**Additional File 1:**

**Tables:**

Table S1. PRISMA Checklist adapted from Moher *et al.*

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Table S3. Number of included studies and isolates

Table S4. Sensitivity analysis

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**Figures:**

Figure S1. Metaanalysis and median prevalence comparison

Figure S2. Sensitivity analysis

Figure S3. MDR *S.* Typi in sub-Saharan Africa

Figure S4. MDR *S.* Typhi in NAME

Figure S5. MDR *S.* Typhi in East Asia

Figure S6. FQNS *S.* Typhi in sub-Saharan Africa

Figure S7. FQNS *S.* Typhi in NAME

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Figure S9. MDR *S.* Paratypi in South Asia

Figure S10. MDR *S.* Paratyphi in Southeast Asia

Figure S11. MDR *S.* Paratyphi in East Asia

Figure S12. FQNS *S.* Paratypi in South Asia

Figure S13. FQNS *S.* Paratyphi in Southeast Asia

Figure S14. FQNS *S.* Paratyphi in East Asia

**Table S1. PRISMA Checklist:** adapted from Moher *et al.*

|  |  |  |  |
| --- | --- | --- | --- |
| **Section/topic** | **#** | **Checklist item** | **Reported** |
| **TITLE** | | |  |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 🗹 |
| **ABSTRACT** | | |  |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 🗹 |
| **INTRODUCTION** | | |  |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 🗹 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 🗹 |
| **METHODS** | | |  |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 🗹 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 🗹 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 🗹 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 🗹 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 🗹 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 🗹 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 🗹 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 🗹 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 🗹 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis. | 🗹 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 🗹 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 🗹 |
| **RESULTS** | | |  |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 🗹 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 🗹 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 🗹 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 🗹 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 🗹 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 🗹 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 🗹 |
| **DISCUSSION** | | |  |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 🗹 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 🗹 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 🗹 |
| **FUNDING** | | |  |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 🗹 |

**Table S2: Database search strategy.** Strategy designed in Ovid MedLine and altered for other databases

|  |  |
| --- | --- |
| **Search number** | **Search term** |
| 1 | Typhoid Fever/ (11123) |
| 2 | typhoid\*.ti,ab. (12200) |
| 3 | paratyphoid\*.ti,ab. (1674) |
| 4 | "enteric fever\*".ti,ab. (1511) |
| 5 | "salmonella typhi".ti,ab. (4311) |
| 6 | "salmonella paratyphi".ti,ab. (821) |
| 7 | paratyphoid fever/ (2380) |
| 8 | 1 or 2 or 3 or 4 or 5 or 6 or 7(20567) |
| 9 | exp Drug Resistance, Bacterial/ (78649) |
| 10 | exp Microbial Sensitivity Tests/ (116858) |
| 11 | "antibacterial resistan\*".ti,ab. (617) |
| 12 | "antibacterial drug resistan\*".ti,ab. (33) |
| 13 | "bacterial drug resistan\*".ti,ab. (208) |
| 14 | "antimicrobial resistan\*".ti,ab. (14949) |
| 15 | "antibiotic drug resistan\*".ti,ab. (67) |
| 16 | "bacterial resistan\*".ti,ab. (5266) |
| 17 | "antibiotics resistan\*".ti,ab. (634) |
| 18 | "bacterial surveillan\*".ti,ab. (40) |
| 19 | "antibiotic surveillan\*".ti,ab. (36) |
| 20 | "antibacterial surveillan\*".ti,ab. (1) |
| 21 | "antimicrobial surveillan\*".ti,ab. (393) |
| 22 | "antimicrobial susceptib\*".ti,ab. (11401) |
| 23 | exp Bacteremia/ (27328) |
| 24 | bacteraemia\*.ti,ab. (5772) |
| 25 | bacteremia\*.ti,ab. (21957) |
| 26 | ("blood culture\*" adj3 result\*).ti,ab. (1319) |
| 27 | (antibacter\* adj3 surveillan\*).ti,ab. (29) |
| 28 | 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 (215387) |
| 29 | 8 and 28 (2202) |
| 30 | 29 (2202) |
| 31 | limit 29 to yr="1990 -Current" (1930) |

**Table S3a: Total number of included studies and isolates.** Displayed are the total number of studies and isolates included by GBD region and five-year time-period. \*Some studies provide data on multiple sites and/or time periods therefore the total number of studies displayed here is higher than the total number of studies included in this review.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **GBD Region** | **Number of studies (Number of isolates)** | | | | | | |
| **1990-1994** | **1995-1999** | **2000-2004** | **2005-2009** | **2010-2014** | **2015-2018** | **Total** |
| Andean Latin America | 1(97) | 0(0) | 0(0) | 0(0) | 1(33) | 0(0) | 2(130) |
| Australasia | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Caribbean | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Central Asia | 0(0) | 1(34) | 1(41) | 1(123) | 0(0) | 0(0) | 3(198) |
| Central Europe | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Central Latin America | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Central Sub-Saharan Africa | 0(0) | 0(0) | 1(29) | 2(410) | 3(363) | 0(0) | 6(802) |
| East Asia | 0(0) | 0(0) | 7(4,916) | 4(443) | 2(463) | 0(0) | 13(5,822) |
| Eastern Europe | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Eastern Sub-Saharan Africa | 2(62) | 3(357) | 2(345) | 6(2,504) | 4(254) | 0(0) | 17(3,522) |
| High-income Asia Pacific | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| High-income North America | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| North Africa & Middle East | 4(643) | 5(1,218) | 4(1,044) | 3(996) | 0(0) | 2(69) | 18(3,970) |
| Oceania | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| South Asia | 57(13,851) | 35(23,253) | 59(19,130) | 60(14,388) | 64(25,886) | 13(2,937) | 288(99,445) |
| Southeast Asia | 5(905) | 12(2,279) | 6(3,795) | 7(421) | 8(1,233) | 1(46) | 39(8,679) |
| Southern Latin America | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Southern Sub-Saharan Africa | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Tropical Latin America | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Western Europe | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Western Sub-Saharan Africa | 0(0) | 4(193) | 3(513) | 7(446) | 7(592) | 1(35) | 22(1,779) |
| Total | 69(15,558) | 60(27,334) | 83(29,813) | 90(19,731) | 89(28,824) | 17(3,087) | \*408(124,347) |

