ASPIRE CLASS 7:
Interpreting Results and Writing an Abstract

Thomas Delate, PhD, MS

Clinical Pharmacy Research Scientist

Kaiser Permanente

KAISER PERMANENTE®

Presentation Objectives

Interpreting Results

Explain measures of frequency

Understand measures of association

Calculate the number needed to treat and number needed to harm

Writing an Abstract

List the essential elements of an abstract

Recognize and apply succinct writing to an abstract

COMPARISON OF UPPER GASTROINTESTINAL TOXICITY OF ROFECOXIB AND NAPROXEN IN PATIENTS WITH RHEUMATOID ARTHRITIS

Claire Bombardier, M.D., Loren Laine, M.D., Alise Reicin, M.D., Deborah Shapiro, Dr.P.H.,
Ruben Burgos-Vargas, M.D., Barry Davis, M.D., Ph.D., Richard Day, M.D., Marcos Bosi Ferraz, M.D., Ph.D.,
Christopher J. Hawkey, M.D., Marc C. Hochberg, M.D., Tore K. Kvien, M.D.,
and Thomas J. Schnitzer, M.D., Ph.D., for the VIGOR Study Group

ABSTRACT

Background Each year, clinical upper gastrointestinal events occur in 2 to 4 percent of patients who are taking nonselective nonsteroidal antiinflammatory drugs (NSAIDs). We assessed whether rofecoxib, a selective inhibitor of cyclooxygenase-2, would be associated with a lower incidence of clinically important upper gastrointestinal events than is the nonselective NSAID naproxen among patients with rheumatoid arthritis.

Methods We randomly assigned 8076 patients who were at least 50 years of age (or at least 40 years of age and receiving long-term glucocorticoid therapy) and who had rheumatoid arthritis to receive either

NONSTEROIDAL antiinflammatory drugs (NSAIDs) are among the most commonly used medications in the world.[1] A major factor limiting their use is gastrointestinal toxicity. Although endoscopic studies reveal that gastric or duodenal ulcers develop in 15 to 30 percent of patients who regularly take NSAIDs,[2] the chief concern is clinically important gastrointestinal problems, such as bleeding. It has been estimated that more than 100,000 patients are hospitalized and 16,500 die each year in the United States as a result of NSAID-associated gastrointestinal events.[3,4]

