

# Long-acting Beta-agonists: Asthma Intubations and Deaths

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# Long-acting Beta-agonists: Asthma Intubations and Deaths

- Potential conflicts of interests
  - No financial ties
    - Pharmaceutical industry
  - Provided expert testimony
    - Litigation case
      - Long-acting beta-agonists
      - Paid on an hourly basis

# Long-acting Beta-agonists: Asthma intubations and deaths

- Pooled data from all available sources
  - LABA with variable inhaled corticosteroids (ICS)
  - LABA with concomitant ICS
- Life-threatening and fatal asthma events
  - Asthma intubations or asthma deaths
- Subgroup analysis: test for interaction
  - Variable and concomitant ICS
  - Salmeterol and formoterol
  - Adults and children
  - Life-threatening and fatal events

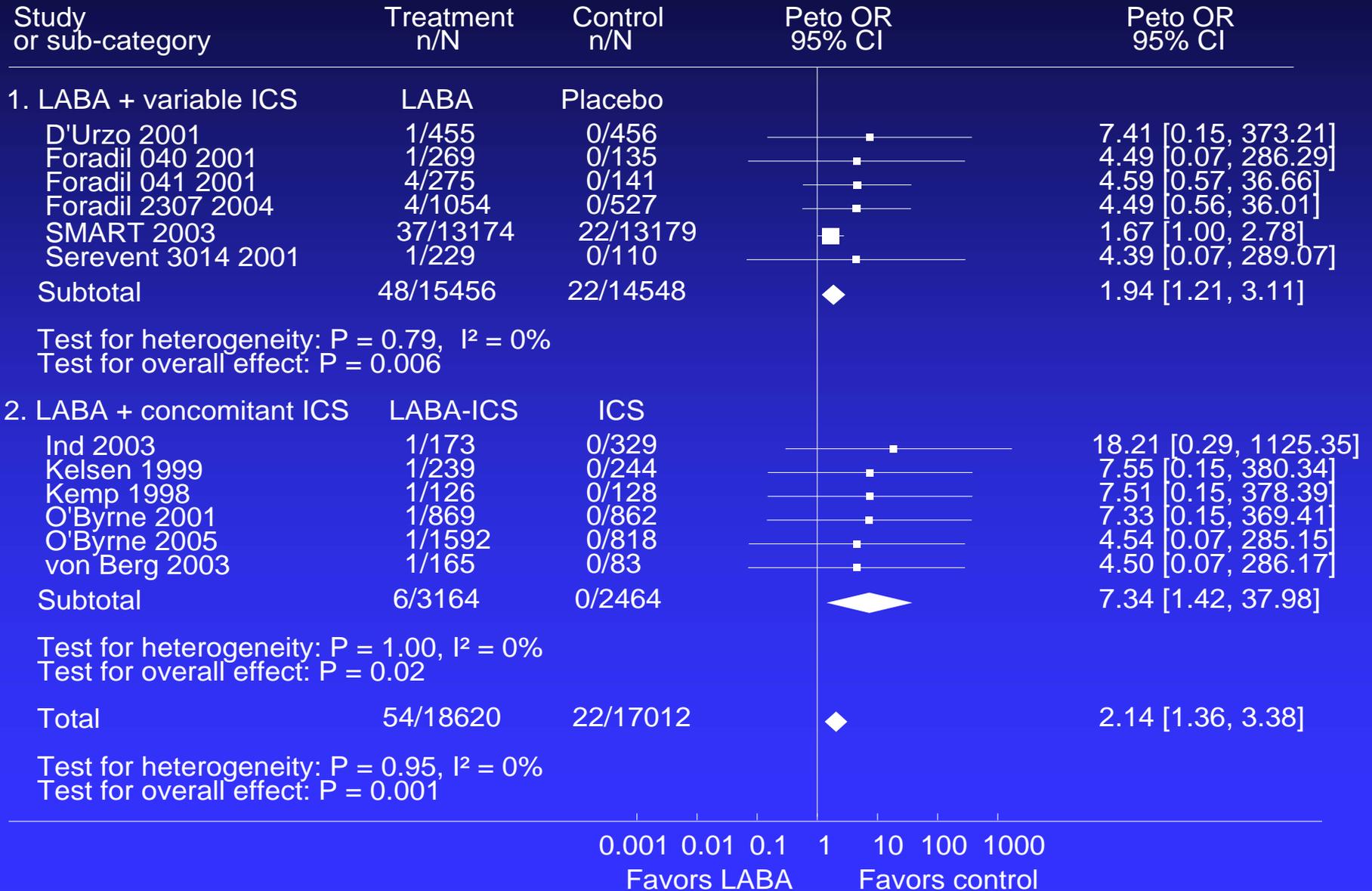
# Long-acting Beta-agonists: Previous Meta-analysis

