Randomized Comparison of IV Procainamide vs. Amiodarone For The Acute Treatment of Tolerated Wide QRS Tachycardia

- PROCAMIO Study -

Ortiz M et al. *European Heart Journal*; Published online 28 June 2016

P: Hemodynamically stable adults with regular wide QRS complex tachycardia (WCT)
I: Procainamide 10mg/kg over 20 minutes
C: Amiodarone 5mg/kg over 20 minutes
O_1: Incidence of major adverse cardiac event (MACE)
O_2: Termination of VT, total adverse events during 24 hours observation period
D: Multi-center, prospective open-labelled randomized control trial

What we already know:

- Current ACLS guidelines give procainamide and amiodarone a class II recommendation for the treatment of regular, stable wide complex tachycardia
- No controlled prospective trial compared these two agents head-to-head in stable WCT

Methods:

- Multi-center, prospective, open-labelled randomized control trial
- 29 participating hospitals in Spain, 16 recruited
- Sample size calculation: *302 patients needed* to determine 15% ARR from baseline rate of 20% in procainamide o8
- *Study period over 6 years; study halted due to very slow recruitment rate*
- Unblinded
- Block randomization- allocation concealment through sealed envelopes
- *Study period* defined as 40 min from infusion initiation (drug administration period 20 mins followed by 20 mins observation), *observation period* included subsequent 24 hr
- Intention-to-treat analysis

Inclusion Criteria:

- Adults (age $\geq$ 18) with WCT (not defined "VT") (HR $\geq$ 120bpm, QRS complex $\geq$ 120ms)
- Hemodynamically stable patients (sBP $\geq$ 90, no SOB, angina or signs of peripheral hypoperfusion)

Exclusion Criteria:

- Administration of procainamide or amiodarone within 24 hrs of recruitment
- Not hemodynamically tolerating mediations (i.e. requiring urgent termination)
- Irregular WCT
- WCT deemed secondary to supraventricular origin
- Contraindication to study drugs

Outcomes:

- *Primary*:
  MACE within 40 min after initiation of infusion of study drug
  i) clinical signs of peripheral hypoperfusion
  ii) signs of HF (dyspnea, orthopnea, pulmonary congestion)
  iii) severe hypotension (sBP $\leq$ 70mmHg or $\leq$ 80 depending on pre-treatment BP)
  ix) tachycardia accelerated by > 20bpm above mean
  x) incidence of rapid polymorphic WCT

- *Secondary*:
  i) termination of WCT
  ii) total adverse events during 24 hr observation period

Results:
- 74 patients were randomized at 16 of the 29 participating hospitals
- 12 patients excluded
- 62 analyzed (32 to procainamide, 29 to amiodarone)
- Similar baseline characteristics (see *Table 1*)
- Time from arrival to infusion 87±21 min for procainamide and 115±36 min for amiodarone (P=0.58)
- *Primary Outcome:* 15 patients (24%) MACE- 9% vs. 41% of patients in procainamide and amiodarone group respectively during study period (OR 0.1; 95% CI 0.03-0.6; p=0.006; **fragility index of 3 patients**)
  - Most common MACE – severe hypotension requiring immediate cardioversion
- *Secondary Outcome:* WCT was terminated 33 patients (53%); 67% vs. 38% of patients in the procainamide and amiodarone group respectively (OR 3.3; 95% CI 1.2-9.3; p=0.026; **fragility index of 1 patient**)
  - Intention-to-treat analysis: 68% vs. 42% (OR 2.7; 95% CI 1.04-7.08; p=0.041; **fragility index of 1**)
  - No significant difference in total adverse events (24% vs. 48%; OR 0.34; 95% CI 0.12-1; p=0.052)
  - No significant difference in adverse events during 24 hr observation period (18% vs. 31%; OR 0.49; 95% CI 0.15-1.61; p=0.24)

Strengths:
- Prospective design, multi-center RCT
- Randomized
- Clinically relevant questions (in patients with dysrhythmias, safety is perhaps most important)

