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# Spousal similarities in cardiometabolic risk factors: A cross-sectional comparison between Dutch and Japanese data from two large biobank studies

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#### ABSTRACT

*Background and aims:* Few studies have examined and compared spousal concordance in different populations. This study aimed to quantify and compare spousal similarities in cardiometabolic risk factors and diseases between Dutch and Japanese populations.

*Methods*: This cross-sectional study included 28,265 Dutch Lifelines Cohort Study spouse pairs (2006–2013) and 5,391 Japanese Tohoku Medical Megabank Organization (ToMMo) Cohort Study pairs (2013–2016). Spousal similarities in cardiometabolic risk factors were evaluated using Pearson's correlation or logistic regression analyses adjusted for spousal age.

*Results*: The husbands' and wives' average ages in the Lifelines and ToMMo cohorts were 50.0 and 47.7 years and 63.2 and 60.4 years, respectively. Significant spousal similarities occurred with all cardiometabolic risk factors and diseases of interest in both cohorts. The age-adjusted correlation coefficients ranged from 0.032 to 0.263, with the strongest correlations observed in anthropometric traits. Spousal odds ratios [95% confidence interval] for the Lifelines vs. ToMMo cohort ranged from 1.45 (1.36–1.55) vs. 1.20 (1.05–1.38) for hypertension to 6.86 (6.30–7.48) vs. 4.60 (3.52–6.02) for current smoking. An increasing trend in spousal concordance with age was observed for sufficient physical activity in both cohorts. The Dutch pairs showed stronger similarities in anthropometric traits and lifestyle habits (smoking and drinking) than their Japanese counterparts.

*Conclusions:* Spouses showed similarities in several cardiometabolic risk factors among Dutch and Japanese populations, with regional and cultural influences on spousal similarities.

and environment) and their interactions [2-6].

glucose tolerance, left ventricular hypertrophy, and low levels of highdensity lipoprotein-cholesterol (HDL-C) are associated with coronary

heart disease [1]. These cardiometabolic risk factors are determined by

genetic and environmental factors (e.g., lifestyle, socioeconomic factors,

#### 1. Introduction

Traditional risk factors for cardiovascular diseases have been explored in many previous epidemiological studies. A previous study showed that hypertension, high cholesterol levels, smoking, impaired

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Moreover, they were reported to be clustered in spouses. A longitudinal study on the association between spousal relationships and obesity showed that if one spouse became obese, the other spouse was also 37% more likely to become obese [7]. Thus, obesity incidence may increase through spousal relationships, indicating that interventions or preventative measures may be more effective if targeted at both spouses rather than at individuals.

Spousal concordance may be explained by assortative mating and cohabitation effects [8]. Assortative mating is the tendency of people to select mates who bear greater similarities in characteristics, such as discernible traits and behaviors (phenotypic assortment), or social and environmental factors (social homogamy). This causes an initial similarity between spouses. Cohabitation effects could be attributed to common environmental factors shared by couples or "partner interaction effects," with partners influencing each other's behavior [9–11]. If concordance is mainly attributed to a cohabitation effect, then it should increase with the partnership duration.

Observational studies have explored spousal similarities in cardiometabolic risk factors, such as blood pressure (BP) [12–18], cholesterol level [13–15,17,18], triglycerides (TG) level [13,15,17], abnormal glucose tolerance [12,13,15–20], and smoking [14,19]. Further, a 2008 meta-analysis, showed statistically significant positive spousal concordances for the main coronary risk factors, such as hypertension and diabetes [21]. However, relatively small sample sizes in many previous studies may have led to insufficient statistical power in identifying moderate spousal similarities for some risk factors. Although some studies had large sample sizes [22,23], they assessed single populations, and none of them compared European and Asian populations.

Therefore, we aimed to quantify and compare the spousal similarities of multiple cardiometabolic risk factors in European and Asian populations from the large-scale Lifelines (Netherlands) and Tohoku Medical Megabank Organization (ToMMo) (Japan) cohorts, collectively including over 30,000 pairs. The examined cardiometabolic risk factors included anthropometric traits, BP, glycated hemoglobin, lipid traits, lifestyle habits, and cardiometabolic diseases, such as hypertension, type 2 diabetes (T2DM), and metabolic syndrome (MetS). We expected to observe positive spousal concordance for these factors in both populations and we examined whether their similarity differed among the Dutch and Japanese populations.

