PROJECT

Article subject: Risks of vaccinations

Title of article "One in a thousand chance"

8

Presented to

Professor James Hanley

Principles of Inferential Statistics

513-607A

McGill University

December 18 2001

QUESTION 1

Suppose an estimated 35% of children would get measles within 2 years if none would be vaccinated. Draw a detailed tree diagram describing the information presented in the 1st paragraph. Include "death" and "disabled" and use your judgment to fill in missing data.

QUESTION 2

Given a population of 1 million children and that none of them were vaccinated

a) **What would be the estimated number of deaths secondary to measles?**
b) **Give an exact number of children that became disabled secondary to measles (or its complications)**

QUESTION 3

As mentioned in the last part of the 1st column," the vaccines only work 85% to 90% of the time". Estimate how many deaths secondary to measles would have been prevented if all that population would have been vaccinated.

QUESTION 4

Using your answers to question 2a) and 2b), find the estimated probability of deaths or disability secondary to measles in an unvaccinated population of 1 million children. Find the relative risk in comparison with the estimated probability of "a more serious problem" (2nd column) in an similar population where 1 million children would have been vaccinated.

QUESTION 5

If 2 SRS of n_1=15 000 n_2=15 000

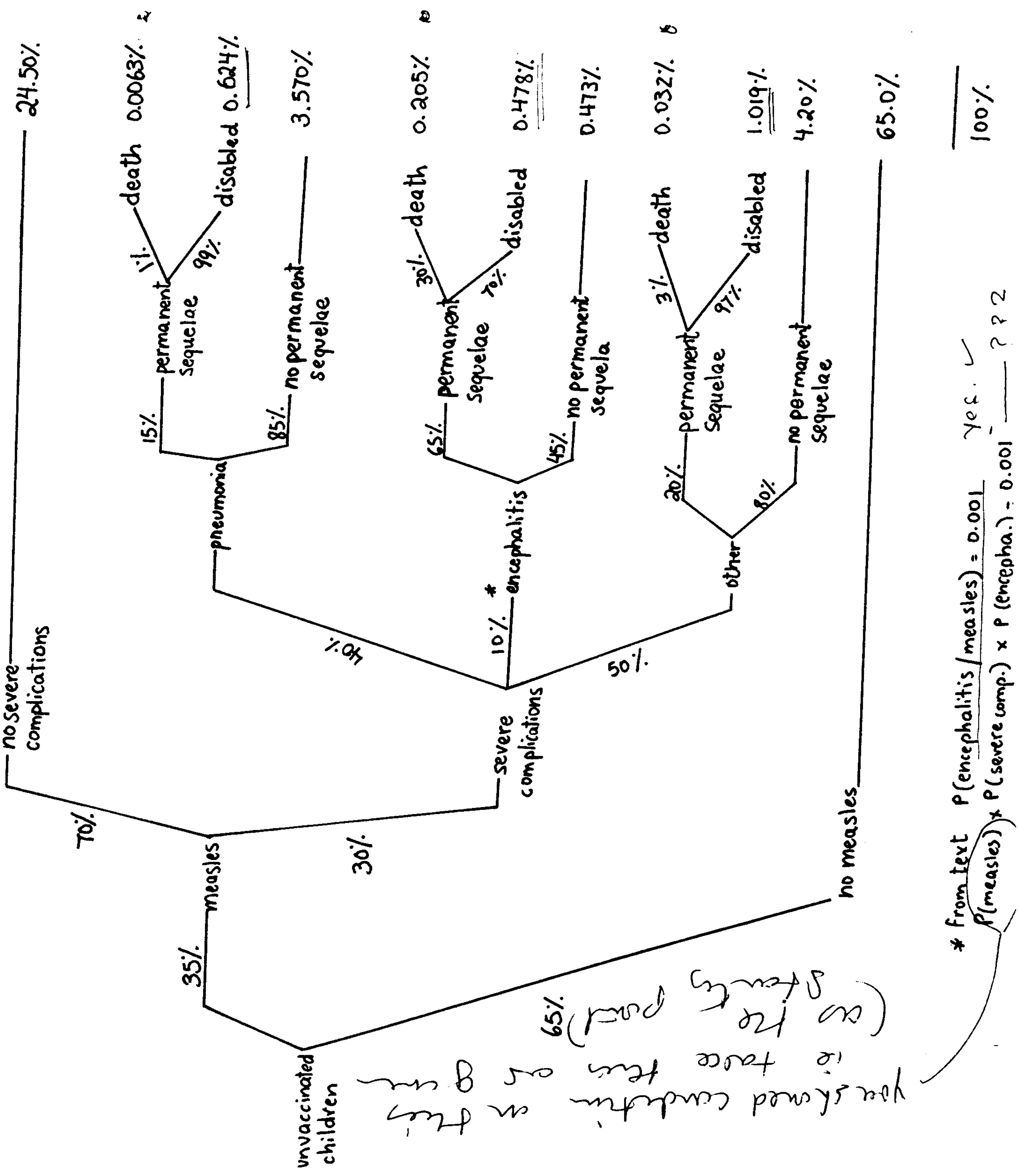
Do a significance test of the difference between the probability of getting encephalitis following measles and the probability of getting encephalitis following mumps.

