having 0–1, 2–3 and ≥ 4 self-reported cardiovascular risk factors, respectively [12,14].

All analyses were performed using Stata version 16 (StataCorp, College Station, TX). The characteristics of the study population were described by IBD and ASCVD status. Variables were summarized using number and percentage, and groups were compared using the Rao-Scott χ^2.

To account for the complex sampling design of the NHIS to estimate annual nationally representative data, we used the *svy* family of commands in Stata. We used the svy: *proportion* command to obtain weighted national estimates for the prevalence of IBD, ASCVD, and of ASCVD by IBD status, overall, across socio-demographic characteristics, and cardiovascular risk factors, with age-adjusted estimates obtained using the US Census Population 2010 Data [15]. Per NCHS guidelines, the *svy: mean* with option *stdize* and *stdweight* were used to obtain age-adjusted prevalence estimates of ASCVD by IBD status [16].

Multivariable logistic regression models were used to assess the association between IBD and ASCVD adjusting for potential confounders. Three hierarchical models were used: Model 1 was unadjusted; Model 2 adjusted for age, sex, and race/ethnicity; and Model 3 further adjusted for traditional cardiovascular risk factors. We tested for interaction by age and sex by including interaction terms in the fully adjusted regression models, and conducted subgroup analyses stratified by age (18–44, 45–64 and ≥65 years) and by sex, respectively.

Finally, in post-hoc analyses we estimated the prevalence of ASCVD comparing those with and without IBD stratifying by cardiovascular risk factor profile, overall and further stratifying by age groups.

Variance estimation and person-level sample weights (representing the inverse probability of a person being selected and household nonresponse adjustment)[17] were obtained from the Integrated Public Use Microdata Series website (http://wwww.ipums.org) [18]. The person-level sample weights were divided by the number of years in the pooled datasets to accurately reflect the total population. For all statistical analyses, a two-tailed alpha level of 0.05 was considered statistically significant.

3. Results

The study included 66,610 surveyed participants, representing approximately 243 million U.S. adults. Overall, 951 (1.3% [95% CI, 1.2–1.4], representing ~3.1 million annually) reported IBD, and 165, representing ~ 500,000, reported ASCVD. Among adults with IBD, the mean age was 52.5 years (SD 17.1), 61% were women, and 77% were non-Hispanic White (Table 1).

Compared to individuals without IBD, those with IBD were older, more frequently female, and more frequently non-Hispanic White. Details on the characteristics of the study population by IBD status are summarized in the Table 1. IBD patients with ASCVD were older than those without ASCVD and had a higher burden of cardiovascular risk factors.

Among participants with IBD, the age-adjusted prevalence of ASCVD was 12.0% (95% CI, 9.7–14.2), while this was 6.9% (95% CI, 6.6–7.1) among those without IBD ($p < 0.001$) (Fig. 1). A higher prevalence of ASCVD among those with vs without IBD was also observed in subgroups defined by age strata, sex, and traditional cardiovascular risk factors. Differences between strata with vs without IBD were statistically significant in all subgroups, except for individuals ≥65 years (26.1% vs 22.8%, $p = 0.50$) and for participants with diabetes ($p = 0.14$).

Compared to not having IBD, presence of IBD was associated with a crude 2.20 odds ratio (95% CI, 1.74–2.78) for ASCVD in unadjusted analyses (Fig. 2, Model 1). In multivariable analyses adjusting for age, sex, and race/ethnicity, individuals with IBD had 95% higher odds of having ASCVD compared with those without IBD (Fig. 2, Model 2). After further adjustment for traditional risk factors, individuals with IBD had

