

RISK FACTORS FOR CHRONIC KIDNEY DISEASE IN SPECIFIC HIGH RISK PATIENTS WITH DIABETES MELLITUS AND HYPERTENSION IN TAIWAN

Chai-Chao Wu¹, Sui-Lung Su², Sen-Yeong Kao², Kuo-Cheng Lu³, and Yuh-Feng Lin⁴

¹Division of Nephrology, Department of Medicine, Tri-Service General Hospital, Taipei, Taiwan

²School of Public Health, National Defense Medical Center, Taipei, Taiwan

³ Division of Nephrology, Department of Medicine, Cardinal Tien Hospital, Taipei, Taiwan

⁴ Division of Nephrology, Department of Medicine, Shuang Ho Hospital, Taipei, Taiwan



Background

Taiwan has the highest prevalence and incidence of end stage renal disease in the world. The majorities were due to diabetes mellitus (DM) or hypertension (HTN). However, the characteristic risk factors for the development of chronic kidney disease (CKD) in each specific high risk population in Taiwan region are still unclear. This study surveyed the most common risk factors and identified their effects on CKD in general population or patients with HTN and/or DM in Taiwan.

Methods

This study included 5328 cases and 5135 controls in CKD/HTN/DM outpatient department and health center of 10 hospitals from 2008 to 2010. Fourteen common risk factors were surveyed (4 of demographic factors, 5 of disease factors and 5 of lifestyle factors) and checked their impact on CKD development. Variables with significant heterogeneity between patients with different comorbidities were stratified analysed.

Result

Male, aging, low incomes, hyperuricemia and no exercise habits were risk factors of CKD; and their impact on people with different comorbidities were the same. Anemia also was a risk factor, and there was an additive effect between anemia and hypertension on CKD. The association between hyperlipidemia related factors and CKD was moderated by HTN; it was a significant risk factor in people without HTN but not in patient with HTN. Based on the power of this study, we considered that hepatitis B, smoking, alcohol intake and groundwater using might not be the important risk factors of CKD. The associations between hepatitis C/betelnut chewing and CKD were not conclusive.

