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Dog ownership and Cardiovascular Risk Factors: a nationwide prospective register-based cohort study

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Abstract (297 words; max 300)

Objective: To study the association between dog ownership and cardiovascular risk factors.

Design: A nationwide register–based prospective cohort study with a cross-sectional study in a subset of the population. Participants were followed up from October 1st, 2006 to December 31st, 2012.

Setting: A cohort of 2,026,865 participants was identified from the Register of the Total Population and linked to other national registers for information on dog ownership, hospital admissions, socio-economic status and country of birth. Participants were followed up to medication for a cardiovascular risk factor, emigration, death or at the end of the study on December 31st, 2012. Cross-sectional associations were further assessed in 10,110 individuals from TwinGene.

Participants: All Swedish residents aged 45-80 years on October 1st, 2006.

Main outcome measures: Initiation of treatment for hypertension, dyslipidemia and diabetes mellitus.

Results

The results indicated slightly higher likelihood of initiating anti-hypertensive (HR, 1.02; 95% CI, 1.01-1.03) and lipid-lowering treatment (HR, 1.02; 95% CI, 1.01-1.04) in dog owners than in non-owners, particularly amongst those aged 45 to 60 and in those owning mixed breed or companion/toy breed dogs. No association of dog ownership with initiation of treatment for diabetes was found in the overall analysis (HR, 0.98; 95% CI, 0.95-1.01). Sensitivity analyses in the TwinGene cohort indicated confounding from factors not available in the national cohort, such as employment status and non-CVD chronic disease status.

Conclusions

In this large cohort study, dog ownership was not associated with any large reduction in initiation of medication for classical cardiovascular risk factors, implying that the previously reported lower risk of cardiovascular mortality among dog owners in this cohort is not explained by reduced hypertension and dyslipidemia.

Strengths and limitations of this study

- This is the largest study to date to examine the impact of dog ownership on cardiovascular risk factors
- The nationwide register-based cohort study with a cross-sectional investigation in a twin registry with a vast array of lifestyle and clinical variables strengthens the results
- The main outcome measures were extracted from nationwide registers thus decreasing the risk of recall and selection bias.
- Misclassification of dog ownership, particularly in the twin register, may have led to some loss of power.
- Some important confounding factors were not available in the national data

Introduction

There is a growing interest in pet ownership as a possible intervention to enhance cardiovascular health and well-being.[1 2] We recently observed that being registered as a dog owner was associated with a lower risk of cardiovascular and all-cause mortality in the general Swedish population (n=3,432,153).[3] Any causal association of dog ownership with lower cardiovascular mortality could potentially be mediated through increased physical activity or through the psychological benefits of companionship, which could in turn reduce other important cardiovascular risk factors such as blood pressure, adiposity, dyslipidemia, and insulin resistance. An alternative explanation could be confounding by socioeconomic, cultural, demographic or psycho-social factors. A large number of cross-sectional and longitudinal studies across different countries support the association of dog ownership with physical activity;[1] however, reports regarding the association of dog ownership with other cardiovascular risk factors are less consistent.[4-11] These inconsistences may be due to low statistical power in small studies, use of restricted or homogenous populations, inability to control for differences across breed of dogs, or simply an absence of effect. As dogs are reported to be more common in rural areas compared to urban areas,[12-14] as well as in households with children,[15 16] it is also important to account for these differences.

The aim of this study was to assess the association of dog ownership with three major clinical risk factors for cardiovascular disease, specifically initiation of treatment of hypertension, dyslipidemia and diabetes mellitus. We investigated this using data from national registers on dog ownership and drug prescriptions. We further sought to explore the association with other cardiovascular risk factors using cross-sectional data from a sub-cohort extracted from the Swedish Twin Registry containing detailed information from questionnaire data, physical examinations and laboratory measurements.

Methods

Design

The main analysis was based on a nationwide cohort study of Swedish residents aged 45-80 followed from October 1st 2006, to December 31st 2012. We additionally used cross-sectional data of participants (aged 47-80) in the TwinGene study, which is a sub-study of the Swedish Twin Registry (**Supplementary Figure 1)**.

Study Population – National Cohort

All Swedish residents (n=3,412,946) aged 45-80 on October 1st 2006, were identified through the Register of the Total Population. We excluded 11,298 individuals with unverified, re-used identification numbers or missing education information, and 137,306 additional individuals that had resided in Sweden for <15 years to ensure complete linkage to medical information and sufficient information regarding dog ownership in Sweden. We also excluded 531,658 individuals with a history of any CVD (International Classification of Disease (ICD)-9 codes 390-459 and ICD-10 I00-I99) or with a history of coronary artery bypass grafts or percutaneous coronary artery intervention medical procedure (Nordic surgical procedure codes FNA, FNC and FNG) from in- and outpatient data from the National Patient Register before October 1st, 2006. Inpatient data was available from 1987 and outpatient data from 2001. Further, using data from the Swedish Prescribed Drug Register, which covers all Swedish dispensed pharmacy prescriptions since it was established on July 1st 2005, individuals (n=705,819) were excluded if they had any recorded dispensed prescription of anti-hypertensive drugs, lipid-lowering drugs, or glucose lowering drugs from 15 months prior to baseline (which was when this register was initiated). Anti-hypertensive drugs were defined based on the Anatomical Therapeutic Chemical Classification System (ATC) as codes: C02 (antihypertensive drugs), C03A, C03EA01 (thiazide diuretics), C07 (beta receptor blockers, excluding sotalol [C07AA07]), C08C (selective calcium antagonists with mainly vascular effects) and C09 (agents acting on the renin-angiotensin system). Lipid-lowering drugs were defined as C10AA (statins), C10AB (fibrates), C10AC (bile acid sequestrants), C10AX (other lipid-modifying agents) and C10B (lipid-lowering drug combinations). Glucose-lowering drugs were defined as ATC-code A10A (insulin and analogues) and A10B (glucose-lowering drugs excluding insulin).

Study population – TwinGene

The TwinGene study originally included 12,614 (of 22,391 invited) twins from the "Screening Across the Lifespan Twin study" (SALT) and was conducted between April 2004 and December 2008 and included a visit to their local health center and blood sampling (**Supplementary Figure 2**).[17] The study-base "SALT" was a sub-study of the Swedish Twin Register in twins born before 1959 and who participated in a telephone-based questionnaire sub-study from March 1998 to March 2002[17] (**Supplementary Table 1).**

We performed a cross-sectional analysis of the association of dog ownership with cardiovascular risk factors in the TwinGene cohort (n=12,105). We excluded 1,373 individuals for having a previous history of CVD recorded in the National Patient Register.[18] We also excluded 622 individuals for having missing or incomplete data (**Supplementary Figure 1**).

Exposure

Dogs in Sweden are required to have a unique identifier (ear tattoo or implanted identity chip) and this is registered alongside their owner's unique personal identity number at the Swedish Board of Agriculture. All dogs sold as purebred are registered by the Swedish Kennel Club. We defined the variable 'dog ownership' in the national cohort as registered dog ownership or having a partner registered as a dog owner in either the Swedish Board of Agriculture and/or the Swedish Kennel Club, in a time-updated manner throughout the study period. The linkage to each respective partner (defined as a married couple, registered same-sex partnership or a cohabiting couple with common children) was possible through annual extracts from the Register of the Total Population.

In the TwinGene data, we did not have access to information on partners' dog ownership and only each person's own dog registrations were used. Dog ownership was defined at the date of inclusion in TwinGene.

If information on a dog's death was missing, we assumed a maximum lifespan of ten years. Where birth or registration dates were discrepant between the two registers, we randomly selected one of the two. We used the Swedish Kennel Club's definition of breed groups to categorize the 331 breeds into ten breed groups **(Supplementary Table 2)**. All non-purebred dogs and those of unknown breed were included in an additional mixed breed group. Where

owners had dogs of different breeds, we defined the breed based on the dog registered first and where owners had several dogs, we restricted ownership to three dogs.

Based on previous findings of owners to hunting dogs having a lower risk of cardiovascular events, we additionally defined a group of hunting dogs consisting of Terriers, Pointing, Scent Hounds and Retrievers for analysis.

Outcome

In the national cohort, time to first dispensed prescription of anti-hypertensive drugs, lipid-lowering drugs or glucose-lowering drugs after baseline was defined from data extracted from the drug register. Participants were censored at emigration, death or at the end of the study on December 31st, 2012. In the analysis of time to anti-hypertensive medication, individuals were additionally censored at a diagnosis of heart failure, unstable angina or acute myocardial infarction in the National Patient Register as the same drugs could be administered for their treatment.

Prevalent use of anti-hypertensive, lipid-lowering or glucose-lowering drugs was defined from the clinical questionnaire data collected during the TwinGene study. Cardiovascular risk factors measured and also used as outcomes in TwinGene included blood glucose, glycosylated hemoglobin A1c (HbA1c), high sensitive C-reactive protein (hsCRP), triglycerides, high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), waist-hip ratio, body mass index (BMI), systolic and diastolic blood pressure and mean arterial pressure (MAP) (**Supplementary methods**). Only fasting measurements of glucose and triglycerides were used (9,873 [97%] of all participants were fasting). hsCRP and triglycerides were transformed to the natural log scale before analysis to approach normality.

Statistical analyses

All statistical analyses were conducted using Stata version MP14.1 (StataCorp). Using age as a time-scale, separate multivariable Cox proportional hazards models were applied to assess the associations between dog ownership and time to initiation of anti-hypertensive, lipid-lowering and glucose-lowering drugs, respectively. Directed acyclic graphs were used to guide the choice of covariates (**Supplementary Figure 3).** A first crude model included age and sex, and a second model additionally included the region of birth, area of residence, level of education, marital status and income. A description of the covariates is provided in the

Supplementary methods. The proportional hazards assumption was verified by plotting Schoenfield residuals and log-log graphs. Results were reported as hazard ratios (HR) and 95% confidence intervals (CI).

We repeated the calculations using the breed group as exposure to examine possible breed group effects and we applied Bonferroni correction (for 11 breed groups) to control for multiple testing. Further analyses were stratified by age group, sex, and whether participants lived alone or not. Individuals considered as "living alone" did not have any spouse, partner with common children, or children living in the same household.

We conducted a sensitivity analysis where we excluded β-blockers as first line anti-hypertensive treatment to estimate the effect of changing treatment guidelines over the study period. In additional sensitivity analysis, in the lipid-lowering medication analysis, we assessed the effect of censoring participants at a diagnosis of heart failure, unstable angina or acute myocardial infarction in the National Patient Register.

Logistic regression was applied in TwinGene for the association of dog ownership with prevalent anti-hypertensive, lipid-lowering and blood-glucose lowering medication and linear regression for the association of dog ownership with continuous variables. In addition to adjusting for age, sex, presence of children in the household, area of residence, population density, marital status, latitude of residence and level of education, we added one covariate at a time to investigate their individual importance: tobacco use, occupational level, employment status, Charlson comorbidity index and disability. In all twin analyses, standard errors were adjusted with the robust sandwich estimator for dependent observations. For blood pressure and lipid levels, associations were further stratified by current medication.

Ethical approval

The regional ethical review board in Stockholm, Sweden, approved the study (national study: 2012/1114-31/2, with amendment 2013-1687-32; TwinGene: 2007/644-31/2 and 2016/1392-31/1).

Patient involvement

No patients were involved in the development, design or analysis of this study. The review board allowed the researchers to waive the requirement for obtaining informed consent in the national study. Participants in TwinGene provided written informed consent.

Results

National Cohort

The baseline characteristics of 2,026,865 Swedish residents are shown in **Table 1**. Dog ownership was directly registered in 189,355 (9.3%) at any time during the follow-up period, and this increased to 295,682 (14.6%) individuals when partners' registration were included. At baseline, the average age of dog owners was 50 years vs 53 years in non-owners. Dog owners were more likely to be married than non-owners (78% vs 60%) and more likely to live in low-density areas than non-owners (median: 49 vs 77 inhabitants per square kilometer). Compared to non-owners, mixed pedigree dog owners (n=32,003) were less likely to be married (59 %), were less likely to have a tertiary education (21%) and had fewer people in the top quintile for income (12.2%). Owners of hunting-type breeds showed similar characteristics to the overall dog owners.

Medication for cardiovascular risk factors

During 10,692,258 person-years of follow-up, dog ownership was associated with a 2% higher risk of initiation of anti-hypertensive drug medication in both crude and multivariable-adjusted analyses (HR, 1.02; 95% CI, 1.01-1.03). During 11,508,349 person-years of follow-up, there was a 2% higher risk of initiating lipid-lowering medication in the multivariable adjusted models (HR, 1.02; 95% CI, 1.01-1.04). During 12,207,964 person-years of follow-up, there was a lower risk of initiating glucose lowering drugs in dog owners in minimally adjusted models (HR, 0.91; 95% CI, 0.89-0.94), but on multivariable adjustment, the association was attenuated and non-significant (HR, 0.98; 95% CI, 0.95-1.01) (**Table 2)**.

Owners of "Companion/toy" breeds and of dogs of mixed pedigree were at higher risk of anti-hypertensive and lipid-lowering drug initiation compared to non-dog owners (**Table 3**). Owners of the Spitz/primitive breed types and the combined group of hunting breed types had lower risks of initiating glucose-lowering medication (HR, 0.83; 95% CI, 0.74-0.93 and HR, 0.92; 95% CI, 0.86-0.97 respectively) while owners of mixed pedigree dogs had higher risk of getting glucose-lowering medication (HR, 1.18; 95% CI, 1.09-1.27) **(Supplementary Figure 4)**.

There was no difference in strength of association when we excluded β-blockers as first-line treatment for anti-hypertension (**Supplementary Table 3)** or when censoring was done in those being investigated for lipid-lowering treatment initiation was made for angina, myocardial infarction or heart failure was conducted **(Supplementary Table 4)**.

In age-stratified analysis, there were some evidence of effect modification by age for both anti-hypertensive and lipid-lowering drugs where an increased risk was observed in those aged below 50 years (HR, 1.04; 95% CI, 1.01-1.08 and HR, 1.10; 95% CI, 1.04-1.15, respectively), with estimates gradually approaching one with increasing age (**Figure 1)**. Inverse associations of dog ownership with glucose-lowering drugs was observed in the lower age groups, in males and those not living alone (HR, 0.89; 95% CI, 0.79-0.99, HR, 0.95; 95% CI, 0.92-0.99 and HR, 0.91; 95% CI, 0.86-0.97, respectively).

TwinGene

On cross-sectional analysis of 10,110 individuals, 484 (5%) were registered as dog owners (partners' dogs not included) and their characteristics are described in **Table 1** and **Supplementary Table 5**. Using similar covariates as in the national cohort, no associations of dog ownership was found with prevalent use of anti-hypertensive drugs (OR, 0.94; 95% CI, 0.74-1.20), lipid-lowering drugs (OR, 0.92; 95% CI, 0.65-1.29) or glucose-lowering drugs (OR, 0.90; 95% CI, 0.50-1.63) (**Table 2).** Upon inclusion of additional covariates, the Charlson comorbidity score and the employment status were found to be the most influential confounders and the fully adjusted model yielded lower but still non-significant estimates: OR, 0.90 (95% CI, 0.70-1.15) for use of anti-hypertensive drugs, OR, 0.87 (95% CI, 0.62-1.22) for lipid-lowering drugs or and OR, 0.78 (95% CI, 0.43-1.43) for glucose-lowering drugs (**Supplementary Table 6**). We found no association between dog ownership and the other clinical and biochemical cardiovascular risk factors (**Figure 2)**.

Discussion

In this nationwide study in a population without previous cardiovascular disease, we observed a minimally higher risk of initiation of treatment for hypertension and dyslipidemia among persons with a dog in their household compared to those without dogs in the household. Associations were most prominent in younger age groups (40-60 years). Owning a dog of mixed pedigree or a dog belonging to the "companion/toy" breed group was associated with hypertension and dyslipidemia, whilst ownership of a dog from the "Spitz/primitive" breed and the combined group of hunting-type breeds (Terriers, Pointing, Scent Hounds and Retrievers) was associated with lower risk of treatment for diabetes mellitus. Cross-sectional analyses in 10,110 participants from TwinGene showed no association of dog ownership with body mass index, waist-to-hip-ratio, blood pressure or biochemical cardiovascular risk factors, and indicated that the association of dog ownership with medication for hypertension,

dyslipidemia and diabetes was confounded by employment status and non-CVD-chronic conditions.

That owners of mixed-breed and "companion/toy" breeds, as well as dog owners in younger age groups, had mildly increased risks for hypertension and dyslipidemia are in line with our previous study regarding higher risk of myocardial infarction and stroke in this group. We note that the proportion of highest education level in the mixed breed group was remarkably lower than the general population (20.9% vs 29.3%). Although we adjusted for educational level, it is likely that there is unmeasured confounding from differences in health-seeking behavior, smoking habits or stress in dog-owners in working age groups. In TwinGene, we noted that additional adjustment for employment status (unemployed, retired, sick leave or unemployed) and a comorbidity index (for diseases other than CVD) were important confounders lowering the estimates. These covariates were not available in the national cohort, implying that the results in the national cohort are likely to have been confounded by these or other factors.

Our findings in TwinGene are different from an Australian cohort study in 5,741 individuals with 13.6% pet ownership who found lower levels of plasma cholesterol, triglycerides and systolic blood pressures in pet-owners than non-owners.[11] Dog owners (6.3%) had better self-rated health but no difference in blood pressure than non-pet owners in cross-sectional analysis of the Nord-Trondelag Health Study (HUNT)-3 study (n=12,297).[4]

There are a limited number of studies of the association between dog ownership and the risk of type 2 diabetes. A study by Lentino et al., (n=916) showed that regular dog walkers (n=399, 44%) in a primarily well-educated Caucasian population had lower BMI and were at lower risk of both dyslipidemia and type 2 diabetes than other study participants.[7] These findings were contradicted by Wright et al, who showed that dog owners were more likely to be overweight, and have diabetes than non-owners in a study of 1179 community dwellers with 30% pet ownership.[10] Differences in findings across countries could be due to differences in study design, or to inherent differences in dog management and the type of dog breeds in the country. The level of dog walking might be lower in the smaller companion/toy dogs breeds as compared to the hunting-type breeds.[19] In TwinGene, 68% of hunting breed owners reporting a high level of physical activity versus 52% in non-dog owners.

Strengths and weaknesses

The main strengths of our study include its size and the population-based approach increasing generalizability beyond healthy volunteers in a cohort study. To the best of our knowledge, this is the largest register-based study to date to explore the association between dog ownership and cardiovascular risk factors. At the same time, while national registers allow for large and unselected populations with no loss to follow-up, we were able to include additional clinical and health measurements and potential confounders using data from the TwinGene study supporting additional confounding from employment status and non-CVD comorbidities. Although our findings show an association between certain dog breeds and cardiovascular risk factors, these observational results do not imply a causal relationship. The main limitation of the study is the possibility of unmeasured confounding by demographics, socioeconomic factors or pre-existing personality traits. However, a large randomized study of dog ownership over several years cannot be done. Further, despite adjustment for several health, socioeconomic and lifestyle indicators, there is still a possibility of residual confounding or reverse causation. For instance, we could not assess health status before pet acquisition in the national cohort. A smaller study population, although not selected in relation to exposure or outcome, and possible misclassification of dog ownership (due to no information on partners' dog ownership) or lifestyle questionnaire data (collected some years earlier) were important limitations in the subcohort analyses.

Conclusion

In this large cohort study, we observed that dog ownership was associated with a minimally higher risk of initiation of treatment for hypertension and dyslipidemia, and that ownership of dogs of the hunting breed types was associated with a lower risk of initiating treatment for diabetes. These observations may suffer from residual confounding despite access to multiple important covariates, and future studies may add valuable information. The observed inverse association of dog ownership and cardiovascular disease previously reported in this population are unlikely to be explained by reduced hypertension and dyslipidemia.

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Competing financial interests

E.I. is a scientific advisor for Precision Wellness and Olink Proteomics for work unrelated to the present project. The authors report that no other competing interests exist.

Contributorship Statement

T.F conceived the study and acquired funding. M.M, A.E, E.I, J.S and L.B contributed to the design of the study. T.F. acquired the national data and P.M is responsible for the Swedish Twin Registry data. M.M performed data cleaning. M.M and T.F ran statistical analyses. M.M drafted the manuscript and all authors reviewed the manuscript.

Data sharing statement

The register data that support the findings of this study were made available by record-linkage with data from Statistics Sweden, the National Board of Health and Welfare, the Swedish Kennel Club, Swedish Board of Agriculture and the Swedish Twin Register. Restrictions apply to the availability of these data, which were used under license and ethical approval for the current study, and so are not publicly available. Data are however available from the

authors upon reasonable request and with permission of the Regional Ethical Review Board in Stockholm, Sweden. There is no additional data available.

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Table 1. Baseline characteristics of Swedish adults aged 45-80 years without cardiovascular disease according to dog ownership status (national cohort, n=2,026,865) and (TwinGene, n=10,110, responses derived from SALT study [1998-2002]). Age is given at baseline. Numbers and % of the respective cohort are reported unless stated otherwise.

	National Cohort					TwinGene				
	All n=2,026,865 (100%)	**Non-dog owners n=1,731,183 (85.4%)**	**Dog owners* n=295,682 (14.6%)**	**Mixed pedigree† n=32,003 (1.6%)**	**Hunting breeds†,‡ n=65,686 (3.2%)**	**All n=10,110 (100%)**	**Non-dog owners n=9,626 (95%)**	**Dog owners* n=484 (5%)**	**Mixed pedigree† n=141 (1.3%)**	**Hunting breeds†,‡ n=143 (1.4%)**
Age - mean ± SD	52.8 (8.7)	53.3 (8.9)	49.9 (7.3)	49.2 (7.1)	50.0 (7.3)	63.6 (7.1)	63.7 (7.1)	62.0 (6.7)	61.9 (6.3)	62.7 (6.7)
Male	981,094 (48.4)	839,321 (48.5)	141,773 (47.9)	11,841 (37.0)	27,961 (42.6)	4,189 (41.4)	3,986 (41.4)	203 (41.9)	60 (42.6)	64 (44.8)
Marital status										
Married/ cohabiting	1,276,074 (63.0)	1,044,915 (60.4)	231,159 (78.2)	18,991 (59.3)	46,638 (71.0)	8,039 (79.5)	7,648 (79.5)	391 (80.8)	110 (78.0)	112 (78.3)
Never married	287,589 (14.2)	265,895 (15.4)	21,694 (7.3)	4,265 (13.3)	6,377 (9.7)	771 (7.6)	734 (7.6)	37 (7.6)	13 (9.2)	14 (9.8)
Divorced	352,209 (17.4)	316,728 (18.3)	35,481 (12.0)	7,522 (23.5)	10,325 (15.7)	855 (8.5)	824 (8.6)	31 (6.4)	11 (7.8)	8 (5.6)
Widowed	110,993 (5.5)	103,645 (6.0)	7,348 (2.5)	1,225 (3.8)	2,346 (3.6)	445 (4.4)	420 (4.4)	25 (5.2)	7 (5.0)	9 (6.3)
Type of family										
Children at home	658,355 (32.4)	521,224 (30.0)	137,131 (46.3)	14,079 (44.0)	28,785 (43.8)	1,500 (14.8)	1,397 (14.5)	103 (21.3)	31 (22.0)	27 (18.9)
No children at home	1,369,617 (67.6)	1,210,920 (69.9)	158,697 (53.7)	17,924 (56.0)	36,901 (56.2)	8,610 (85.2)	8,229 (85.5)	381 (78.7)	110 (78.0)	116 (81.1)
Education										
Compulsory	541,662 (26.7)	473,952 (27.4)	67,710 (22.9)	8,596 (26.9)	13,207 (20.1)	4,069 (40.2)	3,880 (40.3)	189 (39.0)	56 (39.7)	52 (36.4)
Secondary	891,458 (44.0)	751,156 (43.4)	140,302 (47.5)	16,729 (52.3)	29,352 (44.7)	3,107 (30.7)	2,958 (30.7)	149 (30.8)	46 (32.6)	36 (25.2)
University	593,745 (29.3)	506,075 (29.2)	87,670 (29.7)	6,678 (20.9)	23,127 (35.2)	2,934 (29.0)	2,788 (29.0)	146 (30.2)	39 (27.7)	55 (38.5)
Income quintile§										
1 (lowest quintile)	405,929 (20.0)	342,412 (19.8)	63,517 (21.5)	8,222 (25.7)	12,695 (19.3)	-	-	-	-	-
2	405,486 (20.0)	348,254 (20.1)	57,232 (19.4)	7,472 (23.3)	12,461 (19.0)	-	-	-	-	-
3	405,173 (20.0)	347,691 (20.1)	57,482 (19.4)	6,801 (21.3)	12,586 (19.2)	-	-	-	-	-
4	405,175 (20.0)	346,350 (20.0)	58,825 (19.9)	5,620 (17.6)	13,364 (20.3)	-	-	-	-	-
5 (highest quintile)	405,102 (20.0)	346,476 (20.0)	58,626 (19.8)	3,888 (12.1)	14,580 (22.2)	-	-	-	-	-
Country of birth										
Sweden	1,805,438 (89.1)	1,529,664 (88.4)	275,774 (93.3)	29,168 (91.1)	62,160 (94.6)	10,110 (100)	9,626 (100)	484 (100)	141 (100)	143 (100)
Other Nordic countries**	92,043 (4.5)	80,740 (4.7)	11,303 (3.8)	1,650 (5.2)	2,083 (3.2)	0	0	0	0	0
Non-Nordic countries	129,384 (6.4)	120,779 (7.0)	8,605 (2.9)	1,185 (3.7)	1,443 (2.2)	0	0	0	0	0
Population density - median (IQR) inhabitant per square kilometer	72.6 (228.8)	76.7 (315.3)	49.2 (92.8)	45.0 (87.7)	56.8 (106.2)	60.7 (111.1)	60.7 (114.7)	41.8 (72.9)	40.1 (70.3)	45.9 (68.5)
Region of residence										
Norrland	269,897 (13.3)	222,443 (12.8)	47,454 (16.0)	4,791 (15.0)	9,476 (14.4)	1,621 (16.0)	1,518 (15.8)	103 (21.3)	32 (22.7)	22 (15.4)
Svealand	771742 (38.1)	669673 (38.7)	102,069 (34.5)	10,278 (32.1)	23,451 (35.7)	3,391 (33.5)	3,240 (33.7)	151 (31.2)	41 (29.1)	42 (29.4)
Götaland	985,226 (48.6)	839,067 (48.5)	146,159 (49.4)	16,934 (52.9)	32,759 (49.9)	5,098 (50.4)	4,868 (50.6)	230 (47.5)	68 (48.2)	79 (55.2)
Exercise††										

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Little or none	-	-	-	-	2,139 (21.2)	2,064 (21.5)	75 (15.5)	29 (20.7)	16 (11.2)
Average	-	-	-	-	2,611 (25.9)	2,508 (26.2)	103 (21.3)	29 (20.7)	27 (18.9)
Above average	-	-	-	-	5,319 (52.8)	5,014 (52.3)	305 (63.1)	82 (58.6)	100 (69.9)
Tobacco Use††									
No history of tobacco	-	-	-	-	4,314 (42.7)	4,155 (43.2)	159 (32.9)	42 (29.8)	46 (32.2)
Previous tobacco user	-	-	-	-	4,061 (40.2)	3,833 (39.8)	228 (47.1)	69 (48.9)	68 (47.6)
Current tobacco user	-	-	-	-	1,735 (17.2)	1,638 (17.0)	97 (20.0)	30 (21.3)	29 (20.3)

*For descriptive purposes, dog owners here are individuals who had a registered dog at any time point during the study period, and for TwinGene taken as ownership at the clinical test date.
†Proportion of this breed of all participants
‡Hunting breeds comprises all Terriers, Scent hounds, Pointing dog and Retriever dog breed groups.
§Information on income not available for the TwinGene sub-study in the Swedish Twin Register;
**Other Nordic countries include Norway, Denmark, Iceland, Finland, the territories of the Åland Islands and the Faroe Islands
††Information on exercise levels and tobacco use was not available from the Register of the Total Population

Table 2. Association of dog ownership with initiation of medication for hypertension, dyslipidemia and diabetes. For national cohort (n=2,026,865), Cox regression models with hazard ratios (HR) and 95% confidence interval (CI) for incident medication are applied, while logistic models for prevalent use is used in TwinGene (n=10,110) and odds ratios presented (OR).

Cohort	Medication	N treated	Time at risk	Model 1*	Model 2§	Model 3†
National	Hypertension	503,305	10,659,258	**1.02 (1.01-1.03)**	**1.02 (1.01-1.03)**	NA
	Dyslipidemia	276,691	11,508,349	**1.03 (1.02-1.04)**	**1.02 (1.01-1.04)**	NA
	Diabetes	60,038	12,207,964	**0.91 (0.89-0.94)**	0.98 (0.95-1.01)	NA
TwinGene	Hypertension	2,223	NA	0.96 (0.75-1.21)	0.94 (0.74-1.20)	0.90 (0.70-1.15)
	Dyslipidemia	963	NA	0.92 (0.65-1.29)	0.92 (0.65-1.29)	0.87 (0.62-1.22)
	Diabetes	318	NA	0.89 (0.49-1.61)	0.90 (0.50-1.63)	0.78 (0.43-1.43)

*Model 1. Age and sex adjusted

§Model 2. National cohort: Adjusted for sex, age, type of family, area of residence, population density, marital status, region of birth (Sweden, Nordic, Non-Nordic), income, education level, latitude of residence. TwinGene: Adjusted for sex, age, type of family, area of residence, population density, marital status, education level and latitude of residence

† Model 3. Adjusted for sex, age, number of children in the home, area of residence, population density, marital status, tobacco use, occupational level, employment status, disability and Charlson comorbidity index

Table 3. Association of dog ownership with initiation of medication for hypertension drugs, dyslipidemia and diabetes by breed group in the National cohort with non-dog owners as the reference group. Estimates that pass Bonferroni correction for 11 breed groups (p=0.05/11) are marked in bold.

