

Supplementary Table 1. Hazard ratio (HR) of incident diabetes by quartiles of serum total calcium excluding events occurring in the first 3 years and 5 years of follow up.

	Q1	Q2	Q3	Q4	P <sub>Trend</sub>
Cutoff (mmol/l)	<2.33	2.33 to 2.38	2.39 to 2.44	>2.44	
Excluding events in the first 3 years of follow-up	1	1.20 (0.91-1.58)	1.43 (1.08-1.89)	1.35 (1.00-1.80)	0.039
Excluding events in the first 5 years of follow-up	1	1.13 (0.82-1.56)	1.36 (0.99-1.88)	1.40 (1.00-1.96)	0.031

\* Adjusted for age, sex, BMI, smoking status, drinking status, physical activity, serum albumin, serum phosphate, parathyroid hormone, alkaline phosphatase, femoral neck BMD T-score, and season.

Supplementary Table 2. Data summary of selected literatures for meta-analysis.

a) Literatures in serum total calcium group

Study	No. of incident Diabetes/ Sample size	Baseline	Age / Female, %	Follow-up years	Define Serum Calcium, mmol/L	Risk estimates (95% CI)	Diabetes assessment	Adjusted confounding factors	Quality score
Sing 2015, Hong Kong	631/6096	Southern Chinese age 20 or above free of diabetes	52.5±16.2 (mean±sd) / 72%	10.2 (median)	Quartiles: <2.33 2.33-2.38 2.39-2.44 >2.44	Hazard Ratios: 1 1.17 (0.91-1.49) 1.37 (1.07-1.74) 1.32 (1.02-1.70)	Ascertainment of diabetes, with a prescription record of diabetic medication, a lab record of A1C ≥6.5% or fasting plasma glucose >7.0 mmol/l, and enrolled in a diabetic complication screening program	Age, sex, BMI, smoking, drinking, physical activity, serum phosphate, serum parathyroid hormone, serum alkaline phosphatase, serum albumin, femoral neck BMD T-score, season	-

Jorde 2013, Norway	705/27158	Inhabitants of the municipality of Tromsø aged above 25	> 25 / 52.6%	13	Quartiles: 2.20–2.29 2.30–2.39 2.40–2.49 2.50–2.60	Hazard Ratios 1 0.91 (0.72-1.14) 1.08 (0.86-1.36) 1.36 (1.04 1.77),	Non-fasting glucose $\geq$ 11.1 mmol/L, fasting glucose $\geq$ 7.0 mmol/L, 2 h glucose load $\geq$ 11.1 mmol/L or HbA1c >6.5%	Age, sex, BMI, smoking, systolic blood pressure, serum cholesterol	8
Lorenzo 2014, US	140/863	Non-diabetic patient (non-Hispanic whites, African-Americans, Hispanics)	40-69 (range) / 56%	5.2 (mean)	Quintiles: <2.13 2.13–2.24 2.25–2.37 2.38–2.49 $\geq$ 2.50	Odd Ratios: 0.92 (0.40-2.09) 1 1.18 (0.69-2.01) 1.94 (0.96-3.91) 3.15 (1.14, 8.73)	Fasting glucose $\geq$ 7.0 mmol/l and/or 2 h glucose $\geq$ 11.1 mmol/l, impaired glucose tolerance as 2 h glucose 7.8–11.0 mmol/l, and self-reported of glucose-lowering medications	BMI, family history of diabetes, fasting and 2h OGTT glucose concentrations, $\log_e$ insulin sensitivity index, $\log_e$ acute insulin response, eGFR and diuretic drugs	9

