

Electronic Supplementary Material (ESM)

Plasma prostein: a novel risk marker for incidence of diabetes and cancer mortality

Xue Bao^{1,2}, Biao Xu¹, Iram Faqir Muhammad², Peter M. Nilsson², Jan Nilsson² and Gunnar Engström²

¹Department of Cardiology, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, China

²Department of Clinical Sciences, Malmö, Lund University, Malmö, Sweden

Corresponding authors:

Biao Xu xubiao62@nju.edu.cn

Gunnar Engström gunnar.engstrom@med.lu.se

ORCID identifiers:

Xue Bao: 0000-0003-3777-5988

Biao Xu: 0000-0003-3404-8582

Gunnar Engström: 0000-0002-8618-9152

ESM Table 1 Baseline characteristics of the study population ($n = 4658$) across sex-specific quartiles (Q1–Q4) of prostatic

	Whole population	Q1 ($n = 1165$)	Q2 ($n = 1164$)	Q3 ($n = 1165$)	Q4 ($n = 1164$)	p for trend ^a
Prostatic in men (NPX)	8.46 (5.91-9.89)	7.89 (5.91-8.19)	8.35 (8.19-8.48)	8.61 (8.48-8.76)	8.99 (8.76-9.89)	–
Prostatic in women (NPX)	8.19 (6.40-9.78)	7.89 (5.91-8.19)	8.35 (8.19-8.48)	8.61 (8.48-8.76)	8.99 (8.76-9.89)	–
Diabetes	361 (7.75)	57 (4.89)	64 (5.50)	90 (7.73)	150 (12.89)	<0.0001
Age (years)	57.5±5.90	56.6±5.90	57.2±5.90	57.9±5.90	58.2±6.00	<0.0001
Men	1858 (39.9)	465 (39.9)	464 (39.9)	465 (39.9)	464 (39.9)	0.99
Waist circumference (cm)	83.4±12.8	81.1±12.0	82.5±12.2	84.1±13.5	86±12.9	<0.0001
Smoking	1007 (21.6)	119 (10.2)	178 (15.3)	264 (22.7)	446 (38.3)	<0.0001
High alcohol consumption	160 (3.43)	32 (2.75)	31 (2.66)	32 (2.75)	65 (5.58)	0.0004
Systolic BP (mmHg)	140.9±18.9	137.8±18.4	139.6±18.3	142.1±18.7	144.3±19.5	<0.0001
LDL-cholesterol (mmol/l)	4.17±0.98	4.10±0.99	4.12±0.96	4.17±0.95	4.29±1.02	<0.0001
BP-lowering medication	744 (16.0)	133 (11.4)	181 (15.6)	196 (16.8)	234 (20.1)	<0.0001
Fasting blood glucose (mmol/l)	4.90 (4.60-5.30)	4.80 (4.50-5.10)	4.80 (4.60-5.20)	4.90 (4.60-5.30)	5.10 (4.70-5.50)	<0.0001 ^b
Plasma insulin (pmol/l) ($n = 4627$)	41.7 (27.8-62.5)	34.7 (27.8-48.6)	41.7 (27.8-55.6)	48.6 (27.8-62.5)	55.6 (34.7-76.4)	<0.0001 ^b
HOMA2-IR ($n = 4627$)	0.80 (0.50-1.20)	0.70 (0.50-10.0)	0.80 (0.50-1.10)	0.90 (0.60-1.30)	1.10 (0.70-1.60)	<0.0001 ^b
CRP (mg/l) ($n = 4556$)	1.30 (0.70-2.70)	1.00 (0.60-2.10)	1.20 (0.60-2.50)	1.40 (0.70-2.80)	1.70 (0.80-3.70)	<0.0001 ^b
eGFR ($\text{ml min}^{-1} 1.73 \text{ m}^{-2}$) ($n = 4351$)	89.0±13.5	90.8±13.4	89.7±13.0	88.4±13.3	87.1±14.1	<0.0001