Most NSAIDs inhibit both cyclooxygenase-1 and

Describing Results and Making Comparisons

A key feature of all clinical research is measurement. This is typically done in two or three steps:
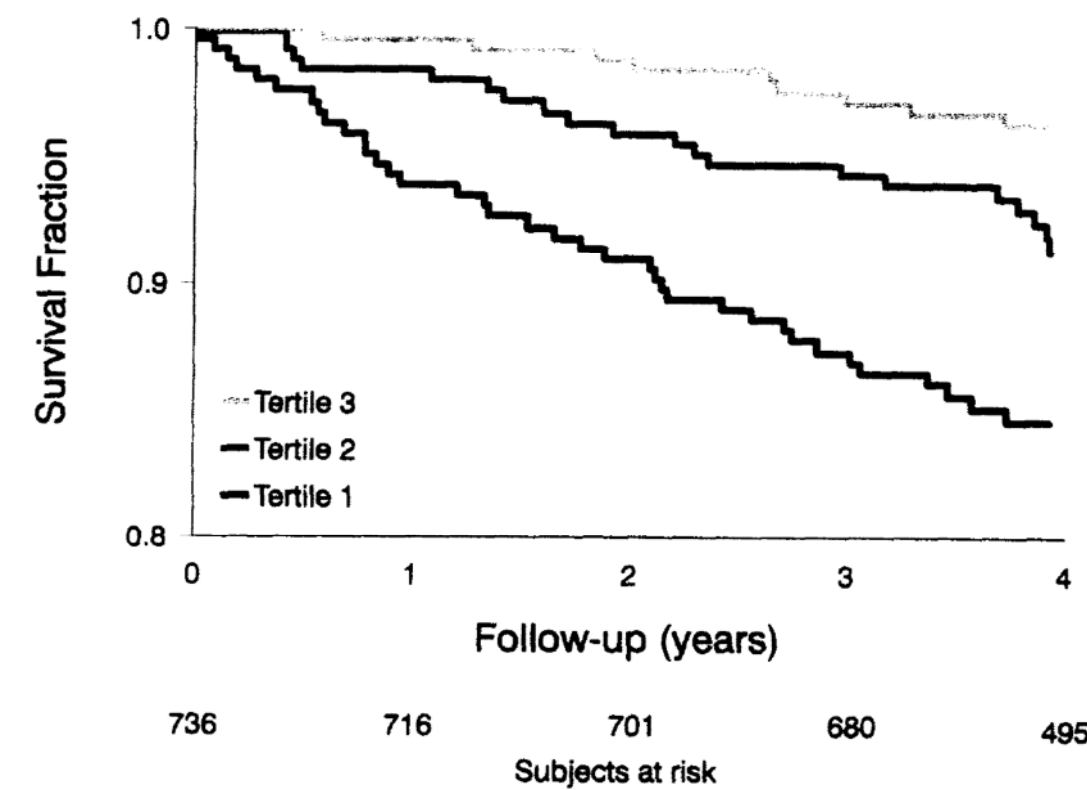1) At what regularity are events occurring in a group or population (***Measures of Frequency***)?
2) Does an exposure have an effect on the frequency of events in different groups (***Measures of Association***)?
3) Does changing the exposure impact the frequency of outcomes (***Measures of Potential Impact***)?
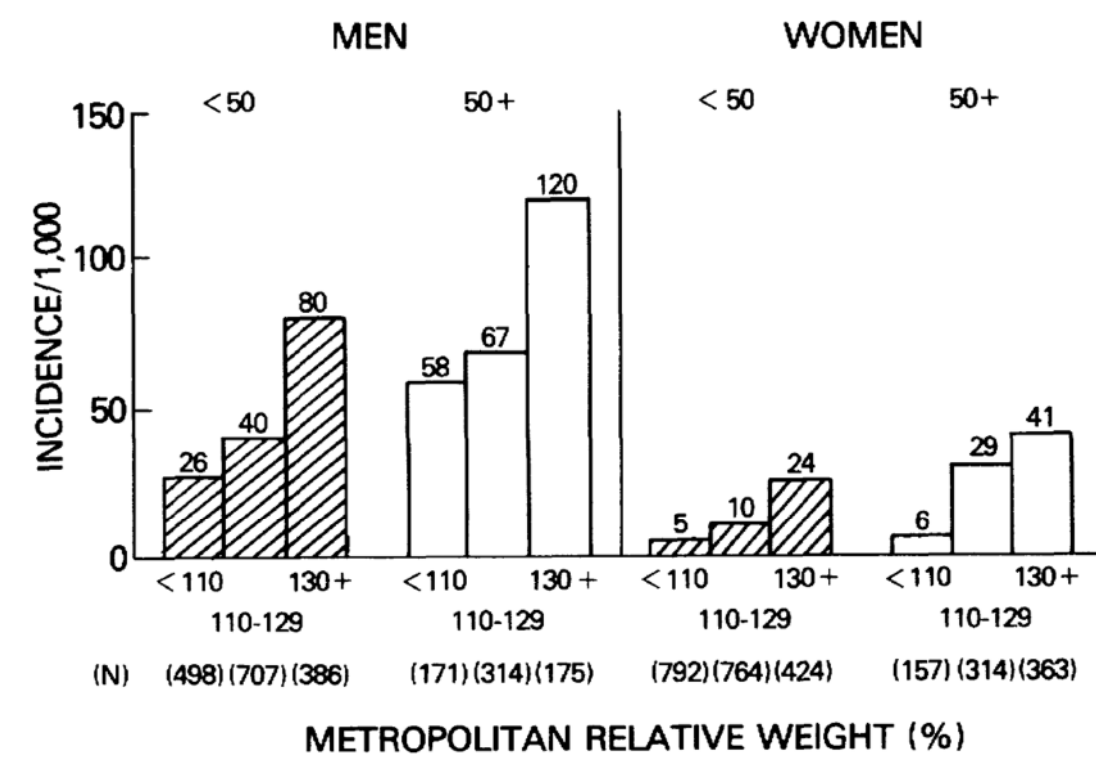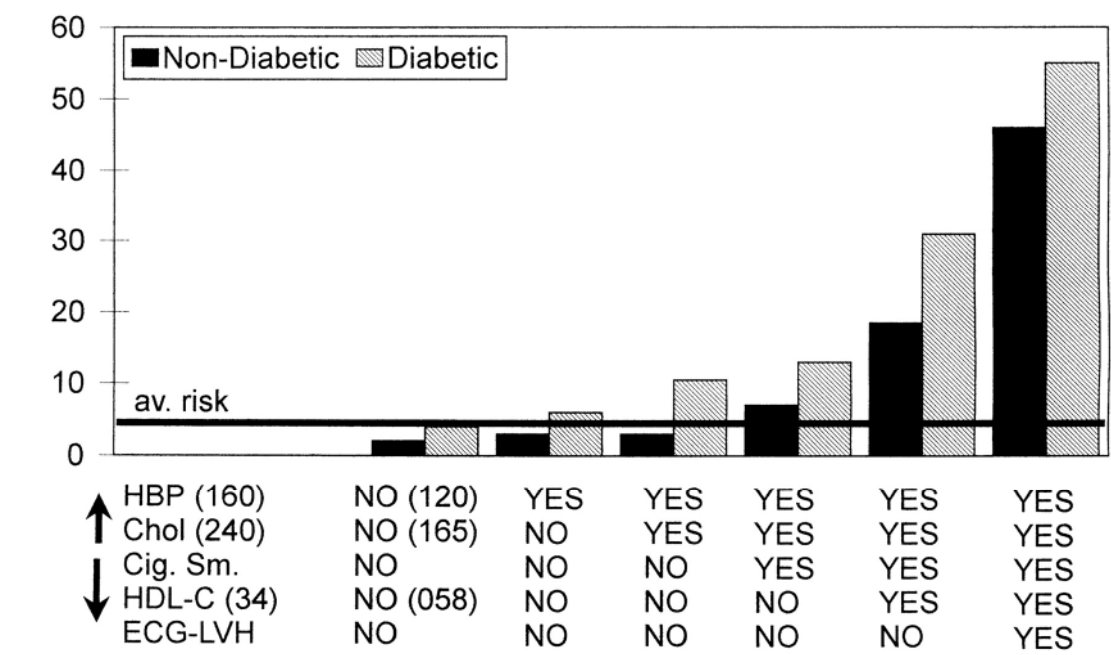

