U.S. Food and Drug Administration

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Estimating Sudden Cardiac Death Rates with Death Certificate Data

Marc B. Stone, M.D.
Senior Medical Reviewer
U.S. Food and Drug Administration

Use and accuracy of state death certificates for classification of sudden cardiac deaths in high-risk populations

Every, Parsons, Hlatky, et al. American Heart Journal 1997

Use and accuracy of state death certificates for classification of sudden cardiac deaths in high-risk populations

- *Prospective* study (registry) of 31,156 Seattle area patients in hospitalized for suspected MI
- 407 deaths outside the hospital with complete paramedic report and death certificate data
- Paramedic findings used as "gold standard"

Use and accuracy of state death certificates for classification of sudden cardiac deaths in high-risk populations

Definite arrhythmic cause
(VF/VT and underlying cardiac cause)

Sudden Cardiac Death?		Death Certificate	
		Y	N
Paramedic	Y	69	20
	N	231	87

Sensitivity 78%
Specificity 27%
Positive Likelihood Ratio 1.07 (95% CI, 0.93-1.23)
Negative Likelihood Ratio 0.82 (95% CI, 0.54 -1.25)
(p=0.41)

→ Death certificates no better than chance

Use and accuracy of state death certificates for classification of sudden cardiac deaths in high-risk populations

Definite or possible arrhythmic cause
(VF/VT *or asystole* and underlying cardiac cause)

Sudden Cardiac Death?		Death Certificate	
		Y	N
Paramedic	Y	255	45
	N	45	62

Sensitivity 85%
Specificity 58%
Positive Likelihood Ratio 2.02 (95% CI, 1.72 -2.37)
Negative Likelihood Ratio 0.26 (95% CI, 0.19 -0.35)
($p<0.00005$)

Validation of death certificate diagnosis of out-of-hospital sudden cardiac death

Iribarren, Crow, Hannan, Jacobs, Luepker
American Journal of Cardiology 1998

Validation of death certificate diagnosis of out-of-hospital sudden cardiac death

- *Prospective* study (Minnesota Heart Health Program) of cardiac disease rates in six communities
- 2035 deaths outside the hospital (ages 30-74)
- 911 death certificates with COPD, neoplasm, poisoning, injury, accident, suicide, or homicide *assumed to be accurate*

Validation of death certificate diagnosis of out-of-hospital sudden cardiac death

1124 other deaths reviewed by physicians using

- Medical records
- Interview with next of kin (1076/1124)
- Autopsy reports (218/1124)

Validation of death certificate diagnosis of out-of-hospital sudden cardiac death

Narrow Definition

Sudden Cardiac Death?		Death Certificate	
		Y	N
Physician review	Y	60	194
	N	262	608

Sensitivity 24%
Specificity 70%
Positive Likelihood Ratio 0.78 (95% CI, 0.62 -0.99)
Negative Likelihood Ratio 1.09 (95% CI, 1.00 -1.19)
(p=0.05)

→ Death certificates *worse* than chance expectation

Validation of death certificate diagnosis of out-of-hospital sudden cardiac death

Broad Definition

Sudden Cardiac Death?		Death Certificate	
		Y	N
Physician review	Y	222	32
	N	613	257

Sensitivity 87%
Specificity 30%
Positive Likelihood ratio 1.24 (95% CI, 1.15 -1.34)
Negative Likelihood ratio 0.43 (95% CI, 0.31 -0.58)
($p<0.00005$)