Fig. 1 Recruitment Process Flow Chart

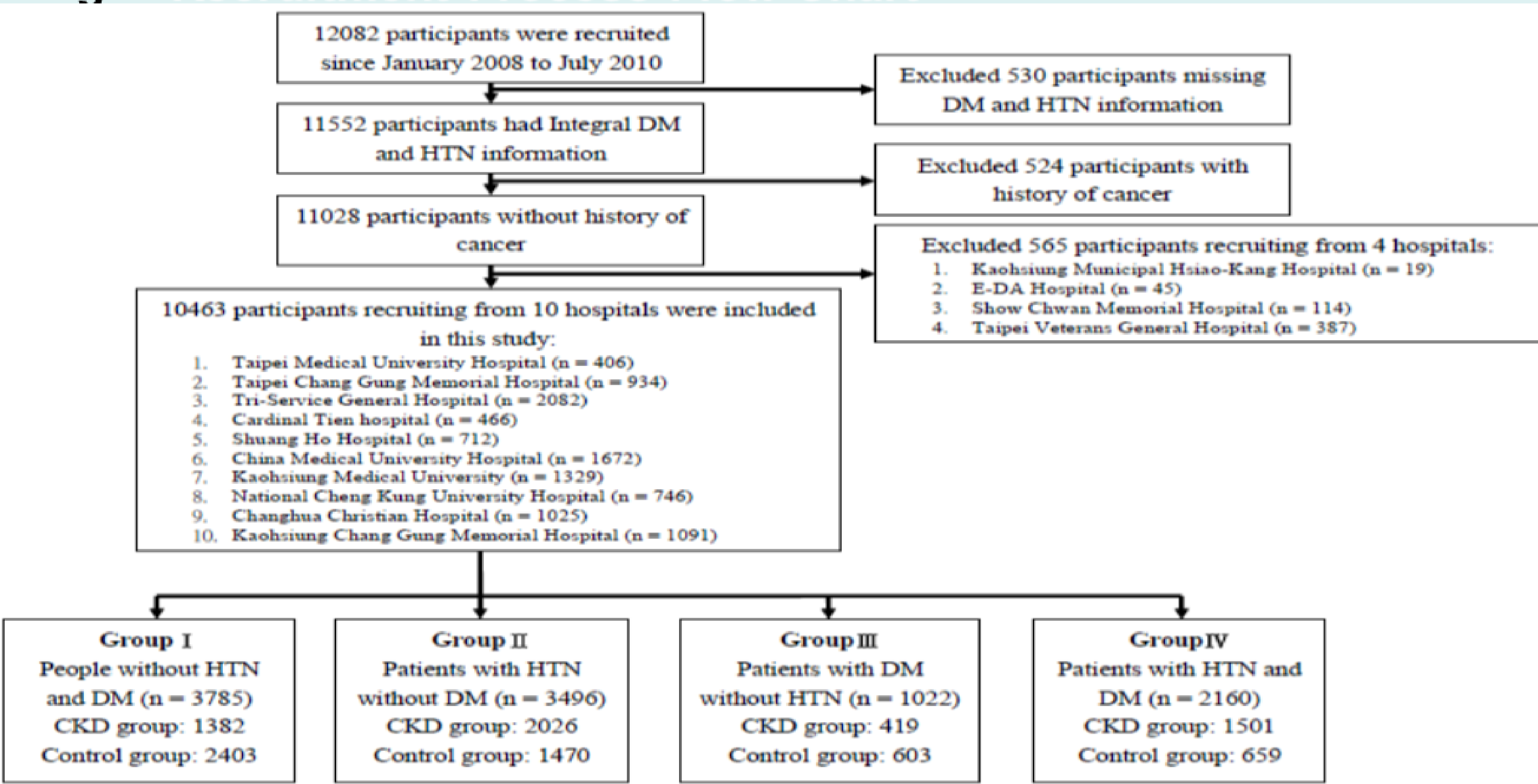


Fig. 2 Stratified analyses for variables with significant heterogeneity between four groups in multivariable analyses

