Understanding The Numbers
SZ is the Editor-in-Chief theNNT.
No financial compensation/No conflict of interest.

JH is Cofounder and CEO of MD Aware LLC, which owns and operates MDCalc and theNNT.
Docs Don’t Make the Best Statisticians
Even doctors need a little help every now and then

Hey girl
You must be $p > .05$, because I fail to reject you.
• Odds Ratio vs Relative Risk
• Relative Risk Reduction
• Absolute Risk Reduction
• Number-Needed-To-Treat (NNT)
Risk of having a 1

1:6 (17%)
Odds of having a 1

1:5 (20%)
Disease in dice:

Only if you roll a 1

1st Risk Group 1:6 = 17%
2nd Risk Group 1:6 = 17%

Risk Ratio: 1

Equal Risk (boring example!)
Disease in cards:

Only if you pick a 1

1st Risk Group 1:5 = 17%
2nd Risk Group 1:5 = 17%

Odds Ratio: 1

Equal Risk (boring example!)
### When prevalence is small, OR and RR are almost the same.

<table>
<thead>
<tr>
<th></th>
<th>Exposure Group N = 100</th>
<th>Control Group N = 100</th>
<th>Odds in Exposure Group</th>
<th>Odds in Control Group</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
<td>10</td>
<td>12</td>
<td>10:90 (11%)</td>
<td>12:88 (14%)</td>
<td>0.79 (11%/14%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Exposure Group N = 100</th>
<th>Control Group N = 100</th>
<th>Risk in Exposure Group</th>
<th>Risk in Control Group</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
<td>10</td>
<td>12</td>
<td>10:100 (10%)</td>
<td>12:100 (12%)</td>
<td>0.83 (10%/12%)</td>
</tr>
</tbody>
</table>
What about RRRs, ARDs and NNTs?

<table>
<thead>
<tr>
<th></th>
<th>Exposure Group N = 100</th>
<th>Control Group N = 100</th>
<th>Risk in Exposure Group</th>
<th>Risk in Control Group</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
<td>10</td>
<td>12</td>
<td>10:100 (10%)</td>
<td>12:100 (12%)</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Relative Risk: **0.83**

Relative Risk Reduction (RRR): \( 1 - \text{RR} : 1 - 0.83 : 0.17 \) (17%)

Absolute Risk Difference (ARD): \( 12\% - 10\% = 2\% \)

NNT: \( 1/\text{ARD} = 1:2\% = 50 \)
LET’s DO The NUMBERS!
TISSUE PLASMINOGEN ACTIVATOR FOR ACUTE ISCHEMIC STROKE

THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE t-PA STROKE STUDY GROUP*

Abstract  Background.  Thrombolytic therapy for acute ischemic stroke has been approached cautiously because there were high rates of intracerebral hemorrhage in early clinical trials. We performed a randomized, double-blind trial of intravenous recombinant tissue plasminogen activator (t-PA) for ischemic stroke after recent pilot studies suggested that t-PA was beneficial when treatment was begun within three hours of the onset of stroke.

Methods. The trial had two parts. Part 1 (in which 291 patients were enrolled) tested whether t-PA had clinical activity, as indicated by an improvement of 4 points over base-line values in the score of the National Institutes of Health stroke scale (NIHSS) or the resolution of the neurologic deficit within 24 hours of the onset of stroke. Part 2 (in which 333 patients were enrolled) used a global test statistic to assess clinical outcome at three months, according to scores on the Barthel index, modified Rankin scale, Glasgow outcome scale, and NIHSS.

Results. In part 1, there was no significant difference between the group given t-PA and that given placebo in the percentages of patients with neurologic improvement at 24 hours, although a benefit was observed for the t-PA group at three months for all four outcome measures. In part 2, the long-term clinical benefit of t-PA predicted by the results of part 1 was confirmed (global odds ratio for a favorable outcome, 1.7; 95 percent confidence interval, 1.2 to 2.6). As compared with patients given placebo, patients treated with t-PA were at least 30 percent more likely to have minimal or no disability at three months on the assessment scales. Symptomatic intracerebral hemorrhage within 36 hours after the onset of stroke occurred in 6.4 percent of patients given t-PA but only 0.6 percent of patients given placebo (P<0.001). Mortality at three months was 17 percent in the t-PA group and 21 percent in the placebo group (P = 0.30).

