

## Supplementary Online Content

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**eTable 1.** Treat vs Don't Treat: Ampicillin/Amoxicillin vs Placebo or Wait-and-See, Prescription-to-Hold Approaches

**eTable 2.** Comparative Effectiveness of Different Antibiotics for Treating Uncomplicated Acute Otitis Media (AOM) in Average-Risk Children

This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1. Treat vs Don't Treat: Ampicillin/Amoxicillin vs Placebo or Wait-and-See, Prescription-to-Hold Approaches**

| Author, Year                                      | Study Quality (Jadad Score) <sup>1</sup> | Age          | Number of Participants (Treat, Don't Treat) | Comparison                                       | Definition of Outcome   | Rate Difference (95% CI)  | Adverse Events Rate difference (95% CI)   |
|---|--|--------------|---|--|---|---|---|
| <b>Ampicillin/Amoxicillin vs. Placebo Studies</b> |  |              |   |  |   |   |   |
| Halsted, 1967 <sup>1</sup>                        | [1,1,1,1,1]                              | 2-66 mos     | 30, 27                                      | Ampicillin 100 mg/kg/d, QID for 10 d vs. Placebo | Success rate 14-18 days (decreased symptoms and improvement of TM appearance)                         | -8% (-21, 5)<br>92% (23/25) vs. 100% (21/21)                      | Not reported  |
| Laxdal, 1970 <sup>2</sup>                         | [1,0,0,1,0]                              | <15 yrs      | 49, 48                                      | Ampicillin vs. Placebo                           | Success at day 7 (no evidence of middle ear inflammation and partial/complete resolution of symptoms) | 27% (11, 43)<br>90% (44/49) vs. 63% (30/48)<br>NNT: 4 (2, 9)      | Mild Diarrhea: 2% (-2, 6)<br>2% (1/49) vs. 0% (0/48)<br>Rash: 4% (-2, 10)<br>4% (2/49) vs. 0% (0/48)<br>Serious complications: 0% (0, 0)<br>0% (0/49) vs. 0% (0/48) |
| Howie, 1972 <sup>3</sup>                          | [1,0,0,0,0]                              | <=2.5 yrs    | 36, 116                                     | Ampicillin vs. Placebo                           | Success at day 2-7 (absence of effusion)  | 27% (9, 44)<br><br>47% (17/36) vs. 21% (24/116)<br>NNT: 4 (2, 11) | Not reported  |
| Burke, 1991 <sup>4</sup>                          | [1,1,0,1,1]                              | 3-<10 yrs    | 114, 118                                    | Amoxicillin 125 mg, TID for 7 d vs. Placebo      | Success at day 7 (no receipt of any additional antimicrobial)   | 13% (6, 19)<br>98% (112/114) vs. 86% (101/118)<br>NNT: 8 (5, 17)  | Vomiting: 6% (-3, 15)<br>18% (20/114) vs. 12% (14/118)<br>Diarrhea: 7% (-3, 17)<br>21% (24/114) vs. 14% (16/118)<br>Rash: 3% (-4, 9)<br>8% (9/114) vs. 5% (6/118)   |
| Kaleida, 1991 <sup>5</sup>                        | [1,1,0,0,0]                              | 7 mos-12 yrs | 488, 492                                    | Amoxicillin vs. Placebo                          | Success at day 14 (resolution of effusion)  | 15% (8, 22)<br>53% (213/401) vs. 38% (155/408)<br>NNT: 7 (5, 13)  | Not reported  |
| Damoiseaux, 2000 <sup>6</sup>                     | [1,1,1,1,1]                              | 6 mos-2yrs   | 117, 123                                    | Amoxicillin 40 mg/kg/d, TID for 10 d vs. Placebo | Clinical success at day 11 (resolution of symptoms- earache, fever, irritability, crying)             | 6% (-6, 18)<br>36% (40/112) vs. 30% (36/120)                      | Diarrhea<br>At day 4: 7% (-2, 16)<br>17% (20/117) vs. 10% (12/123)<br>At day 10: 4 (-4, 12)<br>12% (14/117) vs. 8% (10/123)   |

eTable 1 (Continued)

| Author, Year  | Study Quality (Jadad Score) <sup>1</sup>  | Age          | Number of Participants (Treat, Don't Treat) | Comparison   | Definition of Outcome  | Rate Difference (95% CI)  | Adverse Events Rate difference (95% CI)   |
|---|---|--------------|---|--|--|---|---|
| Le Saux, 2005 <sup>7</sup>  | [1,1,1,1,1]   | 6 mos-5yrs   | 250, 240                                    | Amoxicillin 60 mg/kg/day, TID for 10 d vs. Placebo | Clinical resolution at day 14 (no receipt of any additional antimicrobial) | 9% (3, 14)<br>93% (232/250) vs. 84% (202/240)<br>NNT: 11 (7, 33)                | Any event:<br>Diarrhea: 0% (-6, 6)<br>11% (26/235) vs. 11% (27/240)<br>Rash: -1% (-6, 4)<br>7% (17/235) vs. 8% (20/240) |
| Van Buchen, 1981 <sup>8</sup>   | [1,1,1,0,1]   | 2-12 yr      | 46, 38                                      | Amoxicillin vs. Placebo                            | No pain after 7 days   | 4% (-8, 16)<br>93% (43/46) vs. 89% (34/38)                                      | Not reported  |
| Halsted, 1967 <sup>1</sup><br>Laxdal, 1970 <sup>2</sup><br>Howie, 1972 <sup>3</sup><br>Burke, 1991 <sup>4</sup><br>Kaleida, 1991 <sup>5</sup><br>LeSaux, 2005 <sup>7</sup><br>Damoiseaux, 2000 <sup>6</sup> | [1,1,1,1,1]<br>[1,0,0,1,0]<br>[1,0,0,0,0]<br>[1,1,0,1,1]<br>[1,1,0,0,0]<br>[1,1,1,1,1]<br>[1,1,1,1,1] | 2 mos-14 yrs | 987, 1071                                   | Amoxicillin or Ampicillin vs. Placebo              | Success by day 14  | Pooled:<br>12% (5, 18)<br>73% (934/1079) vs.<br>60% (867/1161)<br>NNT: 9 (6,20) | Diarrhea: 5% (0, 10)<br>13.1% vs. 7.8%<br>Includes Laxdal, Burke, and Damoiseaux  |

