Finding the truth: multivariable analysis and the assassination of Abraham Lincoln

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In my dream last night I went back in time to 1865, and found myself at the trial of John Wilkes Booth for the assassination of President Lincoln at Ford's Theater. While I am aware that Booth was killed while on the run, in my dream he had been captured and brought back to Washington DC for trial. While the evidence against him seemed insurmountable, there were no actual witnesses of the shooting as he had entered Lincoln's box seat from the back while Lincoln and his guests watched the show. However, a guilty verdict seemed imminent, and the crowd was ready, for the tension, anger and resentment were high.

A young Oliver Wendell Holmes was completing an eloquent speech in front of the jury.

'While it may be true that no one actually witnessed the shooting, the evidence that John Wilkes Booth is guilty is beyond reproach. We have numerous witnesses that saw him jump from Lincoln's box seat to the floor immediately after the shooting, and they found his gun on the floor of the box seat and a bullet from his gun in Lincoln's head. Members of the jury, I am convinced you will find Booth guilty. I rest my case.'

The Judge turned to Booth, who sat nervously in the witness stand, and said. 'Do you have any last comments you wish to say in your defense?'

Booth did indeed look troubled. But then the slightest smile crossed his face, and he turned to the judge and spoke softly, 'I do have one person who wishes to provide a defense. He is well learned and a medical scientist, and highly respected in the field. He is an expert of a new field called epidemiology, which is the science that allows one to assess odds, risks and causalities. For such a case as this, an epidemiologist is indispensable. I hope you agree that science should trump simple opinion.'

'Sounds interesting. Please have your 'epidemiologist' give us his argument.'

Booth nodded to an individual sitting not far from me, and the man, dressed in a dark suit and holding his medical bag, rushed up to the front and faced the jury.

'Members of the jury, let me explain. We have identified three bits of evidence. First, John Wilkes Booth was seen jumping from the box seat to the theater floor immediately after the shooting. Second, we have a gun found on the floor of the box seat. Third, we have a bullet found in Lincoln's head. Do we all agree?'

Many of the jury nodded in approval.

'Clearly all three observations are associated with the assassination. In epidemiology we call these risk factors. However, a key question is whether they are independent of each other. Now I have used a sophisticated technique termed multivariable analysis. Using this approach, I can show that neither the gun nor the fact that John Wilkes Booth jumped from the box seat immediately after the shooting are independent of the bullet in Lincoln's head in causing the death of Lincoln. Furthermore, when I control for the bullet and gun, the presence of John Wilkes Booth in Ford's Theater is associated with a decreased risk for Lincoln's death. I am not sure why, but I guess it correlates

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with his frequent presence on stage, and for some unclear reason when he is on stage, there is a decreased risk for Lincoln to die.'

'Thus, it should be obvious that John Wilkes Booth is not an 'independent' risk factor for Lincoln's death and that the presence of Booth in Ford's Theater is actually associated with a lower risk for Lincoln's death. Thus, there is only one reasonable conclusion, and that is the real assassin must still be at large. '

The room was silent. Holmes looked perplexed, the judge was speechless, and the jury appeared dazed.

'There are three kinds of lies; lies, damned lies, and statistics,' said a man next to me, who looked a bit like a writer.

I woke up at this point, and realised the problem, which is already known by many, but which is worth repeating.

The problem is not with the statistics, but with the interpretation.

When one performs multivariable analysis, one is determining whether the risk factors are linked with each other or whether they are independent. Unfortunately, it is common for many authors, editors and readers to think that a factor must be independent to be causal, and some journals only focus on whether a risk factor is independent in order to view it as clinically important, and do not even show the univariate findings.

However, it is important to recognise that risk factors may be causally linked, in which case they will probably not be independent of each other. Sometimes it is readily evident that the two risk factors engage a common causal pathway, such as demonstrated here. In contrast, in some cases it may not be obvious that two factors could be involved in the same causal pathway, leading the reader to expect they should be independent of each other when in fact they are not. This is especially true if one is evaluating risk factors for which it is not fully known how they might contribute to the outcome. Unfortunately, this latter situation is extremely common.

So remember, when reading a scientific paper, the key question is whether there is an association, so the univariate relationship is the most important result. The question of whether it is independent of other risk factors only addresses whether it is linked with another factor, and says nothing about causality.

Next time you read a study that interprets independence as causality, remember the trial of John Wilkes Booth. (1)