**Table S3b: Number of included studies and isolates for *S.* Typhi.** Displayed by GBD region and five-year time-period. \*Some studies provide data on multiple sites and/or time periods therefore the total number of studies displayed here is higher than the total number of studies included in this review.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **GBD Region** | **Number of studies (Number of isolates)** | | | | | | |
| **1990-1994** | **1995-1999** | **2000-2004** | **2005-2009** | **2010-2014** | **2015-2018** | **Total** |
| Andean Latin America | 0(0) | 0(0) | 0(0) | 0(0) | 1(33) | 0(0) | 1(33) |
| Australasia | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Caribbean | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Central Asia | 0(0) | 1(34) | 1(41) | 1(123) | 0(0) | 0(0) | 3(198) |
| Central Europe | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Central Latin America | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Central Sub-Saharan Africa | 0(0) | 0(0) | 1(29) | 2(410) | 3(363) | 0(0) | 6(802) |
| East Asia | 0(0) | 0(0) | 5(618) | 2(164) | 0(0) | 0(0) | 7(782) |
| Eastern Europe | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Eastern Sub-Saharan Africa | 2(62) | 3(357) | 2(345) | 6(2,504) | 4(254) | 0(0) | 17(3,522) |
| High-income Asia Pacific | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| High-income North America | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| North Africa & Middle East | 4(643) | 5(1,218) | 4(1,004) | 3(996) | 0(0) | 2(69) | 18(3,930) |
| Oceania | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| South Asia | 57(13,136) | 31(17,472) | 55(12,726) | 55(10,530) | 62(19,581) | 13(2,274) | 273(75,719) |
| Southeast Asia | 5(761) | 12(2,260) | 6(3,728) | 7(421) | 7(689) | 1(46) | 38(7,905) |
| Southern Latin America | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Southern Sub-Saharan Africa | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Tropical Latin America | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Western Europe | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Western Sub-Saharan Africa | 0(0) | 4(176) | 3(513) | 7(431) | 7(570) | 1(35) | 22(1,725) |
| Total | 68(14,602) | 56(21,517) | 77(19,004) | 83(15,579) | 84(21,490) | 17(2,424) | \*385(94,616) |

**Table S3c: Number of included studies isolates for *S.* Paratyphi A.** Displayed by GBD region and five-year time-period. \*Some studies provide data on multiple sites and/or time periods therefore the total number of studies displayed here is higher than the total number of studies included in this review.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **GBD Region** | **Number of studies (Number of isolates)** | | | | | | |
| **1990-1994** | **1995-1999** | **2000-2004** | **2005-2009** | **2010-2014** | **2015-2018** | **Total** |
| Andean Latin America | 1(97) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 1(97) |
| Australasia | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Caribbean | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Central Asia | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Central Europe | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Central Latin America | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Central Sub-Saharan Africa | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| East Asia | 0(0) | 0(0) | 2(4,298) | 4(279) | 2(463) | 0(0) | 8(5,040) |
| Eastern Europe | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Eastern Sub-Saharan Africa | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| High-income Asia Pacific | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| High-income North America | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| North Africa & Middle East | 0(0) | 0(0) | 1(40) | 0(0) | 0(0) | 0(0) | 1(40) |
| Oceania | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| South Asia | 5(715) | 9(5,781) | 28(6,404) | 30(3,858) | 40(6,305) | 7(663) | 119(23,726) |
| Southeast Asia | 3(144) | 1(19) | 2(67) | 0(0) | 6(544) | 0(0) | 12(774) |
| Southern Latin America | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Southern Sub-Saharan Africa | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Tropical Latin America | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Western Europe | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) |
| Western Sub-Saharan Africa | 0(0) | 1(17) | 0(0) | 1(15) | 2(22) | 0(0) | 4(54) |
| Total | 9(956) | 11(5,817) | 33(10,809) | 35(4,152) | 50(7,334) | 7(663) | \*145(29,731) |

**Table S4a. Sensitivity analysis:** Random effects metaanalysis results for studies on MDR *S.* Typhi in South Asia, comparing results for all studies with only those reporting (a) AST methods used; (b) resistance breakpoints used; (c) internal control strain used and (d) those on over 50 isolates of *S.* Typhi.

|  |  |  |  |
| --- | --- | --- | --- |
| **Time Period** | **Studies (N)** | ***I****²* (%) | **Pooled prevalence [95% CI]** |
| **All studies** | | | |
| 1990\_1994 | 33 | 98% | 63% [54-71] |
| 1995\_1999 | 14 | 100% | 38% [24-52] |
| 2000\_2004 | 33 | 99% | 34% [24-44] |
| 2005\_2009 | 31 | 99% | 12% [6-20] |
| 2010\_2014 | 42 | 98% | 7% [4-12] |
| **Studies reporting AST methods** | | | |
| 1990-1994 | 25 | 99% | 61% [50-71] |
| 1995-1999 | 12 | 100% | 36% [22-51] |
| 2000-2004 | 27 | 99% | 32% [21-44] |
| 2005-2009 | 31 | 99% | 12% [6-20] |
| 2010-2014 | 39 | 98% | 6% [3-10] |
| **Studies reporting resistance breakpoints\*** | | | |
| 1990-1994 | 5 | 100% | 67% [38-91] |
| 1995-1999 | 7 | 100% | 29% [14-47] |
| 2000-2004 | 20 | 99% | 27% [18-38] |
| 2005-2009 | 25 | 99% | 13% [6-22] |
| 2010-2014 | 38 | 98% | 6% [3-10] |
| **Studies reporting internal quality control** | | | |
| 1990-1994 | 33 | 98% | 63% [54-71] |
| 1995-1999 | 14 | 100% | 37% [23-53] |
| 2000-2004 | 33 | 99% | 34% [24-44] |
| 2005-2009 | 31 | 99% | 12% [6-20] |
| 2010-2014 | 42 | 98% | 7% [4-12] |
| **Studies with over 50 isolates** | | | |
| 1990-1994 | 23 | 98% | 61% [51-70] |
| 1995-1999 | 14 | 100% | 38% [24-52] |
| 2000-2004 | 22 | 99% | 34% [22-47] |
| 2005-2009 | 27 | 99% | 10% [4-17] |
| 2010-2014 | 30 | 99% | 8% [4-14] |

\* Testing standards including version or year

**Table S4b. Sensitivity analysis:** Random effects metaanalysis results for studies on FQNS *S.* Typhi in South Asia, comparing results for all studies with only those reporting (a) AST methods used; (b) resistance breakpoints used; (c) internal control strain used and (d) those on over 50 isolates of *S.* Typhi.