	Anti-hypertensive drugs		Lipid-lowering drugs		Glucose -lowering drugs	
Breed Groups	**Crude* HR**	**Adjusted† HR**	**Crude* HR**	**Adjusted† HR**	**Crude* HR**	**Adjusted† HR**
Sheep and cattle dogs	1.04 (1.01-1.07)	1.03 (1.00-1.06)	1.01 (0.97-1.06)	1.01 (0.97-1.06)	1.03 (0.95-1.13)	1.06 (0.96-1.15)
Pinscher and schnauzer	1.03 (0.99-1.06)	1.03 (1.00-1.07)	1.07 (1.02-1.12)	**1.07 (1.02-1.12)**	0.92 (0.82-1.02)	0.98 (0.88-1.09)
Terriers	0.98 (0.95-1.02)	0.99 (0.96-1.03)	1.01 (0.96-1.05)	1.02 (0.97-1.07)	**0.84 (0.76-0.94)**	0.91 (0.81-1.01)
Dachshunds	1.01 (0.96-1.06)	1.02 (0.97-1.07)	1.06 (0.99-1.13)	1.06 (0.99-1.13)	0.96 (0.84-1.11)	1.03 (0.89-1.18)
Spitz and primitive types	1.05 (1.01-1.09)	1.00 (0.97-1.04)	1.04 (0.99-1.09)	1.01 (0.96-1.06)	**0.82 (0.73-0.91)**	**0.83 (0.74-0.93)**
Scent hounds and related	1.05 (1.00-1.09)	1.03 (0.98-1.07)	1.07 (1.01-1.13)	1.05 (0.99-1.11)	**0.86 (0.76-0.98)**	0.88 (0.77-0.99)
Pointing dogs	0.95 (0.89-1.02)	0.95 (0.88-1.02)	0.96 (0.88-1.06)	0.97 (0.89-1.07)	**0.65 (0.51-0.82)**	0.73 (0.58-0.93)
Retrievers	1.00 (0.98-1.03)	1.02 (0.99-1.05)	1.00 (0.96-1.04)	1.02 (0.98-1.06)	**0.87 (0.80-0.95)**	0.98 (0.90-1.06)
Companion and Toy dogs	**1.10 (1.06-1.13)**	**1.09 (1.05-1.12)**	**1.12 (1.08-1.17)**	**1.12 (1.07-1.16)**	1.01 (0.92-1.12)	1.03 (0.93-1.14)
Sight hounds	0.90 (0.79-1.02)	0.90 (0.79-1.02)	0.94 (0.79-1.12)	0.94 (0.79-1.12)	0.84 (0.57-1.26)	0.87 (0.59-1.30)
Mixed Pedigree‡	**1.10 (1.07-1.13)**	**1.07 (1.05-1.11)**	**1.09 (1.06-1.12)**	**1.09 (1.05-1.13)**	**1.22 (1.13-1.32)**	**1.18 (1.09-1.27)**

*Adjusted for age and sex
†Adjusted for age, sex, marital status, presence of children in the home, population density, area of residence, education level, region of birth, income and a correction for latitude of residence.
‡Group comprising all non-pure pedigree dogs.

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Figure legends:

Figure 1 - Hazard ratios (HR) and 95% confidence intervals (CI) for the association of dog ownership and time to initiation of medication for hypertension, dyslipidemia and type 2 diabetes.

Figure 2 - Coefficients and 95% confidence intervals for the exposure to dog ownership compared to non-dog ownership on SD-transformed biochemical and clinical measurements in the TwinGene.

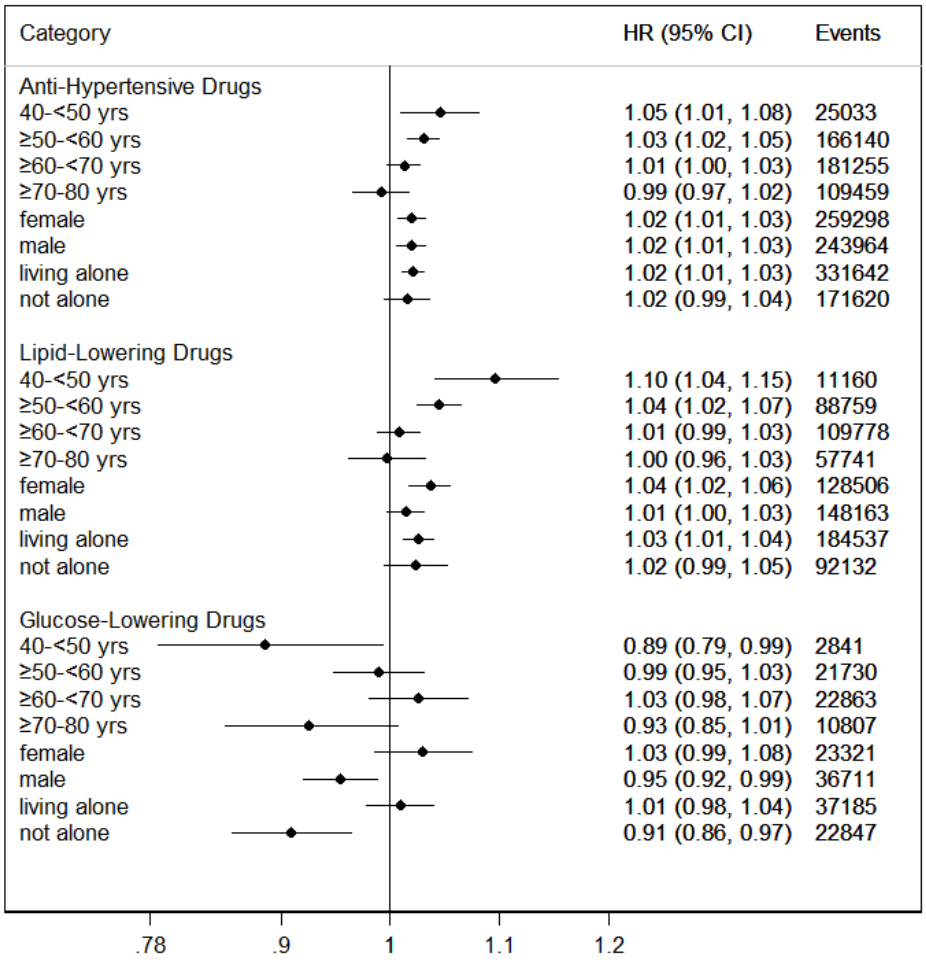

Figure 1 - Hazard ratios (HR) and 95% confidence intervals (CI) for the association of dog ownership and time to initiation of medication for hypertension, dyslipidemia and type 2 diabetes stratified by age category, sex and home occupancy (living alone or with someone) and adjusted for age, sex, marital status, presence of children in the home, population density, area of residence, education level, region of birth, income and a correction for latitude of residence.

257x265mm (72 x 72 DPI)

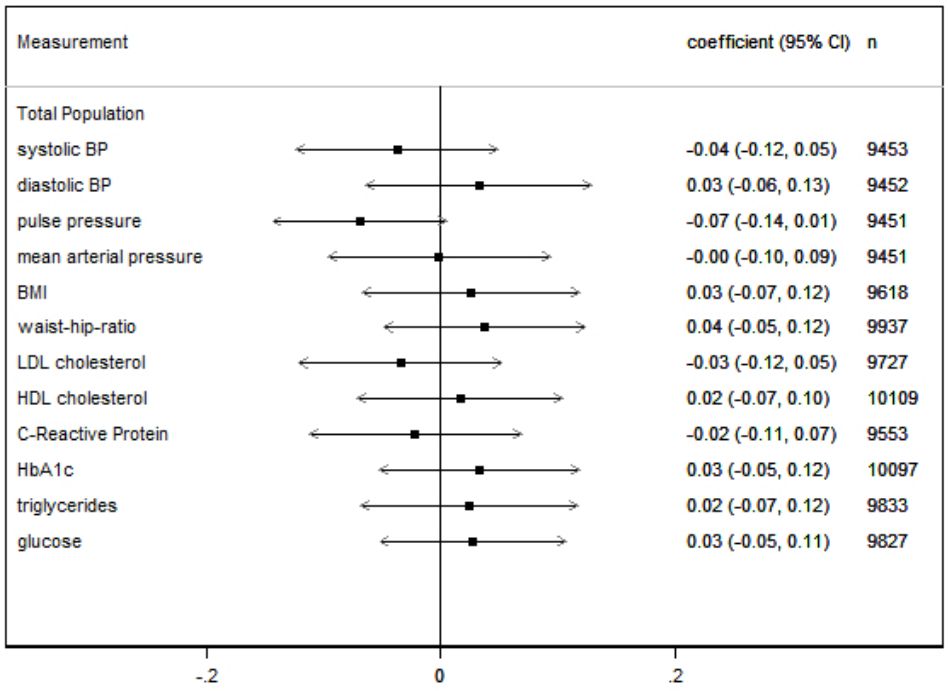

Figure 2 - Coefficients and 95% confidence intervals for the exposure to dog ownership compared to non-dog ownership on SD-transformed biochemical and clinical measurements in the TwinGene adjusted for blood pressure lowering medication, lipid-lowering medication and glucose-lowering medication.

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Supplementary Appendix

Dog ownership and Cardiovascular Risk Factors by Mubanga *et al*.

Content

Supplementary Methods

Data Source and Parameters

Sweden has a structured population registration system that has enabled the collection of individual level information on the total population. By using an identity-protected unique code called the personal identity number (PIN), it is possible to link Swedish residents through different national registers for information such as vital status, socio-demographic data, dog ownership and health outcomes.[1]

Covariates

Covariates extracted at baseline from the Register of the Total Population included sex, birth year, region of birth separated into Sweden, other Nordic countries and non-Nordic countries; and the level of education categorized as compulsory school (≤9 years), secondary school (10-11 years) and tertiary education (≥12 years). We further included annually -updated covariates including marital status categorized as single, married/registered partnership/cohabiting, divorced or widowed; the presence of children in the home (dichotomized as yes/no), the area of residence (Norrland, Svealand and Götaland), the population density in municipality of residence (continuous variable), and annual household income (birth year-standardized quintiles). A north-south gradient was adjusted for by including the latitude of the municipality of residence. To avoid reverse effects of outcomes on covariates, we used covariate data from the preceding year to time-update information on January 1 in every year. A binary variable for home occupancy where individuals were assigned to 'living alone' if the individual lived alone or 'not alone' if they were registered as living with a partner or a child. Co-habiting partners with no children in common could not be accounted for via the registers. Another variable for living with children aged <18 was created to account for those who lived with children in the home. A second stratification variable was created for age group in decades.

From the SALT study conducted in 1998-2002, we used the following self-reported variables as covariates: age, sex, presence of children in the household, area of residence, population density, marital status, and latitude of residence and level of education as defined in the national cohort. Additionally, we adjusted for tobacco use (never, former or current user), employment status (employed, retired, sick leave or unemployed), Charlson comorbidity index and disability (categorized as yes /no). Additionally the socioeconomic index which ranks occupations by the average level of education and job earnings of job holders was also included.[2] By using National Patient Register data from the TwinGene clinic visit date to five years prior, we created a Charlson comorbidity index. This is a widely used index for risk adjustment in health care research.[3 4]

TwinGene

The Swedish Twin Registry is a national register started in 1958 that derives information on all twin births occurring in Sweden from the National Board of Health and Welfare. It contains information on more 190,000 Swedish twin pairs born from 1886 onwards.[5] There have been several sub-studies conducted within this registry that have enabled the enhancement of the phenotypic and genetic data available on each participant. For this study, we limited ourselves to two sub-studies that comprised participants aged 45 to 80 years and who had consented to participate in both studies. Data between the two sub-studies involved was collected a minimum of 2 and a maximum of 10 years apart (**Supplementary Figure 2**).

The first study, the Screening Across the Lifespan Twin study (SALT) interview was conducted as a sub-study of the Swedish Twin Register between 1998 and 2002 targeting all twin-pairs born in 1958 or earlier. Questionnaires were used to collect information on family

status, occupation, education level, anthropometric measurements, alcohol intake, tobacco use, environmental exposures and irritants, medication use and health - including psychosocial /personality outcomes.[5] Information was collected from 44,821 respondents.

The second sub-study, the TwinGene study, was nested in the previous study. Between 2004 and 2008 participants from SALT were invited back as part of the TwinGene Study. TwinGene was set up to enable the collection of biological specimens to investigate gene-environment interactions in participants. 12,614 invited participants gave consent to participate. Questionnaires were mailed and filled in for medication use and health outcomes. Blood was then collected for clinical biochemistry from a local health facility and processed centrally.[6] We used the date of clinic visit as the date of study.

Supplementary Table 1. Description of variables derived from the SALT questionnaire study

Covariate	Questionnaire Option	Variable created	Classification and Derivative from questionnaire
Marital status	What is your civil status?	Married	Married, cohabiting
		Single	Living alone
		Divorced	Divorced, separated, living apart
		Widowed	Widow/ widower
Type of family	Living in a household with children <18 years	Yes/ No	Yes /No
Education level	Highest years of education completed	Primary education or less	9 years or less of education
		Secondary education	10 to 12 years of education
		Tertiary education or more	More than 12 years of education
Employment status	Employment status	Employed	Fully employed, part time employment, owns company, on leave from work, study leave or on military service
		Retired	Pensioner, prematurely retired, partly retired
		Retired for disability or illness	Retired for injury
		Unemployed	Unemployed, housewife/man
Socioeconomic index	Socioeconomic occupation level	Level 1	Unskilled Employees
		Level 2	Lower skilled, non-manual workers
		Level 3	Self-employed excluding independent workers
		Level 4	Intermediate non-manual employees
		Level 5	Highest tier non-manual employees
Tobacco Use	Have you ever smoked or used snuff	Never smoked	No not even tried it, yes but only tried it, smoked now and then (like at parties),
		Former smoker	Smoked regularly, snuffed regularly, smoke now and then (like at parties)
		Current smoker	Smoke regularly, smoke at parties, snuff now and then, snuff regularly
Any movement impairment	Do you have any physical handicap	Yes/no	Yes/ No
Disability	Do you need assistance with personal care/ shopping,/cooking/mobility/	Yes/No	Yes /No
Exercise	How much do you exercise; what fits your annual exercise pattern	Less than average	Almost no exercise, light exercise, much less exercise than average, less than average
		Average	Regular medium exercise, average amount of exercise
		More than average	Hard physical exercise, more exercise than average, much more exercise than normal, maximum amount of exercise

Supplementary Table 2. Description of Breed Classification of the 331 breeds included in the study based on the Nordic Kennel Union Classification

Group Number	Breed Groups	Breed Designation
1	Sheep and cattle dogs	Sheep dogs (Australian, Belgian, Catalan, German, Picardy, Polish, Portuguese, Pyrenean, Shetland, Old English); Shepherd dogs (Belgian, Bergamasco, Croatian, Dutch, German, Majorca, Polish, Romanian, South Russian); Collie (Bearded, Border, Rough, Smooth); Bouvier des Flandres, Beauceron, Briard, Chodsky Pes, Czechoslovakian Wolfdog, Komondor, Kuvasz, Mudi, Lancashire Heeler, Schipperke, Puli, Pumi, Slovakian Chuvach, Welsh Corgie, Australian kelpie, Working kelpie
2	Pinscher and schnauzer dogs	Pincher (Affenpinscher, Austrian, Dobermann, German, Miniature); Schnauzer (Giant, Miniature); Mountain Dog (Appenzeller, Bernese, Caucasian Shepherd, Entlebuch, Great Swiss, Karst, Landseer, Newfoundland, Pyrenean, Serra da Estrela, St Bernard, Tuguayan Cimarron, Yugoslavian Shepherd); Molossian (Aidi, Anatolian Shepherd, Boxer, Bull Mastiff, Broholmer, Cane Corso, Dogo Argentino, Danish-Swedish Farm dog, Dogo Canario, Dogue de Bordeux, English Bulldog, Great Dane, Hovawart, Majorca Mastiff, Mastiff, Neapolitano Mastiff, Pyrenese Mastiff, Rafeiro of Alentejo, Spanish Water Dog, Shar Pei, Tosa); Central Asia Shepherd Dog, Russian Black Terrier
3	Terriers	Airedale, American Staffordshire, Australian, Bedlington, Border, Brazilian, Bull, Cairn, Cesky, Dandie Dinmont, English Toy, Fox, German Hunting, Irish Glen of Imaal, Irish Softcoated Wheaten, Irish, Jack Russel, Kerry Blue, Lakeland, Manchester, Miniature Bull, Norfolk, Norwich, Parson Russell, Sealyham, Australian Silky, Skye, Tenterfield, Welsh, West Highland White, Yorkshire
4	Dachshunds	Miniature, Standard, Kaninchen
5	Spitz and primitive types	Alaskan Malamute, American Akita, Canaan dog, Canarian Warren, Chow Chow, Cirneco dell'Etna, East Siberian Laika, Eurasian, Finnish Lapphund, Finnish Spitz, German Spitz, Greenland dog, Hokkaido, Halleforshund, Icelandic Sheepdog, Japanese Akita, Japanese Spitz, Karelian Beardog, Keeshond, Korea Jindo, Laponian Herder Pharaoh Hound, Mexican Hairless dog, Norwegian Buhund, Norwegian Lundehund, Norwegian Elkhound, Peruvian Hairless dog, Ibizan Hound, Pomeranian, Russian European Laika, Samoyed, Shiba, Siberian Husky, Swedish Elkhound, Swedish Lapphund, Swedish White Elkhound, Swedish Vallhund, Thai Bangkaew, Thai Ridgeback, Volpino italiano, West Siberian Laika
6	Scent hounds and related dogs	Alpine Dachsbracke, American Foxhound, Basset Artesian Normand, Basset Bleu de Gascogne, Basset fauve de Bretagne, Basset Hound, Bavarian Mountain Scent hound, Beagle, Black and Tan Coonhound, Bloodhound, Bluetick Coonhound, Bosnian Coarse-haired hound, Dalmatian, Drever, Dunker Hound, Fawn Brittany Griffon, Finnish Hound, Foxhound, German Hound, Grand Basset Griffon Vendeen, Grand Griffon Vendeen, Griffon Nivernais, Halden Hound, Hamilton Hound, Hygen Hound, Istrian Short-haired hound, Otterhound, Petit Basset Griffon Vendeen, Plott, Polish hunting dog, Porcelain, Posavaz Hound, Rhodesian Ridgeback, Russian Hound, Russian Spotted hound, Small Blue Gascony Hound, Spanish Hound, Schiller Hound, Swiss Hound, Serbian Hound, Slovakian Hound, Småland Hound
7	Pointing dogs	Blue Picardy Spaniel, Bracco Italiano, French Pointing, Brittany, Bohemian wire-haired, Drentse Patridge, English Setter, French Spaniel, Old Danish Pointer, Gordon Setter, French wire-haired Korthals Pointing Griffon, Münsterländer, Irish Red Setter, German Short/Wire-haired pointing dog, Portuguese Pointing dog, Pointer, Pudelpointer, Slovakian Wire-haired Pointing dog, Italian Spinone, Stabyhound, Hungarian Vizsla wire-/short-haired, Weimaraner short-/long-haired
8	Retrievers	American Cocker Spaniel, Barbet, Chesapeake Bay Retriever, Clumber Spaniel, Cocker Spaniel, Curly Coated Retriever, English Springer Spaniel, Field Spaniel, Flat coated Spaniel, German Spaniel, Golden retriever, Irish Water Spaniel, Labrador Retriever, Lagotto romagnolo, Nederlandse Kooikerhondje, Nova Scotia Duck Tolling Retriever, Spanish Water dog, Portuguese Water Dog, Sussex Spaniel, Welsh Springer Spaniel, Wetterhound
9	Companion and toy dogs	Havanese, Bolognese, Boston Terrier, Belgian Griffon, Brussels Griffon, Cavalier King Charles Spaniel, Chihuahua, Chinese Crested, Coton de Tulear, French Bulldog, Japanese Chin, King Charles Spaniel, Kromfohrlander, Lhasa Apso, Lowchen, Maltese, Pug, Papillon, Pekingese, Small Brabant Griffon, Phalene, Prazský krysarík, Poodle, Russian Toy, Shih Tzu, Tibetan Terrier, Tibetan Spaniel
10	Sight hounds	Afghan Hound, Azawakh, Borzoi, Polish Greyhound, Spanish Greyhound, Irish Wolfhound, Italian Greyhound, Hungarian Greyhound, Saluki, Scottish Deerhound, Sloughi, Whippet

Supplementary Table 3. Association of dog ownership with initiation of medication for the treatment of hypertension. This compares the main analysis as shown in Table 2 with a modified analysis that excludes Beta-blockers which have not been recommended first line treatment for hypertension since XX. Cox regression models with hazard ratios (HR) and 95% confidence interval (CI) are reported.

	N treated	Time at risk	Model 1*	Model 2§
With β-blockers	503,305	10,659,258	1.02 (1.01-1.03)	1.02 (1.01-1.03)
Without β-blockers	401,573	11,018,086	1.03 (1.02-1.04)	1.02 (1.01-1.03)

*Model 1. Age and sex adjusted
§Model 2. National cohort: Adjusted for sex, age, type of family, area of residence, population density, marital status, region of birth, income, education level, latitude of residence.

Supplementary Table 4. Association of dog ownership with initiation of lipid lowering medication. This compares the main analysis as shown in Table 2 with a modified analysis that censored participants at an event of angina or heart failure. Cox regression models with hazard ratios (HR) and 95% confidence interval (CI) are reported.

Lipid lowering medication	N treated	Time at risk	Model 1*	Model 2§
Without censoring	276,691	11,508,349	1.03 (1.02-1.04)	1.02 (1.01-1.04)
With censoring	243,797	11,482,789	1.03 (1.02-1.04)	1.04 (1.01-1.04)

*Model 1. Age and sex adjusted
§Model 2. National cohort: Adjusted for sex, age, type of family, area of residence, population density, marital status, region of birth, income, education level, latitude of residence.

Supplementary Table 5. Additional baseline characteristics of 10,110 Swedish adults in the Swedish Twin Register. Information is based on persons who participated in the TwinGene project designed to enhance the Screening Across the Lifespan Twin (SALT) questionnaire-based sub-study in the Swedish Twin Register with biologic specimens. Numbers and % are reported unless stated otherwise. Clinical information was taken during TwinGene study (2004-2008), dog ownership status on the date of clinical examination and other non-clinical details extracted from the SALT questionnaire (1998-2002).

Participant characteristics	n		All n=10,110 (100%)	Non-dog owners n=9,626 (95.0%)	Dog owners n=484 (5.0%)	Mixed pedigree dog owners n=141 (1.4%)*	Hunting dog owners n=143 (1.4%)*
Employment status	10,110	Employed	6,875 (68.0)	6,541 (68.0)	334 (69.0)	97 (68.8)	93 (65.0)
		Retired	2,066 (20.4)	1,992 (20.7)	74 (15.3)	18 (12.8)	29 (20.3)
		Sick leave or illness	875 (8.7)	818 (8.5)	57 (11.8)	18 (12.8)	16 (11.2)
		Unemployed	294 (2.90)	275 (2.9)	19 (3.9)	8 (5.7)	5 (3.5)
Profession†	10,110	Unskilled labor	2,458 (24.3)	2,351 (24.4)	107 (22.1)	32 (22.7)	27 (18.9)
		Lower non-manual labor	3,373 (33.4)	3,205 (33.3)	168 (34.7)	57 (40.4)	43 (30.1)
		Self-employed	430 (4.3)	404 (4.2)	26 (5.4)	6 (4.3)	6 (4.2)
		Intermediate non-manual labor	2,539 (25.1)	2,411 (25.0)	128 (26.4)	32 (22.7)	46 (32.2)
		Higher non-manual employee	1,310 (13.0)	1,255 (13.0)	55 (11.4)	14 (9.9)	21 (14.7)
Type of housing or accommodation	10,110	Independent	10,100 (99.9)	9,616 (99.9)	484 (100.0)	141 (100.0)	143 (100.0)
		Assisted living[2]	6 (0.1)	6 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
		Other	4 (<0.0)	4 (<0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Biochemical Variables							
C-Reactive Protein	9,553	Median (IQR)	1.7 (0.8-3.4)	1.7 (0.8-3.4)	1.8 (0.8-3.2)	2.0 (0.9-3.5)	1.6 (0.7-3.1)
LDL-Cholesterol	9,727	Mean (SE)	3.9 (0.9)	3.9 (0.9)	3.8 (0.9)	3.8 (0.9)	3.9 (0.9)
HDL-Cholesterol	10,109	Mean	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)
Triglyceride (Fasting)	9,261	Median	1.1 (0.8-1.6)	1.1 (0.8-1.6)	1.1 (0.9-1.6)	1.2 (0.9-1.6)	1.2 (0.9-1.5)
Glucose (Non-Diabetic)	9,256	Median	5.3 (5.0-5.7)	5.3 (5.0-5.7)	5.2 (5.0-5.7)	5.3 (5.0-5.8)	5.3 (5.0-5.7)
HbA1c	10,097	Mean	4.8 (0.6)	4.8 (0.6)	4.8 (0.6)	4.8 (0.6)	4.7 (0.5)
Body Mass Index	9,618	Mean	25.9 (4.0)	25.9 (4.0)	26.0 (4.0)	26.3 (4.4)	26.0 (3.8)
Waist-Hip ratio	9,937	Mean	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)
Blood pressure measurements							
Mean systolic BP (all participants)	8010	Mean	138.1 (19.5)	138.2 (19.5)	136.0 (19.2)	139.4 (20.3)	136.2 (18.1)
Mean diastolic BP (all participants)		Mean	82.2 (10.5)	82.2 (10.4)	82.6 (10.9)	84.8 (11.4)	82.7 (10.4)

Pulse pressure (all participants)		Mean	55.9 (15.4)	56.0 (15.4)	53.4 (13.6)	54.6 (13.9)	53.5 (12.5)
Mean systolic BP (On BP treatment)	1,970	Mean	144.9 (18.8)	144.9 (18.9)	144.9 (17.3)	149.4 (14.9)	142.0 (15.8)
Mean diastolic BP (On BP treatment)		Mean	83.9 (10.7)	83.8 (10.8)	85.0 (9.2)	84.5 (8.4)	85.6 (9.3)
Pulse pressure (On BP treatment)		Mean	61.0 (16.0)	61.1 (16.1)	60.0 (13.8)	65.0 (10.1)	56.4 (12.2)
Self-reported health status	10,110	Excellent	3,501 (34.9)	3,330 (34.9)	171 (35.7)	33 (23.6)	58 (40.8)
		Good	5,330 (53.2)	5,085 (53.3)	245 (51.1)	79 (56.4)	73 (51.4)
		Average	963 (9.6)	914 (9.6)	49 (10.2)	19 (13.6)	8 (5.6)
		Not so good	227 (2.3)	213 (2.3)	14 (2.9)	7 (5.0)	3 (2.1)
Blood Pressure Medication	10,110	Number on treatment (%)	2,099 (20.8)	2,010 (20.9)	89 (18.4)	31 (22.0)	22 (15.4)
Lipid Modifying Medication	10,110	Number on treatment (%)	918 (9.1)	880 (9.1)	38 (7.9)	14 (9.5)	13 (8.3)
Diabetes Medication	10,110	Number on treatment (%)	305 (3.0)	293 (3.0)	12 (2.5)	5 (3.5)	5 (3.5)

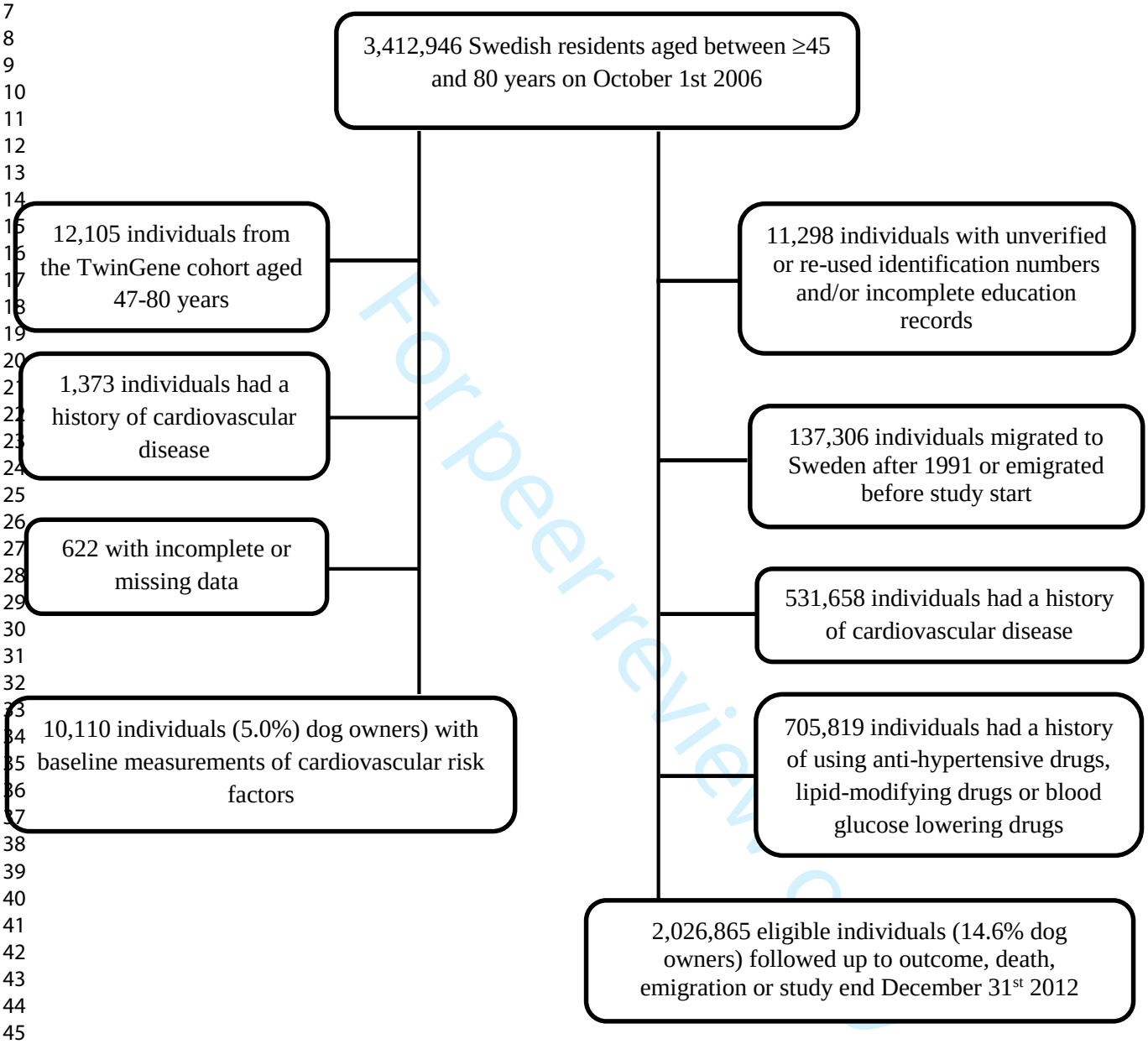
*-Proportion of this breed of total population
†-Defined according to Budoki et al.[7]
‡-Assisted living which includes living in
BP- Blood Pressure

Supplementary Table 6. Stepwise addition of covariates into TwinGene model. Odds ratios (OR) and confidence intervals (CI) for associations of dog ownership and prevalent drug prescriptions for hypertension, dyslipidemia and type 2 diabetes (n=10,110). *