Conclusions. Despite an increased incidence of symptomatic intracerebral hemorrhage, treatment with intravenous t-PA within three hours of the onset of ischemic stroke improved clinical outcome at three months. (N Engl J Med 1995;333:1581-7.)
Favorable Outcomes

Rate in tPA group: **50/168: 30%**

Rate in control group: **38/165: 23%**

Absolute Risk Difference: **30% - 23%: 7%**

NNT: **1/0.07: 14**

Relative risk: **0.30/0.23: 1.3**

Relative risk increase: **1.3 - 1: 0.30 (30%)**

Odds in tPA group: **50/118: 0.42**

Odds in control group: **38/127: 0.30**

Odds Ratio: **0.42/0.30: 1.4**
ORIGINAL ARTICLE

Effect of oseltamivir on the risk of pneumonia and use of health care services in children with clinically diagnosed influenza*

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†Thomson Medstat, Cambridge, MA, USA
‡Children's Hospital San Diego, San Diego, CA, USA

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Key words: Antiviral – Expenditure – Influenza – Oseltamivir – Outcomes – Pediatrics – Pneumonia

ABSTRACT

Objective: To evaluate the effectiveness of oseltamivir in reducing the rate of complications of influenza in children.

Methods and methods: Administrative, chart-based data from MarketScan Research Database between 2006 and 2008 were used to identify children with influenza, aged 1–12 years. Patients who received a prescription for oseltamivir within 1 day of influenza diagnosis were compared with those who received no antiviral therapy.

Main outcome measures: Primary and secondary study outcomes included occurrence of pneumonia within 14 days of onset of influenza, rates of hospitalization for pneumonia, antibiotic use, numbers of healthcare services utilized, and healthcare expenditures.

Results: In total, 4,447 (17.5%) children received a prescription for oseltamivir within 1 day of when they were first clinically diagnosed with influenza, and 26,407 (92.1%) children received no antiviral treatment. Overall, children who received oseltamivir for the treatment of physician-diagnosed influenza were 37.7% less likely to be clinically diagnosed with pneumonia at a subsistence medical encounter (relative risk 0.63; 95% CI: 0.32–0.95; p = 0.03). This benefit was associated with reductions in antibiotics use, outpatient and emergency room visits, and savings in outpatient medical expenditures. Net expenditures per patient were not significantly different between children receiving oseltamivir and those who received no antiviral treatment ($16; 90% CI: -$13 to $50) although pharmacy expenditures were higher with oseltamivir use.

Limitations: The study was restricted to patients with employer-sponsored health insurance. The lack of a prospective diagnosis of influenza, an index date based on the first diagnosis of influenza rather than first exposure or symptom onset, may have resulted in a conservative estimate of treatment effect.

Conclusions: Oseltamivir may reduce the risk of influenza-related morbidity in children when prescribed on presentation of clinically diagnosed influenza. The use of oseltamivir in children may play an important role in managing influenza outbreaks.

* An abstract of this work was submitted to the Congress on Women's Health.
ABSTRACT

Objective: To evaluate the effectiveness of oseltamivir in reducing the rate of complications of influenza in children.

Research design and methods: Anonymous, patient-level data from Medstat’s MarketScan Research Database between 2000 and 2004 were used to identify children with influenza, aged 1–12 years. Patients who received a prescription for oseltamivir within 1 day of influenza diagnosis were compared with those who received no antiviral therapy.

Main outcome measures: Primary and secondary study outcomes included occurrence of pneumonia within 14 days of onset of influenza, rates of hospitalization for pneumonia, antibiotic use, numbers of healthcare services utilized, and healthcare expenditures.

Results: In total, 4447 (17.9%) children received a prescription for oseltamivir within 1 day of when they were first clinically diagnosed with influenza, and 20407 (82.1%) children received no antiviral treatment. Overall, children who received oseltamivir for the treatment of physician-diagnosed influenza were 51.7% less likely to be clinically diagnosed with pneumonia at a subsequent medical encounter (relative risk 0.483; 95% CI: 0.326, 0.717). This benefit was associated with reductions in antibiotic use, outpatient and emergency room visits, and savings in outpatient medical expenditures. Net expenditures per patient were not significantly different between children receiving oseltamivir and those who received no antiviral treatment (−$16; 95% CI: −$13, +$40) although pharmacy expenditures were higher. Wide regional variations in oseltamivir use were noted.

Limitations: The study was restricted to patients with employer-sponsored health insurance. The lack of a virologic diagnosis of influenza, and an index date based on the first diagnosis of influenza rather than first exposure or symptom onset, may have resulted in a conservative estimate of treatment effect.