b) Literatures in albumin-corrected serum calcium

Study	No. of Diabetes/ Sample size	Baseline	Age / Female, %	Follow-up years	Define albumin-corrected serum Calcium, mmol/L	Risk estimates (95% CI)	Diabetes assessment	Adjusted confounding factors	Quality score
Sing 2015, Hong Kong	631/6096	Southern Chinese aged 20 or above, free of diabetes	52.5±16.2 (mean±sd) / 72%	10.2 (median)	Quartiles: <2.25, 2.25-2.29, 2.30-2.35, >2.35	Hazard Ratios: 1 0.96 (0.75-1.24) 1.04 (0.82-1.32) 1.22 (0.96-1.55)	Ascertainment of diabetes, with a prescription record of diabetic medication, a lab record of A1C ≥6.5% or fasting plasma glucose >7.0 mmol/l, and enrolled in a diabetic complication screening program	Age, sex, BMI, smoking, drinking, physical activity, serum phosphate, serum parathyroid hormone, serum alkaline phosphatase, femoral neck BMD T-score, season	-
Becerra-Tomas 2014, Spain	77/707	Men aged 55–80 years and women aged 60–80 years, not previously reported any cardiovascular	67±6 (mean±sd) / 60%	4.78 (median)	Quartiles: 1.97-2.30 2.31-2.40 2.41-2.49 2.5-2.8	Hazard Ratios:* 1 1.77 (0.87-3.62) 0.87 (0.38-2.01) 1.73 (0.84-3.56)	Fasting plasma glucose ≥126.0 mg/dL (7 mmol/L) or 2-hplasma glucose ≥200 mg/dL (11.1 mmol/L) after a 75-g oral glucose load.	Age, sex, BMI, smoking, drinking, leisure-time physical activity, educational level, intervention,	7

		events but who were at high cardiovascular risk and free of diabetes at baseline						group, prevalence of hypertension, prevalence of hypercholesterolemia, use of antihypertensive medication, use of statins, fasting plasma glucose at baseline	
Lorenzo 2014, US	140/863	Non-diabetic patient (non-Hispanic whites, African-Americans, Hispanics)	40-69 (range) / 56%	5.2 (mean)	Quintiles: <2.13 2.13–2.24 2.25–2.37 2.38–2.49 ≥2.50	Odd Ratios:* 1.46 (0.51-4.17) 1 1.43 (0.83-2.48) 1.98 (1.00-3.92) 2.25 (0.71-7.08)	Fasting glucose ≥7.0 mmol/l and/or 2 h glucose ≥11.1 mmol/l, impaired glucose tolerance as 2 h glucose 7.8–11.0 mmol/l, and self-reported of glucose-lowering medications	BMI, family history of diabetes, fasting and 2h OGTT glucose concentrations, log <sub>e</sub> insulin sensitivity index, log <sub>e</sub> acute insulin response, eGFR and diuretic drugs	9

\* Data obtained from the authors

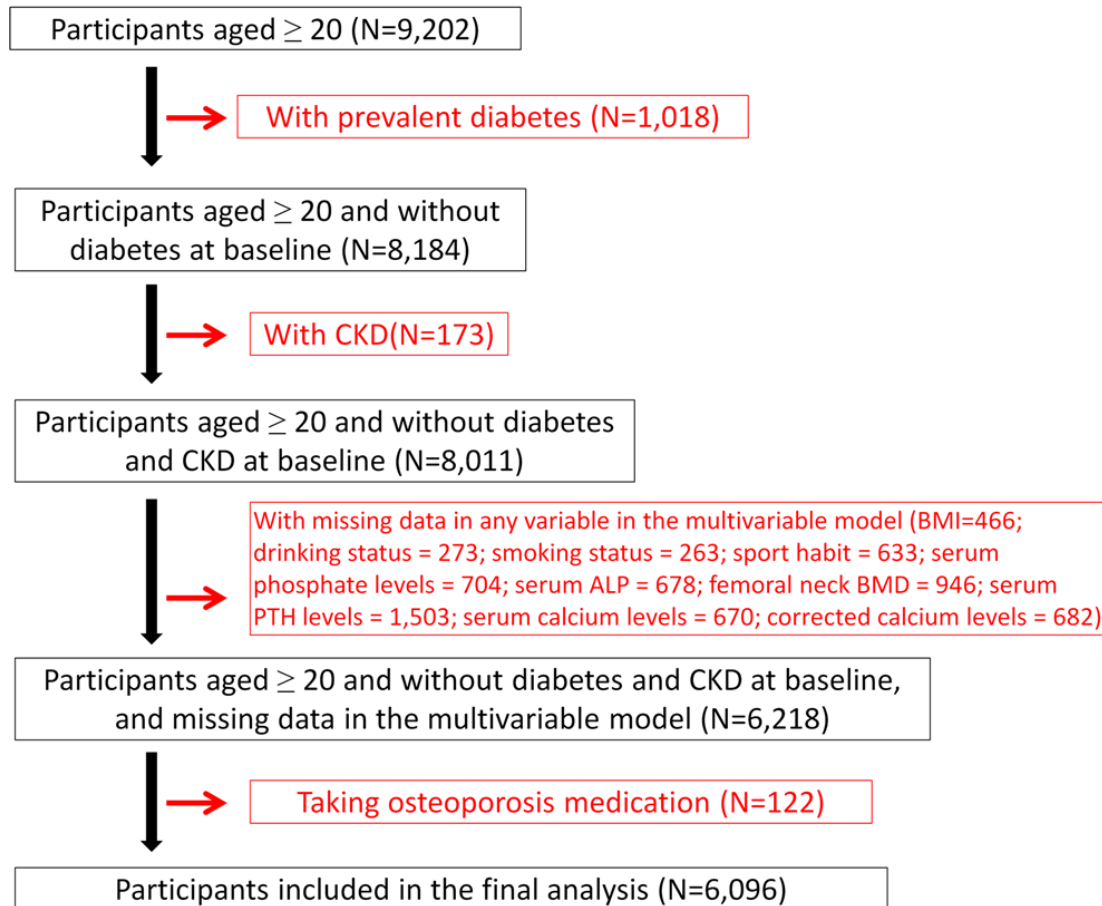
Supplementary Table 3. Associations between serum phosphate and incident diabetes in the IRAS<sup>^</sup> and current study.