#### 2. Materials and methods

#### 2.1. Participants

#### 2.1.1. Lifelines

The Lifelines cohort study (hereafter referred to as Lifelines) [24] is a multi-disciplinary prospective population-based cohort study examining in a unique three-generation design the health and health-related behaviours of 167,729 persons living in the North of the Netherlands. It employs a broad range of investigative procedures in assessing the biomedical, socio-demographic, behavioural, physical and psychological factors which contribute to the health and disease of the general population, with a special focus on multi-morbidity and complex genetics. Between 2006 and 2013, eligible participants aged 20–50 years, were invited by their general practitioners to participate in the study; subsequently, their family members were also invited. In total, 167,729 participants were included at baseline. All participants signed informed consent forms, and the study was approved by the medical ethical committee of the University Medical Center Groningen, the Netherlands.

Spouses (married or in a registered partnership) were identified in Lifelines using the Dutch municipal population register. The reference day of the partner identification was January 1, 2014. Relationships registered after or those ended before this date were excluded. This study included all spouses of the opposite sex, aged  $\geq$ 20 years.

#### 2.1.2. Tohoku Medical Megabank Organization (ToMMo)

The Great East Japan Earthquake and the resulting tsunami of March 11, 2011 caused devastating damage to the Pacific coast of the Tohoku region. The Tohoku Medical Megabank (TMM) Project was launched to plan creative reconstruction and solve medical problems in the aftermath of this disaster. TMM Community-Based Cohort Study (TMM CommCohort Study) is a large-population-based cohort study conducted in the northern Japan, and the details of each cohort were published previously [25,26]. In the TMM CommCohort Study (hereafter referred to as ToMMo) the participants were recruited from May 2013 to March 2016 at baseline using two approaches. They were recruited at the sites of the annual community health examinations, which were conducted for insured persons aged 40-74 years. Additionally, seven "Community Support Center" facilities were established in the Miyagi Prefecture for voluntary admission-type recruitment and health assessment of participants. The Ethics Committee of ToMMo, Tohoku University (Sendai, Japan) reviewed and approved this study protocol (2018-4-021). All participants provided informed consent to the TMM Project.

Patients aged  $\geq 20$  years who lived in Miyagi Prefecture were included. Self-administered family relationship questionnaires were distributed and collected in this study. If a participant's spouse described in the family relationship was identified in the TMM CommCohort Study, then the spouse and the participant were defined as a spouse pair.

#### 2.2. Data collection and variables

Data on a series of cardiometabolic risk factors were collected for both cohorts, including anthropometric traits (height, weight, waist circumference and body mass index (BMI), systolic (SBP) and diastolic BP (DBP), glycated hemoglobin (HbA1c), lipid traits (total cholesterol [TC], TG, HDL-C, and low-density lipoprotein-cholesterol [LDL-C]), and lifestyle factors. Cardiometabolic diseases, such as hypertension, T2DM, and MetS were defined based on the collected data.

#### 2.2.1. Continuous risk factors

Height, weight, and waist circumference of the participants were measured by well-trained staff in the Lifelines and ToMMo cohorts. BMI was calculated as the weight (kg) divided by the height (m) squared. BP was measured using an automated DINAMAP Monitor (GE Healthcare, Chicago, IL, USA) in Lifelines and using a digital automatic BP monitor (HEM-9000AI; Omron Healthcare Co., Ltd, Kyoto, Japan) in ToMMo. In both Lifelines and ToMMo, blood samples were collected using a standard protocol; then, HbA1c and lipid traits including TC, TG, HDL, and LDL were measured.

#### 2.2.2. Lifestyle factors

Lifestyle habits of smoking, drinking, and engagement in physical activity were defined according to the self-reported questionnaires. Smoking was categorized into current smoker, ex-smoker, or non-smoker. Drinking was categorized into current or non-drinker. Regarding physical activity, metabolic equivalent (MET) hours/day was calculated by multiplying the MET score for a specific activity by hours per day spent on that activity. Because different activities were included in Lifelines and ToMMo, we used the 80th percentile of the husband's MET hours/day in each cohort as a cutoff to make the definition more comparable between the two cohorts. Then, we divided physical activity into two categories: (1) sufficiently active and (2) inactive ( $\geq$ 80th and <80th percentile of husband's MET hours/day, respectively).

#### 2.2.3. Diseases

Hypertension was defined based on SBP  $\geq$ 140 mmHg, DBP  $\geq$ 90 mmHg, or the use of antihypertensive medication. Diabetes was defined based on fasting glucose level  $\geq$ 126.0 mg/dL, HbA1c  $\geq$  6.5%, or the use of blood glucose-lowering medication in Lifelines and ToMMo.

