Clinical reasoning & research evidence: How good decisions are really made

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Clinical decisions:
How evidence really informs practice

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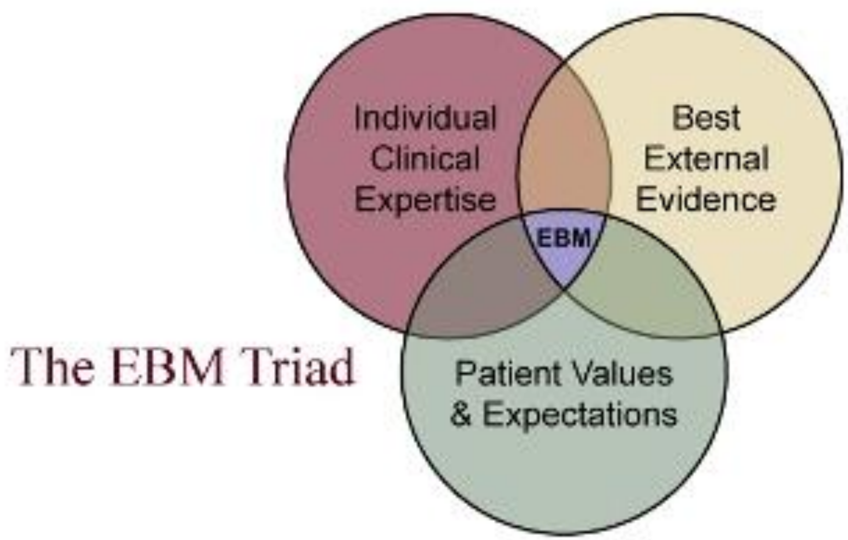
"The pessimist complains about the wind; the optimist expects it to change; the realist adjusts the sails."

-William Arthur Ward

Evidence-Based Practice

- Proponents of evidence-based practice (EBP) argue that research evidence is one of three components that should inform practice
- “Evidence-based medicine is the integration of the best research evidence with clinical expertise and patient values.“



Sackett D et al. Evidence-Based Medicine: How to Practice and Teach EBM, 2nd edition. Churchill Livingstone, Edinburgh, 2000

What Is the Best Evidence?

- Clinical questions concerning effectiveness are most reliably addressed using randomized controlled trials
- Questions about causation and harm are best answered by evidence from cohort or case-control studies
- Feelings and perceptions are commonly addressed using qualitative techniques

- Larger studies are typically more powerful and important than smaller ones
- Large effect sizes that support hypothesis are better than small effect sizes

Evidence for Guidance

- The evidence that we gather and read about shapes clinical practice by providing guidance and reducing uncertainty
- The role of evidence becomes particularly salient when patient encounters generate questions about:
  - Accuracy of diagnostic tests
  - Costs and benefits of therapy
  - Prognosis of diseases
  - Etiology of disorders

Evidence: Mathematical Models

- We quantify evidence using mathematical models
- But, the investigation of physical systems includes a stochastic element: We are not certain about the values of parameters, measurements, expected inputs or disturbances
- So, the effect and sequelae of a clinical decision are estimated probabilistically using mathematical models that approximate reality

Evidence: Probabilistic

- So, evidence is presented probabilistically:
  - 92% sensitivity, 87% specificity
  - 57% probability of full recovery with this therapy
  - 25% relative decrease in acute ankle injury among those in the prevention group
  - 28% probability the condition will recur in this population

