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Applying Study Results to Patient Care: Glossary of Study Design and Statistical Terms

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—Continue to the next section for practical applications of medical statistics followed by our chart, "Drug Therapy of Common Conditions and Number Needed to Treat"—

Absolute risk reduction: The absolute difference in rates of an outcome between treatment and control groups in a clinical trial. Example: A hypothetical clinical trial compares the effect of a new statin and placebo on the incidence of stroke. Over the course of the study, the incidence of stroke is 4% with the statin and 6% with placebo. The absolute risk reduction with the statin is 2%.

Alpha: The probability of concluding there is a difference between groups when there really is no difference between them (making a type I error). A result is usually considered statistically significant if the probability of a type I error is less than 5% ($p<0.05$). This ($p<0.05$) means that the probability that the result is due to chance is less than 1 in 20. The smaller the p-value, the greater the statistical significance.

Beta: The probability of concluding that there is no difference between treatment groups when there really is a difference (making a type II error).

Bias: Flaws in the design or operation of a study that lead to overestimation of the efficacy of treatment. Bias can more easily be introduced into studies that are not blinded. There are many different ways in which bias can be introduced into a study.
Publication bias: Investigators tend not to publish studies with negative outcomes. This can lead to overestimation of efficacy in meta-analysis when studies with positive outcomes are overly represented.
Recall bias: People may remember things differently than how they occurred.
Selection bias: Differences between treatment and control groups that result from the way patients were selected. Randomization and blinding should help prevent selection bias.

Blinding: In a double-blind clinical trial, neither the investigator nor the patient knows which treatment group they are assigned to. If patients or investigators know what group they are assigned to, they may report better results with active treatment and worse results with placebo. In an open-label study, all patients receive active treatment (there is no placebo group) and both the patient and the investigator know this. Open-label studies tend to overestimate efficacy.

Case-control study: A study which selects patients who have the outcome of interest (cases) and patients without that outcome (controls), and looks back in time to identify characteristics that are linked to the outcome in case patients. Case-control studies are retrospective.

Clinical significance: Study results that are important enough to implement in clinical practice. Some studies are so large that very small differences between groups are statistically significant. But the magnitude of the benefit may be so small that it isn't worthwhile to adopt in clinical practice.

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Cohort: A group of patients or study subjects.

Cohort Study: This type of study identifies two groups of patients (cohorts), one which receives active treatment and one which does not (control group). The two cohorts are observed over time to see which develops the outcome of interest. Cohort studies are prospective.

Confidence Interval (CI): An estimate of the range within which the true treatment effect lies. The 95% CI is the range of values within which we are 95% certain that the true value lies. If the confidence interval for the difference in efficacy between two treatments includes 1, then you cannot exclude the possibility that there is no difference in efficacy. The width of the confidence interval is determined by the number of patients studied, the variability of the data, and the confidence level. The confidence level is usually 95%, but could be as narrow as 90% or as wide as 99%.

Confounder: A third factor in a study that affects the statistical relationship between the other two factors. A confounding variable can make it appear that there is a direct relationship between two factors when, in reality, the confounder is responsible for the relationship.

Crossover study: In this study design, each patient receives both treatments. There is less variability in outcomes because the patient serves as his/her own control. Reduced variability means a smaller sample size is needed than for a parallel-group trial. The two phases of the study are usually separated by a washout period. Crossover studies are susceptible to period effects -- differences in the effectiveness of a drug due to the passage of time. Period effects can be attributed to the development of tolerance or resistance, learning effects, or changes in the course of the disease being treated.

Cross-sectional study: This type of study looks at a defined population at a single point in time; it is a snapshot of what is happening at that moment in time.

Effectiveness: How well a drug works in every-day real-world use.

Efficacy: How well a drug works under ideal circumstances, as in a randomized controlled trial.

Endpoint: The outcome that is used to measure drug efficacy in a clinical trial.

Follow-up studies: This type of study begins with patients who have not yet experienced the outcome of interest. Observation continues until this outcome occurs.

Heterogeneity: In a meta-analysis or systematic review, when the results of individual studies are compatible with one another they are considered to be homogenous. Heterogeneity occurs when there is more variation between the study results than would be expected to occur by chance alone. A test for heterogeneity helps determine if it's appropriate to combine studies.

Incidence: The proportion of new cases of a disease occurring in the population at risk during a specified period of time.

