

1 **Risk of cardiovascular disease in Chinese patients with rheumatoid arthritis: a cross-**
2 **sectional study based on hospital medical records in 10 years**

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1 **Abstract**

2 **Objective** Though the risk of cardiovascular disease (CVD) in rheumatoid arthritis (RA) has been
3 established in Western population, little is known about the risk in Chinese people with RA. Our
4 objective was to estimate the risk of CVD in Chinese people with RA using hospital medical records
5 data.

6 **Methods**

7 The inpatients medical record database 2005-2015 of Sichuan provincial people's hospital was
8 examined. All individuals with a primary diagnosis of RA were included as cases, and those of
9 osteoarthritis (OA) were included as controls, which consisted of the unmatched dataset. Then, RA
10 cases and OA controls were matched by sex and age at 1:1 ratio, forming the matched dataset. The
11 morbidity of CVD (including ischemia heart disease (IHD), congestive heart failure (CHF), et al), stroke
12 and atherosclerosis were extracted from the database, so as the demographic data and comorbidities
13 related to CVD. Multiple logistic regression analysis was used to estimate the risk of CVD in RA adjusted
14 for demographics and comorbidities using the unmatched dataset. Sensitivity analysis was conducted
15 1) considering interaction terms between RA and comorbidities, and 2) using multivariable conditional
16 logistic regression for the matched dataset.

17 **Results** The unmatched dataset comprised of 1824 RA cases and 1995 OA controls and the matched
18 dataset comprised of 1022 pairs of sex and age matched RA and OA patients. RA exhibited increased
19 odds of prevalent CVD compared with OA, and the adjusted ORs (95% CIs) for CVD, stroke, IHD, CHF,
20 and atherosclerosis were 1.86(1.42-2.43), 1.11(0.71-1.74), 1.47(0.97-2.24), 2.09(1.03-4.22), and 2.49
21 (1.97-3.13), respectively, and was 2.26 (1.29-3.96) for IHD further adjusted for interaction term. The
22 matched dataset analysis found similar results.

1 **Conclusions** Chinese people with RA were approximated 2 times more likely to have CVD, IHD, CHF and
2 atherosclerosis compared with those with OA. The findings justified the need of further longitudinal
3 study to establish the causal-relationship between RA and CVD and to estimate the precise risk in this
4 population.

5 **Key words:** rheumatoid arthritis, cardiovascular disease, risk, osteoarthritis, Chinese population

6

1 Introduction

2 Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory disease associated with
3 persistent inflammatory synovitis, progressive joint destruction, and an excess mortality when
4 compared to the non-RA individuals.[1-5] RA affects estimated 0.42% of the Chinese population,
5 approximately 5,745,600 people.[6] It is evident that RA increases the risk of cardiovascular diseases
6 (CVD) in addition to traditional CVD risk factors.[2] Systemic inflammation and the 'accelerated
7 atherosclerosis' in RA are considered as the main mechanism linking RA and CVD.[7] Osteoarthritis (OA)
8 – a leading cause of pain and disability, is generally considered as a chronic wear and tear joint condition
9 without systemic inflammation, thus was employed as non-systemic inflammatory comparator in
10 previous studies.[8, 9][4] However, the risk of CVD in Chinese people with RA is unclear and evidence
11 from epidemiological study is lacking. Acknowledge of the relative risk is relevant for optimal
12 management and care of people with RA and prevention of CVD.[10] The objective of this study was to
13 estimate the risk of CVD in Chinese people with RA comparing with those with osteoarthritis (OA) as
14 controls.

