Supplementary Online Content

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

**PUBMED**
‘mycoplasma pneumoniae’ OR mycoplasma pneumonia
AND resistance OR resistant OR macrolide
Filters: Humans; Field: MeSH Major Topic

**EMBASE**
‘mycoplasma pneumoniae’.af.
AND ‘resistant’.af. OR ‘resistance’.af. OR ‘macrolide’.af.

**Cochrane**
‘mycoplasma pneumoniae’.ab.ti.
‘macrolide’.ab.ti.
AND ‘resistance’:ab.ti OR ‘resistant’:ab.ti’ OR ‘macrolide’:ab.ti
**eTable 1. Quality Assessment Scale for Rating the Risk of Bias**

| Bias type                      | Low risk (score=2)                                                                 | Moderate risk (score=1)                                                                 | High risk (score=3)                                                                 |
|-------------------------------|-----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| Sample population             | 1) Sample from the general population, not a select group                         | 1) Sample selected from large population but selection criteria not defined            | 1) Highly select population making it difficult to generalize finding              |
|                               | 2) Consecutive unselected population                                              | 2) Sample selection ambiguous but may be representative                                | 2) Sample selection ambiguous and sample unlikely to be representative             |
|                               | 3) Rationale for case and control selection explained                              | 3) Rationale for cases and controls not explained                                      |                                                                                   |
|                               |                                                                                   | 4) Eligibility criteria not explained                                                  |                                                                                   |
|                               |                                                                                   | 5) Analysis to adjust for sampling strategy bias                                       |                                                                                   |
| Sample size                   | 1) Sample size calculation performed and adequate                                  | 1) Sample size calculation performed and reasons for not meeting sample size given     | 1) Sample size estimation unclear or only subsample studied                       |
|                               |                                                                                   | 2) Sample size calculation not performed but all eligible persons studied              |                                                                                   |
| Participation rate            | 1) High response rate (>85%)                                                      | 1) Moderate response rate (70-85%)                                                    | 1) Low response rate (<70%)                                                      |
|                               |                                                                                   | 2) Response rate not reported                                                          |                                                                                   |
| Outcome assessment            | 1) Diagnosis using consistent criteria and direct examination                      | 1) Assessment from administrative database or register                                 | 1) Assessment from non-validated data or generic estimate from the overall population |
| Analytical methods to control for bias | 1) Analysis appropriate for the type of sample (subgroup analysis/regression etc.) | 1) Analysis does not account for common adjustment                                     | 1) Data confusing                                                                 |
**eTable 2.** Within-Study Bias Assessment for the Included Studies

| Author Year | Sample population | Sample size | Participation | Outcome assessment | Analytical methods | Total score |
|-------------|-------------------|-------------|---------------|--------------------|-------------------|-------------|
| CDC 2010\(^1\) | 2 | 1 | 2 | 1 | 2 | 8 |
| Akaike H, 2012\(^2\) | 2 | 1 | 2 | 1 | 2 | 8 |
| Akashi Y, 2018\(^3\) | 2 | 1 | 2 | 1 | 2 | 8 |
| Ando M, 2018\(^4\) | 1 | 1 | 1 | 1 | 2 | 6 |
| Averbuch D, 2011\(^5\) | 1 | 1 | 1 | 1 | 1 | 5 |
| BAO Fang, 2013\(^6\) | 1 | 1 | 1 | 2 | 1 | 6 |
| Beeton ML, 2020\(^7\) | 2 | 1 | 2 | 2 | 2 | 9 |
| Big Mohammadi H, 2020\(^8\) | 1 | 1 | 1 | 1 | 1 | 5 |
| Brown RJ, 2015\(^9\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Cao B, 2010\(^10\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Cardinale F, 2013\(^11\) | 1 | 1 | 2 | 1 | 7 |
| Chalker VJ, 2012\(^12\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Chalker V, 2011\(^13\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Chalker V, 2012\(^14\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Chang CH, 2021\(^15\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Chen Y, 2018\(^16\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Cheong KN, 2016\(^17\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Chiornna M, 2011\(^18\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Choi JH, 2019\(^19\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Copete AR, 2018\(^20\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Deng H, 2018\(^21\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Diaz MH, 2015\(^22\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Diaz MH, 2015\(^23\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Domthong P, 2016\(^24\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Domthong P, 2014\(^25\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Dong XP, 2013\(^26\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Dou HW, 2020\(^27\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Dumke R, 2013\(^28\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Dumke R, 2010\(^29\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Dumke R, 2019\(^30\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Eshaghi A, 2013\(^31\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Ferguson GD, 2013\(^32\) | 1 | 1 | 1 | 1 | 1 | 5 |
| Goh A, 2014\(^33\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Gullsby K, 2016\(^34\) | 2 | 2 | 2 | 2 | 1 | 9 |
| Gullsby K, 2019\(^35\) | 2 | 1 | 1 | 1 | 1 | 6 |
| Guo D, 2019\(^36\) | 2 | 1 | 1 | 1 | 1 | 6 |
| Guo DX, 2019\(^37\) | 2 | 1 | 2 | 1 | 1 | 7 |
| Han HY, 2021\(^38\) | 2 | 1 | 2 | 1 | 1 | 7 |
| Ho PL, 2015\(^39\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Hong KB, 2013\(^40\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Hung HM, 2021\(^41\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Ishiguro N, 2016\(^42\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Ishiguro N, 2017\(^43\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Ishiguro N, 2021\(^44\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Ishimaru N, 2021\(^45\) | 2 | 1 | 2 | 2 | 1 | 8 |
| Katsukawa C, 2019\(^46\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Katsumiha Y, 2015\(^47\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Kawai Y, 2012\(^48\) | 1 | 1 | 2 | 2 | 1 | 7 |
| Kawai Y, 2013\(^49\) | 2 | 1 | 1 | 2 | 2 | 8 |
| Kawai Y, 2014\(^50\) | 2 | 1 | 1 | 2 | 2 | 8 |
| Kawakami N, 2021\(^51\) | 1 | 1 | 1 | 2 | 2 | 7 |
| Kenri T, 2020\(^52\) | 2 | 1 | 1 | 2 | 2 | 8 |