Measures of Frequency

Incidence   Prevalence

Measures of Association

Absolute   Relative

Measures of Potential Impact

Impact on exposed   Impact on population

Incidence Proportion (Risk)

What is risk?

- The probability that an event will occur in a given period
- Expressed as a %
- Calculated as: $\dfrac{\textit{Patients newly developing outcome}}{\textit{All patients observed for outcome}}$

Characteristics of risk:

- Requires all patients to be observed/at-risk for same duration
- Must know duration of time to interpret

Example from VIGOR:

Outcome	Rofecoxib		Naproxen	
	N total	N event	N total	N event
GI	4047	56	4029	121
MI	4047	17	4029	4

GI events:

$$\text{Rofecoxib} = \frac{56}{4047} = 1.4\%$$

$$\text{Naproxen} = \frac{121}{4029} = 3.0\%$$

MI events:

$$\text{Rofecoxib} = \frac{17}{4047} = 0.4\%$$

$$\text{Naproxen} = \frac{4}{4029} = 0.1\%$$

Incidence Rate

What is a rate?

- The frequency at which an event occurs
- Expressed as events per person-time
- Calculated as: $\dfrac{Patients\ developed\ outcome}{Total\ time\ at\ risk\ for\ outcome}$

Characteristics of rate:

- Assumes the likelihood of an event is constant during at-risk period
- Allows for variable follow-up between patients
- Based on a scale (e.g., per 1000 person-years)

Example from VIGOR:

Outcome	Rofecoxib			Naproxen		
	N total	N event	Person-years	N total	N event	Person-years
GI	4047	56	2667	4029	121	2689
MI	4047	17	2315	4029	4	2316

GI events:

$$Rofecoxib = \frac{56}{2667} = 2.1$$

$$Naproxen = \frac{121}{2689} = 4.5$$

per 100 person-years

MI events:

$$Rofecoxib = \frac{17}{2315} = 7.3$$

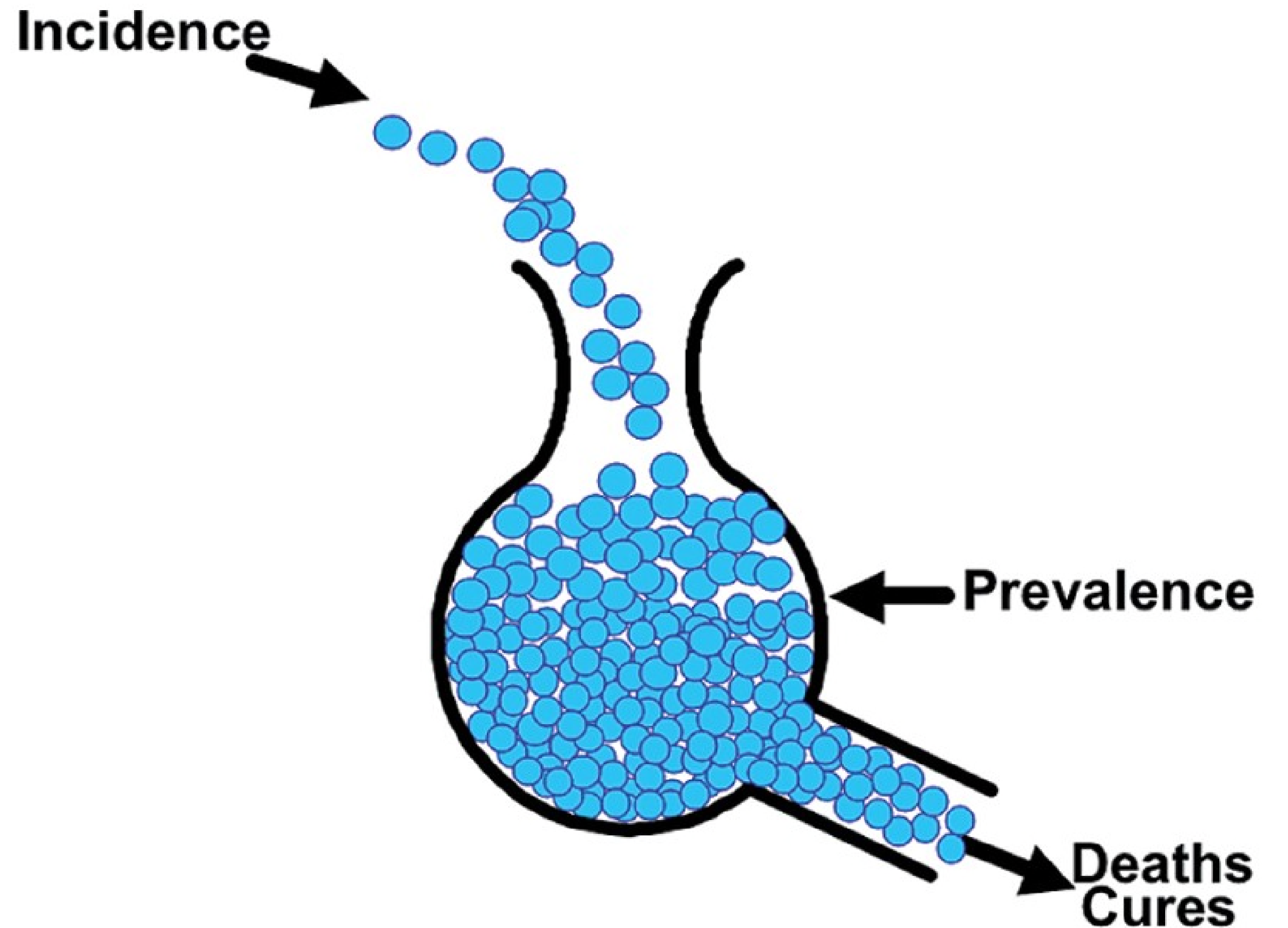$$Naproxen = \frac{4}{2316} = 1.7$$

per 1000 person-years

Prevalence

What is prevalence?

- The existing cases of disease at a given time
- Expressed as a proportion
- Calculated as: $\dfrac{Patients\ with\ a\ give\ disease}{Total\ population}$

Characteristics of prevalence:

- Easily interpreted
- Describes a point or period in time
- Affected by both incidence and duration of disease

Measures of Association – Comparisons Between Groups

Absolute Measures

Risk Difference (RD) and Incidence Rate Difference (IRD)

- The difference in risk or rate between exposed and non-exposed groups
- Measures absolute effect of an exposure
- Calculated as: $Risk1 - Risk0$

Interpretation:

- Difference < 0 Rate lower in the exposed
- Difference > 0 Rate higher in the exposed
- Difference = 0 Exposure has no effect

Example from VIGOR:

Outcome	Rofecoxib		Naproxen	
	Risk (R)	Incidence Rate (IR)	Risk (R)	Incidence Rate (IR)
GI	1.4%	2.1	3.0%	4.5
MI	0.4%	7.3	0.1%	1.7

GI events:

$RD = 1.4 - 3.0 = -1.6\%$

$IRD = 2.1 - 4.5 = -2.4$

MI events:

$RD = 0.4 - 0.1 = 0.3\%$

$IRD = 7.3 - 1.7 = 5.6$

Relative Measures

Risk Ratio/Relative Risk (RR) and Incidence Rate Ratio (IRR)

- The ratio of risk or rates between exposed and non-exposed groups
- Calculated as: $\frac{Risk1}{Risk0}$

Interpretation:

- Difference < 1 Risk lower in the exposed
- Difference > 1 Risk higher in the exposed
- Difference = 1 Exposure has no effect

Example from VIGOR:

Outcome	Rofecoxib		Naproxen	
	Risk (R)	Incidence Rate (IR)	Risk (R)	Incidence Rate (IR)
GI	1.4%	2.1	3.0%	4.5
MI	0.4%	7.3	0.1%	1.7

GI events:

$$RR = \frac{1.4}{3.0} = 0.47$$

$$IRR = \frac{2.1}{4.5} = 0.47$$

MI events:

$$RR = \frac{0.4}{0.1} = 4.20$$

$$IRR = \frac{7.3}{1.7} = 4.29$$

Reporting of Absolute vs Relative Effect Measures

Absolute Effect

- When measuring the effect of an exposure on the health of a population

Relative Effect

- When indicating the extent to which an exposure accounts for the occurrence of disease

Typically, both are reported

Number Needed to Treat (NNT) and Number Needed to Harm (NNH)

- The number of patients who need to be treated to prevent/cause one additional event
- Provides an easily interpretable estimate of the magnitude of an effect
- Calculated from absolute differences
  - 1/ARD
  - People/IRD
- Must consider TIME!