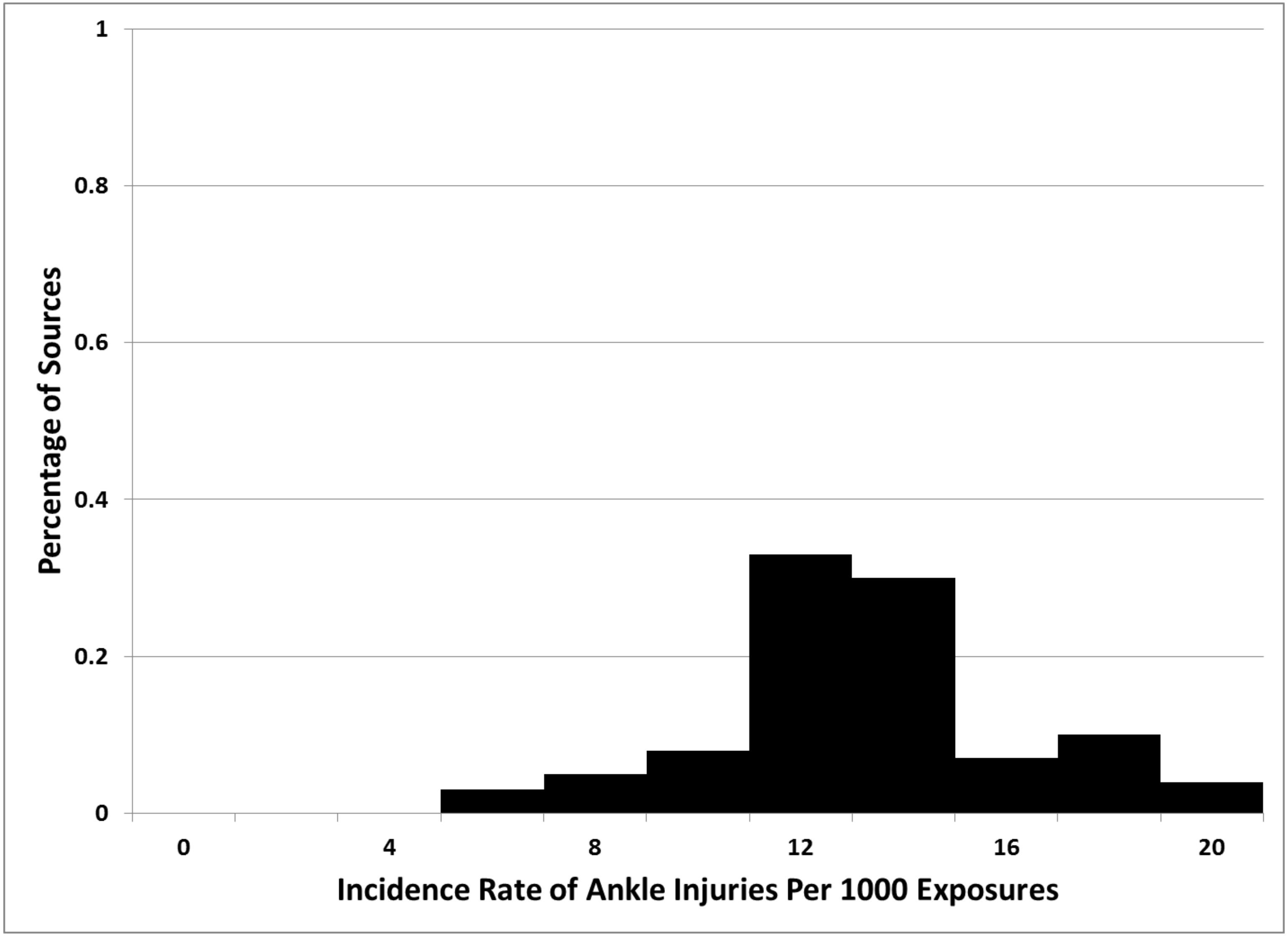
How Is Evidence Used?

- How does new research evidence alter the way you approach a clinical question?

- Example: Epidemiology of ankle sprains for:
  - Diagnostic purposes (sex, sport, age)
  - Risk analysis
  - Cost/benefit analysis of prevention program
- Metric: Incidence rate of ankle injuries per 1000 exposures