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| Name (Year)      | Count | Count | Count | Count | Count | Count |
|------------------|-------|-------|-------|-------|-------|-------|
| Kim JH, 2017    | 2     | 1     | 1     | 2     | 2     | 8     |
| Kim MC, 2018    | 1     | 1     | 1     | 2     | 2     | 7     |
| Kim YJ, 2017    | 1     | 1     | 1     | 2     | 2     | 7     |
| Kogoj R, 2018   | 1     | 1     | 1     | 2     | 2     | 7     |
| Koike C, 2011   | 1     | 1     | 1     | 2     | 2     | 7     |
| Komatsu H, 2014 | 1     | 1     | 1     | 2     | 2     | 7     |
| Kurkela S, 2019 | 2     | 1     | 1     | 2     | 2     | 8     |
| Lanata M, 2021  | 1     | 1     | 1     | 2     | 2     | 7     |
| Leal S, 2020    | 2     | 1     | 1     | 2     | 2     | 8     |
| Lee E, 2017     | 1     | 1     | 1     | 2     | 2     | 7     |
| Lee H, 2021     | 2     | 1     | 1     | 2     | 2     | 8     |
| Lee JK, 2021    | 2     | 1     | 1     | 2     | 2     | 8     |
| Lee JK, 2018    | 2     | 1     | 1     | 2     | 2     | 8     |
| Li SL, 2012     | 1     | 1     | 1     | 2     | 2     | 7     |
| Lin C, 2019     | 1     | 1     | 1     | 2     | 2     | 7     |
| Liu X, 2014     | 1     | 1     | 1     | 2     | 2     | 7     |
| Liu Y, 2009     | 1     | 1     | 1     | 2     | 2     | 7     |
| Liu Y, 2010     | 1     | 1     | 1     | 2     | 2     | 7     |
| Liu Y, 2014     | 1     | 1     | 1     | 2     | 2     | 7     |
| Loconsole D, 2019 | 2   | 1     | 1     | 2     | 2     | 8     |
| Loo LH, 2017    | 1     | 1     | 1     | 2     | 2     | 7     |
| Lu C, 2020      | 1     | 1     | 1     | 2     | 2     | 7     |
| Lung D, 2013    | 1     | 1     | 1     | 2     | 2     | 7     |
| Ma Z, 2014      | 1     | 1     | 1     | 2     | 2     | 7     |
| Matsubara K, 2009 | 1 | 1 | 1 | 2 | 2 | 7 |
| Matsuda K, 2013 | 1     | 1     | 1     | 2     | 2     | 7     |
| Matsuoka M, 2004 | 1     | 1     | 1     | 2     | 2     | 7     |
| Meyer Sauteur, 2014 | 1 | 1 | 1 | 2 | 2 | 7 |
| Meyer Sauteur, 2021 | 1 | 1 | 1 | 2 | 2 | 7 |
| Miyashita N, 2013 | 2 | 1 | 1 | 2 | 2 | 8 |
| Miyashita N, 2011 | 1 | 1 | 1 | 2 | 2 | 7 |
| Miyashita N, 2012 | 2 | 1 | 1 | 2 | 2 | 8 |
| Miyashita N, 2010 | 2 | 1 | 1 | 2 | 2 | 8 |
| Miyashita, 2009 | 1     | 1     | 1     | 2     | 2     | 7     |
| Miyata, 2013    | 1     | 1     | 1     | 2     | 2     | 7     |
| Morimoto K, 2017 | 2 | 1 | 1 | 2 | 2 | 8 |
| Morinaga Y, 2020 | 1 | 1 | 1 | 2 | 2 | 7 |
| Morozumi M, 2013 | 1 | 1 | 1 | 2 | 2 | 7 |
| Morozumi M, 2005 | 1 | 1 | 1 | 2 | 2 | 7 |
| Morozumi M, 2008 | 1 | 1 | 1 | 2 | 2 | 7 |
| Morozumi M, 2020 | 1 | 1 | 1 | 2 | 2 | 7 |
| Muto T, 2021    | 1     | 1     | 1     | 2     | 2     | 7     |
| Nagita A, 2021  | 1     | 1     | 1     | 2     | 2     | 7     |
| Nakamura Y, 2021 | 2 | 1 | 1 | 2 | 2 | 8 |
| Nummi M, 2015   | 1     | 1     | 1     | 2     | 2     | 7     |
| Okada T, 2017   | 2     | 1     | 1     | 2     | 2     | 8     |
| Ouchi K, 2019   | 2     | 1     | 1     | 2     | 2     | 8     |
| Pereyre S, 2012 | 0     | 1     | 2     | 2     | 2     | 7     |
| Pereyre S, 2012 | 0     | 1     | 2     | 2     | 2     | 7     |
| Pereyre S, 2013 | 2     | 1     | 2     | 2     | 2     | 9     |
| Peuchant O, 2009 | 1 | 1 | 0 | 2 | 2 | 6 |
| Pouladi I, 2020 | 0 | 0 | 2 | 2 | 2 | 6 |
| Qu K, 2019      | 2     | 1     | 2     | 2     | 2     | 9     |
| Qu J, 2013      | 2     | 1     | 2     | 2     | 2     | 9     |
| Rivaya B, 2020  | 2     | 1     | 2     | 2     | 2     | 9     |

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| Authors            | Year   | Score | Sentence 1 | Sentence 2 | Sentence 3 | Sentence 4 |
|--------------------|--------|-------|------------|------------|------------|------------|
| Rodriguez N.       | 2019   | 0     | 1          | 0          | 2          | 2          |
| Smith, 2016        |        | 0     | 1          | 0          | 2          | 2          |
| Spuensens E.       | 2012   | 2     | 1          | 1          | 2          | 2          |
| Dumke R, 2009      |        | 0     | 1          | 2          | 2          | 2          |
| Sun H, 2017        |        | 0     | 1          | 0          | 2          | 2          |
| Suzuki S, 2018     |        | 2     | 1          | 0          | 2          | 2          |
| Suzuki Y, 2013     |        | 0     | 1          | 0          | 2          | 2          |
| Suzuki Y, 2017     |        | 0     | 1          | 0          | 2          | 2          |
| Tanaka T, 2017     |        | 2     | 1          | 0          | 2          | 2          |
| Uh Y, 2013         |        | 0     | 1          | 0          | 2          | 2          |
| Uldum S, 2012      |        | 2     | 1          | 1          | 2          | 2          |
| Voronina E, 2020   |        | 0     | 1          | 0          | 2          | 2          |
| Wagner K, 2019     |        | 2     | 1          | 2          | 2          | 2          |
| Waites K, 2019     |        | 2     | 1          | 2          | 2          | 2          |
| Waller J, 2014     |        | 0     | 1          | 0          | 2          | 2          |
| Wang Y, 2012       |        | 0     | 1          | 2          | 2          | 2          |
| Wang Y, 2021       |        | 2     | 1          | 2          | 2          | 2          |
| Wang Y, 2016       |        | 0     | 1          | 2          | 2          | 2          |
| Yin Y, 2017        |        | 2     | 1          | 2          | 2          | 2          |
| Whistler T, 2017   |        | 2     | 1          | 0          | 2          | 2          |
| Wu H, 2013         |        | 2     | 1          | 2          | 2          | 2          |
| Wu P, 2013         |        | 2     | 1          | 2          | 2          | 2          |
| Xiao L, 2020       |        | 1     | 1          | 1          | 2          | 2          |
| Xin D, 2008        |        | 0     | 1          | 0          | 2          | 2          |
| Xin D, 2009        |        | 1     | 1          | 2          | 2          | 2          |
| Xu C, 2021         |        | 2     | 1          | 2          | 2          | 2          |
| Xue G, 2018        |        | 1     | 1          | 2          | 2          | 2          |
| Xue G, 2014        |        | 0     | 1          | 2          | 2          | 2          |
| Yamada M, 2012     |        | 1     | 1          | 2          | 2          | 2          |
| Yan C, 2015        |        | 0     | 1          | 0          | 2          | 2          |
| Yan C, 2020        |        | 2     | 1          | 2          | 2          | 2          |
| Yin Y, 2017        |        | 2     | 1          | 2          | 2          | 2          |
| Yoo S, 2012        |        | 0     | 1          | 2          | 2          | 2          |
| Yu H, 2018         |        | 2     | 1          | 2          | 2          | 2          |
| Zhang W, 2019      |        | 1     | 1          | 2          | 2          | 2          |
| Zhao F, 2013       |        | 2     | 1          | 2          | 2          | 2          |
| Zhao F, 2019       |        | 2     | 1          | 2          | 2          | 2          |
| Zhao F, 2019       |        | 0     | 1          | 0          | 2          | 2          |
| Zhao H, 2014       |        | 1     | 1          | 0          | 2          | 2          |
| Zheng X, 2015      |        | 0     | 1          | 0          | 2          | 2          |
| Zhou Y, 2020       |        | 2     | 1          | 2          | 2          | 2          |
| Zhou Y, 2014       |        | 2     | 1          | 2          | 2          | 2          |
| Zhu M, 2020        |        | 1     | 1          | 1          | 2          | 2          |
Table 3. Summary of the Included Studies