**eTable 1 (Continued)**

| Author, Year                         | Study Quality (Jadad Score) <sup>1</sup> | Age       | Number of Participants (Treat, Don't Treat) | Comparison  | Definition of Outcome   | Rate Difference (95% CI)   | Adverse Events Rate difference (95% CI)   |
|--------------------------------------|--|-----------|---|---|---|--|---|
| <b>Other Antibiotics vs. Placebo</b> |  |           |   |   |   |  |   |
| Halsted, 1967 <sup>1</sup>           | [1,1,1,1,1]                              | 2-66 mos  | 32, 27                                      | Penicillin G 50,000 units/kg/d + sulfisoxazole 150 gm/kg/d QID for 10 d vs. Placebo | Success at day 14-18 (decreased symptoms and improvement of TM appearance)                            | 0% (-15, 15)<br>92% (23/25) vs.<br>92% (23/25)                             | Not reported  |
| Laxdal, 1970 <sup>2</sup>            | [1,0,0,1,0]                              | <15 yrs   | 45, 48                                      | Penicillin vs. Placebo  | Success at day 7 (no evidence of middle ear inflammation and partial/complete resolution of symptoms) | 13% (-7, 30)<br>76% (34/45) vs.<br>63% (30/48)                             | Not reported  |
| Howie, 1972 <sup>3</sup>             | [1,0,0,0,0]                              | <=2.5 yrs | 23, 116                                     | Triple sulfonamide vs. Placebo  | Success at day 2-7 (absence of effusion)  | 9% (-9, 28)<br>30% (7/23) vs.<br>21% (24/116)                              | Not reported  |
| Howie, 1972 <sup>3</sup>             | [1,0,0,0,0]                              | <=2.5 yrs | 25, 116                                     | Erythromycin estolate vs. Placebo   | Success at day 2-7 (absence of effusion)  | 3% (-15, 21)<br>24% (6/25) vs.<br>21% (24/116)                             | Not reported  |
| Howie, 1972 <sup>3</sup>             | [1,0,0,0,0]                              | <=2.5 yrs | 80, 116                                     | Erythromycin estolate-triple sulfonamide vs. Placebo                                | Success at day 2-7 (absence of effusion)  | 30% (17, 43)<br>51% (41/80) vs.<br>21% (24/116)<br>NNT: 3 (2, 6)           | Not reported  |
| Thalin, 1985 <sup>9</sup>            | [1,1,0,1,1]                              | 2-15 yr   | 159, 158                                    | Penicillin vs. Placebo  | Success at day 7 (resolution of signs and symptoms)   | 5% (0.3, 10)<br>97% (155/159)<br>vs. 92%<br>(146/158)<br>NNT: 20 (10, 333) | Rash: 0% (-2, 2)<br>1% (1/159) vs. 1% (1/158)<br>Serious complications:<br>0% (0, 0)<br>0% (0/159) vs. 0% (0/158) |
| Mygind, 1981 <sup>10</sup>           | [1,1,1,0,0]                              | 1-10 yr   | 72, 77                                      | Penicillin V 55mg/kg/d for 7 d vs. Placebo  | Symptom free by 2 days  | 17% (2, 32)<br>79% (57/72) vs.<br>62% (48/77)<br>NNT: 6 (3, 50)            | Not reported  |

**eTable 1 (Continued)**

| Author, Year  | Study Quality (Jadad Score) <sup>1</sup> | Age         | Number of Participants (Treat, Don't Treat) | Comparison   | Definition of Outcome   | Rate Difference (95% CI)  | Adverse Events Rate difference (95% CI)   |
|---|--|-------------|---|--|---|---|---|
| <b>Antibiotic vs. Prescription to Hold and Wait-and-See</b> |  |             |   |  |   |   |   |
| McCormick, 2005 <sup>11</sup>                               | [1,0,1,1,0]                              | 6 mos-12 yr | 111, 108                                    | Amoxicillin 90 mg/kg/day, BID for 10 D vs. Wait-and-see          | Success at day 12 (did not return with symptoms and signs of AOM)                           | 15% (6, 24)<br>95% (102/107) vs. 80% (86/107)<br>NNT: 7 (4, 17) | Antibiotic-related events:<br>7% (-0.4, 14)<br>12% (13/111) vs. 5% (5/108)<br>Serious events related to AOM: 0% (0, 0)<br>0% (0/111) vs. 0% (0/108) |
| Neumark, 2007 <sup>12</sup>                                 | [1,0,1,1,0]                              | 2-16 yr     | 87, 82                                      | Phenoxymethylpenicillin 25 mg/kg/d, bid for 5 d vs. Wait-and-see | Success at day 14 (resolution of symptoms)  | -3% (-14, 8)<br>82% (71/87) vs. 85% (70/82)                     | Not reported  |
| Little, 2001 <sup>13</sup> ; 2006 <sup>14</sup>             | [1,0,1,1,0]<br>[1,1,0,1,0]               | 6 mos-10 yr | 135, 150                                    | Amoxicillin vs. Prescription to Hold                             | Success at day 3 (Patient felt better 3 days after seeing the doctor as reported by parent) | 16% (6, 26)<br>86% (116/135) vs. 70% (105/150)<br>NNT 6 (4, 17) | Rash: 0% (-5, 5)<br>5% (6/133) vs. 5% (8/149)<br><br>Diarrhea: 10% (2, 18)<br>19% (25/133) vs. 9% (14/149)<br>NNH: 10 (6, 50)                       |
| Spiro, 2006 <sup>15</sup>                                   | [1,0,1,1,0]                              | 6 mos-12 yr | 133, 132                                    | Antibiotic vs. Prescription to Hold                              | Parent did not fill antibiotic prescription by day 4-6                                      | -49% (-61, -38)<br>13% (17/133) vs. 62% (82/132)                | Day 4-6:<br>Diarrhea: 14% (6, 22)<br>23% (31/133) vs. 8% (10/132)<br>NNH: 7 (5, 17)<br>Vomiting: -1% (-8, 7)<br>11% (15/133) vs. 11% (15/132)       |

Antibiotic dosing and course provided when available.

Pooled rates are not crude rates.

Abbreviations: d= day; mg=milligrams; kg= kilograms; mos=months; yr= years; QID= four times daily; TID= three times daily; BID= twice daily dosing; amx=amoxicillin; RD=rate difference; CI=confidence interval

<sup>1</sup> Jadad study quality score components (1=present; 0=not present): randomization mentioned; double-blind mentioned; dropouts described; randomization appropriate; double-blinding appropriate. Studies could receive a Jadad score ranging from 0 to 5 points.

