Using Routinely Collected Surveillance Data to Predict TB Outbreaks in the United States

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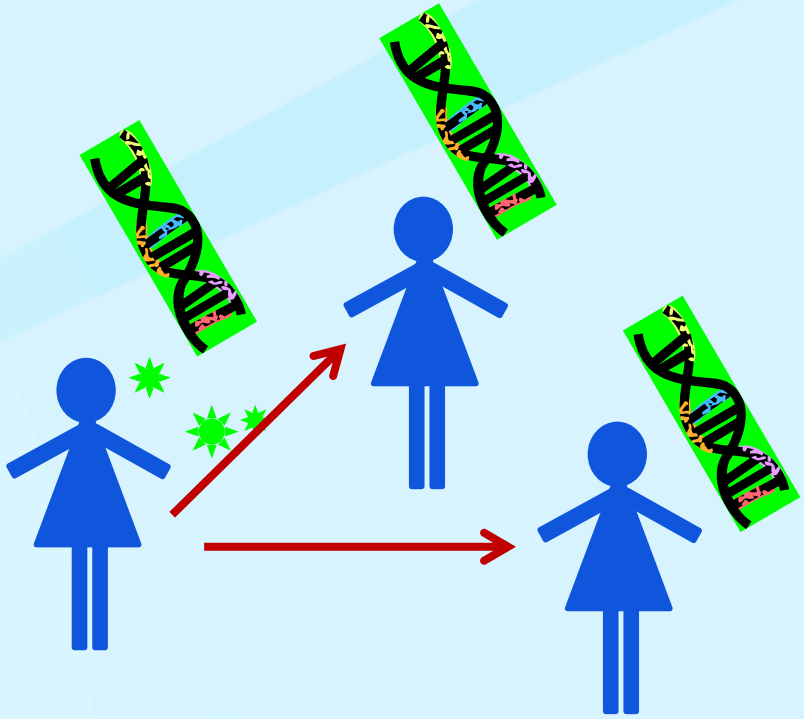
TB genotype background

- Examines genetic variation to determine relatedness of TB strains from different cases
- Only performed with culture-positive cases
- Outbreaks occur when highly infectious TB patients transmit TB
  - "Same" place
  - "Same" time
  - Secondary cases have same genotype

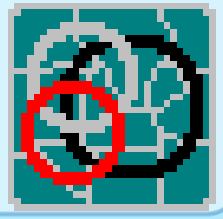


Methods overview

- **Genotyping with spoligotyping + 12-locus MIRU-VNTR**
- **SaTScan**
  - To identify TB clusters (to define our analytic cohort)
- **Decision Tree Analysis**
  - To identify clusters at high risk of becoming outbreaks

