Updates in Therapeutics® 2012:
Ambulatory Care Pharmacy Preparatory Review and Recertification Course

Biostatistics: A Refresher

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Conflict of Interest Disclosures

No conflicts of interest to disclose related to this presentation

Outline

- Purpose: What this is and isn't
- Introduction: What do I need to know?
- Variables
- Descriptive statistics
- Inferential statistics
- Statistical tests
- Hypothesis testing
- Decision errors

Statistics: WHY do you need to know it?

- *Ambulatory Care Pharmacy Specialty Examination Content Outline*
  - Domain 4: Retrieval, Generation, Interpretation, and Dissemination of Knowledge in Pharmacotherapy (15%)
    - Retrieve and interpret biomedical literature with respect to study design methodology, statistical analysis, and significance and applicability of reported data and conclusions.

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Types of Variables/Data
Discrete variables

- Can only take a limited number of values within a given range
  - Nominal: Classified into groups in an unordered manner and with no indication of relative severity
    - Sex (M/F), mortality (yes/no), disease state (present/absent)
  - Ordinal: Ranked in a specific order but with no consistent level of magnitude of difference between ranks
    - NYHA functional class: I, II, III, IV

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Types of Variables/Data
Continuous Variables

- Counting variables, can take on any value within a given range
- Interval Scaled: Data ranked in order with a consistent change in magnitude between units; the zero point is arbitrary
  - degrees Fahrenheit
- Ratio Scaled: Like "interval" but with an absolute zero
  - degrees Kelvin, pulse, BP, time, distance

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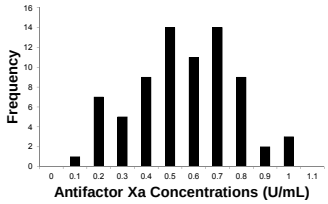
Descriptive statistics
How do we visualize datasets?

- Frequency distribution
- Histogram
- Scatter plot



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Descriptive statistics: Numerical methods
Measures of Central Tendency

- Mean
  - Continuous and normally distributed data
  - Very sensitive to outliers (tends toward the tail)
- Median (a.k.a 50th percentile)
  - Midpoint of the values placed in order from highest→lowest
  - Ordinal or continuous data (especially skewed)
  - Insensitive to outliers
- Mode
  - Most common value in a distribution
  - Nominal, ordinal, or continuous data
  - Data may be bimodal, trimodal, etc.
  - Describes distributions with large range of values

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Measures of Data Spread and Variability
Standard Deviation

- Measure of the variability about the mean
- Applied to continuous data that are ~normally distributed or transformed to be
- Empirical rule: 68% within ±1 SD, 95% within ±2 SD, and 99% within ±3 SD
- Coefficient of Variation (CV)
  - (SD/mean×100%)
- Variance = SD^2

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Measures of Data Spread and Variability
Range

- Difference between the smallest and largest
- Applied to “parametric” and “non-parametric”
- Easy to compute
- Size of range is very sensitive to outliers

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Measures of Data Spread and Variability
Percentiles

- Point in a distribution which a value is larger than some percentage of the other values
- 75th percentile: 75% of the values are smaller
- Does not assume any distribution
- IQR: percentile that describes the middle 50%, encompasses the 25th–75th percentile.

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Measures of Data Spread and Variability
Summary

- What measures of central tendency should be presented with…
  - Continuous, interval scaled data?
  - Ordinal data?
- What measures of spread and variability should be presented with…
  - Means?
  - Medians?

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Dataset
HDL-cholesterol example

- 20 HDL concentrations measured…

64	60	59	65	64	62	54
54	68	67	79	55	48	65
59	65	87	49	46	46	

- Calculate the mean, median, and mode
- Calculate the range, SD and SEM
- Evaluate the visual presentation of the data

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Dataset
HDL-cholesterol example

Measure of Central Tendency	Mean 60.8	Median 61	Mode 65
Measure of Spread	SD 10.4	Range 41 (46-87)	IQR (54-65)

- SEM: 2.3

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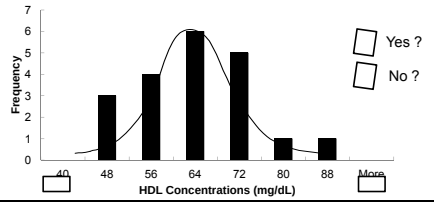
Inferential statistics

- Conclusions made about a population from a study of a sample of that population
- Population distributions
- CIs vs. Hypothesis testing
- Statistical tests
  - Choosing and evaluating

Page 2-121

Population Distributions
Normal (Gaussian) Distribution

- Most common model
- HDL example: Symmetric/"bell-shaped" ?



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Normal (Gaussian) Distribution
How do we assess?

- Frequency distribution and histograms
- Median ~ mean
  - HDL Example: 61 vs. 60.8 mg/dL
  - Formal test: Kolmogorov–Smirnov test
  - Challenging to evaluate when you are reading a paper
- Mean/SD define a normal distribution…….. termed *parametric*

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Normal (Gaussian) Distribution
Standard Error of the Mean (SEM)

- SEM = SD/sqrt(n)
- Quantifies uncertainty in the estimate of the mean, not variability in the sample
- Why is all of this worth knowing the difference between the SEM and SD?
  - Application: 95% CI is ~ mean ± 2 . SEM
  - Deception?

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Confidence Intervals

- 95% Confidence Intervals
  - In repeated samples, 95% of all CIs include true population value
  - Why are 95% CIs most often reported?
  - 95% CI ~ mean ± 1.96 × SEM (or 2 × SEM)
- SD, SEM, and CIs are often used interchangeably (incorrectly)

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Hypothesis Testing

- Null hypothesis (H_0):
  - No difference between comparator groups (Tx A = Tx B)
- Alternative hypothesis (H_a):
  - States that there is a difference (Tx A ≠ Tx B)
- Results of "hypothesis testing" will indicate whether there is enough "evidence" to reject H_0
  - H_0 is "rejected"= statistically significant (SS) difference
  - H_0 is "not rejected" = no SS difference

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Statistical Tests and Choosing a Statistical Test

- Dependent on:
  - Type of data (nominal, ordinal, continuous)
  - Distribution of data (normal, etc.)
  - Study design (parallel, crossover, etc.)
  - Presence of confounding variables
  - One-tailed versus two-tailed
- Parametric vs. nonparametric tests

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Parametric vs. Non-parametric

- Parametric tests assume…
  - Underlying ~normal distribution
  - Continuous data
  - Variances that are ~ equal
- Nonparametric tests…
  - Data are not normally distributed
  - Data do not meet other criteria

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Parametric Tests
Student's t-test(s)

- **One-sample test:** Compares the mean of the study sample with the population mean
- **Two-sample test:** Compares the means of two independent samples
  - Equal variance vs. Unequal variance
- **Paired t-test:** Compares the mean difference of paired or matched or related samples

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Parametric Tests
Analysis of Variance (ANOVA)