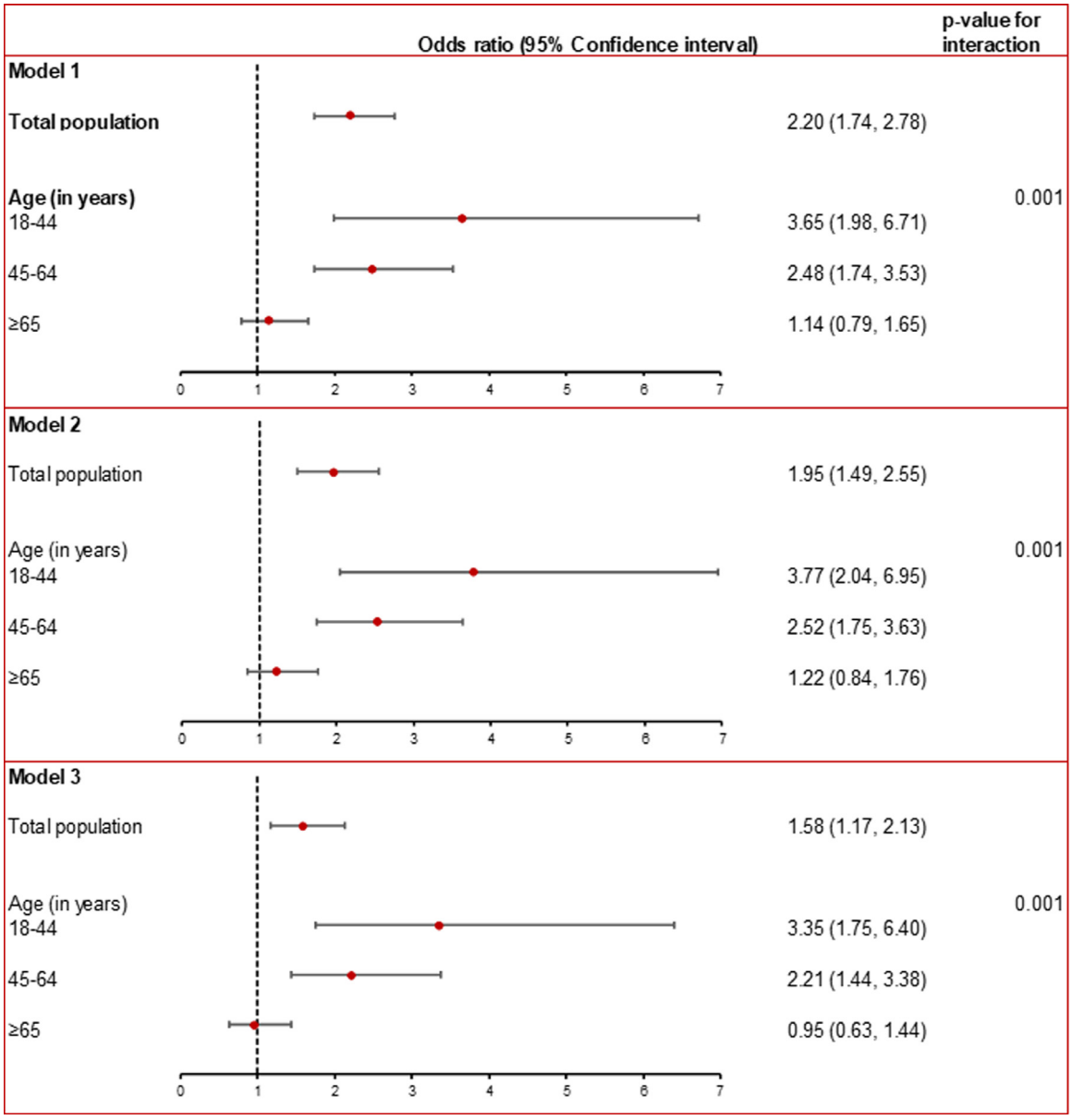

Fig. 2. Multivariable-adjusted associations between IBD and ASCVD, overall and by age strata.
Model 1 was unadjusted; Model 2 adjusted for age, sex and race/ethnicity; Model 3 further adjusted for traditional cardiovascular risk factors (hypertension, diabetes, high cholesterol, smoking, obesity, physical inactivity).
Abbreviations: ASCVD, atherosclerotic cardiovascular disease; IBD, inflammatory bowel disease.

58% higher odds of having ASCVD than those without IBD (Fig. 2, Model 3).