CRP, C-reactive protein; HOMA2-IR, Homeostasis Model Assessment-2 Insulin Resistance; NPX, Normalised protein expression. Values for prostatic are mean (range). Values for fasting glucose, insulin, HOMA2-IR and CRP are median (IQR) due to skewed distributions. Values for other continuous variables are means ± SD. Values for categorical variables are n (%)

^aAnalysis by linear regression or logistic regression

^b p value for natural log-transformed values of fasting glucose, insulin, HOMA2-IR and CRP

ESM Table 2 Prevalence of diabetes in relation to prostatic by sex-specific quartiles (Q1–Q4) and per 1 SD increase ($n = 4658$)

	Q1 ($n = 1165$)	Q2 ($n = 1164$)	Q3 ($n = 1165$)	Q4 ($n = 1164$)	p for trend ^a	Per 1 SD	p^a
No. of diabetes ($n = 361$)	57	64	90	150	–	–	–
OR Model 1 ^b	Reference	1.17 (0.81, 1.69)	1.66 (1.18, 2.35)	2.92 (2.14, 4.05)	<0.0001	1.67 (1.48, 1.87)	<0.0001
OR Model 2 ^c	Reference	1.04 (0.71, 1.52)	1.24 (0.87, 1.79)	2.02 (1.45, 2.84)	<0.0001	1.34 (1.18, 1.52)	<0.0001
OR Model 3 ^d	Reference	1.03 (0.70, 1.50)	1.21 (0.84, 1.74)	1.95 (1.39, 2.76)	<0.0001	1.32 (1.16, 1.50)	<0.0001

^aAnalysis by Multiple logistic regression. Values presented for the models are OR (95% CI)

^bCrude model

^cAdjusted for age, sex and waist circumference

^dAdditionally adjusted for smoking and drinking habits, LDL-cholesterol, systolic blood pressure, and anti-hypertensive drug medication

ESM Table 3 Associations between prostaticin and fasting blood glucose, plasma insulin and HOMA2-IR at baseline in individuals without diabetes

	Standardized β coefficient	Standard error	p^a
Model 1^b			
Fasting blood glucose ($n = 4297$)	0.25	0.016	<0.0001
Plasma insulin ($n = 4247$)	0.23	0.014	<0.0001
HOMA2-IR ($n = 4247$)	0.24	0.013	<0.0001
Model 2^c			
Fasting blood glucose ($n = 4297$)	0.17	0.016	<0.0001
Plasma insulin ($n = 4247$)	0.17	0.015	<0.0001
HOMA2-IR ($n = 4247$)	0.18	0.015	<0.0001
Model 3^d			
Fasting blood glucose ($n = 4297$)	0.14	0.016	<0.0001
Plasma insulin ($n = 4247$)	0.17	0.015	<0.0001
HOMA2-IR ($n = 4247$)	0.18	0.015	<0.0001

HOMA2-IR, Homeostasis Model Assessment-2 Insulin Resistance

^aAnalysis by multivariable linear regression with prostaticin as the dependent variable. Insulin and HOMA2-IR were natural-logarithmically transformed before analyses^bCrude model^cAdjusted for age, sex and waist circumference^dAdditionally adjusted for smoking and drinking habits, LDL-cholesterol, systolic blood pressure, and anti-hypertensive medication

ESM Table 4 Incidence of all-cause mortality and cardiovascular mortality in relation to prostatic by sex-specific quartiles (Q1–Q4) and per 1 SD increase ($n = 4297$)