|  |  |  |  |
| --- | --- | --- | --- |
| **Time Period** | **Studies (N)** | ***I****²* (%) | **Pooled prevalence [95% CI]** |
| **All studies** | | | |
| 1990\_1994 | 6 | 93% | 2% [0-14] |
| 1995\_1999 | 8 | 98% | 49% [26-72] |
| 2000\_2004 | 29 | 99% | 62% [47-77] |
| 2005\_2009 | 38 | 97% | 76% [69-83] |
| 2010\_2014 | 50 | 99% | 82% [75-89] |
| **Studies reporting AST methods** | | | |
| 1990-1994 | 3 | 95% | 10% [0-46] |
| 1995-1999 | 8 | 98% | 49% [26-72] |
| 2000-2004 | 26 | 99% | 59% [42-74] |
| 2005-2009 | 36 | 97% | 77% [70-84] |
| 2010-2014 | 48 | 99% | 82% [74-89] |
| **Studies reporting resistance breakpoints\*** | | | |
| 1990-1994 | 1 | 0% | 0% [0-0] |
| 1995-1999 | 6 | 99% | 51% [21-81] |
| 2000-2004 | 22 | 99% | 68% [53-82] |
| 2005-2009 | 31 | 97% | 77% [69-84] |
| 2010-2014 | 45 | 99% | 83% [74-90] |
| **Studies with control strain stated** | | | |
| 1990-1994 | 6 | 93% | 3% [0-15] |
| 1995-1999 | 8 | 98% | 49% [26-72] |
| 2000-2004 | 29 | 99% | 62% [47-77] |
| 2005-2009 | 38 | 97% | 76% [69-83] |
| 2010-2014 | 50 | 99% | 82% [75-89] |
| **Studies with over 50 isolates** | | | |
| 1990-1994 | 2 | 85% | 1% [0-4] |
| 1995-1999 | 6 | 96% | 39% [23-55] |
| 2000-2004 | 20 | 99% | 65% [48-80] |
| 2005-2009 | 26 | 98% | 75% [66-83] |
| 2010-2014 | 29 | 99% | 82% [72-91] |

\* Testing standards including version or year

**Table S5: Azithromycin resistance in *S.* Typhi.** Resistant isolates are defined as having an MIC >16μg/ml [EUCAST 2014, BSAC 2012] or by disk diffusion, a zone diameter ≤18mm [BSAC 2012]. Sensitive isolates have an MIC ≤16μg/ml or zone diameter ≥19mm.

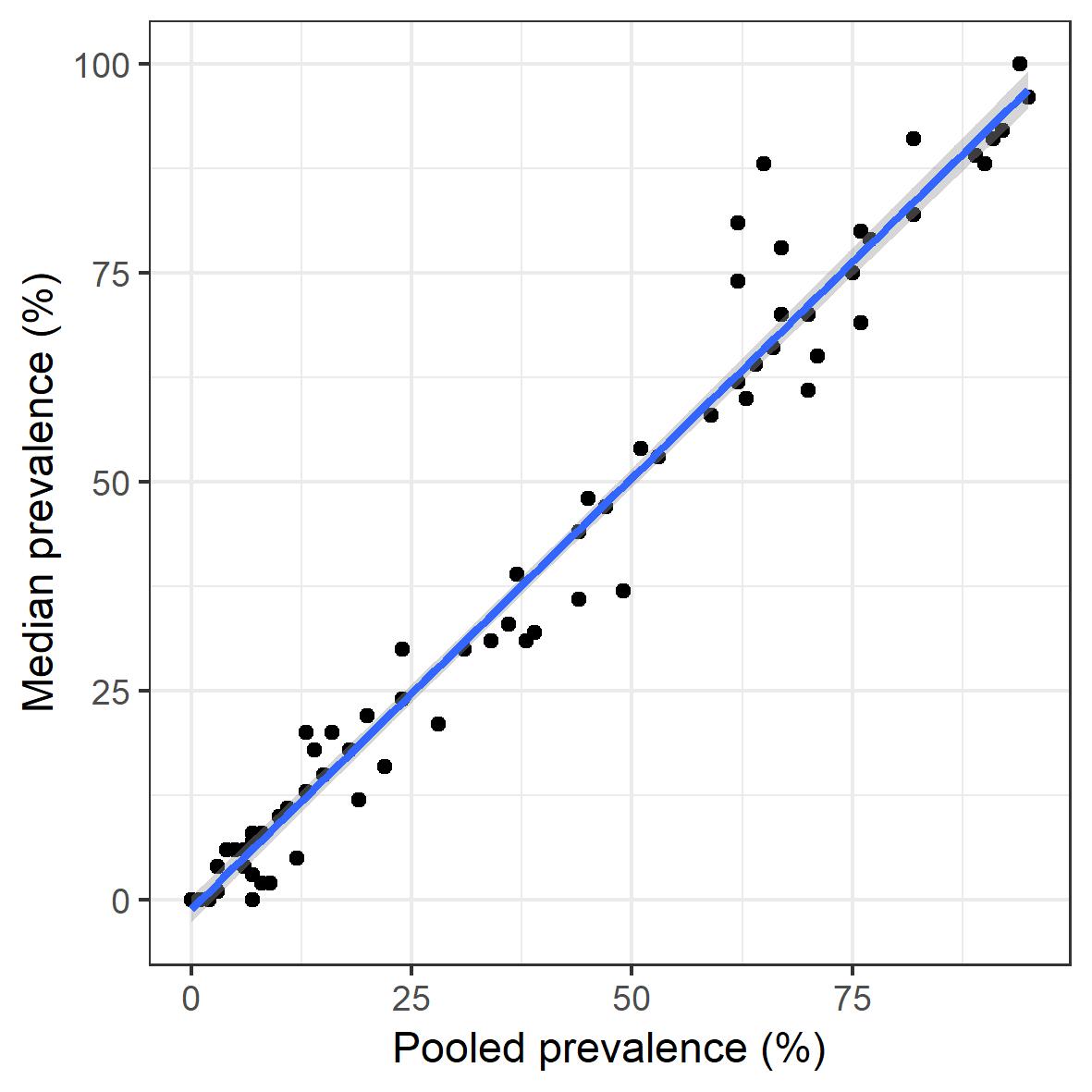
|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author (Year)** | **Country** | **Testing Method** | **Number examined (N)** | **Resistant, N (%)** |
| Chinh (2000) | Viet Nam | Agar dilution | 86 | 0 (0) |
| Capoor (2009) | India | E-test | 149 | 1 (1) |
| Kasper (2010) | Cambodia | E-test | 41 | 0 (0) |
| Ngoun (2012) | Cambodia | E-test | 102 | 0 (0) |
| Rai (2012)ᵇ | India | E-test | 80 | 27 (34) |
| Vlieghe (2012) | Cambodia | E-test | 20 | 1 (5) |
| Garg (2013) | India | E-test | 17 | 3 (7) |
| Jain (2013) | India | Disk-diffusion | 266 | 17 (6) |
| Koirala (2013) | Nepal | E-test | 218 | 0 (0) |
| Venkatesh (2013) | India | E-test | 132 | 0 (0) |
| Dutta (2014) | India | E-test | 77 | 0 (0) |
| Maltha (2014) | Burkina Faso | E-test | 12 | 0 (0) |
| Phoba (2014) | DRC | E-test | 18 | 0 (0) |
| Srirangaraj (2014) | India | E-test | 16 | 2 (13) |
| Ikram (2015) | Pakistan | Disk-diffusion | 71 | 60 (85) |
| Chande (2016) | India | E-test | 108 | 0 (0) |
| Iyer (2017) | India | E-test | 217 | 0 (0) |
| Khanal (2017) | Nepal | Agar dilution | 74 | 0 (0) |
| Kuijpers (2017) | Cambodia | E-test | 64 | 0 (0) |
| Okanda (2018) | Bangladesh | Microdilution | 18 | 0 (0) |
| Sharma (2018) | India | E-test | 95 | 1 (1) |
| Joshi (2019) | India | E-test | 300 | 0 (0) |

