

Supplementary materials

Table S1- Significant variables predicting AGT in BHBHK_HKFDS cohort using forward stepwise logistic regression (n=1054).

	β	OR (95% CI)	P value	Wald-df	VIF
Original RUBY score	0.116	1.123 (1.086 to 1.161)	<0.001	45.292	1.199
FPG (mmol/L)	1.391	4.02 (2.921 to 5.532)	<0.001	71.910	1.149
Creatinine (μ mol/L)	-0.023	0.977 (0.967 to 0.988)	<0.001	16.002	1.192
WBC ($10^9/L$)	0.167	1.181 (1.066 to 1.309)	0.001	9.123	1.038
Urea (mmol/L)	-0.218	0.804 (0.693 to 0.934)	0.004	7.167	1.226
Potassium (mmol/L)	-0.667	0.513 (0.316 to 0.834)	0.007	6.260	1.028
Total protein (g/L)	0.051	1.053 (1.011 to 1.095)	0.012	5.337	1.020

Abbreviations: WBC, white blood cells; FPG, fasting plasma glucose; Wald-df, partial chi-square statistic minus the predictor degrees of freedom, assessed the importance of predictors; VIF, variance inflation factors, assessed the multicollinearity.

Table S2 - Relative contribution of RUBY and biochemical parameters in predicting AGT.

	AUROC		IDI	
	(95% CI)	P value	(95% CI)	P value
RUBY only	0.698 (0.662 to 0.733)	ref	ref	ref
RUBY + FPG (Extended RUBY model 1)	0.756 (0.722 to 0.791)	<0.001	0.201 (0.154 to 0.247)	<0.001
RUBY + Creatinine	0.726 (0.692 to 0.760)	0.002	0.024 (0.006 to 0.042)	0.009
RUBY + WBC	0.711 (0.676 to 0.746)	0.071	0.009 (-0.003 to 0.021)	0.132
RUBY + Creatinine + Urea + Potassium	0.725 (0.690 to 0.761)	0.001	0.047 (0.024 to 0.069)	<0.001
RUBY + FPG (Extended RUBY model 1)	0.756 (0.722 to 0.791)	ref	ref	ref
RUBY + FPG + Creatinine	0.776 (0.742 to 0.809)	0.013	0.029 (0.010 to 0.048)	0.003
RUBY + FPG + WBC	0.763 (0.729 to 0.797)	0.210	0.003 (-0.008 to 0.014)	0.565
RUBY + FPG + Total protein	0.759 (0.725 to 0.794)	0.413	0.003 (-0.005 to 0.010)	0.512
RUBY + FPG + Creatinine + Urea + Potassium (Extended RUBY model 2)	0.778 (0.744 to 0.812)	0.002	0.064 (0.039 to 0.089)	<0.001
RUBY + FPG + Creatinine + Urea + Potassium (Extended RUBY model 2)	0.778 (0.744 to 0.812)	ref	ref	ref
RUBY + FPG + Creatinine + Urea + Potassium + WBC	0.785 (0.752 to 0.819)	0.092	0.008 (-0.004 to 0.021)	0.161
RUBY + FPG + Creatinine + Urea + Potassium + Total protein	0.780 (0.746 to 0.815)	0.462	0.005 (-0.004 to 0.013)	0.315

Abbreviations: AUROC, area under receiver operating characteristics; IDI, integrated discrimination index; FPG, fasting plasma glucose; WBC, white blood cells.

Table S3 - AIC and BIC for different models in predicting AGT.

	AIC	BIC
RUBY	1087.0	1097.0
FPG only	1039.6	1049.5
RUBY + FPG	1001.0	1015
RUBY + FPG + Creatinine	977.9	997.7
RUBY + FPG + WBC	993.4	1013.3
RUBY + FPG + Total protein	997.8	1017.6
RUBY + FPG + Creatinine + Urea + Potassium	965.3	995.1
RUBY + FPG + Creatinine + Urea + Potassium + Total protein	960.8	995.5
RUBY + FPG + Creatinine + Urea + Potassium + WBC	954.4	989.1
RUBY + FPG + Creatinine + Urea + Potassium + Total protein + WBC	951.6	991.3

Abbreviations: AIC, akaike information criterion; BIC, bayesian information criterion

Table S4 - Sensitivity, specificity, PPV and NPV for various cutoff values by Extended RUBY model 2 for AGT at different corresponding absolute risk in percentage.