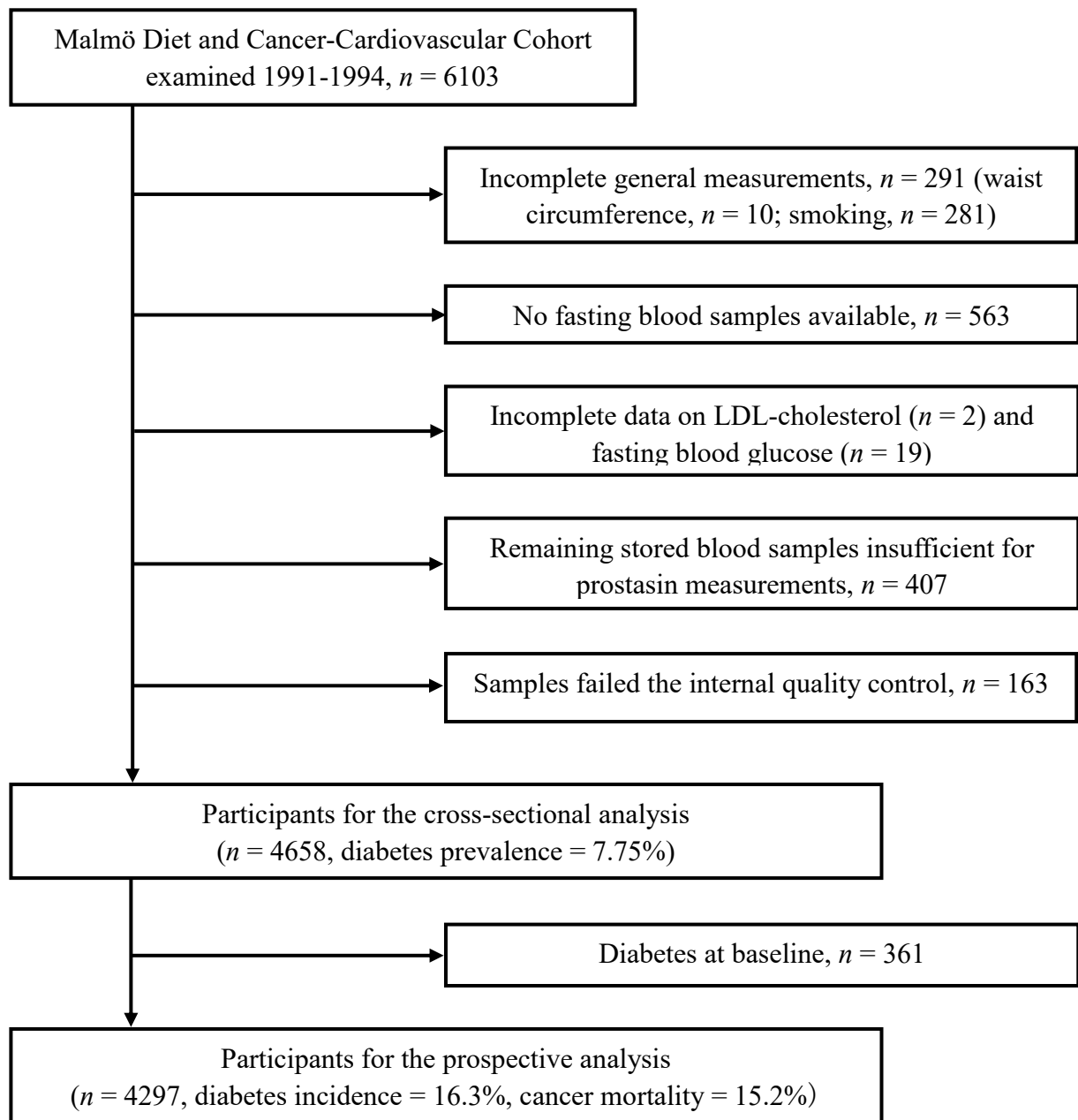
	Q1 ($n = 1075$)	Q2 ($n = 1074$)	Q3 ($n = 1075$)	Q4 ($n = 1073$)	p for trend ^a	Per 1 SD	p^a
All-cause mortality							
Incidence	354	386	434	558	–	–	–
Incidence per 1000 person years	13.4	14.9	17.3	23.7	–	–	–
Model 1 ^b	Reference	1.07 (0.92, 1.23)	1.18 (1.02, 1.36)	1.63 (1.43, 1.87)	<0.0001	1.23 (1.16, 1.29)	<0.0001
Model 2 ^c	Reference	1.04 (0.90, 1.20)	1.07 (0.93, 1.23)	1.33 (1.16, 1.53)	<0.0001	1.12 (1.06, 1.18)	<0.0001
Cardiovascular mortality							
Incidence	108	108	124	156	–	–	–
Incidence per 1000 person years	4.08	4.17	4.95	6.63	–	–	–
Model 1 ^b	Reference	0.92 (0.71, 1.21)	1.00 (0.77, 1.30)	1.35 (1.05, 1.73)	0.0098	1.13 (1.02, 1.24)	0.018
Model 2 ^c	Reference	0.90 (0.69, 1.17)	0.90 (0.70, 1.17)	1.10 (0.85, 1.42)	0.39	1.03 (0.93, 1.14)	0.59
Model 3 ^d	Reference	0.90 (0.69, 1.18)	0.89 (0.68, 1.15)	1.06 (0.82, 1.37)	0.59	1.01 (0.92, 1.12)	0.84
Sensitivity analysis							
Excluding prior cardiovascular events ($n = 4204$)	Reference	0.88 (0.66, 1.16)	0.92 (0.70, 1.2)	1.11 (0.85, 1.44)	0.34	1.03 (0.93, 1.14)	0.59
Accounting for competing risk of death	Reference	0.88 (0.68, 1.15)	0.85 (0.65, 1.11)	0.94 (0.73, 1.21)	0.70	0.97 (0.87, 1.07)	0.51

