REVIEWER'S COMMENTS - REVISION

Srl No.	Manuscript ID: 82424 **Name of Journal:** ***World Journal of Cardiology*** Manuscript type: Observational Study Manuscript Title: A Pharmacoepidemiologic Study of the Association between Apparent Treatment Resistant Hypertension and Risk of Cardiovascular Disease, and the Interaction Effect by Sex and Age		
	Article content	**Comments**	**Authors' point-by-point response to Reviewers' comments**
	Overall	The Observational Study is 'fair'. However, refinements need to be done. Abstract word count needs to be reduced. English needs to be improved.	The Abstract word count has been reduced and is in line with each section's word count limits. The text of the manuscript has been revised for grammar and clarity.
	For clearly pointing focus areas in review and corrections, red/maroon and green font colours are used, respectively.		
1	**ABSTRACT** **Background:** Limited studies have been conducted to test the magnitudes of the association between apparent treatment resistant hypertension (aTRH) and risk of cardiovascular disease (CVD).	Limited studies meaning is not clear. Is it (i) limited number of studies (ii) limited number of patients in studies OR (iii) Methodology limitations	This line has been revised to clarify it is a limited number of studies.
2	**ABSTRACT** **Aim**: We aimed to investigate the association between aTRH) and risk of CVD, and to examine whether sex and age modify this association.	Why aim word is repeated twice?	This line has been revised for clarity.
3	**Methods:** We applied an observational analysis study design …… . The ALLHAT recruited participants (N=25,516) from 625 primary care settings throughout the United States (U.S.), Canada, Puerto Rico, and U.S.	How the effect of additional risk factors for heart disease excluded?	This line is outlining the inclusion criteria for the ALLHAT trial from which secondary data was used for this research. Due to space constraints we did not go into additional detail here. The inclusion/exclusion criteria and protocol for the ALLHAT trial has been described in detail elsewhere and is cited in this manuscript. We adjusted for many of these factors in our analysis including BMI, diabetes, GFR, LVH, and smoking status.

	Virgin Islands, aged 55 and older with hypertension and at least one additional risk factor for heart disease.	What all were these additional risk factors and where these not different in different ages and different sex?	
4	**INTRODUCTION** In addition to the number of antihypertensive medications and blood pressure readings, ideally at least one of the medications should be a diuretic and all medications should be at optimal doses when classifying resistant hypertension.[6]	Dose is optimal when desired effects are there! The quoted reference [6] states: "Before considering someone to have resistant hypertension, treatment with ≥3 antihypertensive medications from different classes should be used together at sufficient doses."	This line has been revised for clarity and information at the end of this paragraph has been revised to clarify these should be sufficient doses.
5	**MATERIALS AND METHODS** **Measures** aTRH was classified as BP ≥ 140/90 while on 3 antihypertensive medications, or being on 4 antihypertensive medications regardless of BP at the year 2 visit.	Is this classification or definition. Is it arbitrary OR by authors OR defined by some textbook/Hypertension association or study?	This classification was based on the definition of aRTH given and cited in the introduction section of this manuscript. This line has been revised for clarity.
6	**Methods:** CVD event defined if one of the following from year 2 follow-up visit: fatal or non-fatal myocardial infarction (MI), coronary revascularization, angina, stroke, heart failure (HF), or peripheral artery disease (PAD).	What grade angina?	Unfortunately this information is unknown. In the secondary data obtained from the ALLHAT trial for this analysis participants were coded as having angina or not. The only definition given for angina in the forms was if the participant was hospitalized or treated for angina.