**eTable 2.** Comparative Effectiveness of Different Antibiotics for Treating Uncomplicated Acute Otitis Media (AOM) in Average-Risk Children

| Author and Publication Year  | Study Quality (Jadad Score) <sup>a</sup>                                | Comparison                                | Age         | Number of Participants (Gp1, Gp2) | Definition of Clinical Success  | Success Rate difference (95% CI)                   | Adverse Events Rate difference (95% CI)   |
|--|---|---|-------------|-----------------------------------|---|--|---|
| <b>Ampicillin/Amoxicillin vs. Other Antibiotic: Pooled Comparisons</b>   |   |   |             |                                   |   |  |   |
| Varsano, 1988 <sup>16</sup><br>Green, 1993 <sup>17</sup><br>Kara, 1998 <sup>18</sup><br>Zhang, 2003 <sup>19</sup>  | [1,1,1,0,1]<br>[1,1,1,0,1]<br>[1,0,0,0,0]<br>[1,0,1,0,0]                | Ampicillin or amoxicillin vs. Ceftriaxone | 5mos- 12yrs | 260, 258                          | Success at 5-14 days (complete or partial resolution of signs and/or symptoms)                | 0% (-7, 7)<br>93% (242/260) vs<br>93% (241/258)    | Rash or loose stool (Data from Kara only): 8% (-3, 19)<br>8% (2/25) vs 0% (0/25)  |
| McLinn, 1987 <sup>20</sup><br>Leigh, 1989 <sup>21</sup><br>Johnson, 1991* <sup>22</sup><br>Principi, 1991 <sup>23</sup><br>Owen, 1993 <sup>24</sup><br><br>*Johnson not included in success pooled analysis because assessed success at 30 d | [1,0,1,1,0]<br>[1,0,1,0,0]<br>[1,0,0,0,0]<br>[1,0,0,1,0]<br>[1,0,1,0,0] | Ampicillin or amoxicillin vs. Cefixime    | <2yrs-16yrs | 374, 380                          | Success at 10-15 (varies; generally partial or complete resolution of signs/symptoms)         | -0.1% (-4, 4)<br>91% (241/265) vs<br>90% (247/274) | Diarrhea:<br>-8% (-13, -4)<br>14% (53/374) vs 21% (80/380)<br>NNH: 12 (8, 25)   |
| Berman, 1983 <sup>25</sup><br>Ploussard, 1984 <sup>26</sup><br>Giebink, 1984 <sup>27</sup><br>McLinn, 1980* <sup>28</sup><br>Jacobson, 1979 <sup>29</sup><br><br>*McLinn not included in pooled analysis because assessed success at 10-21 d | [1,1,1,0,0]<br>[1,0,0,1,0]<br>[1,0,1,1,0]<br>[1,0,0,1,0]<br>[1,1,1,1,1] | Ampicillin or amoxicillin vs. Cefaclor    | <2yrs-12yrs | 95, 90                            | Success at day 3-7 (varies; from complete resolution of MEE to improvement of signs/symptoms) | -5% (-16, 6)<br>83% (79/95) vs 85%<br>(77/90)      | Diarrhea (Data from Berman):<br>4% (-17, 24)<br>14% (3/21) vs 11% (2/19)<br><br>Rash at 1 week (Data from Jacobson):<br>-1% (-20, 18)<br>7% (1/15) vs 8% (1/13) |

**eTable 2 (Continued)**

| Author and Publication Year   | Study Quality (Jadad Score) <sup>a</sup> | Comparison   | Age        | Number of Participants (Gp1, Gp2) | Definition of Clinical Success   | Success Rate difference (95% CI)                  | Adverse Events Rate difference (95% CI)   |
|---|--|--|------------|-----------------------------------|--|---|---|
| <b>Ampicillin/Amoxicillin vs. Other Antibiotics: Single Study Comparisons</b> |  |  |            |                                   |  |   |   |
| Scholz, 1998 <sup>30</sup>  | [1,1,1,0,1]                              | Amoxicillin 50mg/kg/day vs. erythromycin 40mg/kg/day for 10 days <sup>30</sup> | 6mos-11yrs | 151, 151                          | Success on day 9-11 (resolution of signs/symptoms of AOM regardless of residual MEE) | 2% (-3, 7)<br>96% (133/139) vs<br>94% (132/141)   | Any treatment-related<br>2% (-4, 8)<br>7% (11/151) vs 5% (8/151)  |
| Casellas, 2005 <sup>31</sup>  | [1,0,1,0,0]                              | Amoxicillin sulbactam vs. amoxicillin-clavulanate (80mg/kg/day; 10 days)       | 6mos-4yrs  | 149, 140                          | Success at days 12-14 (partial or full resolution of signs and symptoms)             | 0% (-3%, 3%)<br>98% (115/117) vs<br>98% (115/117) | Any: -9% (-20, 2)<br>27% (40/149) vs 36% (50/140)<br>Diarrhea, day 12-14: -3% (-8, 2)<br>3% (4/149) vs 6% (8/140)<br>Diarrhea, day 3: -12% (-19, -5)<br>5% (7/149) vs 16% (23/140)<br>NNH: 8 (5, 20)<br>Severe diarrhea: 0% (-2, 2)<br>0.7% (1/149) vs 0.7% (1/140) |
| Rodriguez 1985 <sup>32</sup>  | [1,1,1,1,1]                              | Amoxicillin 40mg/kg/d vs. erythromycin sulfisoxazole 50mg/kg/d for 10 days     | 2mos-17yrs | 72, 73                            | Success at day 10-14 (resolution of signs and symptoms)                              | 0% (-10, 10)<br>89% (64/72) vs 89% (65/73)        | Not reported  |

**eTable 2 (Continued)**

| Author and Publication Year                            | Study Quality (Jadad Score) <sup>a</sup> | Comparison   | Age        | Number of Participants (Gp1, Gp2) | Definition of Clinical Success  | Success Rate difference (95% CI)   | Adverse Events Rate difference (95% CI)   |
|--|--|--|------------|-----------------------------------|---|--|---|
| <b>Amoxicillin-clavulanate vs. Other Antibiotics</b>   |  |  |            |                                   |   |  |   |
| Feldman, 1990 <sup>33</sup>                            | [1,1,1,1,1]                              | Amoxicillin-clavulanate 50 mg/kg/day of 40/10 vs. trimethoprim-sulfamethoxazole 40mg TMP/200mg SMX for wt<11kg for 10 days | 1-14yrs    | 101, 101                          | Success at day 12-16 (resolution of symptoms and normal otoscopic exam and/or acoustic reflectometry)   | -11% (-20, -2)<br>82% (83/101) vs 93% (94/101)<br>NNT: 9 (5, 50)   | Diarrhea: 51% (38, 65)<br>71% (72/101) vs 20% (20/101)<br>NNH: 2 (2, 3)<br>Rash: -4% (-8, -0.1)<br>0% (0/101) vs 4% (4/101)<br>NNH: 25 (12, 1000)<br>Diaper rash: 13% (6, 20)<br>14% (14/101) vs 1% (1/101)<br>NNH: 8 (5, 17)   |
| Block, 2000 <sup>34</sup><br>Adler, 2000 <sup>35</sup> | [1,0,1,0,0]<br>[1,0,1,0,0]               | Amoxicillin-clavulanate vs. Cefdinir 14mg/kg.day qd for 10 days  | 6mos-12yrs | 379, 376                          | Success at day 2-4 for Block day 11-16 for Adler (complete or partial resolution of signs and symptoms) | Block: 1% (-7, 13)<br>86% (86/100) vs 83% (85/102)<br>Adler: -1% (-7, 5)<br>90% (177/197) vs 91% (177/195) | Block:<br>Any: 28% (17, 39)<br>42% (54/128) vs 14% (18/128)<br>NNH: 4 (3, 6)<br>Diarrhea: 25% (15, 35)<br>35% (45/128) vs 10% (13/128)<br>NNH: 4 (3, 7)<br>Rash: 3% (-3, 9)<br>8% (10/128) vs 5% (6/128)<br>Adler:<br>Any: 10% (3, 17)<br>26% (66/251) vs 16% (41/248)<br>NNH: 10 (6, 33)<br>Diarrhea: 2% (-4, 8)<br>13% (32/251) vs 11% (27/248)<br>Treatment-related: 6% (-0.2, 13)<br>20% (51/251) vs 14% (35/248) |



