

## **High FIB4 index is an independent risk factor of diabetic kidney disease in type 2 diabetes**

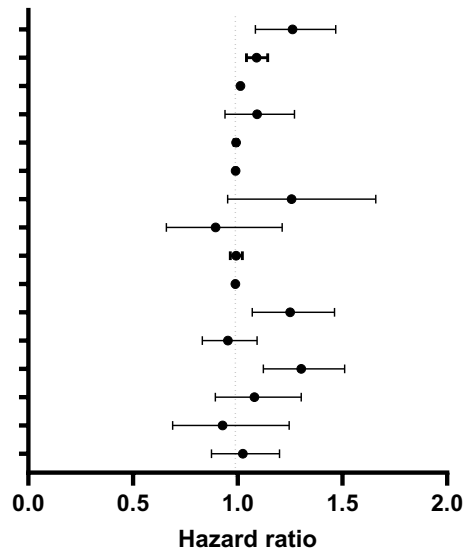
Haruka Saito<sup>1</sup>, Hayato Tanabe<sup>1</sup>, Akihiro Kudo<sup>1</sup>, Noritaka Machii<sup>1</sup>, Moritake Higa<sup>2</sup>, Satoshi Yamaguchi<sup>1,5</sup>, Gulinu Maimaituxun<sup>1</sup>, Kazumichi Abe<sup>3</sup>, Atsushi Takahashi<sup>3</sup>, Kenichi Tanaka<sup>4</sup>, Koichi Asahi<sup>6</sup>, Hiroaki Masuzaki<sup>7</sup>, Hiromasa Ohira<sup>3</sup>, Junichiro J. Kazama<sup>4</sup> and Michio Shimabukuro<sup>1\*</sup>

<sup>1</sup>Department of Diabetes, Endocrinology and Metabolism, <sup>3</sup>Department of Gastroenterology and <sup>4</sup>Department of Nephrology and Hypertension, Fukushima Medical University, Fukushima, Japan; <sup>2</sup>Department of Diabetes and Lifestyle-Related Disease Center, Tomishiro Central Hospital, Okinawa, Japan; <sup>5</sup>Department of Cardiology, Nakagami Hospital, Okinawa, Japan; <sup>6</sup>Division of Nephrology and Hypertension, Iwate Medical University, Iwate, Japan; <sup>7</sup>Division of Endocrinology, Diabetes and Metabolism, Hematology, Rheumatology (Second Department of Internal Medicine), University of the Ryukyus, Okinawa, Japan.

\*Corresponding author at: Department of Diabetes, Endocrinology and Metabolism, Fukushima Medical University, 1 Hikarigaoka, Fukushima City, Fukushima 960-1295, Japan; E-mail address: [mshimabukuro-ur@umin.ac.jp](mailto:mshimabukuro-ur@umin.ac.jp) (M. Shimabukuro); Tel +81-24-547-1305 , Fax +81-24-547-1311

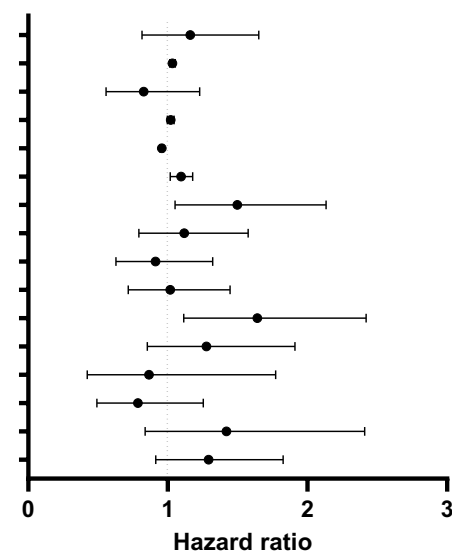
### A. DKD

	Multivariate	P value
FIB4 Quartile	1.202(1.051-1.374)	0.007
Age (per year)	1.003(0.988-1.018)	0.707
Sex (male vs. female)	1.114(0.805-1.542)	0.514
BMI (kg/m <sup>2</sup> )	1.008(0.989-1.028)	0.407
eGFR (mL/min/1.73 m <sup>2</sup> )	0.990(0.981-0.998)	0.017
HbA1c (%)	1.066(1.003-1.132)	0.039
Hypertension (yes vs. no)	1.273(0.962-1.686)	0.092
Dyslipidemia (yes vs. no)	0.969(0.732-1.281)	0.824
Past drinker (yes vs. no)	0.905(0.67-1.224)	0.518
Past smoker (yes vs. no)	1.256(0.952-1.658)	0.107
Sulfonylurea (yes vs. no)	1.395(1.004-1.939)	0.047
Biganide (yes vs. no)	1.086(0.758-1.557)	0.653
Thiazolidine (yes vs. no)	0.978(0.543-1.762)	0.94
αGI (yes vs. no)	0.847(0.568-1.264)	0.416
Insulin (yes vs. no)	1.42(0.901-2.237)	0.13
RAS Inhibitor (yes vs. no)	1.40(1.039-1.887)	0.027