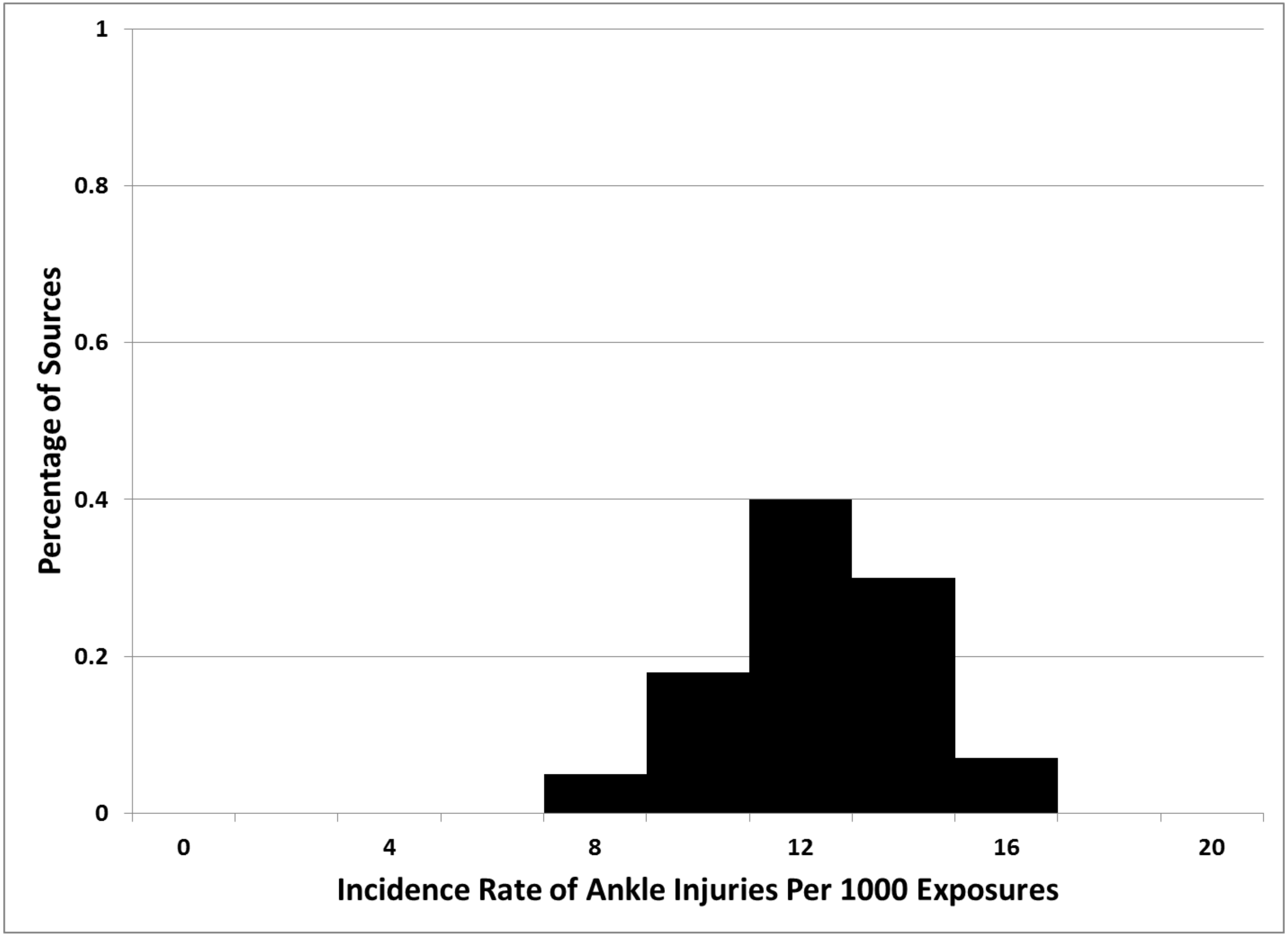
Simple Probability

Novice AT



1
0.8
0.6
0.4
0.2
0
Percentage of Sources
0
4
8
12
16
20
Incidence Rate of Ankle Injuries Per 1000 Exposures