SaTScan

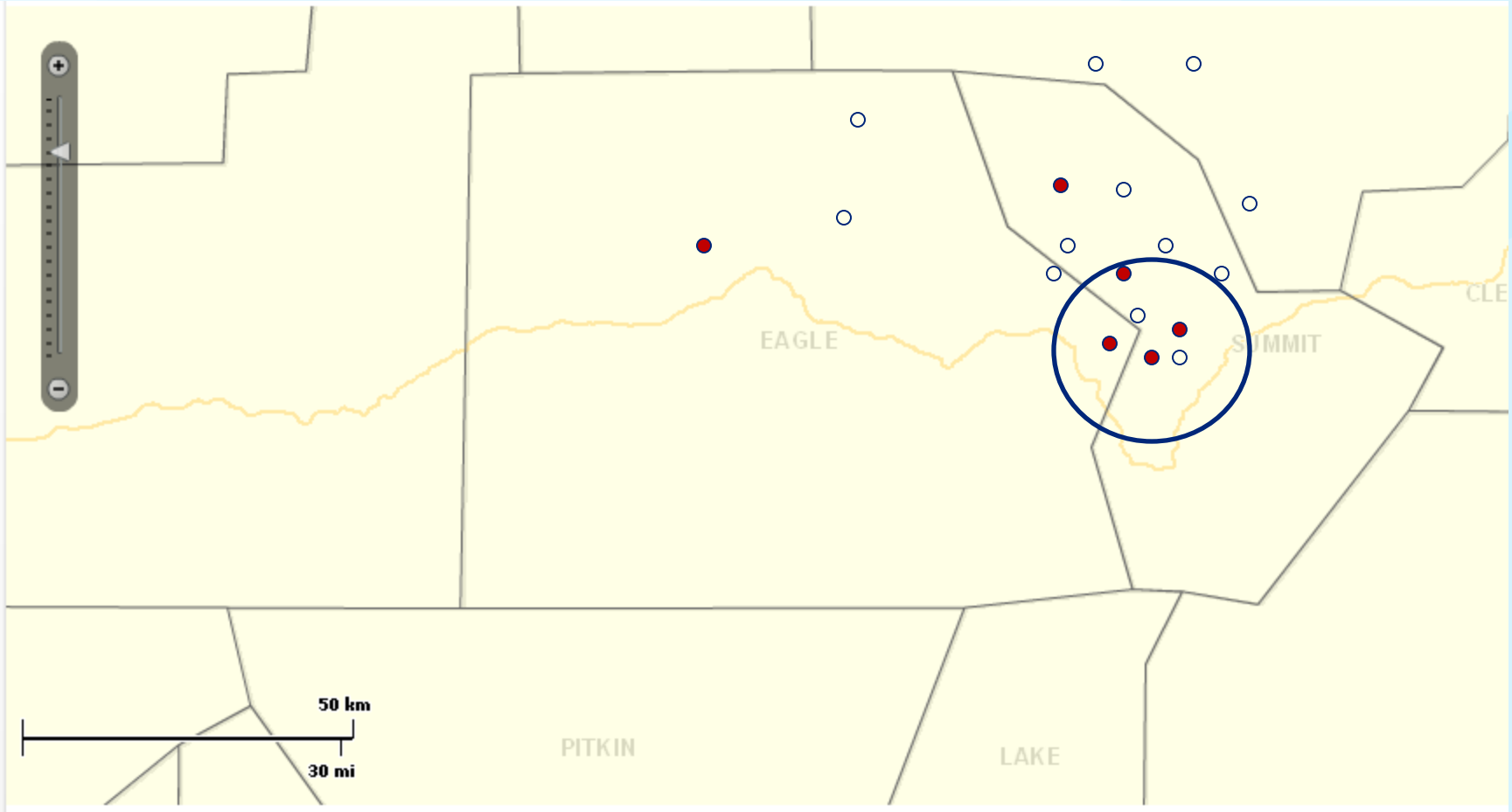
- **GIS software standard**
  - Performing geographical surveillance of disease
  - Detecting spatial disease clusters
- **Poisson-based model**
- **Monte Carlo simulation used to compute p-value for each cluster**



SaTScan parameters

- TB cases with genotyping results reported in U.S. from 2006 through 2010
- Search within 50 km radius
- Significant and non-significant