Intention-to-treat analysis: A statistical analysis for randomized trials that includes all of the patients who were randomized to a treatment arm regardless of whether or not they finished the study. An intention-to-treat analysis is considered to mimic clinical practice more closely than an analysis that includes just the patients who completed the study.

Meta-analysis: The first step in a meta-analysis is the identification of all studies, published and unpublished, that address a clinical question. Criteria for study inclusion in the analysis are established beforehand. In a two-phase process, a result (point estimate or summary statistic with confidence interval) is calculated for the data from each study. Then, if appropriate, data is pooled and a pooled mean result is calculated. Weight is given to studies with the most data. Meta-analysis can be used to increase sample size and statistical power, as well as provide enough patients for subgroup analysis.

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Null hypothesis: Hypothesis that there is no difference between treatment groups in a study.

Number needed to harm (NNH): The number of patients treated with a specific therapy in order for one of them to have a bad outcome.

Number needed to treat (NNT): The number of patients needed to treat with a specified therapy in order for one patient to benefit from treatment. The NNT is the inverse of the absolute risk reduction (1 divided by absolute risk reduction).

Odds ratio (OR): An odds ratio can be used to determine risk in case control studies, as well as prospective cohort studies. In case control studies, the odds ratio is the odds of exposure in cases divided by the odds of exposure in controls. In cohort studies, it is the ratio of the odds of the outcome in the treatment group compared to the odds of the outcome in the control group. Odds ratios and relative risk are comparable when the outcome is rare. But the odds ratio can make risk appear greater when the disease or outcome is more common. In case-control studies evaluating the risk of an adverse effect, an odds ratio of 1 indicates that exposure to the drug is equally likely in cases and controls. If the odds ratio is greater than 1, the risk of exposure is greater in cases than controls. If the odds ratio is less than 1, the risk of exposure is smaller in cases than controls.

p-value: The level of statistical significance. A value of $p<0.05$ means that the probability that the result is due to chance is less than 1 in 20. The smaller the p-value, the greater the statistical significance. The p-value does not provide any information about the size of an effect. It only describes the strength of the result.

Point estimate: The result of a clinical trial or meta-analysis which is used as a best estimate of what the true value is in the population that the study sample came from.

Positive predictive value: Proportion of people who actually have the disease when a diagnostic test is positive. 100 x true positive/ true positive + false positive.

Power: The ability of a study to detect a significant difference between treatment groups; the probability that a study will have a statistically significant result ($p<0.05$). Power = 1- beta (the false-negative rate). By convention, adequate study power is usually set at 0.8 (80%). This corresponds to beta of 0.2 (a false-negative rate of 20%). Power increases as sample size increases. The power of a study should be stated in the methods section of a study report.

Prevalence: The proportion of existing cases of a disease in the population at a given time. Prevalence = 100 x (true positives + false negatives)/ N.

Prospective study: Studies that begin in the present and will evaluate events as they occur in the future.

Randomization: The process of assigning patients to treatment groups in a clinical trial. Each patient should have an equal chance of being assigned to any of the groups. The goal of randomization is to avoid selection bias in the assignment of patients to treatment groups.

Randomized controlled trial (RCT): A prospective study in which patients are randomized into treatment or control groups. These groups are followed up for the variables/outcomes of interest.

Relative risk: The risk of an event in individuals with a particular characteristic compared with the risk of that event in individuals who don't have that characteristic. In a clinical trial, this is the probability of an event in the treatment group divided by the probability of that event in the placebo group.

Relative risk ratio: Statistical method for reporting relative risk in cohort studies; ratio of event rates with treatment vs. control group. A relative risk ratio of 1 indicates no association between treatment and outcome. A relative risk greater than 1 indicates a positive association between treatment and outcome. A relative risk less than 1 indicates a negative association between treatment and outcome.

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Relative risk reduction: Relative risk subtracted from 1.

Retrospective study: Studies that look back in time to evaluate events that occurred in the past.

Sample size: The number of patients required for a study to have valid results. If there is only one sample in a study, the letter "N" is used to designate sample size. If there is more than one sample in a study, the size of these samples is designated with "n." The sample size of a study should be calculated before the study begins. Sample size should increase when: differences between treatment groups are small (as in studies comparing the efficacy of two drugs), as study power increases (as in 90% power instead of 80% power), as statistical significance increases (as in $p<0.001$ instead of $p<0.05$), and if there is more variability in the outcome being measured. The larger the sample size, the narrow the confidence interval. Sample size calculators are available on the Internet (http://www.surveysystem.com /sscalc.htm, http://calculators.stat.ucla.edu/power calc/).