Conclusions: Oseltamivir may reduce the risk of influenza-related morbidity in children when prescribed upon presentation of clinically diagnosed influenza. The use of oseltamivir in children may play an important role in managing influenza outbreaks.
**Table 2.** Relative risk of pneumonia, hospitalization and antibiotic use in children (aged 1–12 years) within 14 days of influenza diagnosis

<table>
<thead>
<tr>
<th></th>
<th>Oseltamivir (n = 4447)</th>
<th>No antiviral (n = 20407)</th>
<th>Unadjusted</th>
<th>Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Relative risk</td>
<td>95% CI</td>
<td>Relative risk</td>
<td>95% CI</td>
</tr>
<tr>
<td>Any pneumonia† diagnosis</td>
<td>0.477</td>
<td>0.326, 0.698</td>
<td>0.483</td>
<td>0.326, 0.717</td>
</tr>
<tr>
<td>Hospitalization due to pneumonia</td>
<td>0.791</td>
<td>0.306, 2.043</td>
<td>0.743</td>
<td>0.277, 1.996</td>
</tr>
<tr>
<td>All hospitalizations</td>
<td>0.854</td>
<td>0.501, 1.454</td>
<td>0.743</td>
<td>0.427, 1.293</td>
</tr>
<tr>
<td>Antibiotic use</td>
<td>0.782</td>
<td>0.738, 0.829</td>
<td>0.741</td>
<td>0.691, 0.795</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, and baseline factors.
**Pneumonia**

Risk Study group: 29/4447 (0.65%)

Risk Control group: 279/20407 (1.4%)

ARD: 0.75%

NNT: 1/0.0075: 133

RR: 0.0065/0.014: 0.46

RRR: 1-RR: 0.54 (54%)

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**Hospitalization:**

Risk Study group: 5/4447 (0.11%)

Risk Control group: 29/20407 (0.14%)

ARD: 0.03%

NNT: 1/0.0003: 3333

RR: 0.0011/0.0014: 0.79

RRR: 1-RR: 0.21 (21%)
Probiotics for the prevention of Clostridium difficile-associated diarrhea in adults and children (Review)

Goldenberg JZ, Yap C, Lytvyn L, Lo CKF, Beardsley J, Mertz D, Johnston BC
Main results

Thirty-nine studies (9955 participants) met the eligibility requirements for our review. Overall, 27 studies were rated as either high or unclear risk of bias. A complete case analysis (i.e. participants who completed the study) among trials investigating CDAD (31 trials, 8672 participants) suggests that probiotics reduce the risk of CDAD by 60%. The incidence of CDAD was 1.5% (70/4525) in the probiotic group compared to 4.0% (164/4147) in the placebo or no treatment control group (RR 0.40, 95% CI 0.30 to 0.52; GRADE = moderate). Twenty-two of 31 trials had missing CDAD data ranging from 2% to 45%. Our complete case CDAD results proved
Risk of CDAD in **probiotic** group: 70/4525: 1.5%

Risk of CDAD in **control** group: 164/4147: 4.0%

**Absolute Risk Difference**: 4% - 1.5% = 2.5%

**Number Needed to Treat**: 1/0.025: 40

**Relative Risk of CDAD**: 0.015 / 0.04: 0.4

**Relative Risk Reduction**: 1 - RR = 1 - 0.4: 0.60 (60%)
The incidence of reported AEs in the probiotic group was 14.3% compared to 17.0% in the placebo or no treatment control group (RR 0.83, 95% CI 0.71 to 0.97), suggesting significantly fewer reported AEs in the probiotic group. Moderate heterogeneity was detected for this comparison; \( P = 0.005; I^2 = 49\% \). Fourteen of the 32 studies were rated as having a low risk of bias and 18 were rated as having a high or unclear risk of bias. The forest plot for this outcome can be found in Figure 4.
Percutaneous Coronary Intervention Outcomes in Patients With Stable Obstructive Coronary Artery Disease and Myocardial Ischemia
A Collaborative Meta-analysis of Contemporary Randomized Clinical Trials

Kathleen Stergiopulos, MD, PhD; William E. Boden, MD; Pamela Hartigan, PhD; et al