- One-way (single factor) ANOVA:
  - Compares the means of ≥3 groups

Young	Group 1	Group 2	Group 3

- Two-way (two factor) ANOVA:
  - Additional factor added

Young	Group 1	Group 2	Group 3
Elderly	Group 1	Group 2	Group 3

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Parametric Tests
Analysis of Variance (ANOVA)

- Repeated Measures ANOVA:
  - Related samples test, extension of paired t-test

	Related Measurements		
Young (Group 1)	Measurement 1	Measurement 2	Measurement 3

- Post-hoc testing

Pages 2-124-5

Non-Parametric Tests

- Tests for independent samples
  - Wilcoxon rank sum/Mann-Whitney U-test
    - Compares 2 independent samples (independent samples t-test)
  - Kruskal-Wallis one-way ANOVA by ranks
    - Compares ≥ 3 independent groups (one-way ANOVA)

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Non-Parametric Tests

- Tests for related or paired samples
  - Sign test and Wilcoxon signed rank test: Compares 2 matched or paired samples (paired t-test)
  - Friedman ANOVA by ranks: Compares ≥3 matched/ paired groups

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Non-Parametric Tests
Nominal Data

- Chi-square (χ^2) test: Compares expected and observed proportions between ≥2 groups
- Fisher exact test: Use of Chi-square test for small groups (cells) containing <5 observations
- McNemar: Paired samples
- Mantel-Haenszel: Controls for the influence of confounders

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Choosing the Most Appropriate Statistical Test: Example

Group	Baseline LDL (mg/dL)	p-value Baseline	Final LDL (mg/dL)	p-value Final
Rosuvastatin (n=25)	152 ± 5	> 0.05	138 ± 7	> 0.05
Simvastatin (n=25)	151 ± 4		135 ± 5	

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Choosing the Most Appropriate Statistical Test: Example

	Rosuvastatin (n=25)	Simvastatin (n=25)
Men/Women	12/13	10/15
Smokers	10	13
Baseline LDL-C (mg/dL)	152 ± 5	151 ± 4

- Appropriate test to determine baseline differences in:
  - Sex distribution?
  - Low-density lipoprotein cholesterol?
  - Percentage of smokers and nonsmokers?

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Appropriate test to determine baseline differences in….

- 1. Sex distribution?
  2. Low-density lipoprotein cholesterol?
  3. Percentage of smokers and nonsmokers?

A. ☐ Wilcoxon signed rank test
B. ☐ Chi-square test
C. ☐ ANOVA
D. ☐ Two-sample t-test

Choosing the Most Appropriate Statistical Test: Example

	Rosuvastatin (n=25)	Simvastatin (n=25)
Baseline LDL (mg/dL)	152 ± 5	151 ± 4
Final LDL (mg/dL)	138 ± 7	135 ± 5
3 mo Δ LDL (mg/dL)	14 ± 6	16 ± 5

- Appropriate test to determine:
  - Effect of rosuvastatin on LDL-C

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Appropriate test to determine

- Effect of rosuvastatin on LDL-C

A. ☐ Wilcoxon signed rank test
B. ☐ Paired t-test
C. ☐ ANOVA
D. ☐ Two-sample t-test

Decision Errors
Type I Error

- Probability of making Type I error = significance level (α), usually 0.05
  - 5.0% of the time, we will conclude there is a SS difference when actually one does not exist
  - Calculated chance that a type I error has occurred is called the "p-value."
  - Lower p-value does not suggest more importance, only SS and less likely attributable to chance

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Decision Errors
Type II error (β) and Power (1-β)

- Type II Error (β), usually 0.10-0.20
  - Concluding that no difference exists when one does
- Power:
  - Ability to detect differences between groups if one actually exists
  - Dependent on:
    - Predetermined α
    - Sample size
    - Effect size
    - Variability of the outcomes that are being measured

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Statistical significance versus clinical significance

- Size of the p-value is not related to the importance of the result.
- Statistically significant not necessarily clinically significant
- Lack of statistical significance does not mean results are not important.
- With nonsignificant findings consider… sample size, estimated power, and observed variability

Pages 2-126-7

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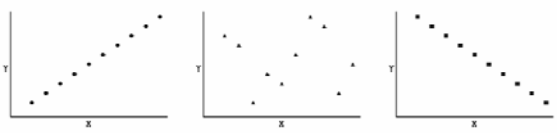
Correlation and Regression

- Correlation examines the strength or degree of the association between two variables
- Does not necessarily imply that one variable is dependent on the other or predicts the other
- Pearson correlation: Parametric test
- Spearman Rank Correlation: Nonparametric test

Pages 2-128-30

Correlation Coefficient



1
Perfect positive linear relationship

0
No linear relationship

-1
Perfect negative linear relationship

Regression

- Regression examines the ability of one or more variables to predict another variable
- Dependent and independent variable
- Development of prediction model: $Y = mx + b$
- Accuracy of prediction: How well the independent variable predicts the dependent variable.
  - Coefficient of determination (r^2) can range 0 to 1.
  - An r^2 of 0.80: 80% of the variability in *Y* is "explained" by the variability in *X*.

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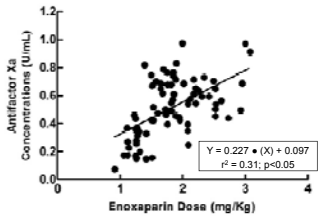
Regression Example



What you should know….

- Slope and intercept?
- r^2 interpretation?
- Predict antifactor Xa concentrations at doses of 2 and 3.75 mg/kg
- What does the $p<0.05$ value indicate?

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Survival Analysis

- Studies the time between entry in a study and some event (e.g., death, myocardial infarction)
  - Censoring makes survival methods unique
  - Subjects do not enter the study at the same time

Pages 2-130-1

Survival Analysis

- Kaplan-Meier method
  - Uses survival times to estimate the proportion of people who would survive a length of time
- Log-Rank Test
  - Compare the survival distributions ≥ 2 groups
- Cox proportional hazards model
  - Evaluate the impact of covariates on survival in two or more groups
  - Allows calculation of a hazard ratio (and CI)

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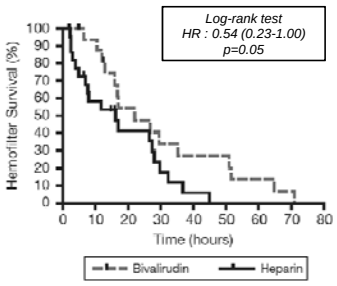
Survival Analysis
Kaplan-Meier method



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Pharmacotherapy 2010; 30:1117-26

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Study Designs: Fundamentals of Design and Interpretation

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Outline

- Validity, Bias and Confounding
- Clinical Study Designs
  - Observational
  - Interventional
- Clinical Trials Analysis and Interpretation
- Summary Measures of Effect
- Miscellaneous

Validity in Study Design

- Internal validity
  - Within the confines of the study methods
  - Does the study design adequately and appropriately test/measure what it purports?
  - Does the study adequately and appropriately address bias, confounding, and measurement of end points?
- External validity
  - Related to generalizing the results outside of the study setting
  - Can the results be applied to other groups, patients, or systems?
  - Addresses issues of representativeness