QUESTION 6

Another study proposes to use SRS of n_1=250 n_2=250 to look at the differences in the probability of encephalitis following measles vs following mumps. They think that a 1% difference would be clinically relevant. Give your advice.

QUESTION 1

Suppose an estimated 35% of children would get measles within 2 years if none would be vaccinated. Draw a detailed tree diagram describing the information presented in the 1st paragraph. Include "death" and "disabled" and use your judgment to fill in missing data.



Q 1. I don't get same #s

(1) 4-5% of those who get measles get pneumonia

Your Percentage is

30% × 40% = 12%

↑
Severe

(2) 1 in 1000 who get Measles develops encephalitis (text)

From your diagram, and STARTING with measles as a given, I get

30% × 10% = 3%

not the 1/1000 the text speaks of

So I think you are 3 x high for pneumonia
30 x high for Encephalitis

Since most of your deaths come via the encephalitis route, the 30 x overestimation makes a huge difference.

QUESTION 2

Given a population of 1 million children and that none of them were vaccinated

a) What would be the estimated number of deaths secondary to measles

Answer: Depending on your invented probabilities your answer will differ. Multiply the probabilities along each branch ending with death outcome by 1 million and add the results. Using my tree you obtain:

*1 million *(probability of dying of pneumonia secondary to measles + probability of dying of encephalitis secondary to measles + probability of dying of other secondary conditions due to measles) =*

*1 million ((35% * 30% * 40% * 15% * 1%) + (35% * 30% * 10% * 65% * 30%) +(35% * 30% * 50% * 20% * 3%))*

*= 1 million * (0.0063% + 0.205% +0.032%) = 1000 000 *0.2433%= 2433 deaths*

b) Give an exact number of children that became disabled secondary to measles (or its complications)

*Answer: Using the same principle of multiplying the total probability of handicapped secondary to measles by 1 million we get an estimated 21 210 children (0.02121 * 1 million). The true value could be determined by this lovely situation where we would completely stop vaccination during many years and then if any researchers are still alive they could calculate exactly how many of 1 million children would have become disabled secondary to measles!!! By that time, even if our initial probability of 35% (getting measles) would have been realistic, after a few years of epidemic infections it would probably have increased dramatically. To get a more realistic number, we could look up past data on the incidence of measles when vaccination did not exist. However, the death and handicapped probabilities would not have been applicable to today since health services have greatly improved in terms of death and disability prevention.*

Conclusion, the number of children that would become disabled following measles is an estimation based on invented probabilities.

My quick check

up front, now $87\frac{1}{2}\%$ protected

other $12\frac{1}{2}\%$ subject to $\frac{15\%}{35\%}$ value than

So it's ~~[illegible]~~ effects

$\frac{1}{8} \times \frac{4}{7} = \frac{1}{14}$.

$\frac{1}{14}$ of 2433

herd immunity is probably even stronger than that

QUESTION 3

As mentioned in the last part of the 1st column," the vaccines only work 85% to 90% of the time". Estimate how many deaths secondary to measles would have been prevented if all that population would have been vaccinated.

Answer:

85% - 90% of the million vaccinated children would have been protected, a range of 850 000 to 900 000 . Therefore 100 000 to 150 000 could still get infected. Lets assume that these unprotected children would now have a probability of 15% of getting infected (because much less people can get infected and transmit it to others). 15% of 100 000 = 1 500

15% of 150 000= 2250

*100 000 ((15% * 30% * 40% * 15% * 1%) + (15% * 30% * 10% * 65% * 30%) +(15% * 30% * 50% * 20% * 3%))=*

*100 000*0.00104= 104 deaths*

*150 000 *0.00104= 156 deaths*

Estimated deaths given vaccinated : from 104 to 156.

Estimated deaths given not vaccinated: 2433

2433 – 104= 2329 2433-156=2277

Again, I think you overshoot everywhere

An estimated 2277 to 2329 deaths would have been prevented if the whole population would have been vaccinated. (Again this is only an estimation using our invented probabilities).

QUESTION 4

Using your answers to question 2a) and 2b), find the estimated probability of deaths or disability secondary to measles in an unvaccinated population of 1 million children. Find the relative risk in comparison with the estimated probability of "a more serious problem" (2nd column) in an similar population where 1 million children would have been vaccinated.