^aAnalysis by Cox proportional hazards model. Values presented for the models are HR (95% CI)

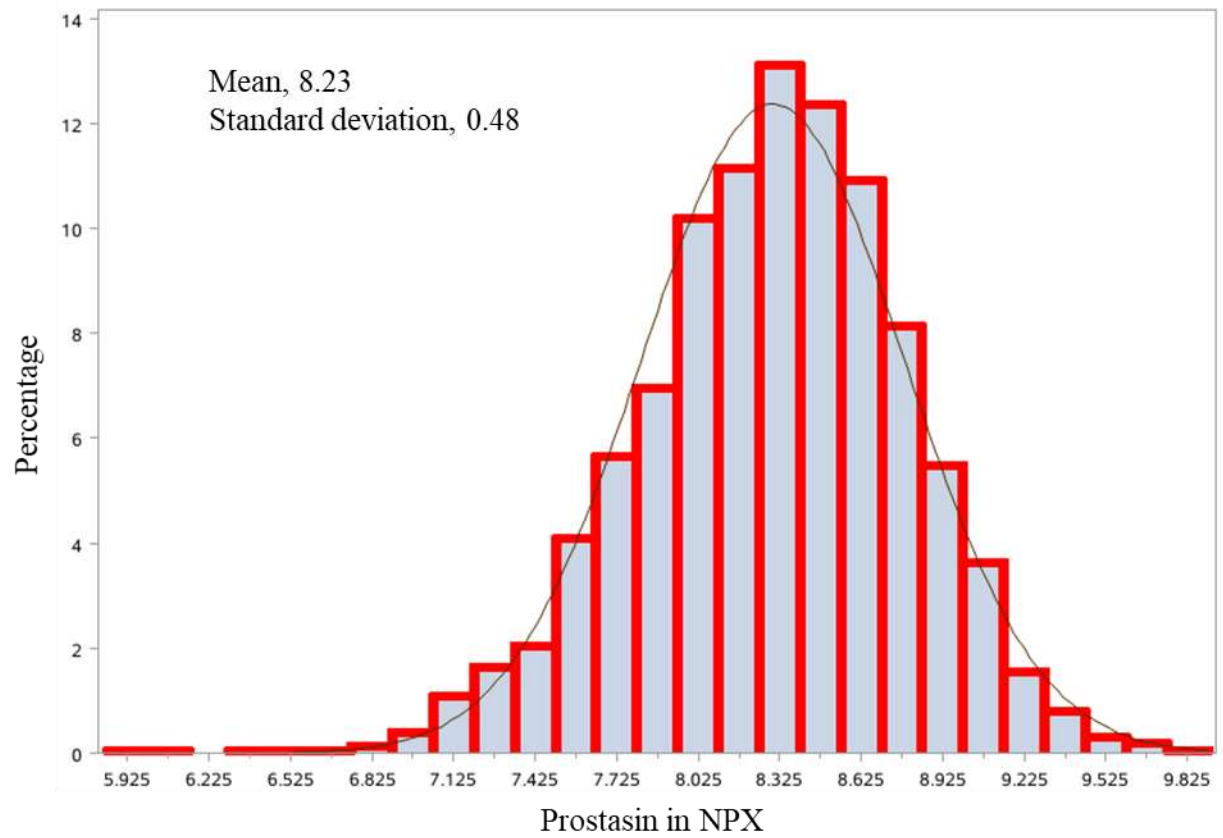
^bAdjusted for age, sex and waist circumference