There was a statistically significant interaction by age in the association between IBD and ASCVD ($p < 0.001$ in all models). Specifically, the association was stronger with lower age: the fully adjusted odds ratio of ASCVD among 18- to 44-year-olds was 3.35 (95% CI, 1.75–6.40), while this was slightly weaker but statistically significant among those aged 45 to <65 years, and null among individuals aged ≥65 years (odds ratio 0.95, 95% CI 0.63–1.44).

Conversely, we found no conclusive evidence of a statistical interaction by sex (Fig. 3). However, the 95% CI crossed the null value (1.00) for men, while this was not the case for women.

Given the relevance of traditional risk factors also among IBD strata, and evidence of effect modification by age in the association between IBD and ASCVD, in post-hoc analyses we explored differences in age-adjusted prevalence of ASCVD by cardiovascular risk factor profile overall and further stratified by age strata. The prevalence of ASCVD was higher among participants with IBD than without IBD across cardiovascular risk factor profiles, overall and among those aged <65 years (Fig. 4). On the other hand, among those with age ≥65 years, the prevalence of ASCVD was not statistically different between participants with and without IBD in any of the cardiovascular risk factor profile strata considered.

4. Discussion

Using nationally representative data from NHIS representing 243 million U.S. adults and ~3.1 million individuals with IBD, we observed a strong, independent association between IBD and prevalent ASCVD. This was true after adjusting for demographics and multiple traditional cardiovascular risk factors. The age-adjusted prevalence of ASCVD was 12.0% (95% CI, 9.7–14.2) among those with IBD while this