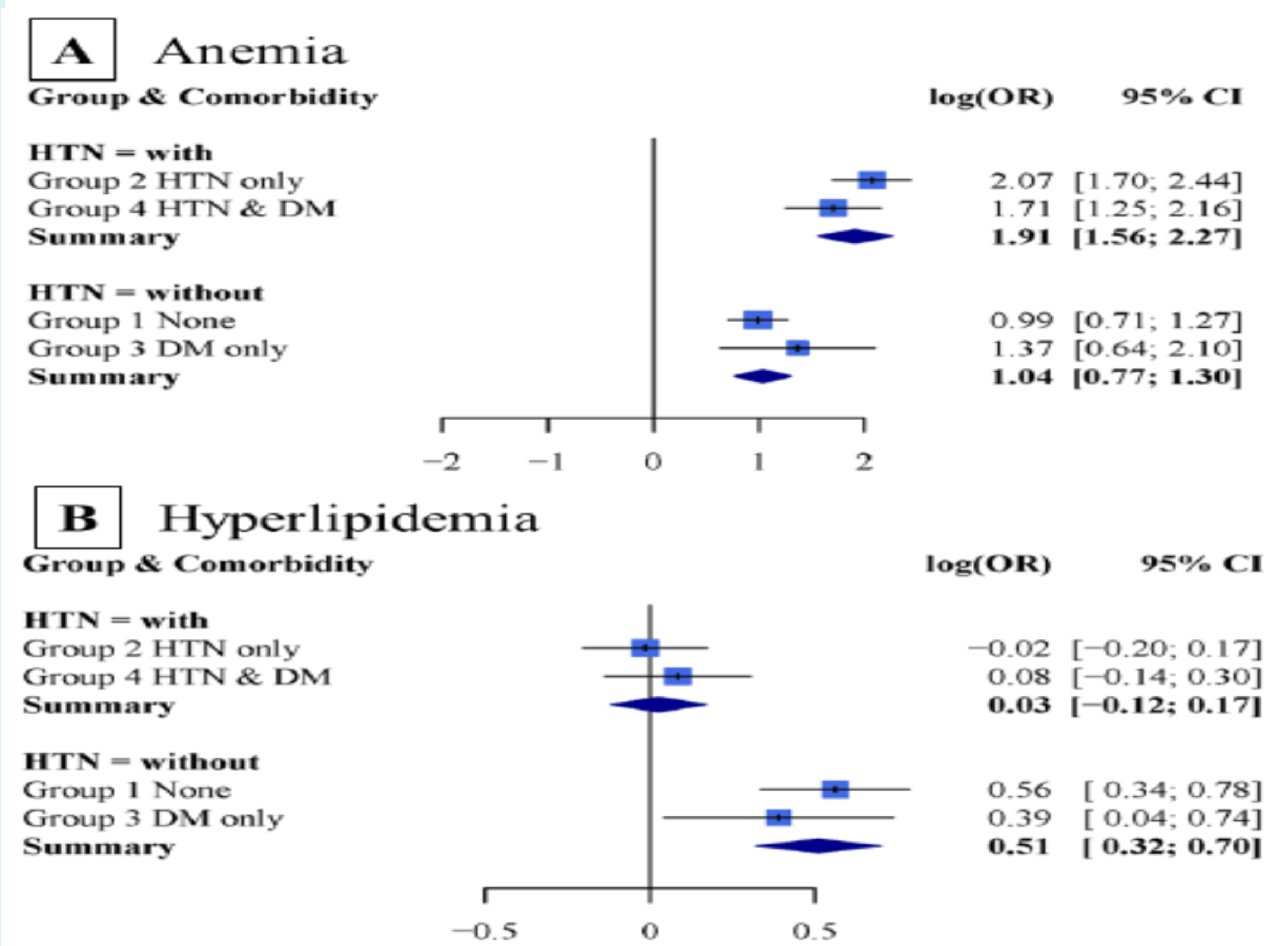


Table 1 Overall proportion of cases and controls with exposure

		CKD	non-CKD	Post power
Gender	Female	2302 (43.2%)	2943 (57.3%)	> 99.9%
	Male	3026 (56.8%)	867 (42.7%)	
Age		59.8±15.2	54.0±15.1	> 99.9%
Obesity (151 missing)	Normal	4634 (88.7%)	4650 (91.4%)	> 99.9%
	Abnormal	592 (11.3%)	436 (8.6%)	
Income (61 missing)	Low	3056 (57.6%)	2039 (40.0%)	> 99.9%
	Median	1416 (26.7%)	1791 (35.1%)	
HB (1 missing)	Normal	5027 (94.4%)	5064 (93.9%)	99.4%
	Abnormal	300 (5.6%)	71 (6.1%)	
HC* (2 missing)	Normal	5228 (98.2%)	5064 (98.6%)	39.6%
	Abnormal	98 (1.8%)	71 (1.4%)	
Hyperuricemia (2 missing)	Normal	4036 (75.8%)	4852 (94.5%)	98.7%
	Abnormal	1291 (24.2%)	282 (5.5%)	
Anemia* (2 missing)	Normal	4463 (83.8%)	4938 (96.2%)	92.1%
	Abnormal	863 (16.2%)	197 (3.8%)	
Hyperlipidemia (1 missing)	Normal	3832 (71.9%)	4196 (81.7%)	> 99.9%
	Abnormal	1495 (28.1%)	939 (18.3%)	
Smoking status (338 missing)	Never	3909 (76.0%)	4126 (82.9%)	> 99.9%
	Ever	1237 (24.0%)	853 (17.1%)	
Alcohol intake (382 missing)	Never	4361 (85.0%)	4340 (87.6%)	> 99.9%
	Ever	767 (15.0%)	613 (12.4%)	
Betelnut chewing* (456 missing)	Never	4876 (95.7%)	4758 (96.9%)	82.2%
	Ever	222 (4.3%)	151 (3.1%)	
Exercise habits (173 missing)	Never	1862 (35.8%)	1511 (29.7%)	> 99.9%
	Ever	3338 (64.2%)	3579 (70.3%)	
Groundwater using (17 missing)	Never	5029 (94.5%)	4890 (95.4%)	96.6%
	Ever	293 (5.5%)	234 (4.6%)	

CKD: patients with CKD; non-CKD: patients without CKD; HB: hepatitis B; HC: hepatitis C.

§: Post power (1-β) estimate based on G*power [23].

Boldface & *: the powers of each variable were less than 95%, and they were defined as lacking of power.

