MEASURE ASSOCIATION

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Learning objectives

- Be able to construct a 2x2 table for summarizing epidemiologic data.
- Be able to explain how to compare the incidence of disease in two or more groups.
- Be able to define, calculate, and interpret:
  - *relative risk*
  - *attributable risk (risk difference)*
  - *attributable risk percent (the attributable proportion)*
  - *odds ratio*
- Be able to demonstrate the uses of these measures of association.
- Be able to explain what is meant by a "reference group"

Look For Association By Making Comparisons

- Cohort
- Case-Control
- Clinical Trial

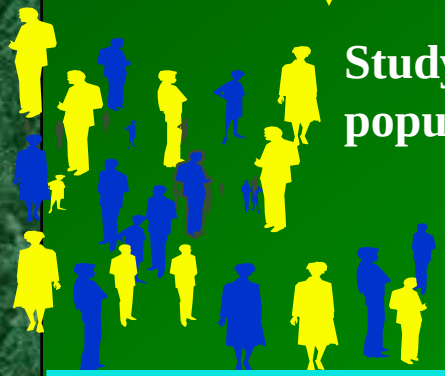
All three types of analytical studies rely on a ***comparison of groups*** to determine whether there is an **association**.

Testing Whether a Factor Causes Disease

Target Population

Inference: factor is associated with disease in *this* population

Sample



Study population

Assess Validity

True?
Alternate explanation?

- Collect data
- Compare frequency

Is there an association?

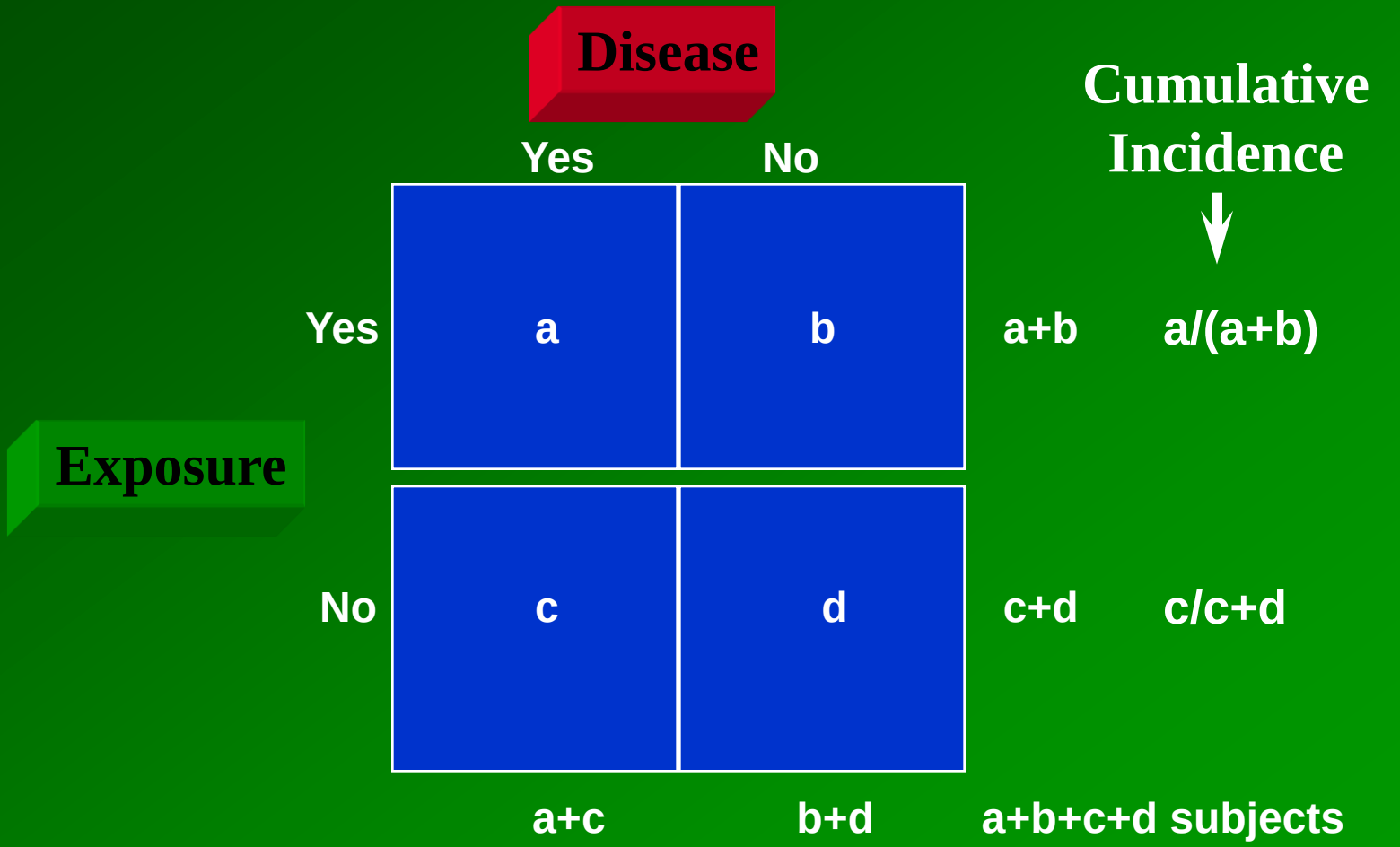
Options For Comparing Incidence

1) Calculate the *ratio* of the incidences for the two groups. (*Divide incidence in exposed group by the incidence in the control group*).