**Table S6: Studies included in the systematic review**

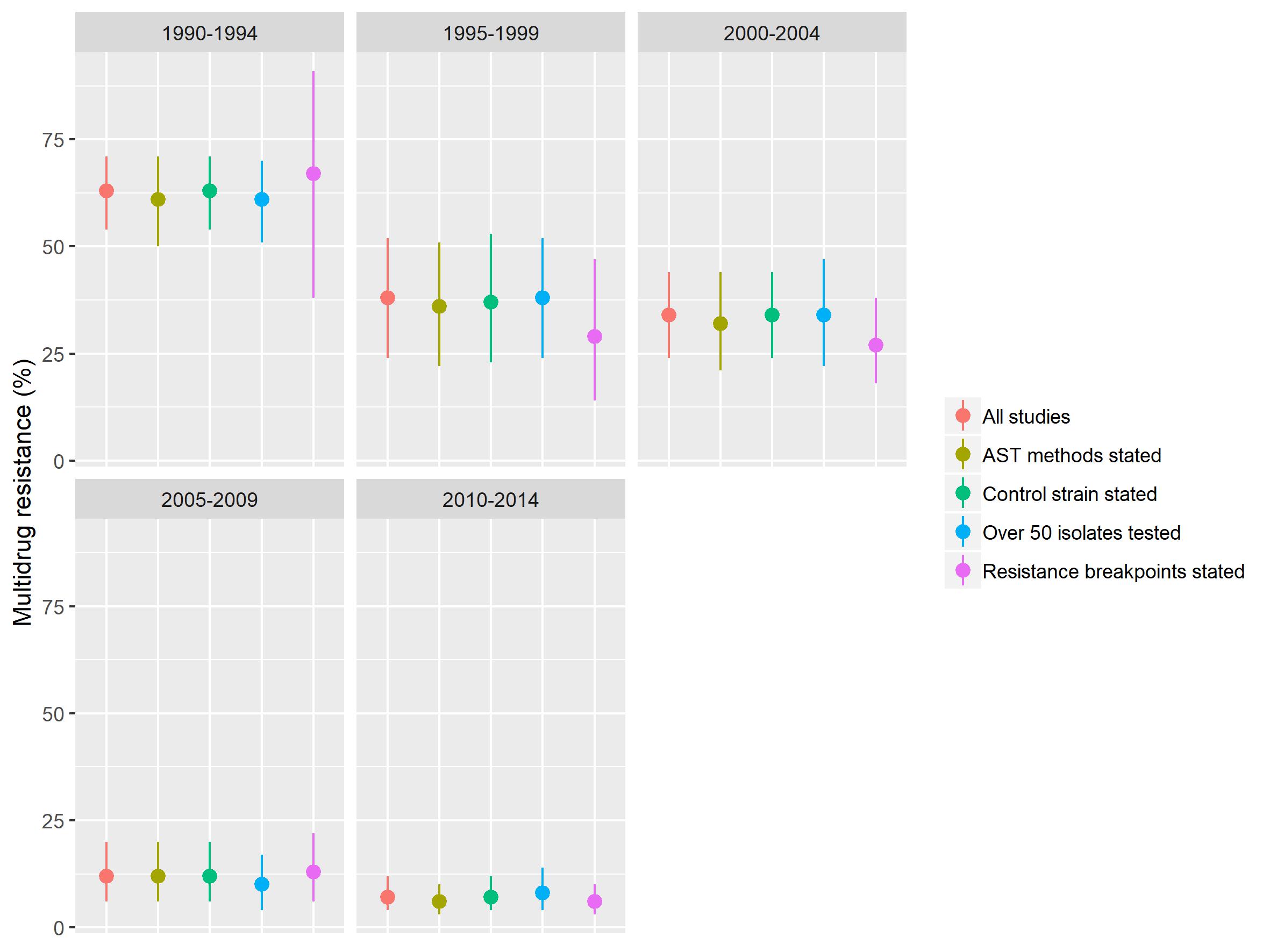
|  |  |
| --- | --- |
| **Author (Year)** | **Citation** |
| Aatekah (2010) | Aatekah O, Shazia S, Umber Z, Arjumand R, Zaidi AKM. Incidence of typhoid bacteremia in infants and young children in southern coastal Pakistan. *Pediatr Infect Dis J* 2010; 29(11): 1035-9. |
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**Figures:**