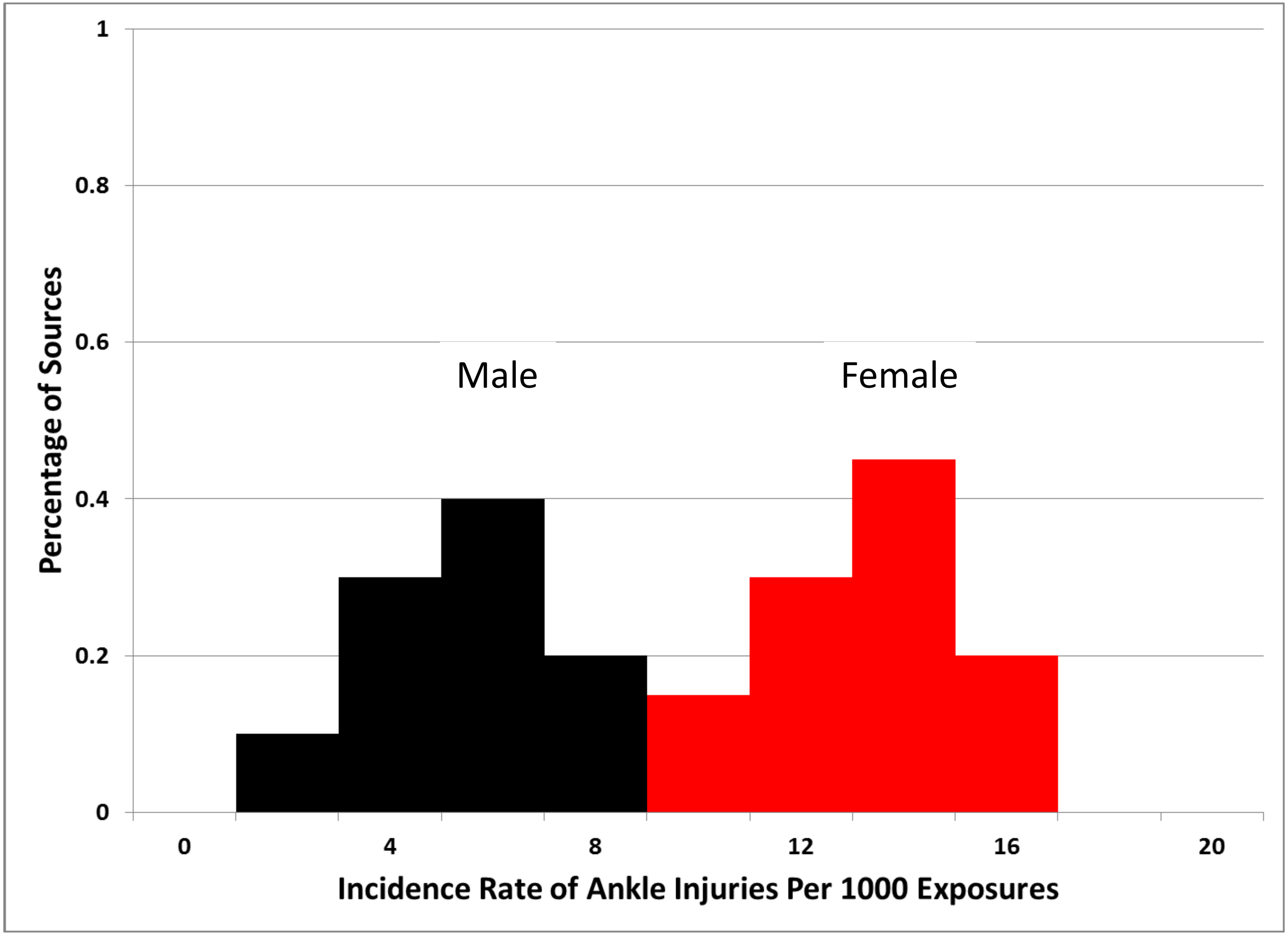
Experienced AT



Conditional Probability

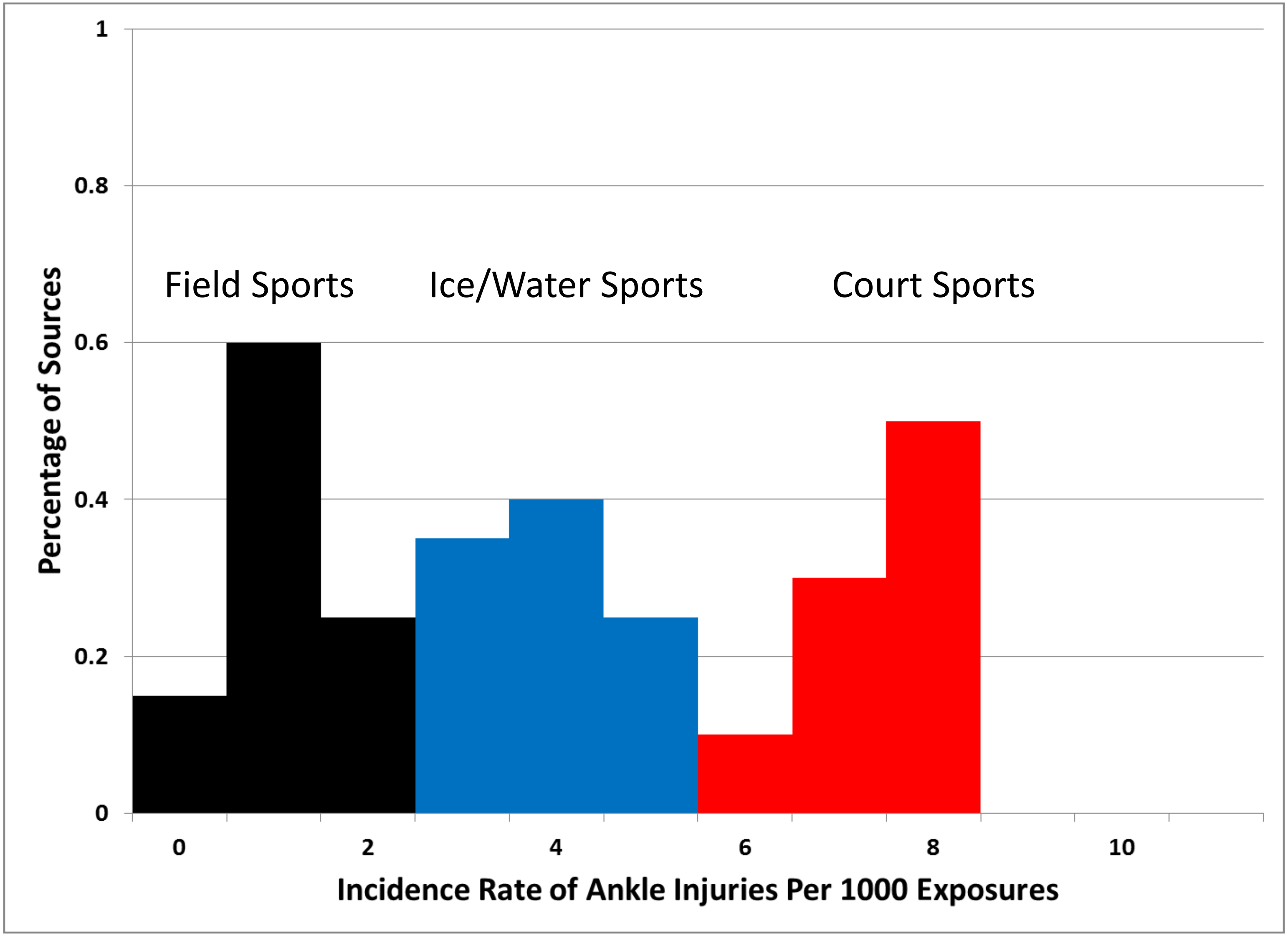
- We might want to "condition" our estimate to match the profile of the population of interest
- Conditional probability: You make an estimate "conditioned on" the fact that . . .
- A change in context alters our expectation