or

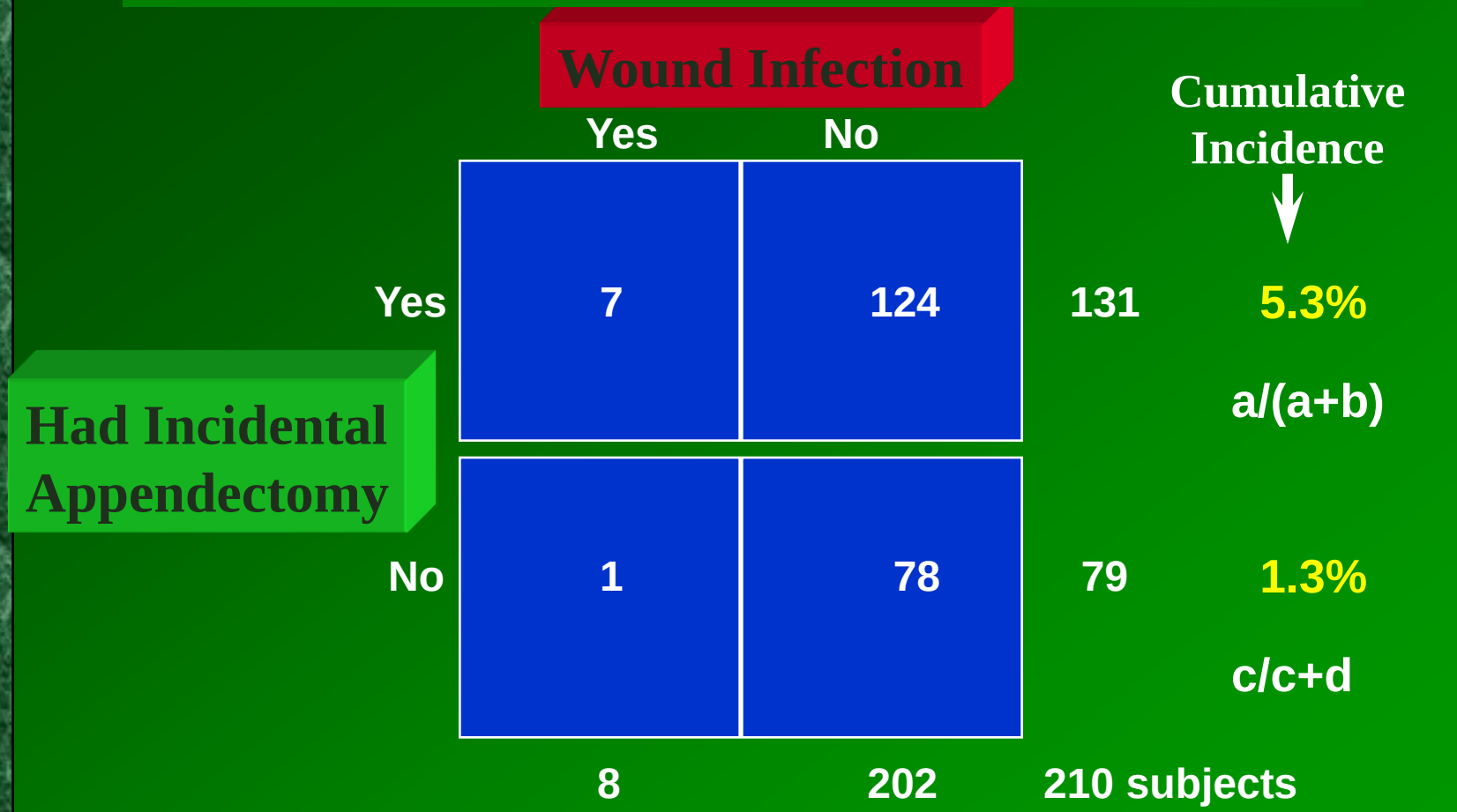
2) Calculate the *difference* in incidence between the two groups. (*Subtract incidence in control group from the incidence in the exposed group*).

Data Summary for Cumulative Incidence



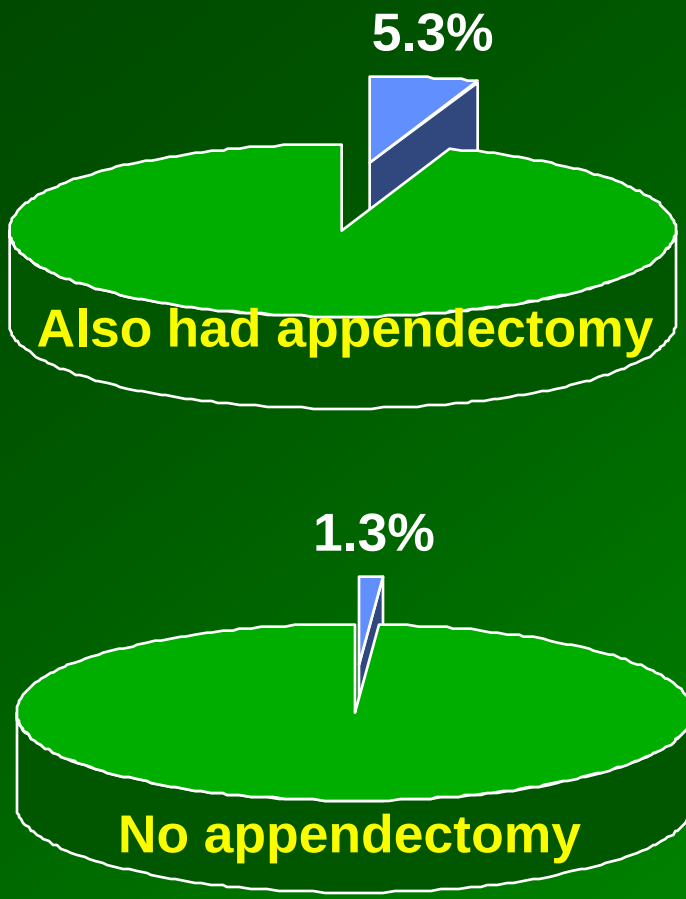
Your conclusion about association depends on a comparison of the frequency of disease (infection)

Measuring Association with Relative Risk



$$RR = \frac{7/131}{1/79} = \frac{5.3}{1.3} = 4.2$$

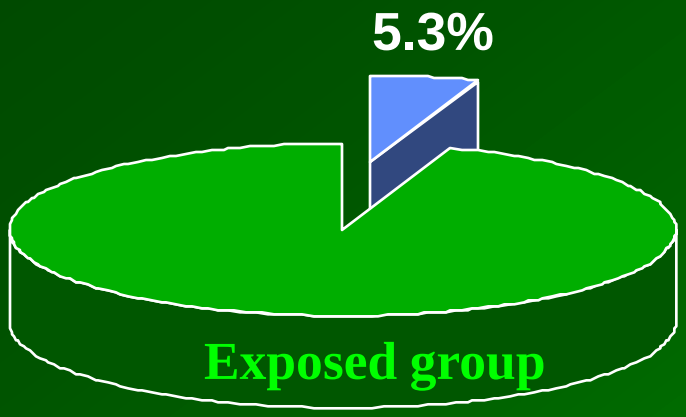
Relative Risk in Appendectomy Study

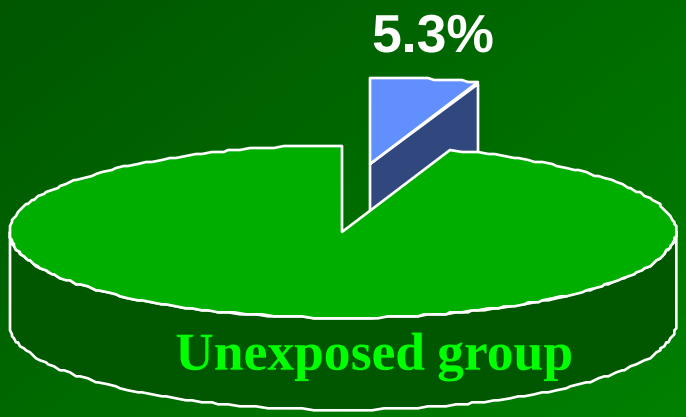


$$RR = \frac{5.3\%}{1.3\%} = 4.2$$

Interpretation: "In this study the risk of wound infection was 4.2 times greater in patients who had incidental appendectomy compared to those who did not have appendectomy."