Slightly different definitions were adopted for MetS in the two cohorts to accommodate the different populations. In Lifelines, participants with three or more of the following five criteria were defined as having MetS [27]: 1) a waist circumference  $\geq$ 102 cm in men and  $\geq$ 88 cm in women; 2) SBP ≥130 mmHg, DBP ≥85 mmHg, and/or use of antihypertensive medication; 3) fasting blood glucose level  $\geq$  5.6 mmol/L, use of blood glucose-lowering medication, and/or a diagnosis of T2DM; 4) HDL-C levels <1.03 mmol/L in men and <1.30 mmol/L in women and/or the use of lipid-lowering medication; and 5) TG levels >1.70 mmol/L and/or use of TG-lowering medication. In ToMMo, participants were defined as having MetS if they met the first criterion and at least two of the following criteria [28]: 1) a waist circumference >85 cm in men and >90 cm in women; 2) high BP (SBP >130 mmHg, DBP  $\geq$  85 mmHg, or use of antihypertensive medication); 3) high glucose (HbA1c > 6.0% or the use of blood glucose-lowering medication); and 4)high TG/HDL-C (TG levels >1.68 mmol/L [150 mg/dL] or HDL-C <1.03 mmol/L [40 mg/dL], or use of lipid-lowering medication).

More details on the measurements in the Lifelines and ToMMo cohorts are given in Supplementary Methods.

#### 2.3. Statistical analyses

All analyses were performed separately for the Lifelines and ToMMo cohorts because we intended to compare the results between these two cohorts from populations with very different cultures and lifestyle habits.

For continuous variables, simple and age-adjusted Pearson's correlation coefficient was used to calculate spousal correlation. Prior to calculating spousal correlations, TG was  $log_{10}$ -transformed as it was not normally distributed. Values of SBP, DBP, TC, and LDL for those using antihypertensive and/or lipid lowering medication were adjusted to reconstruct the original population ranking of these individuals based on expected treatment effects. For those undergoing hypertension treatment, 15 and 10 mmHg were added to the SBP and DBP, respectively [29]. For participants being treated for hyperlipidemia, values for TC and LDL were divided by 0.8 and 0.7, respectively [30,31]. Individuals with diabetes were excluded when analyzing HbA1C. Outliers (>mean + 5 standard deviation [SD] or < mean -5 SD) were excluded for all traits.

For categorical variables, logistic regression analyses were performed to calculate spousal concordance. Odds ratios (ORs) and 95% confidence intervals (CIs) of risk to the husbands were calculated for current smoking, current drinking, and sufficient physical activity. The presence of diseases with the occurrences in their respective wives was considered to be exposure. To adjust for age in the analyses, two new covariates were calculated: the average age of each spouse and the age difference between the spouses. ORs >1.0 indicated higher degrees of concordance for spouse pairs.

As secondary analyses, the aforementioned correlational and logistic regression analyses were performed according to the age groups of the husbands (20–39, 40–59, 60–69, and  $\geq$ 70 years) for two purposes: 1) to compare spousal similarities within the same age groups between the two cohorts because participants' age distributions differed in the two cohorts; and 2) to explore potential changes in spousal similarities with age, which roughly represented marriage duration (the correlation between the age of the husband and marriage duration was 0.866 in the Lifelines cohort).

For every variable, analyses were conducted in the spouse pairs, for husbands and wives with valid values. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and R version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria) in the ToMMo and Lifelines cohorts, respectively.

#### 3. Results

#### 3.1. Basic characteristics in ToMMo and lifelines

In Lifelines, among the 167,729 participants, 28,265 couples were included for the analyses after excluding 142 same-sex couples and three couples aged <20 years. In ToMMo, 76,958 people were asked to participate in the survey. Of these, 54,952 agreed to participate. Among them, 5,391 spousal pairs were identified using family relationship questionnaires.

Table 1 shows the characteristics of the two cohort studies. The participants of ToMMo were older than those of Lifelines. In ToMMo, the mean ages were 63.2 and 60.4 years for husbands and wives, respectively, and approximately two-thirds of the participants were aged  $\geq$ 60 years. In Lifelines, the average age for husbands and wives were 50.0 and 47.7 years, respectively, and the majority were aged between 40 and 59 years. The presence of hypertension, diabetes, and MetS was higher in the ToMMo than in the Lifelines cohort. In both cohorts, the proportions of current smokers, ever smokers, and current drinkers were higher in husbands than in wives; however, these differences were larger in ToMMo.