Sensitivity: The ability of a test to reliably detect the presence of a disease. The proportion of patients with the disease who have a positive test. Sensitivity = 100 x true positives/ true positives + false negatives.

Sensitivity analysis: A statistical method to determine how sensitive the results of a study or systematic review are to changes in the data or methodology. This is particularly important to perform in meta-analyses.

Specificity: The ability of a diagnostic test to reliably rule out a disease. The proportion of patients without the target disease who have a negative test. Specificity = 100 x true negatives/ true negatives + false positives.

Surrogate Endpoint: A surrogate endpoint is an endpoint that stands in for another endpoint. Examples include measurement of blood pressure as a surrogate for reducing cardiovascular events in patients with hypertension, or measurement of CD4 cell counts as surrogate for reducing mortality with antiretroviral therapy.

Statistical vs. Clinical Significance: See explanation above under "clinical significance."

Subgroup analysis: Examination of outcomes in specific groups within a study in order to predict who benefits or is harmed the most by treatment. Large clinical trials will often look at subgroups based on age, sex, or concomitant medical conditions. Ideally, subgroup analyses should be defined before the study starts. Studies usually do not have enough power to perform subgroup analyses. With repeated subgroup analyses, false-positive results will eventually occur due to chance. In general, subgroup analysis should only be used to identify research questions to be addressed in future clinical trials.

Systematic review: Collection, review, and presentation of available studies addressing a particular clinical question. Studies are reviewed according to specific criteria and methods. A systematic review may include meta-analysis as a method of analyzing and quantifying the results. Cochrane reviews (http://www.update-software.com/cochrane/) are a good example of systematic reviews.

Type I error: To conclude there is a difference between treatments when there is really no difference between them; rejection of the null hypothesis when it is actually true.

Type II error: To conclude there is no difference between treatments when there really is a difference between them; accepting the null hypothesis when it is actually false. This type of error is common in clinical trials, often because they don't enroll enough patients.

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Applying Study Results to Patient Care: Relative Risk, Absolute Risk, and Number Needed to Treat

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The manner in which study results are presented affects the way they are viewed. Clinicians are more interested in results that are portrayed as large whole numbers. A recent study illustrates this point.[1] Clinicians were presented with study results in four different formats:

Format A: 91.8% survival with active treatment vs. 88.5% survival with placebo.

Format B: Active treatment led to a 30% reduction in mortality.

Format C: Active treatment reduced mortality by 3.4%.

Format D: One death was avoided for every 30 patients treated.

While 70% of clinicians would implement the results of Formats B and D in their practice, only 20% would act on the Formats A and C. In reality, all four formats present the results of the same study, the milestone 4S study demonstrating cardiovascular risk reduction with simvastatin.[1]

Clinical trials evaluating the safety and efficacy of drug therapy often use three related statistical methods to report results: relative risk, relative risk reduction, and odds ratio. These terms can also be used to calculate two very practical clinical tools: the number needed to treat (NNT) and the number needed to harm (NNH). Format D above illustrates the NNT. Format B illustrates relative risk reduction. Format C illustrates absolute risk reduction. Portraying results as relative rather than absolute risk reduction can make a drug's efficacy appear more impressive. This is why pharmaceutical marketing often focuses on relative risk.[2] Understanding the fundamentals of these statistical tools helps clinicians make more informed choices about drug therapy and makes them less susceptible to pharmaceutical marketing methods. (See box on next page for calculations of above examples).

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	Simvastatin	**Placebo**
Survival	91.8%	88.5%
Mortality	8.2%	11.5%
Absolute risk reduction	11.5% – 8.2%=3.3%*****	
Relative risk	Risk in treatment group divided by risk in control group 8.2% ÷ 11.5%=0.71	
Relative risk reduction	Absolute risk reduction divided by risk in control group 3.3 ÷ 11.5=0.29 or 29%*** OR** 1 minus relative risk (1 – 0.71=0.29 or 29%)	
Number needed to treat	1 divided by absolute risk reduction 1 ÷ 3.3=30 patients treated to avoid one death	