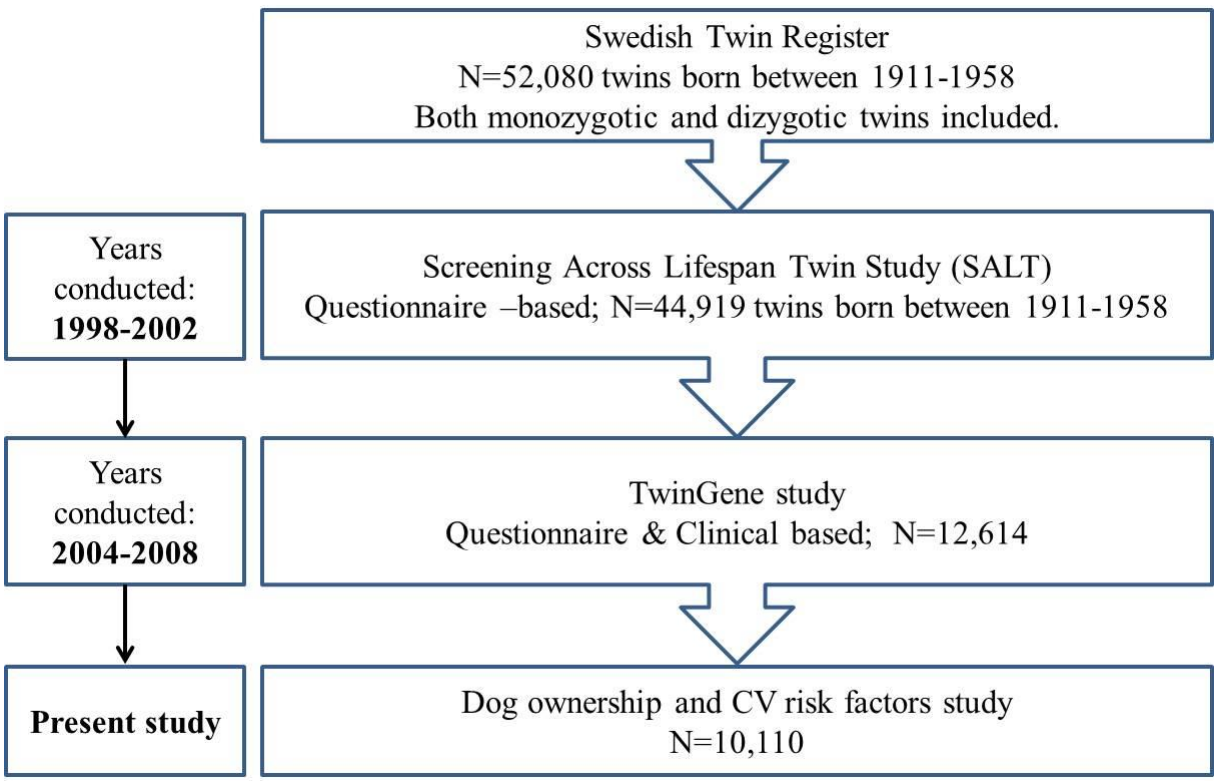
Prescription Medication	N on treatment	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7
Anti-hypertensive drugs	2,223	0.96 (0.75-1.21)	0.94 (0.74-1.20)	0.95 (0.74-1.20)	0.92 (0.72-1.18)	0.90 (0.70-1.15)	0.90 (0.71-1.15)	0.90 (0.70-1.15)
Lipid lowering drugs	963	0.92 (0.65-1.29)	0.92 (0.65-1.29)	0.92 (0.66-1.29)	0.90 (0.64-1.26)	0.87 (0.62-1.22)	0.87 (0.62-1.22)	0.87 (0.62-1.22)
Glucose lowering drugs	318	0.89 (0.49-1.61)	0.90 (0.50-1.63)	0.91 (0.50-1.65)	0.90 (0.50-1.63)	0.80 (0.44-1.46)	0.80 (0.44-1.46)	0.78 (0.43-1.43)

*Model 1, 2 and 7 were reported in the main manuscript Table 2
Model 1. Adjusted for age and sex
Model 2. Adjusted for sex, age, type of family, area of residence, population density, marital status, education level and latitude of residence
Model 3. Model 2 plus professional level
Model 4. Model 3 plus employment status
Model 5. Model 4 plus Charlson comorbidity index
Model 6. Model 5 plus disability
Model 7. Full twin model - Model 6 plus tobacco use

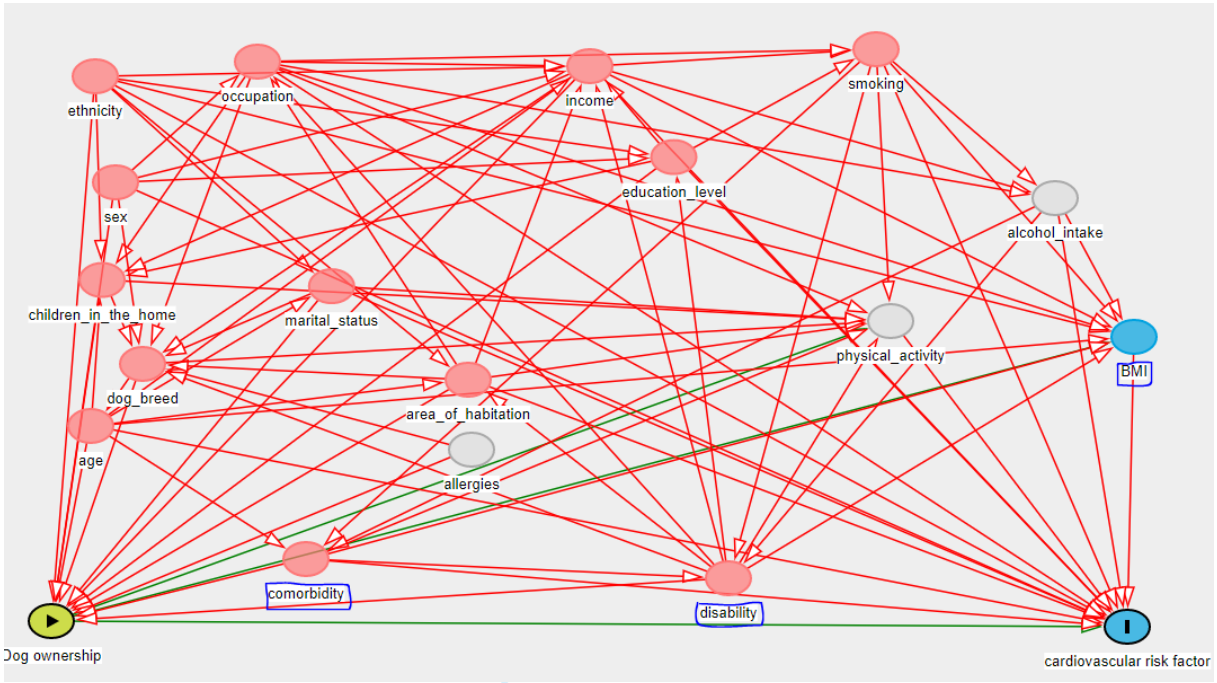
Supplementary Figure 1: Study population



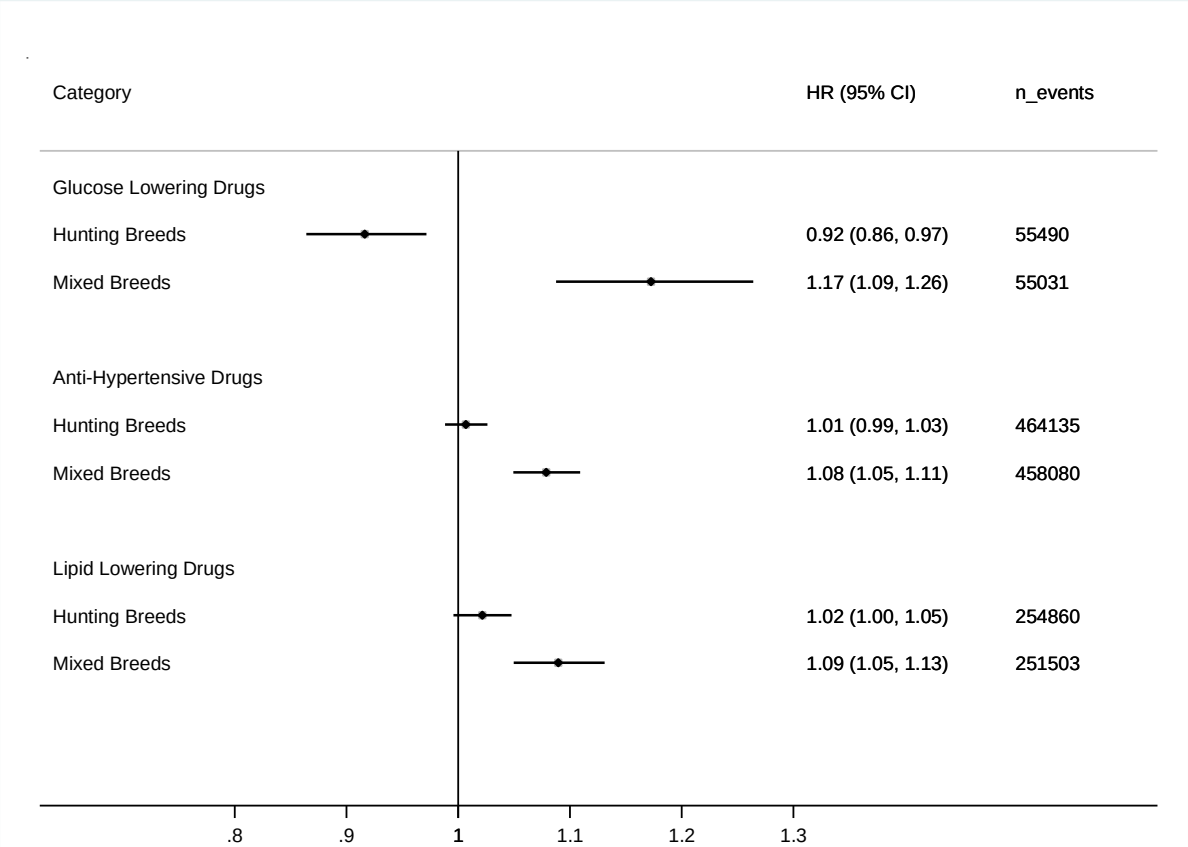
Supplementary Fig 2: Overview of Twin Cohort study recruitment and data collection.



Supplementary Figure 3: Direct Acyclic Graph for dog ownership and cardiovascular risk. The highlighted variables (comorbidity, disability and body mass index) were only available in the TwinGene cohort.



Supplementary Figure 4. Hazard ratios (HR) and 95% confidence intervals (CI) for the association of dog ownership and time to initiation of medication for hypertension, dyslipidemia and type 2 diabetes examining associations in hunting-type breeds (combining Terriers, Scent Hounds, Pointing dogs and Retrievers) and mixed pedigree dogs and adjusted for age, sex, marital status, presence of children in the home, population density, area of residence, education level, region of birth, income and a correction for latitude of residence.



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The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
Dog ownership and Cardiovascular Risk Factors	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	a) Stated in the abstract - Pages 2 b) Abstract Page 2	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Abstract Page 2 Abstract Page 2 Abstract Page 2
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4		
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4		
Methods					
Study Design	4	Present key elements of study design early in the paper	Page 5		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5 & 6		
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the	Page 5, 6 & 7; Also summarised in the	RECORD 6.1: The methods of study population selection (such as codes or	Page 5 & 6

		sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	supplementary material as supplementary figure 1 on page 7 *Not applicable*	algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	This was not applicable to the present study *****
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	Pages 5, 6 & 7	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Full explanations are provided on pages 5-7
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Outlined on Page 6		
Bias	9	Describe any efforts to address potential sources of bias	Pages 8 & 12		
Study size	10	Explain how the study size was		Population-based study including all	

		arrived at	Page 5	adults who met the criteria for inclusion	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	Pages 7 & 8		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	a) Page 7 & 8 b) Page 8 c) Page 6 d) Page 6 e) Page 8		
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	After ethics approval was provided, Statistics Sweden provided de-identified data for the required population. The authors then cleaned the data before analysis

Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	This information is provided on page-7. This was done using the unique personal identity number given to every Swedish resident.
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	a) Supplementary Figure 1 on page 7 of the supplementary material. b) Supplementary Figure 1 on page 7 of the supplementary material. Also provided in main manuscript on page 5 & 6 c) Supplementary Figure 1 on page 7 of the supplementary material.	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Page 5 & Flow diagram on page 7 of the supplementary material and reported as figure 1
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise	a) These baseline characteristic are reported in Table 1on page 14 and 15; as well as in the results in Table 2 on page 16		

		follow-up time (*e.g.*, average and total amount)			
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures	These have been reported on page 16 & in Table 2		
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	These have been reported on page 16 & in Table 2 and in the results section on page 9 & 10 b) This shown in the supplementary methods of the supplementary material		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	This has been reported on Page 8, Table 3 reports the breed group analysis and further material found in the supplementary material as previously described		

			in the methods on page 8		
Discussion					
Key results	18	Summarise key results with reference to study objectives	Page 10 & 11		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	The limitations of this cohort study are discussed on page 12	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Page 13 & 14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 11 & 12	we observed that dog ownership was associated with a minimally higher risk of initiation of treatment for hypertension and dyslipidemia, and that ownership of dogs of the hunting breed types was associated with a lower risk of initiating treatment for diabetes	
Generalisability	21	Discuss the generalisability (external validity) of the study results			
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 13 *The study was funded by the Agria Research Foundation and the Swedish Research Council for Environment, Agricultural Sciences and Spatial Planning (FORMAS), grant number 2013-1673. T.F has personal*		

			funding from the Goran Gustafsson foundation. The Swedish Twin Registry is managed by Karolinska Institutet and receives funding through the Swedish Research Council under the grant no 2017-00641. The funders were not involved in any part of the study design, data collection, analysis manuscript preparation or approval.		
Accessibility of protocol, raw data, and programming code		..	*The register data that support the findings of this study were made available by record-linkage with data from Statistics Sweden, the National Board of Health and Welfare, the Swedish Kennel Club, Swedish Board of Agriculture and the Swedish Twin Register. Restrictions apply to the availability of these data, which were used under license and ethical approval*	RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	

			for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Regional Ethical Review Board in Stockholm, Sweden		

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

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1

Dog ownership and Cardiovascular Risk Factors: a nationwide prospective register-based cohort study

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Abstract (298 words; max 300)

Objective: To study the association between dog ownership and cardiovascular risk factors.

Design: A nationwide register–based cohort study and a cross-sectional study in a subset.

Setting: A cohort of 2,026,865 participants was identified from the Register of the Total Population and linked to national registers for information on dog ownership, hospital admissions, education level, income and country of birth. Participants were followed from October 1st, 2006, to the end of the study on December 31st, 2012, assessing medication for a cardiovascular risk factor, emigration and death. Cross-sectional associations were further assessed in 10,110 individuals from the TwinGene study with additional adjustment for professional level, employment status, Charlson comorbidity index, disability and tobacco use.

Participants: All Swedish residents aged 45-80 years on October 1st, 2006.

Main outcome measures: Initiation of treatment for hypertension, dyslipidemia and diabetes mellitus.

Results

After adjustment for confounders, the results indicated slightly higher likelihood of initiating anti-hypertensive (HR, 1.02; 95% CI, 1.01-1.03) and lipid-lowering treatment (HR, 1.02; 95% CI, 1.01-1.04) in dog owners than in non-owners, particularly amongst those aged 45 to 60 and in those owning mixed breed or companion/toy breed dogs. No association of dog ownership with initiation of treatment for diabetes was found in the overall analysis (HR, 0.98; 95% CI, 0.95-1.01). Sensitivity analyses in the TwinGene cohort indicated confounding of the association between dog ownership and prevalent treatment for hypertension, dyslipidemia and diabetes mellitus, respectively from factors not available in the national cohort, such as employment status and non-CVD chronic disease status.

Conclusions

In this large cohort study, dog ownership was not associated with any large reduction in initiation of medication for classical cardiovascular risk factors, implying that the previously reported lower risk of cardiovascular mortality among dog owners in this cohort is not explained by reduced hypertension and dyslipidemia.

Strengths and limitations of this study

- This is the largest study to date to examine the impact of dog ownership on cardiovascular risk factors.
- The nationwide register-based cohort study with a cross-sectional investigation in a twin registry with a vast array of lifestyle and clinical variables strengthens the results.
- The main outcome measures were extracted from nationwide registers thus decreasing the risk of recall and selection bias.
- Misclassification of dog ownership, particularly in the twin register, may have led to some loss of power.
- Some important confounding factors were not available in the national data.

Introduction

There is a growing interest in pet ownership as a possible intervention to enhance cardiovascular health and well-being.[1, 2] We recently observed that being registered as a dog owner was associated with a lower risk of cardiovascular and all-cause mortality in the general Swedish population (n=3,432,153).[3] Any causal association of dog ownership with lower cardiovascular mortality could potentially be mediated through increased physical activity[4, 5] or through the psychological benefits of companionship,[6] which could in turn reduce other important cardiovascular risk factors such as blood pressure, adiposity, dyslipidemia, and insulin resistance.[7, 8] An alternative explanation could be confounding by socioeconomic,[9] cultural,[10] demographic[9] or psycho-social factors.[11, 12] A large number of cross-sectional and longitudinal studies across different countries support the association of dog ownership with physical activity,[1] however, reports regarding the association of dog ownership with other cardiovascular risk factors are less consistent.[13-20] These inconsistences may be due to low statistical power in small studies, use of restricted or homogenous populations, inability to control for differences across breeds of dogs, or simply an absence of effect. As dogs are reported to be more common in rural areas compared to urban areas,[21-23] as well as in households with children,[24, 25] it is also important to account for these differences. The aim of this study was to assess the association of dog ownership with three major clinical risk factors for cardiovascular disease,[26] specifically initiation of treatment of hypertension, dyslipidemia and diabetes mellitus. We hypothesized that the cardiovascular risk profile of dog owners is better than that of non-dog owners. To overcome limitations of previous studies concerning study size, generalizability and differences between dog breeds, we investigated this hypothesis using data on all Swedish residents aged 45-80 years of age in 2006 from national registers on dog ownership and drug prescriptions. We further sought to explore the association with other cardiovascular risk factors using cross-sectional data from a sub-cohort extracted from the Swedish Twin Registry containing detailed information from questionnaire data, physical examinations and laboratory measurements.

Methods

Design

The main analysis was based on a nationwide cohort study of Swedish residents aged 45-80 followed from October 1st 2006, to December 31st 2012. We additionally used cross-sectional data of participants (aged 47-80) in the TwinGene study, which is a sub-study of the Swedish Twin Registry (**Supplementary Figure 1)**.

Study Population – National Cohort

All Swedish residents (n=3,412,946) aged 45-80 on October 1st 2006, were identified through the Register of the Total Population. To ensure complete linkage to medical information and sufficient information regarding dog ownership in Sweden, we excluded 11,298 individuals with unverified, re-used identification numbers or missing education information, and 137,306 additional individuals that had resided in Sweden for <15 years. We also excluded 531,658 individuals with a history of any CVD (International Classification of Disease (ICD)-9 codes 390-459 and ICD-10 I00-I99) before October 1st, 2006 or with a history of coronary artery bypass grafts or percutaneous coronary artery intervention medical procedure (Nordic surgical procedure codes FNA, FNC and FNG) from in- and outpatient data. Inpatient data was available from 1987 and outpatient data from 2001. Further, using data from the Swedish Prescribed Drug Register, which covers all Swedish dispensed pharmacy prescriptions since it was established on July 1st 2005, individuals (n=705,819) were excluded if they had any recorded dispensed prescription of anti-hypertensive drugs, lipid-lowering drugs, or glucose lowering drugs from 15 months prior to baseline (which was when this register was initiated). Anti-hypertensive drugs were defined based on the Anatomical Therapeutic Chemical Classification System (ATC) as codes: C02 (antihypertensive drugs), C03A, C03EA01 (thiazide diuretics), C07 (beta receptor blockers, excluding sotalol [C07AA07]), C08C (selective calcium antagonists with mainly vascular effects) and C09 (agents acting on the renin-angiotensin system). Lipid-lowering drugs were defined as C10AA (statins), C10AB (fibrates), C10AC (bile acid sequestrants), C10AX (other lipid-modifying agents) and C10B (lipid-lowering drug combinations). Glucose-lowering drugs were defined as ATC-code A10A (insulin and analogues) and A10B (glucose-lowering drugs excluding insulin).

Study population – TwinGene

The TwinGene study originally included 12,614 (of 22,391 invited) twins from the "Screening Across the Lifespan Twin study" (SALT) was conducted between April 2004 and December 2008 and included a visit to their local health center and blood sampling (**Supplementary Figure 2**).[27] The study-base "SALT" was a sub-study of the Swedish Twin Register in twins born before 1959 and who participated in a telephone-based questionnaire sub-study from March 1998 to March 2002[27] (**Supplementary Table 1).**

We performed a cross-sectional analysis of the association of dog ownership with cardiovascular risk factors in the TwinGene cohort (n=12,105). We excluded 1,373 individuals for having a previous history of CVD recorded in the National Patient Register.[28] We also excluded 622 individuals for having missing or incomplete data (**Supplementary Figure 1**).

Exposure

Dogs in Sweden are required to have a unique identifier (ear tattoo or implanted identity chip) and this is registered alongside their owner's unique personal identity number at the Swedish Board of Agriculture. All dogs sold as purebred are registered by the Swedish Kennel Club. We defined the variable 'dog ownership' in the national cohort as registered dog ownership or having a partner registered as a dog owner in either the Swedish Board of Agriculture and/or the Swedish Kennel Club. Exposure to dog ownership was time-updated to include only those periods where each dog was alive and registered to the study participant or their registered partner. The identification of partners was possible through annual extracts from the Register of the Total Population that keeps track of couples that are married, registered in same-sex partnership or are cohabiting with common children.

In the TwinGene data, we did not have access to information on partners' dog ownership and only each person's own dog registrations were used. Dog ownership was defined at the date of inclusion in TwinGene.

If information on a dog's death was missing, we assumed a maximum lifespan of ten years.[29] We conducted sensitivity analyses examining associations with dog death at a maximum lifespan of 8 years and 12 years. Where birth or registration dates were discrepant between the two registers, we randomly selected one of the two.

To define breed groups, we used the Federation Cynologique International standard with some local adaption from Swedish Kennel Club's definition to categorize the 331 breeds into ten breed groups based on character and behaviour attributes **(Supplementary Table 2)**. All non-purebred dogs and those of unknown breed were included in an additional mixed breed group. Where owners had dogs of different breeds, we defined the breed based on the dog registered first and where owners had several dogs, we restricted ownership to three dogs.

Based on previous findings of owners to hunting dogs having a lower risk of cardiovascular events,[3] we additionally defined a group of hunting dogs consisting of Terriers, Pointing, Scent Hounds and Retrievers for analysis.

Outcome

In the national cohort, time to first dispensed prescription of anti-hypertensive drugs, lipid-lowering drugs or glucose-lowering drugs after baseline was defined from data extracted from the drug register. Each outcome was considered separately as we chose to estimate the total effect of dog ownership and not only the direct effects. Participants were censored at emigration, death or at the end of the study on December 31st, 2012. In the analysis of time to anti-hypertensive medication, individuals were additionally censored at a diagnosis of heart failure, unstable angina or acute myocardial infarction in the National Patient Register as the same drugs could be administered for their treatment.

Prevalent use of anti-hypertensive, lipid-lowering or glucose-lowering drugs was defined from the clinical questionnaire data collected during the TwinGene study. Cardiovascular risk factors measured and also used as outcomes in TwinGene included blood glucose, glycosylated hemoglobin A1c (HbA1c), high sensitive C-reactive protein (hsCRP), triglycerides, high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), waist-hip ratio, body mass index (BMI), systolic and diastolic blood pressure and mean arterial pressure (MAP) (**Supplementary methods**). Only fasting measurements of glucose and triglycerides were used (9,873 [97%] of all participants were fasting).

Statistical analyses

All statistical analyses were conducted using Stata version MP14.1 (StataCorp).

Using age as a time-scale, separate multivariable Cox proportional hazards models were applied to assess the associations between dog ownership and time to initiation of anti-hypertensive, lipid-lowering and glucose-lowering drugs, respectively. Directed acyclic graphs were used to guide the choice of covariates (**Supplementary Figure 3).** A first crude model included age and sex, and a second model additionally included the region of birth, area of residence, latitude of residence, population density, level of education, marital status, presence of children in the home and income. A description of the covariates is provided in the **Supplementary methods**. The proportional hazards assumption was verified by plotting Schoenfield residuals and log-log graphs. Results were reported as hazard ratios (HR) and 95% confidence intervals (CI). We repeated the calculations using the breed group as exposure to examine possible breed group effects and we applied Bonferroni correction (for 11 breed groups) to control for multiple testing. Further analyses were stratified by age group, sex, and whether participants lived alone or not. Individuals considered as "living alone" did not have any spouse, partner with common children, or children living in the same household.

We conducted a sensitivity analysis where we excluded β-blockers as first line anti-hypertensive treatment to estimate the effect of changing treatment guidelines over the study period. In additional sensitivity analysis, in the lipid-lowering medication analysis, we assessed the effect of censoring participants at a diagnosis of heart failure, unstable angina or acute myocardial infarction in the National Patient Register.

Logistic regression was applied in TwinGene for the association of dog ownership with prevalent anti-hypertensive, lipid-lowering and blood-glucose lowering medication and linear regression for the association of dog ownership with continuous variables. hsCRP and triglycerides were transformed to the natural log scale before analysis to approach normality. In addition to adjusting for age, sex, presence of children in the household, area of residence, population density, marital status, latitude of residence and level of education, we added further covariates, one at a time to investigate their individual importance: tobacco use, occupational level, employment status, Charlson comorbidity index and disability. In all twin analyses, standard errors were adjusted with the robust sandwich estimator for dependent observations. For blood pressure and lipid levels, associations were further stratified by current medication.

Ethical approval

The regional ethical review board in Stockholm, Sweden, approved the study (national study: 2012/1114-31/2, with amendment 2013-1687-32; TwinGene: 2007/644-31/2 and 2016/1392-31/1).

Patient involvement

No patients were involved in the development, design or analysis of this study. The review board allowed the researchers to waive the requirement for obtaining informed consent in the national study. Participants in TwinGene provided written informed consent.

Results

National Cohort

The baseline characteristics of 2,026,865 Swedish residents are shown in **Table 1**. Dog ownership was directly registered in 189,355 (9.3%) at any time during the follow-up period, and this increased to 295,682 (14.6%) individuals when partners' registration were included. At baseline, the average age of dog owners was 50 years vs 53 years in non-owners. Dog owners were more likely to be married than non-owners (78% vs 60%) and more likely to live in low-density areas than non-owners (median: 49 vs 77 inhabitants per square kilometer). Compared to non-owners, mixed pedigree dog owners (n=32,003) were less likely to be married (59 %), were less likely to have a tertiary education (21%) and had fewer people in the top quintile for income (12.2%). Owners of hunting-type breeds showed similar characteristics to the overall dog owners.

Medication for cardiovascular risk factors

During 10,692,258 person-years of follow-up, dog ownership was associated with a 2% higher risk of initiation of anti-hypertensive drug medication in both crude and multivariable-adjusted analyses (HR, 1.02; 95% CI, 1.01-1.03). During 11,508,349 person-years of follow-up, there was a 2% higher risk of initiating lipid-lowering medication in the multivariable adjusted models (HR, 1.02; 95% CI, 1.01-1.04). During 12,207,964 person-years of follow-up, there was a lower risk of initiating glucose lowering drugs in dog owners in minimally adjusted models (HR, 0.91; 95% CI, 0.89-0.94), but on multivariable adjustment, the association was attenuated and non-significant (HR, 0.98; 95% CI, 0.95-1.01) (**Table 2)**.

Owners of "Companion/toy" breeds and of dogs of mixed pedigree were at higher risk of anti-hypertensive and lipid-lowering drug initiation compared to non-dog owners (**Table 3**). Owners of the Spitz/primitive breed types and the combined group of hunting breed types had lower risks of initiating glucose-lowering medication (HR, 0.83; 95% CI, 0.74-0.93 and HR, 0.92; 95% CI, 0.86-0.97 respectively), while owners of mixed pedigree dogs had higher risk of getting glucose-lowering medication (HR, 1.17; 95% CI, 1.09-1.26) **(Supplementary Figure 4)**.

There was no difference in strength of association when we excluded β-blockers as first-line treatment for anti-hypertension (**Supplementary Table 3)** or when censoring was done in those being investigated for lipid-lowering treatment initiation was made for angina, myocardial infarction or heart failure was conducted **(Supplementary Table 4)**.

In age-stratified analysis, there were some evidence of effect modification by age for both anti-hypertensive and lipid-lowering drugs where an increased risk was observed in those aged below 50 years (HR, 1.04; 95% CI, 1.01-1.08 and HR, 1.10; 95% CI, 1.04-1.15, respectively), with estimates gradually approaching one with increasing age (**Figure 1)**. Inverse associations of dog ownership with glucose-lowering drugs was observed in the lower age groups, in males and those not living alone (HR, 0.89; 95% CI, 0.79-0.99, HR, 0.95; 95% CI, 0.92-0.99 and HR, 0.91; 95% CI, 0.86-0.97, respectively).

TwinGene

On cross-sectional analysis of 10,110 individuals, 484 (5%) were registered as dog owners (partners' dogs not included) and their characteristics are described in **Table 1** and **Supplementary Table 5**. Using similar covariates as in the national cohort, no association of dog ownership was found with prevalent use of anti-hypertensive drugs (OR, 0.94; 95% CI, 0.74-1.20), lipid-lowering drugs (OR, 0.92; 95% CI, 0.65-1.29) or glucose-lowering drugs (OR, 0.90; 95% CI, 0.50-1.63) (**Table 2).** Upon inclusion of additional covariates, the Charlson comorbidity index and the employment status were found to be the most influential confounders and the fully adjusted model yielded lower but still non-significant estimates: OR, 0.90 (95% CI, 0.70-1.15) for use of anti-hypertensive drugs, OR, 0.87 (95% CI, 0.62-1.22) for lipid-lowering drugs and OR, 0.78 (95% CI, 0.43-1.43) for glucose-lowering drugs (**Supplementary Table 6**). We found no association between dog ownership and the other clinical and biochemical cardiovascular risk factors (**Figure 2)**.

Sensitivity analyses on changing the maximum lifespan of dogs in the national cohort that had no dates of death to 8 years or 12 years yielded similar results to the maximum of 10 years used in the main analysis (**Supplementary Table 7).** To provide additional information, the output from the fully adjusted Cox regression models for the association of dog ownership with the initiation of medication for hypertension, dyslipidemia and diabetes mellitus in the national cohort are included in the supplementary material as **Supplementary Table 8**, **Supplementary Table 9** and **Supplementary Table 10,** respectively.

Discussion

In this nationwide study in a population without previous cardiovascular disease, we observed a minimally higher risk of initiation of treatment for hypertension and dyslipidemia among persons with a dog in their household compared to those without dogs in the household. Associations were most prominent in younger age groups (40-60 years). Owning a dog of mixed pedigree or a dog belonging to the "companion/toy" breed group was associated with hypertension and dyslipidemia, whilst ownership of a dog from the "Spitz/primitive" breed and the combined group of hunting-type breeds (Terriers, Pointing, Scent Hounds and Retrievers) was associated with lower risk of treatment for diabetes mellitus. Cross-sectional analyses in 10,110 participants from TwinGene showed no association of dog ownership with body mass index, waist-to-hip-ratio, blood pressure or biochemical cardiovascular risk factors, and indicated that the association of dog ownership with medication for hypertension, dyslipidemia and diabetes was confounded by employment status and non-CVD-chronic conditions. This suggests that the slightly higher associations observed in the national cohort would potentially be attenuated in the presence of the additional confounders.