VIGOR Trial:

- NNT risk = 1 / (0.014 – 0.030) = 62.5
- NNT rate = 100 / (2.1 – 4.5) = 41.7
- 63 patients would need to receive rofecoxib to prevent one additional GI event

- NNH risk = 1 / (0.004 – 0.001) = 333.3
- NNH rate = 1000 / (7.3 – 1.7) = 178.6
- 333 patients would need to receive rofecoxib to cause one additional MI

Other Common Measures

Hazard Ratio (HR)

- Used for time to event analysis
- Calculated from a Cox Proportional Hazards model to compare relative event rates
- Commonly combined with Kaplan-Meier curves and statistics
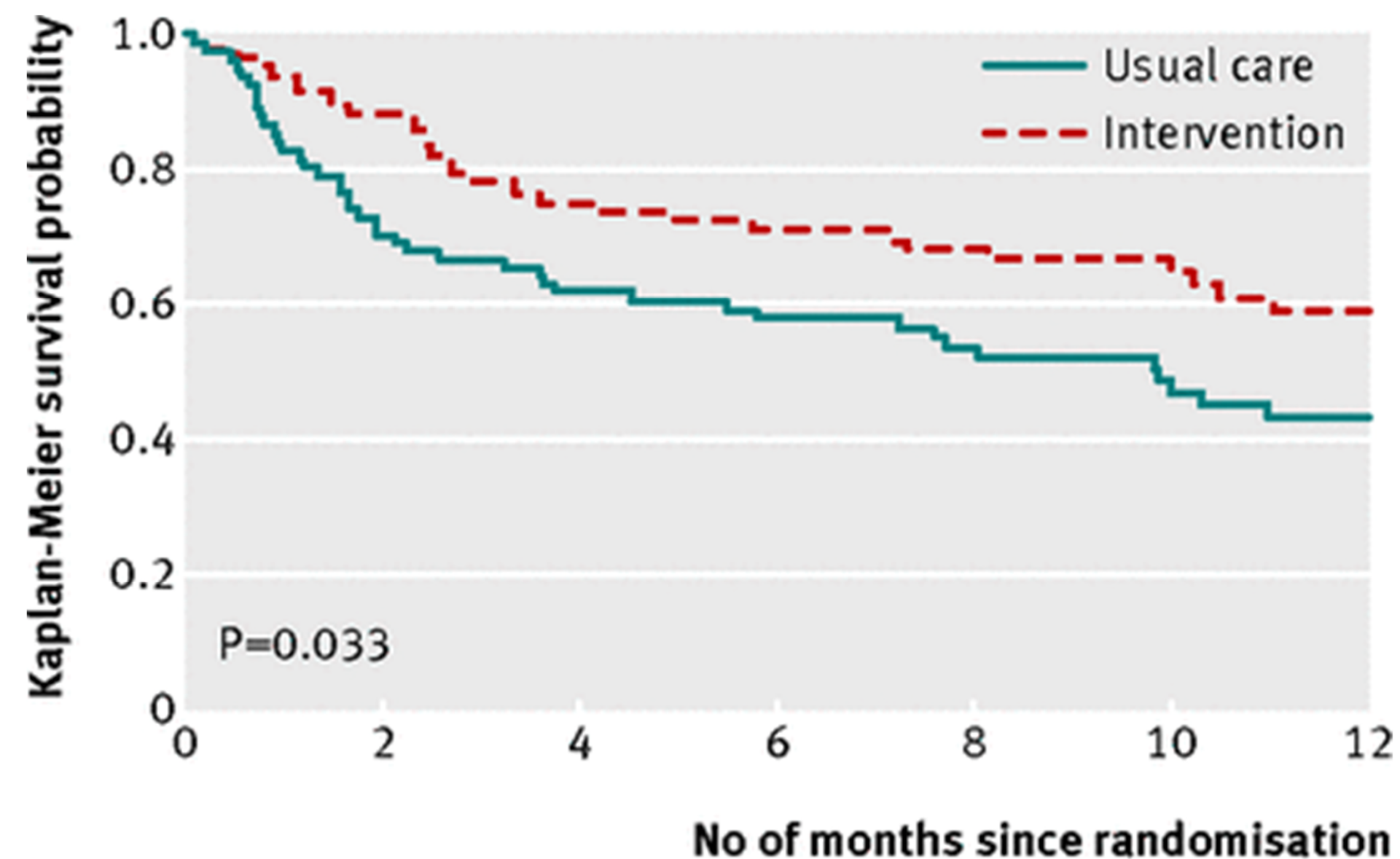
Odds Ratio (OR)

