Developing Pre-Testing Diagnostic Tools for Pandemics Using Predictive Analytics: The Case of COVID-19

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- Setting and Research Objectives
- Optimal Test Admission policies
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Objective: Best use of *Limited* Testing Resources

- COVID: PCR testing ("gold standard") is crucial in identifying infected individuals
- **Testing resources limited**

  During the latest wave, ON had to limit testing to certain groups (symptomatic, high risk, etc.)
- Other **testing limitations**

  Imperfect: PCR estimates are 1% false positive, 20%+ false negative

  Not immediate: results take up to 3 days
- Our approach: use *information available at the time of testing* to *optimally deploy* testing resources

  Information: symptoms, patient characteristics, reason for test

  Optimal deployment: admission, repeated tests, pooled testing

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Prior Work

- ML for predicting test outcome
  - Some, mostly on small datasets (a few exceptions)
  - For some reason, data is either not systematically collected or is not made publically available
- Test design
  - Large literature on pooled testing
  - No(?) prior work on leveraging ML for optimal test resource allocation

Key Assumptions

1. Testing resources constrained: **T**
2. Population presenting for testing: **N** > T
3. **Objective of testing: *discover True Positives (TPs)***
4. Test efficiency: # TPs uncovered
5. Data on previous tests is available
   - Pre-test information
   - Test outcome (P / N)

Patients show up one at a time ("on-line" process). Upon observing the "available info" it is possible to

1. *Accept* or *reject* patient for testing (admission policy)
2. Test a new patient or *re-test* an already tested one (re-test)
3. Direct patients to *individual* or *pooled* testing (mixed testing)

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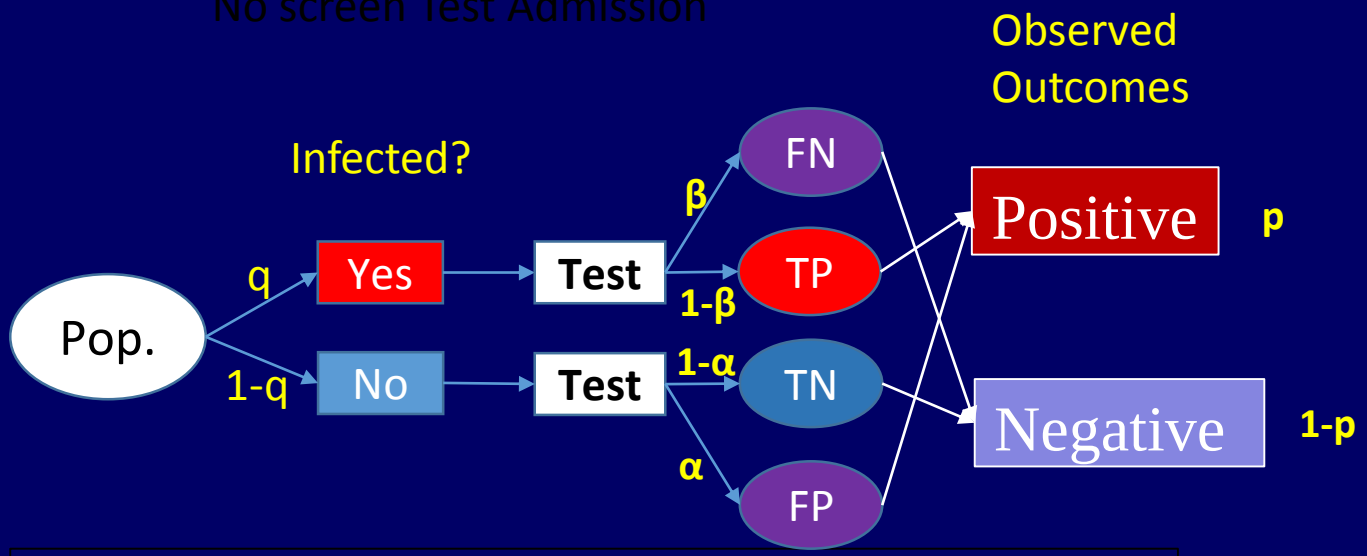
Random Admission Process (Baseline)

No screen Test Admission



Legend:
q – disease prevalence
α –False Positive rate (1 – specificity)
β –False Negative rate (1 – sensitivity)

