SUPPLEMENTAL MATERIAL

Data S1. Detailed Description of Internal- and External Validation, and Measures Used to Evaluate These Metrics.

A clinical prediction models' performance may be evaluated in internal- or external validation. Internal validation reflects a models' reproducibility, and it includes apparent validation, where the model is validated in the derivation cohort; split-sample validation, where the data is randomly split into a training and validation set; bootstrapping, where multiple training and validation datasets are created by random draw; and cross-validation, where training is done in a random segment of the cohort and tested in the remaining part.⁸ External validation conversely reflects a models' generalizability, and it includes geographic validation, where validation is done in another country or center; independent validation, where validation is done by other researchers; and temporal validation, where validation is done using data from a different period.^{8,56}

Model performance is normally evaluated through discrimination and calibration. Discrimination reflects a model's ability to distinguish between patients who do and do not experience an outcome of interest.¹⁴ Discrimination is frequently assessed with measures of concordance (e.g., c-statistic, AUC) and it can range between 0.5 for a model no better than the play of chance to 1.0 for a perfect model.⁵⁷ Concordance estimates the probability that a randomly selected patient who experienced an outcome had a higher predicted risk than a patient who did not. Calibration reflects a model's predictive accuracy: i.e., the agreement between the predicted probability of events and the actual proportion of events observed.¹⁴ Calibration is frequently assessed with statistical tests for goodness-of-fit (e.g., Hosmer-Lemeshow, p<0.05 signifies poor calibration), or graphical plots for visual assessment (e.g., calibration plot slope <0.7 signifies poor calibration).^{58–60} Less common performance measures are described elsewhere and include R², Brier score, sensitivity, specificity, accuracy, and net reclassification.⁶¹

Table S1. Systematic Search Algorithms.

Database: Ovid MEDLINE(R) ALL <1946 to February 24, 2021> 1,054 records

- 1. *diabetes mellitus, type 2/
- 2. (diabet* and ("type 2" or "type ii" or non-insulin* or noninsulin*)).mp.
- 3. (T2DM or DMT2 or TIIDM or DMTII or NIDDM).mp.
- 4. exp *heart failure/
- 5. ((heart or cardiac or myocardial) adj2 failure*).mp.
- 6. ((prognos* or predict* or risk* or strati*) and (model* or tool* or scor* or index or nomogram* or formula* or staging or calculat* or equation* or strati* or chart* or function* or engine* or algorithm*)).ti,ab,kw.
- 7. *risk assessment/ or exp *risk factors/ or *multivariate analysis/ or exp regression analysis/ or exp survival analysis/ or disease-free survival/ or kaplan-meier estimate/ or progression-free survival/ or proportional hazards models/ or logistic models/ or nomograms/ or area under curve/ or exp models, statistical/
- 8. ("disease free survival" or "proportional hazard* model*" or (survival adj2 anal*) or "kaplan-meier estimate*" or "progression-free survival" or develop* or (cox adj3 (model* or anal*)) or (random adj2 forest*) or regress* or (logistic* adj2 model*) or multivari* or (likelihood adj2 function) or (area under adj2 curve) or (statistical adj3 model*) or discrimin* or calibrat* or valid* or "integer-based" or "support vector*" or (machine adj2 learning*) or mathematic* or concordance* or c-statistic* or c-ind* or hosmer-lemeshow* or hazard* or wald* or "survival rate*" or "survival time*" or "survival funct*").mp.

(1 or 2 or 3) and (4 or 5) and 6 and (7 or 8)

Database: Embase Classic+Embase <1947 to February 24, 2021> 3,473 records

- 1. exp *non insulin dependent diabetes mellitus/
- 2. (diabet* and ("type 2" or "type ii" or non-insulin* or noninsulin*)).mp.
- 3. (T2DM or DMT2 or TIIDM or DMTII or NIDDM).mp.
- 4. exp *heart failure/
- 5. ((heart or cardiac or myocardial) adj2 failure*).mp.
- 6. (prognosis/) and (model/)
- 7. ((prognos* or predict* or risk* or strati*) and (model* or tool* or scor* or index or nomogram* or formula* or staging or calculat* or equation* or strati* or chart* or function* or engine* or algorithm*)).ti,ab,kw.
- 8. exp risk assessment/ or exp risk factor/ or exp multivariate analysis/ or exp regression analysis/ or *disease free survival/ or exp proportional hazards model/ or *statistical model/ or exp nomograms/ or *area under the curve/ or exp mathematical phenomena/
- 9. ("disease free survival" or "proportional hazard* model*" or (survival adj2 anal*) or "kaplan-meier estimate*" or "progression-free survival" or develop* or (cox adj3 (model* or anal*)) or (random adj2 forest*) or regress* or (logistic* adj2 model*) or multivari* or (likelihood adj2 function) or (area under adj2 curve) or (statistical adj3 model*) or discrimin* or calibrat* or valid* or "integer-based" or "support vector*" or (machine adj2 learning*) or mathematic* or concordance* or c-statistic* or c-ind* or hosmer-lemeshow* or hazard* or wald* or "survival rate*" or "survival time*" or "survival funct*").mp.