What If Relative Risk = 1.0 ?

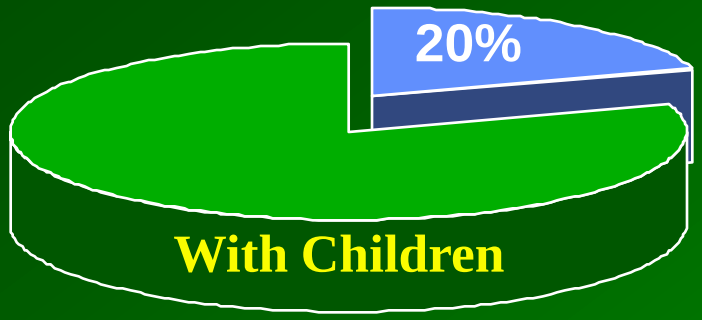


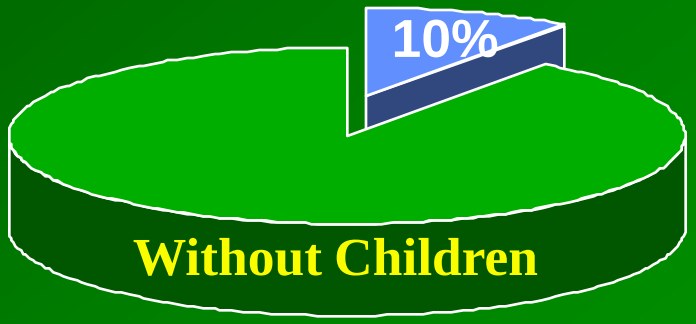


$$RR = \frac{5.3\%}{5.3\%} = 1.0$$

No difference.
Therefore, no association.

Incidence of Colds in Students Living With Children vs. Without Children





Relative Risk = $\frac{20\%}{10\%} = \frac{20\%}{10\%} = 2.0$

"In this study students who lived with small children had 2 times the risk of getting a cold compared to students who did not live with small children."

What If Relative Risk < 1.0 ?

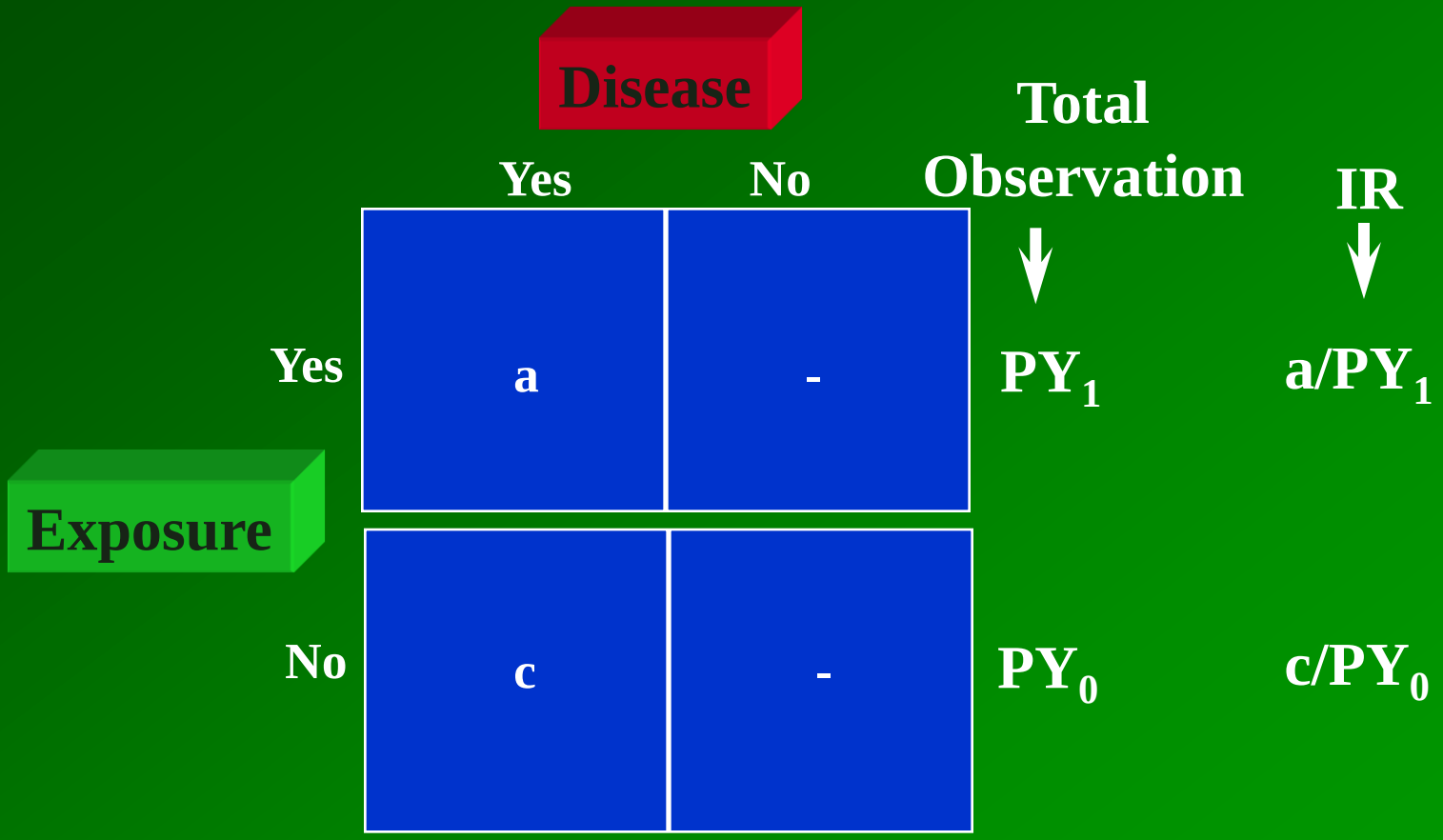
Aspirin Use	Myocardial Infarction: Yes	Myocardial Infarction: No	
Yes	139	10,898	11,037 exposed
No	239	10,795	11,034 not exposed
	378	21,693	22,071 subjects