Estimated Prevalence

$$\hat{q}=\frac{p-\alpha}{1-\alpha-\beta}$$

Test Efficiency

$$\boldsymbol{TE = \hat{q}(1-\beta)}$$

Example:

$$\alpha = 1\%, \beta = 20\%, p = 48\%$$

Then

$$\hat{q} = 59.5\%, \qquad TE = 47.6\%$$

i.e., > 50% of testing capacity is "wasted"

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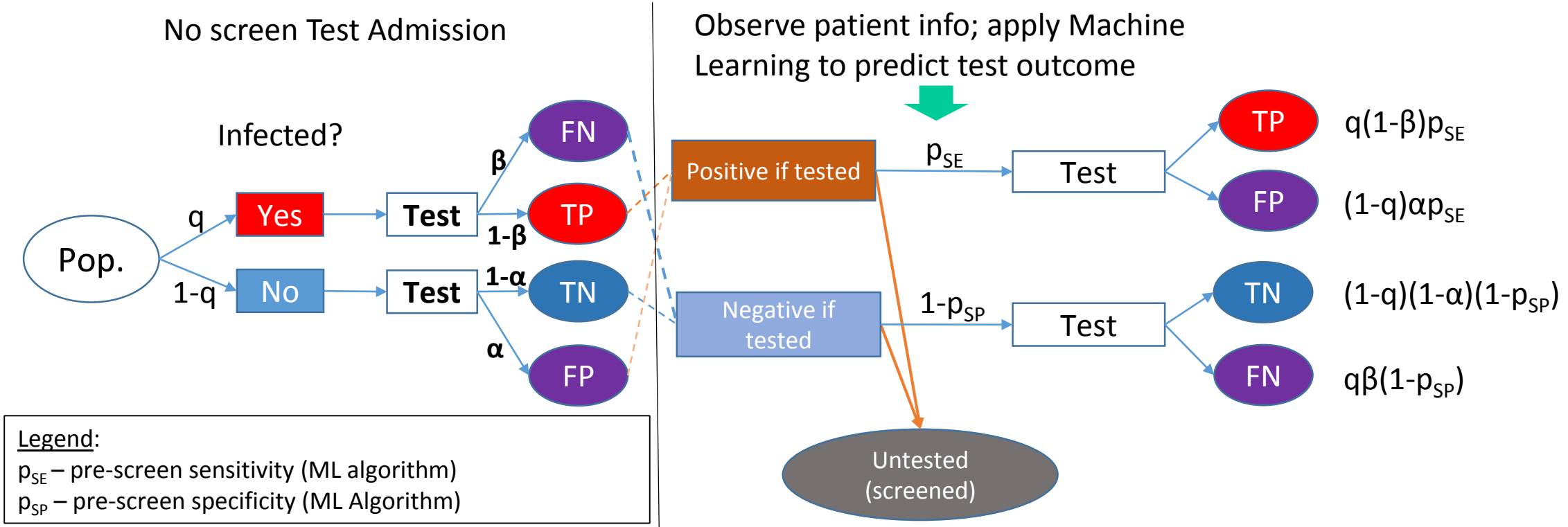
Screened Admission Process