#### 3.2. Spousal similarities in cardiometabolic risk factors

Tables 2 and 3 show the spousal correlations and concordances of cardiometabolic risk factors in the two cohorts. Figs. 1 and 2 show these spousal similarities by age group in the two cohorts (see Supplementary Tables S1 and S2). The correlation coefficients of the husbands' and wives' ages were >0.9 in both Lifelines and ToMMo cohorts.

#### 3.2.1. Continuous risk factors

Age-adjusted correlation coefficients for anthropometric traits ranged from 0.205 to 0.263 in Lifelines and from 0.110 to 0.175 in ToMMo. Spousal correlations for anthropometric traits in Lifelines were stronger than those in ToMMo in every age group. Regarding BMI, an increasing trend of spousal correlation with age was observed in Lifelines but not in ToMMo (Fig. 1).

In both cohorts, spousal correlations of BP and HbA1c decreased considerably after adjusting for the age of spouses (ranges, 0.080–0.123 and 0.073–0.098 in Lifelines and ToMMo, respectively). Regarding SBP and DBP, the oldest ( $\geq$ 70 years) and youngest (20–39 years) age groups in Lifelines and ToMMo, respectively, showed the strongest correlations (Fig. 1).

Age-adjusted correlation coefficients for lipid traits ranged from 0.032 to 0.106 in Lifelines and 0.095 to 0.129 in ToMMo. No clear trend in spousal correlations with age was observed in Lifelines or ToMMo for any lipid traits (Fig. 1).

The strength of spousal correlations varied in risk factors. Overall, spousal correlations for anthropometric traits were stronger than BP, HbA1c, and lipid traits.

#### 3.2.2. Lifestyle factors

Current smoking showed strong spousal concordances in Lifelines (age-adjusted OR = 6.86, 95% CI: 6.30–7.48) and ToMMo (age-adjusted OR = 4.60, 95% CI: 3.52–6.02). Moreover, changes in smoking habits also showed similarity among spouses; thus, compared with a never-smoking husband, an ever-smoking husband was more likely to have a former-smoking wife (OR = 2.59 in Lifelines and OR = 2.56 in ToMMo). For current drinkers, spousal ORs were larger in the Lifelines (age-adjusted OR = 5.14, 95% CI: 4.70–5.61) than in the ToMMo (age-adjusted OR = 2.83, 95% CI: 2.39–3.35) cohort. Spousal concordances for sufficient physical activity were comparable between the Lifelines (age-adjusted OR = 2.14, 95% CI: 1.96–2.35) and ToMMo (age-adjusted OR = 2.76, 95% CI: 2.28–3.32) cohorts. In both cohorts, the spousal ORs showed U-shapes with increasing age for current smoking and an increasing trend with age for sufficient physical activity (Fig. 2).

#### Table 1

Characteristics of the Lifelines and ToMMo cohorts.