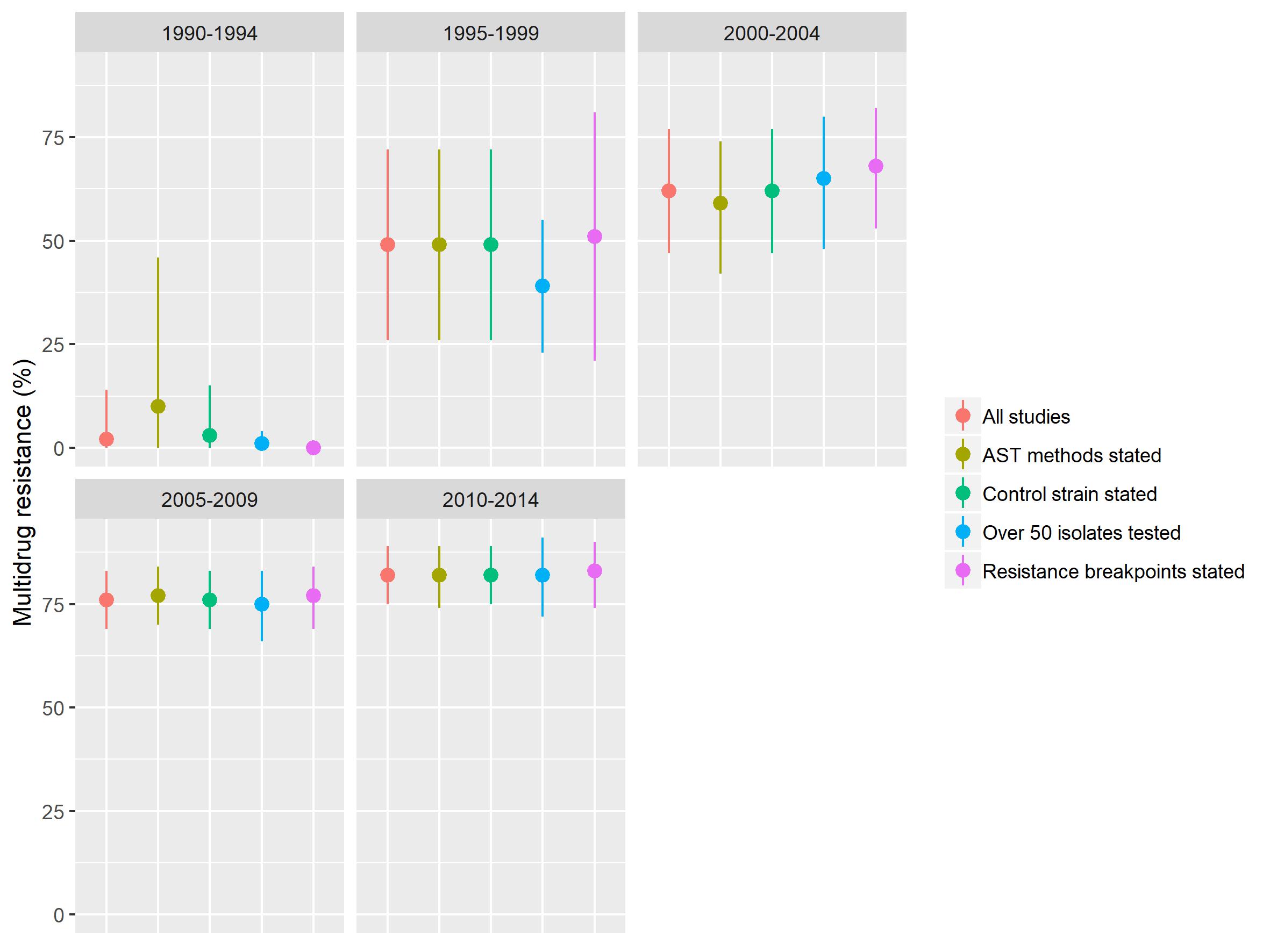
**Figure S1. Meta-analysis and median prevalence comparison.** A scatter graph to compare the median prevalence and pooled prevalence estimates of resistance from a random effects meta-analysis, for every subgroup in the study. Linear regression line fit to the data with an intercept of -1.49 and a coefficient of 1.04. High correlation was observed with an r2 of 0.97 and p<0.001.

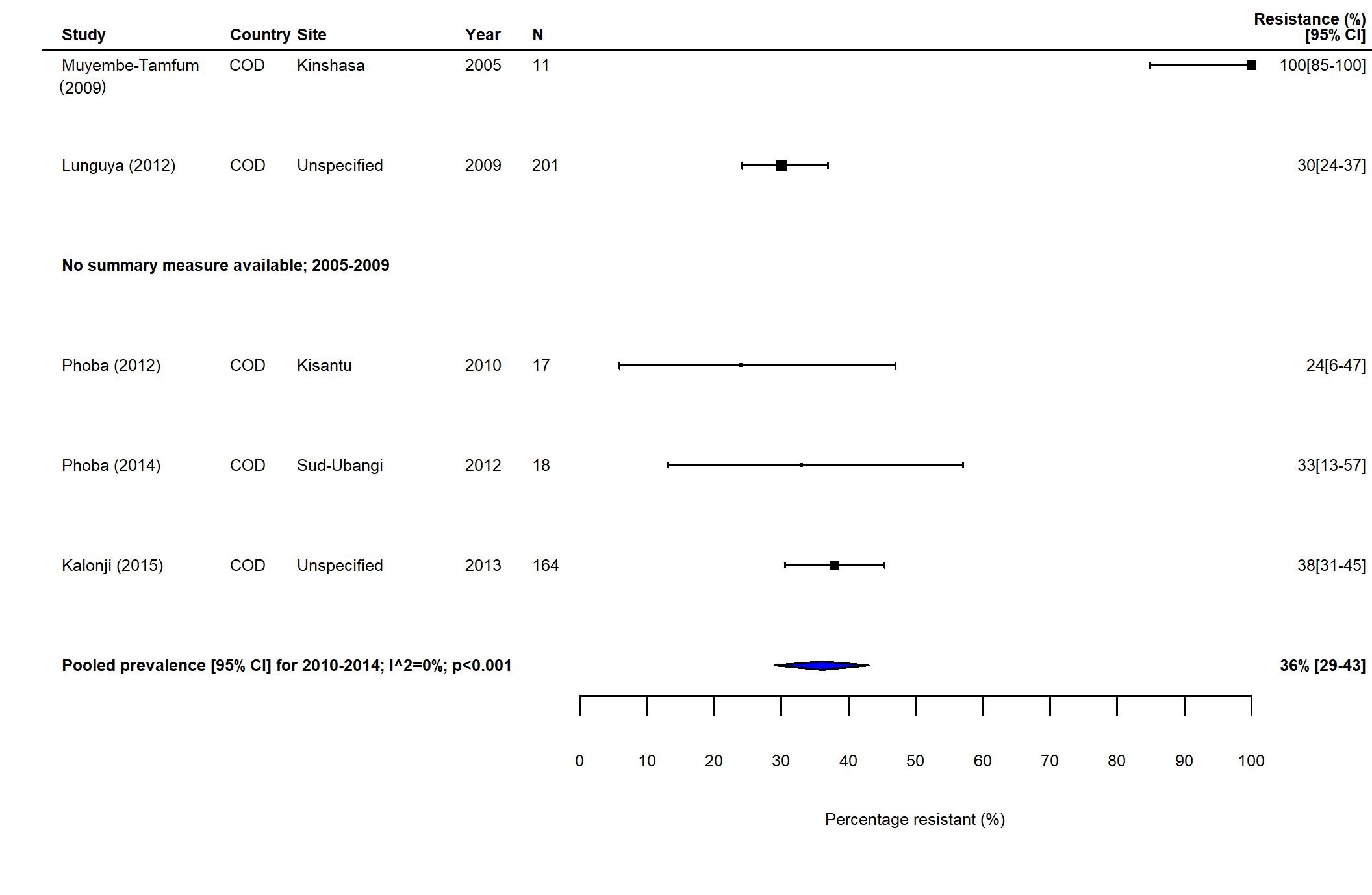


**Figure S2a. Sensitivity analysis:** Random effects metaanalysis results for studies on MDR *S.* Typhi in South Asia, comparing results for all studies (red) with only those reporting AST methods used (olive); (c) internal control strain reported (green), and those on over 50 isolates of *S.* Typhi (blue), resistance breakpoints clearly stated (pink), grouped by 5-year period.