***** Actual calculated numbers differ slightly from examples presented by O'Connell et al.[1]

Relative Risk

Relative risk compares the risk of an event in individuals with a particular characteristic to the risk of that event in individuals without that characteristic. In a clinical trial, this would be the outcome in the treatment group divided by the outcome in the control group.[3] Relative risk can only be used in prospective cohort studies because, by definition, it requires that you determine ahead of time whether patients will receive active treatment or control.[4,5]

A relative risk of 1 indicates no association between treatment and outcome. A relative risk greater than 1 indicates a positive association between treatment and outcome. A relative risk less than 1 indicates a negative association between treatment and outcome.[6,7] A study investigating an anticoagulant for prevention of thrombosis might use relative risk to portray both efficacy and safety. For efficacy, a relative risk less than 1 might indicate a decreased risk of thrombosis. In terms of side effects, a relative risk greater than 1 might indicate an association between the anticoagulant and bleeding.

Relative and Absolute Risk Reduction

Relative risk reduction is 1 minus the relative risk.[3] Portraying the benefits of treatment as relative risk reduction can mislead clinicians about the value of that treatment unless they consider the patient's baseline risk for the outcome the treatment is preventing. For example, when deciding whether to prescribe a drug to prevent myocardial infarction, one should consider the patient's baseline risk of myocardial infarction.

An interactive tutorial prepared by Chris Cates, a general practitioner with a talent for demystifying evidence-based medicine, illustrates this concept very clearly.[8] He considers the decision of whether to prescribe clopidogrel in addition to aspirin based on results of the CURE trial. The relative risk reduction for vascular events with clopidogrel is 20%. The absolute risk reduction in the CURE trial is 2.1% -- from 11.4% to 9.3%. An individual patient's risk for vascular events might vary from that of patients in the CURE trial. If the patient's baseline risk of a vascular event is 15%, treatment with clopidogrel will reduce that patient's absolute risk of a vascular event to 12%. If the patient's baseline risk of a vascular event is only 1%, treatment with clopidogrel will only reduce that patient's absolute risk of an event to 0.8%.[8]

Just as relative risk can make treatment look more effective, it can make adverse effects appear more frightening. Stephen Gehlbach illustrates this point with the following example. In the 1970's, oral contraceptives were found to increase the risk of myocardial infarction by 2.5- to 5-fold. This statistic sounds very alarming until one considers that this is an absolute risk of 3.5 deaths per 100,000 users per year.[4]

Odds Ratio

The *odds* of an event is the ratio of the number of events to the number of non-events (similar to the way the odds of winning or losing a horse race is expressed at a race track).[5] The *odds ratio* is the odds of exposure in cases divided by the odds of exposure in controls.[9] It is analogous to relative risk.[7] Unlike relative risk, it can be used in case-control studies. Case-control studies compare patients with an outcome of interest to patients without that outcome. This type of study is often used to determine whether drugs are the cause of rare adverse events. The odds of exposure to the suspected drug is compared in cases who have the adverse event and controls who do not have the adverse event. Odds ratios and relative risk provide comparable estimates of risk when the outcome is rare. But the odds ratio can exaggerate risk when the disease or outcome is common (incidence greater than 10%).[4,5,7] The

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odds ratio cannot be used directly to calculate an NNT, but it can be done using standard formulas and nomograms.[9] One such nomogram can be viewed at http://www.cebm.net/nnts.asp.

Number Needed to Treat and Harm

The NNT and NNH are statistical concepts that share the simplicity of relative risk reduction, but they have less potential to be misleading because they are based on absolute risk. These very understandable terms can help both clinicians and patients decide whether the risks and benefits of treatment are worthwhile. The NNT is the reciprocal of the absolute risk reduction with drug treatment (1 divided by absolute risk reduction).[3,7] In clinical trials of drug therapy, it is the number of patients who would need to be treated in order to achieve benefit in one patient. The NNH is the reciprocal of the absolute risk increase with a drug side effect. In other words, it is the number of patients who would be treated before you expect to see one patient with an adverse effect. Comparing the NNT and NNH can help give an accurate assessment of the risks and benefits of treatment.

Dr. Cates illustrates this point with the results of a Cochrane review evaluating antibiotics for the treatment of pediatric otitis media. The primary benefit of treatment is pain relief two to seven days after antibiotics are begun. Pain resolves quickly in most children even without antibiotic therapy. Pain tends to persist longer in younger children. In general, 15 children need to be treated with antibiotics to relieve pain in one child (NNT=15). For children under two years of age, the NNT is 9. The primary risk of antibiotic therapy is side effects. Only 12 children need to be treated for one child to develop vomiting, rash, or diarrhea (NNH=12).[10]

Dr. Cates has developed a user-friendly computer program that will calculate the NNT from a meta-analysis of drug therapy, particularly Cochrane reviews. It is called Visual Rx and can be accessed from http://www.nntonline.net/. Another NNT calculator is available at http://www.jr2.ox.ac.uk/bandolier/band59/NNTcalc.html.