Limitations:
- Small sample size (insignificantly powered; did not reach 302 patients)
- Low **Fragility Index**
- Did not compare with other conventional methods (i.e. DC electrical cardioversion)
- Unblinded
- Arbitrary dosing, not the same as what is conventionally used locally

Study Conclusions:
- "In [patients with] acute episodes of sustained monomorphic well-tolerated WCT (probably VT), procainamide therapy was associated with less major cardiac events and a higher proportion of tachycardia termination within 40 minutes"

Presenter's Clinical Bottom Line:
- This is a small, underpowered, non-blinded trial with amiodarone dosing that differs from ACLS suggested dosing. With that being said, this is the best available evidence, and it suggests that there may be improved safety profile and efficacy in terminating stable WCT (probably VT) with the use of 10mg/kg IV procainamide over 20 minutes when compared to 5mg/kg IV amiodarone.
- Be ready for clinical deterioration and have defibrillation pads on the patient

What is Fragility Index?
- The Fragility Index (FI) is a measure of how fragile a trial's result actually is
- Describes the minimum number of patients whose status would have to change from a non-event to an event to turn a statistically significant result into insignificant (i.e. p>0.05)

- The shorter the number of patients one would have to add to the results of either arm to yield insignificant results, the lower the Fragility Index, and the less statistically robust the results are
- FI can be applied to any trial with a binary outcome (e.g. death)
- Calculators for FI can be found online (one: http://clincalc.com/Stats/FragilityIndex.aspx)

Amiodarone, Lidocaine, or Placebo in Out-of-Hospital Cardiac Arrest
- ALPs Study -

Kudenchuk, P.J. et al. *The New England Journal of Medicine*; 2016; Published April 4, 2016

P: In non-traumatic out of hospital cardiac arrest patients with shock refractory V.Fib or pVT after at least one shock plus vascular access.
I: Parenteral Amiodarone, Lidocaine, and Saline Placebo
C: Standard of Care
O_1: Survival to Hospital Discharge
O_2: Favourable neurologic function at discharge
D: Randomized, Double Blinded placebo controlled, pre-hospital trial taking place at 10 NA sites.

What we already know:
- Antiarrhythmic drugs are commonly used in out-of-hospital cardiac arrest for shock refractory V.Fib or pVT – without proven survival benefit.

Methods:
- Setting: The trial was conducted in the communities served by the emergency medical services (EMS) systems participating in the Resuscitation Outcomes Consortium (ROC) – in North America.
- Data Recording:
  - Dispatch records, electronic (ECG) & voice recordings, narrative data from resuscitation
  - EMS providers documented the time each dose of study drug was administered, synchronized whenever possible to the defibrillator clock.
  - Electronic records - analyzed in relationship to times study drug was given for effect on rhythm and hemodynamics.
  - CPR process - monitored in accordance with standard ROC procedures, extending, where feasible, throughout the entire period of resuscitation.
  - Hospital records - reviewed and abstracted.
- Trial drug assignment was not disclosed to anyone, unless emergency un-blinding requested (MD)
- Primary outcome: survival to hospital discharge
- Secondary outcome: survival with favourable neurologic status – defined as a 3 or less on Rankin Scale (0 = no symptoms; 6 = death) – indicating ability to do ADLs independently/minimal assistance
- Data analysis: The trial is designed with a power of 90% to detect a 6.3% absolute difference**.**
  - Survival was evaluated across groups via z-test for comparison of binomial proportions of pooled variance, with one-sided significance level of 0.025 for comparisons between active drug and placebo and two-sided significance of 0.05.
  - Two authors are employees of the NHLBI; they helped in the design and conduct of the trial, data analysis and interpretation…