- Used for retrospective studies to determine likelihood of dichotomous outcome
- Calculated from logistic regression model or 2x2 table
- Odds $= \frac{probability}{1-probability}$
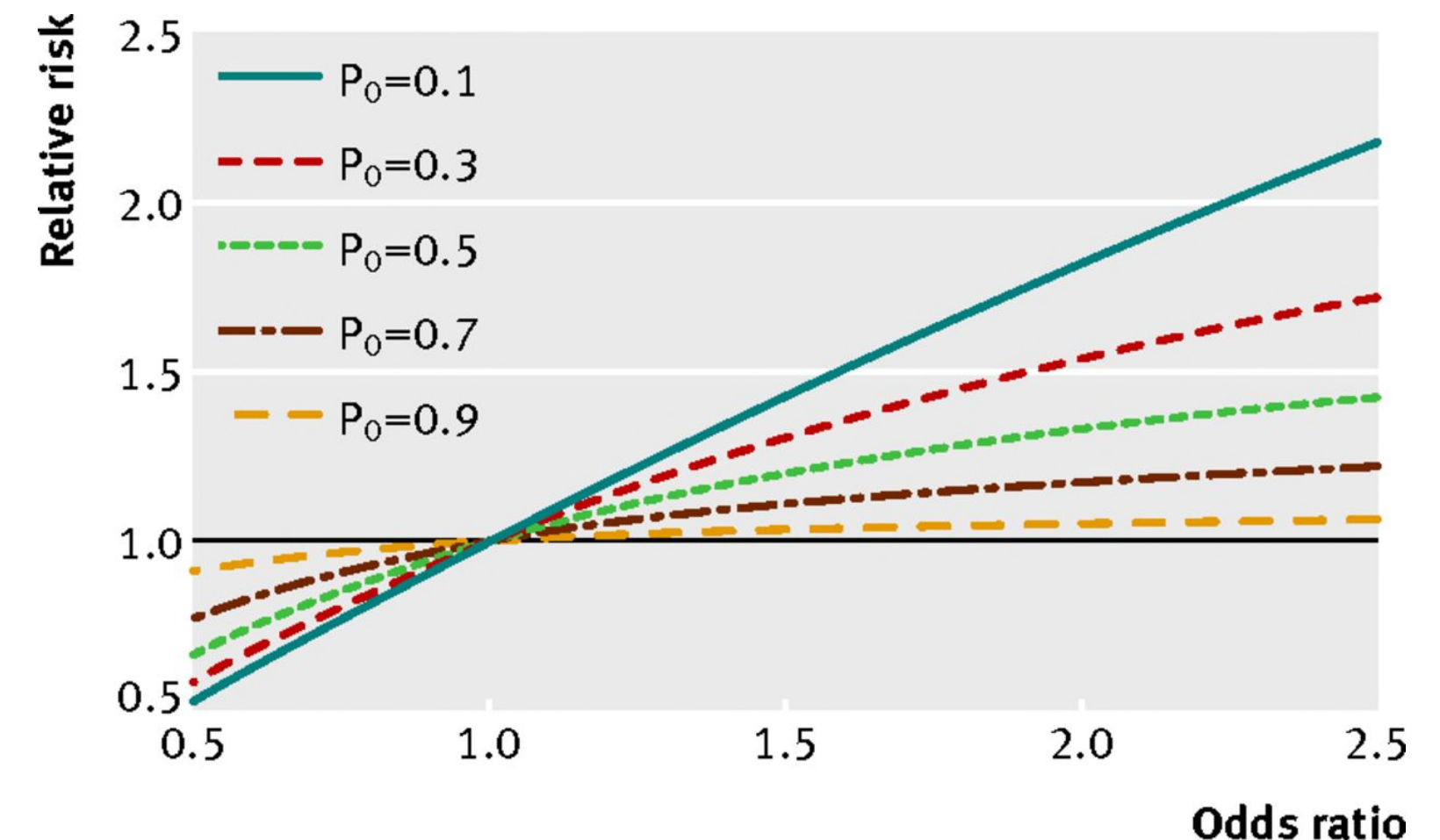
Measures of Variability - 95% Confidence Intervals

Used to express the statistical variation (random error) that underlies our estimate

Interpretation:

"If the level of confidence is set to 95%, it means that if the data collection and analysis could be replicated many times and the study were free of bias, the confidence interval would include within it the correct value of the measure 95% of the time."