Sex



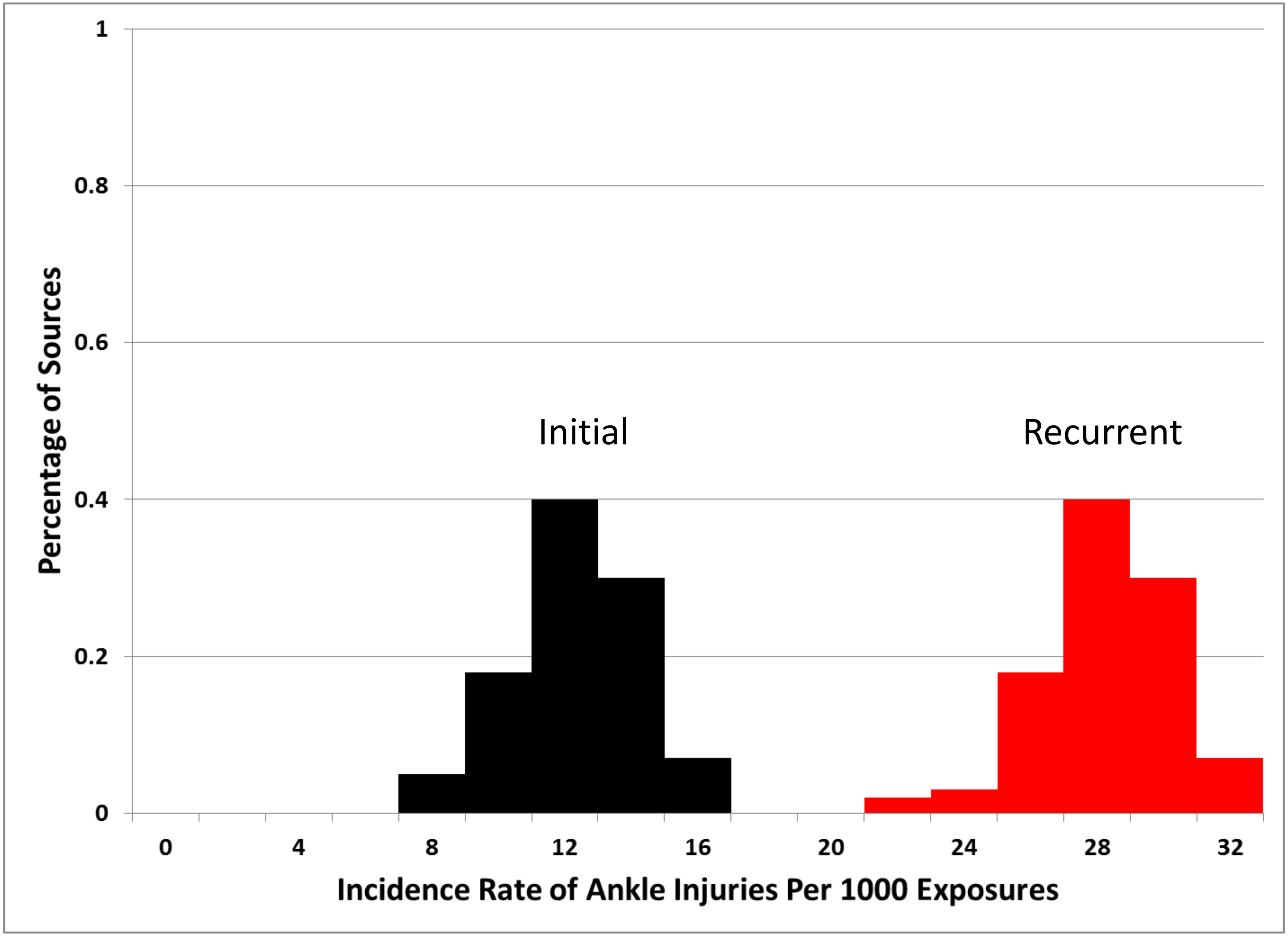
1
0.8
0.6
0.4
0.2
0
Percentage of Sources
Male
Female
0
4
8
12
16
20
Incidence Rate of Ankle Injuries Per 1000 Exposures

Sport



Field Sports
Ice/Water Sports
Court Sports
Percentage of Sources
1
0.8
0.6
0.4
0.2
0
0
2
4
6
8
10
Incidence Rate of Ankle Injuries Per 1000 Exposures

Initial vs Recurrent Injury



Prior Probability

- Based on your clinical experience and familiarity with the evidence, you enter the patient encounter with hypotheses about what is wrong, what will improve the condition, and how things will go in the long term
- These hypotheses are educated guesses, or “prior probabilities”

Posterior Probability

- Evidence obtained subsequently from the history and physical, diagnostic tests, and consulting the literature is used to update prior probabilities to arrive at a final probability estimate (posterior probability)
- How do we get from prior to posterior probability?
- We use conditional logic: If this, then that

Bayes Theorem

- Thomas Bayes (1701 - 1761), a British mathematician and minister, is credited for describing a process for adjusting and updating the likelihood of an event based on data -- as the data are generated
- Bayes' theorem describes the relationships that exist within an array of simple and conditional probabilities

Conditional Probability

- Bayes' Theorem:

$$\Pr(A \mid B) = \frac{\Pr(B \mid A)\Pr(A)}{\Pr(B)}$$

where Pr(A) is the probability of event A (ankle sprain) happening and Pr(A|B) is the probability of event A happening given that event B (prior ankle injury) has happened

- Bayes' Theorem provides a formal mathematical approach to combine our hypotheses with new evidence

Evaluating Potential Ankle Sprains: No Prior Injury

100 patients with ankle pain
manual palpation, then MRI

MRI (Gold Standard)

Manual palpation		D+	D-	Total
	T+	9	8	17
	T-	3	80	83
		12	88	100

Incidence

		MRI		
		D+	D-	Total
Manual palpation	T+	9	8	17
	T-	3	80	83
		12	88	100

$P_{(D+)} = (12/100) = .12$	The probability that the condition will be present in any particular person	Incidence
$P_{(D-)} = 1 - .12 = .88$	The probability that the condition will not be present in any particular person	Complement