	Lifelines Cohort Study		ToMMo Community-based Cohort Study			
	Number of couples	Husband	Wife	Number of couples	Husband	Wife
General characteristics (n, %)						
Age, years (mean $\pm$ SD)	28,265	50.0 (11.6)	47.7 (11.6)	5,391	63.2 (10.5)	60.4 (10.2)
Age group (years)						
20–39		5,102 (18.1%)	6,950 (24.6%)		293 (5.4%)	346 (6.4%)
40–59		16,590 (59.7%)	16,047 (56.8%)		931 (17.3%)	1,373 (25.5%)
60–69		4,959 (17.5%)	4,246 (15.0%)		2,678 (49.7%)	2,995 (55.6%)
≥70		1,614 (5.7%)	1,022 (3.6%)		1,489 (27.6%)	677 (12.6%)
Education (university or graduate school)	26,938	1,746 (6.5%)	1,133 (4.2%)	5,254	1,295 (24.6%)	373 (7.1%)
Education level	26,938			5,254		
Low		8862 (32.9%)	8957 (33.3%)		643 (12.2%)	443 (8.4%)
Medium		9,776 (36.3%)	10823 (40.2%)		3,141 (59.8%)	3,884 (73.9%)
High		8,300 (30.8%)	7158 (26.6%)		1,470 (28.0%)	927 (17.6%)
Risk factors (mean $\pm$ SD)						
Weight, kg	28,241	88.8 (12.8)	74.6 (13.6)	5,390	66.5 (9.6)	54.1 (8.7)
Height, cm	28,242	182.2 (7.0)	169.0 (6.5)	5,391	166.7 (6.0)	154.3 (5.6)
Waist circumference	28,241	96.6 (10.1)	87.6 (11.9)	3,183	85.6 (8.2)	81.9 (9.2)
Body mass index, $kg/m^2$	28,241	26.7 (3.5)	26.1 (4.6)	5,198	23.9 (3.0)	22.7 (3.5)
SBP (mmHg)	28,236	131.4 (14.6)	123.3 (15.9)	5,106	129.7 (16.3)	125.9 (17.7)
DBP (mmHg)	28,236	77.7 (9.2)	72.2 (8.8)	5,106	78.9 (10.6)	75.2 (10.6)
HbA1c (%)	26,962	5.6 (0.5)	5.6 (0.4)	5,373	5.6 (0.6)	5.6 (0.5)
Total cholesterol (mg/dL)	27,244	202.2 (38.3)	198.4 (39.1)	1,964	201.5 (33.5)	213.7 (35.9)
Triglycerides (mg/dL)[IQR]	27,244	103.6	78.0	5,384	126.9	102.3
	27,211	[75.3–147.9]	[58.5–108.1]	0,001	[75.0–151.0]	[64.0-121.0]
HDL-cholesterol (mg/dL)	27,244	51.0 (12.4)	63.0 (15.5)	5,384	57.0 (14.5)	66.5 (15.5)
LDL-cholesterol (mg/dL)	27,238	134.2 (34.8)	123.7 (35.2)	3,191	118.9 (29.8)	128.1 (30.4)
Lifestyle factors (n, %)	27,200	10 112 (0 110)	12017 (0012)	0,151	11015 (2510)	12011 (0011)
Current smoker	24,311	3,771 (15.5%)	2,776 (11.4%)	5,313	1,104 (20.8%)	248 (4.7%)
Ever smoker	24,311	13,800 (56.8%)	11,514 (47.4%)	5,313	3,170 (59.7%)	918 (17.3%)
Current drinker	26,087	23,697 (90.8%)	18,877 (72.4%)	5,356	4,201 (78.4%)	2,187 (40.8%)
Sufficient physical activity ( $\geq$ 80th percentile of	19,365	3,873 (20.0%)	2658 (13.7%)	5,342	1,074 (20.1%)	2,187 (40.8%) 549 (10.3%)
husband's METs)	19,303	3,873 (20.0%)	2038 (13.7%)	3,342	1,074 (20.1%)	549 (10.5%)
Diseases (n, %)						
Hypertension	28,236	10,011 (35.5%)	6,797 (24.1%)	4,260	2,411 (56.6%)	1,770 (41.6%)
Type 2 diabetes	26,001	1,392 (5.4%)	920 (3.5%)	3,469	504 (14.5%)	246 (7.1%)
Metabolic syndrome	25,955	6,971 (26.9%)	4,329 (16.7%)	3,770	1,565 (41.5%)	1,026 (27.2%)

ToMMo, Tohoku Medical Megabank Organization; SD, standard deviation; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MET, metabolic equivalent.

#### Table 2

Spousal correlations of cardiometabolic risk factors in the Lifelines and ToMMo cohorts.

Risk factors	Lifelines Cohort Study		ToMMo Community-based Cohort Study		
	Simple correlation (95% CI)	Age-adjusted correlation (95% CI)	Simple correlation (95% CI)	Age-adjusted correlation (95% CI)	
Age	0.955 (0.954–0.956)		0.934 (0.930–0.937)		
Weight	0.224 (0.212-0.235)	0.225 (0.214-0.236)	0.119 (0.092-0.145)	0.110 (0.084-0.137)	
Height	0.268 (0.257-0.278)	0.205 (0.194-0.216)	0.297 (0.272-0.321)	0.175 (0.149-0.201)	
Waist circumference	0.293 (0.282-0.303)	0.263 (0.252,0.274)	0.132 (0.098-0.166)	0.126 (0.092-0.160)	
Body mass index	0.257 (0.246-0.268)	0.248 (0.237-0.259)	0.134 (0.107-0.161)	0.136 (0.109-0.163)	
SBP	0.256 (0.245-0.267)	0.123 (0.111-0.134)	0.163 (0.136-0.190)	0.086 (0.059-0.113)	
DBP	0.151 (0.140-0.162)	0.086 (0.074-0.097)	0.094 (0.067-0.122)	0.073 (0.046-0.100)	
HbA1c (%)	0.204 (0.192-0.216)	0.098 (0.085-0.110)	0.139 (0.110-0.167)	0.080 (0.051-0.109)	
Total cholesterol	0.114 (0.102-0.126)	0.050 (0.039-0.062)	0.074 (0.030-0.118)	0.101 (0.057-0.145)	
Triglycerides	0.093 (0.081-0.104)	0.093 (0.081-0.105)	0.109 (0.083-0.136)	0.129 (0.102-0.155)	
HDL-cholesterol	0.119 (0.107-0.130)	0.106 (0.094-0.118)	0.098 (0.071-0.124)	0.100 (0.073-0.126)	
LDL-cholesterol	0.085 (0.073–0.096)	0.032 (0.020–0.044)	0.084 (0.050-0.119)	0.095 (0.060–0.129)	