Sample SaTScan map



How we defined an incident TB cluster

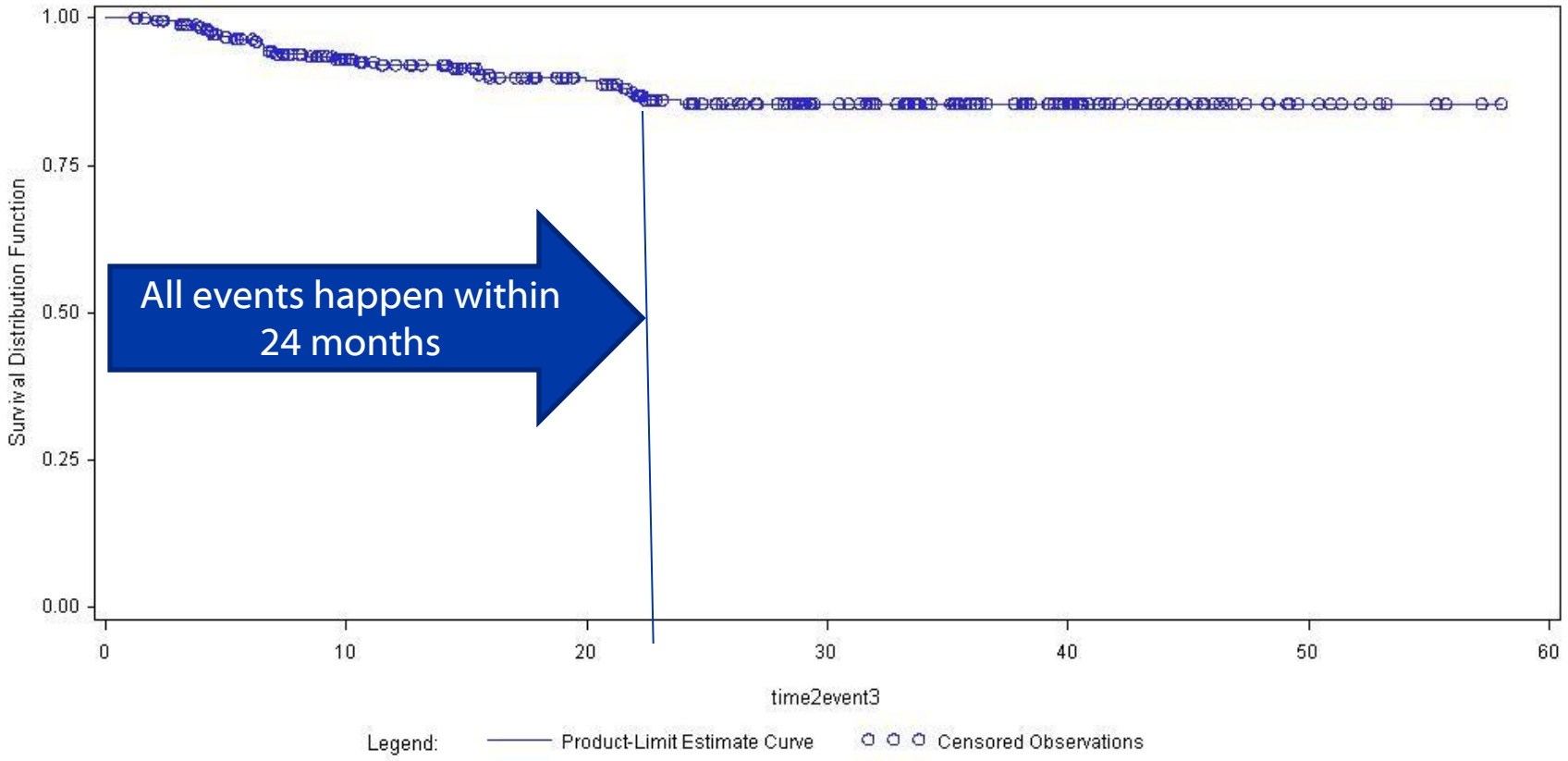
- Identified by SaTScan (2006-2010)
- Clusters ≥3 cases with same genotype
- Annual county genotyping coverage ≥75%
- No matching cases in preceding 24 months
  - Identify new (i.e., incident) clusters

How we defined our outcome: "outbreak"

From beginning (January 2006) to end (Dec 2010) of observation period:

- Grew from 3 to ≥6 cases
- Within 24 months
- Confirmed by local public health officials as an outbreak