| Articles | Design | Country | Subject characteristics | Outcomes; RTI or CAP | Year | Age group | Total number of MP infection cases | Male (%) | A2063 G, n | A2064G, n | Other mutation types (n) | MRMP, n (%) |
|----------|--------|---------|--------------------------|----------------------|------|-----------|-----------------------------------|----------|------------|-----------|------------------------|------------|
| CDC 2010 | Retrospective | USA | Outpatient & ED | CAP | 2000 | Children & Adults | 11 | NA | NA | NA | NA | 2/11 (18.2) |
| Akaike H, 2012 | Retrospective | Japan | NA | RTI | 2009-2011 | Children | 190 | 115 (60.5) | 124 | 0 | 0 | 124/190 (65.2) |
| Akashi Y, 2018 | Retrospective | Japan | NA | RTI | 2016-2017 | Children & Adults | 383 | 200 (52.2) | NA | NA | NA | NA |
| Ando M, 2018 | Retrospective | Japan | NA | RTI | 2002-2016 | Children & Adults | 417 | NA | 163 | 10 | A2063C (10) | 184/417 (44.1) |
| Averbuch D, 2011 | Retrospective | Israel | NA | RTI | 2010-2010 | Children & Adults | 30 | NA | 7 | 0 | A2063G (2) | 9/30 (30.0) |
| BAO Fang, 2013 | Prospective | China | NA | CAP | 2010-2011 | Children | 45 | NA | NA | NA | NA | 44/45 (98.0) |
| Beeton ML, 2020 | Retrospective | Israel | NA | RTI | 2011-2016 | Children & Adults | 209 | NA | NA | NA | NA | 13/209 (1.5) |
| Big Mohammadi H, 2020 | Retrospective | Iran | NA | RTI | NA | Adults | 100 | 48 (48) | 0 | 0 | 2431G & AG2491A (1) | 1/100 (1.0) |
| Brown RJ, 2015 | Retrospective | England | NA | CAP | 2014-2015 | Children & Adults | 43 | NA | 0 | 0 | A2054G (4) | 4/43 (9.3) |
| Cao B, 2010 | Retrospective | China | NA | CAP | 2008-2009 | Children & Adults | 67 | NA | 41 | 4 | A2063T (1) | 46/67 (68.7) |
| Cardinale F, 2013 | Retrospective | Italy | Inpatients | CAP | NA | Children | 46 | 24 (52.2) | NA | NA | NA | 8/46 (17.4) |
| Chalker VJ, 2012 | Retrospective | England | NA | NA | 1995-2005, 2008-2011 | NA | 115 | NA | 1 | 0 | 0 | 1/115 (0.9) |
| Chalker V, 2011 | Retrospective | England | Outpatients | RTI | 2010-2011 | Children & Adults | 12 | NA | 0 | 0 | 0 | 0/12 (0.0) |
| Chalker V, 2012 | Retrospective | England | NA | RTI | 2011-2012 | Children & Adults | 12 | NA | 0 | 0 | 0 | 0/12 (0.0) |
| Authors               | Year    | Study Type   | Country | Setting          | Time Period | Group Type | Total | Children | Adults | Children & Adults | Children | Adults | Children & Adults | Total | Percentage |
|----------------------|---------|--------------|---------|------------------|-------------|------------|-------|-----------|--------|-------------------|-----------|--------|-------------------|-------|-------------|
| Chang CH, 2021       |         | Retrospective | Taiwan  | Inpatients       | 2016-2019   | Children   | 81    | 35 (43.2) | 45     | 0                  | 45        | 81(54.3) |
| Chen, 2018           |         | Retrospective | China   | NA               | 2014-2016   | Children   | 136   | 76 (55.9) | NA     | NA                | 81        | 136 (59.6) |
| Cheong KN, 2016       |         | Retrospective | China   | Inpatients       | 2011-2013   | Children   | 93    | 42 (45.2) | NA     | NA                | 25        | 93 (26.9) |
| Chironna M, 2011      |         | Retrospective | Italy   | Inpatients       | 2010        | Children   | 43    | 22 (51.2) | 7      | 4                  | 11        | 43 (25.6) |
| Choi JH, 2018         |         | Retrospective | Korea   | NA               | 2010-2016   | Adults     | 70    | 34 (48.6) | 2      | 0                  | 2         | 70 (2.9)  |
| Copete AR, 2018       |         | Retrospective | Colombia| Inpatients       | 2011-2012   | Children   | 42    | NA        | 0      | 0                  | 0         | 42 (0.0) |
| Deng H, 2018          |         | Retrospective | China   | NA               | 2014-2015   | Children   | 211   | 108 (51.2)| 195    | 0                  | 195       | 211 (92.4) |
| Diaz MH, 2015         |         | Retrospective | USA     | Inpatients       | 2010-2012   | Children & Adults | 216  | 124 (57.44)| 6      | 1                  | 7         | 216 (3.5) |
| Diaz MH, 2015         |         | Retrospective | USA     | NA               | 2006-2013   | NA         | 176   | NA        | NA     | NA                | 19        | 176 (10.8) |
| Domthong P, 2016      |         | Retrospective | Thailand| NA               | 2012-2015   | NA         | 116   | NA        | 30     | 1                  | 31        | 116 (26.7) |
| Domthong P, 2014      |         | Retrospective | Thailand| NA               | 2012-2013   | NA         | 44    | NA        | 16     | 0                  | 16        | 44 (36.4) |
| Dong XP, 2013         |         | Retrospective | China   | Inpatients       | 2010        | NA         | 53    | NA        | 53     | 0                  | 53        | 53 (100.0) |
| Dou HW, 2020          |         | Retrospective | China   | Outpatients & Inpatients | 2016 | NA | 214 | NA | 134 | 7 | A2063G & A2064G (1) | 142 | 214 (66.4) |
| Dumke R, 2013         |         | Retrospective | Germany | Outpatients & Inpatients | 2009-2012 | Children & Adults | 84  | NA | 3 | 0 | 0 | 3/84 (3.6) |
| Dumke R, 2010         |         | Retrospective | Germany | NA               | 2003-2008, 1991-2009 | Adults | 266 | NA | 3 | 1 | A2064C (1) | 5/266 (1.9) |
| Dumke R, 2019         |         | Retrospective | Germany | NA               | 2016-2018   | NA         | 166   | NA        | 0      | 4                  | 0         | 4/166 (2.4) |
| Eshaghi A, 2013       |         | Retrospective | Canada  | NA               | 2010-2012   | Children & Adults | 91  | NA | 6 | 1 | Mixed with wide & 2063 & | 11/91 (12.1) |