**eTable 2 (Continued)**

| Author and Publication Year                            | Study Quality (Jadad Score) <sup>a</sup> | Comparison  | Age        | Number of Participants (Gp1, Gp2) | Definition of Clinical Success  | Success Rate difference (95% CI)  | Adverse Events Rate difference (95% CI)  |
|--|--|---|------------|-----------------------------------|---|---|--|
| Block, 2000 <sup>34</sup><br>Adler, 2000 <sup>35</sup> | [1,0,1,0,0]<br>[1,0,1,0,0]               | Amoxicillin-clavulanate vs. Cefdinir<br>7mg/kg/day bid for 10 days  | 6mos-12yrs | 379, 381                          | Success at day 2-4 for Block day 11-16 for Adler (complete or partial resolution of signs and symptoms) | Block: 6% (-4, 16)<br>86% (86/100) vs 80% (81/101)<br>Adler: 1% (-5, 7)<br>90% (177/197) vs 89% (180/203) | Block:<br>Any: 20% (8, 31)<br>42% (54/128) vs 23% (29/128)<br>NNH: 5 (3, 12)<br>Diarrhea: 22% (11, 32)<br>35% (45/128) vs 13% (17/128)<br>NNH: 5 (3, 9)<br>Rash: 2% (-5, 8)<br>8% (10/128) vs 6% (8/128)<br>Adler:<br>Any: 3% (-4, 10)<br>26% (66/251) vs 23% (59/253)<br>Diarrhea: -3% (-9, 3)<br>13% (32/251) vs 16% (40/253)<br>Treatment-related: 2% (-4, 9)<br>20% (51/251) vs 18% (45/253) |
| Block, 2000 <sup>34</sup><br>Adler, 2000 <sup>35</sup> | [1,0,1,0,0]<br>[1,0,1,0,0]               | Cefdinir 14mg/kg.day qd for 10 days vs. Cefdinir 7mg/kg/day bid for 10 days   | 6mos-12yrs | 376, 381                          | Success at day 2-4 for Block day 11-16 for Adler (complete or partial resolution of signs and symptoms) | Block: 3% (-7, 14)<br>83% (85/102) vs 80% (81/101)<br>Adler: 2% (-4, 8)<br>91% (177/195) vs 89% (180/203) | Block:<br>Any: -9% (-18, 1)<br>14% (18/128) vs 23% (29/128)<br>Diarrhea: -3% (-11, 5)<br>10% (13/128) vs 13% (17/128)<br>Rash: -2% (-7, 4)<br>5% (6/128) vs 6% (8/128)<br><br>Adler:<br>Any: -7% (-14, 0)<br>16% (41/248) vs 23% (59/253)<br>Diarrhea: 5% (-11, 1)<br>11% (27/248) vs 16% (40/253)<br>Treatment-related: -4% (-11, 4)<br>14% (35/248) vs 18% (45/153)                            |
| Subba Rao, 1998 <sup>36</sup>                          | [1,0,1,1,0]                              | Amoxicillin-clavulanate (>6 yrs old: 250 mg; < 6 yrs old: 125 mg) vs. cefaclor 125 or 250 mg for 7 days <sup>36</sup> | 1-12yrs    | 114, 119                          | Success at end of treatment- day 7 (complete resolution of signs and symptoms)                          | 13% (5, 21)<br>97% (102/105) vs 84% (94/112)<br>NNT: 8 (5, 20)  | Diarrhea: -1% (-8, 6)<br>7% (8/114) vs 8% (10/119)<br>Headache: -3% (-5, 0.4)<br>0% (0/114) vs 3% (3/119)<br>Vomiting: -2% (-7, 2)<br>3% (3/114) vs 5% (6/119)   |

**eTable 2 (Continued)**

| Author and Publication Year                            | Study Quality (Jadad Score) <sup>a</sup> | Comparison   | Age          | Number of Participants (Gp1, Gp2) | Definition of Clinical Success  | Success Rate difference (95% CI)                   | Adverse Events Rate difference (95% CI)  |
|--|--|--|--------------|-----------------------------------|---|--|--|
| <b>Cephalosporins and Other Antibiotic Comparisons</b> |  |  |              |                                   |   |  |  |
| Brodie, 1990 <sup>37</sup>                             | [1,0,1,0,0]                              | Cefuroxime axetil vs. amoxicillin<br>125 mg for < 2 yr<br>250 mg for 2 +yr               | 3mos-12yrs   | 332, 328                          | Success at 1-4 days<br>(clinical cure not defined)  | -0.3% (-4, 4)<br>94% (248/263) vs<br>95% (278/294) | Overall: 5% (-1, 11)<br>20% (68/332) vs 16% (51/328)<br>GI: 6% (2, 10)<br>11% (35/332) vs 4% (14/328)<br>NNH: 17 (10, 50)  |
| Pukander, 1993 <sup>38</sup>                           | [1,0,1,0,0]                              | Clarithromycin vs. amoxicillin   | 1-12yrs      | 39, 49                            | Success at 48 hours<br>(resolution of MEE and improvement of signs and symptoms)  | 3% (-14, 19)<br>93% (25/27) vs 90%<br>(18/20)      | Total: 8% (-10, 26)<br>26% (10/39) vs 18% (7/49)<br>GI: 0.4% (-15, 16)<br>15% (6/39) vs 15% (6/40)   |
| Coles, 1993 <sup>39</sup>                              | [1,0,1,0,0]                              | Clarithromycin bid vs. amoxicillin TID<br>125 mg for <25 kg; 250 mg for 25 kg for 5 days | 1-12yrs      | 132, 127                          | Success at day 6-9<br>(Improvement of signs and symptoms)   | 0.3% (-5, 5)<br>96% (110/114) vs<br>96% (101/105)  | Overall: -3% (-8, 2)<br>3% (4/132) vs 6% (8/127)<br>Diarrhea: -1% (-4, 2)<br>2% (2/132) vs 2% (3/127)<br>Vomiting: -2% (-6, 1)<br>1% (1/132) vs 3% (4/127)                                 |
| Foshee, 1992 <sup>40</sup>                             | [1,1,1,0,1]                              | Loracarbef (30mg/kg/d BID, 7d vs. Amoxicillin 40mg/kg/d, TID, 7d                         | 6mos-12yrs   | 148, 143<br>(419, 422 visits)     | Success at day 7-10<br>(clinical cure not defined)  | -3% (-11, 5)<br>85% (126/148) vs<br>88% (126/143)  | Any: -3% (-8, 2)<br>12% (49/419) vs 15% (62/422)<br>Diarrhea: -1% (-3, 1)<br>2% (8/419) vs 3% (13/422)<br>Vomiting: -2% (-3, -0.4)<br>0% (1/419) vs 2% (9/422)<br>NNH: 50 (33, 250) visits |
| Carvalho, 1998 <sup>41</sup>                           | [1,0,0,0,0]                              | Cefprozil 30 mg/kg/day BID vs. Cefaclor 40 mg/kg/day TID for 10 days                     | Not reported | 21, 19                            | Success at end of treatment (3 <sup>rd</sup> visit)<br>(complete or partial resolution of signs and symptoms, with the exception of TM opacity; no need for additional antibiotics) | 0.5% (-13, 14)<br>95% (20/21) vs 95%<br>(18/19)    | Any: -11% (-24, 3)<br>0% (0/21) vs 11% (2/19)<br>Vomiting: 10% (-4, 23)<br>10% (2/21) vs 0% (0/19)   |