95% Confidence Intervals
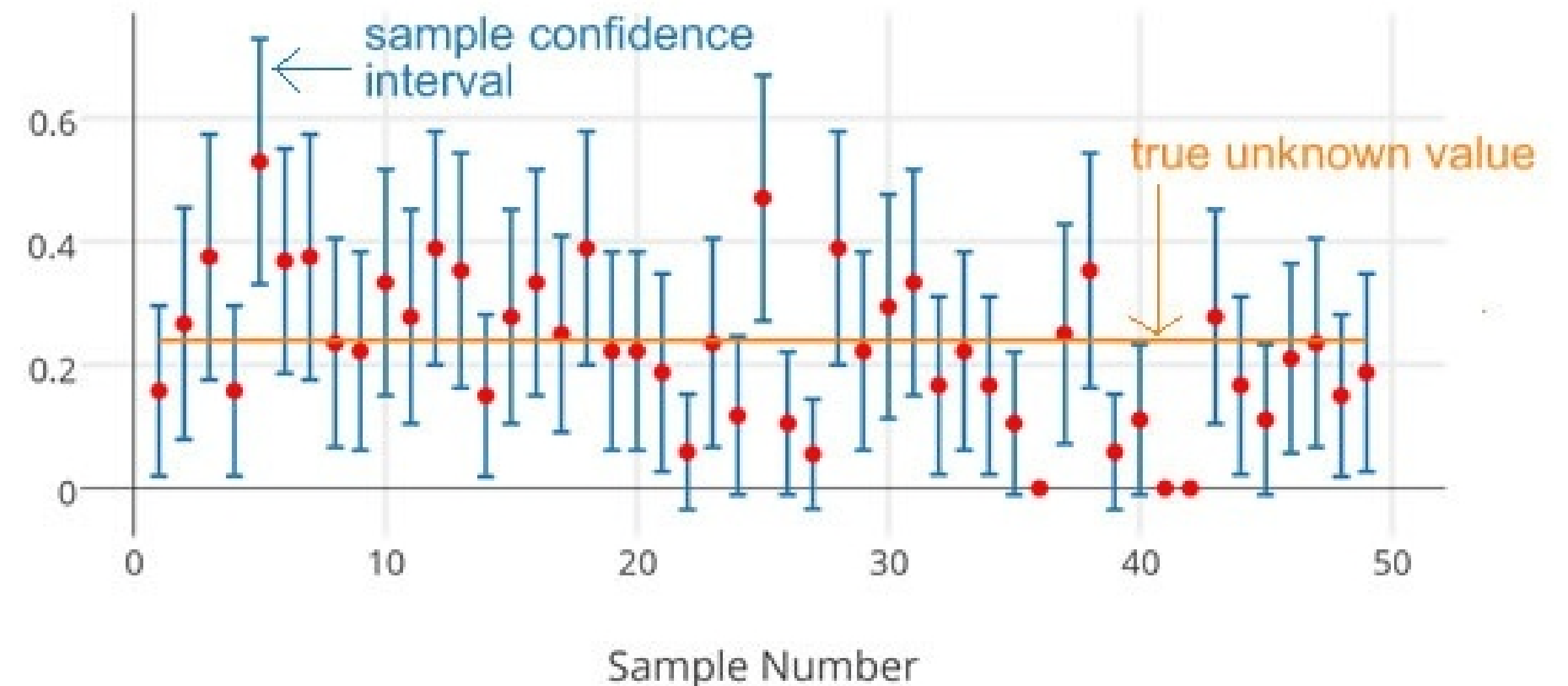
Case Study – Interpreting Results of the VIGOR trial

From the VIGOR abstract:

"During a median follow-up of 9.0 months, 2.1 confirmed gastrointestinal events per 100 patient-years occurred with rofecoxib, as compared with 4.5 per 100 patient-years with naproxen (relative risk, 0.5; 95 percent confidence interval, 0.3 to 0.6; p<0.001)."

- What was the measure of frequency?
- What was the measure of association?
- What was the reference group?
- How do we interpret these values?

From the VIGOR abstract:

"The incidence of myocardial infarction was lower among patients in the naproxen group than among those in the rofecoxib group (0.1 percent vs. 0.4 percent; relative risk, 0.2; 95 percent confidence interval, 0.1 to 0.7)"

- What was the measure of frequency?
- What was the measure of association?
- What was the reference group?
- How do we interpret these values?

Public Health Impact of VIGOR

When using updated MI data:

Incidence Rate

- 7.4 events per 1,000 person-years (rofecoxib)
- 1.5 events per 1,000 person-years (naproxen)

Incidence Rate Difference

- 5.9 MI additional events caused by rofecoxib for every 1,000 patients treated

Number Needed to Harm with rofecoxib

- 1,000/5.9 = 170
- We will harm 1 patient for every 170 patients that are treated with rofecoxib