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| Study | Design | Country | Setting | RTI | Year | Age | Positive | Reference | Mutations |
|-------|--------|---------|---------|-----|------|-----|----------|-----------|-----------|
| Ferguson GD, 2013 | Retrospective | UK | Outpatients & Inpatients | RTI | 2009-2011 | Children & Adults | 32 | NA | 1 | A2064C (1) | 6/32 (18.8) |
| Goh A, 2014 | Retrospective | Singapore | NA | RTI | 2012-2013 | Children | 28 | NA | NA | NA | 8/28 (28.6) |
| Gullsby K, 2016 | Retrospective | Sweden | Outpatients & Inpatients | RTI | 1996-2013 | Children & Adults | 548 | 269 (49.1) | 0 | 0 | 0/548 (0.0) |
| Gullsby K, 2019 | Retrospective | Sweden | Outpatients & Inpatients | RTI | 1996-2017 | NA | 578 | NA | 1 | 0 | 1/578 (0.2) |
| Guo D, 2019 | Retrospective | China | NA | RTI | 2013-2015 | Children | 164 | NA | 91 | 5 | A2063G & A2064G (53) | 149/164 (90.9) |
| Guo DX, 2019 | Retrospective | China | Inpatients | RTI | 2014-2014 | Children | 341 | NA | 199 | 25 | A2063G & A2064G (12) | 236/341 (69.2) |
| Han HY, 2021 | Retrospective | Korea | Inpatients | CAP | 2019-2020 | Children | 56 | 56 | 41 | 0 | 41/56 (73.2) |
| Ho PL, 2015 | Retrospective | Hong Kong | NA | RTI | 2011-2014 | Children & Adults | 241 | NA | 84 | 0 | NA | 84/241 (34.9) |
| Hong KB, 2013 | Retrospective | Korea | NA | RTI | 2000-2011 | Children | 225 | NA | 78 | 2 | 0 | 80/225 (35.6) |
| Hung HM, 2021 | Prospective | Taiwan | NA | CAP | 2017-2019 | Children | 226 | 102 (45.1) | 144 | 2 | A2063T (28) | 174/226 (77.0) |
| Ishiguro N, 2016 | Retrospective | Japan | Outpatients & Inpatients | RTI | 2012-2014 | NA | 95 | NA | 51 | 0 | 51/95 (53.7) |
| Ishiguro N, 2017 | Prospective | Japan | Outpatients & Inpatients | CAP | 2013-2015 | Children | 92 | 62 (67.4) | 42 | 0 | 42/92 (45.7) |

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| Study | Type | Country | Setting | Years | Age | Samples | Controls | Percentage |
|-------|------|---------|---------|-------|-----|---------|----------|------------|
| Ishiguro N, 2021 | Retrospective | Japan | NA | RTI | 2013-2017 | Children | 515 | 153 | 2 | C2617G (2) | 157/515 (30.5) |
| Ishimaru N, 2021 | Retrospective | Japan | Outpatients & Inpatients | CAP | 2016-2018 | Adults | 12 | NA | NA | NA | 10/12 (83.3) |
| Katsukawa C, 2019 | Retrospective | Japan | Outpatients & Inpatients | RTI | 2011-2017 | Children | 419 | NA | 209 | 0 | A2063T (1) | 210/419 (50.1) |
| Katsushima Y, 2015 | Retrospective | Japan | Outpatients | RTI | 2012-2013 | Children | 27 | 16 (59.3) | 23 | 0 | C2617G (1) | 24/27 (88.9) |
| Kawai Y, 2012 | Retrospective | Japan | Outpatients | RTI | 2005-2010 | Children | 30 | 10 (33.3) | 15 | 6 | 0 | 21/30 (70.0) |
| Kawai Y, 2013 | Prospective | Japan | NA | CAP | 2005-2012 | Children | 188 | 106 (56.4) | 134 | 6 | A2063C (2) A2063T (8) | 150/188 (80.0) |
| Kawai Y, 2013 | Prospective | Japan | NA | CAP | 2008-2012 | Children | 769 | 297 (38.6) | 538 | 3 | A2063C (1) C2617G (1) A2063T (18) | 561/769 (73.0) |
| Kawakami N, 2021 | Prospective | Japan | Outpatients | CAP | 2015-2016 | Children | 151 | 72 (47.7) | 83 | 2 | 0 | 85/151 (56.0) |
| Kenri T, 2020 | Retrospective | Japan | NA | NA | 2006-2019 | NA | 554 | NA | 265 | 0 | A2063C (1) A2063T (6) A2064C (5) | 277/554 (50.0) |
| Kim JH, 2017 | Retrospective | Korea | NA | CAP | 2011, 2015 | Children | 250 | 123 (49.2) | 184 | 0 | 0 | 184/250 (74.0) |
| Kim MC, 2018 | Retrospective | Korea | NA | CAP | NA | Adults | 70 | 34 (48.6) | 2 | 0 | 0 | 2/70 (2.9) |
| Kim YJ, 2017 | Retrospective | Korea | NA | RTI | 2010-2015 | Children | 107 | 44 (41.1) | 11 | 0 | 0 | 11/107 (10.3) |
| Kogoj R, 2018 | Retrospective | Slovenia | NA | NA | 2006-2015 | NA | 872 | NA | 0 | 0 | A2058G (7) | 7/872 (0.8) |
| Koike C, 2011 | Retrospective | Japan | NA | CAP | 2006-2008 | Children | 16 | 9 (56.3) | 12 | 0 | 0 | 12/16 (75.0) |
| Komatsu H, 2014 | Retrospective | Japan | NA | RTI | 2010-2012 | Children | 33 | 16 (48.5) | 30 | 1 | 0 | 31/33 (93.9) |