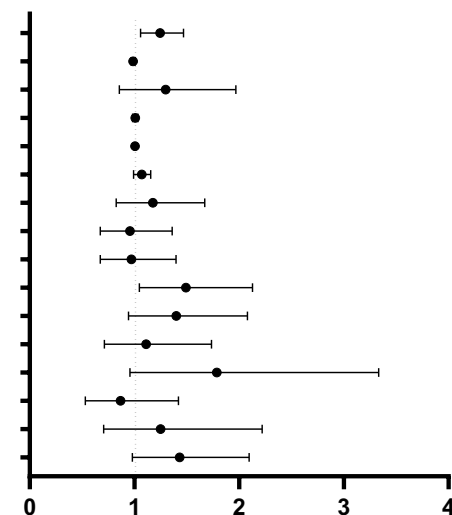
### B. eGFR < 60

	Multivariate	P value
FIB4 Quartile	1.109(0.937-1.314)	0.230
Age (per year)	1.033(1.012-1.054)	0.002
Sex (male vs. female)	0.834(0.553-1.259)	0.388
BMI (kg/m <sup>2</sup> )	1.019(0.996-1.044)	0.112
eGFR (mL/min/1.73 m <sup>2</sup> )	0.958(0.945-0.971)	<0.001
HbA1c (%)	1.109(1.028-1.196)	0.007
Hypertension (yes vs. no)	1.399(0.966-2.025)	0.075
Dyslipidemia (yes vs. no)	1.092(0.767-1.555)	0.625
Past drinker (yes vs. no)	0.859(0.583-1.267)	0.444
Past smoker (yes vs. no)	1.117(0.776-1.609)	0.552
Sulfonylurea (yes vs. no)	1.522(1.028-2.252)	0.036
Biganide (yes vs. no)	1.390(0.922-2.094)	0.116
Thiazolidine (yes vs. no)	1.013(0.492-2.086)	0.971
αGI (yes vs. no)	0.845(0.528-1.352)	0.482
Insulin (yes vs. no)	1.233(0.71-2.142)	0.457
RAS Inhibitor (yes vs. no)	1.402(0.987-1.991)	0.059



### C. Proteinuria

	Multivariate	P value
FIB4 Quartile	1.246(1.058-1.469)	0.009
Age (per year)	0.988(0.969-1.007)	0.207
Sex (male vs. female)	1.299(0.857-1.969)	0.218
BMI (kg/m <sup>2</sup> )	1.008(0.983-1.034)	0.518
eGFR (mL/min/1.73 m <sup>2</sup> )	1.005(0.997-1.014)	0.201
HbA1c (%)	1.071(0.992-1.156)	0.081
Hypertension (yes vs. no)	1.176(0.827-1.672)	0.366
Dyslipidemia (yes vs. no)	0.958(0.675-1.36)	0.81
Past drinker (yes vs. no)	0.971(0.674-1.397)	0.873
Past smoker (yes vs. no)	1.493(1.047-2.127)	0.027
Sulfonylurea (yes vs. no)	1.400(0.943-2.08)	0.095
Biganide (yes vs. no)	1.112(0.713-1.736)	0.639
Thiazolidine (yes vs. no)	1.786(0.957-3.333)	0.069
αGI (yes vs. no)	0.868(0.531-1.42)	0.573
Insulin (yes vs. no)	1.251(0.706-2.219)	0.443
RAS Inhibitor (yes vs. no)	1.433(0.98-2.095)	0.063



**Supplement Figure 3.** Univariate and Cox proportional hazard ratios of FIB4 quartile for the development of (A) diabetic kidney disease (DKD: eGFR < 60 mL/min/1.73 m<sup>2</sup> or proteinuria), (B) eGFR < 60 mL/min/1.73 m<sup>2</sup>, and (C) proteinuria in type 2 diabetic patients. Cox proportional hazard models were adjusted for age, sex, BMI, baseline HbA1c, baseline eGFR, smoking and drinking status (current or past), comorbidities (hypertension, dyslipidemia) and anti-diabetic and anti-hypertensive medications. 95% CI, 95% confidence interval.