That owners of mixed-breed and "companion/toy" breeds, as well as dog owners in younger age groups, had mildly increased risks for hypertension and dyslipidemia are in line with our previous study regarding higher risk of myocardial infarction and stroke in this group. The level of dog walking might be lower in the smaller companion/toy dogs breeds as compared to the hunting-type breeds.[30] In TwinGene, 68% of hunting breed owners reporting a high level of physical activity versus 52% in non-dog owners.[30] We note that the proportion of highest education level in the mixed breed group was remarkably lower than the general population (20.9% vs 29.3%). Although we adjusted for educational level, it is likely that there is unmeasured confounding from differences in health-seeking behavior, smoking habits or stress in dog-owners in working age groups. In TwinGene, we noted that additional adjustment for employment status (unemployed, retired, sick leave or unemployed) and a comorbidity index (for diseases other than CVD) were important confounders lowering the estimates. These covariates were not available in the national cohort, implying that the results in the national cohort are likely to have been confounded by these or other factors.

Our findings in TwinGene are different from an Australian cohort study in 5,741 individuals with 13.6% pet ownership who found lower levels of plasma cholesterol, triglycerides and systolic blood pressures in pet-owners than non-owners.[20] Dog owners (6.3%) had better

self-rated health but no difference in blood pressure than non-pet owners in cross-sectional analysis of the Nord-Trondelag Health Study (HUNT)-3 study (n=12,297).[13]

There are a limited number of studies of the association between dog ownership and the risk of type 2 diabetes. A study by Lentino et al., (n=916) showed that regular dog walkers (n=399, 44%) in a primarily well-educated Caucasian population had lower BMI and were at lower risk of both dyslipidemia and type 2 diabetes than other study participants.[16] These findings were contradicted by Wright et al, who showed that dog owners were more likely to be overweight, and have diabetes than non-owners in a study of 1179 community dwellers with 30% pet ownership.[19] Differences in findings across countries could be due to differences in study design, or to inherent differences in dog management and the type of dog breeds in the country.

A previous study in this population showed a lower risk of cardiovascular disease and all-cause mortality in dog owners.[3] The current study suggests that it is unlikely that hypertension and dyslipidemia mediates these effects. Other potential factors that may explain this reduction in mortality include increased social well-being and decreased psychological stress.[31]

Strengths and weaknesses

The main strengths of our study include its size and the population-based approach increasing generalizability beyond healthy volunteers in a cohort study. To the best of our knowledge, this is the largest register-based study to date to explore the association between dog ownership and cardiovascular risk factors. At the same time, while national registers allow for large and unselected populations with no loss to follow-up, they lack information on individual attributes such body mass index, blood pressure, lipid levels and physical activity. A strength of this study is that we were able to include additional clinical health measurements and socioeconomic variables using data from the TwinGene study supporting the presence of additional confounding of the relationship between dog ownership and cardiovascular risk factors from employment status and non-CVD comorbidities. Although our findings show an association between certain dog breeds and cardiovascular risk factors, these observational results do not imply a causal relationship.

The main limitation of the study is the possibility of remaining unmeasured confounding by unmeasured socioeconomic factors or pre-existing personality traits. Further the register-

based nature of our study made it impossible for us to account for pet-associated factors such as primary pet responsibility, physical activity, the level of dog attachment or indeed the reason for acquiring a dog. Physical activity related to dog walking may however be a mediator of the association between dog ownership and health outcomes and separating activity performed in relation to dog walking and other types of activity would be important. However, a large randomized study of dog ownership over several years cannot be done. Further, despite adjustment for several health, socioeconomic and lifestyle indicators, there is still a possibility of residual confounding or reverse causation. For instance, we could not assess health status before pet acquisition in the national cohort. A smaller study population, although not selected in relation to exposure or outcome, and possible misclassification of dog ownership (due to no information on partners' dog ownership) or lifestyle questionnaire data (collected some years earlier) were important limitations in the sub-cohort analyses. Misclassification of dog ownership was also possible in cohabiting partners without children in common as these would not be registered as cohabiting in the Register of The Total Population. Another important limitation is that we were unable to account for those that did not initiate treatment due to any of the three conditions. The Prescribed Drug Register does not keep a record of adherence to treatment or records of those prescribed lifestyle interventions such as diet or exercise.

Conclusion

In this large cohort study, we observed that dog ownership was associated with a minimally higher risk of initiation of treatment for hypertension and dyslipidemia, and that ownership of dogs of the hunting breed types was associated with a lower risk of initiating treatment for diabetes. These observations may suffer from residual confounding despite access to multiple important covariates, and future studies may add valuable information. The observed inverse association of dog ownership and cardiovascular disease previously reported in this population are unlikely to be explained by reduced hypertension and dyslipidemia.

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Competing financial interests

E.I. is a scientific advisor for Precision Wellness and Olink Proteomics for work unrelated to the present project. The authors report that no other competing interests exist.

Contributorship Statement

T.F conceived the study and acquired funding. M.M, A.E, E.I, J.S and L.B contributed to the design of the study. T.F. acquired the national data and P.M is responsible for the Swedish Twin Registry data. M.M performed data cleaning. M.M and T.F ran statistical analyses. M.M drafted the manuscript and all authors reviewed the manuscript.

Data sharing statement

The register data that support the findings of this study were made available by record-linkage with data from Statistics Sweden, the National Board of Health and Welfare, the Swedish Kennel Club, Swedish Board of Agriculture and the Swedish Twin Register. Restrictions apply to the availability of these data, which were used under license and ethical approval for the current study, and so are not publicly available. Data are however available from the

authors upon reasonable request and with permission of the Regional Ethical Review Board in Stockholm, Sweden. There is no additional data available.

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Table 1. Baseline characteristics of Swedish adults aged 45-80 years without cardiovascular disease according to dog ownership status (national cohort, n=2,026,865) and (TwinGene, n=10,110, responses derived from SALT study [1998-2002]). Age is given at baseline. Numbers and % of the respective cohort are reported unless stated otherwise.

	National Cohort					TwinGene				
	All n=2,026,865 (100%)	**Non-dog owners n=1,731,183 (85.4%)**	**Dog owners* n=295,682 (14.6%)**	**Mixed pedigree† n=32,003 (1.6%)**	**Hunting breeds†,‡ n=65,686 (3.2%)**	**All n=10,110 (100%)**	**Non-dog owners n=9,626 (95%)**	**Dog owners* n=484 (5%)**	**Mixed pedigree† n=141 (1.3%)**	**Hunting breeds†,‡ n=143 (1.4%)**
Age - mean ± SD	52.8 (8.7)	53.3 (8.9)	49.9 (7.3)	49.2 (7.1)	50.0 (7.3)	63.6 (7.1)	63.7 (7.1)	62.0 (6.7)	61.9 (6.3)	62.7 (6.7)
Male	981,094 (48.4)	839,321 (48.5)	141,773 (47.9)	11,841 (37.0)	27,961 (42.6)	4,189 (41.4)	3,986 (41.4)	203 (41.9)	60 (42.6)	64 (44.8)
Marital status										
Married/ cohabiting	1,276,074 (63.0)	1,044,915 (60.4)	231,159 (78.2)	18,991 (59.3)	46,638 (71.0)	8,039 (79.5)	7,648 (79.5)	391 (80.8)	110 (78.0)	112 (78.3)
Never married	287,589 (14.2)	265,895 (15.4)	21,694 (7.3)	4,265 (13.3)	6,377 (9.7)	771 (7.6)	734 (7.6)	37 (7.6)	13 (9.2)	14 (9.8)
Divorced	352,209 (17.4)	316,728 (18.3)	35,481 (12.0)	7,522 (23.5)	10,325 (15.7)	855 (8.5)	824 (8.6)	31 (6.4)	11 (7.8)	8 (5.6)
Widowed	110,993 (5.5)	103,645 (6.0)	7,348 (2.5)	1,225 (3.8)	2,346 (3.6)	445 (4.4)	420 (4.4)	25 (5.2)	7 (5.0)	9 (6.3)
Type of family										
Children at home	658,355 (32.4)	521,224 (30.0)	137,131 (46.3)	14,079 (44.0)	28,785 (43.8)	1,500 (14.8)	1,397 (14.5)	103 (21.3)	31 (22.0)	27 (18.9)
No children at home	1,369,617 (67.6)	1,210,920 (69.9)	158,697 (53.7)	17,924 (56.0)	36,901 (56.2)	8,610 (85.2)	8,229 (85.5)	381 (78.7)	110 (78.0)	116 (81.1)
Education										
Compulsory	541,662 (26.7)	473,952 (27.4)	67,710 (22.9)	8,596 (26.9)	13,207 (20.1)	4,069 (40.2)	3,880 (40.3)	189 (39.0)	56 (39.7)	52 (36.4)
Secondary	891,458 (44.0)	751,156 (43.4)	140,302 (47.5)	16,729 (52.3)	29,352 (44.7)	3,107 (30.7)	2,958 (30.7)	149 (30.8)	46 (32.6)	36 (25.2)
University	593,745 (29.3)	506,075 (29.2)	87,670 (29.7)	6,678 (20.9)	23,127 (35.2)	2,934 (29.0)	2,788 (29.0)	146 (30.2)	39 (27.7)	55 (38.5)
Income quintile§										
1 (lowest quintile)	405,929 (20.0)	342,412 (19.8)	63,517 (21.5)	8,222 (25.7)	12,695 (19.3)	-	-	-	-	-
2	405,486 (20.0)	348,254 (20.1)	57,232 (19.4)	7,472 (23.3)	12,461 (19.0)	-	-	-	-	-
3	405,173 (20.0)	347,691 (20.1)	57,482 (19.4)	6,801 (21.3)	12,586 (19.2)	-	-	-	-	-
4	405,175 (20.0)	346,350 (20.0)	58,825 (19.9)	5,620 (17.6)	13,364 (20.3)	-	-	-	-	-
5 (highest quintile)	405,102 (20.0)	346,476 (20.0)	58,626 (19.8)	3,888 (12.1)	14,580 (22.2)	-	-	-	-	-
Country of birth										
Sweden	1,805,438 (89.1)	1,529,664 (88.4)	275,774 (93.3)	29,168 (91.1)	62,160 (94.6)	10,110 (100)	9,626 (100)	484 (100)	141 (100)	143 (100)
Other Nordic countries**	92,043 (4.5)	80,740 (4.7)	11,303 (3.8)	1,650 (5.2)	2,083 (3.2)	0	0	0	0	0
Non-Nordic countries	129,384 (6.4)	120,779 (7.0)	8,605 (2.9)	1,185 (3.7)	1,443 (2.2)	0	0	0	0	0
Population density - median (IQR) inhabitant per square kilometer	72.6 (228.8)	76.7 (315.3)	49.2 (92.8)	45.0 (87.7)	56.8 (106.2)	60.7 (111.1)	60.7 (114.7)	41.8 (72.9)	40.1 (70.3)	45.9 (68.5)
Region of residence										
Norrland	269,897 (13.3)	222,443 (12.8)	47,454 (16.0)	4,791 (15.0)	9,476 (14.4)	1,621 (16.0)	1,518 (15.8)	103 (21.3)	32 (22.7)	22 (15.4)
Svealand	771742 (38.1)	669673 (38.7)	102,069 (34.5)	10,278 (32.1)	23,451 (35.7)	3,391 (33.5)	3,240 (33.7)	151 (31.2)	41 (29.1)	42 (29.4)
Götaland	985,226 (48.6)	839,067 (48.5)	146,159 (49.4)	16,934 (52.9)	32,759 (49.9)	5,098 (50.4)	4,868 (50.6)	230 (47.5)	68 (48.2)	79 (55.2)
Exercise††										
Little or none	-		-	-	-	2,139 (21.2)	2,064 (21.5)	75 (15.5)	29 (20.7)	16 (11.2)

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Average	-	-	-	-	2,611 (25.9)	2,508 (26.2)	103 (21.3)	29 (20.7)	27 (18.9)
Above average	-	-	-	-	5,319 (52.8)	5,014 (52.3)	305 (63.1)	82 (58.6)	100 (69.9)
Tobacco Use††									
No history of tobacco	-	-	-	-	4,314 (42.7)	4,155 (43.2)	159 (32.9)	42 (29.8)	46 (32.2)
Previous tobacco user	-	-	-	-	4,061 (40.2)	3,833 (39.8)	228 (47.1)	69 (48.9)	68 (47.6)
Current tobacco user	-	-	-	-	1,735 (17.2)	1,638 (17.0)	97 (20.0)	30 (21.3)	29 (20.3)

*For descriptive purposes, dog owners here are individuals who had a registered dog at any time point during the study period, and for TwinGene taken as ownership at the clinical test date.
†Proportion of this breed of all participants
‡Hunting breeds comprises all Terriers, Scent hounds, Pointing dog and Retriever dog breed groups.
§Information on income not available for the TwinGene sub-study in the Swedish Twin Register;
**Other Nordic countries include Norway, Denmark, Iceland, Finland, the territories of the Åland Islands and the Faroe Islands
††Information on exercise levels and tobacco use was not available from the Register of the Total Population

Table 2. Association of dog ownership with initiation of medication for hypertension, dyslipidemia and diabetes. For national cohort (n=2,026,865), Cox regression models with hazard ratios (HR) and 95% confidence interval (CI) for incident medication are applied, while logistic models for prevalent use is used in TwinGene (n=10,110) and odds ratios presented (OR).

Cohort	Medication	N treated	Time at risk	Model 1*	Model 2§	Model 3†
National	Hypertension	503,305	10,659,258	**1.02 (1.01-1.03)**	**1.02 (1.01-1.03)**	NA
	Dyslipidemia	276,691	11,508,349	**1.03 (1.02-1.04)**	**1.02 (1.01-1.04)**	NA
	Diabetes	60,038	12,207,964	**0.91 (0.89-0.94)**	0.98 (0.95-1.01)	NA
TwinGene	Hypertension	2,223	NA	0.96 (0.75-1.21)	0.94 (0.74-1.20)	0.90 (0.70-1.15)
	Dyslipidemia	963	NA	0.92 (0.65-1.29)	0.92 (0.65-1.29)	0.87 (0.62-1.22)
	Diabetes	318	NA	0.89 (0.49-1.61)	0.90 (0.50-1.63)	0.78 (0.43-1.43)

*Model 1. Age and sex adjusted

§Model 2. National cohort: Adjusted for sex, age, type of family, area of residence, population density, marital status, region of birth (Sweden, Nordic, Non-Nordic), income, education level, latitude of residence. TwinGene: Adjusted for sex, age, type of family, area of residence, population density, marital status, education level and latitude of residence

† Model 3. Adjusted for sex, age, number of children in the home, area of residence, population density, marital status, tobacco use, occupational level, employment status, disability and Charlson comorbidity index

Table 3. Association of dog ownership with initiation of medication for hypertension drugs, dyslipidemia and diabetes by breed group in the National cohort with non-dog owners as the reference group. Estimates that pass Bonferroni correction for 11 breed groups (p=0.05/11) are marked in bold.

	Anti-hypertensive drugs		Lipid-lowering drugs		Glucose -lowering drugs	
Breed Groups	**Crude* HR**	**Adjusted† HR**	**Crude* HR**	**Adjusted† HR**	**Crude* HR**	**Adjusted† HR**
Sheep and cattle dogs	1.04 (1.01-1.07)	1.03 (1.00-1.06)	1.01 (0.97-1.06)	1.01 (0.97-1.06)	1.03 (0.95-1.13)	1.06 (0.96-1.15)
Pinscher and schnauzer	1.03 (0.99-1.06)	1.03 (1.00-1.07)	1.07 (1.02-1.12)	**1.07 (1.02-1.12)**	0.92 (0.82-1.02)	0.98 (0.88-1.09)
Terriers	0.98 (0.95-1.02)	0.99 (0.96-1.03)	1.01 (0.96-1.05)	1.02 (0.97-1.07)	**0.84 (0.76-0.94)**	0.91 (0.81-1.01)
Dachshunds	1.01 (0.96-1.06)	1.02 (0.97-1.07)	1.06 (0.99-1.13)	1.06 (0.99-1.13)	0.96 (0.84-1.11)	1.03 (0.89-1.18)
Spitz and primitive types	1.05 (1.01-1.09)	1.00 (0.97-1.04)	1.04 (0.99-1.09)	1.01 (0.96-1.06)	**0.82 (0.73-0.91)**	**0.83 (0.74-0.93)**
Scent hounds and related	1.05 (1.00-1.09)	1.03 (0.98-1.07)	1.07 (1.01-1.13)	1.05 (0.99-1.11)	**0.86 (0.76-0.98)**	0.88 (0.77-0.99)
Pointing dogs	0.95 (0.89-1.02)	0.95 (0.88-1.02)	0.96 (0.88-1.06)	0.97 (0.89-1.07)	**0.65 (0.51-0.82)**	0.73 (0.58-0.93)
Retrievers	1.00 (0.98-1.03)	1.02 (0.99-1.05)	1.00 (0.96-1.04)	1.02 (0.98-1.06)	**0.87 (0.80-0.95)**	0.98 (0.90-1.06)
Companion and Toy dogs	**1.10 (1.06-1.13)**	**1.09 (1.05-1.12)**	**1.12 (1.08-1.17)**	**1.12 (1.07-1.16)**	1.01 (0.92-1.12)	1.03 (0.93-1.14)
Sight hounds	0.90 (0.79-1.02)	0.90 (0.79-1.02)	0.94 (0.79-1.12)	0.94 (0.79-1.12)	0.84 (0.57-1.26)	0.87 (0.59-1.30)
Mixed Pedigree‡	**1.10 (1.07-1.13)**	**1.07 (1.05-1.11)**	**1.09 (1.06-1.12)**	**1.09 (1.05-1.13)**	**1.22 (1.13-1.32)**	**1.18 (1.09-1.27)**

*Adjusted for age and sex
†Adjusted for age, sex, marital status, presence of children in the home, population density, area of residence, education level, region of birth, income and a correction for latitude of residence.
‡Group comprising all non-pure pedigree dogs.

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Figure legends:

Figure 1 - Hazard ratios (HR) and 95% confidence intervals (CI) for the association of dog ownership and time to initiation of medication for hypertension, dyslipidemia and type 2 diabetes.

Figure 2 - Coefficients and 95% confidence intervals for the exposure to dog ownership compared to non-dog ownership on SD-transformed biochemical and clinical measurements in the TwinGene.

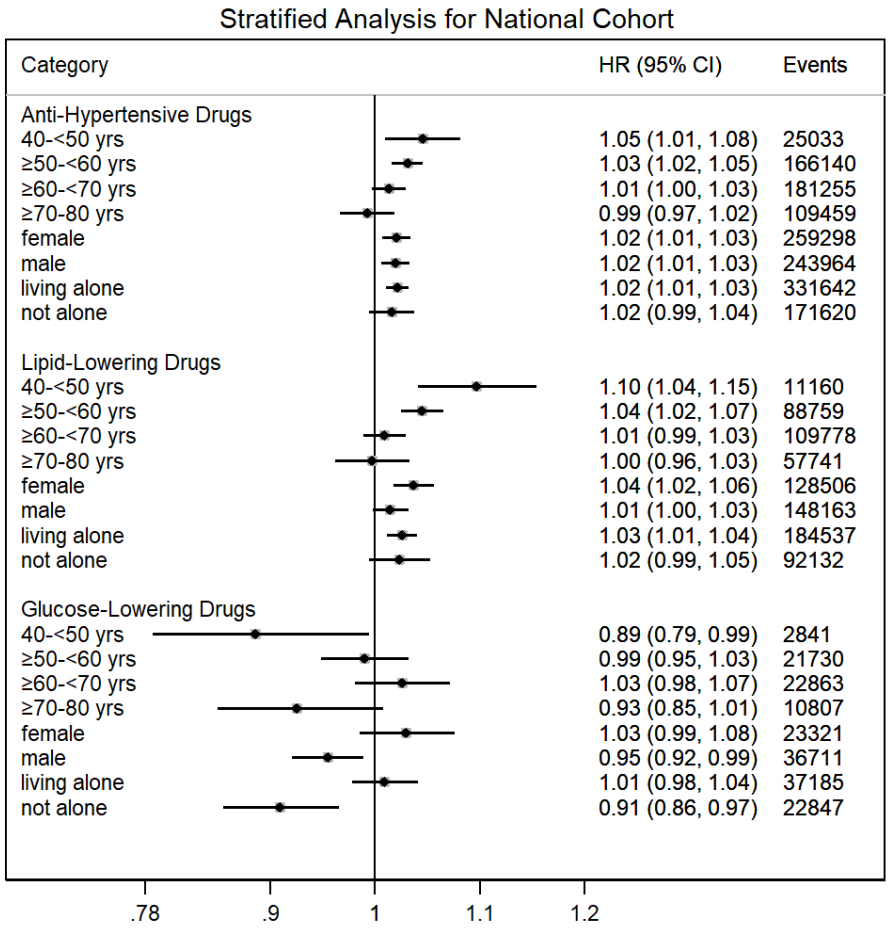

Figure 1. Hazard ratios (HR) and 95% confidence intervals (CI) for the association of dog ownership and time to initiation of medication for hypertension, dyslipidemia and type 2 diabetes stratified by age category, sex and home occupancy (living alone or with someone) and adjusted for age, sex, marital status, presence of children in the home, population density, area of residence, education level, region of birth, income and a correction for latitude of residence.

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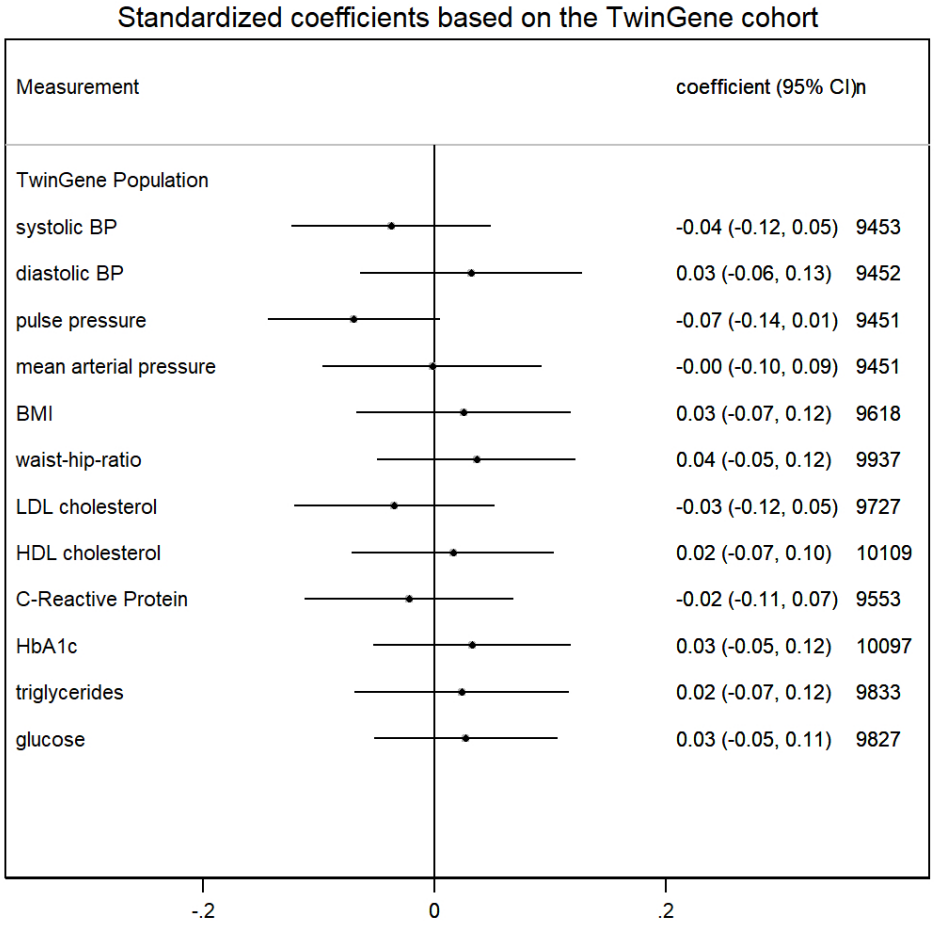

Figure 2. Coefficients and 95% confidence intervals for the exposure to dog ownership compared to non-dog ownership on SD-transformed biochemical and clinical measurements in the TwinGene.

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Supplementary Appendix

Dog ownership and Cardiovascular Risk Factors by Mubanga *et al*.

Content

Supplementary Methods

Data Source and Parameters

Sweden has a structured population registration system that has enabled the collection of individual level information on the total population. By using an identity-protected unique code called the personal identity number (PIN), it is possible to link Swedish residents through different national registers for information such as vital status, socio-demographic data, dog ownership and health outcomes.[1]

Covariates

Covariates extracted at baseline from the Register of the Total Population included sex, birth year, region of birth separated into Sweden, other Nordic countries and non-Nordic countries; and the level of education categorized as compulsory school (≤9 years), secondary school (10-11 years) and tertiary education (≥12 years). We further included annually -updated covariates including marital status categorized as single, married/registered partnership/cohabiting, divorced or widowed; the presence of children in the home (dichotomized as yes/no), the area of residence (Norrland, Svealand and Götaland), the population density in municipality of residence (continuous variable), and annual household income (birth year-standardized quintiles). A north-south gradient was adjusted for by including the latitude of the municipality of residence. To avoid reverse effects of outcomes on covariates, we used covariate data from the preceding year to time-update information on January 1 in every year. A binary variable for home occupancy where individuals were assigned to 'living alone' if the individual lived alone or 'not alone' if they were registered as living with a partner or a child. Co-habiting partners with no children in common could not be accounted for via the registers. Another variable for living with children aged <18 was created to account for those who lived with children in the home. A second stratification variable was created for age group in decades.

From the SALT study conducted in 1998-2002, we used the following self-reported variables as covariates: age, sex, presence of children in the household, area of residence, population density, marital status, and latitude of residence and level of education as defined in the national cohort. Additionally, we adjusted for tobacco use (never, former or current user), employment status (employed, retired, sick leave or unemployed), Charlson comorbidity index and disability (categorized as yes /no). Additionally the socioeconomic index which ranks occupations by the average level of education and job earnings of job holders was also included.[2] By using National Patient Register data from the TwinGene clinic visit-date to five years prior, we created a Charlson comorbidity index. This is a widely used index for risk adjustment in health care research.[3, 4]

TwinGene

The Swedish Twin Registry is a national register started in 1958 that derives information on all twin births occurring in Sweden from the National Board of Health and Welfare. It contains information on more 190,000 Swedish twin pairs born from 1886 onwards.[5] There have been several sub-studies conducted within this registry that have enabled the enhancement of the phenotypic and genetic data available on each participant. For this study, we limited ourselves to two sub-studies that comprised participants aged 45 to 80 years and who had consented to participate in both studies. Data between the two sub-studies involved was collected a minimum of 2 and a maximum of 10 years apart (**Supplementary Table 1, Supplementary Figure 2**).

The first study, the Screening Across the Lifespan Twin study (SALT) interview was conducted as a sub-study of the Swedish Twin Register between 1998 and 2002 targeting all twin-pairs born in 1958 or earlier. Questionnaires were used to collect information on family status, occupation, education level, anthropometric measurements, alcohol intake, tobacco use, environmental exposures and irritants, medication use and health - including psychosocial /personality outcomes.[5] Information was collected from 44,821 respondents.

The second sub-study, the TwinGene study, was nested in the previous study. Between 2004 and 2008 participants from SALT were invited back as part of the TwinGene Study. TwinGene was set up to enable the collection of biological specimens to investigate gene-environment interactions in

participants. 12,614 invited participants gave consent to participate. Questionnaires were mailed and filled in for medication use and health outcomes. Blood was then collected for clinical biochemistry from a local health facility and processed centrally.[6] We used the date of clinic visit as the date of study.

Clinical information was taken during TwinGene study (2004-2008), dog ownership status on the date of clinical examination, and employment, profession and type of housing was extracted from the SALT questionnaire (1998-2002). All variables taken from SALT are described in **Supplementary Table 1**.