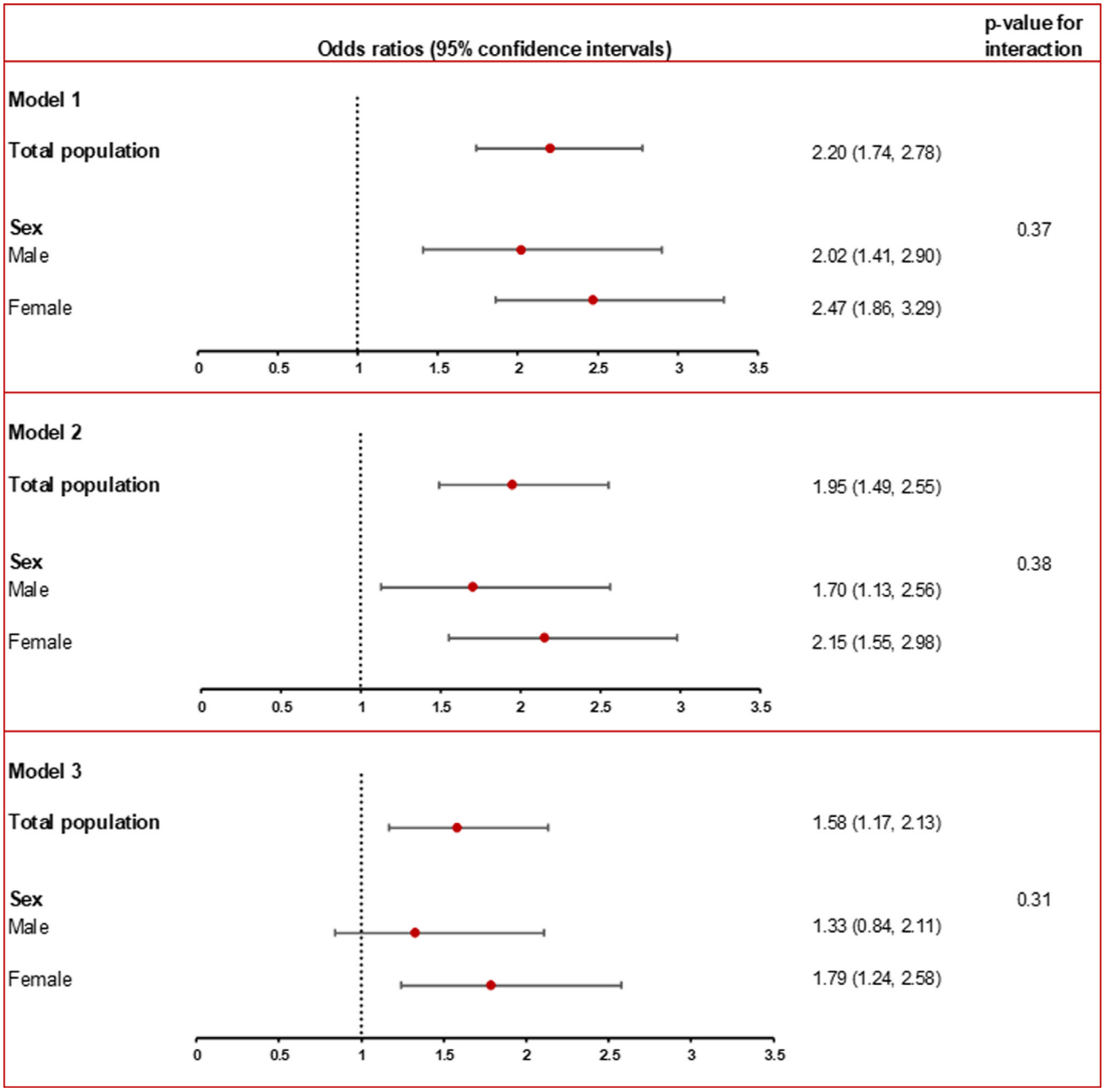

Fig. 3. Multivariable-adjusted associations between IBD and ASCVD, overall and by sex.
Model 1 was unadjusted; Model 2 adjusted for age, sex and race/ethnicity; Model 3 further adjusted for traditional cardiovascular risk factors (hypertension, diabetes, high cholesterol, smoking, obesity, physical inactivity).
Abbreviations: ASCVD, atherosclerotic cardiovascular disease; IBD, inflammatory bowel disease.

was 6.9% (95% CI, 6.6–7.1) among those without IBD ($p < 0.001$). In multivariable-adjusted analyses, the association between IBD and ASCVD was significantly stronger among younger adults, while it became null among those aged ≥65 years.

To the best of our knowledge, this is the first study to evaluate the association between IBD and ASCVD using nationally representative U.S. data. Our findings are consistent with those from a recent analysis combining data from 26 U.S. nationwide healthcare systems, restricted to adults 20–65 years of age and using a history of myocardial infarction as the study outcome [19]. The authors also observed effect modification by age within the 20–65 year age range, with stronger associations between IBD and myocardial infarction in younger adults [19]. Another study by Lee et al. using the nationwide Veterans wIth premaTure AtheroscLerosis (VITAL) registry found that patients with IBD had higher odds of premature (≤55 years) and extremely premature (≤40 years) ASCVD, with the association between stronger among participants in the ≤40 year group [20]. Our findings are also qualitatively consistent with those from 2 recent large meta-analyses combining 10 and 27 cohort studies, respectively, in which IBD was independently associated with a 15–25% increased risk of incident ASCVD events [6,7]. However, the largest contributors to the pooled estimates were non-U.S. populations, and effect modification by age was not evaluated.

Similar to Panhwar and colleagues, we also observed effect modification by age, the association between IBD and ASCVD being stronger in younger ages. Prior studies have suggested that active disease in IBD is associated with cardiovascular events, with higher event rates occurring during flares [21]. Additionally, the risk of ASCVD is higher the first year after IBD diagnosis. The fact that active disease and flares oc-