15 Methods

16 Data source and patient definition

17 The study was approved by the Ethics Committee of Sichuan Provincial People's Hospital (SPPH) on
18 using anonymous medical records data for scientific research purpose (No. 2016-27). This cross-
19 sectional study used the inpatients medical record database (MRD) of SPPH, which records
20 demographics, diagnoses (using ICD-10 codes), procedures (using ICD-CM-9 codes) and expenditure
21 of all inpatients from 2005-2015. All patients with a principal discharge diagnosis of RA (ICD-10 codes:
22 M05.0-M06.9) from 2005-2015 were included, and all patients with a principal discharge diagnosis of

1 OA (ICD-10 codes: M15.0-M19.9) were selected as controls. We focused on the principal diagnosis of
2 discharge to maximize the validity of the case and control definition. Patients with discharge diagnosis
3 of both RA and OA were excluded to avoid the overlapping effect.
4 Two datasets were generated. The first is an unmatched dataset containing all included RA or OA
5 patients. The second was the matched dataset in which patients with RA and OA were matched at 1:1
6 ratio by sex and age (per 5 years), which was used for the sensitivity analysis.

7 **Cardiovascular diseases**

8 The primary outcomes in this study were CVD and stroke. Secondary outcomes were specific
9 cardiovascular conditions: ischaemic heart diseases (IHD), congestive heart failure (CHF) and
10 atherosclerosis (AS). All outcomes were defined by diagnoses recorded in the MRD using ICD-10 codes
11 (S1 Table).[11]

12 **Covariates or confounders**

13 Confounders considered were age, gender, and comorbidities related to CVD including hypertension,
14 hyperlipidemia, diabetes mellitus or hyperglycaemia (referred as the diabetes mellitus in the rest of
15 the text) and chronic obstructive pulmonary disease (COPD).[9, 12-15] Gender and age were extracted
16 from the MRD. Comorbidities were defined by secondary diagnoses of discharge which were recorded
17 in the database using ICD-10 codes (S1 Table).[11]

18 **Statistical analysis**

19 Characteristics of participants were described before the association analyses. Continuous and
20 categorical variables were described using mean and standard deviation (SD) and frequency and
21 percentage, respectively. For univariate analysis, ANOVA was conducted for the former, and Chi square
22 test for the latter.

1 Logistic regression was used to estimate the associations between RA and CVD outcomes using the
2 unmatched dataset, in which unadjusted and adjusted odds ratios (ORs) with its 95% confidence
3 intervals (CIs) were estimated, considering all covariates describe above. Sensitivity analysis was
4 conducted 1) considering significant interaction terms of RA and comorbidities using the unmatched
5 dataset, and 2) using multivariable conditional logistic regression analysis for the matched dataset.
6 Model fit was tested using Bayesian information criterion (BIC).[16]All statistical analyses were
7 conducted using STATA 13.0. The significance level was 0.05.

8 **Results**

9 **Participants and characteristics**

10 There were 2,235 OA patients and 3914 RA patients identified from the database between 2005 and
11 2015. After removing patients with discharge diagnoses of both OA and RA, 2184 patients with OA and
12 2390 with RA remained. Then, readmissions were removed and the last record of a patient
13 hospitalization was selected, leaving 1995 patients with OA and 1824 patients with RA, which consisted
14 of the unmatched dataset of 3819 participants. Finally, RA and OA patients were matched by sex and
15 age (per 5 years), forming the matched dataset of 2044 patients with either OA or RA (1022 each) (Fig
16 1).

17
18 Fig 1 Flow chart of selection of participants

19

20 The characteristics of participants with RA (cases) and OA (controls) are presented and compared in
21 Table 1. In the unmatched dataset, patients with OA were significantly older (63.0 vs. 52.4 years), with
22 more women (74.6% vs. 69.6%), hypertension (22.1% vs. 10.6%), hyperlipidemia (11.6% vs. 5.0%) and
23 less COPD (2.0% vs. 4.3%) compared with patients with RA. There was no significant difference

1 ofdiabetes mellitusbetween the two groups. In the matched dataset, age, sex, and the proportion of
 2 patientswith hypertention, hyperlipdemia, IHD or stroke was similar between the two groups. However,
 3 there were significantly more diabetes mellitus (p=0.01) and COPD (p=0.00)in RA cases than OA
 4 controls.