Risk threshold	Sensitivity	Specificity	PPV	NPV
9.5%	0.919	0.314	0.305	0.922
19.5%	0.765	0.642	0.412	0.893
29.5%	0.635	0.805	0.516	0.871
39.5%	0.492	0.897	0.610	0.844
49.5%	0.373	0.946	0.693	0.822

Abbreviation: PPV, positive predictive value; NPV, negative predictive value. 29.5% was the optimal risk threshold of the Extended model 2 using Youden index.

Table S5 - Baseline characteristics of the cohort for external validation.

	Total	Non-IGT	AGT		P value
	(n = 550)	2hPG < 7.8 (n = 308)	2hPG 7.8 - 11.0 (n = 179)	2hPG ≥ 11.1 (n = 63)	
Age (years)	53 ± 10	51 ± 11	55 ± 10	56 ± 9	<0.001
Female, n (%)	382 (69.5)	220 (71.4)	122 (68.2)	40 (63.5)	0.414
Weight (kg)	67.9 ± 14.5	66.8 ± 15.2	69.1 ± 14.2	69.4 ± 11.6	0.155
Height (cm)	160.9 ± 8.4	161.2 ± 9.1	160.6 ± 7.3	160.3 ± 7.7	0.668
BMI (kg/m ²)	26.1 ± 4.7	25.6 ± 4.8	26.8 ± 4.9	26.9 ± 3.5	0.012
Waist (cm)	89.0 ± 12.7	86.9 ± 13.4	91.6 ± 11.9	91.8 ± 9.6	<0.001
SBP (mmHg)	128.5 ± 17.3	125 ± 16.7	131.6 ± 17.2	136.8 ± 16.3	<0.001
DBP (mmHg)	80.9 ± 11.5	79.5 ± 11.5	81.7 ± 11.3	85.8 ± 11.1	<0.001
DM FH, n (%)	289 (52.5)	156 (50.6)	101 (56.4)	32 (50.8)	0.449
FPG (mmol/L)	5.2 ± 0.6	5.0 ± 0.5	5.3 ± 0.5	5.7 ± 0.5	<0.001
2hPG (mmol/L)	7.8 ± 2.5	6.1 ± 1.2	9.1 ± 0.9	12.6 ± 1.2	<0.001
Creatinine (µmol/L)	68.2 ± 17	68.4 ± 17.2	67.4 ± 16.1	69.1 ± 18.5	0.745
Urea (mmol/L)	5.1 ± 1.3	5.1 ± 1.4	5.2 ± 1.3	5.2 ± 1.1	0.783
Potassium (mmol/L)	4.2 ± 0.4	4.1 ± 0.4	4.2 ± 0.4	4.2 ± 0.4	0.225

Data were shown as mean ± SD or number (%). The one-way ANOVA test was used for continuous variables, chi-square test was used for categorical variables. FPG range, 3.8 - 6.9 mmol/L; Potassium range, 3.2 - 5.5 mmol/L; Urea range, 1.9 - 9.9 mmol/L; Creatinine range, < 129 µmol/L. Abbreviations: BMI, body mass index; FPG, fasting plasma glucose; 2hPG, two-hour post-prandial glucose.

Table S6 - Performance of the extended RUBY models, original RUBY and NCDRS in the external validation cohort (n = 550).

Model	AUROC (95% CI)
Original RUBY	0.637 (0.591, 0.683)
Extended RUBY model 1	0.716 (0.674, 0.759)
Extended RUBY model 2	0.722 (0.680, 0.764)
NCDRS	0.632 (0.586, 0.679)

Abbreviation: AUROC, area under receiver operating characteristics.