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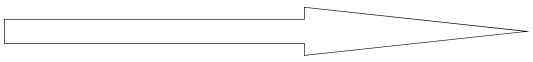
Bias and Confounding in Study Design

- Bias
  - Systematic, non-random variation in study methodology and conductance…introducing error in interpretation
  - Selection bias: Arise from selection of subjects
  - Observation or information bias
- Confounding
  - Variable that impacts the independent/dependent variable altering the ability to determine the true effect on the outcome
  - May hide or exaggerate a true association
  - All relevant information should be collected and evaluated

Pages 2-138-39

Relative Strength of Evidence: Hierarchy of Study Designs



	Descriptive		Observational Studies			Experimental/ Interventional
Ideas, Opinions and Reviews	Case report	Case series	Case-control	Cohort	Cross Sectional	RDBCT
	Systemic Reviews and Meta Analysis					

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Types of Clinical Trial Design
Case Reports/Case Series

- Document and describe experiences, novel treatments and unusual events
- Hypotheses generation
  - Example: QT interval prolongation associated with FQ antibiotics
  - Case report: One patient
  - Case series: > 1 patient with a similar experience or multiple case reports combined
  - Sufficient detail to recognize same/ similar cases
  - Is IRB approval required?

Pages 2-139-140

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Observations Study Designs
Case-control

- Study exposure in those with/without condition of interest
- Determine the association between exposures (risks) and disease (condition)
- Useful to study exposures in rare diseases or ones that take long periods to develop
- Critical assumptions to minimize bias:
  - Cases are selected to be representative of those with the disease
  - Controls are representative of the population without the disease and are as identical as possible to the cases (- Dz)
  - Information is collected from cases and controls in the same way

Pages 2-140-3

Observations Study Designs
Case-control

- Advantages
  - Inexpensive and can be conducted quickly
  - Allows investigation of multiple possible exposures /associations
- Disadvantages
  - Confounding must be controlled for
  - Observation and recall bias: looking back to remember
  - Selection bias: Case selection and control matching is difficult
- Measure of Association: Odds Ratio

Pages 2-140-3

Observations Study Designs
Cohort Study

- Determine the association between exposures/ factors and disease/condition development.
  - Estimate the risk of outcome and study outcome of interest in those with and without exposure
  - Relative risk between the exposure groups
  - Risk of an event or development of a condition relative to exposure
- Describes the incidence or natural history of a disease/condition and measures it in time sequence
- Prospective vs. retrospective

Pages 2-140-3

Observations Study Designs
Cohort Study

Retrospective	Prospective
Begin/end in the present… major backward look to collect data about past events	Begin in the present and progress forward….collecting data on future outcomes
Advantages: Less expensive and time-consuming; no loss to follow-up, ability to investigate issues not amenable to a clinical trial or ethical/safety issues	Advantages: Easier to control for confounding factors, easier to plan for data collection
Disadvantages: Only as good as the data available, little control of confounding variables through nonstatistical approaches, recall bias	Disadvantages: Expensive and time-intensive, loss of follow-up, difficult to study rare diseases/conditions at a reasonable cost

Pages 2-140-3

Observations Study Designs
Cross Sectional or Prevalence Study

- Identify the prevalence or characteristics of a condition in a group of individuals
- Snapshot in time
- Advantages:
  - Easy design, data collected at one time
  - Questionnaire, interview, or other available information
- Disadvantages: Does not allow a study of factors in individual subjects over time, difficult-to-study rare conditions

Pages 2-140-3

Incidence and Prevalence

- Incidence
  - Measure of the instantaneous rate of developing a disease (reflects the rate of disease development)
  - Measured in persons/year
- Prevalence
  - Measure of the number of individuals who have a condition/disease at any given time.

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Interpreting Relative Risks/Odds Ratios

- Estimate the magnitude of association between exposure and disease, not cause and effect
- RR: Cohort studies
- OR: Case control studies (estimate of the RR).
- Interpreted on the basis of their difference from 1
  - If the 95% CI includes 1: no statistical difference

Pages 2-143-44

Interpreting Index of Risk

- Direction of risk

RR	OR	Interpretation
< 1	< 1	Negative association, RR: Risk lower in exposed group, OR: Odds of exposure is lower in diseased group
=1	=1	No association, RR: Risk is the same, OR: Odds of exposure is the same
> 1	> 1	Positive association, , RR: Risk is greater in exposed group OR: Odds of exposure is greater on diseased group

- Magnitude of Risk

RR	OR	Interpretation
0.75	0.75	25% reduction in the risk/odds
1.0	1.0	No difference in risk/odds
1.5	1.5	50% increase in the risk/odds
3.0	3.0	3-fold (or 200%) increase in the risk/odds

Pages 2-143-4

PPA Study Interpretation

	Cases (+ stroke) n=383	Controls (− stroke) n=750	Adjusted OR (95% CI)
Appetite suppressant: Women	6	1	16.6 (1.51–182)
Appetite suppressant: Men	0	0	–
Appetite suppressant: Either	6	1	15.9 (1.38–184)
PPA: Women	21	20	1.98 (1.00–3.90)
PPA: Men	6	13	0.62 (0.20–1.92)
PPA: Either	27	33	1.49 (0.84–2.64)

- Interpret the point estimate and 95% CI in all cases?
  - What does the point estimate mean?
  - What does the CI mean?
  - Which ones are statistically significant?

Page 2-145

N Engl J Med 2000;343:1826–32

Interventional Study Design Randomized, Controlled Trials

- Make intervention and evaluate cause and effect
- Design allows assessment of causality
- Minimizes bias through randomization and/or stratification
- Parallel vs. crossover design
  - Crossover provides practical and statistical efficiency.
  - Crossover not appropriate for certain types of questions….disease that worsens during the study

Pages 2-146-48

Interventional Study Design Randomized, Controlled Trials

- Are the results of the study valid?
- Can I apply the results of this study to my patient population?
- Will they help me care for my patients?
- Other issues related to RCT…
  - Subgroup analyses
  - Primary, Composite and Surrogate Endpoints
  - Superiority, Equivalence, Non-Inferiority

Pages 2-146-48

Randomized, Controlled Trials Subgroup Analysis

- Important part of controlled clinical trials
  - Often overused and over-interpreted
- Many potential pitfalls in identifying and interpreting:
  - Failure to account for multiple comparisons or adjust p-val
  - Problems with sample size, power, classification, and lack of assessment of interaction

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Randomized, Controlled Trials
Primary and Composite End Points

- Primary end point: crucial design decision
- What does the following statement mean?
- "…ramipril…reduces the rate of death, MI, stroke, revascularization, cardiac arrest, HF, complications related to DM, and new cases of DM in…high-risk patients. Treating 1000 patients with ramipril for 4 years prevents about 150 events in around 70 patients.
  - Was there a reduction in all the end points or just some?
  - Are all the outcomes just as likely to occur?
  - Why would this trial have been interested in all of these outcomes?