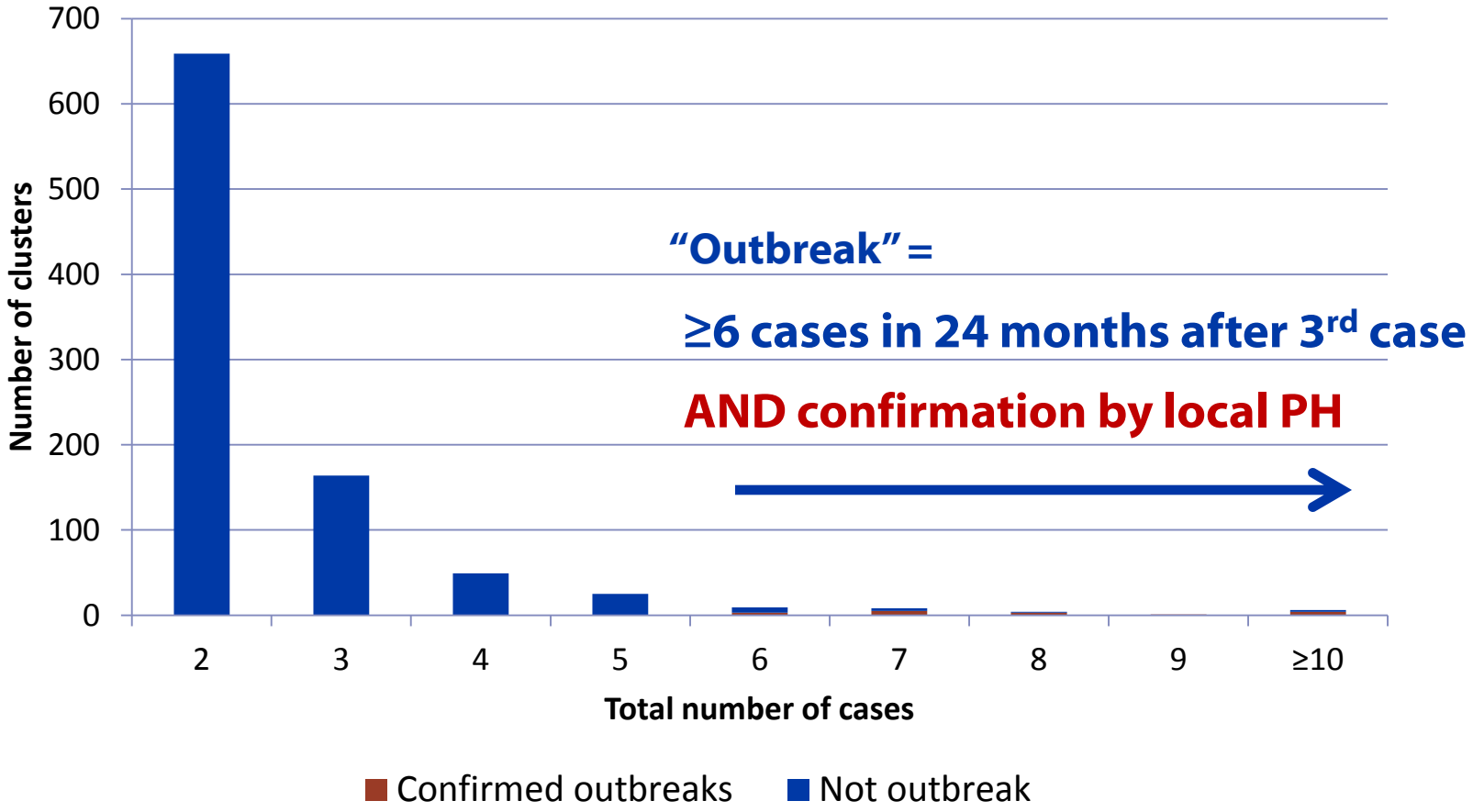
Time to reach 6 cases, N=146



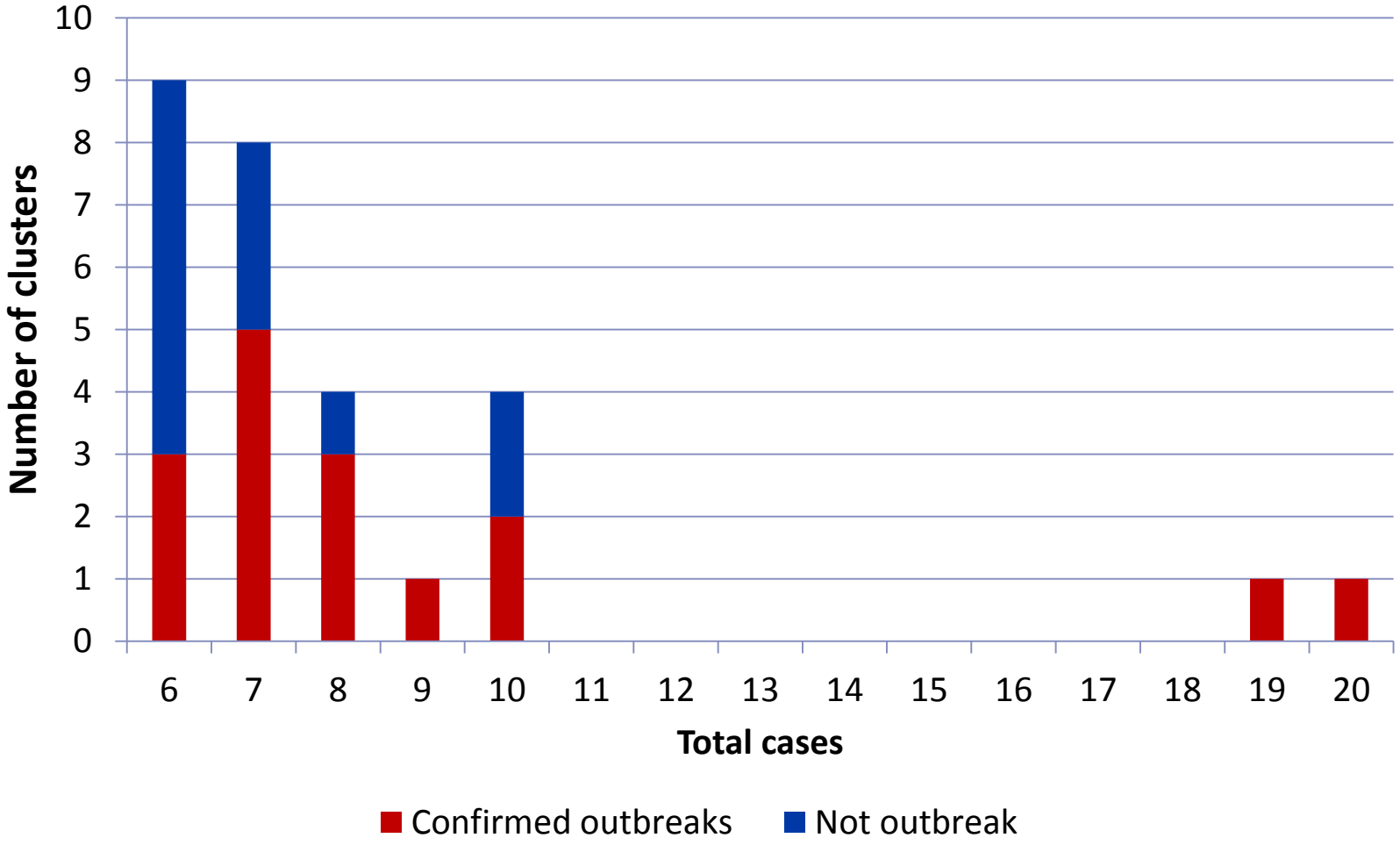
Entry into cohort: 3rd case

Event: 6th case in an outbreak cluster of n>=6, else censored at end of timeline (Dec 2010)