Inclusion Criteria:

a) Age at least 18 years or local age of consent
b) Non-traumatic out-of-hospital cardiac arrest treated by ROC EMS with ALS capability
c) VF or pulseless VT presenting as the initial arrest arrhythmia or results from conversion of another arrhythmia (such as transient asystole or pulseless electrical activity)
d) Incessant or recurrent VF/VT after receipt of ≥ 1 shocks
e) Established vascular access (IV or IO)

Exclusion Criteria:

a) Asystole or PEA as the initial arrest rhythm who never transition to VF or pulseless VT
b) Written advance directive to not attempt resuscitation (DNAR)
c) Blunt, penetrating, or burn-related injury

d) Exsanguination
e) Protected populations (prisoners, pregnancy, children under local age of consent)
f) Treated exclusively by non-ROC EMS agency/provider, or by BLS-only capable ROC EMS
g) Prior receipt of open label Lidocaine or Amiodarone during resuscitation

Results:

- 37,889 patients with non-traumatic out-of-hospital cardiac arrest; 7,051 had shock refractory VF or pVT. 2,384 excluded. 4,653 included - "intention to treat population" & Randomly Assigned to Drug kit
    - Amiodarone n= 970 of 1,539 –, 565 excluded from per-protocol population
    - Lidocaine n = 985 of 1,541 – 548 excluded from per-protocol population
    - Placebo group n= 1056 of 1,573 –514 excluded from per-protocol population
- *Primary Outcome* – survival to hospital: Amiodarone: 237/970 (24.4%); Lidocaine: 233'985 (23.7%); Placebo: 222/1,056 (21.0%)
    - Amiodarone vs. Placebo: p = 0.08
    - Lidocaine vs. Placebo: p = 0.70
    - Amiodarone vs. Lidocaine: p = 0.16
- *Secondary Outcome*– Favourable Neurologic Outcome, Amiodarone: 182/967 (18.8%); Lidocaine: 172/984 (17.5%); Placebo: 175/1,055 (16.6%)
    - Amiodarone vs. Placebo: p = 0.19
    - Lidocaine vs. Placebo: p = 0.59
    - Amiodarone vs. Lidocaine: p = 0.44
- Active drugs were associated with a higher rate of survival to hospital discharge than placebo among patients with witnessed out of hospital arrest (Survival rate amiodarone = 27.7%, lidocaine = 27.8%, placebo = 22.7%).

Strengths:

- Randomized, Double Blinded placebo controlled, pre-hospital trial taking place at 10 NA sites.
- Randomization occurred throughout all studies sites.
- Rigorous methodology with clearly reproducible data entry points.
- Neurologic Outcome + survival benefit (Modified Rankin Scale) – positive patient outcome.

Limitations:

- May be underpowered – 3.2% increase in survival over placebo – yet not significant (p = 0.08), requires at least 9,000 patients to achieve significance.
- Diluted results – failure to exclude unwitnessed cardiac arrests.
- Timing of Drug Administration – relative to in-hospital arrests. Average time to "drug" administration averaged 19.3 +/- 7.4 minutes from EMS activation and after median 3 shocks delivered.

Study Conclusions: In patients with out of hospital cardiac arrest secondary to vfib/vtach treatment with Amiodarone or Lidocaine did not result in a significantly higher rate of survival to hospital discharge nor favourable neurologic outcome at discharge, compared to placebo.

Validity: The methodology and results are generalizable. It was implemented across multiple facilities and EMS systems allowing for minor variations in local practice. The lack of significance between groups, may be attributable to inclusion of patients in whom the likelihood to benefit from ACLS intervention is dismal (i.e. unwitnessed out-of-hospital arrests).

Presenter's Clinical Bottom Line:

- At this time, the best available evidence does not suggest that amiodarone or lidocaine improves survival to neurologically intact hospital discharge in patients with out of hospital cardiac arrest and vfib or pVT. There is also no evidence of harm, so it is likely reasonable to **consider these treatments**.
- This study highlights several interesting, hypothesis generating, secondary outcomes and an adequately powered trial that excludes patients with unwitnessed out of hospital arrest may be of benefit.