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Randomized, Controlled Trials
Composite End Points

- Positives for using composite end points?
- Problems?
  - Difficulties in interpretation
  - Misattribution of statistically beneficial effects of composite to each of its component end points
  - Dilution of effects, Undue influence exerted on composite end point by "softer" end points
  - "Averaging" of overall effect…
  - Should all end points weigh the same, or death "weigh" more?
- Results for each individual end point should be reported with the results for the composite

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Randomized, Controlled Trials
Surrogate End Points

- Parameters thought to be associated with clinical outcomes
  - BP reduction and stroke prevention
  - LDL-C reduction and CV death reduction
    - Statins vs. hormone replacement therapy
  - PVC suppression and mortality reduction
- Surrogate outcomes ≠ predict clinical outcomes
- Short-duration studies with surrogate end points may be too small to detect uncommon AEs

Pages 2-148-49

Randomized, Controlled Trials
Superiority vs. Equivalence vs. Non-inferiority

- Superiority trial: Detect a difference between Txs
  - Typical design in a "traditional" clinical trial
- Equivalence trial: Confirm the absence of meaningful difference(s) between Txs
- Non-inferiority trial: Investigate whether a Tx is not clinically worse (no less effective)
  - Useful if placebo is not possible due to ethical reasons

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Randomized, Controlled Trials
Non-inferiority Design: ONTARGET

- Telmisartan, ramipril, or combination in patients with a high risk of VDz
- Is telmisartan non-inferior in the incidence of CV deaths?
- Non-inferior difference defined as ≤ 13%
- Essentials of non-inferiority design
  - Control group (ramipril) must be effective
  - Study similar to previous study with control (HOPE) and with equal doses, clinical conditions, and design
  - Adequate power is essential, and usually, larger sample sizes are required.

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EXAMPLE: Randomized Trial of ERT-P for Secondary Prevention of CHD in Postmenopausal Women

- Objective: Does ERT-P therapy alter the risk of CHD in postmenopausal women with established CHD?
- Randomized, blinded, placebo controlled
  - CEE 0.625 mg/day plus MPA 2.5 mg/day (ERT-P) and placebo – n=2763 with CAD < 80; mean age = 66.7 years
  - Follow-up averaged 4.1 years; 82% of HRT still taking at the end of 1 year; 75% 3 years

Pages 2-149-50 *JAMA* 1998;280:605–13

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Randomized Trial of ERT-P for Secondary Prevention of CHD in Postmenopausal Women

- End points
  - Primary: Nonfatal MI, CHD death
  - Secondary: Many, including all-cause mortality.
    - Are these composite outcomes appropriate?
- Surrogate end point: LDL-C lowered
- Statistical analysis:
  - Baseline characteristics: t-test and Chi-square
  - Power analysis and sample size calculation
  - Kaplan-Meier with Cox proportional hazards model, intention to treat

Pages 2-149-50 *JAMA* 1998;280:605–13

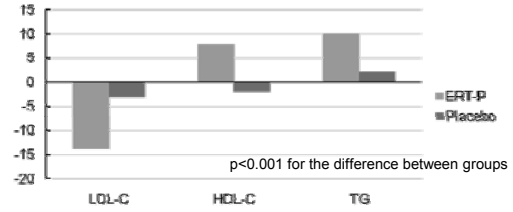
Baseline Characteristics

	ERT-P (n=1380)	Placebo (n=1383)	p-value
Demographics			
Age, mean±SD, yrs	67±7	67±7	0.32
White, %	88	90	0.14
Education, mean±SD, yrs	13±3	13±3	0.84

- Statistical analysis:
  - Baseline characteristics: t-test and Chi-square ☐ ☐

Pages 2-149-50 *JAMA* 1998;280:605–13

Surrogate Endpoints Change in Lipid Profiles after 1 year



- Statistics: No documented test for above comparison
  - "mean LDL-C decreased"
- What is appropriate test?? What does it mean??

Pages 2-149-50 *JAMA* 1998;280:605–13

Randomized, Controlled Trials Composite Endpoint

	ERT-P	Placebo	HR (95% CI)
Primary CHD events	12.4	12.7	0.99 (0.80-1.22)
CHD death	5.1	4.2	1.24 (0.81-1.75)
Any thromboembolic event	2.5	0.9	2.89 (1.50-5.58)
Gall bladder disease	6.1	4.5	1.38 (1.00-1.92)

- Statistics: Kaplan-Meier with Cox proportional hazards model, intention to treat
- Significant time trend: More CHD events in the treatment group than in placebo in year 1 and fewer in years 4 and 5
- Which are statistically different? ☐ Yes ☐ No
- Conclusions

Pages 2-149-50 *JAMA* 1998;280:605–13

Common Approaches to Analyzing Clinical Trials: Intention to treat

- Compares outcomes based on randomization
- How they were "intended to be treated"
- Treatment effects under usual conditions
- Conservative estimate (may underestimate) of differences in treatment
- Most common approach to assessing clinical trial results

Pages 2-150-1

Per-Protocol Analysis

- Those who do not complete/adhere to treatment are not included in the final analysis
- Provides additional information about treatment effectiveness and more generous estimates of differences
- Subject to several issues such as lower sample size and definitions of adherence
- Results are more difficult to interpret

Pages 2-150-1

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As-Treated Analysis

- Analyzed by the actual intervention received
- This analysis essentially ignores the randomization process for those who did not adhere to the study design

Pages 2-150-1

Systematic reviews

- Summary that uses explicit methods to perform a comprehensive literature search, critically appraise it, and synthesize the literature
- Differs from a standard literature review,which combine evaluation with opinions
- Key is a well-documented and described systematic review.
- Some systematic reviews will attempt to statistically combine results from many studies

Pages 2-151-2

Meta-analysis

- Systematic review that uses statistical techniques to summarize the results of the evaluated studies
- These techniques may improve on:
  - Calculation of effect size
  - Increase statistical power
  - Interpretation of disparate results
  - Reduce bias
  - Answers to questions that may not be addressable with additional study

Pages 2-151-2

Issues related to meta-analysis

- Assessment of trial methodology
  - Focused research question?
  - Types of studies were included?
  - How was quality assessed, and how many reviewers were there?
  - How was heterogeneity assessed?
    - Statistical heterogeneity
    - χ^2 and Cochrane *Q* are common tests for heterogeneity
- Sensitivity analysis
- Assessment of risk

Pages 2-151-2

Summary Measures of Effect Absolute vs. Relative Differences

- Absolute differences or absolute changes
- Relative differences or relative changes
- Absolute differences are more important than relative differences
  - Authors highlight the differences observed in their trials with relative differences because they are larger
  - Why? Larger numbers are more convincing
  - Most drug advertisements (both directly to patients and to health care professionals) quote relative differences

Page 2-153

Heart Outcomes Prevention Evaluation (HOPE) Study

- Randomized, double blind, placebo controlled study
- 9297 high-risk patients received ramipril or placebo daily; average follow-up of 5 years
- Primary outcome: Composite of MI, stroke, or death from cardiovascular causes