Tab. 2 Characteristics of subjects by stratification for HTN and DM

		Group I		Group II		Group III		Group IV	
		CKD	non-CKD	CKD	non-CKD	CKD	non-CKD	CKD	non-CKD
Gender	Female	670 (48.5%)	1536 (63.9%)	819 (40.4%)	752 (51.2%)	172 (41.1%)	304 (50.4%)	641 (42.7%)	351 (53.3%)
	Male	712 (51.5%)	867 (36.1%)	1207 (59.6%)	718 (48.8%)	247 (58.9%)	299 (49.0%)	860 (57.3%)	308 (46.7%)
Age		53.0±17.1	47.8±15.2	61.3±15.1	60.5±13.0	61.7±12.1	57.6±12.1	63.5±11.8	60.8±11.8
Obesity (151 missing)	Normal	1278 (93.6%)	2234 (94.0%)	1787 (89.8%)	1311 (90.1%)	356 (86.2%)	538 (89.8%)	1213 (83.3%)	567 (86.6%)
	Abnormal	87 (6.4%)	143 (6.0%)	204 (10.2%)	144 (9.9%)	57 (13.8%)	61 (10.2%)	244 (16.7%)	88 (13.4%)
Income (61 missing)	Low	648 (47.3%)	677 (28.3%)	1153 (57.0%)	736 (50.3%)	265 (63.4%)	260 (44.0%)	990 (66.4%)	366 (56.2%)
	Median	434 (31.7%)	971 (40.0%)	554 (27.4%)	418 (28.0%)	97 (23.2%)	213 (36.0%)	331 (22.2%)	189 (29.0%)
HB (1 missing)	Normal	1273 (92.1%)	2222 (92.5%)	1905 (94.0%)	1399 (95.2%)	402 (95.2%)	574 (95.2%)	1447 (96.5%)	629 (95.4%)
	Abnormal	109 (7.9%)	181 (7.5%)	121 (6.0%)	71 (4.8%)	17 (4.1%)	29 (4.8%)	53 (3.5%)	30 (4.6%)
HC (2 missing)	Normal	1358 (98.3%)	2377 (98.9%)	1984 (97.9%)	1446 (98.4%)	412 (98.3%)	593 (98.3%)	1474 (98.3%)	648 (98.3%)
	Abnormal	23 (1.7%)	26 (1.1%)	42 (2.1%)	24 (1.6%)	7 (1.7%)	10 (1.7%)	26 (1.7%)	11 (1.7%)
Hyperuricemia (2 missing)	Normal	1185 (85.7%)	2335 (97.2%)	1398 (69.0%)	1336 (90.9%)	367 (87.0%)	572 (94.9%)	1086 (72.4%)	609 (92.4%)
	Abnormal	197 (14.3%)	68 (2.8%)	628 (31.0%)	133 (9.1%)	52 (12.4%)	31 (5.1%)	414 (27.6%)	50 (7.6%)
Anemia (2 missing)	Normal	1217 (88.1%)	2285 (95.1%)	1674 (82.6%)	1431 (97.3%)	383 (91.4%)	588 (97.5%)	1189 (79.3%)	634 (96.2%)
	Abnormal	165 (11.9%)	118 (4.9%)	332 (17.4%)	39 (2.7%)	36 (8.6%)	15 (2.5%)	310 (20.7%)	25 (3.8%)
Hyperlipidemia (1 missing)	Normal	1144 (82.8%)	2184 (90.9%)	1478 (73.0%)	1123 (76.4%)	308 (73.5%)	460 (76.3%)	902 (60.1%)	429 (65.1%)
	Abnormal	238 (17.2%)	219 (9.1%)	548 (27.0%)	347 (23.6%)	111 (26.5%)	143 (23.7%)	598 (39.9%)	230 (34.9%)
Smoking status (338 missing)	Never	1088 (80.5%)	2041 (87.6%)	1496 (76.6%)	1148 (80.8%)	288 (71.5%)	438 (74.9%)	1037 (72.2%)	499 (77.2%)
	Ever	263 (19.5%)	290 (12.4%)	457 (23.4%)	273 (19.2%)	117 (28.5%)	147 (25.1%)	400 (27.8%)	143 (22.3%)
Alcohol intake (382 missing)	Never	1203 (89.0%)	2109 (91.1%)	1658 (85.2%)	1209 (85.4%)	338 (83.9%)	480 (82.2%)	1162 (81.4%)	542 (85.0%)
	Ever	148 (11.0%)	207 (8.9%)	289 (14.8%)	206 (14.6%)	65 (16.1%)	104 (17.8%)	265 (18.6%)	96 (15.0%)
Betelnut chewing (456 missing)	Never	1296 (96.7%)	2257 (98.5%)	1870 (95.6%)	1360 (97.0%)	374 (93.0%)	539 (92.8%)	1336 (94.1%)	602 (95.0%)
	Ever	44 (3.3%)	35 (1.5%)	66 (3.4%)	42 (3.0%)	28 (7.0%)	42 (7.2%)	84 (5.9%)	32 (5.0%)
Exercise habits (173 missing)	Never	474 (34.8%)	755 (31.7%)	691 (35.0%)	389 (26.7%)	138 (33.5%)	173 (28.9%)	559 (38.6%)	194 (29.6%)
	Ever	887 (65.2%)	1624 (68.3%)	1286 (65.0%)	1068 (73.3%)	274 (66.5%)	426 (71.1%)	891 (61.4%)	461 (70.4%)
Groundwater using (17 missing)	Never	1312 (95.2%)	2334 (97.3%)	1904 (94.0%)	1349 (92.0%)	394 (94.0%)	574 (95.5%)	1419 (94.7%)	633 (96.2%)
	Ever	66 (4.8%)	65 (2.7%)	125 (6.0%)	117 (8.0%)	25 (6.0%)	27 (4.5%)	80 (5.3%)	25 (3.8%)

Group I: participants without DM and HTN; Group II: participants with HTN without DM; Group III: participants with DM without HTN; Group IV: participants with DM and HTN.