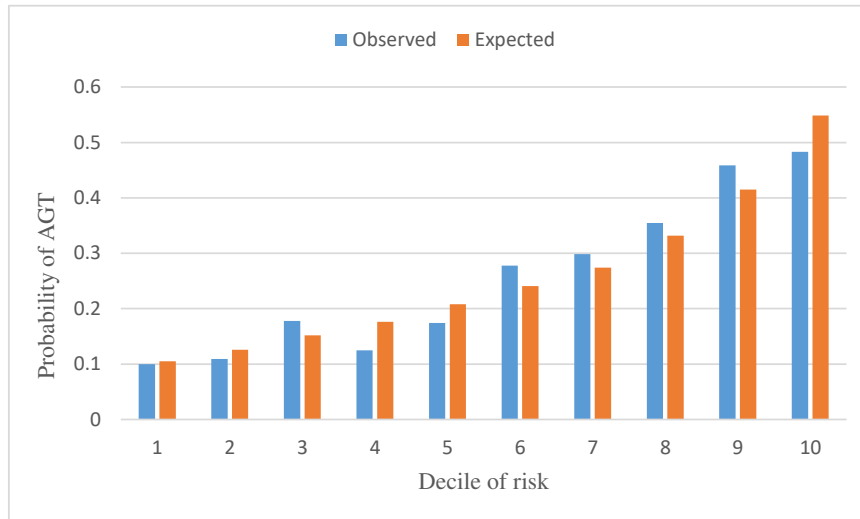
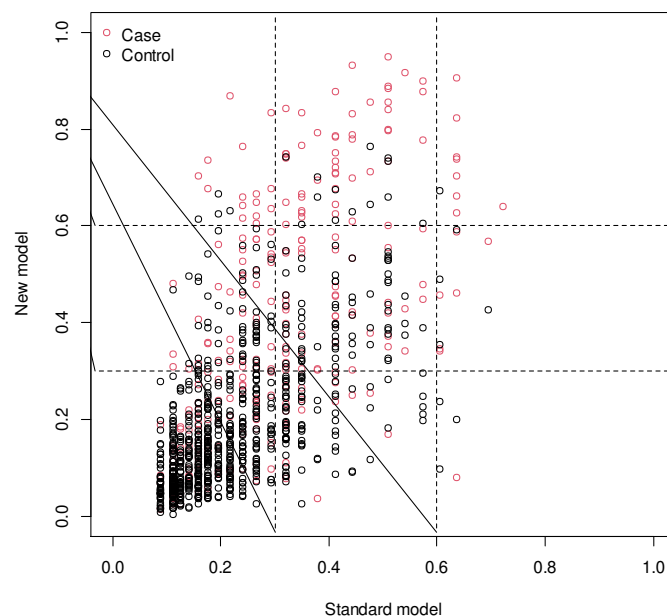


Fig. S1 - Observed vs expected probabilities of AGT as predicted by Extended RUBY model 2 for AGT by decile of risk in the BHBHK-HKFDS cohort.

A.



B.

	Risk threshold of original RUBY score	Risk threshold of Extended RUBY model 2				Cases superiorly detected by Extended RUBY model 2	Cases superiorly detected by RUBY score	NET	NRI
		< 0.3	0.3-0.6	> 0.6	Total				
AGT	< 0.3	79	40	15	134	103, 39.6%	23, 8.8%	30.8%	31.9%
	0.3-0.6	16	47	48	111				
	> 0.6	1	6	8	15				
	Total	96	93	71	260				
Non-IGT	< 0.3	556	63	4	623	89, 11.2%	80, 10.1%	1.1%	31.9%
	0.3-0.6	82	68	13	163				
	> 0.6	3	4	1	8				
	Total	641	135	18	794				

Fig. S2 - Net reclassification index of Extended RUBY model 2 and original RUBY score. A. Figure of NRI. new model, Extended RUBY model 2; standard model, original RUBY score; Case, AGT with 2hPG \geq 7.8 mmol/L; control, non-IGT with 2hPG < 7.8 mmol/L; dash lines, prespecified risk threshold 0.3-0.6. B. Table of NRI indicating the numbers of AGT or non-IGT detected by Extended RUBY model 2 and original RUBY score.