Answer:

We are assuming the "more serious problem" is the same as death or disability.

Because of measles:

Probability of death or disability = probability of death + probability of disability

= 2433 / 1 million + 21 210 / 1 million

= 0.002433 + 0.02121 = 0.02364

Because of vaccination:

Probability of a more serious problem: 1 / 1000 to 1 / 1million or 0.001 to 0.000001

Relative risk:

$\hat{p}_1 / \hat{p}_2 =$ *0.02364 / 0.001 = 23.64*

$\hat{p}_1 / \hat{p}_2 =$ *0.02364 / 0.000001 = 23 640*

The estimated risk of a serious problem following measles is from 24 to 24 000 times higher for unvaccinated children than the risk of a serious problem resulting from the vaccination per se.

QUESTION 5

If 2 SRS of n_1=15 000 n_2=15 000

Do a significance test of the difference between the probability of getting encephalitis following measles and the probability of getting encephalitis following mumps.

Answer:

Ho: p1=p2 *Ha: p1=p2*

probability of encephalitis given measles: 1 / 1000 = 0.001 = $\hat{p}_2$

probability of encephalitis given mumps: 1 / 400 = 0.0025 = $\hat{p}_1$

averaged probability: (0.001 + 0.0025) / 2 = 0.00175

SE_d *= sqrt (*$\hat{p}$ *(1-*$\hat{p}$*) * (1 / n_1 + 1 / n_2)) = sqrt ((0.00175 * 0.99825) * (1 / 15 000 + 1 / 15 000))*

= 0.000483

$z = \hat{p}_1 - \hat{p}_2 / SE_d$ *= 0.0025-0.001 / 0.000483 = 3.106*

2P (z ≥ 3.106) = 0.0018

There is strong evidence that there is a difference in the probability of getting encephalitis from measles and getting encephalitis from mumps.

QUESTION 6

Another study proposes to use SRS of n_1=250 n_2=250 to look at the differences in the probability of encephalitis following measles vs following mumps. They think that a 1% difference would be clinically relevant. Give your advice.

Answer:

The sample sizes are a little too small to detect that 1% difference in proportions.

n per group = 2 (Z α/2 –Z β)^2 (sqrt(π̄(1- π̄)) / Δ)^2 if α=0.05 and 80% power

= 2 (1.96 + 0.84)^2 (sqrt (0.00175 0.99825) / 0.01)^2*

= 273.92 About 275 children would be needed to detect a 1% difference..

Give of where your start for your probs

IMAGINATIVE USE
OF NEWSPAPER ARTICLE.

pity the inputs were off
by an order of magnitude
& more —
(unless I missed something)

Like more realistic inputs, ~~[illegible]~~
I would have given this ~~[illegible]~~ 9/10.
(I've been giving 6 for
7 for average
8 for good (a few)
9 (exceptional)

~~but [illegible] nice~~

1

A child with polio is confined to an iron lung in this 1954 photo. Vaccines have almost wiped out what was once a childhood killer.

One in a thousand chance

VACCINES

Continued from Page D1

"But if you look at the statistics, in the range of 4% to 5% of people who get measles will get pneumonia, severe enough to be hospitalized. And if you think of 350,000 or so cases of measles over a period of years, then you're talking about a substantial numbers of cases of pneumonia."

Worse, one in 1,000 people who get measles suffers a serious brain infection called encephalitis. So does one in 400 people with mumps, and one in 1,000 who get chickenpox. These infections can lead to permanent brain or nerve damage, including deafness and facial paralysis. Some cases are fatal.

While diseases like diphtheria and polio have all but disappeared in Canada, they can return quickly. "Disease knows no borders," says King.

For example, visitors to Canada caused outbreaks of measles recently in religious communities in Alberta and Quebec. In Manitoba, a rubella (German measles) outbreak occurred in 1997, with cases rising to 3,991 from 237 in 1996. The disease is particularly serious for pregnant women because it causes brain damage in fetuses. In British Columbia, rave parties were blamed for an outbreak of mumps among young adults in 1997.

King stresses that vaccines protect more than the individual child getting the needle. There are children who have egg allergies or other conditions and cannot tolerate certain vaccines (some vaccines are grown in an egg medium). And vaccines only work about 85% to 90% of the time. So if one infected child brings measles into a school, up to 15% of vaccinated students and the sprinkling of those who cannot be vaccinated could get infected.

"We have a responsibility, in my opinion, to provide a protective cushion around those individuals by having as many people around them immunized as possible — we call that herd immunity," says King.