(1 or 2 or 3) and (4 or 5) and (6 or 7) and (8 or 9)

Database: Web of Science Core Collection <database inception to February 24, 2021> 1,426 records

- 1. ts= (diabet* and ("type 2" or "type ii" or noninsulin or "non-insulin"))
- 2. ts=((heart or cardiac or myocardial) near/2 failure*)
- 3. ts=((prognos* or predict* or risk* or strati*) and (model* or tool* or scor* or index or nomogram* or formula* or staging or calculat* or equation* or strati* or chart* or function* or engine* or algorithm*))
- 4. ts=("disease free survival" or "proportional hazard* model*" or (survival near/2 anal*) or "kaplan-meier estimate*" or "progression-free survival" or develop* or (cox near/3 (model* or anal*)) or (random near/2 forest*) or regress* or (logistic* near/2 model*) or multivari* or (likelihood near/2 function) or (area under near/2 curve) or (statistical near/3 model*) or discrimin* or calibrat* or valid* or "integer-based" or "support vector*" or (machine near/2 learning*) or mathematic* or concordance* or c-statistic* or c-ind* or hosmer-lemeshow* or hazard* or wald* or "survival rate*" or "survival time*" or "survival funct*")

#1 AND #2 AND #3 AND #4

Database: Google Scholar <database inception to February 24, 2021> first 200 records

- 1.
- "type 2" "diabetes" "heart failure" 2. 3.
- 4. ("risk" or "prediction" or "stratification" or "model")

$1 \mbox{ and } 2 \mbox{ and } 3 \mbox{ and } 4$

Database: Tufts Predictive Analytics and Comparative Effectiveness Clinical Prediction Model Registry <database inception to February 24, 2021> 37 records

- 1. Keyword contains: diabetes
- 2. 3. Outcome contains: heart failure
- Outcome contains: composite Outcome contains: hospitalization 4.

1 and (2 or 3 or 4)

Table S2. List of Excluded Studies Cataloged by Reason for Exclusion.

EXCLUDED: NOT A MODEL DEVLEOPMENT, UPDATE, OR VALIDATION STUDY										
1.	Akter, S., et al. "Predictors of Incident Heart Failure in Community-Dwelling Older Adults with Diabetes									
	Mellitus." Diabetologia, vol. 53, Sept., p. S85.									
2.	Altrabsheh, E., et al. "Pdb64 Association between Cardiovascular Disease Risk Factors and Hypoglycaemic Events in Type 2 Diabetes Using the Iqvia Core Diabetes Model." <i>Value in Health</i> , vol. 22, May, p. S151.									
3.	Ang, Donald SC, et al. "A Comparison between B-Type Natriuretic Peptide, Global Registry of Acute									
	Coronary Events (GRACE) Score and Their Combination in ACS Risk Stratification." <i>Heart</i> , vol. 95, no. 22, 2009, pp. 1836–42.									
4.	Blin, P., et al. "Real World Risk of Major Outcomes for Type 2 Diabetes with Stable Coronary Artery Disease without Prior MI or Stroke and THEMIS-like Patients Using the SNDS French Nationwide Claims Database." <i>European Heart Journal</i> , vol. 41, Nov., p. 1314.									
5.	Breunig, I. M., et al. "Development of Heart Failure in Medicaid Patients with Type 2 Diabetes Treated with Pioglitazone, Rosiglitazone, or Metformin." <i>Journal of Managed Care & Specialty Pharmacy</i> , vol. 20, no. 9, Sept. , pp. 895–903.									
6.	Bucher, S., et al. "Predictive factors of hospitalization in non institutionalized elderly diabetic patients. Data from the S.AGES cohort." <i>Exercer-La Revue Francophone De Medecine Generale</i> , no. 146, Oct., pp. 340–47.									
7.	Davis, W. A., et al. "Contemporary Cardiovascular Risk Assessment for Type 2 Diabetes Including Heart Failure as an Outcome: The Fremantle Diabetes Study Phase II." <i>Journal of Clinical Medicine</i> , vol. 9, no. 5, May									
8.	Fadini, G. P., et al. "Risk of Hospitalization for Heart Failure in Patients with Type 2 Diabetes Newly Treated with DPP-4 Inhibitors or Other Oral Glucose-Lowering Medications: A Retrospective Registry Study on 127,555 Patients from the Nationwide OsMed Health-DB Database." <i>European Heart Journal</i> , vol. 36, no. 36, Sept. , pp. 2454–62.									
9.	Foos, V., et al. "Validation and Evaluation of the Risk-to-Benefit Ratio of Glucose Lowering Therapies in High Cardiovascular Risk Type 2 Diabetes Patients; Projections Using the IMS CORE Diabetes Model." <i>Diabetes</i> , vol. 61, June, p. A36.									
10.	Garcia Carretero, R., et al. "Cardiovascular Prognostic Factors in Prediabetic Patients within a Hypertensive Population." <i>Journal of Hypertension</i> , vol. 36, June , p. e25.									
11.	Gokhale, M., et al. "Calendar Time as an Instrumental Variable in Assessing the Risk of Heart Failure with Antihyperglycemic Drugs." <i>Pharmacoepidemiology and Drug Safety</i> , vol. 25, Aug., pp. 45–46.									
12.	Halon, D. A., et al. "Prediction of Heart Failure in Asymptomatic Type 2 Diabetics: An 8 Year Prospective Study Following Cardiac CT Angiography." <i>European Journal of Heart Failure</i> , vol. 19, May, p. 178.									
13.	Hayes, A. J., et al. "An Improved Model to Estimate Lifetime Health Outcomes of Patients with Type 2 Diabetes Using 30-Year Follow-up Data from the United Kingdom Prospective Diabetes Study." <i>Diabetologia</i> , vol. 54, Sept., p. S8.									
14.	Jhund, P., et al. "NT-ProBNP and HsTnT Improve Cardiovascular Risk Prediction in Patients with Type 2 Diabetes Mellitus, Chronic Kidney or Cardiovascular Disease or Both." <i>Journal of the American College of</i> <i>Cardiology</i> , vol. 63, no. 12, 1, p. A1279.									
15.	Kempf, Tibor, et al. "Prognostic Utility of Growth Differentiation Factor-15 in Patients with Chronic Heart Failure." <i>Journal of the American College of Cardiology</i> , vol. 50, no. 11, 2007, pp. 1054–60.									
16.	Leal, J., et al. "Temporal Validation of the UKPDS Outcomes Model Using 10-Year Posttrial Monitoring Data." <i>Diabetes Care</i> , vol. 36, no. 6, June, pp. 1541–46.									
17.	Maxion-Bergemann, S., et al. "Diabetes Mellitus Model (DMM): Internal Validation of a Computer Simulation Model for Type 1 and Type 2 Diabetes." <i>Journal of Medical Economics</i> , vol. 9, no. 69, 2006, pp. 69–82.									
18.	McAlister, F. A., et al. "Association between Glycated Haemoglobin Levels and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Cardiovascular Disease: A Secondary Analysis of TheTECOSrandomized Clinical Trial." <i>European Journal of Heart Failure</i> , vol. 22, no. 11, Nov. , pp. 2026–34.									
19.	McEwan, P., V. Foos, et al. "Approaches to Standardising Cardiovascular Risk Equation End-Points in Order to Facilitate Their Inclusion within a Type 2 Diabetes Model." <i>Value in Health</i> , vol. 20, May , p. A323.									
ho	$\mathbf{M} = \mathbf{P} \mathbf{H} \mathbf{P} \mathbf{H} \mathbf{P} \mathbf{H} \mathbf{H} \mathbf{H} \mathbf{H} \mathbf{H} \mathbf{H} \mathbf{H} H$									