Supplementary Table 1. Description of variables derived from the SALT questionnaire study

Covariate	Questionnaire Option	Variable created	Classification and Derivative from questionnaire
Marital status	What is your civil status?	Married	Married, cohabiting
		Single	Living alone
		Divorced	Divorced, separated, living apart
		Widowed	Widow/ widower
Type of family	Living in a household with children <18 years	Yes/ No	Yes /No
Education level	Highest years of education completed	Primary education or less	9 years or less of education
		Secondary education	10 to 12 years of education
		Tertiary education or more	More than 12 years of education
Employment status	Employment status	Employed	Fully employed, part time employment, owns company, on leave from work, study leave or on military service
		Retired	Pensioner, prematurely retired, partly retired
		Retired for disability or illness	Retired for injury
		Unemployed	Unemployed, housewife/man
Socioeconomic index	Socioeconomic occupation level	Level 1	Unskilled Employees
		Level 2	Lower skilled, non-manual workers
		Level 3	Self-employed excluding independent workers
		Level 4	Intermediate non-manual employees
		Level 5	Highest tier non-manual employees
Tobacco Use	Have you ever smoked or used snuff	Never smoked	No not even tried it, yes but only tried it, smoked now and then (like at parties),
		Former smoker	Smoked regularly, snuffed regularly, smoke now and then (like at parties)
		Current smoker	Smoke regularly, smoke at parties, snuff now and then, snuff regularly
Any movement impairment	Do you have any physical handicap	Yes/no	Yes/ No
Disability	Do you need assistance with personal care/ shopping,/cooking/mobility/	Yes/No	Yes /No
Exercise	How much do you exercise; what fits your annual exercise pattern	Less than average	Almost no exercise, light exercise, much less exercise than average, less than average
		Average	Regular medium exercise, average amount of exercise
		More than average	Hard physical exercise, more exercise than average, much more exercise than normal, maximum amount of exercise

Supplementary Table 2. Description of Breed Classification of the 331 breeds included in the study based on the Nordic Kennel Union Classification

Group Number	Breed Groups	Breed Designation
1	Sheep and cattle dogs	Sheep dogs (Australian, Belgian, Catalan, German, Picardy, Polish, Portuguese, Pyrenean, Shetland, Old English); Shepherd dogs (Belgian, Bergamasco, Croatian, Dutch, German, Majorca, Polish, Romanian, South Russian); Collie (Bearded, Border, Rough, Smooth); Bouvier des Flandres, Beauceron, Briard, Chodsky Pes, Czechoslovakian Wolfdog, Komondor, Kuvasz, Mudi, Lancashire Heeler, Schipperke, Puli, Pumi, Slovakian Chuvach, Welsh Corgie, Australian kelpie, Working kelpie
2	Pinscher and schnauzer dogs	Pincher (Affenpinscher, Austrian, Dobermann, German, Miniature); Schnauzer (Giant, Miniature); Mountain Dog (Appenzeller, Bernese, Caucasian Shepherd, Entlebuch, Great Swiss, Karst, Landseer, Newfoundland, Pyrenean, Serra da Estrela, St Bernard, Druguayan Cimarron, Yugoslavian Shepherd); Molossian (Aidi, Anatolian Shepherd, Boxer, Bull Mastiff, Broholmer, Cane Corso, Dogo Argentino, Danish-Swedish Farm dog, Dogo Canario, Dogue de Bordeux, English Bulldog, Great Dane, Hovawart, Majorca Mastiff, Mastiff, Neapolitano Mastiff, Pyrenese Mastiff, Rafeiro of Alentejo, Spanish Water Dog, Shar Pei, Tosa); Central Asia Shepherd Dog, Russian Black Terrier
3	Terriers	Airedale, American Staffordshire, Australian, Bedlington, Border, Brazilian, Bull, Cairn, Cesky, Dandie Dinmont, English Toy, Fox, German Hunting, Irish Glen of Imaal, Irish Softcoated Wheaten, Irish, Jack Russel, Kerry Blue, Lakeland, Manchester, Miniature Bull, Norfolk, Norwich, Parson Russell, Sealyham, Australian Silky, Skye, Tenterfield, Welsh, West Highland White, Yorkshire
4	Dachshunds	Miniature, Standard, Kaninchen
5	Spitz and primitive types	Alaskan Malamute, American Akita, Canaan dog, Canarian Warren, Chow Chow, Cirneco dell'Etna, East Siberian Laika, Eurasian, Finnish Lapphund, Finnish Spitz, German Spitz, Greenland dog, Hokkaido, Halleforshund, Icelandic Sheepdog, Japanese Akita, Japanese Spitz, Karelian Beardog, Keeshond, Korea Jindo, Laponian Herder Pharaoh Hound, Mexican Hairless dog, Norwegian Buhund, Norwegian Lundehund, Norwegian Elkhound, Peruvian Hairless dog, Ibizan Hound, Pomeranian, Russian European Laika, Samoyed, Shiba, Siberian Husky, Swedish Elkhound, Swedish Lapphund, Swedish White Elkhound, Swedish Vallhund, Thai Bangkaew, Thai Ridgeback, Volpino italiano, West Siberian Laika
6	Scent hounds and related dogs	Alpine Dachsbracke, American Foxhound, Basset Artesian Normand, Basset Bleu de Gascogne, Basset fauve de Bretagne, Basset Hound, Bavarian Mountain Scent hound, Beagle, Black and Tan Coonhound, Bloodhound, Bluetick Coonhound, Bosnian Coarse-haired hound, Dalmatian, Drever, Dunker Hound, Fawn Brittany Griffon, Finnish Hound, Foxhound, German Hound, Grand Basset Griffon Vendeen, Grand Griffon Vendeen, Griffon Nivernais, Halden Hound, Hamilton Hound, Hygen Hound, Istrian Short-haired hound, Otterhound, Petit Basset Griffon Vendeen, Plott, Polish hunting dog, Porcelain, Posavaz Hound, Rhodesian Ridgeback, Russian Hound, Russian Spotted hound, Small Blue Gascony Hound, Spanish Hound, Schiller Hound, Swiss Hound, Serbian Hound, Slovakian Hound, Småland Hound
7	Pointing dogs	Blue Picardy Spaniel, Bracco Italiano, French Pointing, Brittany, Bohemian wire-haired, Drentse Patridge, English Setter, French Spaniel, Old Danish Pointer, Gordon Setter, French wire-haired Korthals Pointing Griffon, Münsterländer, Irish Red Setter, German Short/Wire-haired pointing dog, Portuguese Pointing dog, Pointer, Pudelpointer, Slovakian Wire-haired Pointing dog, Italian Spinone, Stabyhound, Hungarian Vizsla wire-/short-haired, Weimaraner short-/long-haired
8	Retrievers	American Cocker Spaniel, Barbet, Chesapeake Bay Retriever, Clumber Spaniel, Cocker Spaniel, Curly Coated Retriever, English Springer Spaniel, Field Spaniel, Flat coated Spaniel, German Spaniel, Golden retriever, Irish Water Spaniel, Labrador Retriever, Lagotto romagnolo, Nederlandse Kooikerhondje, Nova Scotia Duck Tolling Retriever, Spanish Water dog, Portuguese Water Dog, Sussex Spaniel, Welsh Springer Spaniel, Wetterhound
9	Companion and toy dogs	Havanese, Bolognese, Boston Terrier, Belgian Griffon, Brussels Griffon, Cavalier King Charles Spaniel, Chihuahua, Chinese Crested, Coton de Tulear, French Bulldog, Japanese Chin, King Charles Spaniel, Kromfohrlander, Lhasa Apso, Lowchen, Maltese, Pug, Papillon, Pekingese, Small Brabant Griffon, Phalene, Prazský krysarík, Poodle, Russian Toy, Shih Tzu, Tibetan Terrier, Tibetan Spaniel
10	Sight hounds	Afghan Hound, Azawakh, Borzoi, Polish Greyhound, Spanish Greyhound, Irish Wolfhound, Italian Greyhound, Hungarian Greyhound, Saluki, Scottish Deerhound, Sloughi, Whippet

Supplementary Table 3. Association of dog ownership with initiation of medication for the treatment of hypertension. This compares the main analysis as shown in Table 2 with a modified analysis that excludes Beta-blockers which have not been recommended first line treatment for hypertension since 2006.[7] Cox regression models with hazard ratios (HR) and 95% confidence interval (CI) are reported.

	N treated	Time at risk	Model 1*	Model 2§
With β-blockers	503,305	10,659,258	1.02 (1.01-1.03)	1.02 (1.01-1.03)
Without β-blockers	401,573	11,018,086	1.03 (1.02-1.04)	1.02 (1.01-1.03)

*Model 1. Age and sex adjusted

§Model 2. National cohort: Adjusted for sex, age, type of family, area of residence, population density, marital status, region of birth, income, education level, latitude of residence.

Supplementary Table 4. Association of dog ownership with initiation of lipid lowering medication. This compares the main analysis as shown in Table 2 with a modified analysis that censored participants at an event of angina or heart failure. Cox regression models with hazard ratios (HR) and 95% confidence interval (CI) are reported.

Lipid lowering medication	N treated	Time at risk	Model 1*	Model 2§
Without censoring	276,691	11,508,349	1.03 (1.02-1.04)	1.02 (1.01-1.04)
With censoring	243,797	11,482,789	1.03 (1.02-1.04)	1.02 (1.01-1.04)

*Model 1. Age and sex adjusted

§Model 2. National cohort: Adjusted for sex, age, type of family, area of residence, population density, marital status, region of birth, income, education level, latitude of residence.

Supplementary Table 5. Additional baseline characteristics of 10,110 Swedish adults in the Swedish Twin Register. Information is based on persons who participated in the TwinGene project designed to enhance the Screening Across the Lifespan Twin (SALT) questionnaire-based sub-study in the Swedish Twin Register with biologic specimens. Numbers and % are reported unless stated otherwise. Clinical information was taken during TwinGene study (2004-2008), dog ownership status on the date of clinical examination and other non-clinical details extracted from the SALT questionnaire (1998-2002).

Participant characteristics	n		All n=10,110 (100%)	Non-dog owners n=9,626 (95.0%)	Dog owners n=484 (5.0%)	Mixed pedigree dog owners n=141 (1.4%)*	Hunting dog owners n=143 (1.4%)*
Employment status	10,110	Employed	6,875 (68.0)	6,541 (68.0)	334 (69.0)	97 (68.8)	93 (65.0)
		Retired	2,066 (20.4)	1,992 (20.7)	74 (15.3)	18 (12.8)	29 (20.3)
		Sick leave or illness	875 (8.7)	818 (8.5)	57 (11.8)	18 (12.8)	16 (11.2)
		Unemployed	294 (2.90)	275 (2.9)	19 (3.9)	8 (5.7)	5 (3.5)
Profession†	10,110	Unskilled labor	2,458 (24.3)	2,351 (24.4)	107 (22.1)	32 (22.7)	27 (18.9)
		Lower non-manual labor	3,373 (33.4)	3,205 (33.3)	168 (34.7)	57 (40.4)	43 (30.1)
		Self-employed	430 (4.3)	404 (4.2)	26 (5.4)	6 (4.3)	6 (4.2)
		Intermediate non-manual labor	2,539 (25.1)	2,411 (25.0)	128 (26.4)	32 (22.7)	46 (32.2)
		Higher non-manual employee	1,310 (13.0)	1,255 (13.0)	55 (11.4)	14 (9.9)	21 (14.7)
Type of housing or accommodation	10,110	Independent	10,100 (99.9)	9,616 (99.9)	484 (100.0)	141 (100.0)	143 (100.0)
		Assisted living[2]	6 (0.1)	6 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
		Other	4 (<0.0)	4 (<0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Biochemical Variables							
C-Reactive Protein	9,553	Median (IQR)	1.7 (0.8-3.4)	1.7 (0.8-3.4)	1.8 (0.8-3.2)	2.0 (0.9-3.5)	1.6 (0.7-3.1)
LDL-Cholesterol	9,727	Mean (SE)	3.9 (0.9)	3.9 (0.9)	3.8 (0.9)	3.8 (0.9)	3.9 (0.9)
HDL-Cholesterol	10,109	Mean	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)
Triglyceride (Fasting)	9,261	Median	1.1 (0.8-1.6)	1.1 (0.8-1.6)	1.1 (0.9-1.6)	1.2 (0.9-1.6)	1.2 (0.9-1.5)
Glucose (Non-Diabetic)	9,256	Median	5.3 (5.0-5.7)	5.3 (5.0-5.7)	5.2 (5.0-5.7)	5.3 (5.0-5.8)	5.3 (5.0-5.7)
HbA1c	10,097	Mean	4.8 (0.6)	4.8 (0.6)	4.8 (0.6)	4.8 (0.6)	4.7 (0.5)
Body Mass Index	9,618	Mean	25.9 (4.0)	25.9 (4.0)	26.0 (4.0)	26.3 (4.4)	26.0 (3.8)
Waist-Hip ratio	9,937	Mean	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)
Blood pressure measurements							
Mean systolic BP (all participants)		Mean	138.1 (19.5)	138.2 (19.5)	136.0 (19.2)	139.4 (20.3)	136.2 (18.1)
Mean diastolic BP (all participants)	8010	Mean	82.2 (10.5)	82.2 (10.4)	82.6 (10.9)	84.8 (11.4)	82.7 (10.4)
Pulse pressure (all participants)		Mean	55.9 (15.4)	56.0 (15.4)	53.4 (13.6)	54.6 (13.9)	53.5 (12.5)

Mean systolic BP (On BP treatment)	1,970	Mean	144.9 (18.8)	144.9 (18.9)	144.9 (17.3)	149.4 (14.9)	142.0 (15.8)
Mean diastolic BP (On BP treatment)		Mean	83.9 (10.7)	83.8 (10.8)	85.0 (9.2)	84.5 (8.4)	85.6 (9.3)
Pulse pressure (On BP treatment)		Mean	61.0 (16.0)	61.1 (16.1)	60.0 (13.8)	65.0 (10.1)	56.4 (12.2)
Self-reported health status	10,110	Excellent	3,501 (34.9)	3,330 (34.9)	171 (35.7)	33 (23.6)	58 (40.8)
		Good	5,330 (53.2)	5,085 (53.3)	245 (51.1)	79 (56.4)	73 (51.4)
		Average	963 (9.6)	914 (9.6)	49 (10.2)	19 (13.6)	8 (5.6)
		Not so good	227 (2.3)	213 (2.3)	14 (2.9)	7 (5.0)	3 (2.1)
Blood Pressure Medication	10,110	Number on treatment (%)	2,099 (20.8)	2,010 (20.9)	89 (18.4)	31 (22.0)	22 (15.4)
Lipid Modifying Medication	10,110	Number on treatment (%)	918 (9.1)	880 (9.1)	38 (7.9)	14 (9.5)	13 (8.3)
Diabetes Medication	10,110	Number on treatment (%)	305 (3.0)	293 (3.0)	12 (2.5)	5 (3.5)	5 (3.5)

*-Proportion of this breed of total population
†-Defined according to Budoki et al.[8]
‡-Assisted living which includes living in
BP- Blood Pressure

Supplementary Table 6. Stepwise addition of covariates into TwinGene model. Odds ratios (OR) and confidence intervals (CI) for associations of dog ownership and prevalent drug prescriptions for hypertension, dyslipidemia and type 2 diabetes (n=10,110). *

Prescription Medication	N on treatment	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7
Anti-hypertensive drugs	2,223	0.96 (0.75-1.21)	0.94 (0.74-1.20)	0.95 (0.74-1.20)	0.92 (0.72-1.18)	0.90 (0.70-1.15)	0.90 (0.71-1.15)	0.90 (0.70-1.15)
Lipid lowering drugs	963	0.92 (0.65-1.29)	0.92 (0.65-1.29)	0.92 (0.66-1.29)	0.90 (0.64-1.26)	0.87 (0.62-1.22)	0.87 (0.62-1.22)	0.87 (0.62-1.22)
Glucose lowering drugs	318	0.89 (0.49-1.61)	0.90 (0.50-1.63)	0.91 (0.50-1.65)	0.90 (0.50-1.63)	0.80 (0.44-1.46)	0.80 (0.44-1.46)	0.78 (0.43-1.43)

*Model 1, 2 and 7 were reported in the main manuscript Table 2
Model 1. Adjusted for age and sex
Model 2. Adjusted for sex, age, type of family, area of residence, population density, marital status, education level and latitude of residence
Model 3. Model 2 plus professional level
Model 4. Model 3 plus employment status
Model 5. Model 4 plus Charlson comorbidity index
Model 6. Model 5 plus disability
Model 7. Full twin model - Model 6 plus tobacco use

Supplementary Table 7: Association of dog ownership with initiation of medication for hypertension, dyslipidaemia and diabetes. Shown for assuming 10-year life-span of dog and a sensitivity analyses at 8-year and 12-year life-span of dog.

Medication	Assuming 10-year life-span of dog		Assuming 8-year life-span of dog		Assuming 12-year life-span of dog	
	Sex-age adjusted model	Fully-adjusted model	Sex-age adjusted model	Fully-adjusted model	Sex-age adjusted model	Fully-adjusted model
Hypertension	1.02 (1.01-1.03)	1.02 (1.01-1.03)	1.02 (1.01-1.03)	1.01 (1.00-1.02)	1.03 (1.02-1.04)	1.02 (1.01-1.03)
Dyslipidemia	1.03 (1.02-1.04)	1.02 (1.01-1.04)	1.02 (1.01-1.04)	1.02 (1.00-1.03)	1.03 (1.02-1.04)	1.02 (1.01-1.04)
Diabetes	0.91 (0.89-0.94)	0.98 (0.95-1.01)	0.90 (0.88-0.93)	0.97 (0.94-1.00)	0.92 (0.90-0.94)	0.99 (0.96-1.02)

§Fully-adjusted models adjusted for sex, age, type of family, area of residence, population density, marital status, education level and latitude of residence

Supplementary Table 8: Output from fully adjusted Cox regression models for the association of dog ownership with initiation of medication for hypertension.

	Haz. Ratio	P>z	[95% Confidence Interval]	
Dog owner	1.018	0.000	1.009	1.028
Sex				
Male	**Ref**			
Female	0.945	0.000	0.939	0.950
Marital status				
Married/ cohabiting	**Ref**			
Never Married	0.904	0.000	0.895	0.912
Divorced	0.993	0.091	0.986	1.001
Widowed	1.064	0.000	1.053	1.076
Children in home				
No	**Ref**			
Yes	0.922	0.000	0.915	0.930
Area of Residence				
Norrland	**Ref**			
Svealand	0.959	0.000	0.946	0.972
Götaland	0.912	0.000	0.895	0.929
Population density	1.000	0.203	0.998	1.001
Education				
Primary level	**Ref**			
Secondary level	0.955	0.000	0.949	0.962
Tertiary level	0.832	0.000	0.826	0.839
Country of birth				
Sweden	**Ref**			
Other Nordic countries	1.143	0.000	1.128	1.157
Non-Nordic countries	1.010	0.114	0.998	1.022
Income				
Income level 1 (lowest tier)	**Ref**			
Income level 2	0.994	0.195	0.985	1.003
Income level 3	0.995	0.297	0.986	1.004
Income level 4	0.991	0.056	0.982	1.000
Income level 5 (highest tier)	0.986	0.004	0.977	0.995
Latitude of residence	1.000	0.000	1.000	1.000

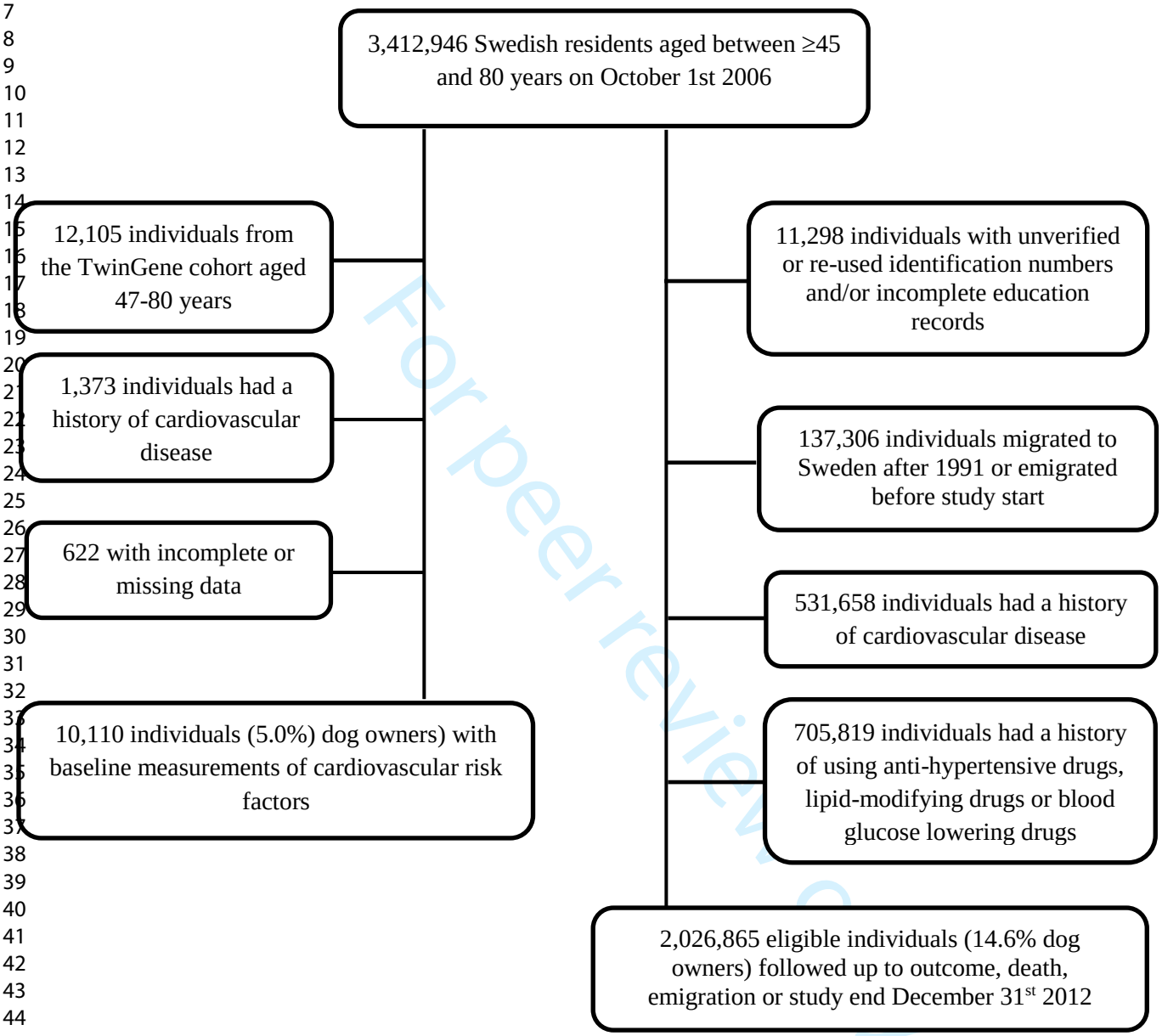
Supplementary Table 9: Output from fully adjusted Cox regression models for the association of dog ownership with initiation of medication for dyslipidaemia

	Haz. Ratio	P>z	[95% Confidence Interval]	
Dog owner	1.024	0.000	1.011	1.036
Sex				
Male	**Ref**			
Female	0.773	0.000	0.767	0.779
Marital status				
Married/ cohabiting	**Ref**			
Never Married	0.835	0.000	0.825	0.846
Divorced	0.992	0.117	0.982	1.002
Widowed	1.022	0.004	1.007	1.038
Children in home				
No	**Ref**			
Yes	0.891	0.000	0.881	0.901
Area of Residence				
Norrland	**Ref**			
Svealand	1.005	0.597	0.987	1.024
Götaland	0.928	0.000	0.905	0.952
Population density	1.000	0.000	0.999	1.001
Education				
Primary level	**Ref**			
Secondary level	0.963	0.000	0.954	0.972
Tertiary level	0.796	0.000	0.787	0.804
Country of birth				
Sweden	**Ref**			
Other Nordic countries	1.169	0.000	1.150	1.189
Non-Nordic countries	1.195	0.000	1.177	1.213
Income				
Income level 1 (lowest tier)	**Ref**			
Income level 2	1.000	0.962	0.988	1.012
Income level 3	1.004	0.504	0.992	1.016
Income level 4	1.010	0.104	0.998	1.022
Income level 5 (highest tier)	1.005	0.450	0.992	1.018
Latitude of residence	1.000	0.813	1.000	1.000

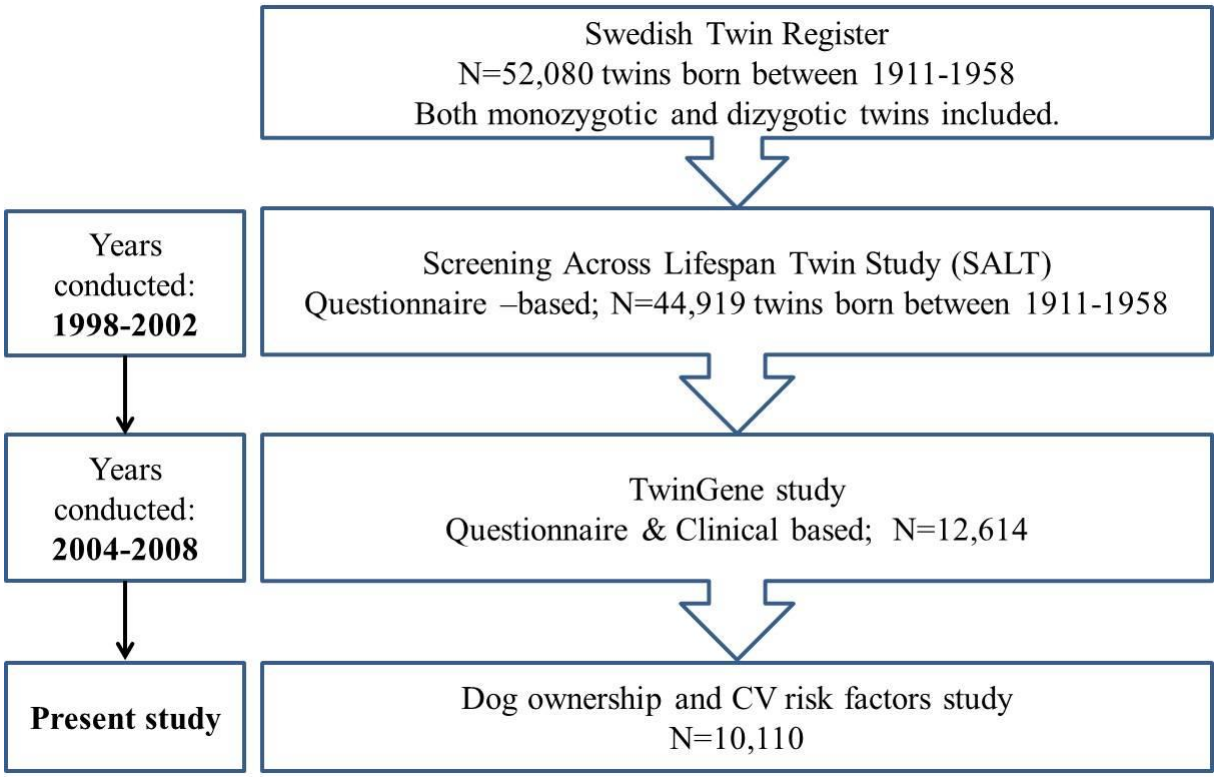
Supplementary Table 10: Output from fully adjusted Cox regression models for the association of dog ownership with initiation of medication for diabetes.

	Haz. Ratio	P>z	[95% Confidence Interval]	
Dog owner	0.982	0.193	0.954	1.009
Sex				
Male	**Ref**			
Female	0.546	0.000	0.536	0.556
Marital status				
Married/ cohabiting	**Ref**			
Never Married	1.244	0.000	1.215	1.274
Divorced	1.196	0.000	1.171	1.223
Widowed	1.290	0.000	1.248	1.334
Children in home				
No	**Ref**			
Yes	0.965	0.002	0.944	0.988
Area of Residence				
Norrland	**Ref**			
Svealand	0.909	0.000	0.874	0.946
Götaland	0.883	0.000	0.837	0.932
Population density	0.999	0.000	0.998	1.001
Education				
Primary level	**Ref**			
Secondary level	0.877	0.000	0.861	0.894
Tertiary level	0.635	0.000	0.620	0.650
Country of birth				
Sweden	**Ref**			
Other Nordic countries	1.116	0.000	1.076	1.159
Non-Nordic countries	1.952	0.000	1.900	2.004
Income				
Income level 1 (lowest tier)	**Ref**			
Income level 2	0.919	0.000	0.896	0.941
Income level 3	0.845	0.000	0.824	0.866
Income level 4	0.777	0.000	0.757	0.797
Income level 5 (highest tier)	0.702	0.000	0.683	0.722
Latitude of residence	1.000	0.001	1.000	1.000

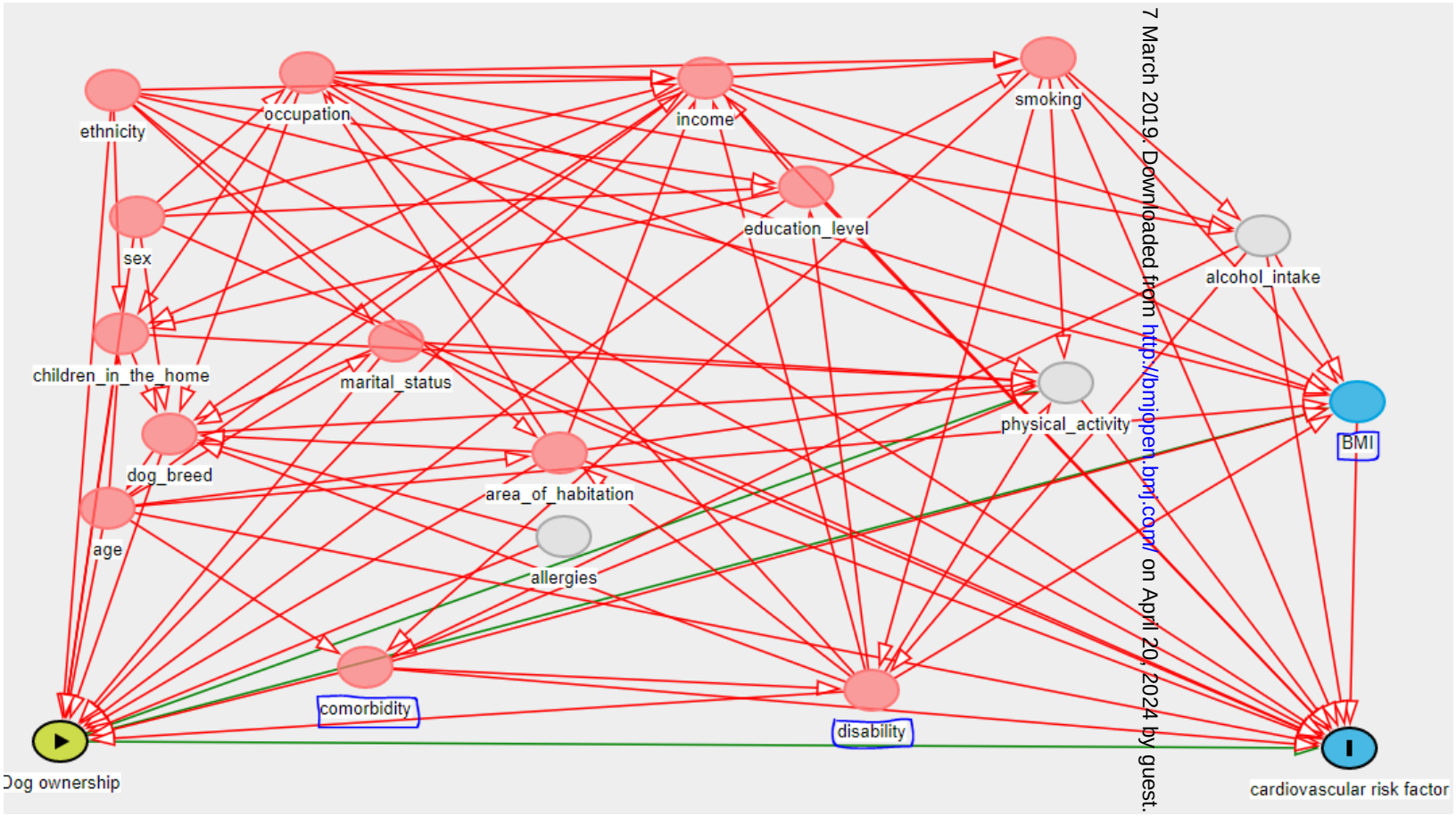
Supplementary Figure 1: Study population



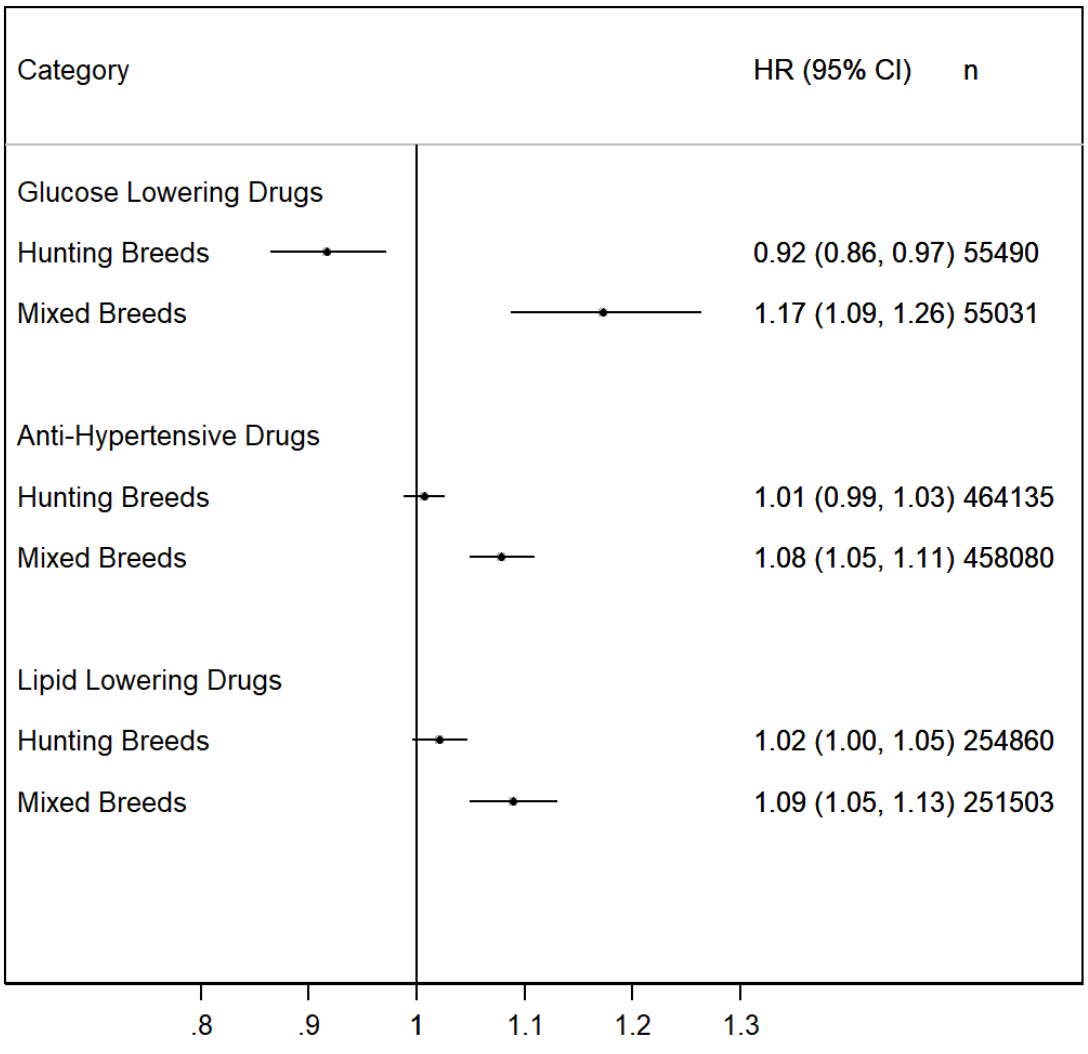
Supplementary Fig 2: Overview of Twin Cohort study recruitment and data collection.