ToMMo, Tohoku Medical Megabank Organization; CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

#### 3.2.3. Diseases

In both cohorts, significant spousal similarities for hypertension and T2DM were observed; however, these decreased considerably after adjusting for age in spouses. Men were at increased risk of hypertension if their wives had the same disease in both Lifelines (OR = 1.45, 95% CI: 1.36–1.55) and ToMMo (OR = 1.20, 95% CI: 1.05–1.38) cohorts. Spousal ORs for T2DM were 1.59 (95% CI: 1.29–1.94) in Lifelines, whereas they became borderline insignificant in ToMMo (OR = 1.34, 95% CI: 0.96–1.83).

Spousal concordance for MetS was similar in Lifelines and ToMMo. Husbands whose wives had MetS were  $\sim$ 70% more likely to have MetS compared with those whose wives did not have MetS (Lifelines: age-adjusted OR = 1.77, 95% CI: 1.65–1.90; ToMMo: age-adjusted OR = 1.72, 95% CI: 1.47–2.02).

Spousal concordance showed a decreasing trend with age for all diseases in Lifelines, whereas no clear trend was observed in ToMMo (Fig. 1).

#### Table 3

Spousal concordance of lifestyle factors and diseases in the two cohorts.

	Lifelines Cohort Study		ToMMo Community-based Cohort Study		
	Crude odds ratio (95% CI)	Age-adjusted odds ratio (95% CI)	Crude odds ratio (95% CI)	Age-adjusted odds ratio (95% CI)	
Smoking					
Current smoker	7.05 (6.47–7.67)	6.86 (6.30-7.48)	5.61 (4.33-7.30)	4.60 (3.52-6.02)	
Ever smoker	2.77 (2.63-2.92)	2.59 (2.45-2.73)	2.39 (1.94-2.98)	2.56 (2.06-3.20)	
Alcohol drinking					
Current drinker	5.09 (4.66-5.56)	5.14 (4.70-5.61)	2.76 (2.30-3.31)	2.83 (2.39–3.35)	
Sufficient physical activity	2.36 (2.16-2.58)	2.14 (1.96-2.35)	2.76 (2.28-3.32)	2.76 (2.28-3.32)	
Diseases					
Hypertension	2.74 (2.59-2.90)	1.45 (1.36–1.55)	1.75 (1.54–1.98)	1.20 (1.05–1.38)	
Type 2 diabetes	3.02 (2.47-3.65)	1.59 (1.29–1.94)	1.78 (1.29-2.42)	1.34 (0.96–1.83)	
Metabolic syndrome	2.51 (2.35-2.69)	1.77 (1.65–1.90)	2.15 (1.85-2.50)	1.72 (1.47-2.02)	

ToMMo, Tohoku Medical Megabank Organization; CI, confidence interval.

#### 3.2.4. Sensitivity analyses

Spousal similarities for continuous risk factors, lifestyle factors, and diseases were robust against adjustment for education. Only after additional adjustment for BMI, spousal similarities of waist circumference, triglycerides, and diseases attenuated in both Lifelines and ToMMo, but mostly remained significant (Supplementary Tables S3 and S4).

#### 4. Discussion

In this international collaborative large sample study from the Netherlands and Japan, we found significant spousal similarities for all cardiometabolic risk factors including continuous risk factors, lifestyle habits, and diseases. Dutch couples showed stronger similarities in anthropometric traits and lifestyle habits (current smoking and drinking) compared with the Japanese couples.