$I_{exposed} = 139/11,037 = .0126$

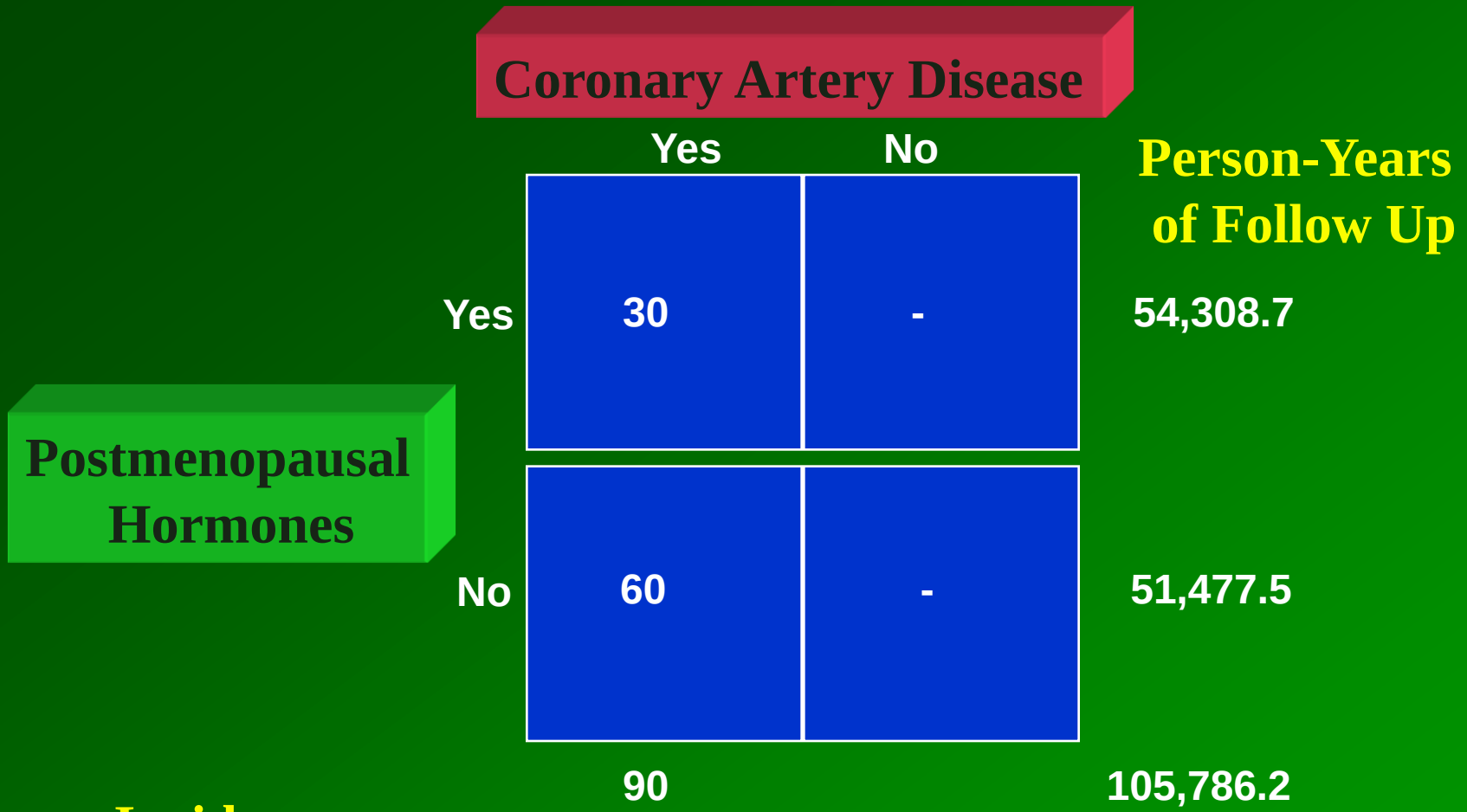
$I_{unexposed} = 239/11034 = .0221$

$RR = \frac{.0126}{.0221} = 0.55$

Data Summary for Incidence Rate



$$\text{Relative risk} = \frac{a/PY_1}{c/PY_0}$$



Incidence

In treated group = 30 / 54,308.7 = 55.2 / 100,000 P-Yrs

In untreated group = 60 / 51,477.5 = 116.6 / 100,000 P-Yrs

$$\text{Relative Risk} = \frac{55.2 \text{ /100,000 P-Yr.}}{116.6 \text{ /100,000 P-Yr.}} = \frac{55.2}{116.6} = 0.47$$

Postmenopausal Hormones	Incidence
Yes	30 / 54,308.7 = 55.2 / 100,000 P-Yrs
No	60 / 51,477.5 = 116.6 / 100,000 P-Yrs

Relative Risk = $\frac{55.2 \text{ /100,000 P-Yr.}}{116.6 \text{ /100,000 P-Yr.}} = \frac{55.2}{116.6} = 0.47$

Interpretation:

Women using hormone replacement therapy had 0.47 times the risk of coronary disease compared to women who did not use HRT.

The Nurse's Health Study

An "r x c" Table – Multiple Rows & Columns

Obesity → ? → Non-fatal Myocardial Infarction

Quetelet Index: $\frac{\text{wgt kg}}{\text{hgt } m^2}$	# MIs (non-fatal)	person-years of observation	rate of MI per 100,000 P-Yrs (incidence)	Relative Risk
<21	41	177,356	23.1	1.0
21-23	57	194,243	29.3	1.3
23-25	56	155,717	36.0	1.6
25-29	67	148,541	45.1	2.0
>29	85	99,573	85.4	3.7