How to Go from Absolute Risk to NNT

Cook and Sackett use the treatment of mild to moderate hypertension to illustrate the relationship between relative risk, absolute risk, and the number needed to treat.[3] About 20% of patients with untreated moderate hypertension are expected to have a stroke over a 5-year period. Antihypertensive therapy reduces this risk to 12%. This provides a relative risk ratio of 0.6 (0.12/0.2) and a relative risk reduction of 40% (1–0.60=0.40). This is an absolute risk reduction of 8% (0.20–0.12=0.08). The reciprocal of absolute risk (1/0.08) is the number needed to treat, in this case approximately 13. Thirteen patients would need to be treated with antihypertensive therapy for five years to prevent one stroke.[3]

They take this example a step further and compare how treatment reduces the risk of stroke in patients with mild hypertension. Over a 5-year period, 1.5% of patients with untreated mild hypertension would have a stroke compared with 0.9% of antihypertensive-treated patients. As is the case with moderate hypertension, treatment provides a relative risk ratio of 0.6 (0.009/0.015) and a relative risk reduction of 40% (1–0.6=0.40). The absolute risk reduction is much lower (0.015–0.009=0.006). The number needed to treat in this case is 167 (1/0.006=166.66). In other words, 167 patients would need to be treated for five years to prevent one stroke.[3]

There is always some uncertainty about how well the NNT represents the true treatment effect in the population at large. This uncertainty can be expressed as a confidence interval. A confidence interval estimates the range within which the true treatment effect lies. A narrow confidence interval suggests less uncertainty and a wide confidence interval suggests more uncertainty. Ideally, a NNT for drug therapy should be accompanied by information about what it was compared to (another drug or placebo), the duration of treatment, the study outcome, and a 95% confidence interval.[12] We have compiled NNTs for drug therapy of common disorders in the table below. Some of these NNTs are based on a single large-scale clinical trial, while others are based on a systematic review or meta-analysis of multiple clinical trials. When comparing the NNT of two drug regimens, make sure that they are based on the same duration of therapy, treat the same condition, and share the same outcome.[14]

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Drug Therapy of Common Conditions and the Number Needed to Treat*

Condition	Drug Duration of therapy	Number Needed to Treat or Harm (95% confidence interval)
Coronary artery disease		
Primary prevention of CHD	Aspirin x 1 year	500 healthy men treated to prevent one MI/death[28]
	Statin x 3 to 5 years	71 treated to prevent one MI/stroke[11]
Coronary artery disease[28]	ACE inhibitor x 1 year	22 to 83 treated to prevent one death
	Beta blocker x 1 year	31 to 81 treated to prevent one death
	Simvastatin x 1 year	163 treated to prevent one death
Unstable angina[28]	Aspirin x 1 year	25 to prevent one MI/death
Myocardial infarction[28]	Streptokinase + 1 month of ASA	NNT: 20 treated to prevent one death at 5 weeks NNH: 1000 treated to cause one hemorrhagic stroke
	tPA vs. streptokinase	100 treated to prevent one extra death
	ACE inhibitor	18 treated to prevent 1 death within 6 months
Intensive lipid-lowering after acute coronary syndrome[13]	Target of 70 mg/dL (atorvastatin) vs. 100 mg/dL (pravastatin)	50 extra patients treated per year to 70 mg/dL rather than 100 mg/dL to prevent one CHD event
Secondary prevention of CHD	Simvastatin x 5 years	15 (10-25) to prevent one major coronary event 29 (18-56) to prevent one coronary death[14]
	Statin x 5 years	21 treated to prevent 1 MI/stroke[11]
Prevention of CHD events in elderly patients with hyperlipidemia, based on 10-year risk of MI or coronary death[22]	Statin x 15 years	Number of patients treated to prevent 1 CHD event 10-year risk of 10%: 10 10-year risk of 20%: 5 10-year risk of 30%: 3 10-year risk of 40%: 2
Hypertension (HTN)		
Mild HTN[14]	Antihypertensive x 1 year	700 treated to prevent one stroke, MI, or death
Mild HTN (10-year CHD risk of at least 15%)[23]	Antihypertensive x 5 years	40 treated to prevent one cardiovascular complication
	Aspirin x 5 years	90 treated to prevent 1 cardiovascular complication
Severe hypertension[14]	Antihypertensive x 1 year	15 treated to prevent 1 stroke, MI, or death
HTN in elderly[28]	Antihypertensive x 5 years	18 treated to prevent 1 cardiovascular complication
Isolated systolic HTN[28]	Chlorthalidone/ atenolol x 1 year	43 treated to prevent 1 stroke
HTN in diabetes[28]	Antihypertensive x 10 years	15 treated to prevent 1 diabetes-related death
Heart failure		
Heart failure, NYHA I-II[14]	ACE inhibitor x 1 year	100 treated to prevent 1 death
Heart failure, NYHA IV[14]	ACE inhibitor x 1 year	6 treated to prevent 1 death
Heart failure post-MI[14]	ACE inhibitor	18 treated to prevent 1 death
Heart failure, NYHA II-IV[32]	Metoprolol ER	25 treated to prevent 1 death
LVD post-MI[34]	Eplerenone	50 treated to prevent 1 death
Thromboembolic events		
Deep vein thrombosis[31]	Low molecular weight heparin vs. heparin	NNT: 61 to avoid 1 death; 114 to avoid 1 recurrent thromboembolism with heparin. NNT: 164 to avoid 1 major bleed with heparin