Study	Estimate	Serum phosphate levels (mmol/l)						
		<1	1.00-1.09		1.10-1.19		≥1.2	
IRAS <sup>1</sup>	OR	1	1.57	(1.00-2.46)	1.11	(0.61-2.01)	2.12	(1.19-3.79)
Current study	OR	1	0.85	(0.65-1.10)	0.97	(0.76-1.25)	0.95	(0.74-1.21)
Current study	HR	1	0.95	(0.74-1.20)	1.08	(0.86-1.37)	1.07	(0.85-1.34)

Results adjusted for age, sex, and ethnicity.

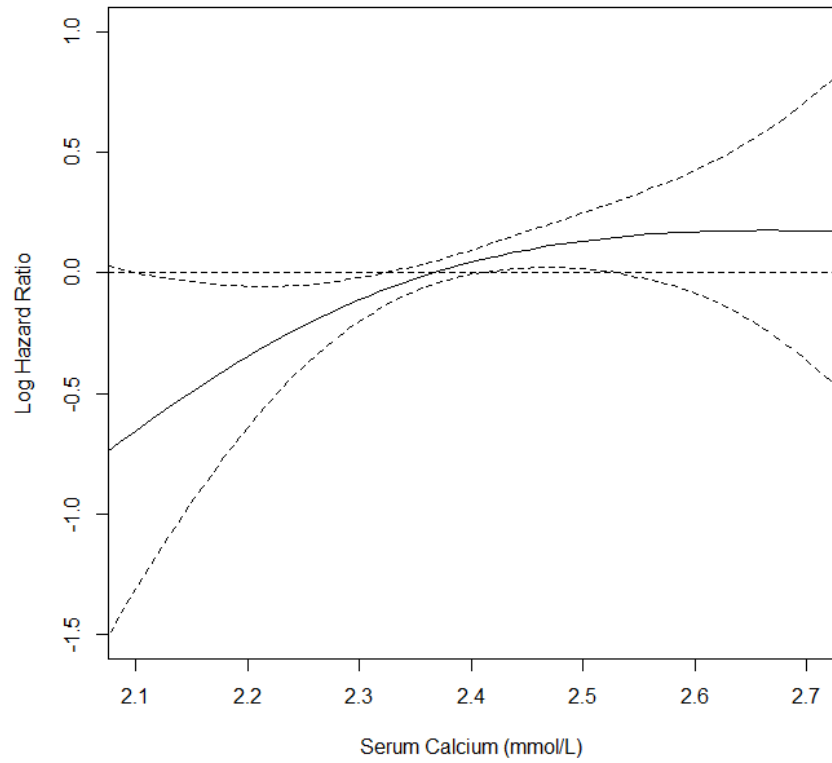
<sup>^</sup> Lorenzo C, Hanley AJ, Rewers MJ, Haffner SM (2014) Calcium and phosphate concentrations and future development of type 2 diabetes: the Insulin Resistance Atherosclerosis Study. *Diabetologia*. doi:10.1007/s00125-014-3241-9

Supplementary Figure 1. Eligibility flow of the study.