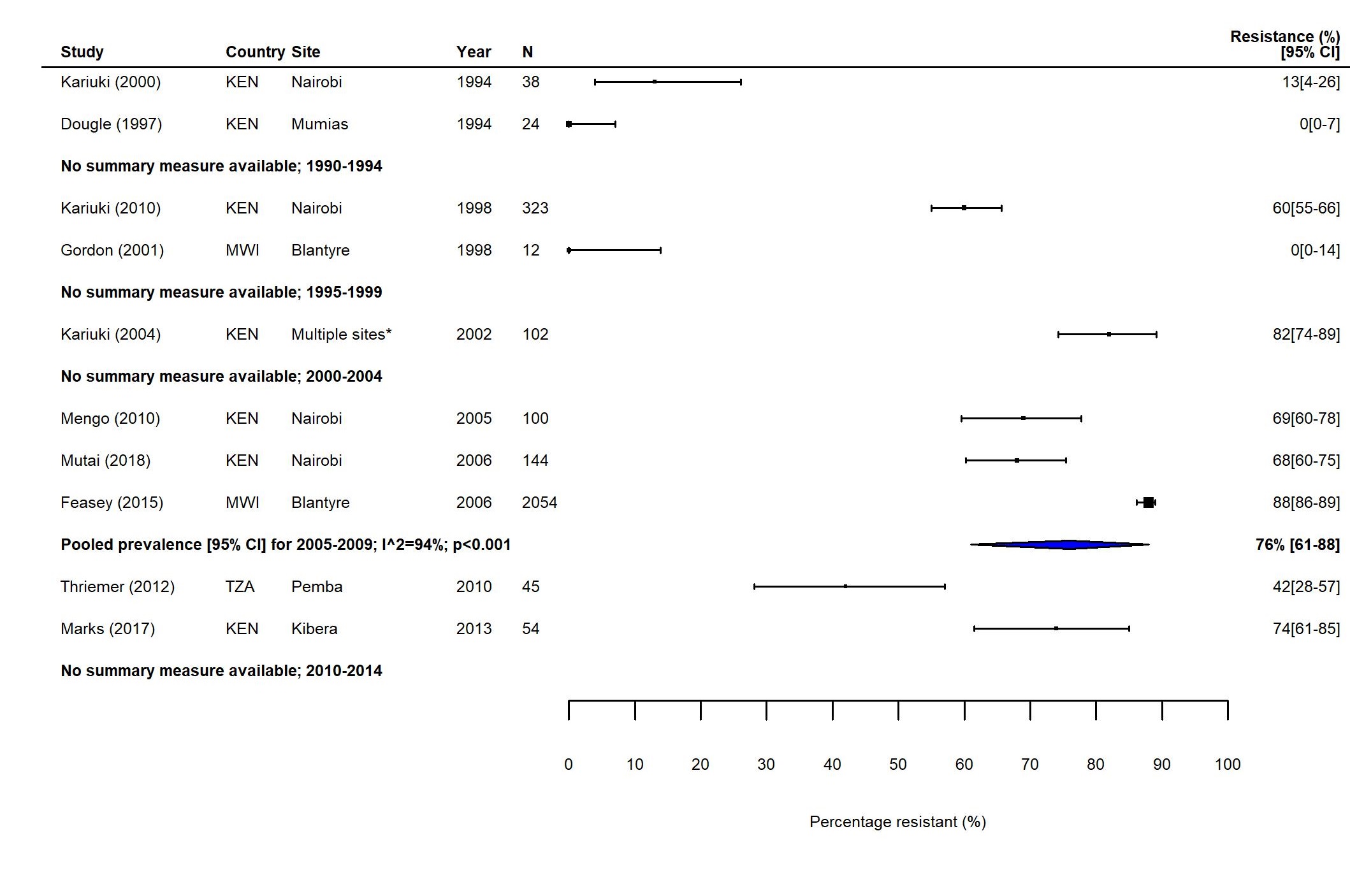
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**Figure S2b. Sensitivity analysis:** Random effects metaanalysis results for studies on FQNS *S.* Typhi in South Asia, comparing results for all studies (red) with only those reporting AST methods used (olive); (c) internal control strain reported (green), and those on over 50 isolates of *S.* Typhi (blue), resistance breakpoints clearly stated (pink), grouped by 5-year period.

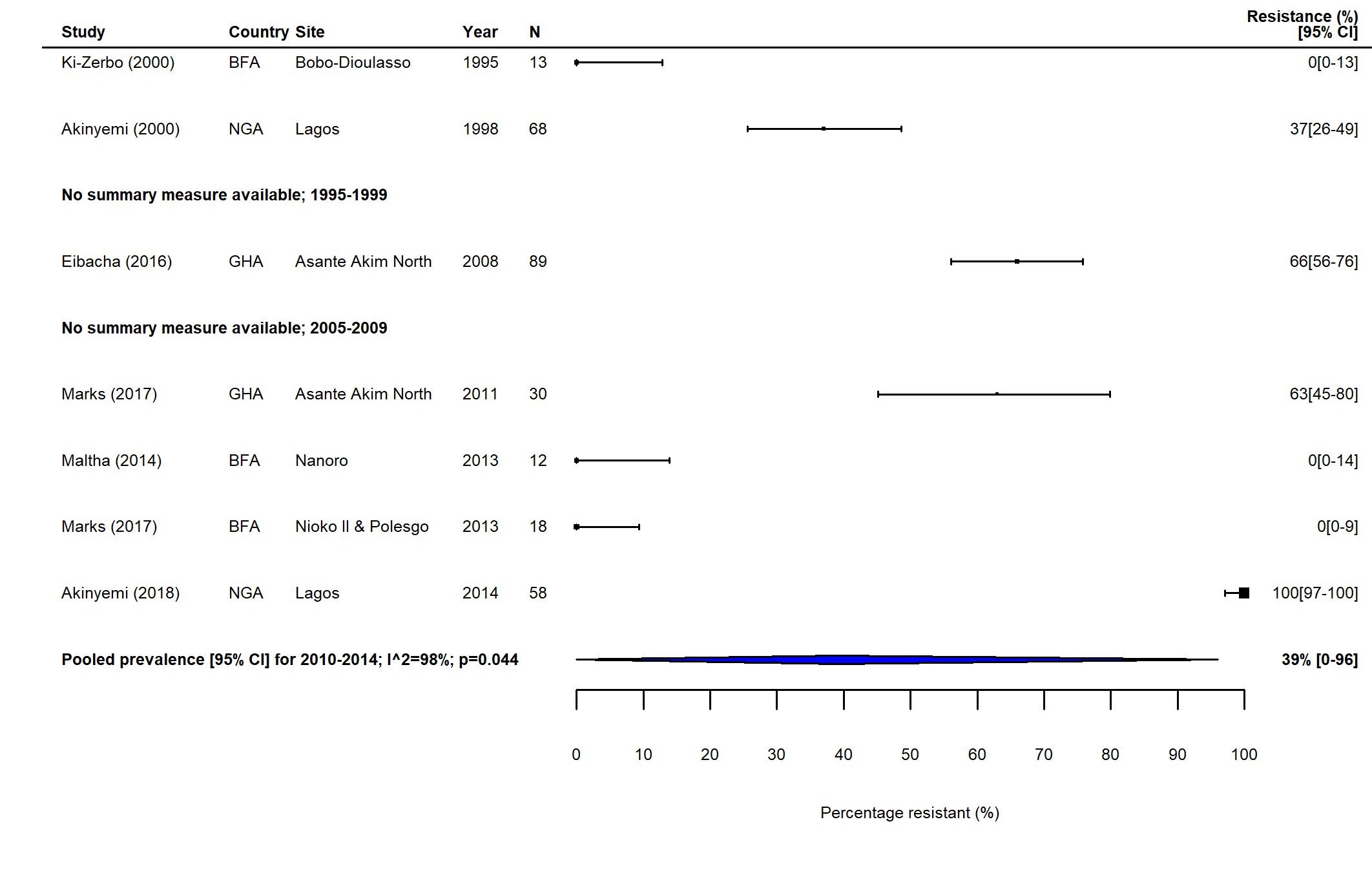
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**Figure S3.** **MDR *S.* Typhi in sub-Saharan Africa:** Forest plots illustrating the prevalence of MDR amongst *S.* Typhi isolates in sub-Saharan Africa, grouped by five-year time-periods. Individual study results are displayed with 95% confidence intervals, the pooled prevalence [95%CI] for each subgroup is represented by the blue diamond: (a) Central sSA; (b) Eastern sSA; (c) Western sSA. Multidrug resistance is defined as concurrent resistance against ampicillin, chloramphenicol and co-trimoxazole. ****