Study Group	Person-Years of Exposure	No. of Myocardial Infarctions	Relative Risk	95% CI
Total				
Rofecoxib	2698	20	5.00	1.68 to 20.13
Naproxen	2699	4		
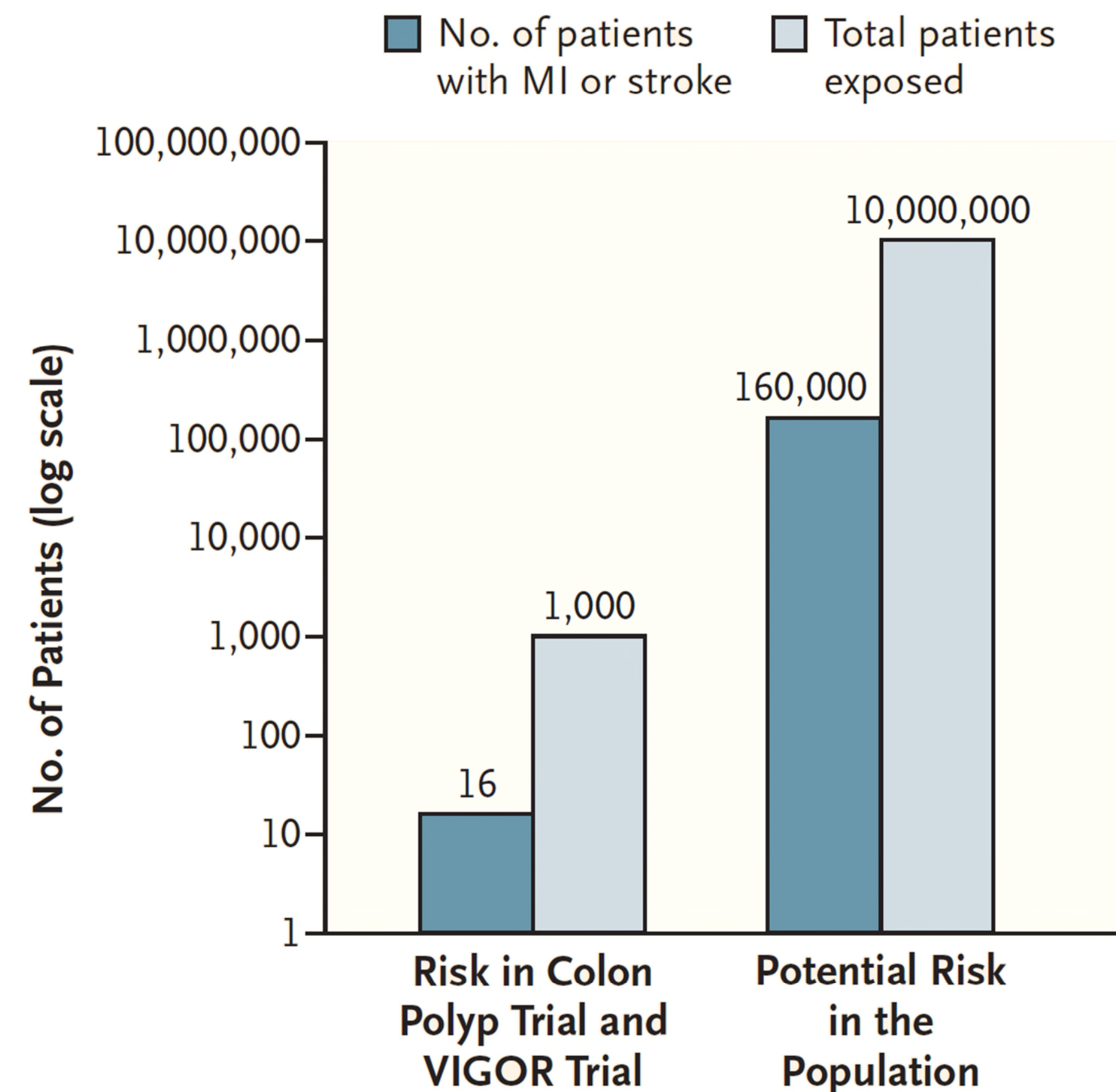
Writing an Abstract

What is an Abstract?

- An abbreviated representation of a study's purpose, methods, results, and interpretation of the study findings

- Provides the essence of the research done

- Designed to tempt a reader to want to know more about a study (e.g., read the rest of the manuscript, accept the study for presentation at a conference)

- It is often the only information on a study that is read

Essential Elements of an Abstract

- **Aim(s)/Objective(s)**: State the rationale for the study and/or hypothesis being tested. (Why was the study done?)

- **Methods:** Describe what was done. Include study design, population, exposure(s) and outcome(s), and main analytic method(s). (What was done and how was it done?)

- **Results:** Report the findings. Include sample size(s), participant characteristics, outcomes (compare numbers & percentages with risk differences), and indicators of statistical significance. (Who was in the study and what was found?)

- **Conclusions:** Summarize the findings and provide clinical context. Do not just repeat the results. (What do the findings mean?)

The format and length requirements differ from journal to journal and conference to conference

Abstract Writing Tips

- Follow the conference/journal writing guide/instructions for authors
- Provide only main objectives, methods, results, and conclusions
  - Space is very limited (use abbreviations when appropriate, don't wallow in background)
  - Only provide outcome results described in the methods
  - Describe statistic used for primary outcome (e.g., Proportional Hazards modeling was used to ….)
  - Some conferences allow for figures, tables, and/or references to be included
- Give enough information to entice a reviewer/editor in seeing more
  - Conference reviewers evaluate the quality of the research from the abstract alone
  - Most conferences will not accept an abstract with results pending

QUESTIONS?

KAISER PERMANENTE.®