Regarding continuous risk factors, age-adjusted correlation coefficients ranged from 0.032 (LDL-cholesterol for Lifelines) to 0.263 (Waist circumference for Lifelines), with the strongest correlations in anthropometric traits. The magnitude of these correlations was consistent with that reported in the literature. Similar spousal correlations (adjusted for age) were reported in a 2008 meta-analysis for anthropometric traits (weight, BMI, and waist circumference), BP (SBP and DBP), and lipid traits (HDL, LDL, TC, and TG) [21] (Supplementary Table S5). Two other meta-analyses have suggested that people are more likely to have hypertension (OR = 1.41) and diabetes (OR = 1.26) if their spouses have the same diseases [32,33]. A study of Korean spouses also found significant spousal concordance for MetS [13]. Regarding lifestyle factors, spousal similarities for smoking, drinking, and physical activity were observed in European and Asian populations [11,22]. Our research, along with previous studies, supported spousal similarities for several cardiometabolic risk factors in diverse populations regardless of region, ethnicity, or culture.

However, the strength of spousal concordance may differ among populations for some factors. Earlier studies found 79.7% agreement for current smoking between spouses in a large Dutch sample [34] and 39.2% agreement in a large study of Chinese couples [22]. Moreover, Dutch couples showed stronger similarities for anthropometric traits, current smoking, and drinking than Japanese couples in all age groups. Interestingly, 20.8% and 4.7% of Japanese husbands and wives were current smokers, respectively, compared with 15.5% and 11.4% in the Dutch sample. Thus, the prevalence of current smoking and drinking was similar across the sexes in the Dutch population. This may partly explain the stronger spousal concordance for current smoking and drinking in the Lifelines cohort, as revealed by Roberts et al. who stated that spousal concordance becomes stronger with narrower female vs. male differences in the prevalence of alternative tobacco products usage [35]. Further, differences between Western and Eastern cultures may partly explain why the degree of spousal similarity for some factors differed between the Dutch and Japanese populations, as cultural factors

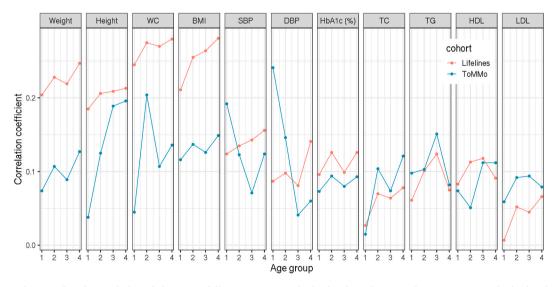
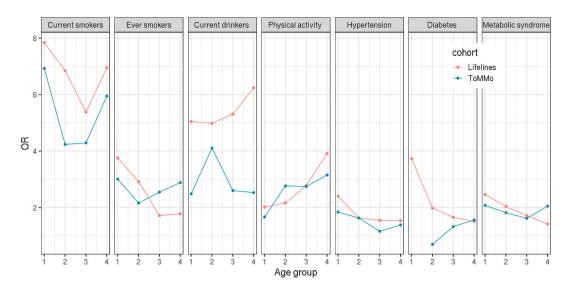


Fig. 1. Spousal correlations of cardiometabolic risk factors in different age groups for husbands in the two cohorts. Age groups for husbands: 1) 20–39 years, 2) 40–59 years, 3) 60–69 years, and 4)  $\geq$ 70 years. WC, waist circumference; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; TC, total cholesterol; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ToMMo, Tohoku Medical Megabank Organization.



**Fig. 2.** Spousal concordances in cardiometabolic risk factors (lifestyle factors and diseases) in different age groups for husbands in the two cohorts. Age groups for husbands: 1) 20–39 years, 2) 40–59 years, 3) 60–69 years, and 4)  $\geq$ 70 years. The OR for diabetes for the 20–39-year age group in ToMMo could not be calculated because of the small number of cases.

ToMMo, Tohoku Medical Megabank Organization; OR, odds ratio.

may have influenced lifestyle habits and attitudes toward mate selection.

Consistent with the findings of a previous study in Korea [19], the magnitude of concordance differed by age group in our study, especially for physical activity and current smoking. As the husbands' ages can be considered a proxy for marriage duration, this difference by age group may indicate differential effects of assortative mating and cohabitation on spousal similarity. We observed an increasing trend of spousal concordance with age for sufficient physical activity in both cohorts, which suggested a contribution of cohabitation effects. This finding was consistent with those of previous studies, which generally supported cohabitation effects on exercise [11,36,37]. Over the course of their relationship, spouses may have a similar performance of physical activity because of some shared environmental factors (e.g., access to resources for exercise) and spousal interaction. Unlike physical activity, regarding current smoking, the youngest age group (20-39 years) showed the strongest concordance between pairs in both cohorts, suggesting that assortative mating may account for the spousal resemblance in smoking habits. This finding was in line with an earlier evidence. Ask et al. found a high similarity between future couples in smoking, before marriage, suggesting a high level of non-random mating [11]. A recent study in a Dutch population revealed the underlying mechanism in phenotypic assortment, that is, individuals more often choose a spouse with similar smoking habits [34]. We noticed that the oldest age group (≥70 years) showed the second strongest spousal concordance for current smoking. Further analyses showed a declined percentage of pairs of current smokers with age, while the percentage of spouse pairs who were non-smokers increased with age (Supplementary Table S6). Therefore, the high concordance level for current smoking in the oldest age group was caused by the increase in the proportion of concordant non-smoker couples.