**eTable 2 (Continued)**

| <b>Author and Publication Year</b> | <b>Study Quality (Jadad Score)<sup>a</sup></b> | <b>Comparison</b>  | <b>Age</b> | <b>Number of Participants (Gp1, Gp2)</b> | <b>Definition of Clinical Success</b>   | <b>Success Rate difference (95% CI)</b>     | <b>Adverse Events Rate difference (95% CI)</b>   |
|------------------------------------|--|--|------------|--|---|---|--|
| Tsai, 1998 <sup>42</sup>           | [1,0,1,0,0]                                    | Cefpodoxime 10 mg/kg/day vs. Cefaclor 45 mg/kg/day for 10 days | 3mos-15yrs | 23, 34                                   | Success at day 10-14 (resolution of signs/symptoms with/without residual MEE)           | 5% (-10, 20)<br>95% (20/21) vs 90% (27/30)  | Any: 16% (-6, 37)<br>30% (7/23) vs 15% (5/34)<br><br>Diarrhea: 14% (-1, 30)<br>17% (4/23) vs 3% (1/34)<br><br>Pruritis: 4% (-3, 11)<br>4% (1/23) vs 0% (0/34)<br><br>Skin rash: -6% (-16, 4)<br>0% (0/23) vs 6% (2/34) |
| Turik, 1998 <sup>43</sup>          | [1,0,1,0,0]                                    | Cefuroxime 30 mg/kg/day vs. Cefaclor 40 mg/kg/day for 10 days  | 3mos-12yrs | 101, 104                                 | Success at day 10 (resolution of signs/symptoms and no need for additional antibiotics) | -0.7% (-9, 7)<br>93% (65/70) vs 94% (73/78) | Any: 5% (-8, 18)<br>36% (36/101) vs 31% (32/104)<br>Diarrhea: -1% (-4, 2)<br>1% (11/101) vs 2% (2/104)<br>Diarrhea during treatment: 8% (3, 13)<br>8% (8/101) vs 0% (0/104)<br>NNH: 12 (8, 33)                         |

eTable 2 (Continued)

| Author and Publication Year        | Study Quality (Jadad Score) <sup>a</sup> | Comparison   | Age        | Number of Participants (Gp1, Gp2) | Definition of Clinical Success  | Success Rate difference (95% CI)               | Adverse Events Rate difference (95% CI)   |
|------------------------------------|--|--|------------|-----------------------------------|---|--|---|
| <b>High vs. Low Dose Treatment</b> |  |  |            |                                   |   |  |   |
| Bottenfield, 1998 <sup>44</sup>    | [1,0,0,0,0]                              | Amoxicillin-clavulanate 90mg/kg/d vs. amoxicillin-clavulanate 45 mg/kg/d for 10 days                             | 3mos-12yrs | 223, 230                          | Success at end of therapy (defined by clinical response)                              | 5% (-3, 13)<br>84% (149/177) vs 79% (149/189)  | Any: 3% (-6,12)<br>45% (101/223) vs 43% (98/230)<br>Diaper Rash: -1% (-5, 3)<br>4% (9/223) vs 5% (11/230)<br>Severe diarrhea: 2% (-4, 7)<br>10% (22/223) vs 8% (19/230)<br>Severe Rash: 1% (-0.2, 3)<br>1% (3/223) vs 0% (0/230)<br>Severe GI: -0.4% (-1, 0.4)<br>0% (0/223) vs 0% (1/230)<br>Vomiting -1%(-6, 3)<br>6% (13/223) vs 7% (16/230) |
| Principi, 1986 <sup>45</sup>       | [1,0,1,0,0]                              | High-dose amoxicillin bid vs. tid  | 6mos-1yr   | 55, 55                            | Clinical cure at day 15   | -4% (-14, 7)<br>89% (49/55) vs 93% (51/55)     | Not reported  |
| Damrikarnlert, 2000 <sup>46</sup>  | [1,0,1,1,0]                              | Amoxicillin-clavulanate 45/6.4 mg/kg/day vs. Amoxicillin-clavulanate 40/10 mg/kg/day for 7-10 days <sup>46</sup> | 2mos-12yrs | 209, 206                          | Success at day 7-12 (complete resolution of signs and symptoms of AOM, excluding MEE) | 0.1% (-5, 5)<br>94% (187/199) vs 94% (175/186) | Any: -6% (-13, 0.9)<br>12% (25/209) vs 18% (37/206)<br>Diarrhea: -4% (-9, 3)<br>7% (15/209) vs 11% (22/206)   |