126 lb @ 5'6" = 21
175 lb @ 5'6" = 29

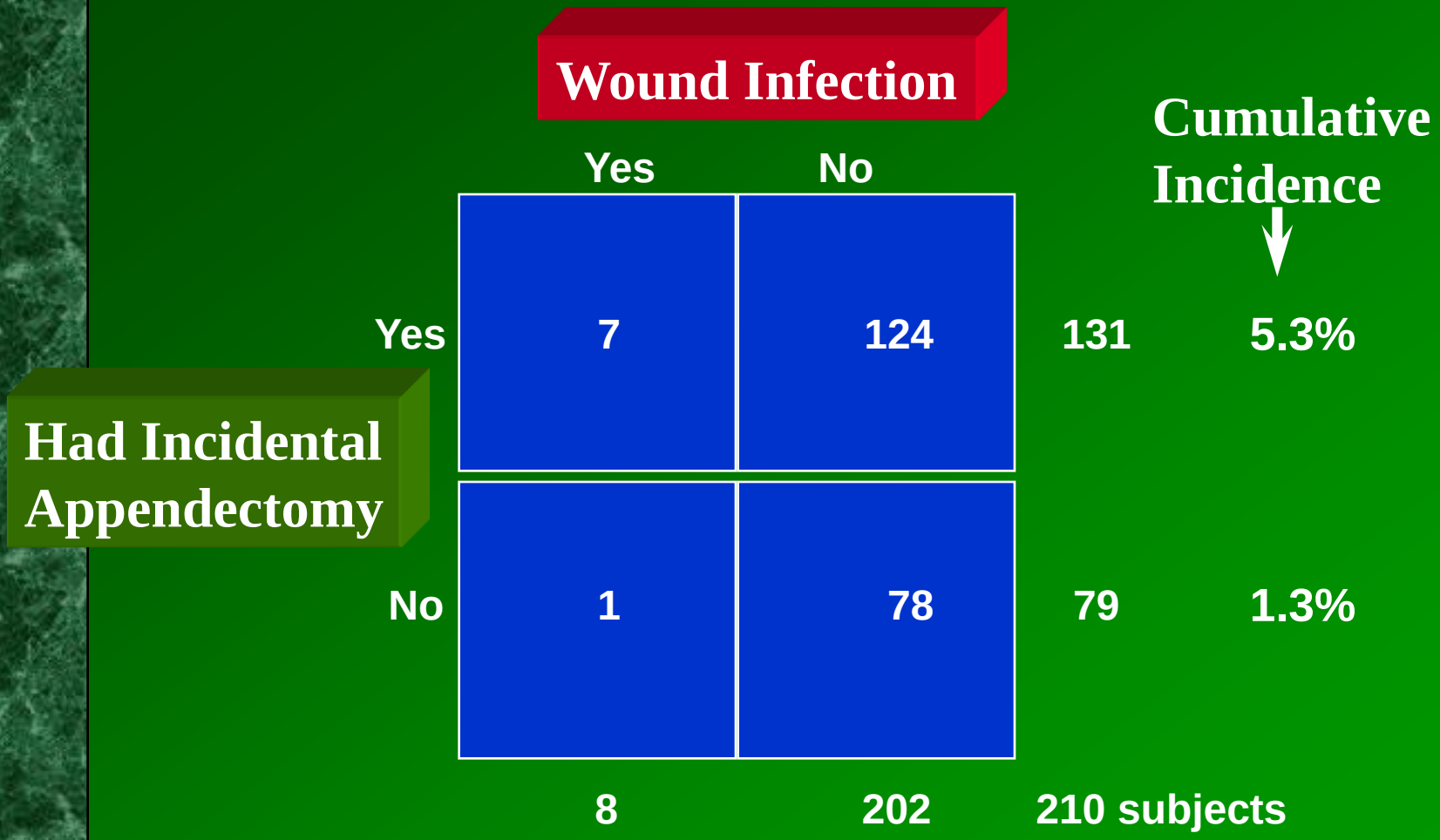
How would you interpret in words the RR= 3.7 in the heaviest group?

Attributable Risk – The Risk Difference

AR = Incidence in exposed - Incidence in unexposed

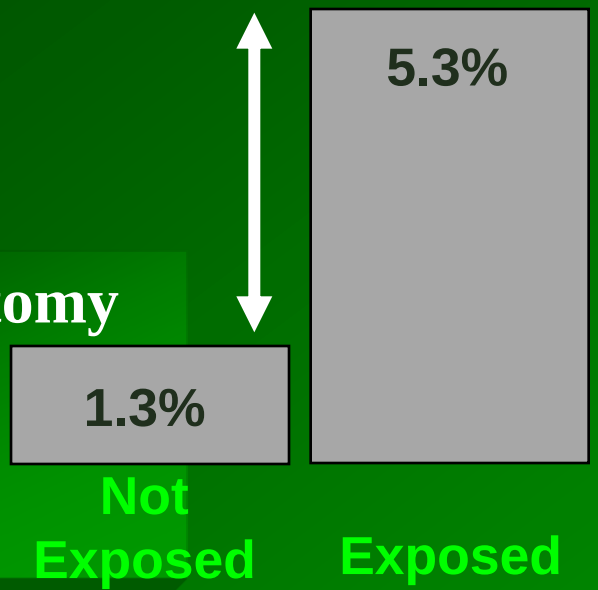
$$AR = I_e - I_0$$

Attributable Risk in Appendectomy Study



AR = 5.3% - 1.3% = 4% (4 per 100)

Attributable Risk Gives a Different Perspective on the Same Information



Even if appendectomy is not done, there is a risk of wound infection (1.3%).

But, adding an appendectomy appears to increase the risk by 4% (4 per 100), so ...

… the **AR** is the ***excess risk*** in those who have the factor, i.e., the risk of wound infection that can be ***attributed*** to having an appendectomy, assuming there is a cause-effect relationship.

Tip #1 for Interpretation of Attributable Risk – Convert % to a Decimal Fraction

Example:

Incidence with appendectomy = 5.3% = .053
Incidence with appendectomy = 1.3% = .013
Attributable Risk = .040

i.e., 4 per 100 incidental appendectomies
or 40 per 1,000

***Interpretation*:**
***In the group that underwent incidental appendectomy* there were 4 excess wound infection per 100 subjects.**

Tip #2 for Interpretation of Attributable Risk – Focus on the Increase in the Exposed Group

In the group that underwent incidental appendectomy **there were 4 excess wound infection per 100 subjects.**

or

If incidental appendectomy were performed on another 100 subjects **having staging surgery, we would expect 4 excess wound infections which could be attributed to the incidental appendectomy.**

Attributable Risk in The Nurse's Health Study

Obesity → ? → Non-fatal Myocardial Infarction

Quetelet Index: wgt kg / hgt m^2	# MIs (non-fatal)	person-years of observation	rate of MI per 100,000 P-Yrs (incidence)	Relative Risk
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Attributable Risk = 85.4/100,000 - 23.1/100,000
= 62.3 excess cases / 100,000 P-Y in the heaviest group

Interpretation

Among the heaviest women there were 62 excess cases of heart disease per 100,000 person-years of follow up that could be attributed to their excess weight.

Or

If we followed 50,000 women with BMI > 29 for 2 years we might expect 62 excess myocardial infarctions due to their weight. (Or one could prevent 62 deaths by getting them to reduce their weight.)