Study Conclusions

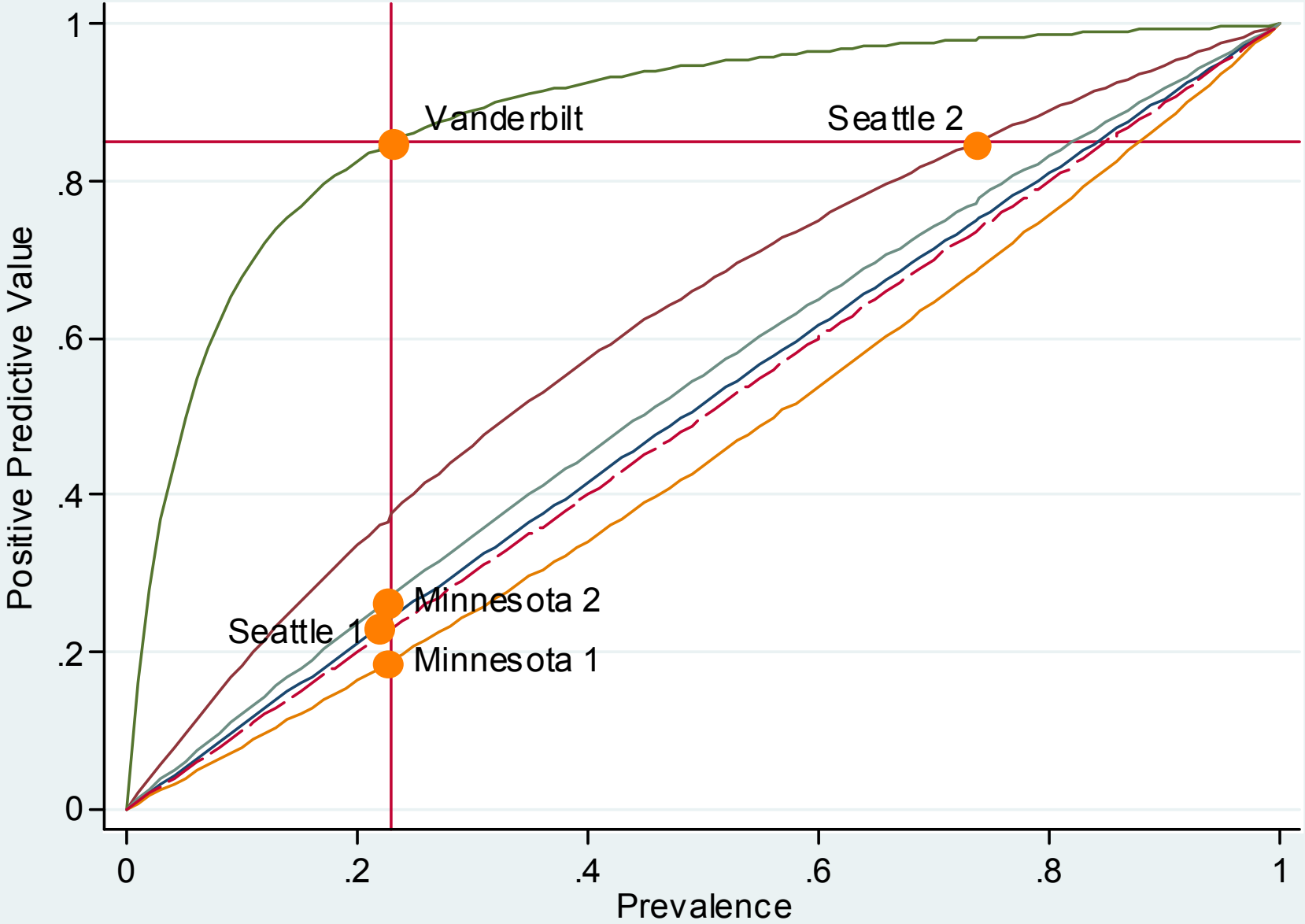
(Emphasis added)

Seattle:

- "We conclude that the death certificate can be used to identify cases of sudden cardiac death *in patients at high risk*; however, there is a substantial rate of false-positive sudden death classification."

Minnesota:

- "Death certificate diagnosis of OOH-SCD included many erroneous cases, and *may not have been suitable for study of etiologic factors, such as cardiac dysrhythmias.*"


Vanderbilt
Seattle 2
Minnesota 2
Seattle 1
Minnesota 1
Positive Predictive Value
Prevalence
0
.2
.4
.6
.8
1

IF

- 23% of non-excluded out of hospital deaths are Sudden Cardiac Deaths
- Positive Predictive Value from Death Certificates is 86%

What is the Positive Likelihood Ratio?

$$\frac{\text{Sensitivity}}{1\text{-Specificity}} = \frac{\text{PPV} * (1 - \text{Prevalence})}{(\text{Prevalencœ}) * (1\text{-PPV})}$$