Sensitivity

MRI

		D+	D-	Total
Manual palpation	T+	9	8	17
	T-	3	80	83
		12	88	100

$P_{(T+\|D+)}$ = (9/12)=.75	The probability that the test will yield a positive result [T+] **if** the condition is present [D+]	Sensitivity
$P_{(T-\|D+)}$ = 1—.75 = .25	The probability that the test will yield a negative result [T-] **if** the condition is present [D+]	Complement

Specificity

		MRI		
		D+	D-	Total
Manual palpation	T+	9	8	17
	T-	3	80	83
		12	88	100

$P_{(T-\|D-)}$ = (80/88)=.91	The probability that the test will yield a negative result [T-] **if** the condition is not present [D-]	Specificity
$P_{(T+\|D-)}$ = 1-.91 = .09	The probability that the test will yield a positive result [T+] **if** the condition is not present [D-]	Complement

A Practical Example of Conditional Probability

- Sensitivity and specificity describe a medical test's accuracy if we know whether or not the patient has the condition:
- Sensitivity: The probability that the test is positive if the condition is present
  - $\Pr(T+|D+)$
- Specificity: The probability that the test is negative if the condition is absent
  - $\Pr(T-|D-)$
- Is this helpful?

A Practical Example of Conditional Probability

- We need to know the inverse to assess diagnosis:
  – If the test is positive, what is the probability the patient has the condition, Pr(D+|T+):
    - <u>Positive Predictive Value</u>
  – If the test is negative, what is the probability the patient does not have the condition, Pr(D-|T-):
    - <u>Negative Predictive Value</u>

A Practical Example of Conditional Probability

- We use Bayes' to convert sensitivity/specificity to what we really want to know: How strongly we should believe in the test results, given the new data, i.e., positive and negative predictive values

$$PPV = \frac{(Sensitivity\ x\ Incidence)}{Probability\ of\ Positive\ Test}$$

= [.75 x .12] / .17
= .53

$$NPV = \frac{(Specificity\ x\ Incidence)}{Probability\ of\ Negative\ Test}$$

= [.91 x .88] / .83
= .96

Evaluating Potential Ankle Sprains: Prior Injury

100 patients with ankle pain
manual palpation, then MRI

		MRI		
		D+	D-	Total
Manual palpation	T+	21	6	27
	T-	7	66	73
		28	72	100

Sensitivity = .75; Specificity = .91

Same SnS/SpC, Different Incidences

Assuming the properties of the test remain constant, the PPV will increase with increasing incidence; and NPV decreases with an increase in incidence

$$PPV = \frac{(Sensitivity\ x\ Incidence)}{Probability\ of\ Positive\ Test} \qquad NPV = \frac{(Specificity\ x\ Incidence)}{Probability\ of\ Negative\ Test}$$

Incidence	PPV	NPV
.12	= [.75 x .12] / .17 = **.53**	= [.91 x .88] / .83 = **.96**
.28	= [.75 x .28] / .27 = **.77**	= [.91 x .72] / .73 = **.90**

Bayes' Theorem

- A high prior probability makes it easier to confirm the hypothesis of the presence of the target condition
- A low prior probability will make it easier to accept the hypothesis of absence of the condition
- If the probability of a new ankle sprain is (conditionally) related to a previous ankle sprain, Bayes' theorem can be used to more accurately assess the probability of a new ankle sprain

Beyond the Diagnostic Test

- Each piece of evidence that a clinician discovers (e.g., aspects of the history and physical examination) may be viewed as a separate test, each with its own test characteristics and associated probabilities
- So, the results of each test may be used to form a conditional statement
- Bayes' theorem allows clinicians to explicitly apply published test characteristics to their probability assessment