**eTable 2 (Continued)**

| Author and Publication Year  | Study Quality (Jadad Score) <sup>a</sup>                                | Comparison   | Age        | Number of Participants (Gp1, Gp2) | Definition of Clinical Success  | Success Rate difference (95% CI)                  | Adverse Events Rate difference (95% CI)   |
|--|---|--|------------|-----------------------------------|---|---|---|
| <b>Short vs. Long Treatment Duration:<sup>c</sup> Pooled Comparisons</b>   |   |  |            |                                   |   |   |   |
| Varsano, 1988 <sup>16</sup><br>Green, 1993 <sup>17</sup><br>Kara, 1998 <sup>18</sup><br>Zhang, 2003 <sup>19</sup>                                    | [1,1,1,0,1]<br>[1,1,1,0,1]<br>[1,0,0,0,0]<br>[1,0,1,0,0]                | Ampicillin or amoxicillin (7-10 days) vs. Ceftriaxone (1 dose) | 5 mos-12 y | 260, 258                          | Success at day 5-14 (complete or partial resolution of signs and/or symptoms)           | 0% (-7, 7)<br>93% (242/260) vs<br>93% (241/258)   | Rash or loose stool (Kara study only): 8% (-3, 19)<br>8% (2/25) vs 0% (0/25)  |
| Bauchner, 1996 <sup>47</sup><br>Varsano, 1997 <sup>48</sup><br>Cohen, 1999 <sup>49</sup><br>Wang, 2004 <sup>50</sup><br>Biner, 2007 <sup>51</sup>    | [1,0,0,1,0]<br>[1,0,1,1,0]<br>[1,0,1,1,0]<br>[1,0,1,0,0]<br>[1,0,0,0,0] | Amoxicillin-Clavulanate (7-10 days) vs. Ceftriaxone (1 dose)   | 3m-10y     | 676, 686                          | Success at day 3, and 10-16 (resolution or improvement of signs and/or symptoms)        | 3% (-2, 7)<br>80% (513/676) vs<br>77% (497/686)   | Diarrhea (No data from Bauchner):<br>11% (7, 16)<br>20% (92/458) vs 9% (42/452)<br>NNH: 9 (6,15)  |
| Rodriguez, 1996 <sup>52</sup><br>Dagan, 2000 <sup>53</sup><br>Oguz, 2003 <sup>54</sup>   | [1,0,1,0,0]<br>[1,0,1,0,0]<br>[1,0,1,1,0]                               | Cefaclor (7-10 days) vs. Azithromycin (3 days)                 | 6m-13y     | 285, 286                          | Success at day 10-14 (varies; resolution of signs and symptoms)                         | -0.7 (-4, 3)<br>94% (198/212) vs<br>93% (200/215) | Diarrhea:<br>3% (0.4, 6)<br>5% (15/285) vs 2% (5/286)<br>NNH: 29 (16, 250)  |
| Aronovitz, 1996 <sup>55</sup><br>McLinn, 1996 <sup>56</sup><br>Khurana, 1996 <sup>45</sup><br>Dagan, 2000 <sup>57</sup><br>Biner, 2007 <sup>51</sup> | [1,0,1,0,0]<br>[1,1,1,0,1]<br>[1,0,1,0,0]<br>[1,0,1,0,0]<br>[1,0,0,0,0] | Amoxicillin-clavulanate (7-10 days) vs. Azithromycin (5 days)  | 6 m-15y    | 636, 666                          | Clinical success days 3-14 (varies; resolution or improvement in signs and/or symptoms) | 5% (-2, 11)<br>89% (576/636) vs<br>86% (573/666)  | Diarrhea (Biner, McLinn, and Khurana only):<br>10% (4, 15)<br>12% (74/633) vs 2% (11/634)<br>NNH: 10 (7, 24)<br>Vomiting (No data from Aronovitz):<br>4% (0.2, 8)<br>5% (38/751) vs 1% (8/754)<br>NNH: 26 (13, 500)<br>Any (No data from Biner):<br>16% (7, 25)<br>26% (209/796) vs 9% (76/808)<br>NNH: 6 (4, 14) |

**eTable 2 (Continued)**

| <b>Author and Publication Year</b>   | <b>Study Quality (Jadad Score)<sup>a</sup></b>  | <b>Comparison</b>  | <b>Age</b>   | <b>Number of Participants (Gp1, Gp2)</b> | <b>Definition of Clinical Success</b>   | <b>Success Rate difference (95% CI)</b>          | <b>Adverse Events Rate difference (95% CI)</b>   |
|--|---|--|--------------|--|---|--|--|
| Pestalozza, 1992 <sup>58</sup><br>Daniel, 1993 <sup>59</sup><br>Schaad, 1993 <sup>60</sup><br>Principi, 1995 <sup>61</sup><br>Arguedas, 1996 <sup>62</sup><br>Dunne, 2003 <sup>63</sup><br>Guven, 2006 <sup>64</sup> | [1,0,0,0,0]<br>[1,0,1,0,0]<br>[1,0,1,0,0]<br>[1,0,1,0,0]<br>[1,0,1,1,0]<br>[1,1,1,1,1]<br>[1,0,1,0,0] | Amoxicillin-clavulanate (7-10 days) vs. Azithromycin (≤3 days) | 6 mos-12 yrs | 766, 847                                 | Clinical success days 7-20 (varies; resolution or improvement in signs and/or symptoms) | -2% (-9, 5)<br>83% (668/766) vs<br>87% (761/847) | Diarrhea (Data from Principi, Dunne, and Guven only):<br>3% (-5, 10)<br>6% (33/509) vs 4% (19/521)<br>Rash (No data from Pestalozza or Guven):<br>2% (-1, 5)<br>3% (21/716) vs 1% (5/778)<br>Vomiting (Data from Principi, Arguedas, and Dunne only):<br>1% (-2, 3)<br>2% (9/472) vs 1% (11/953)<br>Any (No data from Pestalozza, Principi, or Arguedas):<br>4 (-4, 11)<br>13% (65/515) vs 9% (50/515) |