- Salpeter et al, 2006
  - Ann Intern Med 2006;144:904-912
  - Meta-analysis on LABA:
    - Asthma hospitalizations, intubations, deaths
    - Included trials: LABA vs. placebo
      - Varying amounts of concomitant ICS
    - LABA: two- to four-fold increased risk
      - Serious, life-threatening and fatal asthma events
      - Compared with placebo
    - Average: 50% participants
      - Concomitant ICS

# Long-acting Beta-agonists: Data Sources

- Previous meta-analyses as sources
  - LABA with variable ICS
    - Salpeter et al, Ann Intern Med 2006;144:904-912
      - LABA: intubations, death
    - Sears et al, Eur Respir J 2008; epub ahead of print
      - Formoterol: death
    - Cates et al, Cochrane Database 2008; Issues 2, 3
      - Formoterol: deaths
      - Salmeterol: deaths
  - LABA with concomitant ICS
    - Jaeschke et al, Am J Respir Crit Care Med 2008;178:1009-16
      - LABA in adults: intubations, death
    - Bateman et al, Ann Intern Med 2008;149:33-42
      - Salmeterol: intubations, death
    - Sears et al, Eur Respir J 2008; epub ahead of print
      - Formoterol: deaths

# Long-acting Beta-agonists: Asthma Intubations and Deaths



# Long-acting Beta-agonists: Subgroup Analysis

- No significant difference in results
  - Use of inhaled corticosteroids
    - Variable ICS (OR 2.0 [CI, 1.2 to 3.1])
    - Concomitant ICS (OR 7.3 [CI, 1.4 to 38.0])
  - Fatal vs. life-threatening events
    - Variable ICS
      - Life-threatening (OR 1.5 [CI, 0.9 to 2.7])
      - Asthma death (OR 3.7 [CI, 1.5 to 9.2])
    - Concomitant ICS
      - Life-threatening (OR 7.5 [CI, 0.5 to 120.3])
      - Asthma death (OR 7.3 [CI, 0.9 to 55.8])

# Long-acting Beta-agonists: Subgroup Analysis

- No significant difference in results
  - Type of LABA or age
    - Variable ICS
      - Salmeterol (OR 2.0 [CI, 1.2 to 3.0])
      - Formoterol (OR 4.5 [CI, 1.2 to 16.9])
      - Adults (OR 1.9 [CI, 1.2 to 3.1])
      - Children (OR 4.4 [CI, 0.1 to 289])
    - Concomitant ICS
      - Salmeterol (OR 9.9 [CI, 1.0 to 98.9])
      - Formoterol (OR 5.4 [CI, 0.5 to 56.3])
      - Adults (OR 8.0 [CI, 1.3 to 48.1])
      - Children (OR 4.5 [CI, 0.2 to 84.8])

# Long-acting Beta-agonists: Increase Asthma Intubations and Deaths

- Conclusion:
  - LABAs significantly increase risk
    - Life-threatening or fatal asthma events
    - With and without use concomitant ICS
  - No protective effect ICS was seen
    - Relative risk asthma intubations or deaths
    - Not able to assess absolute increase risk
      - Only trials with at least one event included
    - Possible ICS reduced baseline risk
      - Treatment and control groups
      - Absolute increase risk of LABA reduced