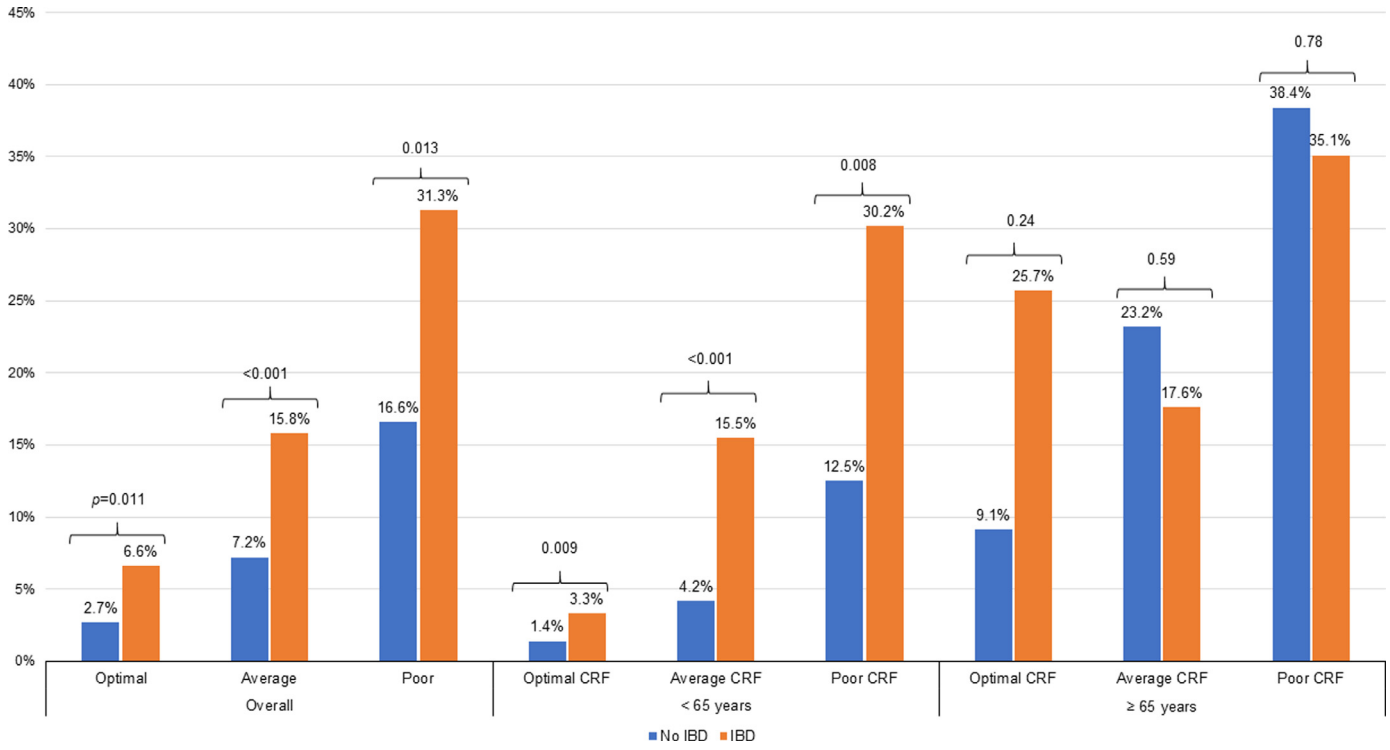

Fig. 4. Age-adjusted prevalence of ASCVD by IBD status, age and cardiovascular risk factor profile.
P values comparing proportions among individuals with vs. without IBD were calculated using chi-squared tests.
Abbreviations: ASCVD, atherosclerotic cardiovascular disease; CRF, cardiovascular risk factors; IBD, inflammatory bowel disease.

cur in younger individuals could account for the relatively stronger association between IBD and ASCVD in this age group, with cardiovascular risk factors (which accumulate over time) having a stronger impact on ASCVD events than IBD during later years of life. More research is needed to better understand the mechanisms driving the stronger association among younger patients with IBD. Because the U.S. has the largest prevalence of diagnosed IBD, understanding such mechanisms can inform ASCVD prevention approaches tailored to young adults with IBD [9,22,23].

In our study, the association between IBD and ASCVD was independent of traditional cardiovascular risk factors, which is consistent with prior reports [6,7,19]. Several mechanisms have been proposed as underlying the IBD–ASCVD connection. These include chronic inflammation leading to vascular damage, endothelial dysfunction, prothrombosis, lipid dysfunction, microbiome abnormalities which further activate the other mechanisms, and the cardiovascular effects of corticosteroids, among other mechanisms [24–26]. Observational research suggests that anti-TNF agents may hold some promise in reducing ASCVD risk in IBD patients [27], however, experimental studies are needed to confirm these findings. These findings are consistent with those from studies involving other chronic inflammatory conditions such as psoriasis and human immunodeficiency syndrome, where the use of immunomodulators and biologics have shown the potential for ASCVD risk reduction [28,29]. Specifically, Elnabawi et al. showed that in patients with psoriasis, biologic therapy was associated with a favorable modulation of coronary atherosclerotic plaque indices at one year of follow-up [28]. More generally, and as discussed above, further mechanistic research is needed to identify targeted opportunities for ASCVD risk reduction in patients with IBD [23]. Also, a detailed phenotyping of coronary plaque prevalence, characteristics, and changes over time in patients with IBD can provide further insights into the pathophysiology of ASCVD in these individuals, inform personalized risk assessment approaches, and perhaps even develop novel ASCVD risk-reduction paradigms tailored to this patient population.