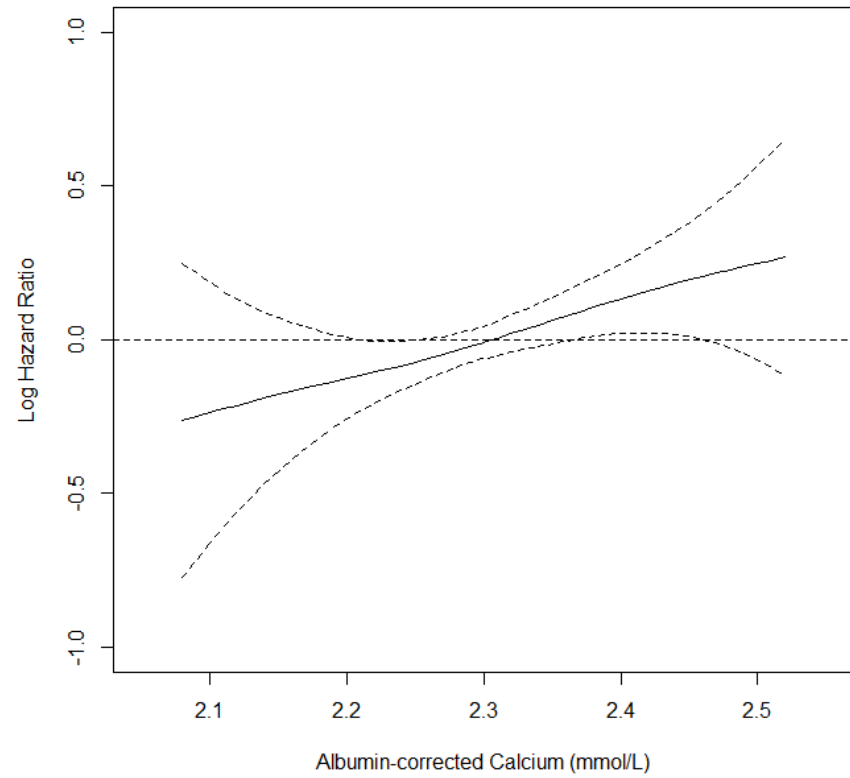


Supplementary Figure 2. Association between serum calcium and incident diabetes assessed via penalized regression splines.