RR & AR
Provide Different Perspectives

- **Relative Risk: shows the *strength* of the association.**
  - **RR = 1.0 suggests no association**
  - **RR close to 1.0 suggests weak association**
  - **RR >> 1.0 or RR << 1.0 suggests a strong association**

- **Attributable Risk: a better measure of *public health impact*.**
  How much impact would prevention have?
  How many people would benefit?

A large study looked at whether a program for fecal occult blood testing (FOBT) could decrease mortality from colorectal cancer (CRC).

Relative Risk Perspective:

FOBT decreased mortality from CRC by 33% !
(RR = .67 for FOBT compared to no screening)

Attributable Risk Perspective:

FOBT decreased mortality from 9 per 1,000 people to 6 per 1,000.
So, RR= 0.67 (i.e., 0.006/0.009
BUT
The risk difference was only 3 per 1,000 people screened.

The ratio of these two numbers is more impressive than the actual difference.

Contrast RR & AR For Two Disease

	Annual Mortality per 100,000
Lung Cancer	
Cigarette smokers	140
Non-smokers	10

RR= 14
AR= 130 per 100,00

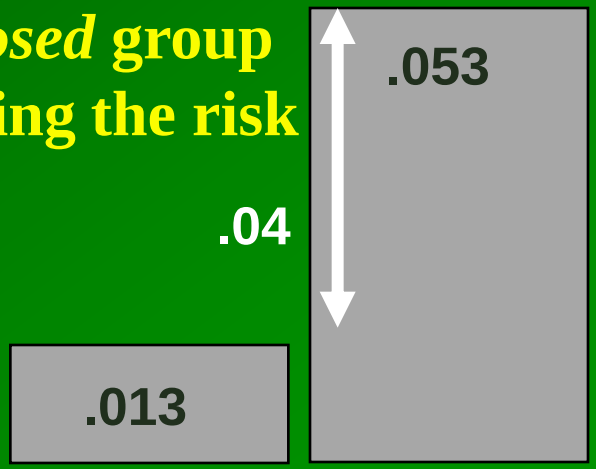
	Annual Mortality per 100,000
Coronary Heart Disease	
Cigarette smokers	669
Non-smokers	413

RR= 1.6
AR= 256 per 100,00

Attributable Risk % - The Attributable Proportion

The *proportion* (%) of disease in the exposed group that can be attributed to the exposure, i.e., the proportion of disease in the *exposed* group that could be prevented by eliminating the risk factor.

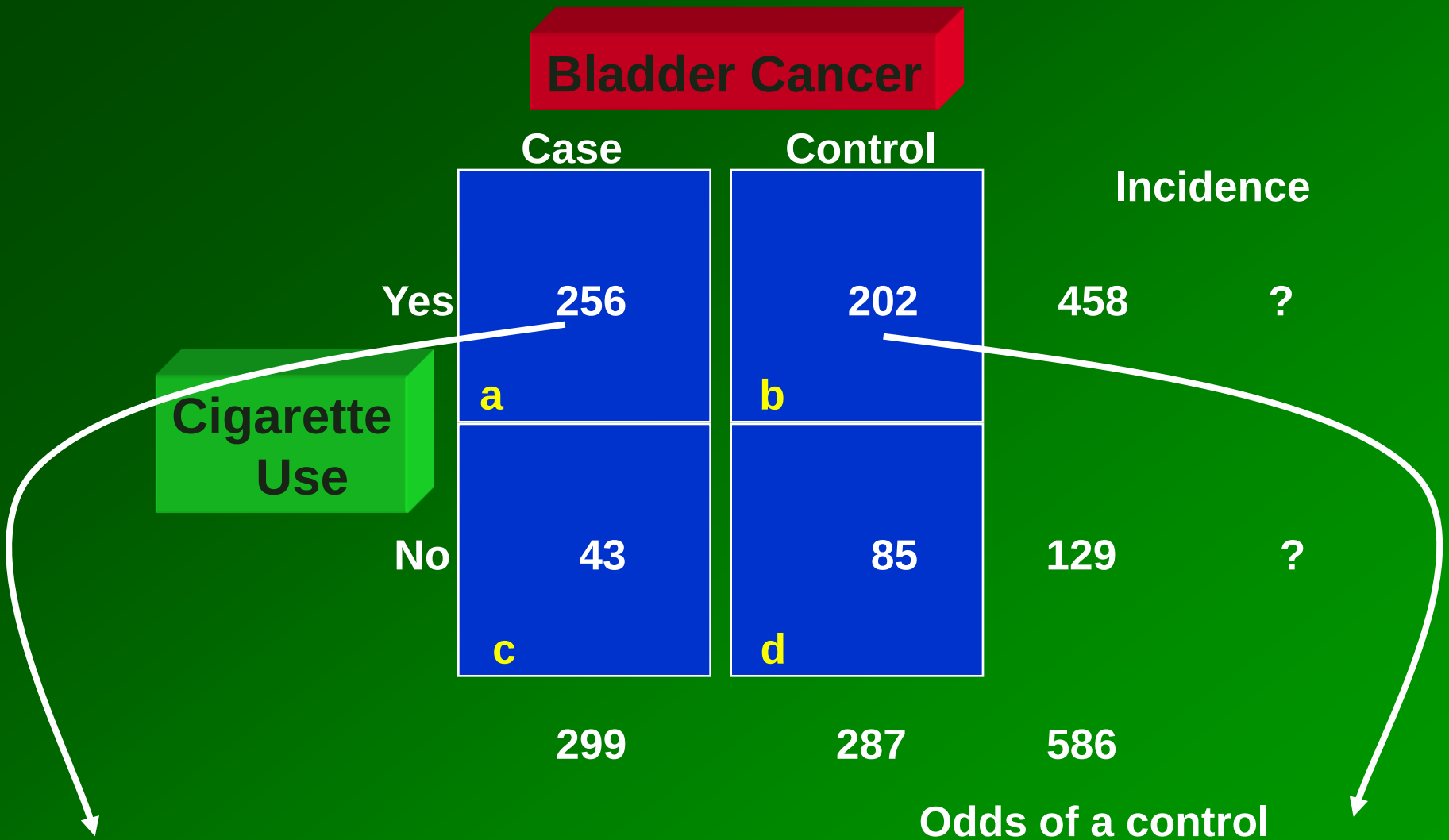
$$AR\% = \frac{AR}{I_e} \times 100$$



What % of infections in the exposed group can be attributed to having the exposure?