The findings for young adults in this and prior studies have important implications moving forward. Young adults with IBD may benefit from a team approach to their cardiovascular risk management, ideally involving preventive cardiologists early in the process [23]. An optimized management of IBD, particularly of flares may reduce the risk of ASCVD events, and an exhaustive screening of traditional cardiovascular risk factors and an aggressive management once detected will most likely be beneficial as well. Additionally, considering the consistency of our finding with those of recent studies [6,7,20,23], we believe that there is enough evidence to explicitly include IBD as an example risk enhancing factor in future ACC/AHA prevention guidelines.

We did not observe a statistically significant interaction by sex in the association between IBD and ASCVD. Of note, the published literature is not completely consistent in this aspect. In their meta-analysis of cohort studies, Singh and colleagues found a stronger association between IBD and ASCVD among women [30]. The same was true in the meta-analysis by Sun and colleagues combining 27 studies. Conversely, in their large cross-sectional analysis focused on myocardial infarctions, Panhwar and colleagues found a stronger independent association between IBD and MI among men [19]. Further research is needed to better understand these differences by sex.

4.1. Study limitations

Some limitations should be acknowledged. IBD and ASCVD were self-reported, which may have introduced information bias. While this would be expected to result in an underestimation of the prevalence of IBD, particularly among subgroups with lower access to care and health literacy, prior studies using NHIS have actually pointed to some potential for IBD prevalence overestimation [31]. Although this was not the main purpose of our study, our prevalence estimates are consistent with prior reports from the CDC, thereby, we expect the impact of any potential misclassification of either IBD and ASCVD on the reported associations to be small, if any. With regards to the IBD-ASCVD associ-

ation, it is important to note that any information bias would be expected to be non-differential: while young patients with IBD may have greater contact with the healthcare system than those without IBD and be more aware of their overall health, we would not expect differential reporting of *hard* cardiovascular events such as angina, myocardial infarctions, and strokes by IBD status. The same would be expected with regards to IBD reporting among individuals with vs without ASCVD. Non-differential misclassification of IBD/ASCVD status would be expected to have biased the associations towards the null, at least in the unadjusted analyses.

Conversely, self-reported information on cardiovascular risk factors as categorical variables, may have led to residual confounding in multivariable regression analyses. This may explain the stronger associations observed in our study compared to some prior research [6,7].

Although the NHIS has remained a reliable source of information on the health of the non-institutionalized US population, studies have shown that survey respondents tend to be healthier than the general population [32]. Therefore, our prevalence estimates might have been conservative. Nevertheless, our prevalence estimate for IBD (1.3%, translating into 3.1 million) was identical to that reported in the literature [11], further reinforcing the validity of our estimates.

Finally, NHIS did not include information on IBD subtypes, which prevented evaluating the specific associations between ulcerative colitis and Crohn's disease and ASCVD. Nevertheless, prior studies suggest that the association with ASCVD events is consistent across IBD subtypes [6,7]. Related to this was our inability to assess the effect of IBD severity, duration, and medications for both IBD and ASCVD on the association between our exposure and outcome. Further analyses using more granular clinical databases will shed light on these aspects, although those analyses will not be as generalizable to the US population as these current one using NHIS.

5. Conclusions

In a nationally representative adult U.S. population, there was an independent association between IBD and ASCVD. This association was significantly stronger in younger adults, while it was absent among individuals aged ≥65 years. Additionally, there was no statistical evidence of a differential association between IBD and ASCVD by sex. Mechanistic and interventional studies are needed to confirm a causal association between IBD and ASCVD and identify opportunities to enhance ASCVD prevention in young and middle-aged adults with IBD.