Page 2-153 *N Engl J Med* 2000;342:145–53

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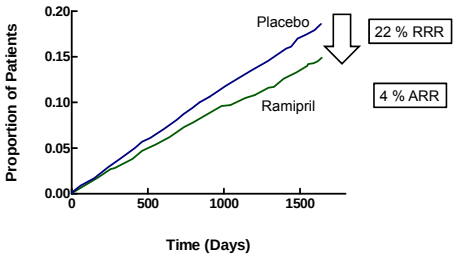
Absolute vs. Relative Differences
Risk reduction of Primary End Point



Page 2-153

Data extracted and adapted from *NEJM* 2000;342:145-53

Summary Measures of Effect
Number Needed to Treat

- Another means to characterize changes or differences in absolute risk
- Definition: The reciprocal of the ARR
  - NNT = 1/(ARR)…Rounded to the next highest whole num
- Applied to clinical outcomes with dichotomous data
- Cautions: Assumes the baseline risk is the same for all (or that it is unrelated to RR)
- Extrapolation beyond studied time duration
- NNTs should only be provided for significant effects

Page 2-153

NNT Application
HOPE study

- Results NNT = 1/(0.178 − 0.140) = 1/0.038 = 26.3, rounded up to 27
- NNT for each endpoint

Outcome	Ramipril (%)	Placebo (%)	Relative Risk	RRR	ARR	NNT
Combined	14.0	17.8	0.79	0.21	0.038	27
Death from CV causes	6.1	8.1	0.74	0.25	0.02	50
Myocardial infarction	9.9	12.3	0.80	0.20	0.024	42
Stroke	3.4	4.9	0.68	0.31	0.015	67

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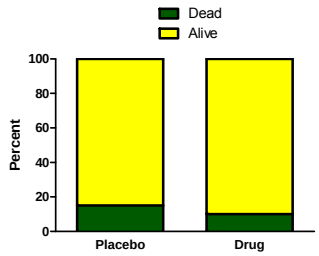
N Engl J Med 2000;342:145–53

Summary

Absolute vs. Relative Differences



- ARR
  - 15%-10%=
  - 5%
- RRR
  - (15%-10%)/15%
  - 33%

Interventional Study Design
Randomized, Controlled Trials

- Examples:
  - Clinical trial: Comparison of two drugs, two behavioral modifications...
  - Educational intervention: Online course versus lecture class format
  - Health care intervention: RPh vs. non-RPh-based health care team

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Calculation of RR, OR……

Phenylpropanolamine and the risk of hemorrhagic stroke

		Disease? Hemorrhagic Stroke	
		Yes	No
Exposure? Use Appetite Suppression	Yes	*6*	*377*
	No	*1*	*749*

$$RR = \frac{A/(A+B)}{C/(C+D)}$$

$$OR = \frac{\frac{A}{C}}{\frac{B}{D}} = \frac{\frac{6}{1}}{\frac{377}{749}}$$

N Engl J Med 2000;343:1826–32

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Updates in Therapeutics® 2012:
Ambulatory Care Pharmacy Preparatory Review and Recertification Course

Bone/Joint & Rheumatology
Daniel S Longyhore, Pharm.D., BCACP
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Conflict of Interest Disclosures

None

Learning Objectives and/or Agenda

- Systematically identify patients to screen for osteoporosis and use the screening results to guide the decision on how to treat the patient.
- Use a STEPS-wise approach for comparing, recommending, and justifying a drug therapy regimen for osteoporosis.

Learning Objectives and/or Agenda

- Evaluate the severity and prognostic indicators of rheumatoid arthritis in order to choose the most appropriate initial regimen with disease-modifying antirheumatic drugs (DMARDs).
- Identify appropriate health maintenance interventions when caring for a patient receiving biologic and nonbiologic DMARD therapy.

OSTEOPOROSIS

Patient Case 1

F.R. is a 74-year-old woman with a history of a right hip replacement after a fall and fracture. In addition to her hip fracture, the patient has a history of type 2 diabetes mellitus, hypothyroidism, and dyslipidemia, for which she receives treatment. A DXA revealed F.R.'s T-score at her femoral neck to be −2.7 and −2.1. The Z-score associated with her femoral neck T-score was −2.1. Her physician believes that this was a fracture secondary to drug-induced bone density loss.

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Patient Case 1

Which one of the following medications most likely contributed to her BMD loss and fracture?

- Metformin.
- Glipizide.
- Levothyroxine.
- Lovastatin.

Page 2-162
Answer 2-203

Osteoporosis

- Risk Factors
  - Women > 65 years
    Men > 70 years
  - Smoking
  - Rheumatoid arthritis
    Type 2 diabetes
    Asthma/COPD
    History of falls
  - Gender-specific factors
- Medication-induced
  - Anti-epileptic agents
  - Immunosuppressants
  - Proton-pump inhibitors
  - Corticosteroids
  - SSRI / TCA use
  - Excessive T3/T4 supp.
  - Warfarin / heparin use

Page 2-161

Patient Case 1

Which one of the following medications most likely contributed to her BMD loss and fracture?

- Metformin.
- Glipizide.
- Levothyroxine.
- Lovastatin.

Page 2-162
Answer 2-203

Ostoporosis

- Screening Recommendations

Table 3. Screening Recommendations

National Osteoporosis Foundation (2010)	U.S. Preventive Services Task Force (2011)	Am. Assoc. of Clinical Endocrinologists (2010)
Women: Older than 65 years Postmenopausal with clinical risk factors Menopausal woman with risk factors (low BMI, prior low-trauma fracture, high-risk medication use)	**Women:** 65 years or older without known fractures or secondary causes of osteoporosis 50–65 years with 10-year major osteoporotic risk (FRAX) greater than 9.3%	**Women:** 65 years or older 65 years or younger at an increased risk of fracture, based on risk factors
Men: Older than 70 years Age 50–69 years with clinical risk factors	**Men:** No recommendation	**Men:** No recommendation
Any adult: Fracture after age 50 Condition associated with bone loss Use of medication associated with bone loss		

Page 2-162

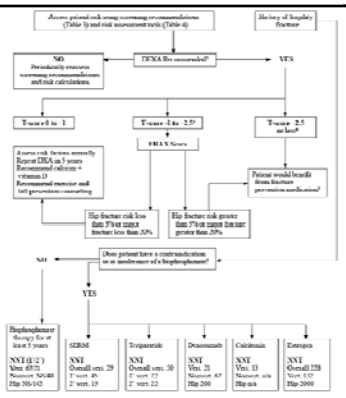
Osteoporosis

- Diagnostic Criteria

Diagnosis	Criteria (T-score)
"Normal"	Zero to 1 standard deviation below average
Osteopoenia	One to 2.5 standard deviations below average
Osteoporosis	Greater than 2.5 standard deviations below average

*Consider a diagnosis of osteoporosis if two individual lumbar spine measurements are greater than 2.5 standard deviations below the mean, regardless of the lumbar spine average.
**A patient with osteopenia and a FRAX score of greater than 3% in the hip or 20% for major osteoporotic fracture are treated the same as a person with osteoporosis.