Adjunctive Glucocorticoid Therapy in Patients with Septic Shock

- ADRENAL Trial -

Venkatesh B et. al. *New England Journal of Medicine*; Published online 19 January 2018 NEJM.org

P: Mechanically ventilated critically ill adults (age ≥ 18) with septic shock
I: Hydrocortisone (HC) infusion (200mg/day) for 7 days or until death or ICU discharge
C: Sterile air-filled vial (placebo)
O_1: 90-day all-cause mortality
O_2: 28-day mortality, time to resolution of shock, recurrence of shock, length of hospital/ICU stay, time to discharge, no. days alive and out of hospital/ICU, frequency and duration of mechanical ventilation or treatment with renal-replacement therapy, incidence of new-onset bacteremia or fungemia, blood transfusion requirements
D: International, pragmatic, double-blind, parallel-group randomized control trial

What we already know:

- Current Surviving Sepsis Guidelines (2016) recommend corticosteroids in septic shock patients not achieving hemodynamic instability after adequate fluid resuscitation and vasopressors (Level 2C)
- There is conflicting evidence on utility of corticosteroids in the management of septic shock

Methods:

- Double-blinded RCT
- March 2013-April 2017; 69 medical-surgical ICUs in Australia (45), United Kingdom (12), New Zealand (8), Saudi Arabia (3), and Denmark (1)
- Published trial protocol and statistical analysis plan revealed prior to enrollment
- All other aspects of care at discretion of treating clinicians
- Intention-to-treat analysis
- Sample size calculation- 3800 would provide 90% power to detect absolute difference of 5% in 90 day mortality from estimated baseline mortality of 33% and alpha level of 0.05
- Primary outcome: death from any case at 90 days after randomization.
    - Primary outcome examined in 6 pre-specified subgroups: *admission type*, *dose of catecholamine infusion*, *primary site of sepsis*, *sex*, *APACHE II score*, and *duration of shock*
- Secondary outcomes: Death from any cause at 28 days, time to resolution of shock

Inclusion Criteria:

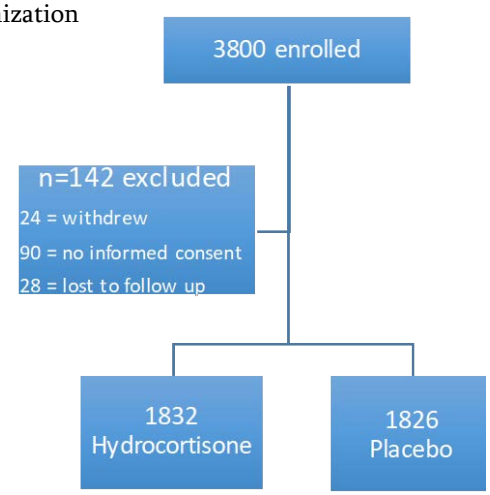
- Adults (age ≥ 18) undergoing mechanical ventilation with documented strong clinical suspicion of infection, ≥ 2 SIRS criteria, and treatment with vasopressors/inotropes for ≥ 4 hours prior to randomization

Exclusion Criteria:

- Received systemic glucocorticoids for any other indication other than septic shock
- Administered etomidate
- Considered likely to die from pre-existing disease within 90 days after randomization
- Treatment limitations in place (i.e. DNR)
- Met all inclusion criteria for ≥ 24 hours

Results:

- Similar baseline characteristics. No statistically significant difference in use of inotropes, vasopressors, etomidate, statins and antibiotics
- Assigned trial regimen received in 99.8% (HC) and 99.7% (placebo) of patients; infusion median 5.1 vs. 5.6 days respectively