Supplementary Figure 3: Direct Acyclic Graph for dog ownership and cardiovascular risk. The highlighted variables (comorbidity, disability and body mass index) were only available in the TwinGene cohort.



Supplementary Figure 4. Hazard ratios (HR) and 95% confidence intervals (CI) for the association of dog ownership and time to initiation of medication for hypertension, dyslipidemia and type 2 diabetes examining associations in hunting-type breeds (combining Terriers, Scent Hounds, Pointing dogs and Retrievers) and mixed pedigree dogs and adjusted for age, sex, marital status, presence of children in the home, population density, area of residence, education level, region of birth, income and a correction for latitude of residence.



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The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
Dog ownership and Cardiovascular Risk Factors	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	a) Stated in the abstract - Pages 2 b) Abstract Page 2	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Abstract Page 2 Abstract Page 2 Abstract Page 2
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4		
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4		
Methods					
Study Design	4	Present key elements of study design early in the paper	Page 5		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5 & 6		
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the	Page 5, 6 & 7; Also summarised in the	RECORD 6.1: The methods of study population selection (such as codes or	Page 5 & 6

		sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	supplementary material as supplementary figure 1 on page 7 *Not applicable*	algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	This was not applicable to the present study *****
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	Pages 5, 6 & 7	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Full explanations are provided on pages 5-7
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Outlined on Page 6		
Bias	9	Describe any efforts to address potential sources of bias	Pages 8 & 12		
Study size	10	Explain how the study size was		Population-based study including all	

		arrived at	Page 5	adults who met the criteria for inclusion	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	Pages 7 & 8		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	a) Page 7 & 8 b) Page 8 c) Page 6 d) Page 6 e) Page 8		
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	After ethics approval was provided, Statistics Sweden provided de-identified data for the required population. The authors then cleaned the data before analysis

Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	This information is provided on page-7. This was done using the unique personal identity number given to every Swedish resident.
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	a) Supplementary Figure 1 on page 7 of the supplementary material. b) Supplementary Figure 1 on page 7 of the supplementary material. Also provided in main manuscript on page 5 & 6 c) Supplementary Figure 1 on page 7 of the supplementary material.	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Page 5 & Flow diagram on page 7 of the supplementary material and reported as figure 1
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise	a) These baseline characteristic are reported in Table 1on page 14 and 15; as well as in the results in Table 2 on page 16		

		follow-up time (*e.g.*, average and total amount)			
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures	These have been reported on page 16 & in Table 2		
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	These have been reported on page 16 & in Table 2 and in the results section on page 9 & 10 b) This shown in the supplementary methods of the supplementary material		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	This has been reported on Page 8, Table 3 reports the breed group analysis and further material found in the supplementary material as previously described		

			in the methods on page 8		
Discussion					
Key results	18	Summarise key results with reference to study objectives	Page 10 & 11		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	The limitations of this cohort study are discussed on page 12	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Page 13 & 14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 11 & 12	we observed that dog ownership was associated with a minimally higher risk of initiation of treatment for hypertension and dyslipidemia, and that ownership of dogs of the hunting breed types was associated with a lower risk of initiating treatment for diabetes	
Generalisability	21	Discuss the generalisability (external validity) of the study results			
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 13 *The study was funded by the Agria Research Foundation and the Swedish Research Council for Environment, Agricultural Sciences and Spatial Planning (FORMAS), grant number 2013-1673. T.F has personal*		

			funding from the Goran Gustafsson foundation. The Swedish Twin Registry is managed by Karolinska Institutet and receives funding through the Swedish Research Council under the grant no 2017-00641. The funders were not involved in any part of the study design, data collection, analysis manuscript preparation or approval.		
Accessibility of protocol, raw data, and programming code		..	*The register data that support the findings of this study were made available by record-linkage with data from Statistics Sweden, the National Board of Health and Welfare, the Swedish Kennel Club, Swedish Board of Agriculture and the Swedish Twin Register. Restrictions apply to the availability of these data, which were used under license and ethical approval*	RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	

			for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Regional Ethical Review Board in Stockholm, Sweden		

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

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Dog ownership and Cardiovascular Risk Factors: a nationwide prospective register-based cohort study

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Dog ownership and Cardiovascular Risk Factors: a nationwide prospective register-based cohort study

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Abstract

Objective: To study the association between dog ownership and cardiovascular risk factors.

Design: A nationwide register–based cohort study and a cross-sectional study in a subset.

Setting: A cohort of 2,026,865 participants was identified from the Register of the Total Population and linked to national registers for information on dog ownership, hospital admissions, education level, income and country of birth. Participants were followed from October 1st, 2006, to the end of the study on December 31st, 2012, assessing medication for a cardiovascular risk factor, emigration and death. Cross-sectional associations were further assessed in 10,110 individuals from the TwinGene study with additional adjustment for professional level, employment status, Charlson comorbidity index, disability and tobacco use.

Participants: All Swedish residents aged 45-80 years on October 1st, 2006.

Main outcome measures: Initiation of medication for hypertension, dyslipidemia and diabetes mellitus.

Results: After adjustment for confounders, the results indicated slightly higher likelihood of initiating anti-hypertensive (HR, 1.02; 95% CI, 1.01-1.03) and lipid-lowering treatment (HR, 1.02; 95% CI, 1.01-1.04) in dog owners than in non-owners, particularly amongst those aged 45 to 60 and in those owning mixed breed or companion/toy breed dogs. No association of dog ownership with initiation of treatment for diabetes was found in the overall analysis (HR, 0.98; 95% CI, 0.95-1.01). Sensitivity analyses in the TwinGene cohort indicated confounding of the association between dog ownership and prevalent treatment for hypertension, dyslipidemia and diabetes mellitus, respectively from factors not available in the national cohort, such as employment status and non-CVD chronic disease status.

Conclusions: In this large cohort study, dog ownership was associated with a minimally higher risk of initiation of treatment for hypertension and dyslipidemia implying that the previously reported lower risk of cardiovascular mortality among dog owners in this cohort is not explained by reduced hypertension and dyslipidemia. These observations may suffer from residual confounding despite access to multiple important covariates, and future studies may add valuable information.

Strengths and limitations of this study

- This is the largest study to date to examine the impact of dog ownership on cardiovascular risk factors.
- The nationwide register-based cohort study with a cross-sectional investigation in a twin registry with a vast array of lifestyle and clinical variables strengthens the results.
- The main outcome measures were extracted from nationwide registers thus decreasing the risk of recall and selection bias.
- Misclassification of dog ownership, particularly in the twin register, may have led to some loss of power.
- Some important confounding factors were not available in the national data.

Introduction

There is a growing interest in pet ownership as a possible intervention to enhance cardiovascular health and well-being.[1, 2] We recently observed that being registered as a dog owner was associated with a lower risk of cardiovascular and all-cause mortality in the general Swedish population (n=3,432,153).[3] Any causal association of dog ownership with lower cardiovascular mortality could potentially be mediated through increased physical activity[4, 5] or through the psychological benefits of companionship,[6] which could in turn reduce other important cardiovascular risk factors such as blood pressure, adiposity, dyslipidemia, and insulin resistance.[7, 8] An alternative explanation could be confounding by socioeconomic,[9] cultural,[10] demographic[9] or psycho-social factors.[11, 12] A large number of cross-sectional and longitudinal studies across different countries support the association of dog ownership with physical activity,[1] however, reports regarding the association of dog ownership with other cardiovascular risk factors are less consistent.[13-20] These inconsistences may be due to low statistical power in small studies, use of restricted or homogenous populations, inability to control for differences across breeds of dogs, or simply an absence of effect. As dogs are reported to be more common in rural areas compared to urban areas,[21-23] as well as in households with children,[24, 25] it is also important to account for these differences. The aim of this study was to assess the association of dog ownership with three major clinical risk factors for cardiovascular disease,[26] specifically initiation of treatment of hypertension, dyslipidemia and diabetes mellitus. We hypothesized that the cardiovascular risk profile of dog owners is better than that of non-dog owners. To overcome limitations of previous studies concerning study size, generalizability and differences between dog breeds, we investigated this hypothesis using data on all Swedish residents aged 45-80 years of age in 2006 from national registers on dog ownership and drug prescriptions. We further sought to explore the association with other cardiovascular risk factors using cross-sectional data from a sub-cohort extracted from the Swedish Twin Registry containing detailed information from questionnaire data, physical examinations and laboratory measurements.

Methods

Design

The main analysis was based on a nationwide cohort study of Swedish residents aged 45-80 followed from October 1st 2006, to December 31st 2012. We additionally used cross-sectional data of participants (aged 47-80) in the TwinGene study, which is a sub-study of the Swedish Twin Registry (**Supplementary Figure 1)**.

Study Population – National Cohort

All Swedish residents (n=3,412,946) aged 45-80 on October 1st 2006, were identified through the Register of the Total Population. To ensure complete linkage to medical information and sufficient information regarding dog ownership in Sweden, we excluded 11,298 individuals with unverified, re-used identification numbers or missing education information, and 137,306 additional individuals that had resided in Sweden for <15 years. We also excluded 531,658 individuals with a history of any CVD (International Classification of Disease (ICD)-9 codes 390-459 and ICD-10 I00-I99) before October 1st, 2006 or with a history of coronary artery bypass grafts or percutaneous coronary artery intervention medical procedure (Nordic surgical procedure codes FNA, FNC and FNG) from in- and outpatient data. Inpatient data was available from 1987 and outpatient data from 2001. Further, using data from the Swedish Prescribed Drug Register, which covers all Swedish dispensed pharmacy prescriptions since it was established on July 1st 2005, individuals (n=705,819) were excluded if they had any recorded dispensed prescription of anti-hypertensive drugs, lipid-lowering drugs, or glucose lowering drugs from 15 months prior to baseline (which was when this register was initiated). Anti-hypertensive drugs were defined based on the Anatomical Therapeutic Chemical Classification System (ATC) as codes: C02 (antihypertensive drugs), C03A, C03EA01 (thiazide diuretics), C07 (beta-receptor blockers, excluding sotalol [C07AA07]), C08C (selective calcium antagonists with mainly vascular effects) and C09 (agents acting on the renin-angiotensin system). Lipid-lowering drugs were defined as C10AA (statins), C10AB (fibrates), C10AC (bile acid sequestrants), C10AX (other lipid-modifying agents) and C10B (lipid-lowering drug combinations). Glucose-lowering drugs were defined as ATC-code A10A (insulin and analogues) and A10B (glucose-lowering drugs excluding insulin).

Study population – TwinGene

The TwinGene study originally included 12,614 (of 22,391 invited) twins from the "Screening Across the Lifespan Twin study" (SALT). It was conducted between April 2004 and December 2008 and included a visit to the participants' local health center and blood sampling (**Supplementary Figure 2**).[27] The study-base "SALT" was a sub-study of the Swedish Twin Register in twins born before 1959 and who participated in a telephone-based questionnaire sub-study from March 1998 to March 2002[27] (**Supplementary Table 1).**

We performed a cross-sectional analysis of the association of dog ownership with cardiovascular risk factors in the TwinGene cohort (n=12,105). We excluded 1,373 individuals for having a previous history of CVD recorded in the National Patient Register.[28] We also excluded 622 individuals for having missing or incomplete data (**Supplementary Figure 1**).

Exposure

Dogs in Sweden are required to have a unique identifier (ear tattoo or implanted identity chip) and this is registered alongside their owner's unique personal identity number at the Swedish Board of Agriculture. All dogs sold as purebred are registered by the Swedish Kennel Club. In Sweden, there are virtually no stray dogs,[29] and compliance to regulations is thought to be high due to a general high level of social and institutional trust.[30]

We defined the variable 'dog ownership' in the national cohort as registered dog ownership or having a partner registered as a dog owner in either the Swedish Board of Agriculture and/or the Swedish Kennel Club registers. Exposure to dog ownership was time-updated to include only those periods where each dog was alive and registered to the study participant or their registered partner. The identification of partners was possible through annual extracts from the Register of the Total Population that keeps track of couples that are married, registered in same-sex partnership or are cohabiting with common children. It is presently not possible to identify cohabiting non-married partners who have no children in common in the population registers.

In the TwinGene data, we did not have access to information on partners' dog ownership and only each person's own dog registrations were used. Dog ownership was defined at the date of inclusion in TwinGene.

If information on a dog's death was missing, we assumed a maximum lifespan of ten years.[31] We conducted sensitivity analyses examining associations with dog death at a maximum lifespan of 8 years and 12 years. Where birth or registration dates were discrepant between the two registers, we randomly selected one of the two.

To define breed groups, we used the Federation Cynologique International standard with some local adaption from Swedish Kennel Club's definition to categorize the 331 breeds into ten breed groups based on character and behaviour attributes **(Supplementary Table 2)**. All non-purebred dogs and those of unknown breed were included in an additional mixed breed group. Where owners had dogs of different breeds, we defined the breed based on the dog registered first and where owners had several dogs, we restricted ownership to three dogs.

Based on previous findings [3] that ownership to four different breed groups was associated with a lower risk of cardiovascular events, we defined a group of these dog breeds (Terriers, Pointing, Scent Hounds and Retrievers) for additional exploratory analysis. This group is hereafter referred to as 'active dog breeds' as these breeds also generally demand high levels of physical activity.

Outcome

In the national cohort, time to first dispensed prescription of anti-hypertensive drugs, lipid-lowering drugs or glucose-lowering drugs after baseline was defined from data extracted from the drug register. Each outcome was considered separately as we chose to estimate the total effect of dog ownership and not only the direct effects. Participants were censored at emigration, death or at the end of the study on December 31st, 2012. In the analysis of time to anti-hypertensive medication, individuals were additionally censored at a diagnosis of heart failure, unstable angina or acute myocardial infarction in the National Patient Register as the same drugs could be administered for their treatment.

Prevalent use of anti-hypertensive, lipid-lowering or glucose-lowering drugs was defined from the clinical questionnaire data collected during the TwinGene study. Cardiovascular risk factors measured and also used as outcomes in TwinGene included blood glucose, glycosylated hemoglobin A1c (HbA1c), high sensitive C-reactive protein (hsCRP), triglycerides, high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), waist-hip ratio, body mass index (BMI), systolic and diastolic blood pressure and mean arterial pressure (MAP) (**Supplementary methods**). Only fasting

measurements of glucose and triglycerides were used (9,873 [97%] of all participants were fasting).

Statistical analyses

All statistical analyses were conducted using Stata version MP14.1 (StataCorp).

Using age as a time-scale, separate multivariable Cox proportional hazards models were applied to assess the associations between dog ownership and time to initiation of anti-hypertensive, lipid-lowering and glucose-lowering drugs, respectively. Directed acyclic graphs were used to guide the choice of covariates (**Supplementary Figure 3).** A first crude model included age and sex, and a second model additionally included the region of birth, area of residence, latitude of residence, population density, level of education, marital status, presence of children in the home and income. A description of the covariates is provided in the **Supplementary methods**. The proportional hazards assumption was verified by plotting Schoenfield residuals and log-log graphs. Results were reported as hazard ratios (HR) and 95% confidence intervals (CI). We repeated the calculations using the breed group as exposure to examine possible breed group effects and we applied Bonferroni correction (for 11 breed groups) to control for multiple testing. Further analyses were stratified by age group, sex, and whether participants lived alone or not. Individuals considered as "living alone" did not have any spouse, partner with common children, or children living in the same household.

We conducted a sensitivity analysis where we excluded β-blockers as first line anti-hypertensive treatment to estimate the effect of changing treatment guidelines over the study period. In additional sensitivity analysis, in the lipid-lowering medication analysis, we assessed the effect of censoring participants at a diagnosis of heart failure, unstable angina or acute myocardial infarction in the National Patient Register.

Logistic regression was applied in TwinGene for the association of dog ownership with prevalent anti-hypertensive, lipid-lowering and blood-glucose lowering medication and linear regression for the association of dog ownership with continuous variables. hsCRP and triglycerides were transformed to the natural log scale before analysis to approach normality. In addition to adjusting for age, sex, presence of children in the household, area of residence, population density, marital status, latitude of residence and level of education, we added further covariates, one at a time to investigate their individual importance: tobacco use, occupational level, employment status, Charlson comorbidity index and disability. In all twin analyses, standard errors were adjusted with the robust sandwich estimator for dependent observations. For blood pressure and lipid levels, associations were further stratified by current medication.

Ethical approval

The regional ethical review board in Stockholm, Sweden, approved the study (national study: 2012/1114-31/2, with amendment 2013-1687-32; TwinGene: 2007/644-31/2 and 2016/1392-31/1).

Patient involvement

No patients were involved in the development, design or analysis of this study. The review board allowed the researchers to waive the requirement for obtaining informed consent in the national study. Participants in TwinGene provided written informed consent.

Results

National Cohort

The baseline characteristics of 2,026,865 Swedish residents are shown in **Table 1**. Dog ownership was directly registered in 189,355 (9.3%) at any time during the follow-up period, and this increased to 295,682 (14.6%) individuals when partners' registration were included. At baseline, the average age of dog owners was 50 years vs 53 years in non-owners. Dog owners were more likely to be married than non-owners (78% vs 60%) and more likely to live in low-density areas than non-owners (median: 49 vs 77 inhabitants per square kilometer). Compared to non-owners, mixed pedigree dog owners (n=32,003) were less likely to be married (59 %), were less likely to have a tertiary education (21%) and had fewer people in the top quintile for income (12.2%). Owners of 'active dog breeds' showed similar characteristics to the overall dog owners.

Medication for cardiovascular risk factors

During 10,692,258 person-years of follow-up, dog ownership was associated with a 2% higher risk of initiation of anti-hypertensive drug medication in both crude and multivariable-adjusted analyses (HR, 1.02; 95% CI, 1.01-1.03). During 11,508,349 person-years of follow-up, there was a 2% higher risk of initiating lipid-lowering medication in the multivariable adjusted models (HR, 1.02; 95% CI, 1.01-1.04). During 12,207,964 person-years of follow-up, there was a lower risk of initiating glucose lowering drugs in dog owners in minimally adjusted models (HR, 0.91; 95% CI, 0.89-0.94), but on multivariable adjustment, the association was attenuated and non-significant (HR, 0.98; 95% CI, 0.95-1.01) (**Table 2)**.

Owners of "Companion/toy" breeds and of dogs of mixed pedigree were at higher risk of anti-hypertensive and lipid-lowering drug initiation compared to non-dog owners (**Table 3**). Owners of the Spitz/primitive breed types and the combined group of 'active dog breeds' breed-types had lower risks of initiating glucose-lowering medication (HR, 0.83; 95% CI, 0.74-0.93 and HR, 0.92; 95% CI, 0.86-0.97 respectively), while owners of mixed pedigree dogs had higher risk of getting glucose-lowering medication (HR, 1.17; 95% CI, 1.09-1.26) **(Supplementary Figure 4)**.

There was no difference in strength of association when we excluded β-blockers as first-line treatment for anti-hypertension (**Supplementary Table 3)** or when censoring was done in those being investigated for lipid-lowering treatment initiation was made for angina, myocardial infarction or heart failure was conducted **(Supplementary Table 4)**.

In age-stratified analysis, there were some evidence of effect modification by age for both anti-hypertensive and lipid-lowering drugs where an increased risk was observed in those aged below 50 years (HR, 1.04; 95% CI, 1.01-1.08 and HR, 1.10; 95% CI, 1.04-1.15, respectively), with estimates gradually approaching one with increasing age (**Figure 1)**. Inverse associations of dog ownership with glucose-lowering drugs was observed in the lower age groups, in males and those not living alone (HR, 0.89; 95% CI, 0.79-0.99, HR, 0.95; 95% CI, 0.92-0.99 and HR, 0.91; 95% CI, 0.86-0.97, respectively).

TwinGene

On cross-sectional analysis of 10,110 individuals, 484 (5%) were registered as dog owners (partners' dogs not included) and their characteristics are described in **Table 1** and **Supplementary Table 5**. Using similar covariates as in the national cohort, no association of dog ownership was found with prevalent use of anti-hypertensive drugs (OR, 0.94; 95% CI, 0.74-1.20), lipid-lowering drugs (OR, 0.92; 95% CI, 0.65-1.29) or glucose-lowering drugs (OR, 0.90; 95% CI, 0.50-1.63) (**Table 2).** Upon inclusion of additional covariates, the Charlson comorbidity index and the employment status were found to be the most influential confounders and the fully adjusted model yielded lower but still non-significant estimates: OR, 0.90 (95% CI, 0.70-1.15) for use of anti-hypertensive drugs, OR, 0.87 (95% CI, 0.62-1.22) for lipid-lowering drugs and OR, 0.78 (95% CI, 0.43-1.43) for glucose-lowering drugs (**Supplementary Table 6**). We found no association between dog ownership and the other clinical and biochemical cardiovascular risk factors (**Figure 2)**.

Sensitivity analyses on changing the maximum lifespan of dogs in the national cohort that had no dates of death to 8 years or 12 years yielded similar results to the maximum of 10 years used in the main analysis (**Supplementary Table 7).** To provide additional information, the output from the fully adjusted Cox regression models for the association of dog ownership with the initiation of medication for hypertension, dyslipidemia and diabetes mellitus in the national cohort are included in the supplementary material as **Supplementary Table 8**, **Supplementary Table 9** and **Supplementary Table 10,** respectively.

Discussion

In this nationwide study in a population without previous cardiovascular disease, we observed a minimally higher risk of initiation of treatment for hypertension and dyslipidemia among persons with a dog in their household compared to those without dogs in the household. Associations were most prominent in younger age groups (45-60 years). Owning a dog of mixed pedigree or a dog belonging to the "companion/toy" breed group was associated with hypertension and dyslipidemia, whilst ownership of a dog from the "Spitz/primitive" breed and the combined group of 'active dog breeds', consisting of breeds identified in our previous study (Terriers, Pointing, Scent Hounds and Retrievers),[3] was associated with lower risk of treatment for diabetes mellitus. Cross-sectional analyses in 10,110 participants from TwinGene showed no association of dog ownership with body mass index, waist-to-hip-ratio, blood pressure or biochemical cardiovascular risk factors, and indicated that the association of dog ownership with medication for hypertension, dyslipidemia and diabetes was confounded by employment status and non-CVD-chronic conditions. This suggests that the slightly higher associations observed in the national cohort would potentially be attenuated in the presence of the additional confounders.

That owners of mixed-breed and "companion/toy" breeds, as well as dog owners in younger age groups, had mildly increased risks for hypertension and dyslipidemia are in line with our previous study regarding higher risk of myocardial infarction and stroke in this group.[3] The level of dog walking might be lower in the smaller companion/toy dogs and mixed breed dogs as compared to the 'active dog breeds' group, which consists of dog breeds originally bred for hunting.[32] This was also supported by data from TwinGene where 69.9% of active dog breeds' breed owners reported a high level of physical activity versus 52.3% in non-dog owners and 58.6% for mixed-breed dog-owners.[32] We chose to analyze these four 'active dog breeds' together (Terriers, Pointing, Scent Hounds and Retrievers) to explore the association with CVD risk factors as they were all associated with lower risk of incident CVD events in our previous study [3], but should not be viewed as the only active breed groups in the study. We also note that the proportion of highest education level in the mixed breed group was remarkably lower than the general population (20.9% vs 29.3%). Although we adjusted for educational level, it is likely that there is unmeasured confounding from differences in health-seeking behavior, smoking habits or stress in dog-owners in working age groups. In TwinGene, we noted that additional adjustment for employment status (unemployed, retired, sick leave or unemployed) and a comorbidity index (for diseases other

than CVD) were important confounders lowering the estimates. These covariates were not available in the national cohort, implying that the results in the national cohort are likely to have been confounded by these or other factors.

Our findings in TwinGene are different from an Australian cohort study in 5,741 individuals with 13.6% pet ownership who found lower levels of plasma cholesterol, triglycerides and systolic blood pressures in pet-owners than non-owners.[20] Dog owners (6.3%) had better self-rated health but no difference in blood pressure than non-pet owners in cross-sectional analysis of the Nord-Trondelag Health Study (HUNT)-3 study (n=12,297).[13]

There are a limited number of studies of the association between dog ownership and the risk of type 2 diabetes. A study by Lentino et al., (n=916) showed that regular dog walkers (n=399, 44%) in a primarily well-educated Caucasian population had lower BMI and were at lower risk of both dyslipidemia and type 2 diabetes than other study participants.[16] These findings were contradicted by Wright et al, who showed that dog owners were more likely to be overweight, and have diabetes than non-owners in a study of 1179 community dwellers with 30% pet ownership.[19] Differences in findings across countries could be due to differences in study design, or to inherent differences in dog management and the type of dog breeds in the country.

A previous study in this population showed a lower risk of cardiovascular disease and all-cause mortality in dog owners.[3] The current study suggests that it is unlikely that hypertension and dyslipidemia mediates these effects. Other potential factors that may explain this reduction in mortality include increased social well-being and decreased psychological stress.[33]

Strengths and weaknesses

The main strengths of our study include its size and the population-based approach increasing generalizability beyond healthy volunteers in a cohort study. To the best of our knowledge, this is the largest register-based study to date to explore the association between dog ownership and cardiovascular risk factors. At the same time, while national registers allow for large and unselected populations with no loss to follow-up, they lack information on individual attributes such as body mass index, blood pressure, lipid levels and physical activity. A strength of this study is that we were able to include additional clinical health measurements and socioeconomic variables using data from the TwinGene study supporting

the presence of additional confounding of the relationship between dog ownership and cardiovascular risk factors from employment status and non-CVD comorbidities. Although our findings show an association between certain dog breeds and cardiovascular risk factors, these observational results do not imply a causal relationship.

The main limitation of the study is the possibility of remaining unmeasured confounding by unmeasured socioeconomic factors or pre-existing personality traits. Further, the register-based nature of our study made it impossible for us to account for pet-associated factors such as primary pet responsibility, physical activity, the level of dog attachment or indeed the reason for acquiring a dog. Physical activity related to dog walking may however be a mediator of the association between dog ownership and health outcomes and separating activity performed in relation to dog walking and other types of activity would be important. However, a large randomized study of dog ownership over several years cannot be done. Further, despite adjustment for several health, socioeconomic and lifestyle indicators, there is still a possibility of residual confounding or reverse causation. For instance, we could not assess health status before pet acquisition in the national cohort. A smaller study population, although not selected in relation to exposure or outcome, and possible misclassification of dog ownership (due to a lack of information on partners' dog ownership) or lifestyle questionnaire data (collected some years earlier) were important limitations in the sub-cohort analyses. Misclassification of dog ownership was also possible in non-married cohabiting partners without children in common as these would not be registered as cohabiting in the Register of The Total Population. Another important limitation is that we were unable to account for those that did not initiate treatment due to any of the three conditions. The Prescribed Drug Register does not keep a record of adherence to treatment or records of those prescribed lifestyle interventions such as diet or exercise.

Conclusion

In this large cohort study, we observed that dog ownership was associated with a minimally higher risk of initiation of treatment for hypertension and dyslipidemia, and that ownership of dogs of the previously identified 'active dog breeds' was associated with a lower risk of initiating treatment for diabetes. These observations may suffer from residual confounding despite access to multiple important covariates, and future studies may add valuable information. The observed inverse association of dog ownership and cardiovascular disease

previously reported in this population are unlikely to be explained by reduced hypertension and dyslipidemia.

Acknowledgements

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Competing financial interests

E.I. is a scientific advisor for Precision Wellness and Olink Proteomics for work unrelated to the present project. The authors report that no other competing interests exist.

Contributorship Statement

T.F conceived the study and acquired funding. M.M, A.E, E.I, J.S and L.B contributed to the design of the study. T.F. acquired the national data and P.M is responsible for the Swedish Twin Registry data. M.M performed data cleaning. M.M and T.F ran statistical analyses. M.M drafted the manuscript and all authors reviewed the manuscript.

Data sharing statement

The register data that support the findings of this study were made available by record-linkage with data from Statistics Sweden, the National Board of Health and Welfare, the Swedish Kennel Club, Swedish Board of Agriculture and the Swedish Twin Register. Restrictions

apply to the availability of these data, which were used under license and ethical approval for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Regional Ethical Review Board in Stockholm, Sweden. There is no additional data available.

Table 1. Baseline characteristics of Swedish adults aged 45-80 years without cardiovascular disease according to dog ownership status (national cohort, n=2,026,865) and (TwinGene, n=10,110, responses derived from SALT study [1998-2002]). Age is given at baseline. Numbers and % of the respective cohort are reported unless stated otherwise.