5 **Table 1 Characteristics of rheumatoid arthritis (RA) cases and osteoarthritis controls (OA)**

| | Unmatched dataset | | | Matched dataset | | |
|-----------------------|-------------------|-------------|------|-----------------|-----------|------|
| | OA (%) | RA (%) | p | OA (%) | RA (%) | p |
| No. of participants | 1,995 | 1,824 | | 1,022 | 1,022 | |
| Mean age (SD), year | 63.0(0.3) | 52.4(0.4) | 0.00 | 58.5(0.4) | 57.8(0.4) | 0.25 |
| Age group, year | | | 0.00 | | | 1.00 |
| <45 | 146(7.3) | 553(30.3) | | 142(13.9) | 142(13.9) | |
| 45-49 | 111(5.6) | 191(10.5) | | 105(10.3) | 105(10.3) | |
| 50-54 | 174(8.7) | 202(11.1) | | 103(10.1) | 103(10.1) | |
| 55-59 | 265(13.3) | 243(13.3) | | 152(14.9) | 152(14.9) | |
| 60-64 | 334(16.7) | 229(12.6) | | 183(17.9) | 183(17.9) | |
| 65-69 | 327(16.4) | 178(9.8) | | 151(14.8) | 151(14.8) | |
| 70-74 | 303(15.2) | 114(6.3) | | 99(9.7) | 99(9.7) | |
| 75-79 | 221(11.1) | 66(3.6) | | 58(5.7) | 58(5.7) | |
| 80-84 | 83(4.2) | 37(2.0) | | 22(2.2) | 22(2.2) | |
| 85+ | 31(1.6) | 11(0.6) | | 7(0.7) | 7(0.7) | |
| Women | 1,488(74.6) | 1,270(69.6) | 0.00 | 702(68.7) | 702(68.7) | 1.00 |
| Comorbidity | | | | | | |
| Hypertension | 441(22.1) | 194(10.6) | 0.00 | 148(14.5) | 167(16.3) | 0.24 |
| Hyperlipdemia | 231(11.6) | 92(5.0) | 0.00 | 75(7.3) | 69(6.8) | 0.60 |
| Diabetes mellitus | 251(12.6) | 198(10.9) | 0.10 | 103(10.1) | 144(14.1) | 0.01 |
| COPD | 39(2.0) | 78(4.3) | 0.00 | 12(1.2) | 64(6.3) | 0.00 |
| Outcomes | | | | | | |
| CVD | 166(8.3) | 139(7.6) | 0.43 | 53(5.2) | 105(10.3) | 0.00 |
| IHD | 76(3.8) | 44(2.4) | 0.01 | 23(2.3) | 34(3.3) | 0.14 |
| Myocardial infarction | 3 (0.15) | 2 (0.11) | | | | |
| CHF | 17(0.9) | 21(1.2) | 0.35 | 5(0.5) | 18(1.8) | 0.01 |
| Stroke | 74(3.7) | 34(1.9) | 0.00 | 29(2.8) | 27(2.6) | 0.79 |
| Arthrosclerosis | 216(10.8) | 234(12.8) | 0.06 | 65(6.4) | 203(19.9) | 0.00 |

6 Numbers are frequencies (percentages) unless otherwise specified, CVD: cardiovascular disease, IHD:
 7 ischaemic heart disease, CHF: congestive heart disease, COPD: chronic obstructive pulmonary disease
 8

9 Association analysis

10 For the unmatched dataset, significant more patients with RA had CVD (adjusted OR: 1.86, 95%CI 1.42-

1 2.43), CHF (adjusted OR: 2.09, 1.03-4.22) and atherosclerosis (adjusted OR: 2.49, 1.97-3.13) than OA
2 patients adjusted for age, sex, hypertension, hyperlipidemia, diabetes mellitus and COPD. However, no
3 difference was found for stroke (adjusted OR: 1.11, 0.71-1.74) and IHD (adjusted OR: 1.47, 0.97-2.24)
4 between the two groups adjusted for other variables. (Table 2)
5 In the sensitivity analysis using matched dataset, the findings were similar to that of unmatched
6 dataset analysis. Significant more patients with RA had CVD (adjusted OR: 2.19, 1.49-3.21), CHF
7 (adjusted OR: 6.95, 1.50-32.21) and atherosclerosis (adjusted OR:4.95, 3.36-7.28) than OA controls.
8 Still, no difference of patients with stroke (adjusted OR: 1.13, 0.57-2.25) and IHD (adjusted OR:1.83,
9 0.94-3.56) was found between the two groups adjusted for other variables.(Table 2)