Distribution of clusters by final cluster size, stratified by outcome, N=925

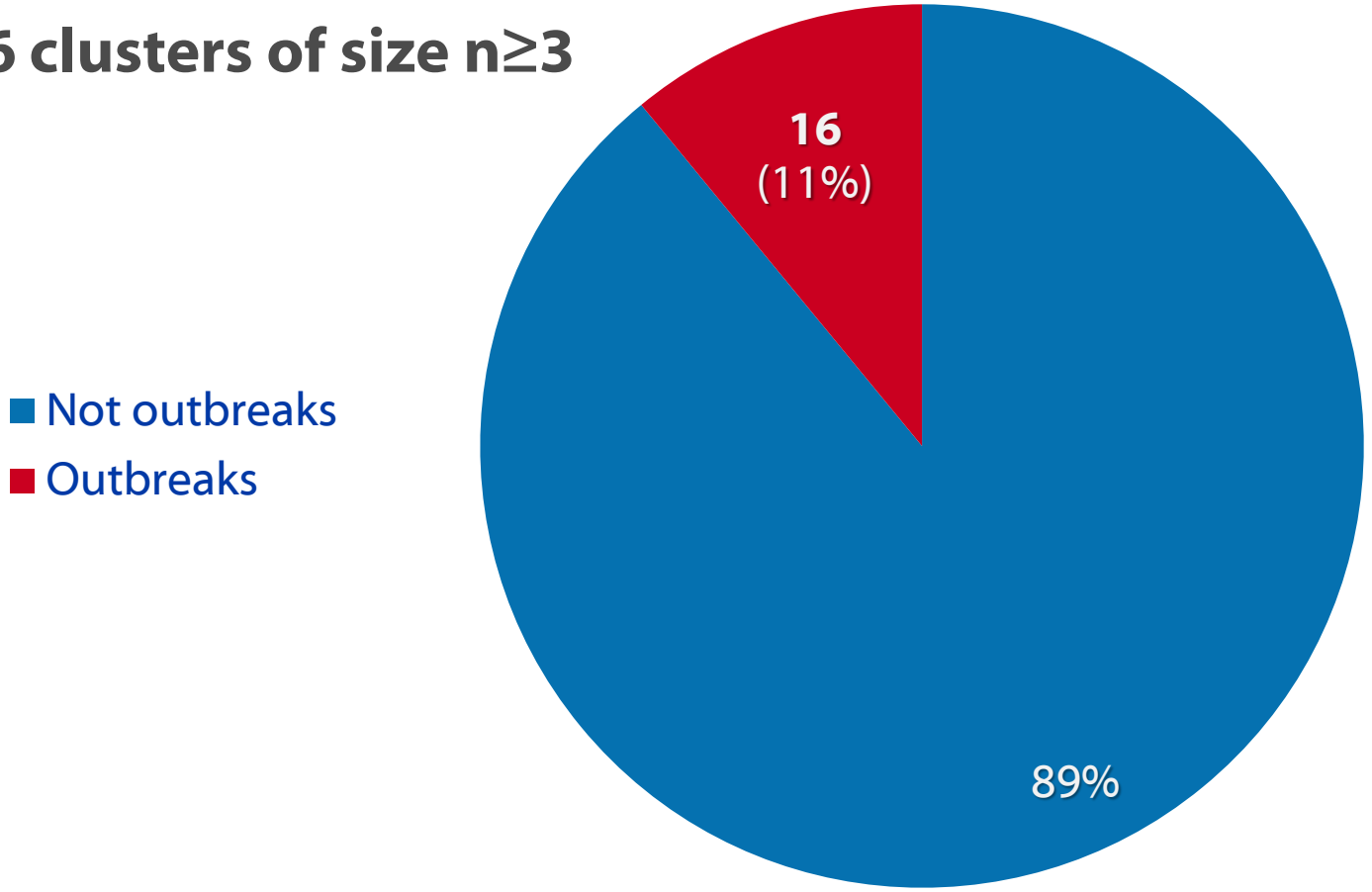


Distribution of clusters by final cluster size, stratified by outcome, n>=6



Outcomes

- 146 clusters of size n≥3



Characteristics of 146 TB clusters and associated risk factors of cluster becoming an outbreak case

Cluster characteristic	Outbreak clusters (n=16) with characteristic		Relative risk in predicting outbreaks	
Patient risk factors	n	%	RR	95% CI
Homeless or excess alcohol use or illicit drug use or incarceration at diagnosis	**15**	**22.4**	**17.7**	**2.4, 130.4**
Homeless or alcohol or drug use	**14**	**21.9**	**9.0**	**2.1, 38.0**
Drug use	**12**	**25.5**	**6.3**	**2.2, 18.6**
Alcohol use	**11**	**25.0**	**5.1**	**1.9, 13.8**
Homeless or alcohol use	**11**	**22.0**	**4.2**	**1.6, 11.5**
Homeless and alcohol use	**6**	**30.0**	**3.8**	**1.5, 9.3**
Incarceration	**5**	**29.4**	**3.4**	**1.4, 8.7**
Homeless	**6**	**23.1**	**2.8**	**1.1, 6.9**