	National Cohort					TwinGene				
	All n=2,026,865 (100%)	**Non-dog owners n=1,731,183 (85.4%)**	**Dog owners* n=295,682 (14.6%)**	**Mixed pedigree† n=32,003 (1.6%)**	**'Active dog breeds' †,‡ n=65,686 (3.2%)**	**All n=10,110 (100%)**	**Non-dog owners n=9,626 (95%)**	**Dog owners* n=484 (5%)**	**Mixed pedigree† n=141 (1.3%)**	**'Active dog breeds' †,‡ n=143 (1.4%)**
Age - mean ± SD	52.8 (8.7)	53.3 (8.9)	49.9 (7.3)	49.2 (7.1)	50.0 (7.3)	63.6 (7.1)	63.7 (7.2)	62.0 (6.7)	61.9 (6.3)	62.7 (6.7)
Male	981,094 (48.4)	839,321 (48.5)	141,773 (47.9)	11,841 (37.0)	27,961 (42.6)	4,189 (41.4)	3,986 (41.4)	203 (41.9)	60 (42.6)	64 (44.8)
Marital status										
Married/ cohabiting	1,276,074 (63.0)	1,044,915 (60.4)	231,159 (78.2)	18,991 (59.3)	46,638 (71.0)	8,039 (79.5)	7,648 (79.5)	391 (80.8)	110 (78.0)	112 (78.3)
Never married	287,589 (14.2)	265,895 (15.4)	21,694 (7.3)	4,265 (13.3)	6,377 (9.7)	771 (7.6)	734 (7.6)	37 (7.6)	13 (9.2)	14 (9.8)
Divorced	352,209 (17.4)	316,728 (18.3)	35,481 (12.0)	7,522 (23.5)	10,325 (15.7)	855 (8.5)	824 (8.6)	31 (6.4)	11 (7.8)	8 (5.6)
Widowed	110,993 (5.5)	103,645 (6.0)	7,348 (2.5)	1,225 (3.8)	2,346 (3.6)	445 (4.4)	420 (4.4)	25 (5.2)	7 (5.0)	9 (6.3)
Type of family										
Children at home	658,355 (32.4)	521,224 (30.0)	137,131 (46.3)	14,079 (44.0)	28,785 (43.8)	1,500 (14.8)	1,397 (14.5)	103 (21.3)	31 (22.0)	27 (18.9)
No children at home	1,369,617 (67.6)	1,210,920 (69.9)	158,697 (53.7)	17,924 (56.0)	36,901 (56.2)	8,610 (85.2)	8,229 (85.5)	381 (78.7)	110 (78.0)	116 (81.1)
Education										
Compulsory	541,662 (26.7)	473,952 (27.4)	67,710 (22.9)	8,596 (26.9)	13,207 (20.1)	4,069 (40.2)	3,880 (40.3)	189 (39.0)	56 (39.7)	52 (36.4)
Secondary	891,458 (44.0)	751,156 (43.4)	140,302 (47.5)	16,729 (52.3)	29,352 (44.7)	3,107 (30.7)	2,958 (30.7)	149 (30.8)	46 (32.6)	36 (25.2)
University	593,745 (29.3)	506,075 (29.2)	87,670 (29.7)	6,678 (20.9)	23,127 (35.2)	2,934 (29.0)	2,788 (29.0)	146 (30.2)	39 (27.7)	55 (38.5)
Income quintile§										
1 (lowest quintile)	405,929 (20.0)	342,412 (19.8)	63,517 (21.5)	8,222 (25.7)	12,695 (19.3)	-	-	-	-	-
2	405,486 (20.0)	348,254 (20.1)	57,232 (19.4)	7,472 (23.3)	12,461 (19.0)	-	-	-	-	-
3	405,173 (20.0)	347,691 (20.1)	57,482 (19.4)	6,801 (21.3)	12,586 (19.2)	-	-	-	-	-
4	405,175 (20.0)	346,350 (20.0)	58,825 (19.9)	5,620 (17.6)	13,364 (20.3)	-	-	-	-	-
5 (highest quintile)	405,102 (20.0)	346,476 (20.0)	58,626 (19.8)	3,888 (12.1)	14,580 (22.2)	-	-	-	-	-
Country of birth										
Sweden	1,805,438 (89.1)	1,529,664 (88.4)	275,774 (93.3)	29,168 (91.1)	62,160 (94.6)	10,110 (100)	9,626 (100)	484 (100)	141 (100)	143 (100)
Other Nordic countries**	92,043 (4.5)	80,740 (4.7)	11,303 (3.8)	1,650 (5.2)	2,083 (3.2)	0	0	0	0	0
Non-Nordic countries	129,384 (6.4)	120,779 (7.0)	8,605 (2.9)	1,185 (3.7)	1,443 (2.2)	0	0	0	0	0
Population density - median (IQR) inhabitant per square kilometer	72.6 (228.8)	76.7 (315.3)	49.2 (92.8)	45.0 (87.7)	56.8 (106.2)	60.7 (111.1)	60.7 (114.7)	41.8 (72.9)	40.1 (70.3)	45.9 (68.5)
Region of residence										
Norrland	269,897 (13.3)	222,443 (12.8)	47,454 (16.0)	4,791 (15.0)	9,476 (14.4)	1,621 (16.0)	1,518 (15.8)	103 (21.3)	32 (22.7)	22 (15.4)
Svealand	771742 (38.1)	669673 (38.7)	102,069 (34.5)	10,278 (32.1)	23,451 (35.7)	3,391 (33.5)	3,240 (33.7)	151 (31.2)	41 (29.1)	42 (29.4)
Götaland	985,226 (48.6)	839,067 (48.5)	146,159 (49.4)	16,934 (52.9)	32,759 (49.9)	5,098 (50.4)	4,868 (50.6)	230 (47.5)	68 (48.2)	79 (55.2)
Exercise††										
Little or none	-		-	-	-	2,139 (21.2)	2,064 (21.5)	75 (15.5)	29 (20.7)	16 (11.2)

Average	-	-	-	-	2,611 (25.9)	2,508 (26.2)	103 (21.3)	29 (20.7)	27 (18.9)
Above average	-	-	-	-	5,319 (52.8)	5,014 (52.3)	305 (63.1)	82 (58.6)	100 (69.9)
Tobacco Use††									
No history of tobacco	-	-	-	-	4,314 (42.7)	4,155 (43.2)	159 (32.9)	42 (29.8)	46 (32.2)
Previous tobacco user	-	-	-	-	4,061 (40.2)	3,833 (39.8)	228 (47.1)	69 (48.9)	68 (47.6)
Current tobacco user	-	-	-	-	1,735 (17.2)	1,638 (17.0)	97 (20.0)	30 (21.3)	29 (20.3)

*For descriptive purposes, dog owners here are individuals who had a registered dog at any time point during the study period, and for TwinGene taken as ownership at the clinical test date.
†Proportion of this breed of all participants
‡'Active dog breeds' which comprises all Terriers, Scent hounds, Pointing dog and Retriever dog breed groups.
§Information on income not available for the TwinGene sub-study in the Swedish Twin Register;
**Other Nordic countries include Norway, Denmark, Iceland, Finland, the territories of the Åland Islands and the Faroe Islands
††Information on exercise levels and tobacco use was not available from the Register of the Total Population

Table 2. Association of dog ownership with initiation of medication for hypertension, dyslipidemia and diabetes. For national cohort (n=2,026,865), Cox regression models with hazard ratios (HR) and 95% confidence interval (CI) for incident medication are applied, while logistic models for prevalent use is used in TwinGene (n=10,110) and odds ratios presented (OR).

Cohort	Medication	N treated	Time at risk	Model 1*	Model 2§	Model 3†
National	Hypertension	503,305	10,659,258	**1.02 (1.01-1.03)**	**1.02 (1.01-1.03)**	NA
	Dyslipidemia	276,691	11,508,349	**1.03 (1.02-1.04)**	**1.02 (1.01-1.04)**	NA
	Diabetes	60,038	12,207,964	**0.91 (0.89-0.94)**	0.98 (0.95-1.01)	NA
TwinGene	Hypertension	2,223	NA	0.96 (0.75-1.21)	0.94 (0.74-1.20)	0.90 (0.70-1.15)
	Dyslipidemia	963	NA	0.92 (0.65-1.29)	0.92 (0.65-1.29)	0.87 (0.62-1.22)
	Diabetes	318	NA	0.89 (0.49-1.61)	0.90 (0.50-1.63)	0.78 (0.43-1.43)

*Model 1. Age and sex adjusted

§Model 2. National cohort: Adjusted for sex, age, type of family, area of residence, population density, marital status, region of birth (Sweden, Nordic, Non-Nordic), income, education level, latitude of residence. TwinGene: Adjusted for sex, age, type of family, area of residence, population density, marital status, education level and latitude of residence

† Model 3. Adjusted for sex, age, number of children in the home, area of residence, population density, marital status, tobacco use, occupational level, employment status, disability and Charlson comorbidity index

Table 3. Association of dog ownership with initiation of medication for hypertension drugs, dyslipidemia and diabetes by breed group in the National cohort with non-dog owners as the reference group. Estimates that pass Bonferroni correction for 11 breed groups (p=0.05/11) are marked in bold.

	Anti-hypertensive drugs		Lipid-lowering drugs		Glucose -lowering drugs	
Breed Groups	**Crude* HR**	**Adjusted† HR**	**Crude* HR**	**Adjusted† HR**	**Crude* HR**	**Adjusted† HR**
Sheep and cattle dogs	1.04 (1.01-1.07)	1.03 (1.00-1.06)	1.01 (0.97-1.06)	1.01 (0.97-1.06)	1.03 (0.95-1.13)	1.06 (0.96-1.15)
Pinscher and schnauzer	1.03 (0.99-1.06)	1.03 (1.00-1.07)	1.07 (1.02-1.12)	**1.07 (1.02-1.12)**	0.92 (0.82-1.02)	0.98 (0.88-1.09)
Terriers	0.98 (0.95-1.02)	0.99 (0.96-1.03)	1.01 (0.96-1.05)	1.02 (0.97-1.07)	**0.84 (0.76-0.94)**	0.91 (0.81-1.01)
Dachshunds	1.01 (0.96-1.06)	1.02 (0.97-1.07)	1.06 (0.99-1.13)	1.06 (0.99-1.13)	0.96 (0.84-1.11)	1.03 (0.89-1.18)
Spitz and primitive types	1.05 (1.01-1.09)	1.00 (0.97-1.04)	1.04 (0.99-1.09)	1.01 (0.96-1.06)	**0.82 (0.73-0.91)**	**0.83 (0.74-0.93)**
Scent hounds and related	1.05 (1.00-1.09)	1.03 (0.98-1.07)	1.07 (1.01-1.13)	1.05 (0.99-1.11)	**0.86 (0.76-0.98)**	0.88 (0.77-0.99)
Pointing dogs	0.95 (0.89-1.02)	0.95 (0.88-1.02)	0.96 (0.88-1.06)	0.97 (0.89-1.07)	**0.65 (0.51-0.82)**	0.73 (0.58-0.93)
Retrievers	1.00 (0.98-1.03)	1.02 (0.99-1.05)	1.00 (0.96-1.04)	1.02 (0.98-1.06)	**0.87 (0.80-0.95)**	0.98 (0.90-1.06)
Companion and Toy dogs	**1.10 (1.06-1.13)**	**1.09 (1.05-1.12)**	**1.12 (1.08-1.17)**	**1.12 (1.07-1.16)**	1.01 (0.92-1.12)	1.03 (0.93-1.14)
Sight hounds	0.90 (0.79-1.02)	0.90 (0.79-1.02)	0.94 (0.79-1.12)	0.94 (0.79-1.12)	0.84 (0.57-1.26)	0.87 (0.59-1.30)
Mixed Pedigree‡	**1.10 (1.07-1.13)**	**1.07 (1.05-1.11)**	**1.09 (1.06-1.12)**	**1.09 (1.05-1.13)**	**1.22 (1.13-1.32)**	**1.18 (1.09-1.27)**

*Adjusted for age and sex
†Adjusted for age, sex, marital status, presence of children in the home, population density, area of residence, education level, region of birth, income and a correction for latitude of residence.
‡Group comprising all non-pure pedigree dogs.

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Figure legends:

Figure 1 - Hazard ratios (HR) and 95% confidence intervals (CI) for the association of dog ownership and time to initiation of medication for hypertension, dyslipidemia and type 2 diabetes.

Figure 2 - Coefficients and 95% confidence intervals for the exposure to dog ownership compared to non-dog ownership on SD-transformed biochemical and clinical measurements in the TwinGene.

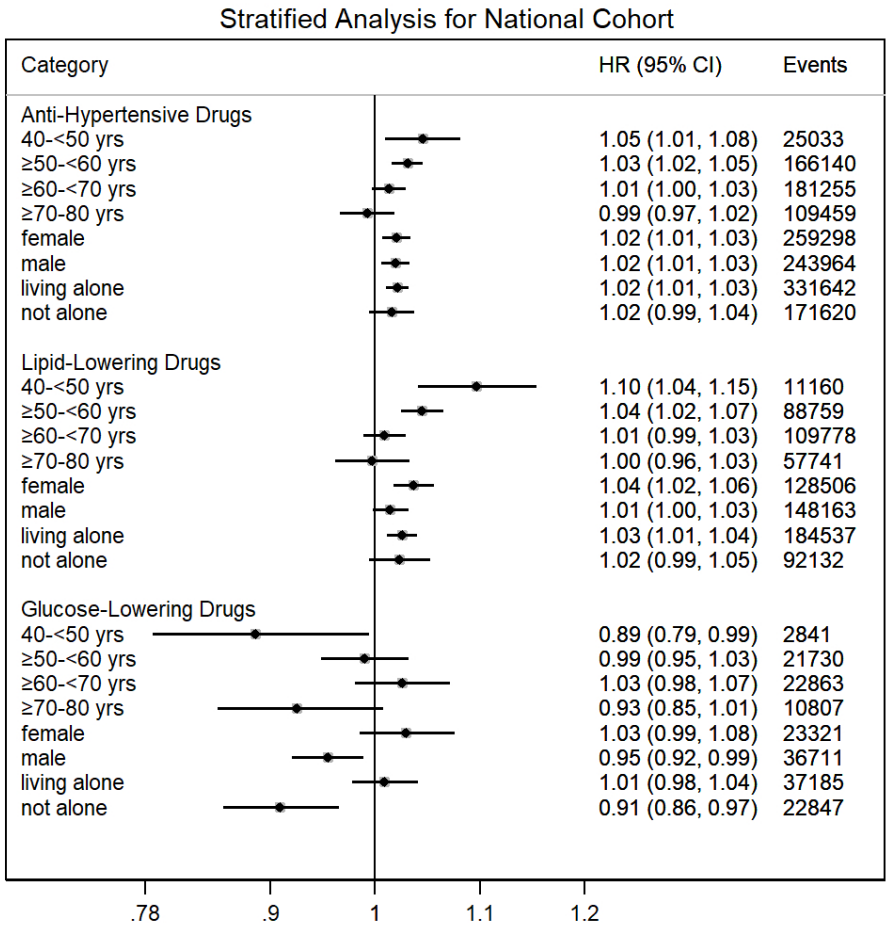

Figure 1. Hazard ratios (HR) and 95% confidence intervals (CI) for the association of dog ownership and time to initiation of medication for hypertension, dyslipidemia and type 2 diabetes stratified by age category, sex and home occupancy (living alone or with someone) and adjusted for age, sex, marital status, presence of children in the home, population density, area of residence, education level, region of birth, income and a correction for latitude of residence.

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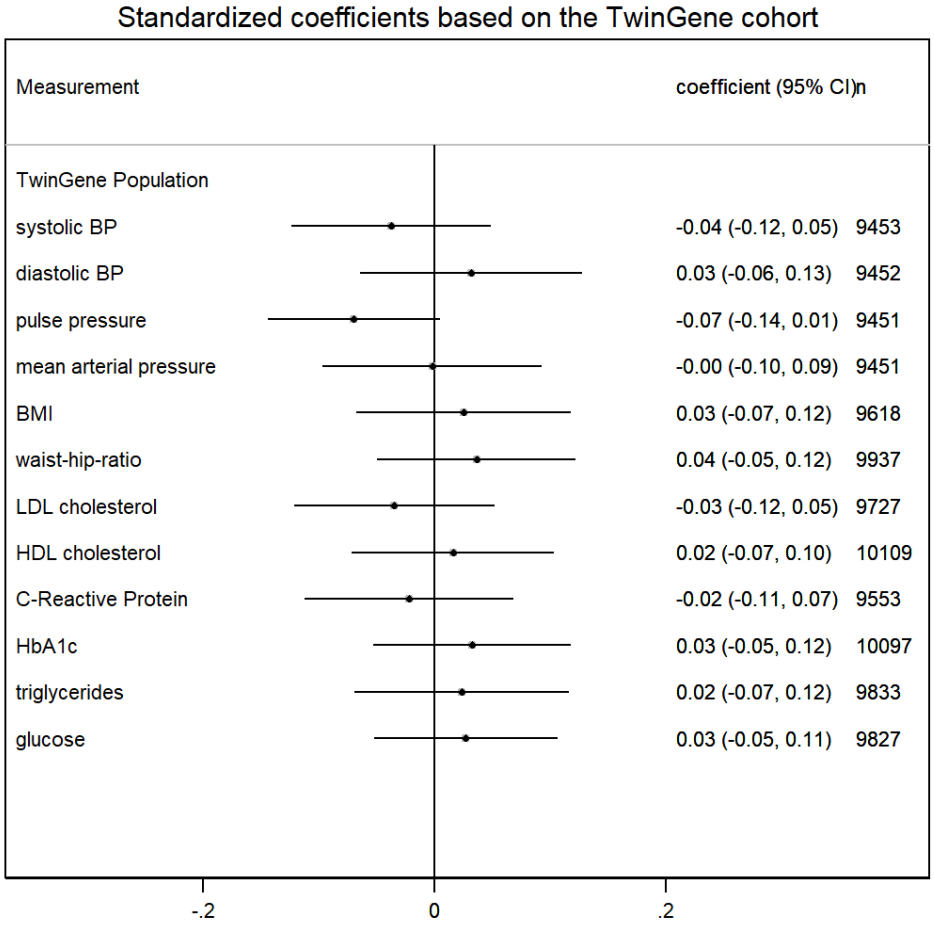

Figure 2. Coefficients and 95% confidence intervals for the exposure to dog ownership compared to non-dog ownership on SD-transformed biochemical and clinical measurements in the TwinGene.

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Supplementary Appendix

Dog ownership and Cardiovascular Risk Factors by Mubanga *et al*.

Content

Supplementary Methods

Data Source and Parameters

Sweden has a structured population registration system that has enabled the collection of individual level information on the total population. By using an identity-protected unique code called the personal identity number (PIN), it is possible to link Swedish residents through different national registers for information such as vital status, socio-demographic data, dog ownership and health outcomes.[1]

Covariates

Covariates extracted at baseline from the Register of the Total Population included sex, birth year, region of birth separated into Sweden, other Nordic countries and non-Nordic countries; and the level of education categorized as compulsory school (≤9 years), secondary school (10-11 years) and tertiary education (≥12 years). We further included annually -updated covariates including marital status categorized as single, married/registered partnership/cohabiting, divorced or widowed; the presence of children in the home (dichotomized as yes/no), the area of residence (Norrland, Svealand and Götaland), the population density in municipality of residence (continuous variable), and annual household income (birth year-standardized quintiles). A north-south gradient was adjusted for by including the latitude of the municipality of residence. To avoid reverse effects of outcomes on covariates, we used covariate data from the preceding year to time-update information on January 1 in every year. A binary variable for home occupancy where individuals were assigned to 'living alone' if the individual lived alone or 'not alone' if they were registered as living with a partner or a child. Co-habiting partners with no children in common could not be accounted for via the registers. Another variable for living with children aged <18 was created to account for those who lived with children in the home. A second stratification variable was created for age group in decades.

From the SALT study conducted in 1998-2002, we used the following self-reported variables as covariates: age, sex, presence of children in the household, area of residence, population density, marital status, and latitude of residence and level of education as defined in the national cohort. Additionally, we adjusted for tobacco use (never, former or current user), employment status (employed, retired, sick leave or unemployed), Charlson comorbidity index and disability (categorized as yes /no). Additionally the socioeconomic index which ranks occupations by the average level of education and job earnings of job holders was also included.[2] By using National Patient Register data from the TwinGene clinic visit-date to five years prior, we created a Charlson comorbidity index. This is a widely used index for risk adjustment in health care research.[3 4]

TwinGene

The Swedish Twin Registry is a national register started in 1958 that derives information on all twin births occurring in Sweden from the National Board of Health and Welfare. It contains information on more 190,000 Swedish twin pairs born from 1886 onwards.[5] There have been several sub-studies conducted within this registry that have enabled the enhancement of the phenotypic and genetic data available on each participant. For this study, we limited ourselves to two sub-studies that comprised participants aged 45 to 80 years and who had consented to participate in both studies. Data between the two sub-studies involved was collected a minimum of 2 and a maximum of 10 years apart (**Supplementary Figure 1, Supplementary Figure 5**).

The first study, the Screening Across the Lifespan Twin study (SALT) interview was conducted as a sub-study of the Swedish Twin Register between 1998 and 2002 targeting all twin-pairs born in 1958 or earlier. Questionnaires were used to collect information on family status, occupation, education level, anthropometric measurements, alcohol intake, tobacco use, environmental exposures and irritants, medication use and health - including psychosocial /personality outcomes.[5] Information was collected from 44,821 respondents.

The second sub-study, the TwinGene study, was nested in the previous study. Between 2004 and 2008 participants from SALT were invited back as part of the TwinGene Study. TwinGene was set up to enable the collection of biological specimens to investigate gene-environment interactions in

participants. 12,614 invited participants gave consent to participate. Questionnaires were mailed and filled in for medication use and health outcomes. Blood was then collected for clinical biochemistry from a local health facility and processed centrally.[6] We used the date of clinic visit as the date of study.

Clinical information was taken during TwinGene study (2004-2008), dog ownership status on the date of clinical examination, and employment, profession and type of housing was extracted from the SALT questionnaire (1998-2002). All variables taken from SALT are described in Supplementary Table 1.

Supplementary Table 1. Description of variables derived from the SALT questionnaire study

Covariate	Questionnaire Option	Variable created	Classification and Derivative from questionnaire
Marital status	What is your civil status?	Married	Married, cohabiting
		Single	Living alone
		Divorced	Divorced, separated, living apart
		Widowed	Widow/ widower
Type of family	Living in a household with children <18 years	Yes/ No	Yes /No
Education level	Highest years of education completed	Primary education or less	9 years or less of education
		Secondary education	10 to 12 years of education
		Tertiary education or more	More than 12 years of education
Employment status	Employment status	Employed	Fully employed, part time employment, owns company, on leave from work, study leave or on military service
		Retired	Pensioner, prematurely retired, partly retired
		Retired for disability or illness	Retired for injury
		Unemployed	Unemployed, housewife/man
Socioeconomic index	Socioeconomic occupation level	Level 1	Unskilled Employees
		Level 2	Lower skilled, non-manual workers
		Level 3	Self-employed excluding independent workers
		Level 4	Intermediate non-manual employees
		Level 5	Highest tier non-manual employees
Tobacco Use	Have you ever smoked or used snuff	Never smoked	No not even tried it, yes but only tried it, smoked now and then (like at parties),
		Former smoker	Smoked regularly, snuffed regularly, smoke now and then (like at parties)
		Current smoker	Smoke regularly, smoke at parties, snuff now and then, snuff regularly
Any movement impairment	Do you have any physical handicap	Yes/no	Yes/ No
Disability	Do you need assistance with personal care/ shopping,/cooking/mobility/	Yes/No	Yes /No
Exercise	How much do you exercise; what fits your annual exercise pattern	Less than average	Almost no exercise, light exercise, much less exercise than average, less than average
		Average	Regular medium exercise, average amount of exercise
		More than average	Hard physical exercise, more exercise than average, much more exercise than normal, maximum amount of exercise

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Supplementary Table 2. Description of Breed Classification of the 331 breeds included in the study based on the Nordic Kennel Union Classification

Group Number	Breed Groups	Breed Designation
1	Sheep and cattle dogs	Sheep dogs (Australian, Belgian, Catalan, German, Picardy, Polish, Portuguese, Pyrenean, Shetland, Old English); Shepherd dogs (Belgian, Bergamasco, Croatian, Dutch, German, Majorca, Polish, Romanian, South Russian); Collie (Bearded, Border, Rough, Smooth); Bouvier des Flandres, Beauceron, Briard, Chodsky Pes, Czechoslovakian Wolfdog, Komondor, Kuvasz, Mudi, Lancashire Heeler, Schipperke, Puli, Pumi, Slovakian Chuvach, Welsh Corgie, Australian kelpie, Working kelpie
2	Pinscher and schnauzer dogs	Pincher (Affenpinscher, Austrian, Dobermann, German, Miniature); Schnauzer (Giant, Miniature); Mountain Dog (Appenzeller, Bernese, Caucasian Shepherd, Entlebuch, Great Swiss, Karst, Landseer, Newfoundland, Pyrenean, Serra da Estrela, St Bernard, Druguayan Cimarron, Yugoslavian Shepherd); Molossian (Aidi, Anatolian Shepherd, Boxer, Bull Mastiff, Broholmer, Cane Corso, Dogo Argentino, Danish-Swedish Farm dog, Dogo Canario, Dogue de Bordeux, English Bulldog, Great Dane, Hovawart, Majorca Mastiff, Mastiff, Neapolitano Mastiff, Pyrenese Mastiff, Rafeiro of Alentejo, Spanish Water Dog, Shar Pei, Tosa); Central Asia Shepherd Dog, Russian Black Terrier
3	Terriers	Airedale, American Staffordshire, Australian, Bedlington, Border, Brazilian, Bull, Cairn, Cesky, Dandie Dinmont, English Toy, Fox, German Hunting, Irish Glen of Imaal, Irish Softcoated Wheaten, Irish, Jack Russel, Kerry Blue, Lakeland, Manchester, Miniature Bull, Norfolk, Norwich, Parson Russell, Sealyham, Australian Silky, Skye, Tenterfield, Welsh, West Highland White, Yorkshire
4	Dachshunds	Miniature, Standard, Kaninchen
5	Spitz and primitive types	Alaskan Malamute, American Akita, Canaan dog, Canarian Warren, Chow Chow, Cirneco dell'Etna, East Siberian Laika, Eurasian, Finnish Lapphund, Finnish Spitz, German Spitz, Greenland dog, Hokkaido, Halleforshund, Icelandic Sheepdog, Japanese Akita, Japanese Spitz, Karelian Beardog, Keeshond, Korea Jindo, Laponian Herder Pharaoh Hound, Mexican Hairless dog, Norwegian Buhund, Norwegian Lundehund, Norwegian Elkhound, Peruvian Hairless dog, Ibizan Hound, Pomeranian, Russian European Laika, Samoyed, Shiba, Siberian Husky, Swedish Elkhound, Swedish Lapphund, Swedish White Elkhound, Swedish Vallhund, Thai Bangkaew, Thai Ridgeback, Volpino italiano, West Siberian Laika
6	Scent hounds and related dogs	Alpine Dachsbracke, American Foxhound, Basset Artesian Normand, Basset Bleu de Gascogne, Basset fauve de Bretagne, Basset Hound, Bavarian Mountain Scent hound, Beagle, Black and Tan Coonhound, Bloodhound, Bluetick Coonhound, Bosnian Coarse-haired hound, Dalmatian, Drever, Dunker Hound, Fawn Brittany Griffon, Finnish Hound, Foxhound, German Hound, Grand Basset Griffon Vendeen, Grand Griffon Vendeen, Griffon Nivernais, Halden Hound, Hamilton Hound, Hygen Hound, Istrian Short-haired hound, Otterhound, Petit Basset Griffon Vendeen, Plott, Polish hunting dog, Porcelain, Posavaz Hound, Rhodesian Ridgeback, Russian Hound, Russian Spotted hound, Small Blue Gascony Hound, Spanish Hound, Schiller Hound, Swiss Hound, Serbian Hound, Slovakian Hound, Småland Hound
7	Pointing dogs	Blue Picardy Spaniel, Bracco Italiano, French Pointing, Brittany, Bohemian wire-haired, Drentse Patridge, English Setter, French Spaniel, Old Danish Pointer, Gordon Setter, French wire-haired Korthals Pointing Griffon, Münsterländer, Irish Red Setter, German Short/Wire-haired pointing dog, Portuguese Pointing dog, Pointer, Pudelpointer, Slovakian Wire-haired Pointing dog, Italian Spinone, Stabyhound, Hungarian Vizsla wire-/short-haired, Weimaraner short-/long-haired
8	Retrievers	American Cocker Spaniel, Barbet, Chesapeake Bay Retriever, Clumber Spaniel, Cocker Spaniel, Curly Coated Retriever, English Springer Spaniel, Field Spaniel, Flat coated Spaniel, German Spaniel, Golden retriever, Irish Water Spaniel, Labrador Retriever, Lagotto romagnolo, Nederlandse Kooikerhondje, Nova Scotia Duck Tolling Retriever, Spanish Water dog, Portuguese Water Dog, Sussex Spaniel, Welsh Springer Spaniel, Wetterhound
9	Companion and toy dogs	Havanese, Bolognese, Boston Terrier, Belgian Griffon, Brussels Griffon, Cavalier King Charles Spaniel, Chihuahua, Chinese Crested, Coton de Tulear, French Bulldog, Japanese Chin, King Charles Spaniel, Kromfohrlander, Lhasa Apso, Lowchen, Maltese, Pug, Papillon, Pekingese, Small Brabant Griffon, Phalene, Prazský krysarík, Poodle, Russian Toy, Shih Tzu, Tibetan Terrier, Tibetan Spaniel
10	Sight hounds	Afghan Hound, Azawakh, Borzoi, Polish Greyhound, Spanish Greyhound, Irish Wolfhound, Italian Greyhound, Hungarian Greyhound, Saluki, Scottish Deerhound, Sloughi, Whippet

Supplementary Table 3. Association of dog ownership with initiation of medication for the treatment of hypertension. This compares the main analysis as shown in Table 2 with a modified analysis that excludes Beta-blockers which have not been recommended first line treatment for hypertension since 2006.[7] Cox regression models with hazard ratios (HR) and 95% confidence interval (CI) are reported.

	N treated	Time at risk	Model 1*	Model 2§
With β-blockers	503,305	10,659,258	1.02 (1.01-1.03)	1.02 (1.01-1.03)
Without β-blockers	401,573	11,018,086	1.03 (1.02-1.04)	1.02 (1.01-1.03)

*Model 1. Age and sex adjusted
§Model 2. National cohort: Adjusted for sex, age, type of family, area of residence, population density, marital status, region of birth, income, education level, latitude of residence.

Supplementary Table 4. Association of dog ownership with initiation of lipid lowering medication. This compares the main analysis as shown in Table 2 with a modified analysis that censored participants at an event of angina or heart failure. Cox regression models with hazard ratios (HR) and 95% confidence interval (CI) are reported.