Page 2-163



Page 2-164

Osteoporosis

- Preventative Counseling
  - Supplemental Calcium intake
    - 1,200 to 1,500 mg (elemental) per day
  - Vitamin D intake
    - 800 to 1000 units per day
  - Physical activity
  - Social habits
  - Fall assessments

Page 2-166

Patient Case 4

E.U. is a 58-year-old woman with a medical history significant for primary progressive multiple sclerosis with severe limitation, for which she spends most of her time in bed or lying on a couch. She attempts to ambulate but is unable to do so without a walker and/or assistance. She has been given a diagnosis of osteoporosis of the lumbar spine by DEXA, and she now requires treatment. She already takes 1200 mg of calcium carbonate daily (600 mg twice daily) and 800 units of vitamin D (400 units twice daily).

Page 2-165

Patient Case 4

Which one of the following agents is best for E.U. for prevention of vertebral fracture?

- [ ] Zoledronic acid 5-mg infusion once yearly.
- [ ] Risedronate 150-mg tablet once monthly.
- [ ] Raloxifene 60-mg tablet once daily.
- [ ] Calcitonin nasal spray, 1 spray per nostril each day.

Page 2-165
Answer 2-203

Osteoporosis

- Calcium Supplementation
  - Improves and sustain bone mineral density
  - Recommend use in conjunction with all other medications to treat osteoporosis
  - Target daily intake of 1,000 to 1,500 mg per day (depending on age, hormone replacement status)
  - Slight increase risk of nephrolithiasis with calcium carbonate use
  - Account for other medications and acid-suppression status when choosing calcium formulation

Page 2-166

Osteoporosis

- Vitamin D supplementation
  - Used in conjunction with calcium to increase calcium absorption
  - Unclear if Vitamin D alone will decrease fracture risk (100,000 units every 3 months; NNT 44)
  - Has demonstrated a decrease risk of falls when used in elderly patients
  - Annual dosing alternative (500,000 units per year) has a higher rate of falls and fractures

Page 2-167

Osteoporosis

- Bisphosphonates
  - First-line option for the treatment of osteoporosis
    - Effective for preventing glucocorticoid-induced bone disease
  - All bisphosphonates will prevent fractures
    - Vertebral: alendronate, ibandronate, risedronate, zoledronic acid
    - Non-vertebral: alendronate, risedronate, zoledronic acid
  - Use caution in patients with a low creatinine clearance
    - Less than 30 mL/minute: risedronate & ibandronate
    - Less than 35 mL/minute: alendronate & zoledronic acid

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Osteoporosis

- Bisphosphonates
  - Safety concerns surrounding FDA warning of atypical femur fractures
    - Likelihood of event increases over time and is greatest when treatment is for greater than 5 years
    - Cohort study of 83,000 women treated with bisphosphonates showed absolute risk difference of 0.0005 (NNH 2,000)
  - Osteonecrosis of the Jaw
    - Oncology patients: 1-12% after 36 months of exposure
    - Osteoporosis patients: < 1 case per 100,000 person-years of exposure

Page 2-167

Osteoporosis

- Bisphosphonates
  - Patient counseling points
    - Most doses should be taken with 6 to 8 ounces of water 30 to 60 minutes before the first meal of the day
      - Exception: risedronate delayed-release should be dosed immedately after breakfast
    - Remain upright for 30 to 60 minutes after dosing
    - If the patient is unable to tolerate because of gastrointestinal or musculoskeletal adverse events, discontinue the agent until the symptoms resolve and then restart a different bisphosphonate

Page 2-167

Patient Case 4

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- Risedronate 150-mg tablet once monthly.
- Raloxifene 60-mg tablet once daily.
- Calcitonin nasal spray, 1 spray per nostril each day.

Page 2-165
Answer 2-203

Osteoporosis

- Estrogen Replacement Therapy
  - Reduces the risk of both vertebral and non-vertebral fractures
  - Risk of hormone replacement therapy-induced heart disease, stroke, venous thromboembolism, and breast cancer are approximately equal to that of the benefit of fracture prevention.

Page 2-168

Osteoporosis

- Selective Estrogen Receptor Modulator (SERM)
  - Increases bone mineral density and reduces the risk of clinical vertebral fractures
  - Ideal agent for patients with osteoporosis and history of invasive breast cancer
  - The rates of venous thromboembolism are approximately the same as the rates for clinical fracture prevention
  - Other adverse events
    - Arthralgias, hot flashes/flushes, peripheral edema, sweating

Page 2-169

Osteoporosis

- Biosynthetic parathyroid hormone 1-34
  - Decreases the incidence of vertebral fractures in women
  - Increases bone mineral density in the vertebrae and hip
  - Effective for preventing fracture and bone mineral density loss in patients receiving chronic corticosteroids
  - Diminished effect when used concurrently with a bisphosphonate
    - Used with a bisphosphonate in sequential therapy

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Osteoporosis

- Biosynthetic Parathyroid Hormone 1-34
  - Avoid using in patients:
    - With alkaline phosphatase elevations
    - With prior skeletal radiation
    - For greater than 24 months
  - Counsel patients regarding adverse events
    - Influenza-like symptoms
    - Injection site pain and/or rash
    - Urolithiasis

Page 2-169

Osteoporosis

- Calcitonin
  - Inferior for bone mineral density preservation when compared to alendronate
  - Suggested to help with "bone pain" associated with osteoporotic fractures
    - Should not be considered for a compelling indication or chosen over any other available agent to preserve bone mineral density or prevent fracture
  - Injection is associated with anaphylactoid and anaphylaxis reactions

Page 2-170

Osteoporosis

- Denosumab
  - Relatively new to the U.S. market and is not included in most clinical guidelines, yet.
  - NICE guidelines (U.K.) recommend using denosumab for patients who are unable to adhere to or tolerate the use of a bisphosphonate.
  - Most serious adverse events include cellulitis and osteonecrosis of the jaw.
  - Administered as a subcutaneous injection every 6 months

Page 2-170

Osteoporosis

- Follow-up
  - If not using drug therapy
    - Recheck DEXA every 5 years or sooner if a new risk factor for premature bone mineral density loss is present
  - If using drug therapy
    - Recheck DEXA 24 months after starting drug therapy
    - Do not be concerned if there is a new bone loss over this time
    - Questionable if continued DEXA monitoring is necessary
    - Medication adherence at least every 6 months

Page 2-170

Osteoporosis

Physician Quality Reporting System (CMS) 2011

Number	Category
24	Osteoporosis: Communication with the Physician Managing Ongoing Care Post Fracture
39	Screening or Therapy for Osteoporosis for Women Aged 65 Years and Older
40	Osteoporosis: Management Following Fracture
41	Osteoporosis: Pharmacologic Therapy

Page 2-171

RHEUMATOID ARTHRITIS

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Patient Case 5

F.T. is a 38-year-old man recently referred from his primary care provider to a rheumatologist for assessmentand treatment of RA. During the initial interview, the rheumatologist assesses the patient for various subjectiveand objective markers of disease activity. Of the following four markers used to assess disease activity, which one is a clinically relevant prognostic marker?