**eTable 2 (Continued)**

| Author and Publication Year  | Study Quality (Jadad Score) <sup>a</sup> | Comparison   | Age       | Number of Participants (Gp1, Gp2) | Definition of Clinical Success  | Success Rate difference (95% CI)                              | Adverse Events Rate difference (95% CI)  |
|--|--|--|-----------|-----------------------------------|---|---|--|
| <b>Short vs. Long Treatment Duration:<sup>c</sup> Single Study Comparisons</b> |  |  |           |                                   |   |   |  |
| Morris, 2010 <sup>65</sup>   | [1,1,1,0,0]                              | Amoxicillin 50 mg/kg/day (7 days) vs. Azithromycin 30 mg/kg/dose (1 day)                             | 6mos-6yrs | 155, 165                          | Success at day 6-11 (resolution of pain, bulging TM and middle ear drainage)  | -4% (-15, 7)<br>46% (72/155) vs. 50% (83/165)                 | Not reported   |
| Bain, 1985 <sup>66</sup>   | [1,0,1,1,0]                              | Amoxicillin 2 days vs. Amoxicillin 7 days  | 3-10yrs   | 125, 118                          | Success at end of therapy (resolution of signs/symptoms)  | -0.5% (-6, 5)<br>94% (118/125) vs 95% (112/118)               | Not reported   |
| Puczynski, 1987 <sup>67</sup>  | [1,1,1,0,0]                              | 1 dose of amoxicillin followed by 10 d of placebo vs first dose placebo followed by 10 d amoxicillin | >2yrs     | 7, 10                             | Success at 48-72 hours (clinical improvement)   | -43% (-80, -6)<br>57% (4/7) vs 100% (10/10)<br>NNT: 2 (1, 17) | Not reported   |
| Hedrick, 2001 <sup>68</sup>  | [1,0,1,0,0]                              | Amoxicillin-clavulanate 90/6.4 mg/kg/day vs. Cefprozil 30 mg/kg/day for 10 days                      | 6mos-7yrs | 153, 150                          | Success at days 4-7 after treatment (resolution or improvement in signs/symptoms without need for additional antibiotics) | 2% (-6, 10)<br>89% (116/130) vs 87% (110/127)                 | Any: 13% (4, 23)<br>32% (49/153) vs 19% (28/150)<br>NNH: 8 (4, 25)<br>Diarrhea: 10% (2, 18)<br>19% (29/153) vs 9% (14/150)<br>NNH: 10 (6, 50)<br>Rash: 5% (-2, 11)<br>11% (16/153) vs 6% (9/150)<br>Vomiting: 4% (-0.5, 8)<br>6% (9/153) vs 2% (3/150) |
| Pessey, 1999 <sup>69</sup>   | [1,0,1,0,0]                              | Amoxicillin-clavulanate 40 mg/kg/day for 10 days vs. Cefuroxime 30 mg/kg/day for 5 days              | 6mos-3yrs | 255, 252                          | Success at end of treatment (resolution of signs and symptoms, exclusive of MEE)  | 2% (-4, 8)<br>88% (181/205) vs 86% (175/203)                  | Any: 8% (1, 14)<br>22% (57/255) vs 15% (37/252)<br>NNH: 12 (7, 100)<br>Diarrhea: 8% (2, 14)<br>18% (46/255) vs 20% (25/252)<br>NNH: 12 (7, 50)   |

**eTable 2 (Continued)**

| Author and Publication Year | Study Quality (Jadad Score) <sup>a</sup> | Comparison   | Age        | Number of Participants (Gp1, Gp2)   | Definition of Clinical Success  | Success Rate difference (95% CI)                            | Adverse Events Rate difference (95% CI)   |
|-----------------------------|--|--|------------|---|---|---|---|
| Dagan, 2000 <sup>57</sup>   | [1,0,1,0,0]                              | Amoxicillin-clavulanate 45/6.4 mg/kg/d (10 days) vs. azithromycin 10 mg/kg/d (1 day), 5 mg/kg/d (4 days) | 6mos-6yrs  | 70, 73 evaluated for clinical efficacy<br>118, 120 evaluated for treatment-related adverse events | Success days 12-14 (resolution or improvement in MEI with or without MEE)             | 16% (2, 30)<br>86% (60/70) vs 70% (51/73)<br>NNT: 6 (3, 50) | Any: 3% (-11, 2)<br>27% (32/118) vs 22% (26/120)<br>Related to treatment: 8% (3, 14)<br>10% (12/118) vs 2% (2/120)<br>NNH: 12 (7, 33)<br>Diarrhea: 3% (-3, 9)<br>8% (9/118) vs 4% (5/120)<br>Vomiting: 8% (3, 14)<br>8% (10/118) vs 0% (0/120)<br>NNH: 12 (7, 33) |
| Block, 2004 <sup>70</sup>   | [1,0,1,0,0]                              | Amox-clav 45/6.4 for 10 d vs. Cefdinir 14 mg for 5 d   | 6mos-6yrs  | 214, 211  | Success at end of treatment (complete or partial resolution of signs and/or symptoms) | -2% (-9, 5)<br>85% (164/192) vs 88% (170/194)               | Diarrhea and rash: 2% (-4, 7)<br>10% (21/214) vs 8% (17/211)<br>Diarrhea: 3% (-3, 8)<br>10% (21/214) vs 7% (15/211)<br>Vomiting: 4% (1, 8)<br>5% (11/214) vs 1% (2/211)<br>NNH: 25 (12, 100)  |
| Güven, 2006 <sup>64</sup>   | [1,0,1,0,0]                              | Amoxicillin-clavulanate 45/6.4 mg/kg/d (10d) vs. azithromycin 10 mg/kg/d (3 days) <sup>64</sup>          | 6mos-12yrs | 84, 90  | Clinical cure at day 11-13 (complete resolution of signs and symptoms)                | 3% (-9, 15)<br>81% (68/84) vs 78% (70/90)                   | Any: 1% (-5, 7)<br>5% (4/84) vs 4% (4/90)<br>Abdominal pain: 5% (0.3, 9)<br>5% (4/84) vs 0% (0/90)<br>NNH: 20 (11, 333)<br>Diarrhea: -4% (-9, 0)<br>0% (0/84) vs 4% (4/90)  |



**eTable 2 (Continued)**

| <b>Author and Publication Year</b> | <b>Study Quality (Jadad Score)<sup>a</sup></b> | <b>Comparison</b>  | <b>Age</b> | <b>Number of Participants (Gp1, Gp2)</b> | <b>Definition of Clinical Success</b>                                     | <b>Success Rate difference (95% CI)</b>        | <b>Adverse Events Rate difference (95% CI)</b>  |
|------------------------------------|--|--|------------|--|---|--|---|
| Catania, 2004 <sup>71</sup>        | [1,0,1,1,0]                                    | Cefaclor 50mg/kg/d; 5 days) vs. cefaclor 40mg/kg/d; 10days)                                    | 2-6yrs     | 204, 206                                 | Success at end of therapy (no persistence of fever, otalgia, or otorrhea) | 1% (-4, 5)<br>96% (195/204) vs 95% (195/206)   | Any: -2% (-7, 3)<br>6% (12/204) vs 8% (17/206)<br>Abd pain: -1% (-4, 2)<br>1% (3/204) vs 2% (5/206)<br>Diarrhea: -0.4% (-3, 2)<br>2% (4/204) vs 2% (5/206)<br>Rash: -1% (-4, 2)<br>2% (5/204) vs 3% (6/206)                     |
| Barnett, 1997 <sup>72</sup>        | [1,0,1,1,0]                                    | Ceftriaxone (1 IM dose) vs. trimethoprim-sulfamethoxazole (8 mg TMP/ 40 mg SMZ/kg/day 10 days) | 3mos-3yrs  | 241, 243                                 | Success at day 14 (partial or complete resolution of signs/symptoms)      | -2% (-10, 6)<br>80% (158/197) vs 82% (174/212) | Adverse event on day 3<br>Pain at site: 4% (2, 7)<br>4% (10/225) vs 0% (0/243)<br>NNH: 25 (14, 50)<br>Diarrhea: 14% (7, 22)<br>24% (46/195) vs 9% (19/207)<br>NNH: 7 (5, 14)<br>Rash: 3% (-2, 9)<br>10% (21/206) vs 7% (14/201) |