10

11 **Table 2 Risk of cardiovascular diseases in rheumatoid arthritis (RA) compared with osteoarthritis**
12 **(OA)**

| | Unmatched dataset OR (95%CI) | | Matched dataset OR (95%CI) | |
|--------------------------------|------------------------------|-------------------------|----------------------------|--------------------------|
| | Unadjusted | Adjusted | Unadjusted | Adjusted |
| Cardiovascular disease | | | | |
| RA vs. OA | 0.91(0.72-1.15) | <u>1.86(1.42-2.43)*</u> | 2.09(1.49-2.95)* | <u>2.19 (1.49-3.21)*</u> |
| Age, per 5 years | 1.42(1.34-1.50)* | 1.38(1.30-1.47)* | 1.42(1.31-1.54)* | / |
| Women | 0.90(0.69-1.16) | 0.94(0.71-1.24) | 0.70(0.50-0.98)* | / |
| Hypertension | 4.64(3.63-5.93)* | 2.72(2.07-3.57)* | 3.79(2.68-5.38)* | 1.98(1.07-3.65)* |
| Hyperlipidemia | 2.33(1.68-3.23)* | 1.81(1.26-2.58)* | 1.67(0.98-2.85) | 1.66(0.64-4.32) |
| Diabetes mellitus | 2.74(2.07-3.63)* | 1.51(1.11-2.04)* | 2.34(1.57-3.49)* | 1.57(0.76-3.25) |
| COPD | 2.63(1.62-4.29)* | 1.21(0.71-2.05) | 3.43(1.93-6.11)* | 1.94(0.63-6.01) |
| Stroke | | | | |
| RA vs. OA | 0.49(0.33-0.74)* | 1.11(0.71-1.74) | 0.93(0.55-1.58) | 1.13(0.57-2.25) |
| Age, per 5 years | 1.58(1.43-1.74)* | 1.47(1.32-1.64)* | 1.54(1.35-1.76)* | / |
| Women | 0.83(0.55-1.26) | 0.78(0.50-1.21) | 0.75(0.44-1.31) | / |
| Hypertension | 7.38(4.99-10.92)* | 3.84(2.50-5.90)* | 7.44(4.33-12.79)* | 4.80(1.65-13.93)* |
| Hyperlipidemia | 2.72(1.67-4.45)* | 1.84(1.08-3.12)* | 1.93(0.86-4.34) | 1.21(0.26-5.62) |
| Diabetes mellitus | 2.60 (1.66-4.06)* | 1.22(0.76-1.96) | 2.51(1.35-4.67)* | 1.33(0.41-4.25) |
| COPD | 1.91 (0.82- 4.44) | 0.83(0.34-2.04) | 2.05(0.72-5.81) | 0.38(0.07-1.93) |
| Ischaemic heart disease | | | | |
| RA vs. OA | 0.62(0.43-0.91)* | 1.47(0.97-2.24) | 1.49(0.87-2.56) | 1.83(0.94-3.56) |
| Age, per 5 years | 1.66(1.51-1.82)* | 1.59(1.43-1.76)* | 1.74(1.51-2.01)* | / |
| Women | 1.01(0.68-1.52) | 1.08(0.70-1.67) | 0.78(0.45-1.34) | / |