Condition	Drug Duration of therapy	Number Needed to Treat or Harm (95% confidence interval)
Stroke		
Prevention of stroke in atrial fibrillation[29]	Warfarin, primary prevention x 1 year	37 treated to prevent 1 major vascular event
	Warfarin, secondary prevention x 1 year	13 treated to prevent 1 major vascular event
	Aspirin, primary prevention x 1 year	67 treated to prevent 1 major vascular event
	Aspirin, secondary prevention x 1 year	40 treated to prevent 1 major vascular event
Primary prevention of stroke[28]	Pravastatin x 1 year	641 patients with hyperlipidemia treated to prevent 1 stroke
Secondary prevention of stroke[29]	Smoking cessation x 1 year	43 to prevent 1 major vascular event
	Aspirin x 1 year	38 to prevent 1 stroke after TIA or minor stroke[28] 100 to prevent 1 major vascular event
	Antihypertensive x 1 year	42 to 45 treated to prevent 1 major vascular event
	Statin x 1 year	59 treated to prevent 1 major vascular event
Acute ischemic stroke[29]	Thrombolytic (tPA) within 3 hours	7 treated to improve outcome in 1 patient
Modification of Cardiovascular Risk Factors		
Smoking cessation[14]	Nicotine gum, patch, spray, or inhaler	14 treated for 1 success over 6 to 12 months of follow-up
Weight reduction in obesity[14]	Sibutramine x 6 months	2.7 treated for 1 to have 5% weight reduction
	Orlistat x 1 year	3.9 treated for 1 to have 5% weight reduction
	Orlistat x 1 year	5.6 treated for 1 to have 10% weight reduction
Dermatologic conditions		
Athletes foot[17]	Topical azoles	2 treated to achieve one extra cure
	Undecylenic acid or tolnaftate	2 treated to achieve one extra cure
Warts[18]	Self-administered salicylic acid	4 (3-12) treated for 1 cure
Onychomycosis[14]	Terbinafine 250 mg vs. griseofulvin 500 mg x 12 weeks	2.7 treated with terbinafine for 1 extra patient with cured fingernail
	Terbinafine x 16 weeks vs. griseofulvin 500 mg x 52 weeks	2.5 treated with terbinafine for 1 extra patient with cured toenail
	Terbinafine x 24 weeks vs. griseofulvin 1000 mg x 48 weeks	4.6 treated with terbinafine for 1 extra patient with cured toenail