According to immunization experts, most side effects to vaccines are no more serious than a sore arm or mild fever, which can be controlled by taking acetaminophen before or after the shot. But in a few cases — ranging from one in 1,000 to one in a million — children suffer a more serious problem. This can include hypo- or hypersensitivy, which are forms of allergic reactions, and even anaphylactic shock.

"Vaccines are never going to be 100% safe," says King. "There will always be some small risk involved. But what we're saying is, the risk is a fraction of what you'd face with the infectious diseases you're vaccinating against."

Historically, vaccines were deliberately made from substances that cause disease. For example, early typhoid vaccine was made from the excrement of typhoid patients. Pertussis (whooping cough) vaccine came from the mucous of infected children. These crude extracts contained the bacterial cells or toxins that triggered an immune response, but they also contained impurities that caused serious side effects, including fatal allergic reactions. And some versions of polio vaccine in the 1960s were tainted with cancer cells.

Today, advances in cell biology have made vaccines that are much "cleaner" and safer. "We can now slice a bacterium or virus apart, putting only the protective bits into vaccines, and discard the rest," says Dr. Luis Barreto, a senior official with Pasteur Mérieux Connaught, the vaccine manufacturer.

What about mercury? Thimerosal, a preservative containing mercury, helps prevent bacterial contamination when a vaccine vial is opened. But virtually none of the vaccines sold for infants in Canada, including Pentacel, the most widely used, contain any mercury at all.

Many parents also worry that a child's immature immune system can be overwhelmed by being bombarded with so many vaccines. This concern is sharply dismissed by experts. "We are bombarded with thousands and millions of foreign antigens every day of our lives and we're coping with those just fine," says King.

Numerous studies have shown that giving combinations of vaccines at the same time is not only safe, it may be more practical, since it means fewer visits to a doctor's office. Doctors don't like giving multiple shots because children cry or scream blue murder at the prospect of a second needle.

If vaccines are so safe, why are so many people skeptical? The backlash against immunization began in Britain and the United States, initiated by a handful of critics who say vaccines damaged their children.

One of the most prominent is Barbara Loe Fisher, a U.S. mother whose oldest son was a bright, precocious infant until he got his fourth diphtheria-pertussis-tetanus (DPT) shot at 18 months. Since then, the boy has struggled with neurological problems, she says. The experience prompted Loe Fisher to found the U.S.-based National Vaccine Information Center, now a powerful voice among vaccine skeptics.

'THE RISK IS A FRACTION OF WHAT YOU'D FACE WITH THE INFECTIOUS DISEASE'

"What we're having here in this country is control of childhood infectious diseases but [also] an explosion of chronic disease and disability," she says. "Our special-education classrooms are filled with children with brain and immune-system damage. In the last two decades we've had a doubling of learning disabilities, a doubling of AD/HD, a doubling of asthma, a tripling of diabetes, and autism now affects one in 150 children. What we're saying is that science and medicine have not given us an adequate explanation; in fact, they've given us no explanation as to what's happening to our children. What we're saying is, let's examine what we do to every child. And vaccination is one of those things, in ever-increasing numbers and doses."

Loe Fisher's organization is pushing for biological studies that examine the effects of vaccines on children's brains, which develop quickly during the first three years of life — the period when most kids get all their shots. "We think that there may be genetic differences between children and their responses to vaccines," she says. "So what we're criticizing is the one-size-fits-all approach with vaccines."

Perhaps the best known theory of this kind comes from a British report linking autism to the measles, mumps and rubella (MMR) vaccine. The 1998 case study of 12 infants suggested the MMR vaccine causes irritable bowel syndrome, which is linked to autism. The article, published in the British medical journal *The Lancet*, caused worldwide headlines.

Subsequent population studies in England and elsewhere have shown no big increase in the rate of autism since the MMR vaccine was introduced in 1988, but the damage in perception may take years to dispel.

"Anyone can make an allegation," says Halperin, who co-ordinates a Canadian program that monitors the adverse effects of vaccines. "It takes a long time to prove it's not true."

Halperin says most children are diagnosed with autism at 12 to 14 months, the age when they normally learn to speak. Coincidentally, it's also the age they get the MMR vaccination. "Parents have a child with autism, and they want to know why," Halperin says. "They link it to vaccination as a possible cause."

While public health officials find the vaccine critics a bother, such groups have been catalysts for vaccine improvements. Today, the National Vaccine Information Center and its allies are credited with helping to accelerate the development of a new form of pertussis vaccine, engineered to cause fewer side effects.

Since the Canadian introduction of this new vaccine in 1997, Halperin said pediatric hospitals report an 80% drop in the rate of febrile seizures after an inoculation, a huge improvement over the old formula. Ironically for the critics, these safety improvements will lead to more vaccines, since safer products mean their benefits outweigh the potential dangers.

"We are going to see vaccines for many more diseases," predicts King.

National Post