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| Study                        | Type      | Country | Study Period | Age Group | Total | Participants | A2063T | A2063C | Unknown |
|------------------------------|-----------|---------|--------------|------------|-------|--------------|--------|--------|---------|
| Kurkela S, 2019              | Retrospective | Finland     | 2017-2018 | Children & Adult | 12 | NA | 0 | 0 | 0 | 0/12 (0.0) |
| Lanata M, 2020               | Retrospective | US          | 2015-2019 | Children | 499 | NA | 11 | 3 | 0 | 14/499 (2.8) |
| Leal S, 2020                 | Retrospective | US          | 2015-2019 | NA | 212 | NA | NA | NA | NA | 21/212 (9.9) |
| Lee E, 2017                  | Retrospective | Korea       | 2015      | Children | 94 | 37 (39.4) | 82 | 0 | 0 | 82/94 (87.2) |
| Lee H, 2021                  | Retrospective | Korea       | 2014-2015, 2019-2020 | Children | 145 | 59 (40.7) | NA | NA | NA | 59/145 (40.7) |
| Lee JK, 2021                 | Retrospective | Korea       | 2019-2020 | NA | 93 | NA | NA | NA | NA | 73/93 (78.5) |
| Lee JK, 2018                 | Retrospective | Korea       | 2000-2016 | Children | 146 | NA | 58 | 1 | 0 | 59/146 (40.4) |
| Li SL, 2012                  | Retrospective | China       | 2009-2010 | Children | 97 | 54 (55.7) | 85 | 1 | A2063T (2) | 88/97 (90.7) |
| Lin C, 2010                  | Retrospective | China       | 2009      | Children | 64 | 38 (59.4) | 57 | 0 | A2063T (1) | 58/64 (90.6) |
| Liu X, 2014                  | Retrospective | China       | 2003-2007 | NA | 76 | NA | 64 | 5 | A2063C (1) | 70/76 (92.1) |
| Liu Y, 2009                  | Retrospective | China       | 2005-2008 | Children | 53 | NA | 44 | 0 | 0 | 44/53 (83.0) |
| Liu Y, 2010                  | Retrospective | China       | 2008-2009 | Children | 100 | NA | 88 | 1 | A2063T (1) | 90/100 (90.0) |
| Liu Y, 2014                  | Retrospective | China       | 2005-2008 | Children | 101 | NA | 81 | 1 | 0 | 82/101 (81.2) |
| Loconsole D, 2019            | Retrospective | Italy       | 2013-2015 | Adults | 15 | 8 (53.3) | 2 | 1 | 0 | 3/15 (20.0) |
| Loo LH, 2017                 | Retrospective | Singapore   | 2013-2014 | Children | 200 | NA | 26 | 0 | 0 | 26/200 (13.0) |
| Lu C, 2020                   | Retrospective | Taiwan      | 2016      | Children | 180 | NA | 37 | 1 | A2063T (5) | 43/180 (23.9) |
| Lung D, 2013                 | Retrospective | Hong Kong   | 2010-2013 | Children | 48 | NA | 34 | 0 | 0 | 34/48 (70.8) |
| Ma Z, 2014                   | Retrospective | China       | 2010-2011 | Children | 57 | 39 (68.4) | 36 | 0 | 0 | 36/57 (63.2) |
| Matsubara K, 2009            | Retrospective | Japan       | 2002-2006 | Children | 94 | NA | 26 | 3 | Unknown (1) | 30/94 (31.9) |

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| Study                        | Design            | Country | Age Group | Year(s)   | Participants | Genotype  | Genotype  | Genotype  |
|------------------------------|-------------------|---------|-----------|-----------|--------------|-----------|-----------|-----------|
| Matsuda K, 2013²⁸           | Prospective       | Japan   | Children  | 2010-2011 | 65           | 32 (49.2) | 31        | 0         |
| Matsuoka M, 2004³⁹          | Retrospective     | Japan   | NA        | 2000-2003 | 76           | NA        | 10        | 1         |
| Meyer Sauteur, 2014³⁰       | Retrospective     | Switzerland | NA   | 2011-2013 | 50           | NA        | 1         | 0         |
| Meyer Sauteur, 2021³¹       | Prospective       | Switzerland | NA   | 2016-2017 | 25           | NA        | NA        | NA        |
| Miyashita N, 2013³²         | Retrospective     | Japan   | NA        | 2008-2012 | Children & Adults | 73   | 38 (52.1) | 27        |
| Miyashita N, 2011³³         | Retrospective     | Japan   | NA        | 2005-2010 | Children     | 30      | NA        | NA        |
| Miyashita N, 2012³⁴         | Retrospective     | Japan   | NA        | 2008-2011 | Children & Adults | 99   | 52 (52.5) | 42        |
| Miyashita N, 2010³⁵         | Retrospective     | Japan   | NA        | 2000-2009 | Adults       | 84      | NA        | 1         |
| Miyashita, 2009³⁶           | Retrospective     | Japan   | NA        | 2005-2008 | Children     | 21      | NA        | NA        |
| Miyata, 2013³⁷              | Retrospective     | Japan and US | NA   | NA        | Children     | Japan(21) US(18) | NA   | Japan(16) US(1) | Japan(0) US(0) |
| Morimoto K, 2017³⁸          | Retrospective     | Japan   | NA        | 2012-2015 | Adults       | 55      | NA        | NA        |
| Morinaga Y, 2020³⁹          | Retrospective     | Japan   | NA        | 2016-2018 | NA           | 249     | NA        | 2         |
| Morozumi M, 2013³⁰          | Prospective       | Japan   | NA        | 2008-2009 | Children     | 54      | NA        | 22        |
| Morozumi M, 2005³¹          | Prospective       | Japan   | NA        | 2002-2004 | Children     | 195     | NA        | 9         |
| Morozumi M, 2008³²          | Prospective       | Japan   | NA        | 2002-2006 | Children     | 380     | NA        | 50        |

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| Study                  | Design          | Country     | Sample Type | Time Frame   | Age Group   | Total   | NA | 0 | 0 | % (95% CI)   |
|----------------------|-----------------|-------------|-------------|--------------|-------------|---------|----|---|---|-------------|
| Morozumi M. 2020     | Prospective     | Japan       | NA          | CAP          | Children    | 53      | NA | 6 | 0 | 6/53 (11.3) |
| Muto T. 2021         | Retrospective   | Japan       | NA          | NA           | Children    | 21      | 10 (47.6) | NA | NA | 14/21 (66.7) |
| Nagita A. 2021       | Prospective     | Japan       | NA          | CAP          | Children    | 38      | 19 (50.0) | 24 | 0  | 24/38 (63.1) |
| Nakamura Y. 2021     | Retrospective   | Japan       | NA          | RTI          | Children    | 1949    | NA | 1140 | 7 | A2063C (3) C2617G (2) A2063T (30) 1182/1949 (60.6) |
| Nummi M. 2015        | Retrospective   | Finland     | NA          | NA           | NA          | 42      | NA | 3  | 1 | 0        4/42 (9.5) |
| Okada T. 2012        | Prospective     | Japan       | NA          | CAP          | Children    | 202    | 106 (52.5) | 160 | 4  | A2063C (1) A2063T (11) 176/202 (87.1) |
| Ouchi K. 2019        | NA              | Japan       | NA          | NA           | Children    | 1702   | NA | NA | NA | 1180/1702 (69.3) |
| Pereyre S. 2011      | Retrospective   | France, Israel | NA     | RTI          | Children & Adults | France (29) Israel (41) | NA | France (0) Israel (9) | France (1) Israel (0) | France 1/29 (3.4) Israel 9/41 (22.0) |
| Pereyre S. 2013      | Retrospective   | France      | NA          | RTI          | Children    | 6      | NA | 0  | 0 | 0        0/6 (0.0) |
| Pereyre S. 2013      | Retrospective   | France      | NA          | NA           | Children    | 72      | NA | 0  | 0 | A2058G (4) A2059G (1) A2062G (1) 6/72 (8.3) |
| Peuchant O. 2009      | Retrospective   | France      | NA          | NA           | Children & Adults | 67      | NA | 0  | 0 | A2058G (3) A2059G (1) C2611G 5/67 (7.5) |