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Condition	Drug Duration of therapy	Number Needed to Treat or Harm (95% confidence interval)
Endocrine Disorders		
Prevention of type 2 diabetes[19]	Lifestyle	7 treated to prevent 1 case in 3 years
	Metformin	14 treated to prevent 1 case in 3 years
Treatment of type 2 diabetes[20]	Metformin x 1 year	Obese patients: 141 treated to prevent 1 death; 74 treated to prevent 1 diabetes-related outcome
	Tight blood pressure control x 1 year	152 to prevent 1 diabetes-related death; 61 treated to prevent 1 complication
	Tight glucose control x 1 year	196 patients treated to prevent 1 complication
	Aspirin, primary prevention x 5 years	45 treated to prevent 1 major cardiovascular event[28]
	Simvastatin x 5 years	6 patients with known CHD treated to prevent 1 major cardiovascular event[28]
Polycystic ovary disease[25]	Metformin	4 women treated for 1 to achieve ovulation
Postmenopausal hormone replacement therapy[35]	*Premarin* plus medroxyprogesterone acetate	NNT for 5 years: 333 to prevent 1 hip fracture; 333 to prevent 1 colorectal cancer NNH for 5 years of treatment: 250 to cause 1 CHD event; 250 to cause 1 stroke; 100 to cause 1 venous thromboembolism; 200 to cause 1 breast cancer
Gastrointestinal disorders		
Prevention of GI complications with NSAIDs[13]	Misoprostol x 1 year	83 treated to prevent 1 serious GI complication; NNT as low as 7 for age over 75 years + history of GI bleed
	Misoprostol 800 mcg x 6 months	6 treated to prevent one GI complication
	Omeprazole 20 mg x 6 months	3 treated to prevent one GI complication
Prevention of GI events with coxib over traditional NSAID[33]	Rofecoxib vs. naproxen x 1 year	41 treated with rofecoxib instead of naproxen to avoid 1 upper GI complication†
	Celecoxib vs. NSAID x 1 year	100 treated with celecoxib instead of NSAID to avoid 1 upper GI complication†
GERD, symptom relief[21]	Antacids and/or famotidine	For excellent/good symptom relief in 1 patient: 14 patients treated with either; 6 treated with both
GERD, short-term healing	Omeprazole vs. ranitidine x 8 weeks	For every 3 treated with omeprazole, 1 extra patient healed than would have healed with ranitidine
GERD, long-term maintenance[14]	Omeprazole vs. ranitidine x 1 year	For every 3 treated with omeprazole, 1 extra patient still healed at 1 year than expected with ranitidine
Postoperative nausea and vomiting[24]	Droperidol	7 treated to prevent nausea in 1
	Ondansetron	5-6 treated to prevent nausea in 1
Peptic ulcer disease[14]	Triple antibiotics vs. antacids alone	NNT for *H. pylori* eradication is 1.1 at 6 weeks and 1.8 at 1 year; NNT is 5 for ulcer healing at 6 weeks

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Condition	Drug Duration of therapy	Number Needed to Treat or Harm (95% confidence interval)
Infectious Diseases		
Pediatric ear infections[10]	Antibiotics	NNT: 15 treated to relieve pain in 1 NNT for <2 year old: 9 treated to relieve pain in 1 NNH: 12 treated to cause 1 case of vomiting, rash, or diarrhea
Influenza[14]	Flu vaccine	23 immunized to prevent 1 case of influenza
Prophylaxis of infection after dog bite[12]	Antibiotics	16 (9-92) treated to prevent 1 infection
Streptococcal pharyngitis[26]	Penicillin	3000-4000 patients treated to prevent 1 case of acute rheumatic fever
Common cold[14]	Ipratropium nasal inhalation	For 1 patient to have improvement in runny nose, the NNT is 6.3 vs saline and 1.6 vs no treatment
	Zinc lozenges	3 treated for 1 to have cold symptoms resolved between days 6 to 12
Neurology		
Dementia[14]	Ginkgo x 1 year	8 treated for 1 to have 4-point improvement on ADAS-cog
Multiple sclerosis, secondary progressive[14]	Interferon beta-1b x 2 years	9 treated to prevent confirmed progression in 1; 11 treated to prevent 1 moderate/severe relapse; 13 treated to prevent 1 becoming wheel-chair bound
Multiple sclerosis, remitting-relapsing[14]	Interferon beta-1a x 2 years	5 patients treated to prevent 1 moderate/severe relapse
Pain		
Acute migraine[14]	PO sumatriptan 100 mg	3 treated for one 2-hour headache response
	SC sumatriptan 6 mg	2 treated for one 2-hour headache response
	PO eletriptan 80 mg	2.6 treated for one 2-hour headache response 3.7 treated for one to be pain-free at 2 hours 2.8 for 1 response sustained at 24 hours
	PO eletriptan 40 mg	2.9 treated for one 2-hour headache response 4.5 treated for 1 to be pain-free at 2 hours 3.6 for 1 response sustained at 24 hours
	PO eletriptan 20 mg	4.4 treated for one 2-hour headache response 9.9 treated for 1 to be pain-free at 2 hours 5.4 for 1 response sustained at 24 hours
	PO rizatriptan 10 mg	2.7 treated for one 2-hour headache response 3.1 treated for 1 to be pain-free at 2 hours 5.6 for 1 response sustained at 24 hours
	PO rizatriptan 5 mg	3.9 treated for one 2-hour headache response 4.7 treated for 1 to be pain-free at 2 hours 8.3 for 1 response sustained at 24 hours
	Excedrin	3.9 treated for one 2-hour headache response
Neuropathic pain	Tricyclic antidepressants	For 1 patient with at least 50% reduction in pain: Treat 3 with diabetic neuropathy[12, 27] Treat 4 (2.6-8.9) with postherpetic neuralgia[15]
	Topical capsaicin	3-6 treated for 1 to experience pain relief[14,27]
	Opioids	3 (1.9-4.2) treated for 1 with at least 50% pain relief[15]
	Gabapentin	3 (2.4-8.7) treated for 1 to experience pain relief[27]

