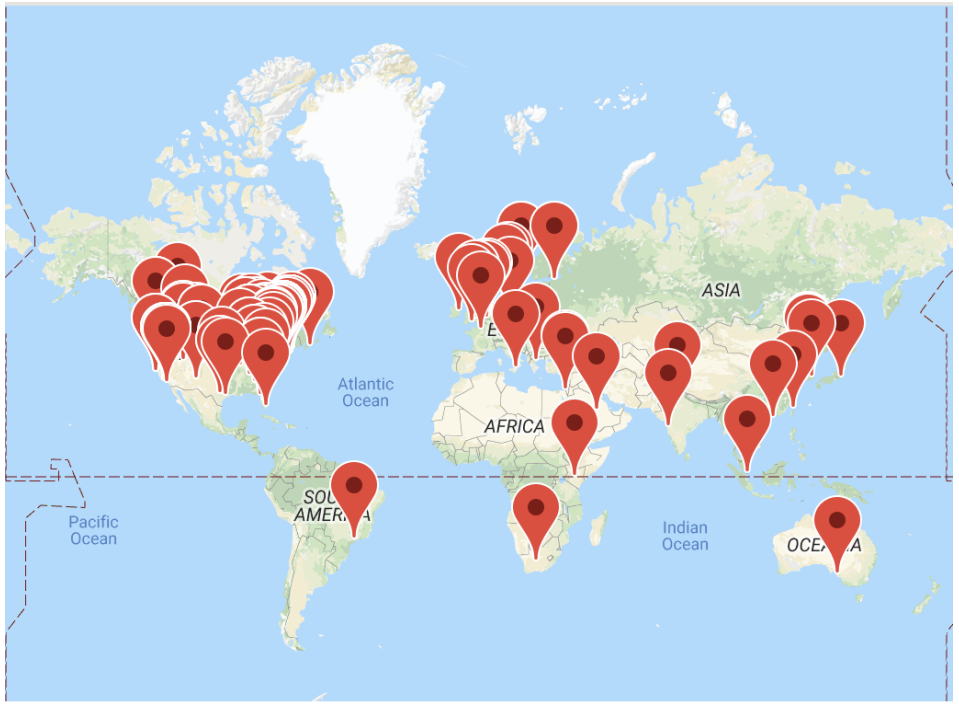
External Validation of Existing Stroke Risk Models

Evaluating Existing Risk Models Using the Patient-Level Prediction Package

We now have functions that enable you to add existing risk score or generalized linear models for evaluation across the OHDSI network

Studies have shown external validation before OHDSI took years… at the symposium we showed it can be done in hours!



Part 1: Evaluating Existing Risk Models Using the Patient-Level Prediction Package

You need three tables:

1. Model table (specifies the coefficient value for each covariate of the model)
2. Covariate definition tables (specifies a set of standard covariates from the Feature Extraction package that make up the model covariate)
3. Intercept table (the intercept value for the model)

You also need to specify the analysis_id settings for the standard covariates with a covariateSetting

Model table

modelId	modelCovariateName	modelCovariateId	coefficientValue
1	Age 50-54	1	1.0
1	Type 2 diabetes condition occurrance longterm	2	1.0
1	Type 2 diabetes group condition longterm	3	0.5
1	Type 2 diabetes group condition anytime	4	0.5

The same model so the id is 1 (can do multiple models at a time by using different modelIds)

Specifies the coefficient value for each of the model's covariates

Covariate table

This columns are not needed but are used to construct the covariateId

modelCovariateId	covariateId	conceptId	analysisId
1	10003	0	3
2	201826102	201826	102
2	443732102	443732	102
3	201826210	201826	210
3	443732210	443732	210
4	201826209	201826	209
4	443732209	443732	209