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| Study  | Design | Country  | Source | Start-Year | End-Year | Age Group  | n   | NA | n   | %   | (1)                  |
|--------|--------|----------|--------|------------|----------|------------|-----|-----|-----|-----|----------------------|
| Pouladi I, 2020 | Prospective | Iran | NA | RTI | 2018 | Adults | 17 | NA | 0 | 0 | 0 | 0/17 (0.0) |
| Qu K, 2020 | Prospective | China | NA | CAP | 2010-2012 | Children & Adults | 205 | 95 (46.3) | 181 | 0 | 0 | 181/205 (88.3) |
| Qu J, 2013 | Prospective | China | NA | CAP | 2010-2012 | Children & Adults | 136 | 61 (44.9) | 114 | 0 | 0 | 114/136 (83.8) |
| Rivaya B, 2020 | Prospective | Spain | 3 NA | CAP | 2013-2017 | Children | 127 | NA | 7 | 2 | A2063T & C2617A (1) | 10/127 (7.8) |
| Rodriguez N, 2019 | Retrospective | Cuba | NA | CAP | 2012, 2017 | Children & Adults | 27 | NA | 3 | 2 | 0 | 5/27 (18.5) |
| Smith, 2016 | Retrospective | Australia | NA | NA | 1998-2014 | Children & Adults | 123 | NA | 0 | 0 | 0 | 0/123 (0.0) |
| Spuesens E, 2012 | Prospective | Netherlands | NA | RTI | 1997-2008 | Children & Adults | 96 | 41 (42.7) | 0 | 0 | 0 | 0/96 (0.0) |
| Dumke R, 2009 | Prospective | Germany | NA | CAP | 1991-2009 | Adults | 266 | NA | 2 | 1 | A2063C (1) A2063G (1) | 5/266 (1.9) |
| Sun H, 2017 | Retrospective | China | NA | NA | 2003-2007, 2014-2015 | Children | 149 | NA | 131 | 0 | G2611T & T2613C (1) | 132/149 (88.6) |
| Suzuki S, 2018 | Prospective | Japan | NA | RTI | 2016-2017 | Children | 25 | NA | 7 | 0 | 0 | 7/25 (28.0) |
| Suzuki Y, 2013 | Retrospective | Japan | NA | RTI | 2009-2010 | Children | 47 | NA | 0 | 0 | A2063T (39) | 39/47 (83.0) |
| Suzuki Y, 2017 | Retrospective | Japan | NA | NA | 2004-2014 | Children | 347 | NA | 129 | 0 | 0 | 129/347 (37.2) |
| Tanaka T, 2017 | Prospective | Japan | NA | RTI | 2008-2015 | Children | 1448 | 818 (56.5) | 973 | 6 | A2063C (3) A2063T (31) C2617G (2) C2617T (1) | 1016/1448 (70.2) |
| Uh Y, 2020 | Prospective | Korea | NA | RTI | 2010 | Children | 17 | 7 (41.2) | 3 | 0 | 0 | 3/17 (17.6) |

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| Year   | Study Type    | Country      | Design         | Children/Adults | Samples | Cases | % Cases (95% CI) | A2063C | A2063T | A2063G | Other Mutations |
|--------|---------------|--------------|----------------|----------------|---------|-------|-----------------|--------|--------|--------|-----------------|
| 2013   | Prospective   | Denmark      | NA             | 2010-2011       | NA      | 248   | 5/248 (2.0)     |        |        |        |                 |
| 2012   | Retrospective | Denmark      | NA             | 2010-2011       | NA      | 99    | 7/99 (7.1)      |        |        |        |                 |
| 2012   | Prospective   | Russia       | NA             | 2015-2018       | NA      | 22    | 0               |        |        |        |                 |
| 2012   | Retrospective | Switzerland  | NA             | 2014-2017       | NA      | 163   | 15/163 (9.0)    |        |        |        |                 |
| 2012   | Retrospective | Russia       | NA             | 2015-2018       | Children| 360   | 204 (56.7)     |        |        |        | A2063T & A2063G (1) |
| 2012   | Retrospective | China        | NA             | 2012-2012       | Adults  | 21    | 0               |        |        |        |                 |
| 2012   | Retrospective | China        | NA             | 2011           | Children| 15    | 12/15 (80.0)    |        |        |        | 2063 or 2617 mutation (12) |
| 2012   | Retrospective | China        | NA             | 2016-2019       | Children| 1524  | 824 (54.1)     |        |        |        | 1386/1524 (90.9) |
| 2012   | Retrospective | China        | NA             | 2014           | Children| 25    | 10 (40.0)      |        |        |        | 18/25 (72.0)   |
| 2012   | Prospective   | China        | NA             | 2010-2012       | Adults  | 75    | 56             |        |        |        | 56/75 (74.7)   |
| 2012   | Retrospective | Thailand     | NA             | 2009-2012       | Children & Adults | 141  | 0               |        |        |        | 0/141 (0.0)    |
| 2012   | Retrospective | Taiwan       | NA             | 2011           | Children| 73    | 33 (45.2)      |        |        |        | 9/73 (12.3)    |
| 2012   | Prospective   | Taiwan       | NA             | 2010-2011       | Children| 60    | 14             |        |        |        | 14/60 (23.3)  |
| 2012   | Retrospective | USA          | NA             | 2012-2014       | Children| 446   | 32             |        |        |        | Unknown (5)    |
| 2012   | Retrospective | China        | NA             | 2004-2005       | NA      | 64    | 35             |        |        |        | 37/446 (8.3)  |
| 2012   | Retrospective | China        | NA             | 2003-2006       | Children| 50    | 40             |        |        |        | 46/50 (92.0)  |
| 2012   | Prospective   | China        | NA             | 2014-2016       | Children| 276   | 137 (49.6)     |        |        |        | A2063G and G (1) |