- Joint involvement (quantity).
- Erythrocyte sedimentation rate (ESR).
- Rheumatoid factor (RF).
- C-reactive protein (CRP).

Page 2-172
Answer 2-203

Rheumatoid Arthritis

- Patient Presentation
  - Diffuse pain
  - Variable time to symptoms onset
  - Morning joint stiffness lasting greater than 60 minutes
  - Affected joints include:
    - Elbow
    - Foot and ankle
    - Hands and wrists
    - Hip
    - Knee

Page 2-171

Rheumatoid Arthritis

- 2010 ACR/EULAR Classification Criteria
  - Test patients with at least one joint with clinical synovitis not otherwise explained by another disease
  - The tool is not diagnostic, but a score of 6 out of 10 is considered "definite RA"
  - A score of 6 or higher may also be a good indicator for individuals with the highest probability of persistent or erosive disease

Page 2-172

Rheumatoid Arthritis

Table 16. 2010 ACR/EULAR Classification Criteria for Rheumatoid Arthritis

Classification Criteria	Scoring (points)
1. Joint involvement	
More than 10 joints including at least 1 small joint	5
4–10 small joints	3
1–3 small joints	2
2–10 large joints	1
1 large joint	0
2. Serology	
Positive RF or positive ACPA greater than 3 times the upper limit of normal	3
Positive RF or positive ACPA up to 3 times the upper limit of normal	2
Negative RF and ACPA	0
Acute-phase reactants	
Abnormal CRP or ESR	1
Normal CRP and ESR	0
Duration of symptoms	
At least 6 weeks	1
Less than 6 weeks	0
Total points	

ACPA = anti-citrullinated protein antibody; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; RF = rheumatoid factor.

Page 2-172

Rheumatoid Arthritis

- Disease Prognosis
  - Functional limitations
  - Positive RF or ACPA
  - Radiographic evidence of bony erosions
  - Extra-articular disease
- Other markers
  - Disease activity in the first three to six months

Page 2-173

Patient Case 5

F.T. is a 38-year-old man recently referred from his primary care provider to a rheumatologist for assessmentand treatment of RA. During the initial interview, the rheumatologist assesses the patient for various subjectiveand objective markers of disease activity. Of the following four markers used to assess disease activity, which one is a clinically relevant prognostic marker?

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- Rheumatoid factor (RF).
- C-reactive protein (CRP).

Page 2-172
Answer 2-203

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Rheumatoid Arthritis

- Pretreatment Education
  - Physical / Occupational therapy
  - Social work and/or counseling services
  - Energy conservation
  - Joint protection
  - Range-of-motion exercises
  - Strengthening exercises

Page 2-173

Rheumatoid Arthritis

- Immunizations

Live Vaccines	Avoid administration with concurrent biologic therapy or within 3 months of discontinuation
Influenza Vaccine	Administer annually
Pneumococcal Vaccine	Administer to all patients receiving biologic DMARDs, methotrexate, leflunomide, and/or sulfasalazine
Hepatitis B Vaccine series	Administer to all patients with risk factors and receiving biologic therapy, methotrexate, and/or leflunomide

Page 2-174

Rheumatoid Arthritis

- ACR treatment recommendations
  - Choice of drug driven by disease duration, activity, and prognosis
  - Non-DMARDs for pain control:
    - NSAIDs
    - Low-dose systemic corticosteroids
    - Local corticosteroid injections
  - Initiate treatment within the first 3 months of diagnosis
  - Consider the patient's ability to pay for and continue paying for therapy

Page 2-178

Rheumatoid Arthritis

- EULAR treatment recommendations
  - Initiate DMARD therapy, specifically methotrexate, early
  - Adding a TNF antagonist is appropriate for patients if:
    - Treatment naïve and poor prognosis
    - Not responding adequately to methotrexate
  - If the patient shows evidence of remission:
    - Taper the corticosteroid dose
    - Taper the biologic DMARD use
    - And/or decrease nonbiologic DMARDs to the lowest effective dose

Page 2-178

Rheumatoid Arthritis

- Non-Steroidal Anti-Inflammatory Drugs
  - Effective at reducing the pain associated with RA, but will not change joint destruction or progression of RA
  - All available NSAIDs are equally effective, but not all patients will respond to the same NSAID
  - After a 14- to 28-day trial, try at least one other NSAID before saying treatment is ineffective
  - Various strategies to reduce or manage GI complaints associated with chronic NSAID use
  - Evaluate NSAID related cardiovascular event risk prior to choosing the most appropriate agent

Page 2-178

Rheumatoid Arthritis

- Corticosteroids
  - Short-term, low-dose corticosteroids are effective for symptom flares
  - Early introduction and continued low-dose corticosteroids will help prevent joint reduction and increased likelihood of clinical remission
  - Adverse events associated with continued use
    - Metabolic abnormalities
    - Calcium and vitamin D supplementation
    - Bisphosphonates in select groups

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Rheumatoid Arthritis

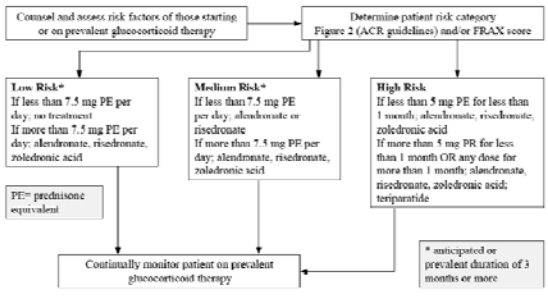

Figure 4. Preventing corticosteroid-induced BMD loss in postmenopausal women and men older than 50.
Reprinted with permission Arthritis Care Res 2010;62:1515–26.

Listed as Figure 5 on Page 2-180

Rheumatoid Arthritis

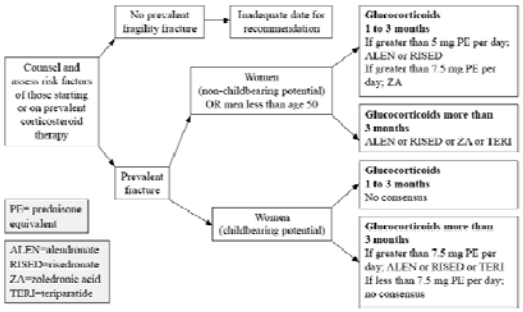

Figure 5. Preventing corticosteroid induced BMD loss in premenopausal women and men under age 50.
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Listed as Figure 6 on Page 2-180

Patient Case 8

T.D. is a 28-year-old graduate student meeting with a rheumatologist regarding worsening RA symptoms. She currently takes methotrexate 20 mg by mouth weekly, folic acid 1 mg by mouth daily, and naproxen 500 mg by mouth twice daily as needed for pain Her symptoms have been increasingly worse during the past 3 months, and she has been using naproxen around-the-clock for the past 30 days. She is unable to afford biologic DMARDs and is unwilling to use daily corticosteroids (prednisone 10 mg/day) because of potential weight gain and bone density loss.