^cAdditionally adjusted for smoking and drinking habits, LDL-cholesterol, systolic BP, and anti-hypertensive medication

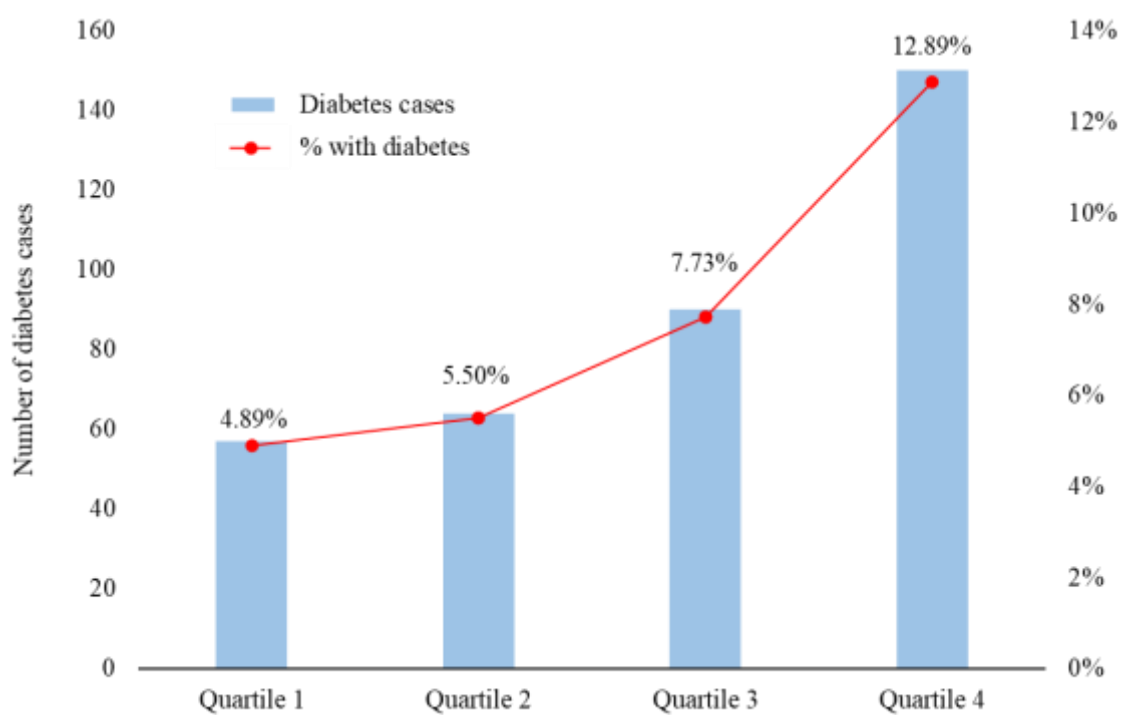
^dAdditionally adjusted for prior cardiovascular events