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| Study | Study Type | Region | Age Group | Year | Sample Size | Genotypes | Insertion 1 | Insertion 2 | Insertion 3 | Insertion 4 | Insertion 5 | Insertion 6 | Insertion 7 |
|-------|------------|--------|-----------|------|-------------|------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Xue G, 2018 | Retrospective | China | Children | 2016 | 213 | NA | 137 | 0 | A2063G & A2065C (1), A2063G & wild type (3), A2064G & wild type (1) | 142/213 (76.3) |
| Xue G, 2014 | Retrospective | Australia, China | Children & Adults | 2008-2012 | 49 | NA | 2 | 0 | wild type (2) | 4/49 (8.2) |
| Yamada M, 2012 | Retrospective | Japan | Children | 2007-2010 | 59 | NA | 7 | 0 | 0 | 7/59 (11.9) |
| Yan C, 2015 | Retrospective | USA | Children | 2012-2014 | 247 | NA | 209 | 5 | A2063T (2) C2617T (1) | 217/247 (87.9) |
| Yan C, 2020 | Prospective | China | Children & Adults | 2014-2015 | 75 | 30 (40.0) | 53 | 1 | 0 | 54/75 (77.1) |
| Yin Y, 2017 | Prospective | China | Adults | 2010-2012 | 91 | 39 (42.9) | 27 | 0 | 0 | 27/91 (29.7) |
| Study Year & Authors | Study Type | Country | Cohort | Year Range | Number of Subjects | Number of Subjects (n) | Number of T2611C (n) | Number of A2063G (n) | Number of A2063T (n) |
|---------------------|------------|---------|--------|------------|--------------------|------------------------|----------------------|----------------------|---------------------|
| 2012140             | Retrospective | China   | NA     | 2015-2016  | Adults             | 27                     | 11 (40.7)            | 27                   | 0                   | 0                   |
| 2018141             | Retrospective | China   | NA     | 2018      | Children          | 19                     | NA                   | 19                   | 0                   | 0                   |
| 2018142             | Retrospective | China   | NA     | 2008-2012 | Children & Adults | 309                    | NA                   | 272                  | 7                   | A2063T (1)          |
| 2019143             | Retrospective | China   | NA     | 2007-2012 | Children          | 129                    | NA                   | 116                  | 0                   | A2063G & T2611C (1) |
| 2019144             | Retrospective | China   | NA     | 2012-2014 | Children & Adults | 91                     | NA                   | 10                   | NA                  | Unknown (2)         |
| 2015147             | Retrospective | China   | NA     | 2016-2019 | Children          | 107                    | 55 (51.4)            | 60                   | 0                   | 60/107 (56.1)      |
| 2014148             | Retrospective | China   | NA     | 2009-2010 | Children          | 235                    | 149 (63.4)           | 199                  | 1                   | A2063T (6)          |
| 2020149             | Retrospective | China   | NA     | 2015-2018 | Children          | 315                    | 177 (56.2)           | 164                  | 0                   | 164/315 (52.1)     |

CAP, community-acquired pneumonia; MP, *M. pneumoniae*; MRMP, macrolide resistant *M. pneumoniae*; n, number; NA, not applicable; RTI, respiratory tract infection.

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### eTable 4. Proportion of MRMP in Each Country

| WHO regions | Country | Number of studies in each country | MRMP/total, n (%) | Summary estimate (95% CI) |
|-------------|---------|----------------------------------|-------------------|--------------------------|
| AMR         | Cuba    | 14                               | 163/2269 (7.2)    | 8.4% (6.1-11.6)          |
|             | Canada  | 1                                | 5/27 (18.5)       | 18.5% (8.4-40.9)         |
|             | USA     | 11                               | 111/91 (12.1)     | 12.1% (7.0-21.0)         |
|             | Colombia| 1                                | 0/42 (0.0)        | 1.2% (0.1-18.5)          |
| EMR         | Iran    | 2                                | 1/117 (0.9)       | 1.4% (0.3-7.0)           |
| EUR         | Italy   | 3                                | 22/104 (21.2)     | 21.7% (15.0-31.4)        |
|             | Israel  | 3                                | 31/280 (11.1)     | 15.9% (6.2-41.1)         |
|             | Slovenia| 1                                | 7/872 (8.0)       | 0.8% (0.4-1.7)           |
|             | Spain   | 1                                | 10/127 (7.9)      | 7.9% (4.3-14.3)          |
|             | Finland | 2                                | 4/54 (7.4)        | 8.7% (3.6-21.0)          |
|             | Russia  | 1                                | 7/99 (7.1)        | 7.1% (3.5-14.4)          |
|             | France  | 4                                | 12/174 (6.9)      | 7.4% (4.4-12.7)          |
|             | Switzerland | 3                           | 16/238 (6.7)    | 5.1% (1.5-16.7)          |
|             | UK      | 5                                | 11/214 (5.1)      | 6.4% (2.1-19.4)          |
|             | Germany | 4                                | 18/782 (2.3)      | 2.4% (1.5-3.8)           |
|             | Denmark | 1                                | 5/248 (2.0)       | 2.0% (0.9-4.8)           |
|             | Sweden  | 2                                | 1/1126 (0.1)      | 0.1% (0.0-0.7)           |
|             | Netherlands | 1                      | 0/96 (0.0)      | 0.5% (0.0-8.2)           |
| SEAR        | Thailand| 3                                | 47/301 (15.6)     | 9.8% (0.8-100.0)         |
| WPR         | Thailand| 3                                | 47/301 (15.6)     | 9.8% (0.8-100.0)         |
|             | China   | 39                               | 12634/20307 (62.2)| 53.4% (47.4-60.3)        |
|             | Japan   | 41                               | 5210/6385 (81.6)  | 79.5% (74.6-84.8)        |
|             | Japan   | 41                               | 6363/11268 (56.5) | 47.3% (38.9-57.5)        |
|             | Taiwan  | 5                                | 285/620 (46.0)    | 32.4% (17.1-61.2)        |
|             | Korea   | 12                               | 623/1364 (45.7)   | 30.0% (16.6-54.1)        |
|             | Hong Kong| 2                               | 118/289 (40.8)   | 49.7% (24.8-99.5)        |
|                |      |                   |          |                  |
|----------------|------|-------------------|----------|------------------|
| Singapore      | 2    | 34/228 (14.9)     | 18.6% (8.6-40.1) |
| Australia      | 2    | 1/153 (0.7)       | 1.5% (0.2-11.1)   |
| Total          | 153  | 12989/27408 (47.0)| 27.5% (22.5-33.5) |

AMR, Region of the Americas; EMR, Eastern Mediterranean Region EUR, European Region; NA, not applicable; SEAR, South-East Asian Region; WPR, Western Pacific Region.
**eTable 5.** The Proportion of A2063G and A2064G Mutations by Year of Testing According to World Health Organization Regions in Studies With Information on Mutation Types Associated With Macrolide Resistance of *M pneumoniae*

| Year of testing | Global proportion, % | Region of the Americas, % | European Region, % | Western Pacific Region, % |
|-----------------|----------------------|---------------------------|--------------------|--------------------------|
|                 | A2063G | A2064G | A2063G | A2064G | A2063G | A2064G | A2063G | A2064G |
| 2001            | 76.9   | 7.7    | NA     | NA     | 76.9   | 7.7    |
| 2002            | NA     | NA     | NA     | NA     | NA     | NA     |
| 2003            | 56.3   | 12.5   | NA     | NA     | 81.8   | 18.2   |
| 2004            | 94.0   | 5.4    | NA     | NA     | 94.0   | 5.4    |
| 2005            | 92.9   | 5.2    | NA     | NA     | 94.7   | 4.7    |
| 2006            | 94.7   | 0.8    | NA     | NA     | 99.2   | 0.8    |
| 2007            | 82.4   | 17.6   | NA     | NA     | 81.8   | 18.2   |
| 2008            | 92.4   | 3.7    | NA     | NA     | 92.5   | 3.5    |
| 2009            | 89.6   | 1.6    | NA     | NA     | 89.6   | 1.     |
| 2010            | 93.7   | 1.5    | NA     | NA     | 94.7   | 1.1    |
| 2011            | 95.4   | 0.8    | 66.7   | 11.1   | NA     | 95.7   | 0.7    |
| 2012            | 96.9   | 0.0    | NA     | NA     | 100.0  | 0.0    | 96.7   | 0.0    |
| 2013            | 96.6   | 0.6    | 96.1   | 0.0    | NA     | 96.7   | 0.6    |
| 2014            | 90.5   | 3.4    | NA     | NA     | 90.8   | 3.3    |
| 2015            | 97.3   | 1.8    | NA     | NA     | 99.0   | 0.6    |
| 2016            | 95.7   | 2.3    | 81.5   | 14.8   | 100.0  | 0.0    | 96.4   | 1.6    |
| 2017            | 95.5   | 4.5    | 78.6   | 21.4   | 0.0    | 100.0  | 97.6   | 2.4    |
| 2018            | 84.9   | 1.0    | NA     | NA     | NA     | 84.9   | 1.     |
| 2019            | 100.0  | 0.0    | NA     | NA     | NA     | 100.0  | 0.0    |

