

## SUPPLEMENTARY FILE

### **Mortality is increased in patients with rheumatoid arthritis or diabetes compared to the general population – the Nord-Trøndelag Health Study**

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**Supplementary Table S1: Baseline and disease-specific characteristics including participants with missing covariates <sup>1,2,3</sup>**

	<b>RA</b>	<b>Diabetes</b>	<b>RA + Diabetes</b>	<b>Controls</b>
	<b>N=475</b>	<b>N=3,820</b>	<b>N=41</b>	<b>N=72,582</b>
<b>Baseline characteristics</b>				
Sex				
Female	326 (69)	1,852 (48)	25 (61)	38,571 (53)
Male	149 (31)	1,969 (52)	16 (39)	34,024 (47)
Age (years)	58 (49, 68)	62 (51, 73)	66 (59, 73)	46 (34, 60)
Smoking status				
Never smoker	152 (32)	1,527 (40)	18 (44)	31,569 (43)
Former smoker	160 (34)	846 (22)	9 (22)	19,788 (27)
Current smoker	140 (29)	1,156 (30)	14 (34)	16,407 (23)
Previous CVD <sup>4</sup>	51 (11)	754 (20)	10 (24)	4,685 (6)
BMI (kg/m <sup>2</sup> )	26.1 (23.8, 29.0)	28.9 (26.1, 32.2)	27.8 (24.4, 30.9)	25.7 (23.4, 28.4)
Hypertension <sup>5</sup>	233 (49)	2,711 (71)	29 (71)	27,609 (38)
Waist/hip ratio	0.84 (0.79, 0.90)	0.90 (0.84, 0.96)	0.88 (0.84, 0.93)	0.85 (0.79, 0.90)
Non- fasting glucose	5.2 (4.7, 5.9)	7.3 (5.7, 10.7)	6.7 (5.5, 9.6)	5.1 (4.7, 5.6)

(mmol/L)

Creatinine ( $\mu\text{mol/L}$ )	83 (76, 92)	89 (80, 99)	85 (79, 96)	85 (77, 94)
Triglycerides (mmol/L)	1.4 (1.0, 2.0)	2.1 (1.4, 3.1)	1.6 (1.3, 2.4)	1.4 (1.0, 2.1)
Total cholesterol (mmol/L)	5.9 (5.2, 6.8)	6.0 (5.2, 6.9)	6.0 (5.2, 6.8)	5.6 (4.8, 6.5)
HDL cholesterol (mmol/L)	1.4 (1.1, 1.7)	1.2 (0.9, 1.4)	1.3 (1.1, 1.6)	1.3 (1.1, 1.6)
Total cholesterol/HDL cholesterol ratio	4.2 (3.4, 5.4)	5.1 (4.1, 6.5)	4.5 (3.6, 5.5)	4.2 (3.3, 5.3)

Observation time (years)	18.0 (12.1, 18.8)	17.4 (7.5, 18.4)	14.6 (7.2, 18.2)	17.9 (8.0, 18.7)
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#### **RA-specific variables**

Seropositive <sup>6</sup>	348 (73)		31 (76)	
Age when diagnosed (years)	55 (44, 65)		61 (53, 70)	
RA duration before first HUNT participation with diagnosis (years)	6 (3, 9)		7 (4, 9)	

#### **Diabetes-specific variables**

Peroral diabetes medication		1,469 (38)	15 (37)	
Insulin		722 (19)	10 (24)	
Age when diagnosed (years)		59 (49, 68)	61 (50, 69)	

Diabetes duration before first HUNT participation with diagnosis (years)	5 (2, 11)	6 (3, 12)
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<sup>1</sup>Number (%) or median (25<sup>th</sup> and 75<sup>th</sup> percentile)

<sup>2</sup>RA: rheumatoid arthritis, CVD: cardiovascular disease, BMI: body mass index, HDL: high-density lipoprotein

<sup>3</sup>Missing data – <4% missing data except for smoking, blood pressure, creatinine, triglycerides and diabetes-specific variables. Smoking missing for 3,176 (5 %) and 1,970 (13%) with baseline in HUNT2 and HUNT3, respectively. Blood pressure missing for 1,900 (13%) with baseline in HUNT3. Creatinine and triglycerides missing for 3,777 (25%) with baseline in HUNT3. Diabetes-specific variables: peroral diabetes medication use missing for 1,058 (27%), insulin use missing for 1,072 (28 %), duration of diabetes and age of diabetes onset missing for 299 (8%).

<sup>4</sup>Previous cardiovascular disease: self-reported angina, stroke, or myocardial infarction

<sup>5</sup>Hypertension: Systolic blood pressure  $\geq 140$ , diastolic blood pressure  $\geq 90$ , or on blood pressure-lowering medication

<sup>6</sup>Seropositive – positive for either rheumatoid factor and/or anti-citrullinated protein antibodies

**Supplementary Table S2: Sensitivity analyses 1, 4, and 5**

	<b>Hazard ratio</b>	<b>95 % Confidence interval</b>	<b>P-value</b>
<b>Sensitivity analysis 1: Cox regression for mortality by age groups</b>			
Rheumatoid arthritis ≤75 years	1.21	0.79-1.62	0.25
Rheumatoid arthritis >75 years	1.24	1.01-1.48	0.035
Diabetes age ≤75 years	1.83	1.61-2.05	<0.001
Diabetes age >75 years	1.49	1.39-1.59	<0.001
<b>Sensitivity analysis 4: Cox regression for mortality after multiple imputation of missing adjustment variables</b>			
Rheumatoid arthritis	1.20	1.03-1.40	0.021
Diabetes age ≤75 years	1.90	1.70-2.12	<0.001
Diabetes age >75 years	1.43	1.27-1.62	<0.001
<b>Sensitivity analysis 5: Cox regression for mortality excluding patients with both diseases</b>			
Rheumatoid arthritis	1.24	1.02-1.46	0.017
Diabetes age ≤75 years	1.83	1.61-2.06	<0.001
Diabetes age >75 years	1.52	1.39-1.59	<0.001

All models are from Step 3, i.e. adjusted for sex, hypertension <sup>1</sup>, smoking <sup>2</sup>, BMI <sup>3</sup>, creatinine, total cholesterol, and previous cardiovascular disease <sup>4</sup>

Age was used as the time variable and was thereby adjusted for in all models

Abbreviations: BMI – body mass index

<sup>1</sup>Hypertension: Systolic blood pressure  $\geq 140$ , diastolic blood pressure  $\geq 90$ , or on blood pressure-lowering medication

<sup>2</sup>Smoking: never smoker, current smoker or former smoker

<sup>3</sup>BMI: categorised as  $<18.5 \text{ kg/m}^2$ ,  $18.5\text{-}24.9 \text{ kg/m}^2$ ,  $25\text{-}29.9 \text{ kg/m}^2$ ,  $30\text{-}34.9 \text{ kg/m}^2$  and  $\geq 35 \text{ kg/m}^2$

<sup>4</sup>Previous cardiovascular disease: self-reported angina, stroke, or myocardial infarction