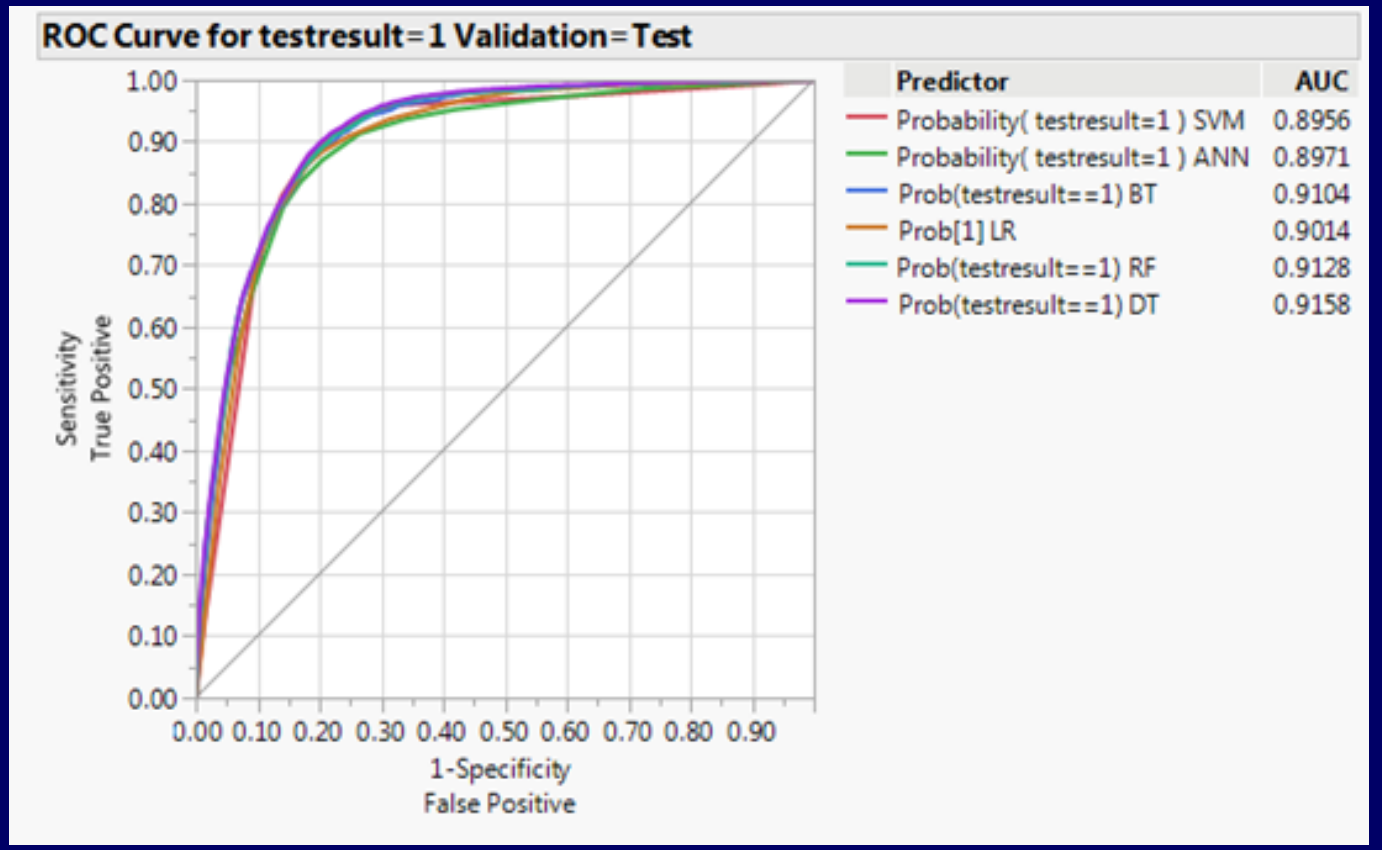


Test Efficiency: TP for tested

$$TE_s = \frac{qp_{SE}(1-\beta)}{1-[q(1-\beta)+(1-q)\alpha](1-p_{SE})-[(1-q)(1-\alpha)+q\beta]p_{SP}}.$$

Linking ML to Admission Process: ROC

p_{SE}



$1 - p_{SP}$

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Optimal Admission Process

- Policy: Admit if predicted probability of positive test > $\mathcal{P}(\frac{T}{N})$ – predicted prob. for percentile $\frac{T}{N}$
  - (p_{SE}, p_{SP}) are sensitivity/specificity for $\mathcal{P}(\frac{T}{N})$
- **Thm 1:** (better than random): If $p_{SE} + p_{SP} \geq 1$ then screen-based testing yields efficiency gains
- **Thm 2**: If Thm 1 holds and $\alpha + \beta \leq 1$, then the policy above is optimal