Page 2-183

Patient Case 8

Which one of the following is the best strategy to help T.D. control her symptoms?

- Recommend that she change to subcutaneous, injectable methotrexate.
- Increase her methotrexate to 30 mg/week.
- Add minocycline to her current methotrexate regimen.
- Use naproxen around-the-clock and add hydrocodone/acetaminophen 5/500 mg every 6 hours as needed.

Page 2-183
Answer 2-204

Rheumatoid Arthritis

- Methotrexate
  - First choice in DMARD therapy
  - Substantial treatment response
  - May have treatment benefits outside of RA
    - Decreased risk of cardiovascular disease
  - Likelihood of methotrexate toxicity in reduced with daily folic acid supplementation

Page 2-181

Rheumatoid Arthritis

- Methotrexate
  - Contraindicated in pregnancy and breastfeeding
    - Pregnancy should be avoided for at least 3 months with males and at least one ovulatory cycle for females taking methotrexate.
  - Increased incidence of malignancy, lung cancer, melanoma, and Non-Hodgkins lymphoma
  - Adverse events include:
    - Anorexia, nausea, stomatitis, abdominal cramping, infection, increased AST/ALT

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Rheumatoid Arthritis

- Leflunomide
  - Alternative to methotrexate therapy
  - May be added on to methotrexate for patients who have not adequately responded to initial therapy
  - Risk of Steven-Johnson Syndrome / Toxic Epidermal Necrolysis in patients using leflunomide
  - Women who wish to become pregnant or men who wish to father children should discontinue leflunomide use and use cholestyramine to achieve plasma (leflunomide) active metabolites less than 0.02 mg/L

Page 2-182

Rheumatoid Arthritis

- Sulfasalazine
  - Alternative for women who are (or are planning to become) pregnant
  - GI side effects may be attenuated by using an enteric coated formulation
  - Dosing may be inconvenient for patients
    - Two to 4 tablets per dose, twice daily

Page 2-182

Patient Case 8

Which one of the following is the best strategy to help T.D. control her symptoms?

- ☐ Recommend that she change to subcutaneous, injectable methotrexate.
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- ☐ Add minocycline to her current methotrexate regimen.
- ☐ Use naproxen around-the-clock and add hydrocodone/acetaminophen 5/500 mg every 6 hours as needed.

Page 2-183
Answer 2-204

Rheumatoid Arthritis

- TNF Inhibitors
  - ACR recommends using in patients who cannot tolerate or failed nonbiologic DMARD therapy
  - ACR also recommends in patients with high disease activity and/or poor prognosis
  - EULAR recommends using in patients after failure of a sufficient trial of methotrexate
  - Superior to nonbiologic DMARDs, but combination with methotrexate yields better results than either agent alone

Page 2-184

Rheumatoid Arthritis

- TNF Inhibitors
  - All patients should undergo tuberculosis evaluation and treatment, if necessary
  - Increased risk of bacterial/fungal infection and malignancy
  - Linked with new or worsening heart failure
  - Subcutaneous dosing:
    - Weekly: etanercept
    - Every other week: adalimumab
    - Every 4 weeks: golimumab, certolizumab

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Rheumatoid Arthritis

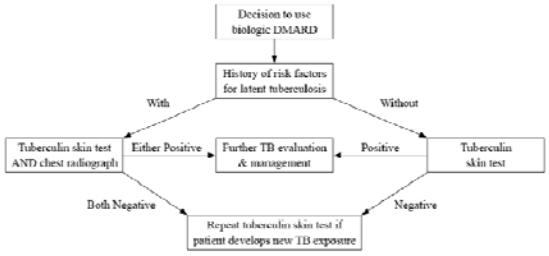

Figure 4. ACR recommendations for tuberculosis screening before biologic DMARD use.

Listed as Figure 7 on page 2-186

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Patient Case 9

D.K. is a 37-year-old woman with RA for the past 8 years. She was initially treated with leflunomide for 4 years, but she started using etanercept after that time because of worsening symptoms. She returns to the rheumatology office today with worsening RA symptoms (classified as moderate to severe disease). She had the same complaints 6 months ago, but she was given a course of oral corticosteroids in the hope that they would cause her symptoms to remit. Unfortunately, her symptoms are still present and worsening.

Page 2-187

Patient Case 9

Which one of the following is the best next step to help control the patient's RA and symptoms?

- ☐ Start another course of prednisone, but increase the dose to 20 mg/day and continue indefinitely.
- ☐ Add another anti-TNF to the patient's regimen, such as adalimumab.
- ☐ Discontinue etanercept and initiate the patient on abatacept.
- ☐ Continue etanercept and initiate the patient on abatacept.

Page 2-187
Answer 2-204

Rheumatoid Arthritis

- Abatacept
  - Recommended for patients with moderate to severe disease for greater than 6 months and have not responded to nonbiologic DMARDs
  - Patients should also try and not respond to a TNF inhibitor before using abatacept
  - Linked to adverse pulmonary events in patients with COPD
  - Acute infusion reactions possible with dosing (monthly)

Page 2-184

Rheumatoid Arthritis

- Rituximab
  - Recommended to use in patients who have failed an adequate trial with methotrexate and/or TNF inhibitor
  - Effective as monotherapy and may be used in combination with methotrexate
  - Safety concerns for:
    - Acute renal failure
    - Cardiac arrhythmias
    - Linked to fatal infusion-related adverse reactions
    - Mucocutaneous reactions

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Rheumatoid Arthritis

- Anakinra
  - Effective for treating RA, but not as effective as the TNF inhibitors
  - Not included in the ACR recommendations because of limited available data during last guideline iteration
  - Higher doses are associated with an increased risk of serious infection

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Rheumatoid Arthritis

- Tocilizumab
  - Recommended for patients who have not adequately responded to TNF inhibitors
  - Used in addition to methotrexate
  - Not in ACR recommendations because it was not available during development of last version
  - GI perforation has been reported in patients using tocilizumab concurrently with NSAIDs, corticosteroids, or methotrexate

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Patient Case 9

Which one of the following is the best next step to help control the patient's RA and symptoms?

- ☐ Start another course of prednisone, but increase the dose to 20 mg/day and continue indefinitely.
- ☐ Add another anti-TNF to the patient's regimen, such as adalimumab.
- ☐ Discontinue etanercept and initiate the patient on abatacept.
- ☐ Continue etanercept and initiate the patient on abatacept.

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Rheumatoid Arthritis

Physician Quality Reporting System 2011

Number	Category
108	Rheumatoid Arthritis (RA): Disease Modifying Anti- Rheumatic Drug (DMARD) Therapy
176	Rheumatoid Arthritis (RA): Tuberculosis screening
177	Rheumatoid Arthritis (RA): Periodic Assessment of Disease Activity
178	Rheumatoid Arthritis (RA): Functional Status Assessment
179	Rheumatoid Arthritis (RA): Assessment and Classification of Disease Prognosis
180	Rheumatoid Arthritis (RA): Glucocorticoid Management

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Bone/Joint & Rheumatology
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