| | | | | |
|---------------------------------|-------------------|-------------------------|-------------------|--------------------------|
| Hypertension | 6.49(4.48-9.39)* | 3.37(2.25-5.05)* | 4.57(2.67-7.83)* | 4.40(1.28-15.05)* |
| Hyperlipidemia | 1.83(1.08-3.10)* | 1.24(0.70-2.18) | 1.58(0.66-3.74) | 0.62(0.11-3.64) |
| Diabetes mellitus | 2.61(1.71-3.99)* | 1.30(0.83-2.05) | 1.99(1.04-3.81)* | 1.09(0.35-3.32)* |
| COPD | 2.35(1.12-4.94)* | 0.98(0.44-2.17) | 2.59(1.01-6.69)* | 1.38(0.28-6.87) |
| Congestive heart disease | | | | |
| RA vs. OA | 1.36(0.71-2.58) | <u>2.09(1.03-4.22)*</u> | 3.65(1.35-9.86)* | <u>6.95(1.50-32.21)*</u> |
| Age, per 5 years | 1.36(1.18-1.57)* | 1.27(1.08-1.49)* | 1.29(1.07-1.57)* | / |
| Women | 0.47(0.25-0.90)* | 0.57(0.29-1.10) | 0.41(0.18-0.94)* | / |
| Hypertension | 4.62(2.43-8.78)* | 3.59(1.77-7.29)* | 5.18(2.26-11.84)* | 13.69(1.13-166.48)* |
| Hyperlipidemia | 0.29(0.04-2.12) | 0.22(0.03-1.64) | Exactly the same | (omitted) |
| Diabetes mellitus | 2.72(1.31-5.64)* | 1.57(0.73-3.36) | 2.04(0.75-5.55) | 1.27(0.18-9.18) |
| COPD | 4.96(1.90-12.95)* | 2.05(0.72-5.80) | 4.00(1.16-13.77)* | 3.95(0.19-82.30) |
| Atherosclerosis | | | | |
| RA vs. OA | 1.21 (1.00- 1.48) | <u>2.49(1.97-3.13)*</u> | 3.65(2.72-4.90)* | <u>4.95(3.36-7.28)*</u> |
| Age, per 5 years | 1.31(1.26-1.37)* | 1.31(1.25-1.38)* | 1.30(1.22-1.38)* | / |
| Women | 0.92(0.74-1.14) | 0.96(0.76-1.21) | 0.92(0.70-1.21) | / |
| Hypertension | 3.88(3.14-4.81)* | 2.47(1.94-3.15)* | 3.34(2.49-4.46)* | 1.83(0.98-3.42) |
| Hyperlipidemia | 3.75(2.89-4.88)* | 3.51(2.63-4.69)* | 3.55(2.43-5.17)* | 5.62(2.23-4.14)* |
| Diabetes mellitus | 2.20(1.71-2.84)* | 1.21(0.92-1.60) | 1.73(1.22-2.44)* | 0.91(0.43- 1.92) |
| COPD | 3.24(2.14-4.89)* | 1.61(1.02-2.54)* | 3.05(1.84-5.07)* | 1.31(0.35-4.87) |

1 CI: confidence interval, COPD: chronic obstructive pulmonary disease. The number of observations for
2 multivariate conditional logistic regression analysis for cardiovascular disease, ischaemic heart disease,
3 congestive heart disease,, stroke and atherosclerosis was 292, 106, 46, 108 and 404
4 respectively. *p<0.05

5

6 Moreover, findings were similar for CVD, stroke, CHF and atherosclerosis in the sensitivity analysis
7 considering interaction terms of RA and comorbidities using the unmatched dataset. However,
8 patients with RA were significantly more likely to have IHD (adjusted OR: 2.26, 1.29-3.96) than patients
9 with OA adjusted for other variables and the interaction term of RA and hypertension. (S2 Table)

10

11 Discussion

12 This study included 3819 Chinese patients with RA or OA consecutively admitted to a medical centre
13 between 2005 and 2015. Important covariables such as age, sex, and comorbidities related to CVD were
14 adjusted in the estimate of association between RA and CVD. RA and OA, CVD, and comorbidities

1 related to CVD were defined by physician's diagnoses recorded as ICD-10 codes in MRD, which reduced
2 information bias and enhanced the accuracy of variable definition. We found 1) the prevalence of CVD
3 in Chinese patients with RA admitted to hospital was 7.6%-10.3%; 2) RA patients were approximately
4 twice more likely to have CVD, IHD, CHF and atherosclerosis than people with OA; and 3) the risk
5 of stroke were not significantly different between the two groups, while an incremental (from non-
6 significant to significant) risk of IHD was found when more covariables or their interaction were
7 adjusted.