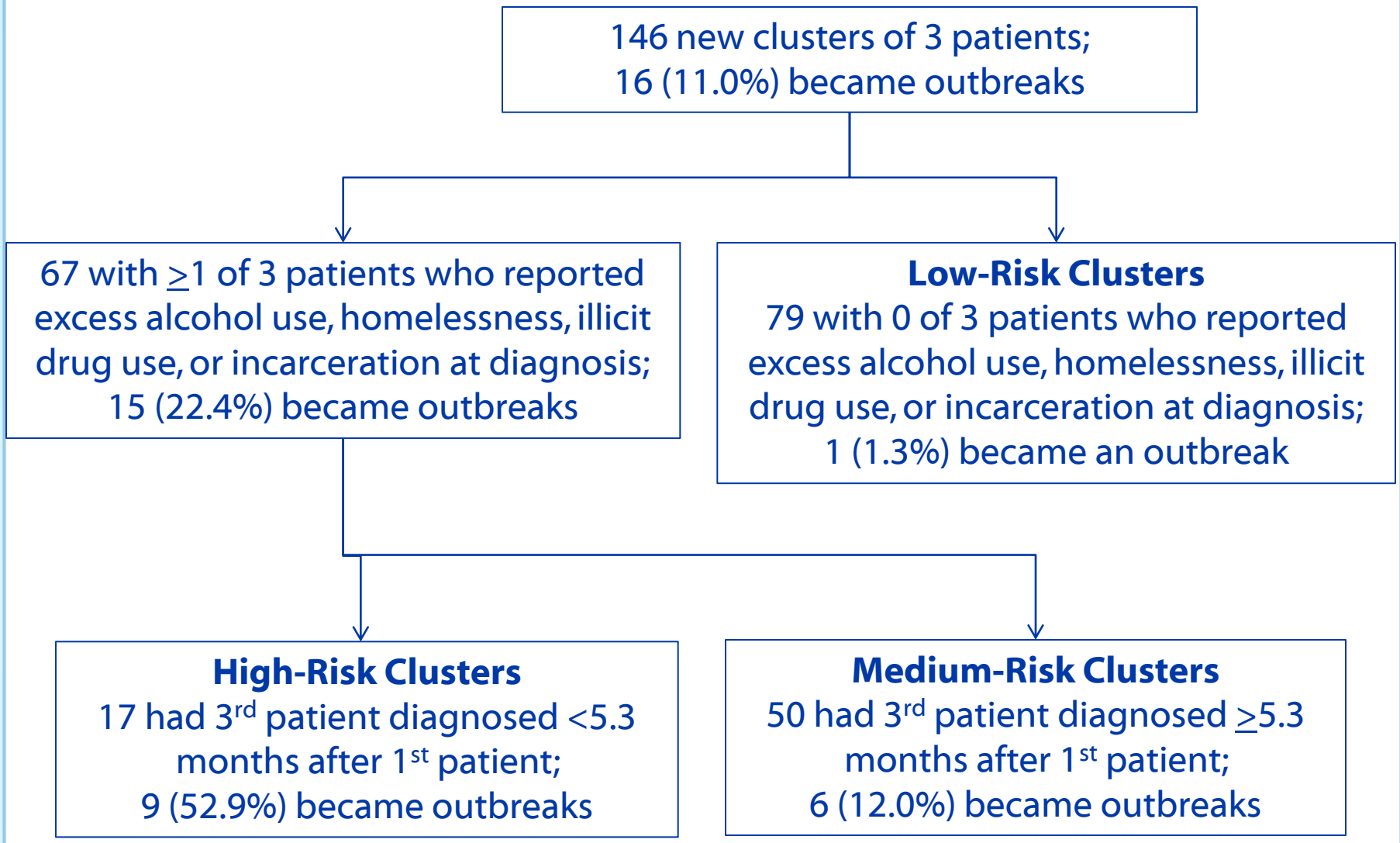
Characteristics of 146 TB clusters and associated risk factors of cluster becoming an outbreak case

Cluster characteristic	Outbreak clusters (n=16) with characteristic		Relative risk in predicting outbreaks	
Cluster risk factors	n	%	RR	95% CI
T1 to T3 <5.3 months	**9**	**21.4**	**3.2**	**1.3, 8.0**
T1 to T2 <4.4 months	**12**	**16.9**	**3.2**	**1.1, 9.4**
T2 to T3 <0.9 months	**7**	**21.2**	**2.7**	**1.1, 6.6**
Sig. LLR at 3rd case	**13**	**16.3**	**3.5**	**1.0, 11.6**