MRMP, macrolide-resistant *M pneumoniae*; NA, not applicable.
### eTable 6. Proportion of Each Mutation Type Associated With Macrolide Resistance of *M. pneumoniae* in Each Country

| Countries | A2063G, n (%) | A2064G, n (%) | Other mutations, n (%) |
|-----------|---------------|---------------|------------------------|
| Australia | 0 (0.0%)      | 1 (100.0%)    | 0 (0.0%)               |
| Canada    | 6 (54.5%)     | 1 (9.1%)      | 4 (36.4%)              |
| China     | 3493 (95.1%)  | 73 (2.0%)     | 107 (2.9%)             |
| Cuba      | 3 (60.0%)     | 2 (40.0%)     | 0 (0.0%)               |
| Finland   | 3 (75.0%)     | 1 (25.0%)     | 0 (0.0%)               |
| France    | 0 (0.0%)      | 1 (8.3%)      | 11 (91.7%)             |
| Germany   | 8 (44.4%)     | 6 (33.3%)     | 4 (22.2%)              |
| Hong Kong | 118 (100.0%)  | 0 (0.0%)      | 0 (0.0%)               |
| Iran      | 0 (0.0%)      | 0 (0.0%)      | 1 (100.0%)             |
| Israel    | 16 (88.9%)    | 0 (0.0%)      | 2 (11.1%)              |
| Italy     | 9 (64.3%)     | 5 (35.7%)     | 0 (0.0%)               |
| Japan     | 4579 (94.1%)  | 75 (1.5%)     | 214 (4.4%)             |
| Korea     | 488 (99.4%)   | 3 (0.6%)      | 0 (0.0%)               |
| Russia    | 7 (100.0%)    | 0 (0.0%)      | 0 (0.0%)               |
| Singapore | 26 (100.0%)   | 0 (0.0%)      | 0 (0.0%)               |
| Slovenia  | 0 (0.0%)      | 0 (0.0%)      | 7 (100.0%)             |
| Spain     | 7 (63.6%)     | 2 (18.2%)     | 2 (18.2%)              |
| Sweden    | 1 (100.0%)    | 0 (0.0%)      | 0 (0.0%)               |
| Switzerland | 10 (62.5%)  | 5 (31.2%)     | 1 (6.2%)               |
| Taiwan    | 249 (87.4%)   | 3 (1.1%)      | 33 (11.6%)             |
| Thailand  | 46 (97.9%)    | 1 (2.1%)      | 0 (0.0%)               |
| UK        | 5 (45.5%)     | 1 (9.1%)      | 5 (45.5%)              |
| USA       | 89 (89.0%)    | 8 (8.0%)      | 3 (3.0%)               |
| Variable | No. of articles | Positive samples/total samples | Proportion (95% CI) | p value for \( \chi^2 \) |
|----------|----------------|--------------------------------|---------------------|--------------------------|
|          |                |                                |                     | Q test | Egger test | Begg test |
| Children with CAP |                |                                |                     |        |            |            |
| MRMP in studies with or without information on mutation types | 39 | 4315/6606 | 43.9\% (34.2-56.4) | <0.001 | <0.001 | <0.001 |
| A2063G  | 30            | 2510/2642                      | 96.1\% (94.1-98.0)  | <0.001 | <0.001 | 0.1045   |
| A2064G  | 24            | 45/2642                        | 4.2\% (2.4-7.6)    | <0.001 | 0.0718 | 0.024    |
| Other mutations | 15 | 87/2642                      | 4.7\% (2.7-8.1)    | <0.001 | 0.0654 | 0.255    |
| MRMP in studies with information on mutation types | 30 | 2642/6606 | 39.8\% (29.2-54.2) | <0.001 | <0.001 | 0.001    |
| Children with RTI |                |                                |                     |        |            |            |
| MRMP in studies with or without information on mutation types | 29 | 2751/5814 | 41.1\% (29.0-58.2) | <0.001 | 0.004  | 0.0055   |
| A2063G  | 26            | 2588/2746                      | 98.0\% (96.6-99.4)  | <0.001 | 0.0239 | 0.0051   |
| A2064G  | 20            | 47/2746                        | 2.5\% (1.2-5.1)    | <0.001 | 0.0103 | 0.0015   |
| Other mutations | 17 | 111/2746                      | 3.8\% (1.6-9.2)    | <0.001 | <0.001 | 0.6211   |
| MRMP in studies with information on mutation types | 29 | 2746/5814 | 40.8\% (28.6-58.1) | <0.001 | 0.0039 | 0.0055   |
| Adults with CAP |                |                                |                     |        |            |            |
| MRMP in studies with or without information on mutation types | 7  | 142/531 | 12.4\% (2.6-59.0) | <0.001 | 0.0115 | 0.6523   |
| A2063G  | 4             | 138/142                        | 99.5\% (97.6-100.0) | 0.3209 | 0.1380 | 0.1742   |
| A2064G  | 2             | 2/142                          | 6.3\% (0.6-65.0)   | 0.0746 | NA      | NA       |
| Other mutations | 2  | 2/142                          | 7.6\% (0.2-100.0)  | 0.0124 | NA      | NA       |
| MRMP in studies with information on mutation types | 5  | 142/531 | 20.3\% (3.3-100.0) | <0.001 | 0.028  | 0.3272   |
| Adults with RTI |                |                                |                     |        |            |            |
| MRMP in studies with or without information on mutation types | 6  | 1290/2423 | 11.2\% (2.6-48.0) | <0.001 | 0.3114 | 0.3476   |
| A2063G  | 4             | 1234/1288                      | 96.6\% (95.6-97.6)  | 0.055  | 0.2515 | 0.4969   |
| A2064G  | 4             | 13/1288                        | 5.2\% (0.3-56.9)   | <0.001 | 0.3422 | 0.4969   |
| Other mutations | 5  | 41/1288                     | 11.3\% (2.2-58.1)  | <0.001 | 0.3756 | 0.6242   |
| MRMP in studies with information on mutation types | 6  | 1288/2423 | 10.7\% (2.4-47.6) | <0.001 | 0.3172 | 0.3476   |

CAP, community-acquired pneumonia; CI, confidence interval; MRMP, macrolide resistant *M pneumoniae*; NA, not applicable; RTI, respiratory tract infection.

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eFigure. Funnel Plots for the Proportion of Macrolide Resistance of *M pneumoniae* Against Study Sample Sizes and the Egger Test for Investigation of the Small Study Biases. (A) Studies for A2063G mutation associated with macrolide resistance of *M pneumoniae*. (B) Studies for A2064G mutation associated with macrolide resistance of *M pneumoniae*. 
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