a) Serum total calcium



b) Albumin-corrected calcium

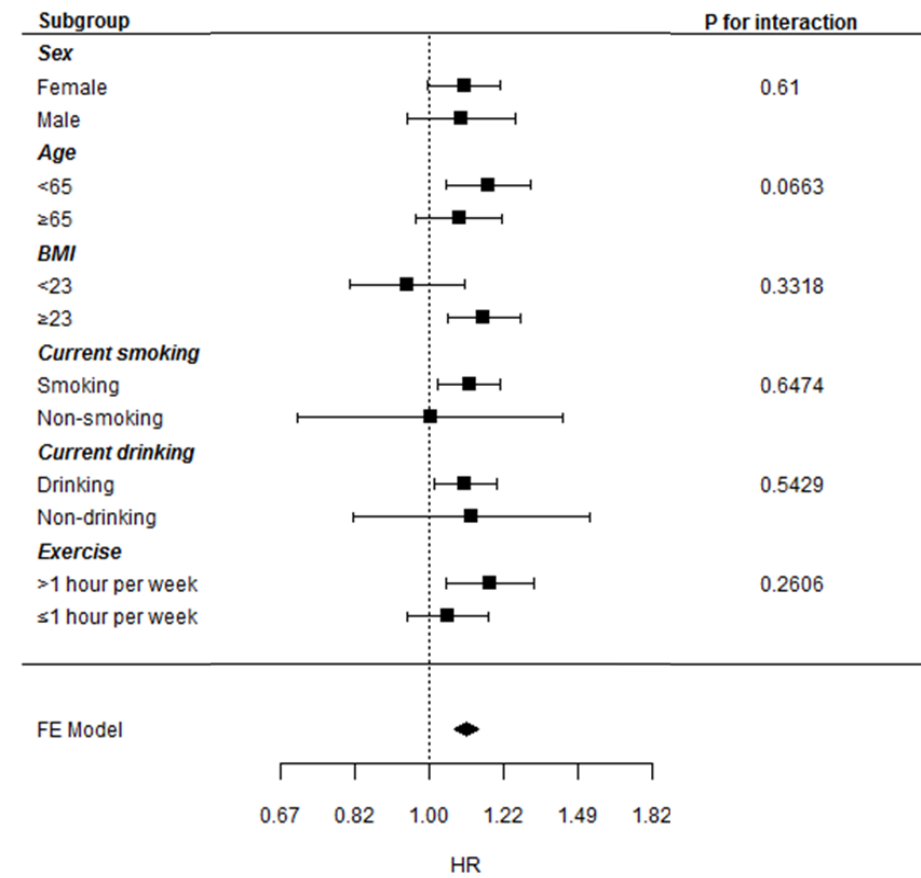
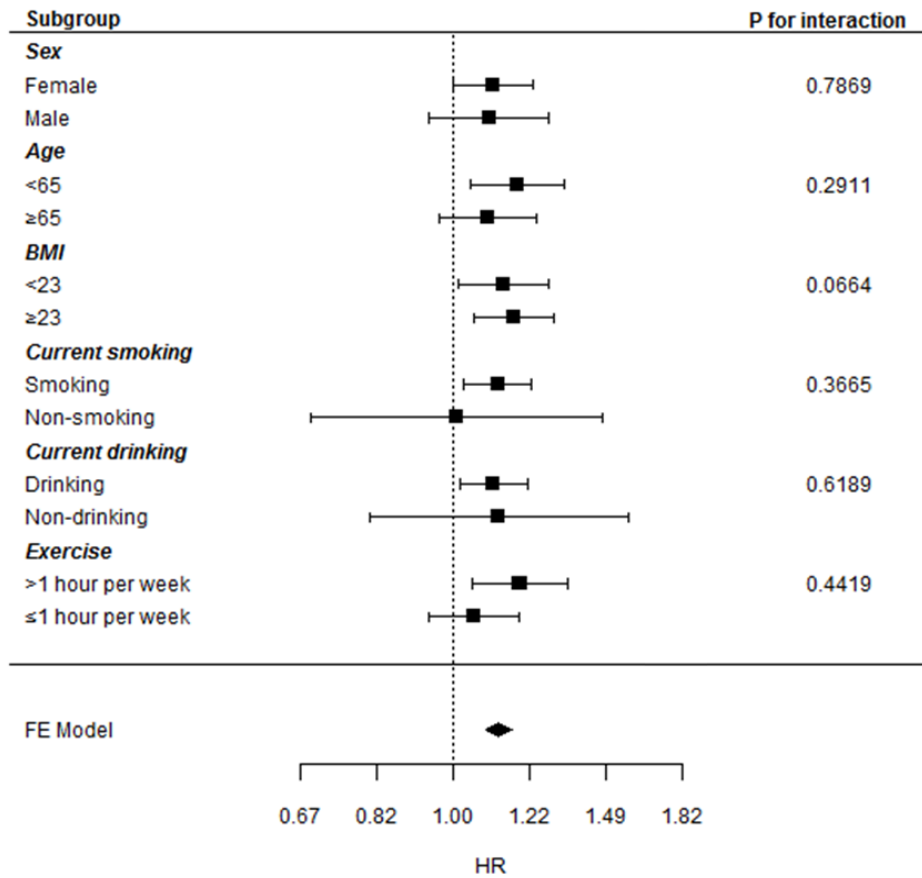