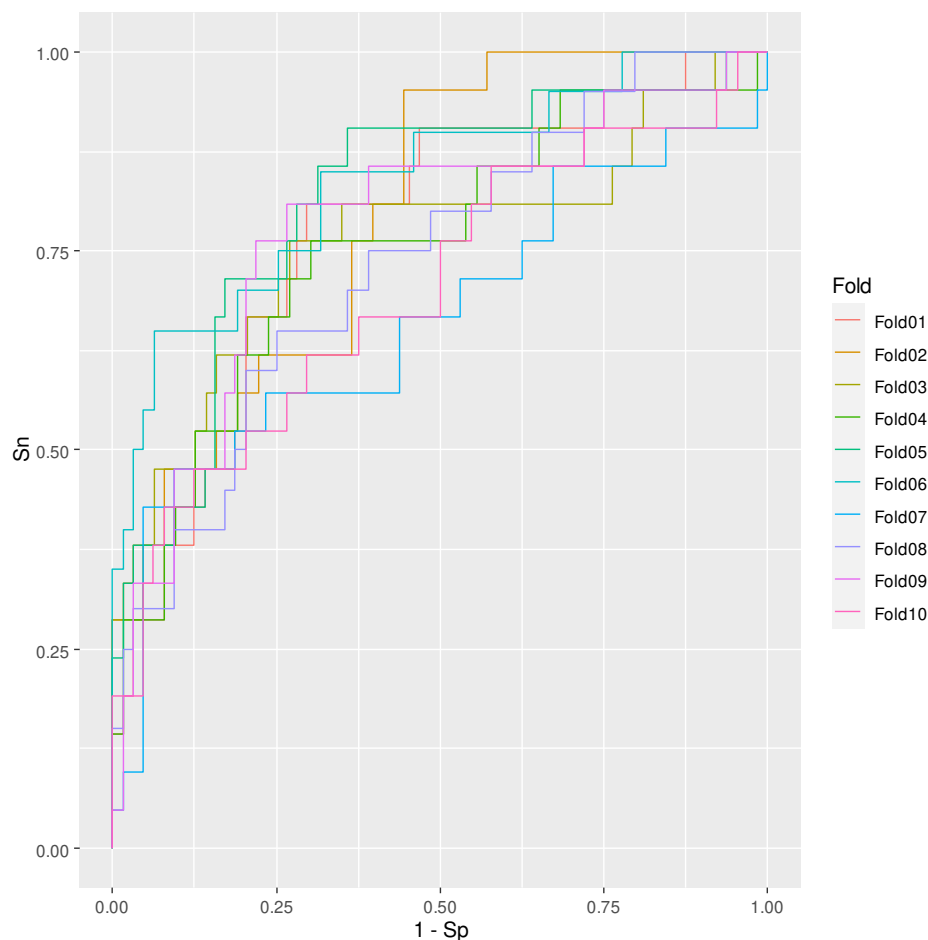


Fig. S3 - ROC of 10-fold resampling of the dataset divided into testing (1-fold) and training datasets (9-fold) in cross-validation for Extended RUBY model 2. Every fold sample had a chance to be the testing data to generate a ROC curve. AUROC of the 1st testing data (Fold 01): 0.788; AUROC of 2nd testing data (Fold 02): 0.780; AUROC of 3rd testing data (Fold 03): 0.810; AUROC of 4th testing data (Fold 04): 0.810; AUROC of 5th testing data (Fold 05): 0.800; AUROC of 6th testing data (Fold 06): 0.843; AUROC of 7th testing data (Fold 07): 0.800; AUROC of 8th testing data (Fold 08): 0.786; AUROC of 9th testing data (Fold 09): 0.812; AUROC of 10th testing data (Fold 10): 0.788. The average ROC was 0.814.

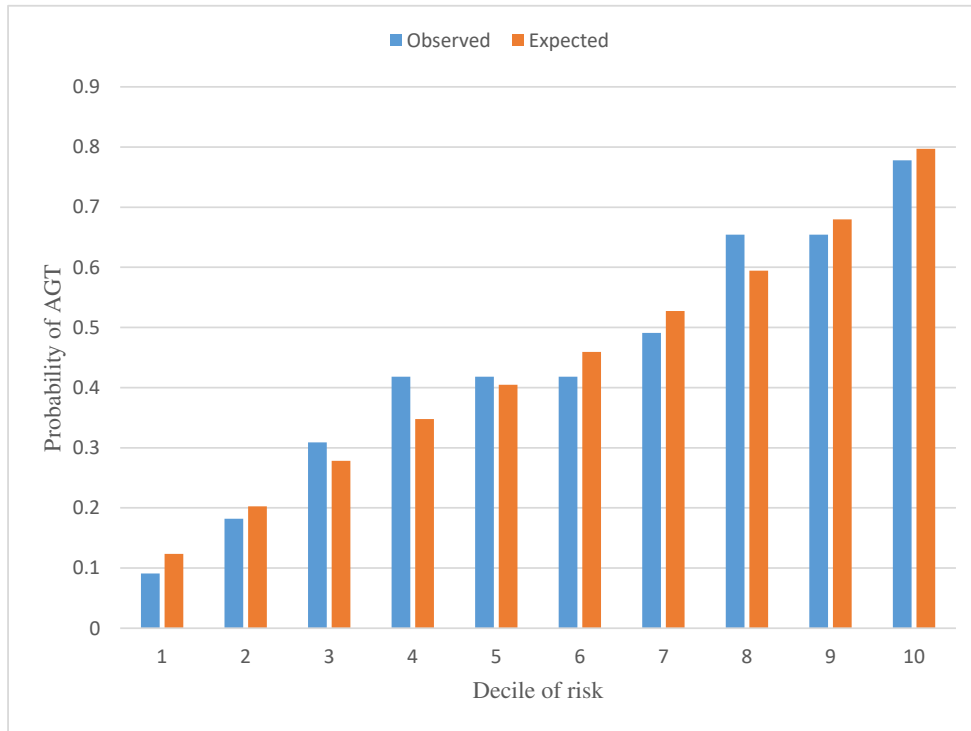


Fig. S4 - Observed vs expected as predicted by Extended RUBY model 2 for AGT by decile of risk in the external cohort.