This columns are needed

Intercept table

No intercept – so set to 0

modelId	interceptValue
1	0

CovariateSettings

```
covSettings <- FeatureExtraction::createCovariateSettings(useDemographicsAgeGroup = T, #3
                                                          useConditionOccurrenceLongTerm = T, #102
                                                          useConditionGroupEraAnyTimePrior = T, #209
                                                          useConditionGroupEraLongTerm = T, #210
                                                          longTermStartDays = -400)
```

This needs to link up to any analysisIds you used in the covariate table (in the example on slide 5 I used analysisIds: 3 (ageGroup), 102 (conditionOccurrenceLongTerm), 210 (conditionGroupEraLongTerm) and 209 (conditionGroupEraAnyTimePrior)

102/209/210 are all longTerm – so I can set the model to use the prior 400 days for the variables by setting longTermStartDays = - 400

Putting it all together

```r
result <- PatientLevelPrediction::evaluateExistingModel(
  #Existing model settings
  modelTable = modelTable[,c("modelId", "modelCovariateId", "coefficientValue")],
  covariateTable = covariateTable[,c("modelCovariateId", "covariateId")],
  interceptTable = interceptTable,
  type = 'score',
  covariateSettings = covSettings,

  # Data settings
  connectionDetails = connectionDetails,
  cdmDatabaseSchema = cdmDatabaseSchema,
  cohortDatabaseSchema = cohortDatabaseSchema,
  cohortTable =  'cohort',
  cohortId = 1,
  outcomeDatabaseSchema = cohortDatabaseSchema,
  outcomeTable = 'cohort',
  outcomeId = 2,

  # TAR/Population settings
  riskWindowStart = 1,
  riskWindowEnd =  365,
  requireTimeAtRisk = T,
  minTimeAtRisk = 364,
  includeAllOutcomes = T,

  # Output settings
  covariateSummary = T)
```

This code will then apply the score model previously specified for the target population (cohort definition 1 in the cohort table) and evaluate it using the ground truth (outcome defined as cohort definition 2 in the cohort table) where TAR is 1 day to 365 days after the target cohort start date.

Part 2: External Validation of Stroke Risk Models

Prediction Question 1: Within a target population of female patients with newly diagnosed atrial fibrillation predict who will develop a stroke 1 day until 365 days after diagnosis of atrial fibrillation.

Prediction Question 2: Within a target population of female patients ages 65+ with newly diagnosed atrial fibrillation predict who will develop a stroke 1 day until 365 days after diagnosis of atrial fibrillation.

Part 2: External Validation of Stroke Risk Models

We used the framework previously described to add **five** existing stroke risk models:

Variable	ATRIA	Framingham	CHADS2	CHADS2VASc	Qstroke
Age	x	x	x	x	
Female	x	x		x	
Diabetes	x	x	x	x	x
CHF	x		x		x
Prior Stroke or TIA		x	x	x	
Hypertension	x		x	x	x
Systolic blood pressure		x			x
Total cholesterol:HDL cholesterol ratio					x
Townsend deprivation score					x
Proteinuria	x				
eGFR<45 or ESRD	x				
Vascular disease				x	
CHF or LV disease				x	
Smoking status					x
Ethnicity					x
CHD					x
FH of CHD					x
Atrial fibrillation					x
Rheumatoid arthritis					x
Chronic renal disease					x
Valvular heart disease					x

Part 2: External Validation of Stroke Risk Models

Validation:

	ATRIA	Framingham	CHADS2	CHADS2VASc	Qstroke
Internal AUROC					
	0.72		0.82	0.61	0.81
External AUROCs					
UK EMR 2015 [8]	0.7 (0.69-0.71)	-	0.68 (0.67-0.69)	0.68 (0.67-0.69)	-
Swedish EMR 2016 [9]	0.71 (0.70-0.71)	-	0.69 (0.69-0.70)	0.69 (0.69-0.70)	-
Taiwan 2016 [10]	-	-	0.66	0.70	-
New Zealand, Russia and the Netherlands 2014 [11]	-	0.70 (0.68-0.73)	-	-	0.71 (0.69-0.73)
UK EMR 2010 [12]	-	0.65 (0.63-0.68)	0.66 (0.64-0.68)	0.67 (0.65-0.69)	-