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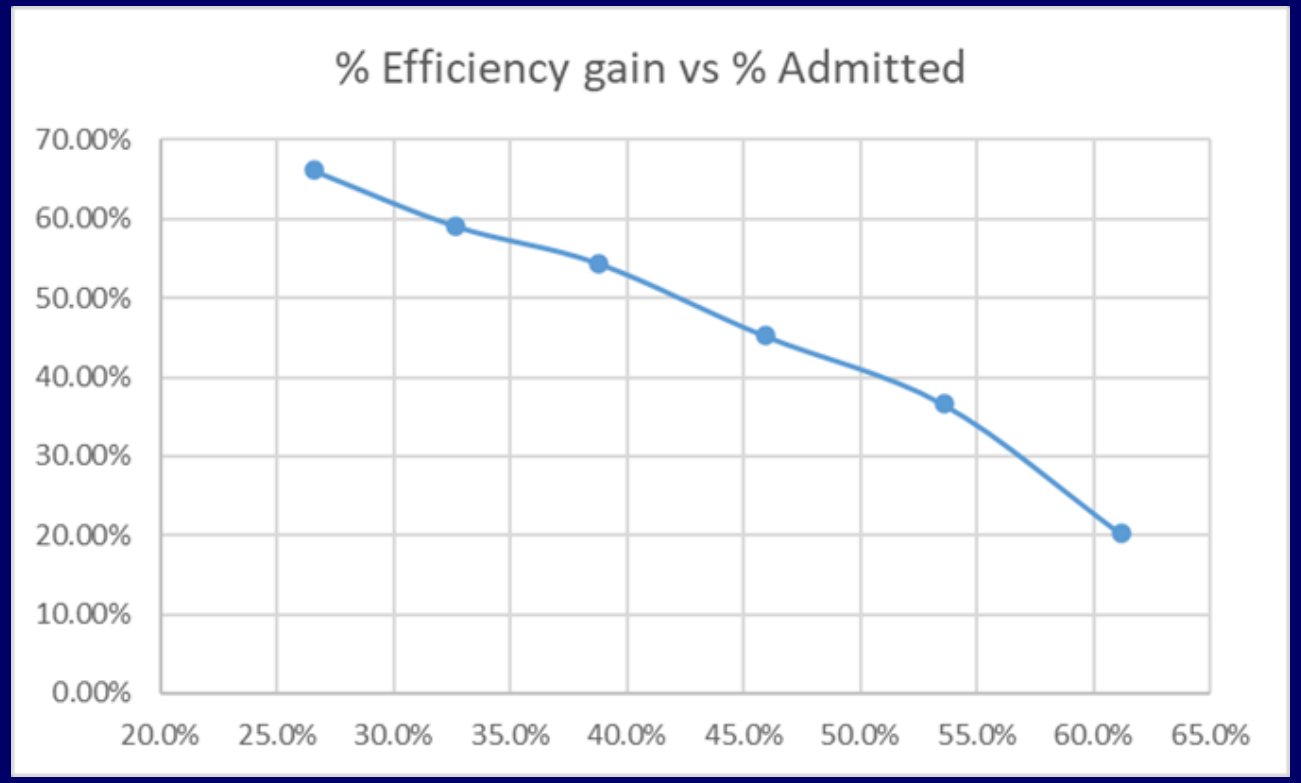
Expected Efficiency Gains (case study)



Screening most important when test resources are constrained

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Re-Testing "Probable" Cases

- Q: Given high false negative rate of the PCR, does it make sense to re-test a negative patient ahead of testing a new one?
- A1: with random admission policy, *NO*
- A2: with screened admission, *possibly*
  - Use ML model to classify patients into m groups with decreasing predicted probability of positive outcome
  - Let j(T) = $\min\{j: \sum_{i=1}^{j} n_i \geq T\}$
    - Under single test policy would test groups 1,…,j(T)-1 and part of group j
  - Let q_i be prevalence of infections in group i
  - If $\boldsymbol{q_1\beta > q_{j(T)}}$ then optimal policy must involve some retesting
    - Optimal re-testing strategy can be computed via mathematical programming

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Pooled Testing

- Divide all patients into groups of size s (max group size ≈64)
- Mix the samples from each group (pool)
- If sample for group j tests positive, then test each member of the group individually
  - Otherwise, the whole group is classified as Negative
- To test the whole population set s so that exp # test = T
  - Allows us to test everyone rather than just a random selection
  - Q: Is this more efficient (with respect to discovering TP's)?
  - A: Yes if $N(1-\beta) \geq T$

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Combining Pooled and Screening

- Suppose N_i highest-scoring patients are tested individually
- The remaining N_p = N- Ni are pooled (no one is turned away)
- Results:
  - Can derive conditions under which combined testing is better than pooled
    - Intuitively: ML model must be accurate enough
  - Optimal policy structure: use individual tests as much as possible; use max group size for all else