8 The approximately 2 fold risk of total CVD, IHD and CHF in Chinese people with RA found in this study
9 is comparable to previous studies in other populations (mainly Caucasians). [2, 17, 18] For Chinese
10 population, Chung and colleagues found a 38% increase of risk of acute myocardial infarction in patients
11 with RA comparing with non-RA population in a cohort study in Taiwan; unfortunately the risk of total
12 CVD and other specific CVD were not estimated. [19] The association between RA and CVD is further
13 supported by our finding that the risk of atherosclerosis increased in RA, for it is considered as the main
14 mechanism underlying RA and CVD morbidity linked by systemic inflammation. [7, 20] However, we
15 found a positive but non-significant risk of stroke, and an incremental risk (from non-significant to
16 significant) of IHD in people with RA when more covariables or interaction were adjusted. The increased
17 risk of stroke and IHD in RA has been shown in large sample sized longitudinal studies and meta-analysis
18 in other population. [2, 18] The non-significant finding of stroke and IHD may be due to the small
19 number of events and lack of power in this study. Furthermore, the risk of CVD in RA compared with
20 OA may not be able to be directly interpreted as the risk compared with non-RA general population.
21 Because evidence has emerged recently that OA may also increase the risk of CVD compared with the

1 general population, though it is still controversial.[21, 22] Therefore, the CVD risk in Chinese people with
2 RA comparing with the general population might be higher than the estimate in our study.

3 This study has several limitations. Firstly, the participants in this study were all inpatients consecutively
4 admitted to a medical centre. Therefore, selection bias may be introduced, for inpatients are generally
5 more severe in disease status than outpatients or community patients, but this situation may be
6 even between RA cases and OA controls. Secondly, some covariables or confounders of CVD were not
7 included in the analysis for they were absent in the database such as obesity, smoking and anti-
8 rheumatic drugs. There is evidence that obesity is more prevalent in patients with OA than in RA.[17,
9 21] Thus, the risk of CVD in RA compared with OA may be higher if obesity was controlled for.
10 Furthermore, diabetes and COPD were adjusted in the analysis, which are positively associated with
11 obesity and smoking, thus their effect on CVD may be indirectly and partially adjusted. Thirdly, detailed
12 analysis on sub-category of CVDs such as myocardial infarction was not possible due to the small
13 number of events. Finally, the nature of the cross-sectional study design prevented us to yield a causal-
14 relationship between RA and CVD.

15 In conclusion, Chinese people with RA were approximated 2 times more likely to have CVD, IHD, CHF
16 and atherosclerosis compared with people with OA. Further longitudinal study is needed to establish
17 the risk of total and specific CVD in Chinese people with RA.

18

19 **Contribution of authors:** KZ, WZ conceptualized the study, KZ, CFG, WZ contributed to the study design,
20 FKX acquired the data, KZ conducted the analysis and wrote the first draft, all authors contributed to
21 critically appraisal and intellectual interpretation of the findings and revision of the final report.

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10 Supporting information

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12 **S1Table. ICD-10 codes of outcomes and covariates**

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14 **S2Table. Sensitivity analysis using unmatched dataset adjusted for covariables and interaction terms**
15 **with rheumatoid arthritis (RA).** RA: rheumatoid arthritis; OA: osteoarthritis, COPD: chronic obstructive
16 pulmonary disease; & Diabetes mellitus or hyperglycemia; § No significant interaction term was
17 detected; †Bayesian information criterion in favor of the model; *p<0.05