Condition	Drug Duration of therapy	Number Needed to Treat or Harm (95% confidence interval)
Pain (cont.)		
Acute pain[14]	Celecoxib 200 mg	2.8 (2.1 to 4.4) for 1 with at least 50% pain reduction
	Rofecoxib 50 mg	1.9 (1.6 to 2.2) for 1 with at least 50% pain reduction
	Ibuprofen 400 mg	2.1 (1.7 to 2.6) for 1 with at least 50% pain reduction
Postoperative pain, moderate to severe[14]	PO NSAID	2-3 treated for 1 with at least 50% pain reduction
	PO valdecoxib	1.7 treated for 1 with at least 50% pain reduction
	IM morphine 10 mg	2.9 treated for 1 with at least 50% pain reduction
	PO APAP 650 mg + codeine 60 mg	3 treated for 1 with at least 50% pain reduction
	IM ketorolac 30 mg	3.4 treated for 1 with at least 50% pain reduction
	IM ketorolac 10 mg	5.7 treated for 1 with at least 50% pain reduction
	PO APAP 1000 mg	4.5 treated for 1 with at least 50% pain reduction
	PO tramadol 75 mg	5 treated for 1 with at least 50% pain reduction
Rheumatology		
Osteoarthritis[14]	Glucosamine	5 treated for improved symptoms in 1
	Topical capsaicin	3 treated for pain relief in 1
Prevention of hip fracture in ambulatory elderly[14]	Calcium1200 mg + vitamin D x 3 years	14 treated to prevent any fracture; 20 to 40 treated to prevent 1 hip fracture
Rheumatoid arthritis[30]	Anti-TNF agents Infliximab and etanercept	2 treated for 1 extra patient to achieve ACR20; 4 treated for 1 extra patient to achieve ACR50; 8 treated for 1 extra patient to achieve ACR70.
	Sulfasalazine	4 treated for 1 patient to achieve ACR20 5-6 treated for 1 extra patient to achieve ACR50
	Leflunomide	4 treated for 1 patient to achieve ACR20 5-6 treated for 1 extra patient to achieve ACR50
Severe postmenopausal osteoporosis[12]	Bisphosphonate x 3 years (risedronate)	9 women treated to prevent 1 new spinal fracture
Urology		
Benign prostatic hypertrophy	Finasteride x 2 years	26 to 38 men treated to prevent prostatectomy or acute urinary retention[16]
	Finasteride + alpha blocker x 4 years	9 men treated to prevent clinical progression in 1 (based on MTOPS)[13]
Erectile dysfunction, mixed etiology/diabetes[14]	Sildenafil	2 men treated for 1 to have erection suitable for intercourse

Abbreviations: ACR20 = 20% reduction in American College of Rheumatology criteria; ACR50 = 50% reduction in American College of Rheumatology criteria; ACR70 = 70% reduction in American College of Rheumatology criteria; CVD = coronary vascular disease; HTN = hypertension; LVD = left ventricular dysfunction; MI = myocardial infarction; NYHA = New York Heart Association.

* Unless stated in the table, NNTs are based on comparisons of drug regimens with placebo.
† Differences in NNT between rofecoxib and celecoxib may be due to differences in the population in which they were studied.

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