 McEwan, P., H. Bennett, et al. "Refitting of the UKPDS 68 Risk Equations to Contemporary Routine Clinical Practice Data in the UK." *Pharmacoeconomics*, vol. 33, no. 2, Feb., pp. 149–61.

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EXCLUDED: INCORRECT OUTCOME

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EXCLUDED: INCORRECT PATIENT POPULATION

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EXCLUDED: DUPLICATES NOT REMOVED AT TITLE / ABSTRACT SCREENING

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EXCLUDED: MISSING PERFORMANCE MEASURES

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Figure S1. Risk of Bias and Applicability of Included Clinical Prediction Model Development Studies.



Risk of Bias in Prediction Model Development Studies

Figure S2. Risk of Bias and Applicability of Included Clinical Prediction Model Validation Studies.



Risk of Bias in Prediction Model Validation Studies

Figure S3. Risk of Bias and Applicability of Included Clinical Prediction Model Development Studies.



🛨 Low

Study

		Risk of bias domains				Applicability domains				
		D1	D2	D3	D4	Overall Risk of Bias	D1	D2	D3	Overall Applicability
	TRSHFDM 2019 Validation	+	+	×	×		+	+	+	+
	TRSHFDM 2020 Validation (Elharram)	+	+	×	×	8	+	+	+	+
	TRSHFDM 2021 Validation (Razaghizad)	+	+	×	+	8	×	+	+	8
	Segar 2018 Validation	×	+	×	×		+	×	8	8
Study	Kim 2018 Validation	×	+	×	×		×	+	+	8
	Bravo 2018 Validation	+	+	×	-		8	+	+	8
	Basu 2017 Validation	+	+	+	+	+	+	+	+	+
	Basu 2018 Validation	+	+	+	+	+	+	+	+	+
	Hippisley Cox 2015 Validation	×	-	×	+		+	+	8	8
		D1: Participant Select	tion		D1: Participant Applicability					Judgement

Figure S4. Risk of Bias and Applicability of Included Clinical Prediction Model Validation Studies.

D1: Predictor Inclusion D2: Predictor Inclusion D3: Outcome Definition D4: Multivariate Analysis

D2: Predictor Applicability D3: Outcome Applicability

🗙 High - Unclear + Low