Supporting information

S1 Table. ICD-10 codes of outcomes and covariates

| Variable | ICD-10 code |
|--|---------------------|
| Outcomes | |
| Cardiovascular disease | |
| Rheumatic heart disease | I05.0-I09.9 |
| Ischemic heart disease | I20.0-I25.9 |
| Myocardial infarction | I21.x, I22.x, I25.2 |
| Pericarditis | I30.0-I32.9 |
| Endocarditis | I33.0-I33.9 |
| Valve disorders | I34.0-I37.9 |
| Myocarditis | I40.0-I41.9 |
| Cardiomyopathy | I42.0-I43.9 |
| Conduction disorders | I44.0-I45.9 |
| Arrhythmias | I46.0-I49.9 |
| Congestive heart failure | I50.0-I50.9 |
| Other heart disease | I51.0-I51.9 |
| Atherosclerosis | I70.0-I70.9 |
| Stroke | I60.0-I64.9 |
| | H34.1 |
| | G45.0-G45.9 |
| Covariable | |
| Hypertension | I10.0-I15.9 |
| Hyperlipidemia | E78.0-E78.5 |
| Diabetes mellitus | E10.0-E14.9 |
| Hyperglycaemia | R73.0-R73.9 |
| Chronic obstructive pulmonary diseases | J40.0-J44.9 |
| | J47.0-J47.9 |

Supporting information

S2 Table. Sensitivity analysis using unmatched dataset adjusted for covariables and interaction terms with rheumatoid arthritis (RA)

| | Adjusted OR (95%CI) | |
|---|---------------------|---------------------|
| Cardiovascular disease⁺ | | |
| RA vs. OA | 2.12 | <u>(1.60-2.83)*</u> |
| Age (per 5 years) | 0.93 | (0.70-1.23) |
| Women | 1.38 | (1.30-1.47)* |
| Hypertension | 2.76 | (2.10-3.63)* |
| Hyperlipidemia | 2.47 | (1.64-3.71)* |
| Diabetes mellitus ^{&} | 1.49 | (1.10-2.02)* |
| COPD | 1.17 | (0.69-2.00) |
| RA # Hyperlipidemia | 0.29 | (0.11-0.71)* |
| Stroke[§] | | |
| RA vs. OA | 1.11 | (0.71-1.74) |
| Age (per 5 years) | 0.78 | (0.50-1.21) |
| Women | 1.47 | (1.32-1.64)* |
| Hypertension | 3.84 | (2.50-5.90)* |
| Hyperlipidemia | 1.84 | (1.08-3.12)* |
| Diabetes mellitus ^{&} | 1.22 | (0.76-1.96) |
| COPD | 0.83 | (0.34-2.04) |
| Ischemic heart disease | | |
| RA vs. OA | 2.26 | <u>(1.29-3.96)*</u> |
| Age (per 5 years) | 1.08 | (0.70-1.67) |
| Women | 1.59 | (1.43-1.76)* |
| Hypertension | 4.84 | (2.87-8.18)* |
| Hyperlipidemia | 1.23 | (0.70-2.17) |
| Diabetes mellitus ^{&} | 1.25 | (0.79-1.96) |
| COPD | 1.01 | (0.46-2.23) |
| RA # Hypertension | 0.37 | (0.16-0.88)* |
| Congestive heart failure | | |
| RA vs. OA | 2.69 | <u>(1.28-5.65)*</u> |
| Age (per 5 years) | 0.54 | (0.28-1.04) |
| Women | 1.28 | (1.09-1.51)* |
| Hypertension | 3.65 | (1.80-7.42)* |
| Hyperlipidemia | 0.20 | (0.03-1.54) |
| Diabetes mellitus ^{&} | 1.54 | (0.71-3.30) |
| COPD | 6.93 | (1.82-26.31)* |
| RA # COPD | 0.12 | (0.02-0.93)* |
| Atherosclerosis | | |
| RA vs. OA | 2.60 | <u>(2.05-3.31)*</u> |

| | | |
|------------------------------------|------|--------------|
| Age (per 5 years) | 0.95 | (0.75-1.20) |
| Women | 1.32 | (1.25-1.39)* |
| Hypertension | 2.47 | (1.94-3.15)* |
| Hyperlipidemia | 3.50 | (2.62-4.68)* |
| Diabetes mellitus ^{&} | 1.21 | (0.92-1.60) |
| COPD | 2.73 | (1.32-5.63)* |
| RA # COPD | 0.44 | (0.17-1.09) |

RA: rheumatoid arthritis; OA: osteoarthritis, COPD: chronic obstructive pulmonary disease; & Diabetes mellitus or hyperglycemia; [§] No significant interaction term was detected; [†]Bayesian information criterion in favor of the model; *p<0.05