- Between days 1-7, patients in HC group had higher MAP (5.39mmHg difference, P<0.001) as well as lower HR (6.6bpm, P<0.001); no significant between-group difference in daily dose of norepinephrine between days 1-14
- Primary Outcome: No statistically significant difference in 90 day mortality
    - 511 (27.9%) vs. 526 (28.8%) died in the HC and placebo group (OR 0.95; 95%CI 0.82-1.10; P=0.50)
    - No significant between-group difference in rate of death in the time-to-event analysis during 90 days after randomization (HR 0.95; 95%CI 0.84-1.07; P=0.42)
    - No significant heterogeneity in six pre-specified subgroups, with exception of those in 6 to < 12 hours' time from shock onset to randomization; these patients did statistically significantly better
- *Secondary Outcome:*
    - Time to shock resolution shorter in HC group median 3 vs. 4d (HR 1.32; 95% CI 1.23-1.41; P<0.001)
    - Shorter time to discharge from ICU in HC group: median 10 vs. 12d (HR 1.14; 95% CI 1.06-1.23; P<0.001)
    - Shorter duration of initial mechanical ventilation in HC group: median 6 vs. 7 days (HR 1.13; 95% CI 1.05-1.22; P<0.001)
    - Fewer patients in HC received blood transfusion: 37.0% vs 41.7% (OR 0.92; 95% CI 0.72-0.94; P=0.004)
    - No significant between-group difference in all-cause mortality at 28 days (410/1841 vs. 448/1840, OR 0.89; 95% CI 0.76-1.03; P=0.13)
    - No significant between-group difference in the other secondary outcomes

Adverse Events:

- Total of 33 adverse events- higher in HC group (1.1% vs 0.3%; P=0.009); 6 serious adverse events; 4 versus 2 in HC and placebo group respectively.

Strengths:

- Large, prospective design, pragmatic multi-center RCT with intention to treat analysis
- Primary outcome clinically important and patient centered
- Ensured concealment and blinding of trial-group assignments
- Similar baseline characteristics between the patients
- Statistical analysis plan published prior to commencement of trial
- High proportion of eligible patients received trial intervention as planned, few lost to follow-up
- Ratio of patients undergoing randomization to those eligible for inclusion was high: 0.69:1

Limitations:

- Data on only adverse events related to the trial regimen as judged by managing physicians
- No data on remainder of care (eg antibiotic, IV fluids, mechanical ventilation settings)
- Time from shock onset to randomization > 20 hours for both groups
- Time from randomization to administration of study drug > 1 hour
- ~7-8% of patients from both groups received open-label steroids
- Hydrocortisone infusion not typically used in practice (although 200mg / day is a common dose)

Study Conclusions:

- "In patients with septic shock who were undergoing mechanical ventilation, the administration of continuous infusion of hydrocortisone did not result in lower mortality at 90 days than placebo"

Presenter's Clinical Bottom Line:

- Use of hydrocortisone infusion does not result in a mortality benefit to intubated patients with septic shock. It may, however, yield more rapid improvement in hemodynamics, quicker resolution from shock, shorter duration spent in ICU, less days on the ventilator, and less blood transfusions without the increased risk of bacteremia and fungemia so would **consider** administration as adverse outcomes may also increase.

Corticosteroids for Pneumonia (Review)

Stern A, Skalsky K, Avni T, Carrara E, Leibovici L, Paul M; First Published on December 13, 2017

P: Adults and Pediatrics with Pneumonia
I: Systemic Corticosteroids + Antibiotics (not specified)
C: Placebo or No corticosteroids
O_1: 30 day all cause mortality
O_2: 1. Early clinical failure. 2. Time to clinical cure. 3. Development of Respiratory Failure. 4. Development of Shock. 5. In-patient Transfer to ICU. 6. Duration of Hospitalization. 7. Duration of ICU stay. 8. Pneumonia complications. 9. Secondary infections 10. Adverse events
D: Systematic Review and Meta-Analysis of RCTs

What we already know:
- Clinical use of corticosteroids for treatment of pneumonia varies.
- CAP 5.5 per 1000 ppl/year, 20% admitted to hospital and 10 to 20% are admitted to ICU; 10 to 12% of admitted patients die at 30 days (higher in ICU admitted)
- Current guidelines do not address use of systemic steroids as an adjunct to treatment of pneumonia.