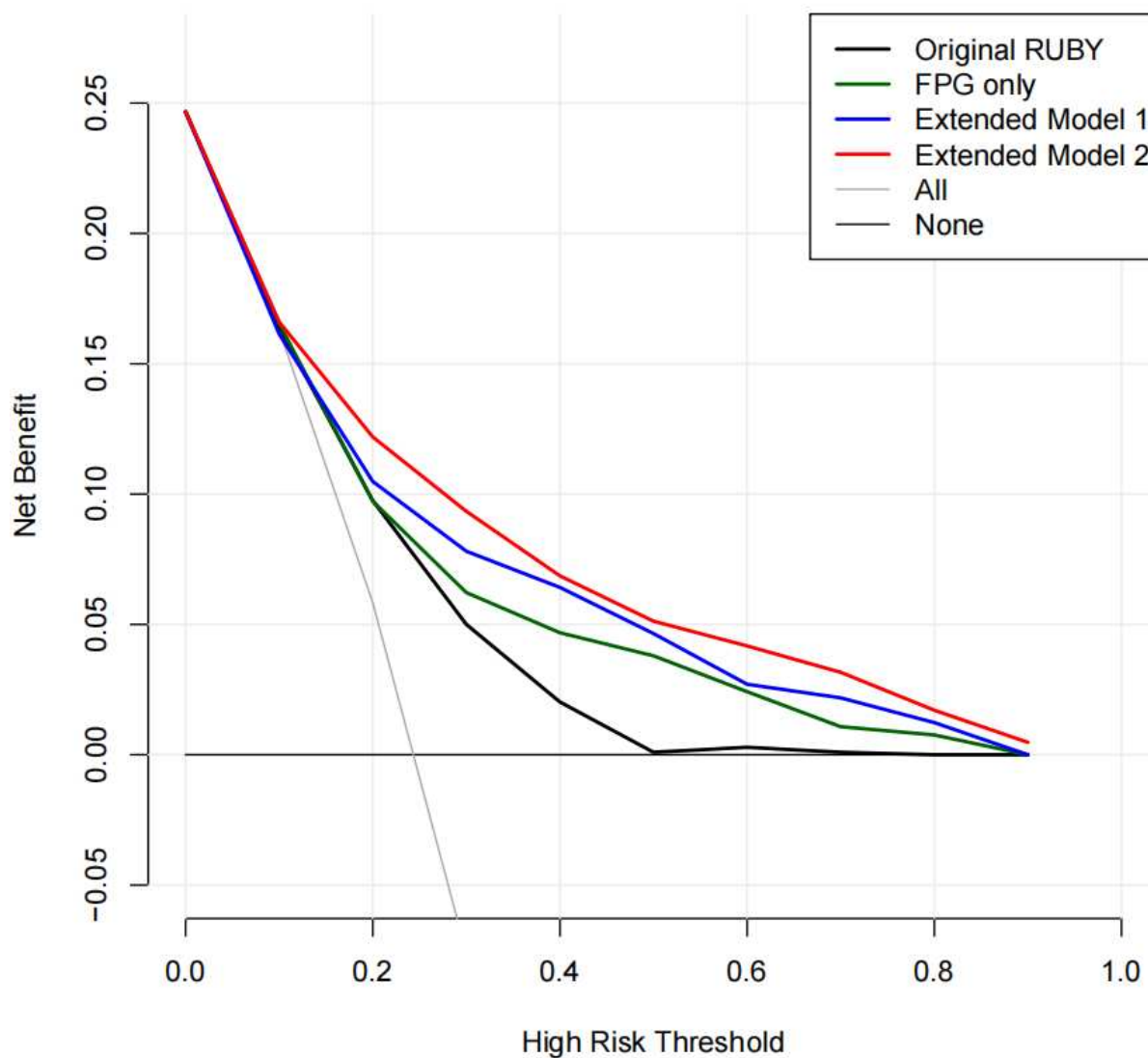


Fig. S5 – Decision curve analysis (DCA) of original RUBY, FPG only, Extended RUBY Model 1 and 2 in predicting AGT in the BHBHK-HKFDS cohort. Black line represents original RUBY score, the green one represents the model with FPG only, the blue and red for the Extended RUBY Model 1 and 2 respectively, and the light grey line represents treating all patients and dark grey line for treating no patient. Risk threshold is defined as 0.25 in this study.