Lipid lowering medication	N treated	Time at risk	Model 1*	Model 2§
Without censoring	276,691	11,508,349	1.03 (1.02-1.04)	1.02 (1.01-1.04)
With censoring	243,797	11,482,789	1.03 (1.02-1.04)	1.02 (1.01-1.04)

*Model 1. Age and sex adjusted
§Model 2. National cohort: Adjusted for sex, age, type of family, area of residence, population density, marital status, region of birth, income, education level, latitude of residence.

Supplementary Table 5. Additional baseline characteristics of 10,110 Swedish adults in the Swedish Twin Register. Information is based on persons who participated in the TwinGene project designed to enhance the Screening Across the Lifespan Twin (SALT) questionnaire-based sub-study in the Swedish Twin Register with biologic specimens. Numbers and % are reported unless stated otherwise. Clinical information was taken during TwinGene study (2004-2008), dog ownership status on the date of clinical examination and other non-clinical details extracted from the SALT questionnaire (1998-2002).

Participant characteristics	n		All n=10,110 (100%)	Non-dog owners n=9,626 (95.0%)	Dog owners n=484 (5.0%)	Mixed pedigree dog owners n=141 (1.4%)*	Active dog breed owners n=143 (1.4%)*
Employment status	10,110	Employed	6,875 (68.0)	6,541 (68.0)	334 (69.0)	97 (68.8)	93 (65.0)
		Retired	2,066 (20.4)	1,992 (20.7)	74 (15.3)	18 (12.8)	29 (20.3)
		Sick leave or illness	875 (8.7)	818 (8.5)	57 (11.8)	18 (12.8)	16 (11.2)
		Unemployed	294 (2.90)	275 (2.9)	19 (3.9)	8 (5.7)	5 (3.5)
Profession†	10,110	Unskilled labor	2,458 (24.3)	2,351 (24.4)	107 (22.1)	32 (22.7)	27 (18.9)
		Lower non-manual labor	3,373 (33.4)	3,205 (33.3)	168 (34.7)	57 (40.4)	43 (30.1)
		Self-employed	430 (4.3)	404 (4.2)	26 (5.4)	6 (4.3)	6 (4.2)
		Intermediate non-manual labor	2,539 (25.1)	2,411 (25.0)	128 (26.4)	32 (22.7)	46 (32.2)
		Higher non-manual employee	1,310 (13.0)	1,255 (13.0)	55 (11.4)	14 (9.9)	21 (14.7)
Type of housing or accommodation	10,110	Independent	10,100 (99.9)	9,616 (99.9)	484 (100.0)	141 (100.0)	143 (100.0)
		Assisted living[2]	6 (0.1)	6 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
		Other	4 (<0.0)	4 (<0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Biochemical Variables							
C-Reactive Protein	9,553	Median (IQR)	1.7 (0.8-3.4)	1.7 (0.8-3.4)	1.8 (0.8-3.2)	2.0 (0.9-3.5)	1.6 (0.7-3.1)
LDL-Cholesterol	9,727	Mean (SE)	3.9 (0.9)	3.9 (0.9)	3.8 (0.9)	3.8 (0.9)	3.9 (0.9)
HDL-Cholesterol	10,109	Mean	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)
Triglyceride (Fasting)	9,261	Median	1.1 (0.8-1.6)	1.1 (0.8-1.6)	1.1 (0.9-1.6)	1.2 (0.9-1.6)	1.2 (0.9-1.5)
Glucose (Non-Diabetic)	9,256	Median	5.3 (5.0-5.7)	5.3 (5.0-5.7)	5.2 (5.0-5.7)	5.3 (5.0-5.8)	5.3 (5.0-5.7)
HbA1c	10,097	Mean	4.8 (0.6)	4.8 (0.6)	4.8 (0.6)	4.8 (0.6)	4.7 (0.5)
Body Mass Index	9,618	Mean	25.9 (4.0)	25.9 (4.0)	26.0 (4.0)	26.3 (4.4)	26.0 (3.8)
Waist-Hip ratio	9,937	Mean	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)
Blood pressure measurements							
Mean systolic BP (all participants)	8010	Mean	138.1 (19.5)	138.2 (19.5)	136.0 (19.2)	139.4 (20.3)	136.2 (18.1)
Mean diastolic BP (all participants)		Mean	82.2 (10.5)	82.2 (10.4)	82.6 (10.9)	84.8 (11.4)	82.7 (10.4)
Pulse pressure (all participants)		Mean	55.9 (15.4)	56.0 (15.4)	53.4 (13.6)	54.6 (13.9)	53.5 (12.5)

Mean systolic BP (On BP treatment)	1,970	Mean	144.9 (18.8)	144.9 (18.9)	144.9 (17.3)	149.4 (14.9)	142.0 (15.8)
Mean diastolic BP (On BP treatment)		Mean	83.9 (10.7)	83.8 (10.8)	85.0 (9.2)	84.5 (8.4)	85.6 (9.3)
Pulse pressure (On BP treatment)		Mean	61.0 (16.0)	61.1 (16.1)	60.0 (13.8)	65.0 (10.1)	56.4 (12.2)
Self-reported health status	10,110	Excellent	3,501 (34.9)	3,330 (34.9)	171 (35.7)	33 (23.6)	58 (40.8)
		Good	5,330 (53.2)	5,085 (53.3)	245 (51.1)	79 (56.4)	73 (51.4)
		Average	963 (9.6)	914 (9.6)	49 (10.2)	19 (13.6)	8 (5.6)
		Not so good	227 (2.3)	213 (2.3)	14 (2.9)	7 (5.0)	3 (2.1)
Blood Pressure Medication	10,110	Number on treatment (%)	2,099 (20.8)	2,010 (20.9)	89 (18.4)	31 (22.0)	22 (15.4)
Lipid Modifying Medication	10,110	Number on treatment (%)	918 (9.1)	880 (9.1)	38 (7.9)	14 (9.5)	13 (8.3)
Diabetes Medication	10,110	Number on treatment (%)	305 (3.0)	293 (3.0)	12 (2.5)	5 (3.5)	5 (3.5)

*-Proportion of this breed of total population
†-Defined according to Budoki et al.[8]
‡-Assisted living which includes living in
BP- Blood Pressure

Supplementary Table 6: Association of dog ownership with initiation of medication for hypertension, dyslipidaemia and diabetes. Shown for assuming 10-year life-span of dog and a sensitivity analyses at 8-year and 12-year life-span of dog.

Medication	Assuming 10-year life-span of dog		Assuming 8-year life-span of dog		Assuming 12-year life-span of dog	
	Sex-age adjusted model	Fully-adjusted model	Sex-age adjusted model	Fully-adjusted model	Sex-age adjusted model	Fully-adjusted model
Hypertension	1.02 (1.01-1.03)	1.02 (1.01-1.03)	1.02 (1.01-1.03)	1.01 (1.00-1.02)	1.03 (1.02-1.04)	1.02 (1.01-1.03)
Dyslipidemia	1.03 (1.02-1.04)	1.02 (1.01-1.04)	1.02 (1.01-1.04)	1.02 (1.00-1.03)	1.03 (1.02-1.04)	1.02 (1.01-1.04)
Diabetes	0.91 (0.89-0.94)	0.98 (0.95-1.01)	0.90 (0.88-0.93)	0.97 (0.94-1.00)	0.92 (0.90-0.94)	0.99 (0.96-1.02)

§Fully-adjusted models adjusted for sex, age, type of family, area of residence, population density, marital status, education level and latitude of residence

Supplementary Table 7. Stepwise addition of covariates into TwinGene model. Odds ratios (OR) and confidence intervals (CI) for associations of dog ownership and prevalent drug prescriptions for hypertension, dyslipidemia and type 2 diabetes (n=10,110). *

Prescription Medication	N on treatment	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7
Anti-hypertensive drugs	2,223	0.96 (0.75-1.21)	0.94 (0.74-1.20)	0.95 (0.74-1.20)	0.92 (0.72-1.18)	0.90 (0.70-1.15)	0.90 (0.71-1.15)	0.90 (0.70-1.15)
Lipid lowering drugs	963	0.92 (0.65-1.29)	0.92 (0.65-1.29)	0.92 (0.66-1.29)	0.90 (0.64-1.26)	0.87 (0.62-1.22)	0.87 (0.62-1.22)	0.87 (0.62-1.22)
Glucose lowering drugs	318	0.89 (0.49-1.61)	0.90 (0.50-1.63)	0.91 (0.50-1.65)	0.90 (0.50-1.63)	0.80 (0.44-1.46)	0.80 (0.44-1.46)	0.78 (0.43-1.43)

*Model 1, 2 and 7 were reported in the main manuscript Table 2
Model 1. Adjusted for age and sex
Model 2. Adjusted for sex, age, type of family, area of residence, population density, marital status, education level and latitude of residence
Model 3. Model 2 plus professional level
Model 4. Model 3 plus employment status
Model 5. Model 4 plus Charlson comorbidity index
Model 6. Model 5 plus disability
Model 7. Full twin model - Model 6 plus tobacco use

Supplementary Table 8: Output from fully adjusted Cox regression models for the association of dog ownership with initiation of medication for hypertension.

	Haz. Ratio	P>z	[95% Confidence Interval]	
Dog owner	1.018	0.000	1.009	1.028
Sex				
Male	**Ref**			
Female	0.945	0.000	0.939	0.950
Marital status				
Married/ cohabiting	**Ref**			
Never Married	0.904	0.000	0.895	0.912
Divorced	0.993	0.091	0.986	1.001
Widowed	1.064	0.000	1.053	1.076
Children in home				
No	**Ref**			
Yes	0.922	0.000	0.915	0.930
Area of Residence				
Norrland	**Ref**			
Svealand	0.959	0.000	0.946	0.972
Götaland	0.912	0.000	0.895	0.929
Population density	1.000	0.203	0.998	1.001
Education				
Primary level	**Ref**			
Secondary level	0.955	0.000	0.949	0.962
Tertiary level	0.832	0.000	0.826	0.839
Country of birth				
Sweden	**Ref**			
Other Nordic countries	1.143	0.000	1.128	1.157
Non-Nordic countries	1.010	0.114	0.998	1.022
Income				
Income level 1 (lowest tier)	**Ref**			
Income level 2	0.994	0.195	0.985	1.003
Income level 3	0.995	0.297	0.986	1.004
Income level 4	0.991	0.056	0.982	1.000
Income level 5 (highest tier)	0.986	0.004	0.977	0.995
Latitude of residence	1.000	0.000	1.000	1.000

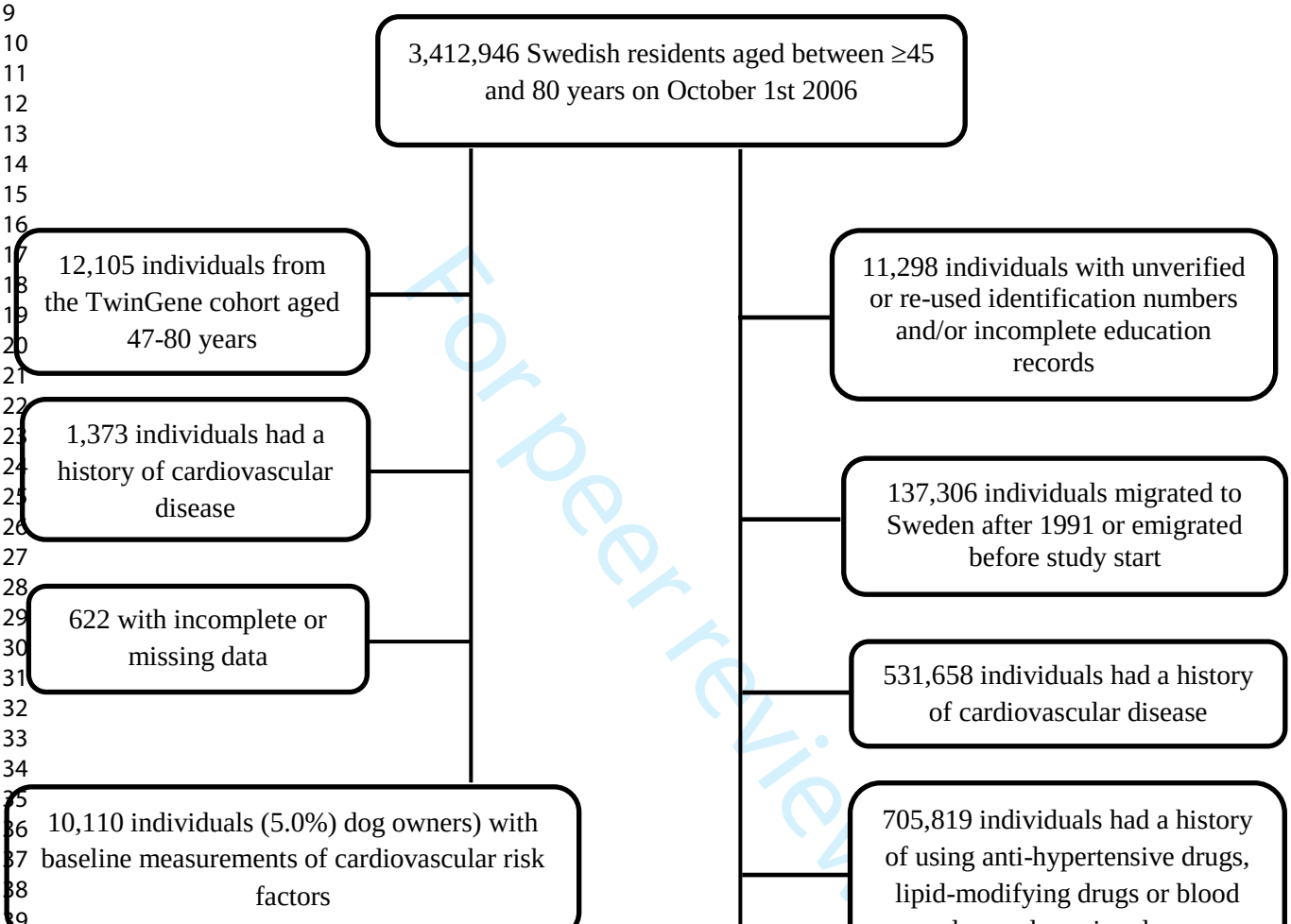
Supplementary Table 9: Output from fully adjusted Cox regression models for the association of dog ownership with initiation of medication for dyslipidaemia

	Haz. Ratio	P>z	[95% Confidence Interval]	
Dog owner	1.024	0.000	1.011	1.036
Sex				
Male	**Ref**			
Female	0.773	0.000	0.767	0.779
Marital status				
Married/ cohabiting	**Ref**			
Never Married	0.835	0.000	0.825	0.846
Divorced	0.992	0.117	0.982	1.002
Widowed	1.022	0.004	1.007	1.038
Children in home				
No	**Ref**			
Yes	0.891	0.000	0.881	0.901
Area of Residence				
Norrland	**Ref**			
Svealand	1.005	0.597	0.987	1.024
Götaland	0.928	0.000	0.905	0.952
Population density	1.000	0.000	0.999	1.001
Education				
Primary level	**Ref**			
Secondary level	0.963	0.000	0.954	0.972
Tertiary level	0.796	0.000	0.787	0.804
Country of birth				
Sweden	**Ref**			
Other Nordic countries	1.169	0.000	1.150	1.189
Non-Nordic countries	1.195	0.000	1.177	1.213
Income				
Income level 1 (lowest tier)	**Ref**			
Income level 2	1.000	0.962	0.988	1.012
Income level 3	1.004	0.504	0.992	1.016
Income level 4	1.010	0.104	0.998	1.022
Income level 5 (highest tier)	1.005	0.450	0.992	1.018
Latitude of residence	1.000	0.813	1.000	1.000

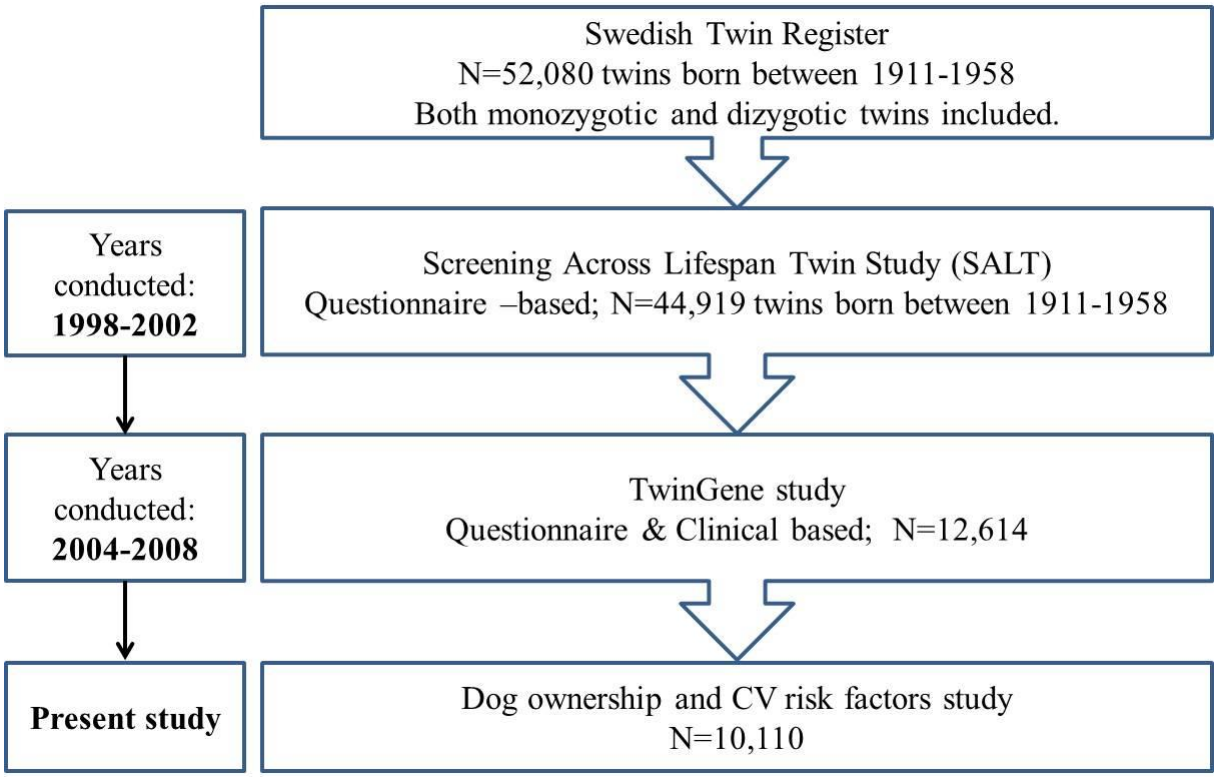
Supplementary Table 10: Output from fully adjusted Cox regression models for the association of dog ownership with initiation of medication for diabetes.

	Haz. Ratio	P>z	[95% Confidence Interval]	
Dog owner	0.982	0.193	0.954	1.009
Sex				
Male	**Ref**			
Female	0.546	0.000	0.536	0.556
Marital status				
Married/ cohabiting	**Ref**			
Never Married	1.244	0.000	1.215	1.274
Divorced	1.196	0.000	1.171	1.223
Widowed	1.290	0.000	1.248	1.334
Children in home				
No	**Ref**			
Yes	0.965	0.002	0.944	0.988
Area of Residence				
Norrland	**Ref**			
Svealand	0.909	0.000	0.8741825	0.946
Götaland	0.883	0.000	0.8366307	0.932
Population density	0.999	0.000	0.998	1.001
Education				
Primary level	**Ref**			
Secondary level	0.877	0.000	0.861	0.894
Tertiary level	0.635	0.000	0.620	0.650
Country of birth				
Sweden	**Ref**			
Other Nordic countries	1.116	0.000	1.076	1.159
Non-Nordic countries	1.952	0.000	1.900	2.004
Income				
Income level 1 (lowest tier)	**Ref**			
Income level 2	0.919	0.000	0.896	0.941
Income level 3	0.845	0.000	0.824	0.866
Income level 4	0.777	0.000	0.757	0.797
Income level 5 (highest tier)	0.702	0.000	0.683	0.722
Latitude of residence	1.000	0.001	1.000	1.000

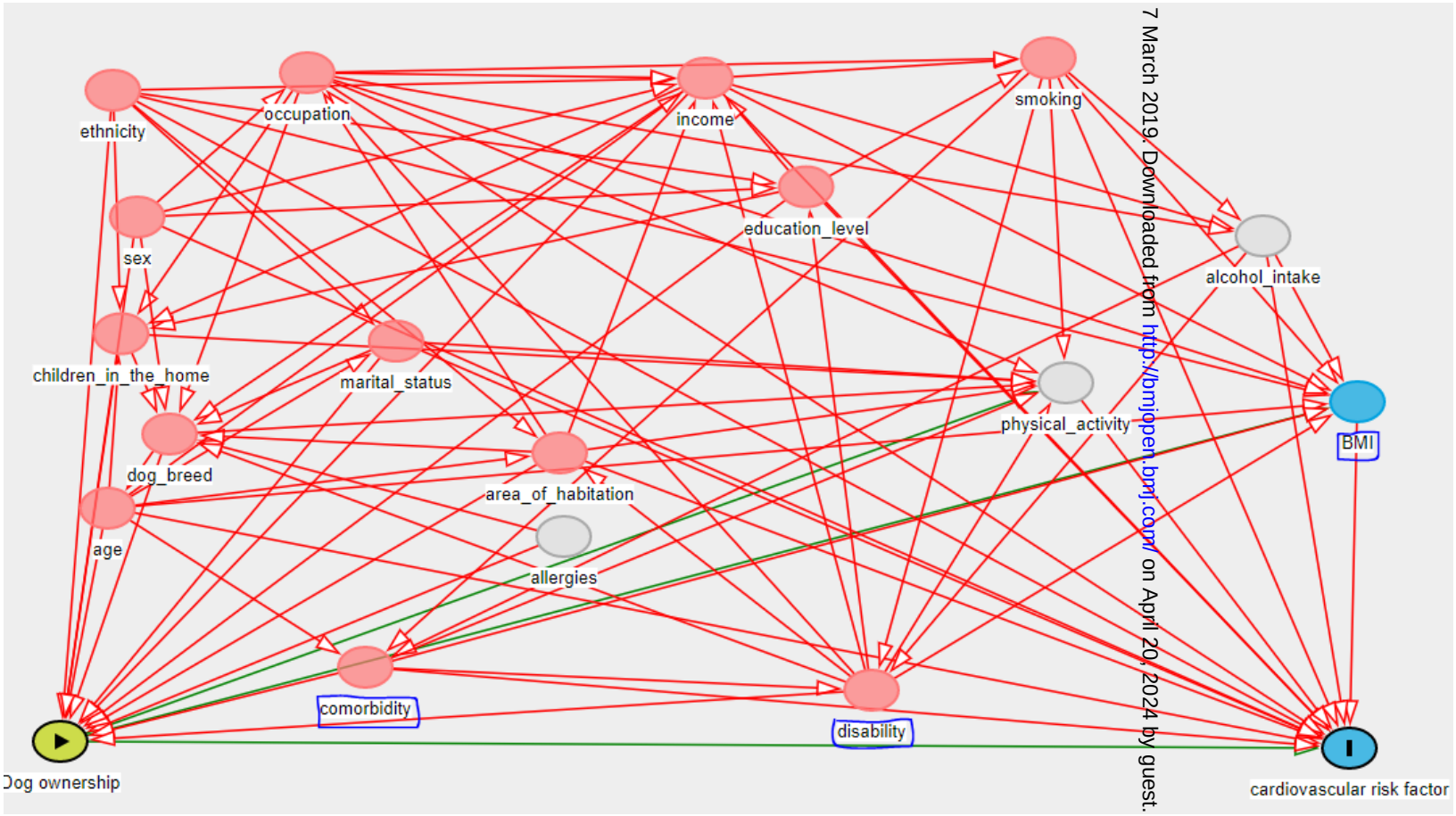
Supplementary Figure 1: Study population



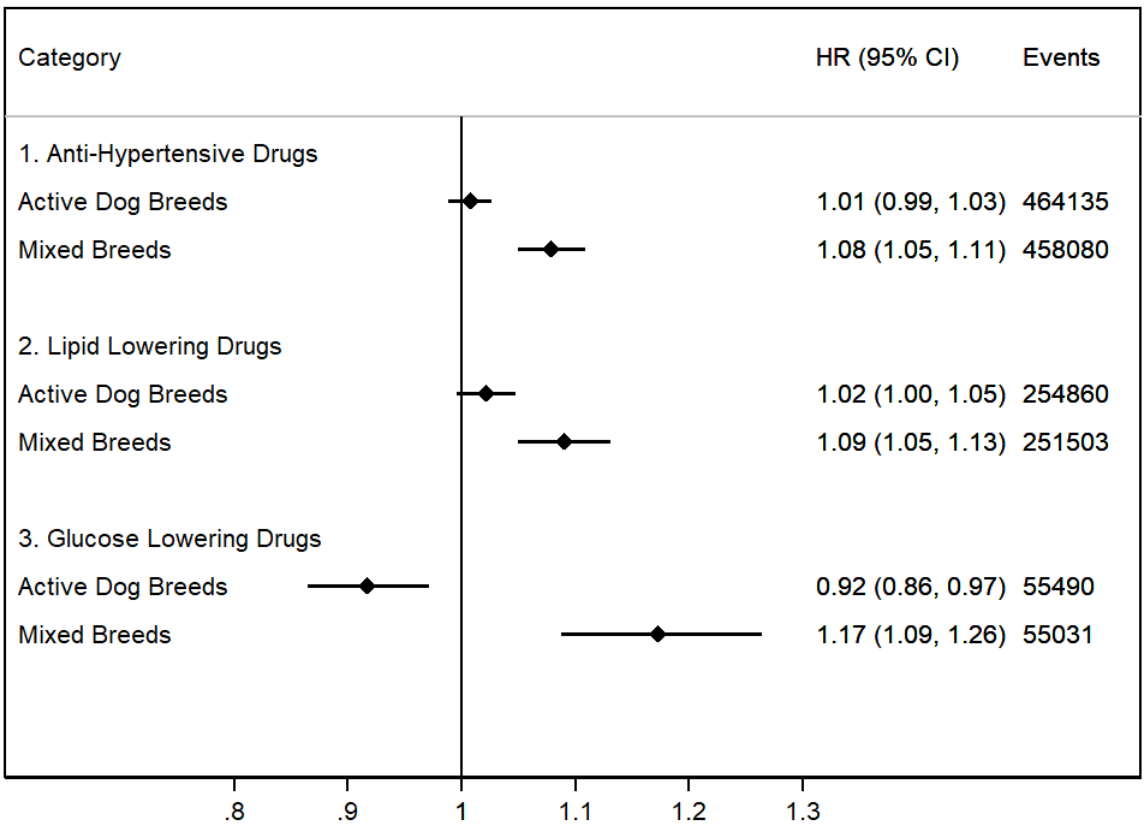
Supplementary Fig 2: Overview of Twin Cohort study recruitment and data collection.



Supplementary Figure 3: Direct Acyclic Graph for dog ownership and cardiovascular risk. The highlighted variables (comorbidity, disability and body mass index) were only available in the TwinGene cohort.



Supplementary Figure 4. Hazard ratios (HR) and 95% confidence intervals (CI) for the association of dog ownership and time to initiation of medication for hypertension, dyslipidaemia and type 2 diabetes examining associations in breeds previously identified to be associated with 'active dog breeds' (combining Terriers, Scent Hounds, Pointing dogs and Retrievers)[9] and mixed pedigree dogs and adjusted for age, sex, marital status, presence of children in the home, population density, area of residence, education level, region of birth, income and a correction for latitude of residence.



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The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
Dog ownership and Cardiovascular Risk Factors	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	a) Stated in the abstract - Pages 2 b) Abstract Page 2	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Abstract Page 2 Abstract Page 2 Abstract Page 2
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4		
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4		
Methods					
Study Design	4	Present key elements of study design early in the paper	Page 5		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5 & 6		
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the	Page 5, 6 & 7; Also summarised in the	RECORD 6.1: The methods of study population selection (such as codes or	Page 5 & 6

		sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	supplementary material as supplementary figure 1 on page 7 *Not applicable*	algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	This was not applicable to the present study *****
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	Pages 5, 6 & 7	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Full explanations are provided on pages 5-7
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Outlined on Page 6		
Bias	9	Describe any efforts to address potential sources of bias	Pages 8 & 12		
Study size	10	Explain how the study size was		Population-based study including all	

		arrived at	Page 5	adults who met the criteria for inclusion	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	Pages 7 & 8		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	a) Page 7 & 8 b) Page 8 c) Page 6 d) Page 6 e) Page 8		
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	After ethics approval was provided, Statistics Sweden provided de-identified data for the required population. The authors then cleaned the data before analysis

Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	This information is provided on page-7. This was done using the unique personal identity number given to every Swedish resident.
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	a) Supplementary Figure 1 on page 7 of the supplementary material. b) Supplementary Figure 1 on page 7 of the supplementary material. Also provided in main manuscript on page 5 & 6 c) Supplementary Figure 1 on page 7 of the supplementary material.	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Page 5 & Flow diagram on page 7 of the supplementary material and reported as figure 1
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise	a) These baseline characteristic are reported in Table 1on page 14 and 15; as well as in the results in Table 2 on page 16		

		follow-up time (*e.g.*, average and total amount)			
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures	These have been reported on page 16 & in Table 2		
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	These have been reported on page 16 & in Table 2 and in the results section on page 9 & 10 b) This shown in the supplementary methods of the supplementary material		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	This has been reported on Page 8, Table 3 reports the breed group analysis and further material found in the supplementary material as previously described		

			in the methods on page 8		
Discussion					
Key results	18	Summarise key results with reference to study objectives	Page 10 & 11		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	The limitations of this cohort study are discussed on page 12	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Page 13 & 14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 11 & 12	we observed that dog ownership was associated with a minimally higher risk of initiation of treatment for hypertension and dyslipidemia, and that ownership of dogs of the hunting breed types was associated with a lower risk of initiating treatment for diabetes	
Generalisability	21	Discuss the generalisability (external validity) of the study results			
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 13 *The study was funded by the Agria Research Foundation and the Swedish Research Council for Environment, Agricultural Sciences and Spatial Planning (FORMAS), grant number 2013-1673. T.F has personal*		

			funding from the Goran Gustafsson foundation. The Swedish Twin Registry is managed by Karolinska Institutet and receives funding through the Swedish Research Council under the grant no 2017-00641. The funders were not involved in any part of the study design, data collection, analysis manuscript preparation or approval.		
Accessibility of protocol, raw data, and programming code		..	*The register data that support the findings of this study were made available by record-linkage with data from Statistics Sweden, the National Board of Health and Welfare, the Swedish Kennel Club, Swedish Board of Agriculture and the Swedish Twin Register. Restrictions apply to the availability of these data, which were used under license and ethical approval*	RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	

			for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Regional Ethical Review Board in Stockholm, Sweden		

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.