Methods:
- Extensive search methodology
- Data Selection: two author independent review of titles and abstracts. Followed PRISMA protocol.
- Performed *Assessment of Risk of Bias in Included studies*. i.e.: Randomization, blinding etc.
- Used five GRADE considerations to assess quality of evidence.
- Data Synthesis via Meta-Analysis: pooled risk ratios (RR) and mean differences with 95% CI
- Subgroup analysis a priori for adults and pediatrics.
- Investigation for Heterogeneity - Subgroup analysis if data provided or Meta-regression if no data.

Inclusion:
- RCTs assessing the effectiveness of systemic corticosteroids + antibiotics for treatment of pneumonia.
- Radiographically confirmed Pneumonia
- Use of steroids of any dose, mode, or duration

Exclusion:
- Excluded studies including only Neonates, Pneumocystis pneumonia, and people with HIV.
- Reason for study Exclusion:
    - Examined the use of inhaled corticosteroids
    - Corticosteroids administered to both study groups.
    - Prospective, non-randomised trial
    - Participants in the control group were subsequently given either corticosteroids or intravenous immunoglobulin therapy
    - Population included people with and without pneumonia, and outcomes were not reported separately for participants with pneumonia
    - Quasi-randomised controlled trial

Results: (Bolded = Significance Achieved)
- Search found 5,545 references, narrowed down to 17 RCTs (conducted world-wide) included in the review. (PRISMA). Six of the studies were Multi-centre trials (2 to 7 centres)
- All trials included limited participants to CAP or HCAP treated as inpatients

- Totals: 2,264 randomized participants. 1,122 received systemic corticosteroids. 1,954 were adults,13 RCTs; 307 pediatric patients 4 RCTs.
- Duration of corticosteroids use ranged from 1 dose to 10 days (40 to 50mg equiv of prednisone/day).
- **Primary Outcome – All cause Mortality**
    - *Adults:* corticosteroids – significantly lower all-cause mortality RR 0.66 95% CI (0.47 to 0.92)
        - Severe Pneumonia: RR 0.58 CI 95% [0.40 to 0.84] – significant
        - Non-severe Pneumonia: RR 0.95 [0.45 to 2.00] – not significant
    - Pediatrics: No reported deaths in any of the trials. RR 0.0 [-0.03 to 0.03]

- **Secondary Outcomes:**
    1. **Early clinical failure.** Pooled Adult + Peds RR 0.40 [0.26 to 0.63]
        a. Adults – both significant RR 0.40 [0.23 to 0.70]
            i. Severe CAP RR 0.32 [0.15 to 0.70]
            ii. Non-Severe CAP 0.68 [0.56 to 0.83]
        b. Peds – RR 0.41 [0.24 to 0.70]
    2. **Time to clinical cure**. Mean Difference in Days
        a. Adults: MD -1.83 [-2.45 to -1.21]
        b. Peds: **Bacterial Pneumonia** MD -1.57 [-2.55 to -0.60]
            Viral Pneumonia MD 1.70 [-2.50 to 5.90]
    3. Development of Resp. Failure/Need for Mechanical Ventilation
        a. Adults: RR 0.40 [0.20 to 0.77]
    4. Development of Shock.
        a. Adults: RR 0.18 [0.09 to 0.34]
    5. In-patient Transfer to ICU.
        a. Adults: RR 0.73 [0.45 to 1.18]
    6. **Length of Hospitalization.** Mean Difference in Days
        a. Adults: MD -2.91 [-4.92 to -0.89]
        b. Peds: 1 Study **Bacterial Pneumonia** MD -4.70 [-7.50 to -1.90]
            1 Study Viral Pneumonia: MD 2.60 [-2.61 to 7.81]
    7. **Duration of ICU stay.** Mean Difference in Days
        a. Adults: MD -1.88 [-2.96 to -0.81]
    8. Development of pneumonia complications.
        a. Pooled Adult + Peds: RR 0.58 [0.40 to 0.84]
    9. Secondary infections ≥72 hours after randomization.
        a. Adults: RR 1.19 [0.73 to 1.93]
        b. Peds: RR 0.0 [-0.03 to 0.03]
    10. *Adverse events* (Any hyperglycemia requiring new insulin treatment, neuro-psych, GI bleeds, Cardiac events)
        a. Adults: Any RR 1.21 [0.99 to 1.47] almost significantly favours control*
            i. Hyperglycemia: RR 1.72 [1.32 to 2.14]
            ii. GI Bleed: 0.91 [0.40 to 2.05]
            iii. Neuropsych: RR 1.95 [0.70 to 5.42]
            iv. Cardiac: RR 0.60 [0.32 to 1.13]
        b. Peds: RR 0.0 -0.05 to 0.05