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ML Modeling and Implementation

- Two-step process
- **Step 1**: Data processing and model selection

  Scoring algorithm uploaded to the website
- **Step 2**: Interactive website
  - Enter available test capacity T (for current period)
  - Enter information for the presenting patient
  - Compute model score; compare to threshold
  - Recommend "test" or "no test"
    - Easy to extend to repeated testing and pooled testing regimes

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Interactive Website

Provide test information:

Test sensitivity (True pos rate):
.85

Test specificity (True neg rate):
.99

Estimated Testing Capacity (this period):
15000

Estimated no. of patients available for testing*:
(with group satisfying filter condition below)
30000

Provide patient information:

Cough:	No
Fever:	No
Sore throat:	Yes
Shortness of breath:	Yes
Headache:	Yes
Age:	Above 60
Gender:	Female
Reason for the test:	Contact

Average positive test % in the last 7 days:
75

Submit

| **Cough** : No | **Fever** : No | **Sore throat** : Yes | **Shortness of breath** : Yes |

| **Test sensitivity** : 85.0% | **Test specificity** : 99.0% | **Estimated testing cap**

Model score (probability of positive PCR) : 77.9%

Model percentile : 63.6

Policy advice : Test

Model used : Random Forest Classifier

Model accuracy report :

sensitivity : 88.6%
specificity : 81.8%
accuracy : 85.1%
AUC : 91.7%

Data Analysis and Summary:

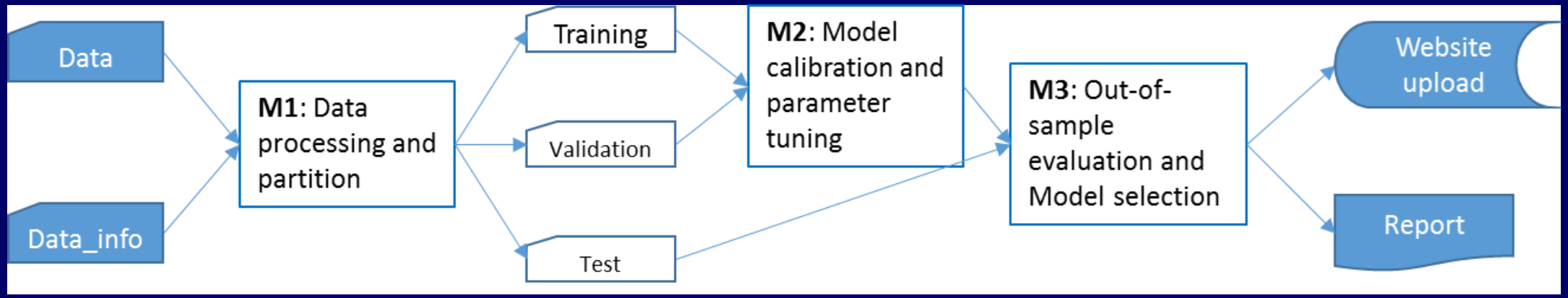
Filter applied:	Symptomatic = Yes
Observed positive rate:	47.9%
Corrected positive rate:	55.9%

Note : Results are only applicable for patients exhibiting at least one symptom.

ML Models

- Used a variety of ML Models
- Created software to
  - automatically tune hyper-parameters
  - select best model
  - Output scoring procedure (python code)

- Logistic Regression
  - With L1, L2 regularization
- Decision Tree
- Random Forest
- Boosted Tree
- Neural Network
- Support Vector Machine
- Ensemble



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Case Study

- IMOH Data for March 2020 – Sept 2020
  - Total tests: 1.5M, 7% positive
  - Symptomatic: 108K, 48% positive

Information available prior to the test: not much!