$$\frac{.04}{.053} \times 100 = 75\%$$

Interpretation: 75%of infections in the *exposed* group could be attributed to doing an incidental appendectomy.



$$\text{Odds Ratio} = \frac{a/c}{b/d} = \frac{ad}{bc} = \frac{256/43}{202/85} = 2.5$$

The Odds Ratio Is Interpreted Just Like Relative Risk

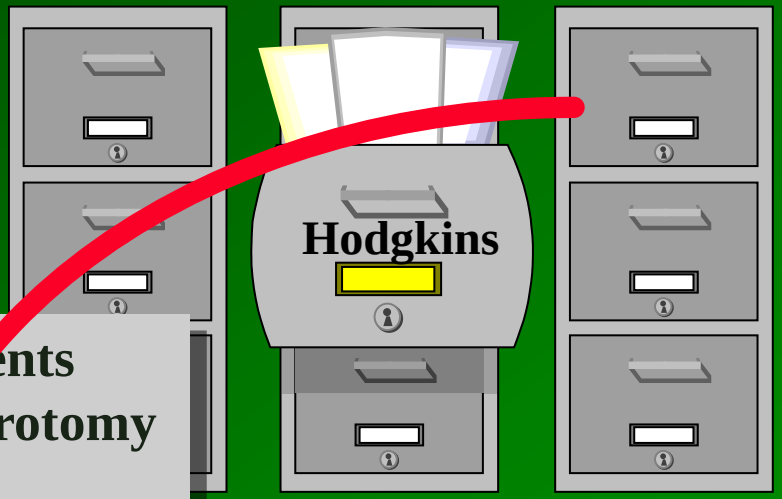
Example:

Smoking and bladder cancer; Odds Ratio = 2.5:

"In this study individuals who smoked had 2.5 times the risk of bladder cancer compared to those who did not smoke."

An Odds Ratio is usually a legitimate estimate of Relative Risk.

Cohort Study or Case-Control Study
RR or OR

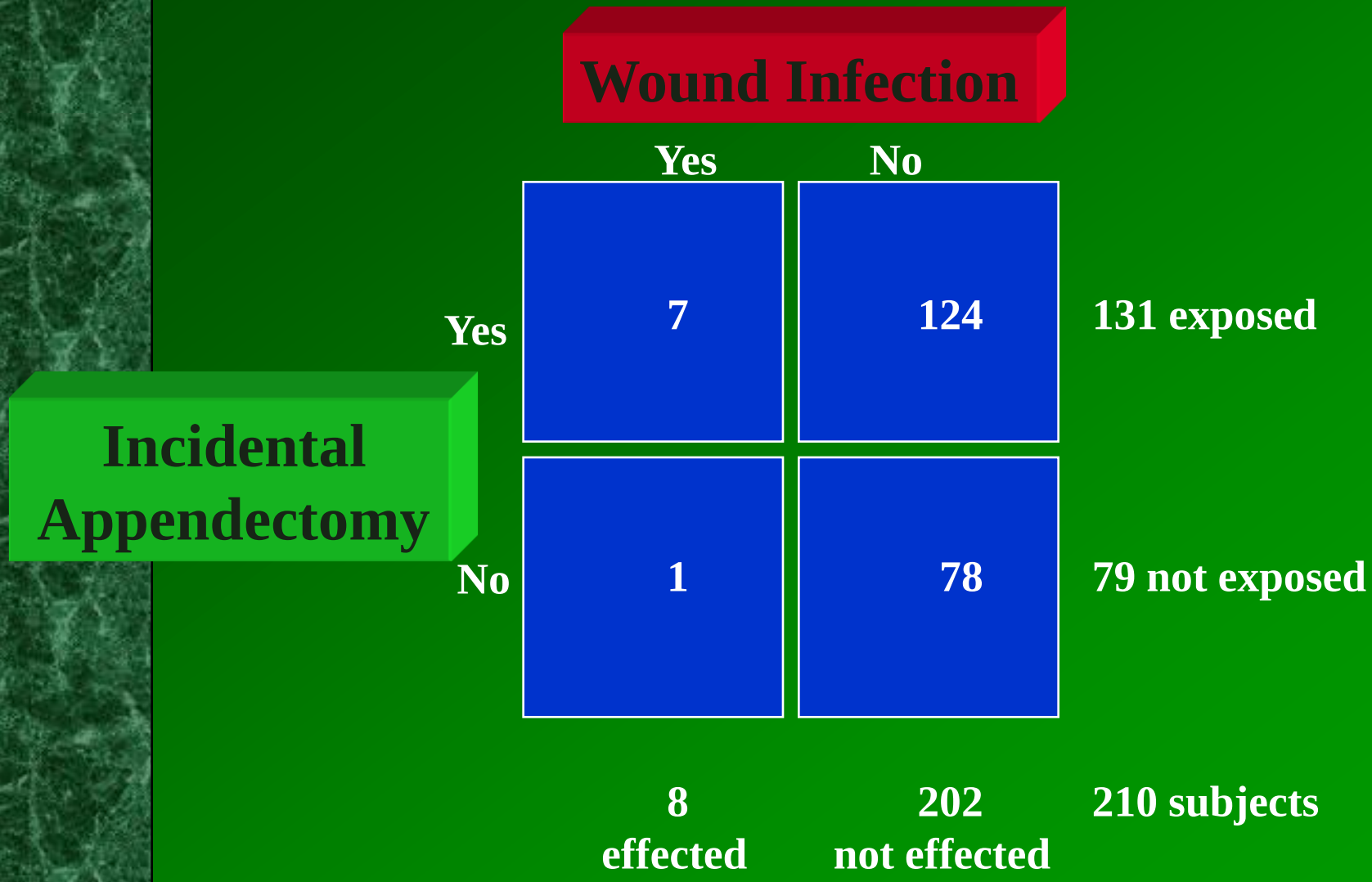


Review Records of Patients
Who Had Staging Laparotomy
for Hodgkins Disease

Sort into 4 piles:

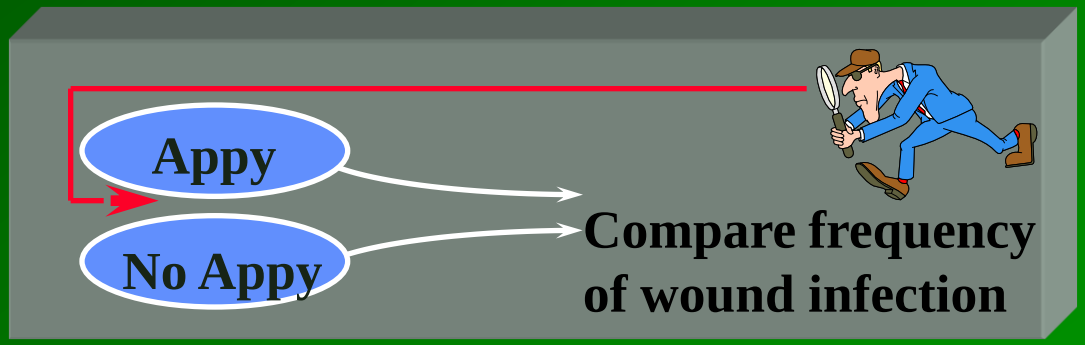
1) Appendectomy / No wound infection
2) Appendectomy / With wound infection
3) No appendectomy / No wound infection
4) No appendectomy / With wound infection

Results of the Record Review



Viewed as a Retrospective Cohort Study By Comparing:

Those Who Had Appendectomy to Those Who Did Not

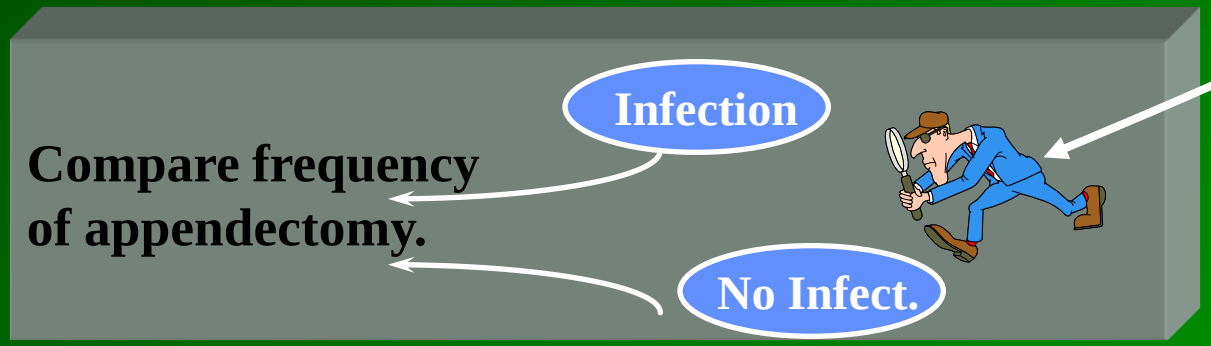


	Wound Infection: Yes	Wound Infection: No	Incidence
Appy	7	124	7 / 131 = 5.3%
vs.			
No Appy	1	78	1 / 79 = 1.3%

Relative Risk = 4.2

Viewed as a Case-Control Study By Comparing:

Patients With Infections to
Patients Without Infections



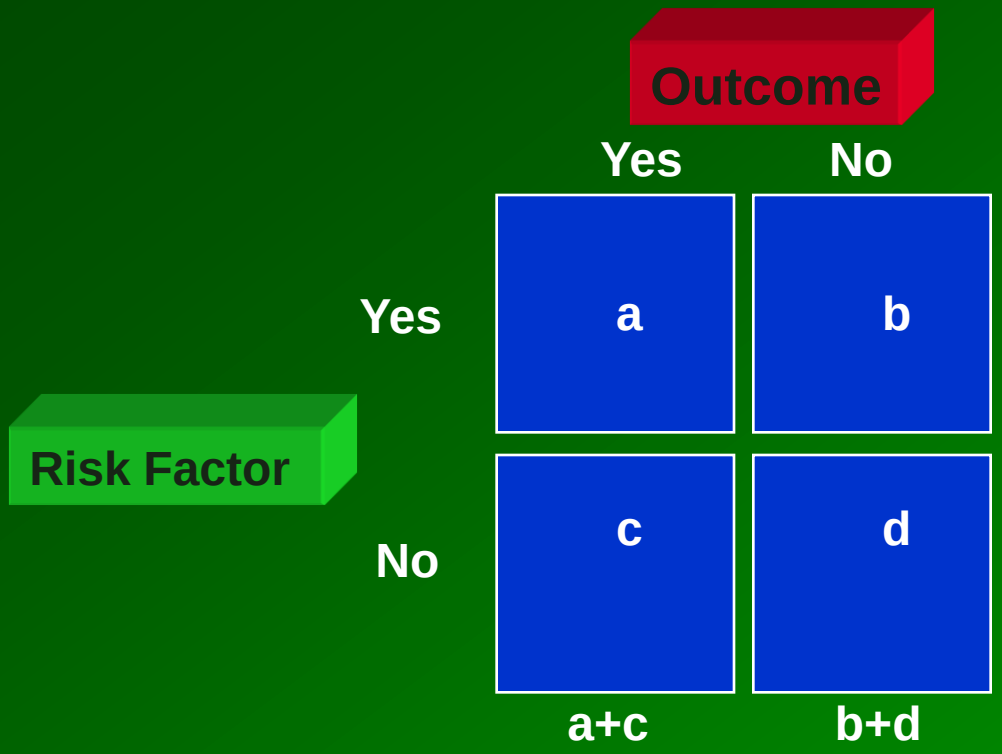
	Infection	No Infect.
Appy	7	124
No Appy	1	78

Odds of Having Had an Appy → 7 / 1 124 / 78

Odds = 7/1
Ratio 124/78

= 4.4

Why an Odds Ratio Is A Legitimate Estimate of Relative Risk



$$I_{exposed} = \frac{a}{a+b}$$

$$I_{unexposed} = \frac{c}{c+d}$$

$$RR = \frac{I_{exposed}}{I_{unexposed}} = \frac{a\,/\,(a+b)}{c\,/\,(c+d)}$$

$$OR = \frac{a/c}{b/d} = \frac{ad}{bc}$$

BUT
If ‘a’ and ‘c’ are small relative to ‘b’ and ‘d’

then $RR \simeq \frac{a/b}{c/d} = \frac{ad}{bc}$

same

Summary

	Fast Driving	Drunk Driving
Relative risk	5.0	10.7
Risk difference	4%	13,6%
Attributable risk %	80%	91%
% all drivers with risk	20%	3%
Population attributable risk	44%	22%

Where will you put your money to have the greatest impact for reducing automobile-related deaths?

	Measure of association	Measure of impact	Question
RR / OR	Yes	No	How much the association could be?
Risk difference	Yes	Yes	What is the excess risk between exposed and unexposed persons?
Attributable risk %	No	Yes	What proportion of the exposed persons had an outcome presumably due to the exposure?
Population attributable risk	No	Yes	What proportion of persons in the total population had the outcome presumably because of the exposure?