Part 2: External Validation of Stroke Risk Models

The package is on Github:

https://github.com/OHDSI/StudyProtocolSandbox/tree/master/ExistingStrokeRiskExternalValidation

Results

We have results from 5 databases at the moment:

Target Population	Model	CCAE	MDCD	MDCR	Optum claims	Optum EHR
T1: Females aged 65+ with atrial fibrillation no prior stroke or anticoagulants	ATRIA	-	0.57 (0.55-0.58)	0.63 (0.62-0.64)	0.61	0.62
	CHADS2	-	0.54 (0.53-0.56)	0.60 (0.59-0.61)	0.59	0.60
	CHADS2VAS	-	0.55 (0.53-0.57)	0.60 (0.59-0.61)	0.59	0.62
	Framingham	-	0.55 (0.53-0.56)	0.59 (0.58-0.60)	0.56	0.58
	QStroke	-	0.53 (0.52-0.55)	0.56 (0.55-0.57)	0.55	0.56
T2: Females with atrial fibrillation no prior stroke or anticoagulants	ATRIA	0.62 (0.60-0.64)	0.58 (0.56-0.59)	-	0.65	0.65
	CHADS2	0.61 (0.59-0.62)	0.56 (0.55-0.57)	-	0.62	0.63
	CHADS2VAS	0.63 (0.61-0.65)	0.58 (0.56-0.59)	-	0.64	0.65
	Framingham	0.61 (0.59-0.63)	0.56 (0.55-0.58)	-	0.61	0.62
	QStroke	0.61 (0.59-0.63)	0.54 (0.53-0.56)	-	0.57	0.58

Results

But now we want you to run it:

Target Population	Model	CCAE	MDCD	MDCR	Optum claims	Optum EHR	Your Database
T1: Females aged 65+ with atrial fibrillation no prior stroke or anticoagulants	ATRIA	-	0.57 (0.55-0.58)	0.63 (0.62-0.64)	0.61	0.62	
	CHADS2	-	0.54 (0.53-0.56)	0.60 (0.59-0.61)	0.59	0.60	
	CHADS2VAS	-	0.55 (0.53-0.57)	0.60 (0.59-0.61)	0.59	0.62	
	Framingham	-	0.55 (0.53-0.56)	0.59 (0.58-0.60)	0.56	0.58	
	QStroke	-	0.53 (0.52-0.55)	0.56 (0.55-0.57)	0.55	0.56	
T2: Females with atrial fibrillation no prior stroke or anticoagulants	ATRIA	0.62 (0.60-0.64)	0.58 (0.56-0.59)	-	0.65	0.65	
	CHADS2	0.61 (0.59-0.62)	0.56 (0.55-0.57)	-	0.62	0.63	
	CHADS2VAS	0.63 (0.61-0.65)	0.58 (0.56-0.59)	-	0.64	0.65	
	Framingham	0.61 (0.59-0.63)	0.56 (0.55-0.58)	-	0.61	0.62	
	QStroke	0.61 (0.59-0.63)	0.54 (0.53-0.56)	-	0.57	0.58	

Discussion – Methodology

1. The framework enables quick external validation of risk models (existing or new)
2. Open repository means people can add new models for benchmarking

Discussion – Clinical

1. We found the performance of the existing models depended on the definition of stroke (need improved phenotype)
2. None of the models performed well in older females – do we need a different model for older patients?
3. Can the kitchen sink approach in PLP lead to an improved model? If it does, is there value in a more complex model?

Conclusion

1. The OHDSI standardizations mean we can improve the external validation process to see how models perform across a variety of datasets
2. The github repository for models makes benchmarking easy
3. Maybe we need better stroke risk models – specifically for older patients
4. If you want to be involved in this study please run the github package – we will submit this for publication soon and anyone who runs the package will be an author (if you review the paper and are happy with it).

Questions?

jreps@its.jnj.com