Strengths:
- Systematic Review of 17 RCTs with Meta-Analyses
- Rigorous revision of previously performed systematic review
- Large number of international adult studies
- Thorough evaluation of secondary outcomes – increases utility of review for more than just a mortality benefit.

Limitations:
- Heterogeneity in pneumonia severity reporting
- Variable steroid administration that was not analysed for significance.

- Pediatrics - small number of studies with heterogeneous pool of pathologies. In addition to significant variation in potential pathophysiology amongst age groups in pediatrics.
- Antibiotic selection was not reported
- Poorly defined Exclusion criteria of studies for review

Study Conclusions:
- Corticosteroids reduced morbidity and mortality in adults with severe CAP (NNT = 18)
- Corticosteroids reduce morbidity but not mortality in adults and children with non-severe CAP.
- Corticosteroids are associated with adverse events (hyperglycemia) but benefit outweighs risk.

Validity:
- The results of this study as, they apply to adult patients, appear valid and generalizable to most populations.
- Quality of evidence for all-cause mortality, rated as moderate
- Quality of evidence for clinical failure, rated as high.
- The validity for the use of corticosteroids in pediatrics with CAP is questionable, a more robust body of literature is required.

Presenter's Clinical Bottom Line:
- Corticosteroids should be started on all adult patients being admitted to hospital for moderate to severe pneumonia to reduce complications, length of stay in ICU/hospital, time to clinical cure and reduce all-cause mortality in severe pneumonia.
- Routine, use of systemic corticosteroids in children with bacterial pneumonia is not supported by this study. However, the risk of a short-course of systemic corticosteroids are minimal and could have a morbidity benefit and decrease hospital admission time.

EBM PEARL: Understanding Risk

Risk terms:

Absolute risk = risk = incidence rate = # of events in treated or control groups, divided by the number of people in the group

AR_C = absolute risk of events in the control group

AR_T = the AR of events in the treatment group

ARR = Absolute risk reduction = absolute risk difference = risk difference = $AR_C - AR_T$

RR = risk ratio = AR_T / AR_C

RRR = relative risk reduction = 1 – RR

NNT = number needed to treat = 1/ARR

Example:

Corticosteroids	Dead	Not dead	Total
Y	51	874	925
N	77	861	938

AR_T = 51/925 = 0.055
AR_C = 77/ 938 = 0.082
ARR = ARC – ART = 0.027
RR = ART / ARC = 0.67
NNT = 1/0.027 = 37

What does this mean?
- **RR > 1 =** events are **more likely in the treatment group** than the control group
- **RR < 1 =** events are **less likely in the treatment group** than the control group
- The closer the RR is to 1 the less significant of effect there is
- Can interpret as **% effect** → RR of 0.67 = 1 – 0.67 = **33% less likely to die** than those who did not receive steroids
- When verbalizing risk ratios: try to say "RR times the risk of x in the treatment vs the control group" Eg: patients with CAP who received corticosteroids have 0.67 times the risk of death

- **NNT =** 37 patients with CAP would have to be **treated for 1 patient death to be prevented**