Declaration of Competing Interest

Dr. Nasir is on the advisory board of Amgen, Novartis, Medicine Company, and his research is partly supported by the Jerold B. Katz Academy of Translational Research.

Dr. Virani receives research support from the Department of Veterans Affairs, World Heart Federation, Tahir and Jooma Family. He is also a steering committee member of the Patient and Provider Assessment of Lipid Management (PALM) registry at the Duke Clinical Research Institute. He receives honorarium from the American College of Cardiology as their Associate Editor for Innovations, acc.org.

All other authors have nothing to disclose.

Credit Author statement

Khurram Nasir: Conceptualization, methodology, supervision, writing-review & editing. **Isaac Acquah**: Data curation, formal analysis, writing-original draft. **Amit K Dey and Tanushree Agrawal**: Validation, writing-review & editing. **Syed Zawahir Hassan, Kerri Glassner, Bincy Abraham, Eamonn Quigley, Ron Blankstein, Salim S. Virani and Michael J. Blaha**: Methodology, writing-review & editing. **Javier Valero-Elizondo**: Formal analysis, validation, writing-review & editing. **Miguel Cainzos-Achirica** and **Nehal N. Mehta**: Methodology, validation, writing-review & editing. All authors gave final approval and agreed to be accountable for all aspects of this work.

References

[1] Virani Salim S, Alonso Alvaro, Aparicio Hugo J, et al. Heart disease and stroke statistics—2021 update: a report from the American Heart Association. Circulation 2022 0:CIR.0000000000000950.

[2] Mahtta D, Gupta A, Ramsey DJ, et al. Autoimmune rheumatic diseases and premature atherosclerotic cardiovascular disease: an analysis from the VITAL registry. Am J Med 2020. 0. Available at: https://www.amjmed.com/article/S0002-9343(20)30524-6/abstract [Accessed September 10, 2020].

[3] Gelfand JM, Neimann AL, Shin DB, et al. Risk of myocardial infarction in patients with psoriasis. JAMA 2006;296:1735.

[4] Knight JS, Kaplan MJ. Cardiovascular disease in lupus: insights and updates. Curr Opin Rheumatol 2013;25:597–605.

[5] Rungoe C, Basit S, Ranthe MF, et al. Risk of ischaemic heart disease in patients with inflammatory bowel disease: a nationwide Danish cohort study. Gut 2013;62:689–94.

[6] Feng W, Chen G, Cai D, et al. Inflammatory bowel disease and risk of ischemic heart disease: an updated meta-analysis of cohort studies. J Am Heart Assoc Cardiovasc Cerebrovasc Dis 2017;6. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5586435 /[Accessed August 13, 2020].

[7] Sun H-H, Tian F. Inflammatory bowel disease and cardiovascular disease incidence and mortality: a meta-analysis. Eur J Prev Cardiol 2018;25:1623–31.

[8] Alatab S, Sepanlou SG, Ikuta K, et al. The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol 2020;5:17–30.

[9] Virani SS, Alonso A, Benjamin EJ, et al. Heart disease and stroke statistics—2020 update: a report from the american heart association. Circulation 2020;141. Available at: https://www.ahajournals.org/doi/10.1161/CIR.0000000000000757 [Accessed August 13, 2020].

[10] Anon. NHIS - national health interview survey. 2020. Available at: https://www.cdc.gov/nchs/nhis/index.htm [Accessed January 22, 2021].

[11] Dahlhamer JM. Prevalence of inflammatory bowel disease among adults aged ≥18 years — United States, 2015. MMWR Morb Mortal Wkly Rep 2016;65. Available at: https://www.cdc.gov/mmwr/volumes/65/wr/mm6542a3.htm [Accessed May 11, 2020].

[12] Valero-Elizondo J, Khera R, Saxena A, et al. Financial hardship from medical bills among nonelderly U.S. adults with atherosclerotic cardiovascular disease. J Am Coll Cardiol 2019;73:727–32.