Naïve Bayes Classifiers

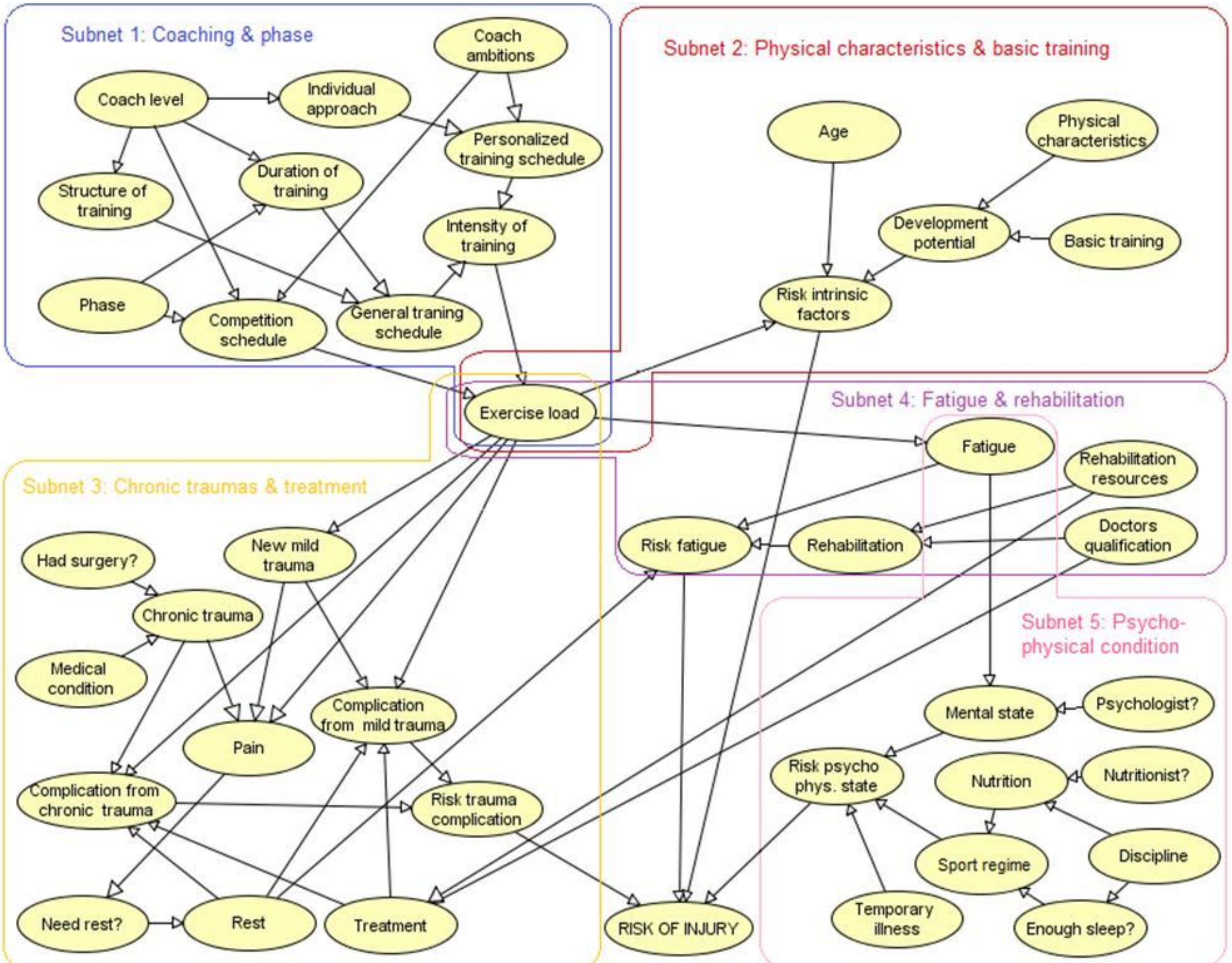
- This diagnostic test example illustrates the use of a single "naïve" Bayes classifier: The predictor (initial vs recurrent) ankle injury is assumed to operate independently of information gleaned from other tests
- Obviously, the results of multiple tests on a patient are inter-connected and dependent
- Complex Bayesian models incorporating many inter-related predictors are possible and feasible

Continuous Predictors

- Bayes' theorem also applies to continuous variables, e.g. heart rate, systolic and diastolic blood pressure
- The Bayesian theorem for conditional densities are related this way:

$$f(x|y) = f(y|x)\frac{f(x)}{f(y)}$$

- Like probabilities, densities are ≥ 0, and sum to 1



Dimitrova L & Petkova K. Bayesian network-based causal analysis of injury risk in elite rhythmic gymnastics. International Journal of Computer Science and Software Engineering, Volume 2, Issue 1, 2014. 50-61.