Results In 5 trials enrolling 5286 patients, myocardial ischemia was diagnosed in 4064 patients by exercise stress testing, nuclear or echocardiographic stress imaging, or fractional flow reserve. Follow-up ranged from 231 days to 5 years (median, 5 years). The respective event rates for PCI with MT vs MT alone for death were 6.5% and 7.3% (OR, 0.90 [95% CI, 0.71-1.16]); for nonfatal MI, 9.2% and 7.6% (OR, 1.24 [95% CI, 0.99-1.56]); for unplanned revascularization, 18.3% and 28.4% (OR, 0.64 [95% CI, 0.35-1.17]); and for angina, 20.3% and 23.3% (OR, 0.91 [95% CI, 0.57-1.44]).
Association of Aspirin Use for Primary Prevention With Cardiovascular Events and Bleeding Events - A Systematic Review and Meta-analysis

Sean L. Zheng, BM, BCh, MA, MRCP; Alistair J. Roddick, BSc

IMPORTANCE The role for aspirin in cardiovascular primary prevention remains controversial, with potential benefits limited by an increased bleeding risk.

OBJECTIVE To assess the association of aspirin use for primary prevention with cardiovascular events and bleeding.

DATA SOURCES PubMed and Embase were searched on Cochrane Library Central Register of Controlled Trials from the earliest available date through November 1, 2018.

STUDY SELECTION Randomized clinical trials enrolling at least 1000 participants with no known cardiovascular disease and a follow-up of at least 12 months were included. Included studies compared aspirin use with no aspirin (placebo or no treatment).

DATA EXTRACTION AND SYNTHESIS Data were screened and extracted independently by both investigators. Bayesian and frequentist meta-analyses were performed.

MAIN OUTCOMES AND MEASURES The primary cardiovascular outcome was a composite of cardiovascular mortality, nonfatal myocardial infarction, and nonfatal stroke. The primary bleeding outcome was any major bleeding (defined by the individual studies).
### Cardiovascular and Bleeding Outcomes in all Participants

<table>
<thead>
<tr>
<th>Cardiovascular Outcomes</th>
<th>No. of Studies</th>
<th>Aspirin</th>
<th>No Aspirin</th>
<th>Absolute Risk Reduction, % (95% CI)</th>
<th>HR (95% Crl)</th>
<th>Favors Aspirin</th>
<th>Favors No Aspirin</th>
<th>p²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite CV outcome</td>
<td>11</td>
<td>2911</td>
<td>79717</td>
<td>0.38 (0.20 to 0.55)</td>
<td>0.89 (0.84-0.95)</td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td></td>
<td></td>
<td>3072</td>
<td>78147</td>
<td></td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>CV mortality</td>
<td></td>
<td>81623</td>
<td>3588</td>
<td>80057</td>
<td>0.13 (-0.07 to 0.32)</td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>NNT: 357</td>
<td>81623</td>
<td>997</td>
<td>80057</td>
<td>0.07 (-0.04 to 0.17)</td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>NNT: 625</td>
<td>65316</td>
<td>942</td>
<td>63752</td>
<td>0.28 (0.05 to 0.47)</td>
<td></td>
<td></td>
<td>18</td>
</tr>
</tbody>
</table>

### Bleeding Outcomes

<table>
<thead>
<tr>
<th>Bleeding Outcomes</th>
<th>No. of Studies</th>
<th>Aspirin</th>
<th>No Aspirin</th>
<th>Absolute Risk Increase, % (95% CI)</th>
<th>HR (95% Crl)</th>
<th>Favors Aspirin</th>
<th>Favors No Aspirin</th>
<th>p²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major bleeding</td>
<td>NNH: 212</td>
<td>74715</td>
<td>834</td>
<td>73143</td>
<td>0.47 (0.34 to 0.62)</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Intracranial bleeding</td>
<td>NNH: 909</td>
<td>80985</td>
<td>257</td>
<td>79419</td>
<td>0.11 (0.04 to 0.18)</td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Major GI bleeding</td>
<td>NNH: 330</td>
<td>70336</td>
<td>380</td>
<td>70465</td>
<td>0.30 (0.20 to 0.41)</td>
<td></td>
<td></td>
<td>2</td>
</tr>
</tbody>
</table>
Considerations

Absolute Risk Reduction for NNT calculation:
RCT vs. meta-analysis

NNT when RR is not significant
(95% CI crosses 1)
Questions?

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Relative Risk (RR)

- AKA: Risk Ratio, Rate Ratio, Incidence Ratio
- Only calculated in prospective studies
- Represents the ratio of the frequency of disease in exposed individuals vs. unexposed

Odds Ratios (OR)

- Usually calculated in retrospective studies as an estimate of the RR
- Is the odds of disease in the exposed vs unexposed
- Stable mathematical properties
- OR automatically produced by logistic regression model formulas