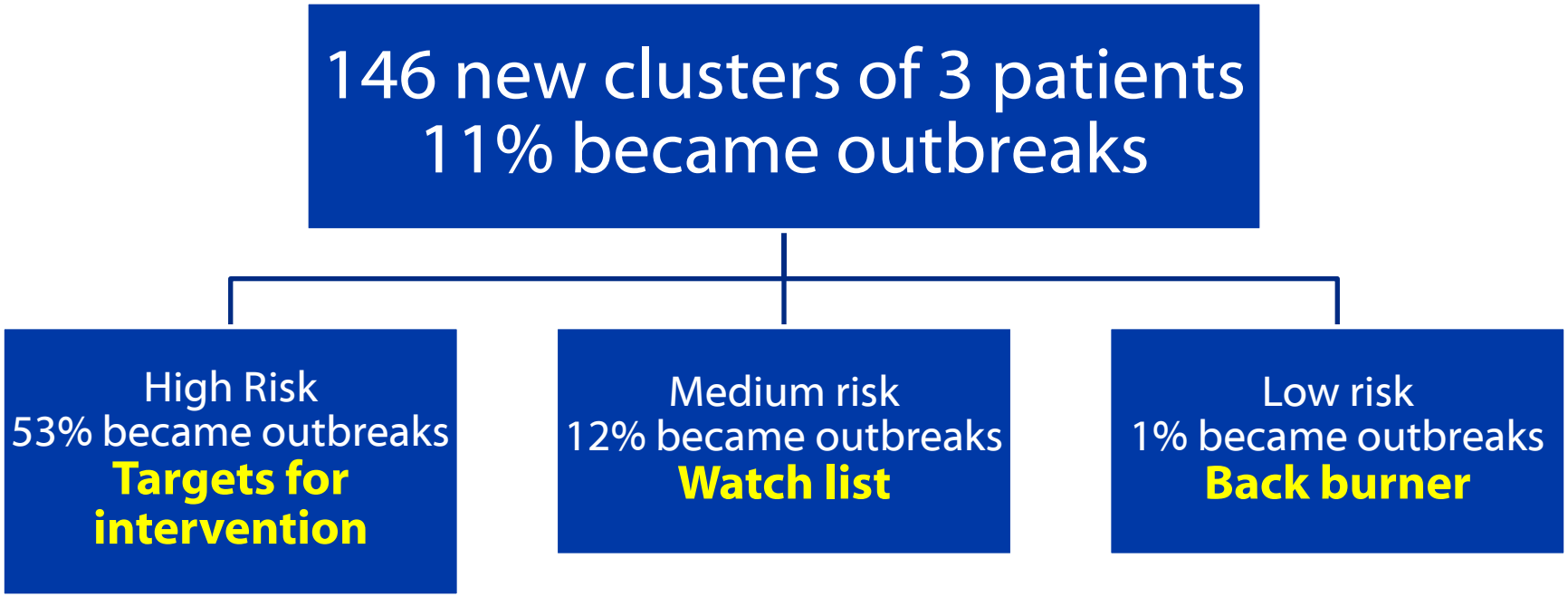
Decision Tree analysis using JMP

- **SAS Predictive modeling software**
- **Recursive partitioning function**
  - "enables users to systematically analyze large data sets to discover unsuspected or unknown relationships.
  - finds a set of cuts or groupings of X values that best predict an outcome by exhaustively searching all possible cuts or groupings, recursively forming a tree of decision rules until the desired fit is reached."

Algorithm for predicting outbreaks at 3rd case



Predicting outbreaks at 3rd case



Limitations

- Surveillance data
- Observation period of only 5 years
- 75% genotyping coverage
  (We now have >90% coverage)
- Based on 12-locus MIRU
  (We now have 24-locus MIRU data)

Conclusion

- With this methodology, we are able to predict half of clusters that would become outbreaks
- This provides an approach to prioritizing clusters for early intervention

Acknowledgements

- **CDC**
  - Sandy Althomsons
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