- Gender, Age (<=60, 60+), Reason (Contact, Travel, Other)
- Symptoms: Cough, Fever, Sore Throat, Shortness of Breath, Headache

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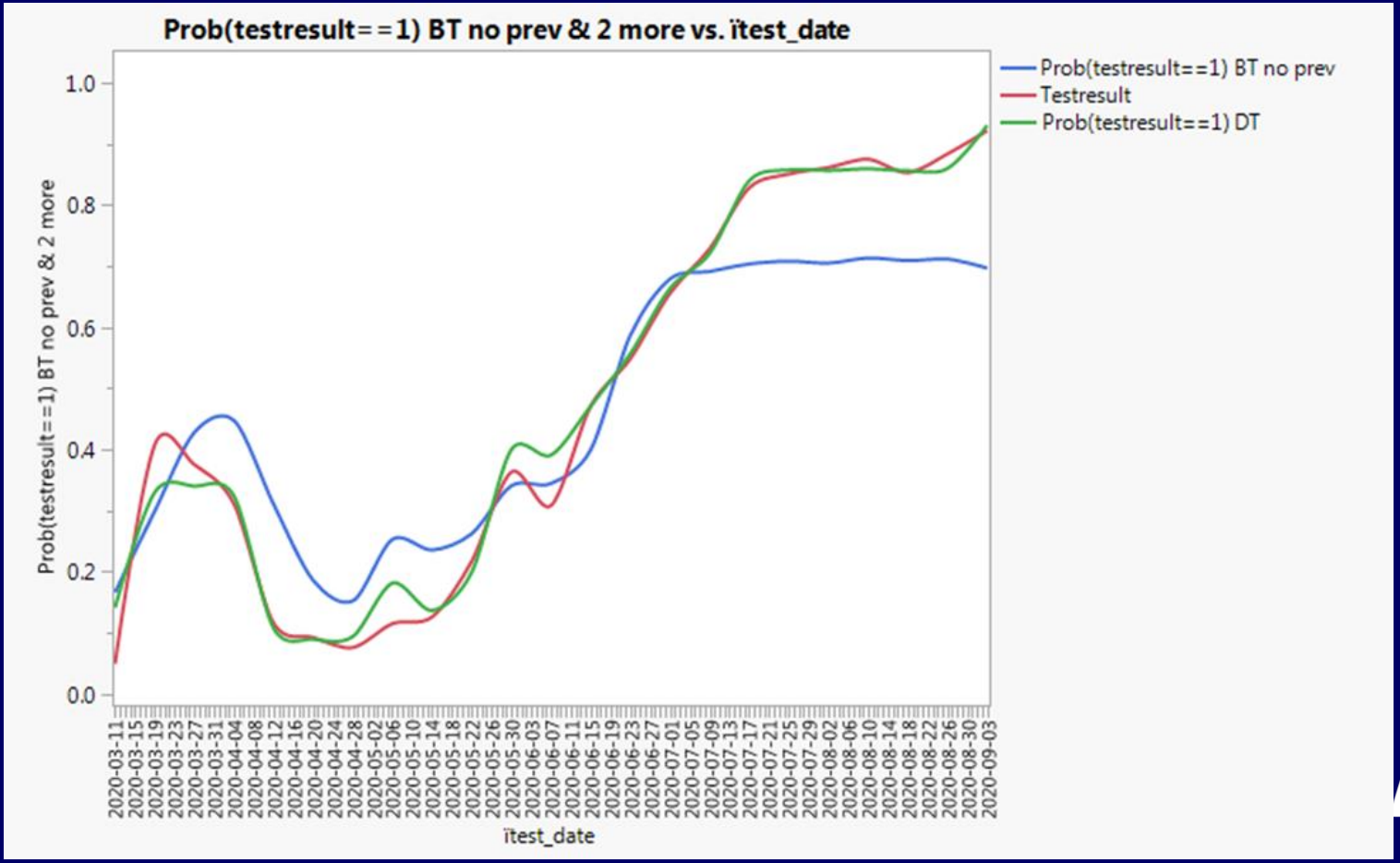
Key Additional Predictors: Prevalence

- Prevalence is very unstable over time
- Added time series terms such as average prev over last 7 days, average tests over last 7 days, etc.