[13] Grandhi GR, Mszar R, Vahidy F, et al. Sociodemographic disparities in influenza vaccination among adults with atherosclerotic cardiovascular disease in the United States. JAMA Cardiol 2021;6:87–91.

[14] César Caraballo, Javier Valero-Elizondo, Rohan Khera, et al. Burden and consequences of financial hardship from medical bills among nonelderly adults with diabetes mellitus in the United States. Circ Cardiovasc Qual Outcomes 2020;13:e006139.

[15] Li C, Ford ES, Zhao G, et al. Age adjustment of diabetes prevalence: use of 2010 U.S. Census data. J Diabetes 2014;6:451–61.

[16] Anon. NHANES tutorials - module 8 - age standardization and population estimates. Available at: https://wwwn.cdc.gov/nchs/nhanes/tutorials/module8.aspx [Accessed January 29, 2021].

[17] Parsons VL, Moriarity C, Jonas K, et al. Design and estimation for the national health interview survey, 2006-2015. Vital Health Stat 2014;2:1–53.

[18] Blewett LA, Rivera Drew JA, King ML, et al. IPUMS Health Surveys: national Health Interview Survey, Version 6.2. IPUMS 2019. Available at: https://ipums.org/projects/ipums-health-surveys/d070.v6.2 [Accessed August 13, 2020].

[19] Panhwar MS, Mansoor E, Al-Kindi SG, et al. Risk of myocardial infarction in inflammatory bowel disease: a population-based national study. Inflamm Bowel Dis 2019;25:1080–7.

[20] Lee MT, Mahtta D, Chen L, et al. Premature atherosclerotic cardiovascular disease risk among patients with inflammatory bowel disease. Am J Med 2021;134 1047-1051.e2.

[21] Kristensen SL, Ahlehoff O, Lindhardsen J, et al. Disease activity in inflammatory bowel disease is associated with increased risk of myocardial infarction, stroke and cardiovascular death – a danish nationwide cohort study. PLoS ONE 2013;8:e56944.

[22] Zeitouni M, Nanna MG, Sun J-L, et al. Performance of guideline recommendations for prevention of myocardial infarction in young adults. J Am Coll Cardiol 2020;76:653–64.

[23] Cainzos-Achirica M, Glassner K, Zawahir HS, et al. Inflammatory bowel disease and atherosclerotic cardiovascular disease. J Am Coll Cardiol 2020;76:2895–905.

[24] Glassner KL, Abraham BP, Quigley EMM. The microbiome and inflammatory bowel disease. J Allergy Clin Immunol 2020;145:16–27.

[25] Principi M, Mastrolonardo M, Scicchitano P, et al. Endothelial function and cardiovascular risk in active inflammatory bowel diseases. J Crohns Colitis 2013;7:e427–33.

[26] Senchenkova E, Seifert H, Granger DN. Hypercoagulability and platelet abnormalities in inflammatory bowel disease. Semin Thromb Hemost 2015;41:582–9.

[27] Kirchgesner J, Nyboe Andersen N, Carrat F, et al. Risk of acute arterial events associated with treatment of inflammatory bowel diseases: nationwide French cohort study. Gut 2020;69:852–8.
[28] Elnabawi YA, Dey AK, Goyal A, et al. Coronary artery plaque characteristics and treatment with biologic therapy in severe psoriasis: results from a prospective observational study. Cardiovasc Res 2019;115:721–8.
[29] Titanji B, Gavegnano C, Hsue P, et al. Targeting inflammation to reduce atherosclerotic cardiovascular risk in people with HIV infection. J Am Heart Assoc 2020;9:e014873.
[30] Singh S. Risk of cerebrovascular accidents and ischemic heart disease in patients with inflammatory bowel disease: a systematic review and meta-analysis. 2014;12:13.
[31] Nguyen GC, Chong CA, Chong RY. National estimates of the burden of inflammatory bowel disease among racial and ethnic groups in the United States. J Crohns Colitis 2014;8:288–95.
[32] Keyes KM, Rutherford C, Popham F, et al. How healthy are survey respondents compared with the general population?: using survey-linked death records to compare mortality outcomes. Epidemiology 2018;29:299–307.