**eTable 2 (Continued)**

| <b>Author and Publication Year</b> | <b>Study Quality (Jadad Score)<sup>a</sup></b> | <b>Comparison</b>   | <b>Age</b>  | <b>Number of Participants (Gp1, Gp2)</b>              | <b>Definition of Clinical Success</b>  | <b>Success Rate difference (95% CI)</b>                            | <b>Adverse Events Rate difference (95% CI)</b>   |
|------------------------------------|--|---|-------------|---|--|--|--|
| Block, 2000 <sup>73</sup>          | [1,0,1,0,0]                                    | Cefprozil 30 mg/kg/day 10 days vs. Cefdinir 14 mg/kg/day for 5 days         | 6mos-6yrs   | 190, 183  | Success at day 9-11 (complete or partial resolution of signs and/or symptoms and no need for additional antibiotics) | -2% (-5, 10)<br>80.0% (152/190) vs 82.5% (151/183)                 | Diarrhea: 4% (-1, 8)<br>8% (15/190) vs 4% (8/183)<br>Rash: -0.6% (-4, 3)<br>3% (6/190) vs 4% (7/183)   |
| Hoberman, 1997 <sup>74</sup>       | [1,0,1,0,0]                                    | Amoxicillin-clavulanate (5 day) vs. Amoxicillin-clavulanate (7-10 day, BID) | 2mos-12yrs  | 197, 178 patients (293, 287 intent-to-treat estimate) | Success at day 12-14 (resolution of signs/symptoms)  | -16% (-24, -8)<br>71% (140/197) vs 87% (155/178)<br>NNT: 6 (4, 12) | Diaper rash: -3% (-7, 1)<br>5% (15/293) vs 8% (23/287)<br>Vomiting: -3% (-8, 2)<br>7% (21/293) vs 10% (29/287)<br>Diarrhea: 1% (-3, 5)<br>6% (18/293) vs 5% (15/287)   |
| Hoberman, 1997 <sup>74</sup>       | [1,0,1,0,0]                                    | Amoxicillin-clavulanate (5 day) vs. Amoxicillin-clavulanate (7-10 day, TID) | 2mos-12yrs  | 197, 189 patients (293, 288 intent-to-treat estimate) | Success at day 12-14 (resolution of signs/symptoms)  | -8% (-16, 1)<br>71% (140/197) vs 79% (149/189)                     | Diaper rash: -5% (-10, -1)<br>5% (15/293) vs 10% (30/288)<br>NNH: 20 (10, 100)<br>Vomiting: -4% (-8, 1)<br>7% (21/293) vs 11% (31/288)<br>Diarrhea: -4% (-8, 1)<br>6% (18/293) vs 10% (28/288)                   |
| Cohen, 1998 <sup>75</sup>          | [1,1,1,1,1]                                    | Amoxicillin-clavulanate 5 days vs. 10 days                                  | 4mos-2.5yrs | 194, 188  | Success at day 12-14 (resolution of signs/symptoms)  | -11% (-20, -3)<br>77% (125/163) vs 88% (148/168)<br>NNT: 9 (5, 33) | All types: 3% (-7, 13)<br>45% (88/194) vs 43% (80/188)<br>Treatment related: 2% (-8, 11)<br>31% (60/194) vs 29% (55/188)   |
| Adam, 1995 <sup>76</sup>           | [1,0,1,0,0]                                    | Cefpodoxime-proxetil (5 day) vs. Cefaclor (7-10 day)                        | 3mos-6yrs   | 50, 50  | Success at day 11-13 (resolution of signs/symptoms)  | 0% (0, 0)<br>100% (50/50) vs 100% (50/50)                          | Total: 0% (-13, 13)<br>12% (6/50) vs 12% (6/50)<br>Diarrhea: 2% (-9, 13)<br>10% (5/50) vs 8% (4/50)<br>Abdominal pain: -4% (-10, 2)<br>0% (0/50) vs 4% (2/50)<br>Urticaria: 2% (-2, 6)<br>2% (1/50) vs 0% (0/50) |

**eTable 2 (Continued)**

| Author and Publication Year  | Study Quality (Jadad Score) <sup>a</sup> | Comparison  | Age        | Number of Participants (Gp1, Gp2) | Definition of Clinical Success                                       | Success Rate difference (95% CI)                                 | Adverse Events Rate difference (95% CI)   |
|------------------------------|--|---|------------|-----------------------------------|--|--|---|
| Simon, 1997 <sup>77</sup>    | [1,1,0,0,0]                              | Ceftibuten (5 day) vs. Ceftibuten (10 day) at (9mg/kg/d)            | 6mos-14yrs | 99, 133                           | Success at day 14 (recurrence of infection)                          | -20% (-28, -12)<br>78% (77/99) vs 98% (130/133)<br>NNT: 5 (3, 8) | Not reported  |
| Arguedas, 1997 <sup>78</sup> | [1,0,1,1,0]                              | Azithromycin (10mg/kg once daily for 3 d) vs. clarithromycin (10 d) | 6mos-12yrs | 50, 47                            | Success at end of treatment (resolution of symptoms or ear drainage) | 4% (-1, 10)<br>100% (50/50) vs 96% (45/47)                       | Loose stool: -7% (-18, 5)<br>6% (3/50) vs 13% (6/47)<br>Rash: -2% (-6, 2)<br>0% (0/50) vs 2% (1/47)<br>Vomiting: -2% (-9, 5)<br>2% (1/50) vs 4% (2/47)<br>Nausea: -2% (-9, 5)<br>2% (1/50) vs 4% (2/47) |

Table Notes: Abbreviations: d= day; mg=milligrams; kg= kilograms; mos=months; yr= years; QID= four times daily; TID= three times daily; BID= twice daily dosing; RD=rate difference; CI=confidence interval; NNT number needed to treat; NNH: number needed to harm; MEE: middle ear effusion; MEI: middle ear inflammation

Pooled rates are not crude rates.

<sup>a</sup> Jadad study quality score components (1=present; 0=not present): randomization mentioned; double-blind mentioned; dropouts described; randomization appropriate; double-blinding appropriate. Studies could receive a Jadad score ranging from 0 to 5 points.

<sup>b</sup> Individual study quality scores available upon request

<sup>c</sup> Short vs. long term duration refers to the length of treatment from the patient perspective, rather than from the perspective of drug action

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