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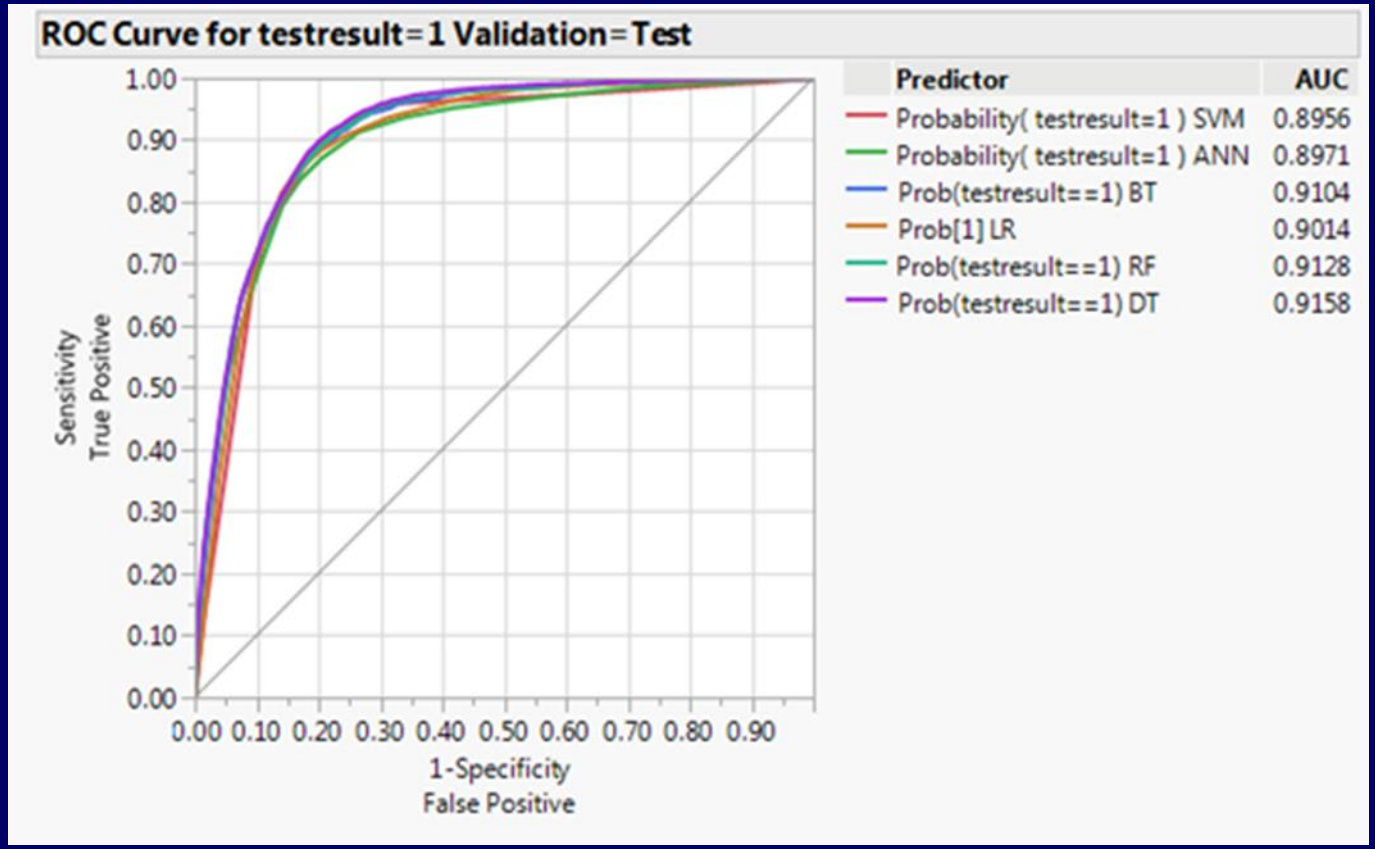
ML Models: surprisingly accurate!

- Note that AUC is the key measure for our purposed
- Evaluated on 25% Holdout Sample



*AUC values for RF and BT improve slightly after parameter tuning

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Comments on Case Study

- Best models extremely accurate in the top deciles
  - Predicted model score can be used in place of PCR result (unlike PCR, available instantly)
- Random Forest tends to perform the best, with other tree-based models close behind
- Extended results to asymptomatic patients with similar accuracy levels (but asymptomatic never in the top risk group)
- Data of the format we need should be easy to collect – our models show it is of great value
- Very significant improvements in efficiency, particularly when resources are scarce 

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Conclusions

- Developed optimal testing policies for maximizing test efficiency when test resources are scarce
  - Combined ML and decision analysis
  - Used data that (should be) readily available
  - Automated modeling pipeline and interactive implementation

- Questions?

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