CKD: patients with CKD; non-CKD: patients without CKD; HTN: hypertension; DM: diabetes mellitus; HB: hepatitis B; HC: hepatitis C.

Tab. 3 Pooled effect of each risk factor on CKD and heterogeneity between four groups

	Univariable analyses			Multivariable analyses		
	OR (95% CI)	I ²	Q test	OR (95% CI)	I ²	Q test
Gender (Female is ref.)	1.65 (1.49 to 1.82)*	25.5%	0.296	1.61 (1.45 to 1.78)*	0.0%	0.934
Age (per 10 years)	1.19 (1.09 to 1.29)*	85.7%	< 0.001*	1.44 (1.13 to 1.83)*	24.1%	0.323
Obesity (Normal is ref.)	1.14 (0.93 to 1.40)	43.9%	0.163	1.07 (0.86 to 1.33)	39.0%	0.204
Income (Low is ref.)	Median 0.57 (0.45 to 0.72)*	80.8%	< 0.001*	0.58 (0.47 to 0.73)*	71.9%	0.011
	High 0.50 (0.38 to 0.67)*	82.3%	< 0.001*	0.55 (0.43 to 0.70)*	65.0%	0.022
HB (Normal is ref.)	1.08 (0.88 to 1.33)	21.6%	0.263	1.25 (1.03 to 1.52)	0.0%	0.523
HC (Normal is ref.)	1.29 (0.93 to 1.79)	0.0%	0.707	1.22 (0.85 to 1.74)	0.0%	0.778
Hyperuricemia (Normal is ref.)	4.56 (3.96 to 5.26)*	0.0%	0.213	3.63 (3.11 to 4.24)*	0.0%	0.806
Anemia (Normal is ref.)	4.89 (2.76 to 8.66)*	88.5%	< 0.001*	4.64 (2.81 to 7.65)*	82.2%	< 0.001*
Hyperlipidemia (Normal is ref.)	1.48 (1.17 to 1.88)*	80.5%	0.001	1.28 (0.97 to 1.67)*	81.3%	0.001*
Smoking status (Never is ref.)	1.45 (1.28 to 1.64)*	26.6%	0.305	1.17 (1.02 to 1.34)	0.0%	0.559
Alcohol intake (Never is ref.)	1.15 (1.00 to 1.33)	22.3%	0.248	0.83 (0.71 to 0.97)	0.0%	0.701
Betelnut chewing (Never is ref.)	1.35 (1.03 to 1.77)	29.0%	0.233	1.10 (0.85 to 1.44)	0.0%	0.836
Exercise habits (Never is ref.)	0.74 (0.65 to 0.85)*	50.9%	0.106	0.71 (0.64 to 0.79)*	0.0%	0.859
Groundwater using (Never is ref.)	1.44 (1.13 to 1.83)	24.1%	0.323	1.29 (1.04 to 1.61)	0.0%	0.534

§: four groups were Group I (participants without DM and HTN), Group II (participants with HTN without DM), Group III (participants with DM without HTN) and Group IV (participants with DM and HTN).

HB: hepatitis B; HC: hepatitis C.

OR: pooled odds ratio for variation groups compared with reference groups on CKD; 95% CI: 95% confidence interval of OR; ref.: reference groups.

I²: heterogeneity between four groups in each variable; Q test: the significant test of I² using Cochrane Q test.

Boldface & *: significance after Bonferroni adjustment; p value < 0.05/14 = 0.0036.

†: The pooled results were unreliable because the difference between coefficients in four group were significant, please refer the results of stratified analyses in Supplementary File (univariable analyses: Appendix Table 1; multivariable analyses: Appendix Table 2).

Conclusion

Several risk factors in each specific high risk population had been identified in Taiwan. We considered that screening/preventing strategy on CKD in high risk patients might differ from health population. Further larger studies are needed for more strong statistical power.

Chai-Chao Wu: wucc@mail.ndmctsgh.edu.tw