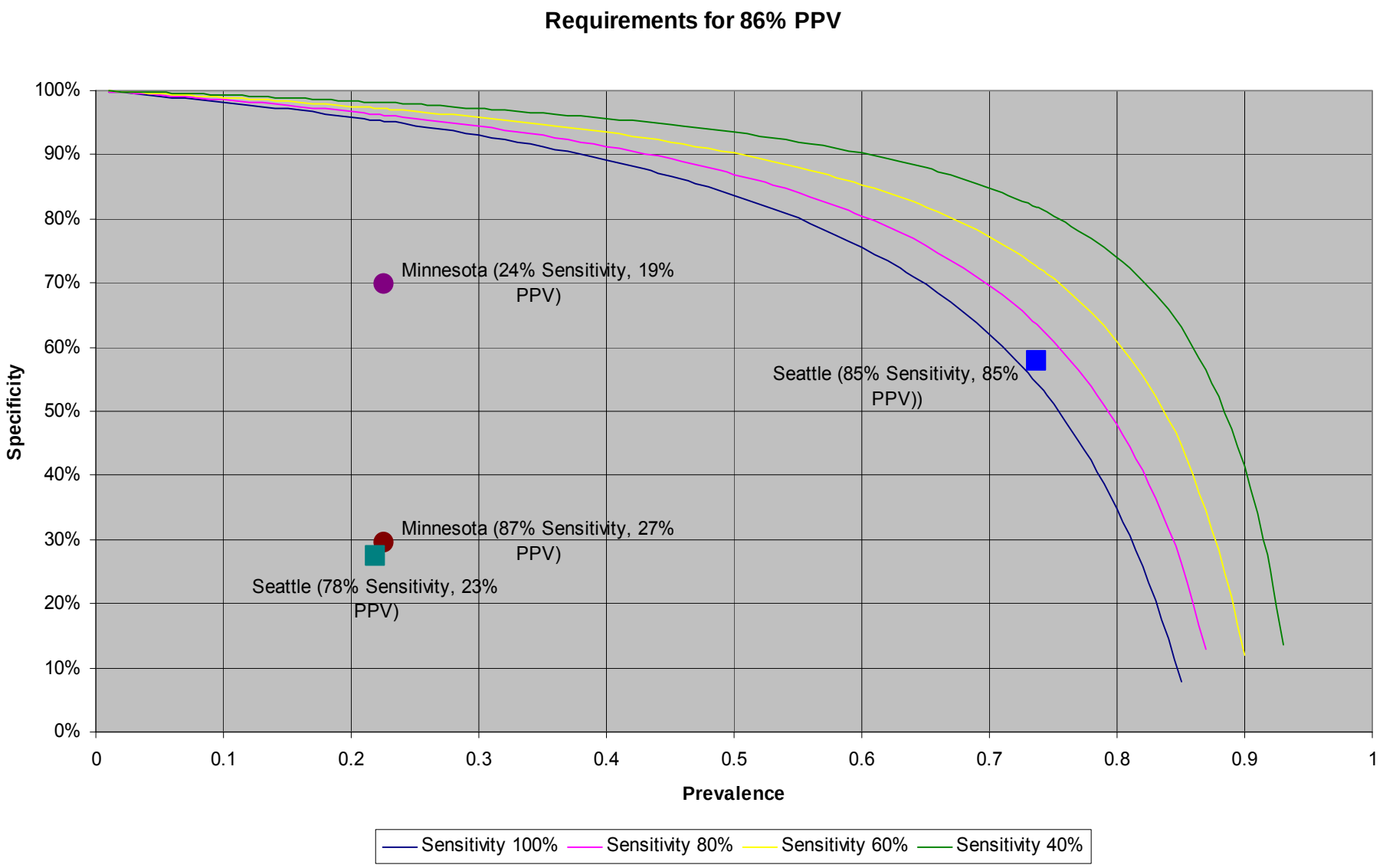
The positive likelihood ratio is

20.6

(Compared to 1.24 in Minnesota, 2.02 in Seattle)