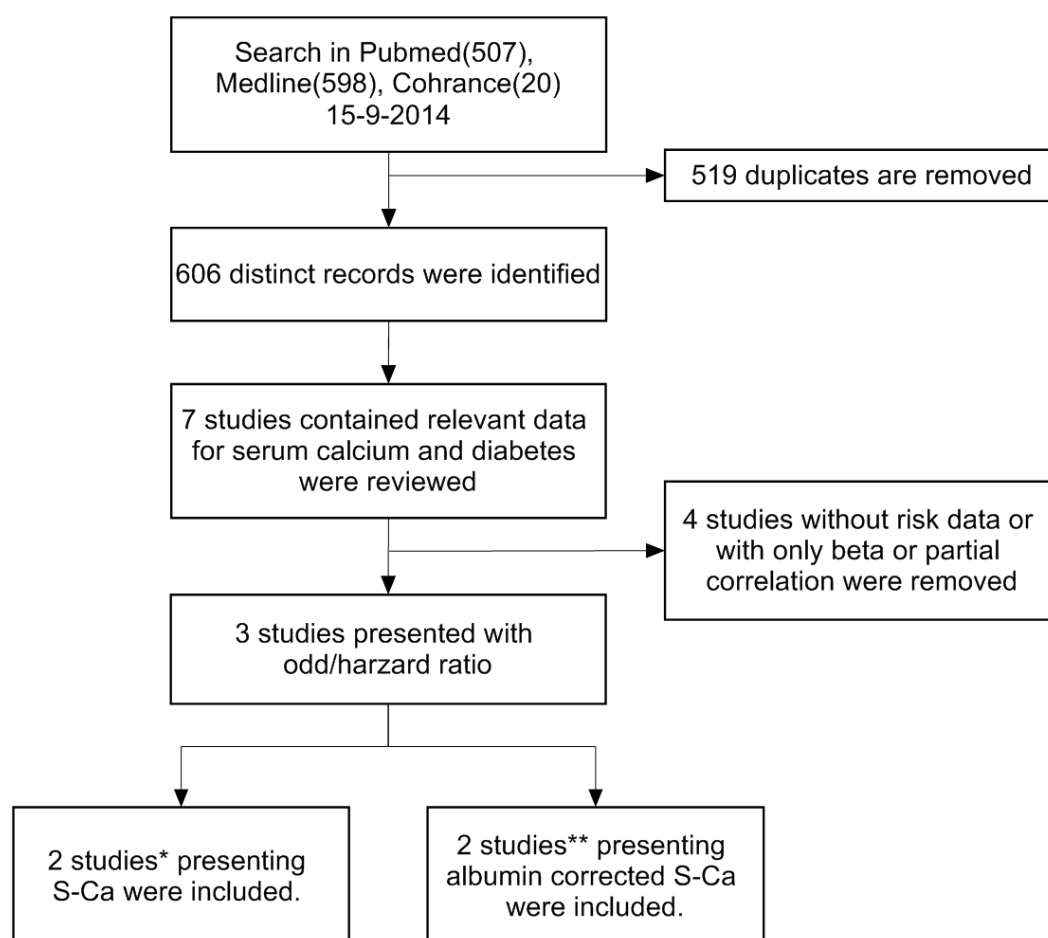
Supplementary Figure 3. Association of serum calcium and incident diabetes stratified by predefined subgroups.

a) Serum total calcium

b) Albumin-corrected calcium



Supplementary Figure 4. Flow chart of paper collection for meta-analysis of serum calcium and incident diabetes.



#### Selected studies

\*Lorenzo C, Hanley AJ, Rewers MJ, et al. Calcium and phosphate concentrations and future development of type 2 diabetes: the Insulin Resistance Atherosclerosis Study. *Diabetologia* 2014.

\*Jorde R, Schirmer H, Njolstad I, et al. Serum calcium and the calcium-sensing receptor polymorphism rs17251221 in relation to coronary heart disease, type 2 diabetes, cancer and mortality: the Tromso Study. *Eur J Epidemiol* 2013;28:569-578.

\*\*Lorenzo C, Hanley AJ, Rewers MJ, et al. Calcium and phosphate concentrations and future development of type 2 diabetes: the Insulin Resistance Atherosclerosis Study. *Diabetologia* 2014.

\*\*Becerra-Tomas N, Estruch R, Bullo M, Casas R, Diaz-Lopez A, Basora J, Fito M, et al. Increased Serum Calcium Levels and Risk of Type 2 Diabetes in Individuals at High Cardiovascular Risk. *Diabetes Care* 2014.