Moreover, partner selection based on phenotypic similarity (i.e., positive assortative mating) may also generate genetic similarity between spouses. Robinson et al. confirmed this and found evidence for genetic correlations among partners for height, BMI, waist-to-height ratio, BP, and educational attainment [38]. Thus, phenotypic similarities between spouses may be partly explained by these underlying genetic similarities.

Interestingly, given the large sample size of our study, even small effects would be statistically significant. Thus, we did not define statistical significance based on *p*-value thresholds and we admit that some

small effect sizes (e.g., the spousal correlation of 0.032 for LDL in the Lifelines cohort) may not be very meaningful clinically although magnitudes of our spousal correlations are in line with the findings of a previously published meta-analysis (Supplementary Table S5). Furthermore, spousal similarities for diseases and lifestyle factors, which are expressed as ORs, might be helpful in terms of clinical relevance and prevention.

In this study, the spousal concordance for cardiometabolic risk factors was quantified, suggesting that prevention and interventions targeted at pairs rather than at individuals may be more effective [39]. For example, a randomized controlled trial focusing on the weight loss effect of exercise training reported a significant effect of weight reduction for both spouses [40]. In the future, it may become increasingly important to explore the effects of spouse-specific interventions.

To our knowledge, this is the first study to explore and compare spousal similarities in two populations (European and Asian). The similarities and differences in the spousal resemblance between the two populations provide a new dimension to the study of concordance between spouse pairs. Additionally, the large sample size (28,265 spouses in Lifelines and 5,391 pairs in ToMMo) helped us obtain stable and accurate estimates. Besides, our study analyzed a comprehensive number of cardiometabolic risk factors, thus, improving the understanding of spousal similarities for major cardiovascular risk factors. Moreover, the detailed analyses of similarities between spouse pairs were conducted according to the age group, and the results may help design future intervention trials.

There were some limitations to this study. First, marriage duration was not measured in ToMMo; therefore, we could not investigate the relationship between this factor and spousal similarity. However, we used the husbands' ages as a surrogate because it was found to be highly correlated with marriage duration in Lifelines. Second, because this was a cross-sectional design study using only baseline data of two cohorts, we could not clearly distinguish effects of cohabitation and assortative mating. However, we could compare concordances in different age groups as an indication of the potential effect of different marriage durations. Third, participants who undergo health check-ups may have higher health consciousness compared to those who do not [41], which could have caused a volunteer bias in our study. However, it is unlikely to be a major concern, as Lifelines has been shown to be broadly representative of the general Dutch population [42]. Fourth, the self-report measures of lifestyle behaviors were subject to reporting and recall bias. For example, a participant may underreport smoking and drinking because of attitudes, beliefs, and cultural context. The latter would influence our estimations of spousal similarities if men and women have different underreporting rates.

In conclusion, this international collaborative study identified significant spousal similarities for a wide variety of cardiometabolic risk factors in Dutch and Japanese populations. Differences in the strength of spousal similarities for some risk factors between populations clearly indicated regional and cultural influences on spousal resemblance. Our study provides a basis for preventive strategies and interventions targeting spouses, rather than individuals. Future studies are needed to evaluate the effectiveness of couple-based interventions to simultaneously reduce the cardiovascular risk of both spouses.

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#### CRediT authorship contribution statement

Naoki Nakaya: Methodology, Formal analysis, Writing – original draft. Tian Xie: Methodology, Formal analysis, Writing – original draft. Bart Scheerder: Methodology, Writing – original draft. Naho Tsuchiya: Writing – original draft. Akira Narita: Writing – original draft. Tomohiro Nakamura: Writing – original draft. Hirohito Metoki: Writing – original draft. Taku Obara: Writing – original draft. Mami Ishikuro: Writing – original draft. Atsushi Hozawa: Methodology, Writing – original draft. Harold Snieder: Writing – original draft, managers of this study. Shinichi Kuriyama: Writing – original draft, managers of this study.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.atherosclerosis.2021.08.037.

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