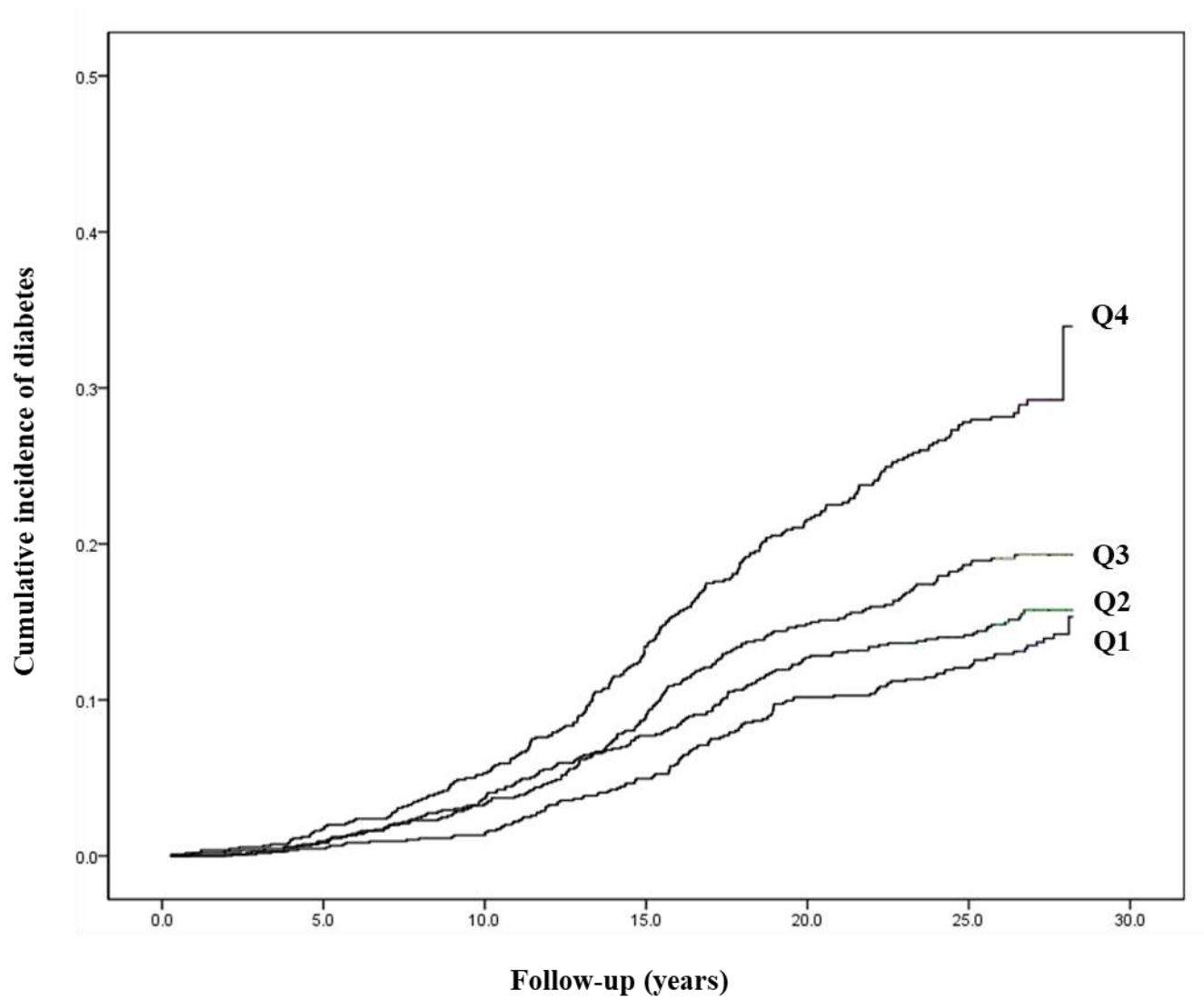
ESM Fig. 1 Study population flow chart



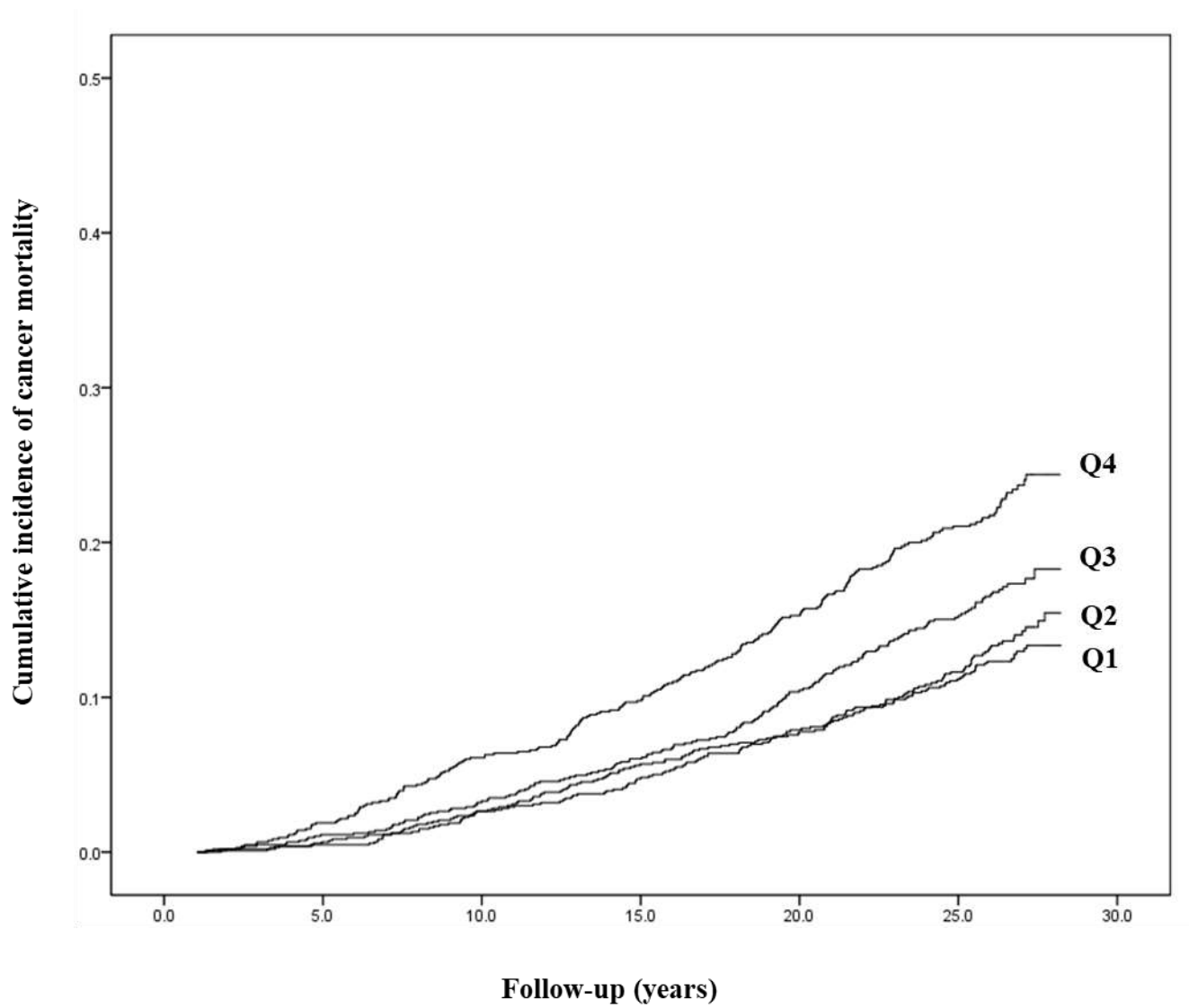
ESM Fig. 2 Distribution plot of prostin



ESM Fig. 3 Number of prevalent diabetes cases and the percentage (%) of people with diabetes in each quartile of prostatic



ESM Fig. 4 Cumulative incidence of diabetes in relation to prostatic quartiles (Q1–Q4)



ESM Fig. 5 Cumulative cancer mortality in relation to prostatic acid phosphatase quartiles (Q1–Q4)