Which requires

>95% Specificity


Requirements for 86% PPV
Specificity
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
Prevalence
Minnesota (24% Sensitivity, 19% PPV)
Seattle (85% Sensitivity, 85% PPV))
Minnesota (87% Sensitivity, 27% PPV)
Seattle (78% Sensitivity, 23% PPV)
Sensitivity 100%
Sensitivity 80%
Sensitivity 60%
Sensitivity 40%

ICD-9 Codes in SCD Definition

- 401.9 Unspecified Essential Hypertension
- 402 Hypertensive Heart Disease
- 410 - 414 Ischemic Heart Disease
- 425.4 Other Primary Cardiomyopathies
- 427.1 Paroxysmal Ventricular Tachycardia
- 427.4 Ventricular Fibrillation And Flutter
- 427.5 Cardiac Arrest

ICD-9 Codes in SCD Definition

- 427.8 Other Specified Cardiac Dysrhythmias
- 427.9 Cardiac Dysrhythmia, Unspecified
- 429.2 Cardiovascular Disease, Unspecified
- 429.9 Heart Disease, Unspecified
- 440.9 Generalized And Unspecified Atherosclerosis

ICD-9 Codes in SCD Definition

- 798.2 Death Occurring In Less Than 24 Hours From Onset Of Symptoms, Not Otherwise Explained
- 798.9 Death in circumstances where the body of the deceased was found and no cause could be discovered; Found dead

Interpreting the Results of the Vanderbilt Study

Estimating the Risk Ratio

We want to know:

$$\frac{\text{Sudden Cardiac Deaths (Anti - Psychotics)}}{\text{Sudden Cardiac Deaths (Comparators)}}$$

Estimating the Risk Ratio

Which is the same as:

$$\frac{\text{True Positives(AP)} + \text{False Negatives(AP)}}{\text{True Positives(C)} + \text{False Negatives(C)}}$$

Estimating the Risk Ratio

But what we measure is:

$$\frac{\text{True Positives(AP)} + \text{False Positives(AP)}}{\text{True Positives(C)} + \text{False Positives(C)}}$$

False Negatives

$$\frac{\text{True Positives(AP)} + \text{False Negatives(AP)}}{\text{True Positives(C)} + \text{False Negatives(C)}}$$

$$\text{What if } \frac{TP(AP)}{TP(C)} > 1 \text{ BUT } \frac{\text{FN(AP)}}{\text{FN(C)}} < 1\text{?}$$

Excluded Deaths

- Deaths in Nursing Homes
- Deaths in Hospitals
- Deaths < 30 days after Hospital Discharge

Could these be more common in Comparator groups?

Could these be more common in Comparator groups?

- More Hospital/Nursing Home Admissions?
- Longer stays?
- Admissions that coincide with a period of high risk for SCD?

  (Medical vs. psychiatric admission)

False Positives

$$\frac{\text{True Positives(AP)} + \text{False Positives(AP)}}{\text{True Positives(C)} + \text{False Positives(C)}}$$

$$\text{Could } \frac{\text{False Positives(AP)}}{\text{False Positives(C)}} > 1?$$

Sudden Cardiac Death or Social Isolation?

If someone dies,

Sudden Cardiac Death or Social Isolation?

and no one else is around to see it,

Sudden Cardiac Death or Social Isolation?

Would it be more likely to be classified (incorrectly) as a
sudden cardiac death?

Confounding Factors

Smoking

Antipsychotic users are

- More likely to smoke
- Likely to smoke more heavily

Less Effective Medical Care

Antipsychotic users may

- Get less non-psychiatric care
- Be less likely to have CAD symptoms or risk factors recognized or treated (or entered on claims even when recognized)
- Be less compliant with treatment for CAD risk

Conclusions

- Death certificate data are unlikely to be a reliable means of identifying sudden cardiac death
  - They may have adequate predictive value in high-risk populations, however
  - If prevalence is high, an effect should be detectable looking at total deaths; death certificate classification should be unnecessary and would be more subject to bias

Conclusions

- The findings of the Vanderbilt study could have been significantly influenced by both false positives and false negatives

Conclusions

- Confounding could also have strongly influenced the Vanderbilt results