(a)

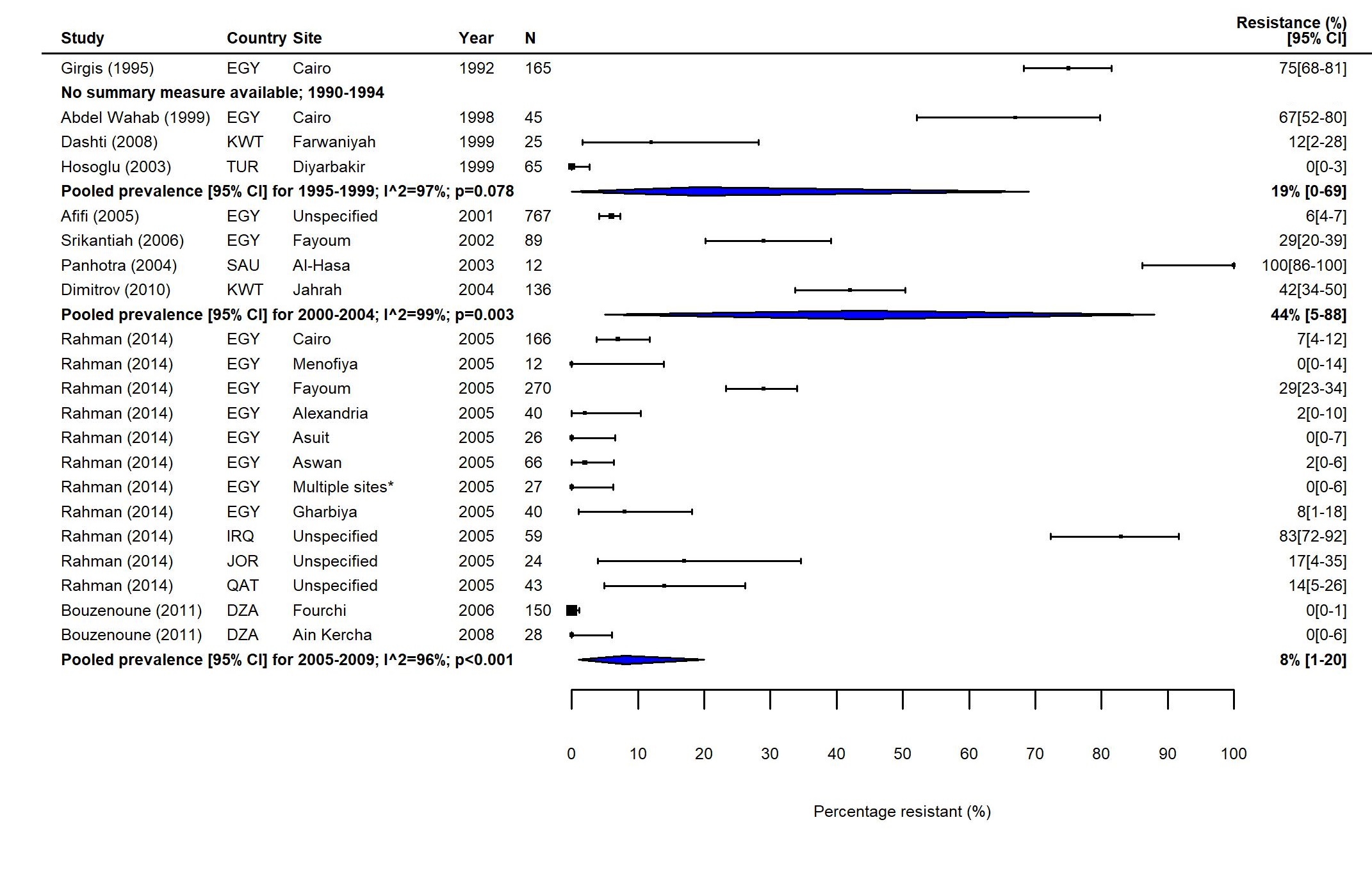


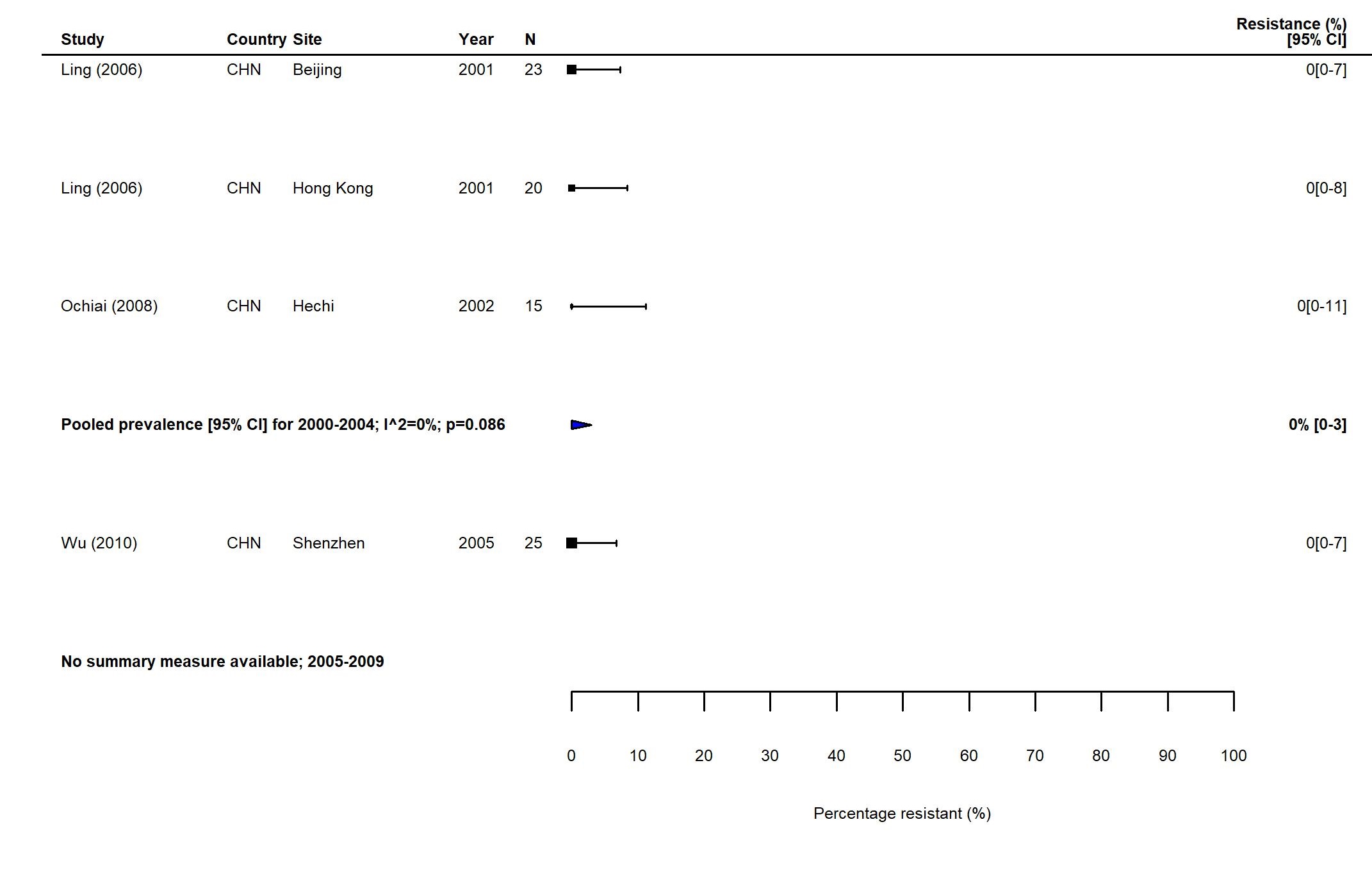
(b)



(c)

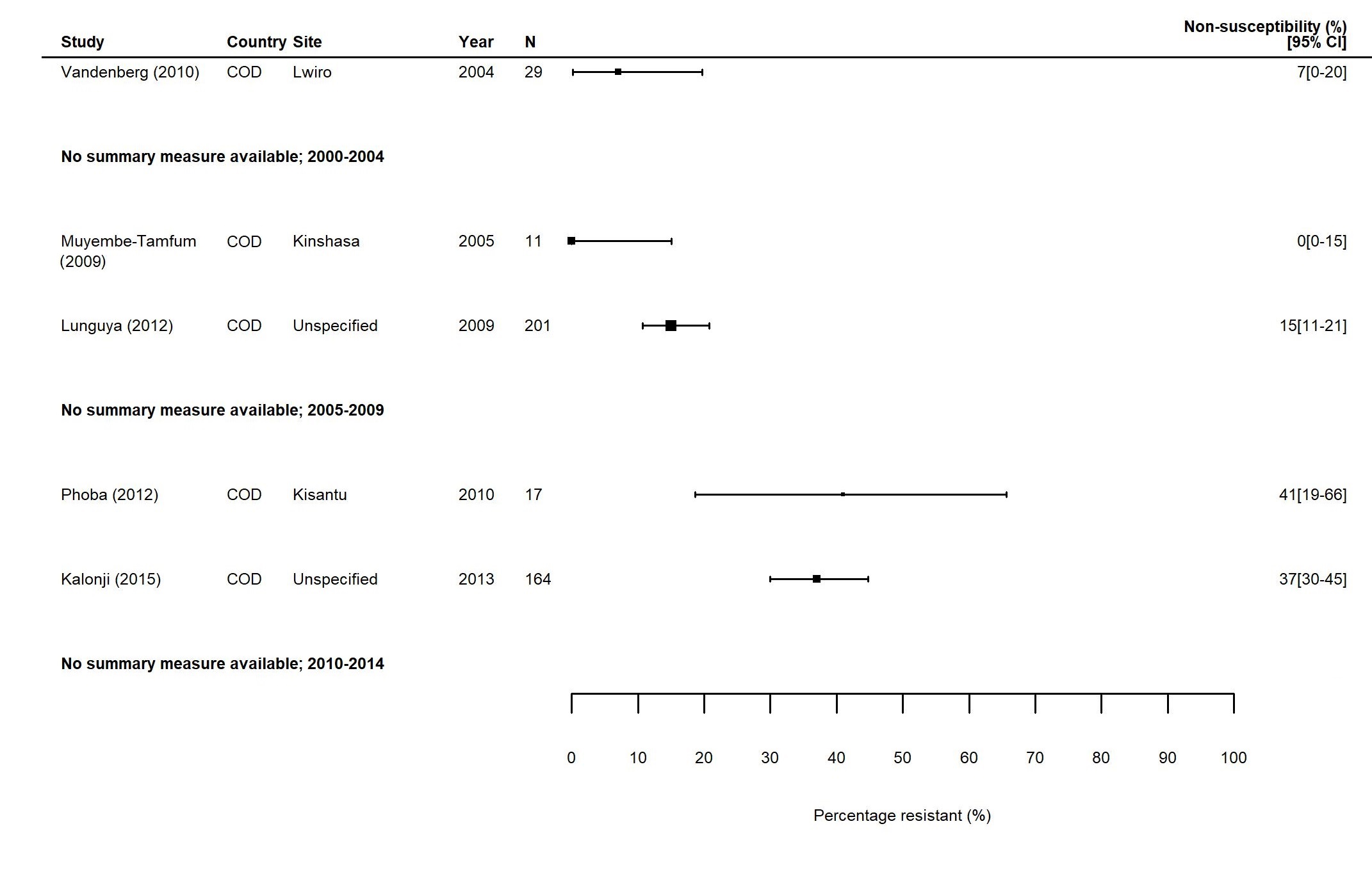
**Figure S4. MDR *S.* Typhi in North Africa and the Middle East (NAME):** Forest plots illustrating the prevalence of MDR amongst *S.* Typhi isolates in NAME, grouped by five-year time-periods. Individual study results are displayed with 95% confidence intervals, the pooled prevalence [95%CI] for each subgroup is represented by the blue diamond. Multidrug resistance is defined as concurrent resistance against ampicillin, chloramphenicol and co-trimoxazole.

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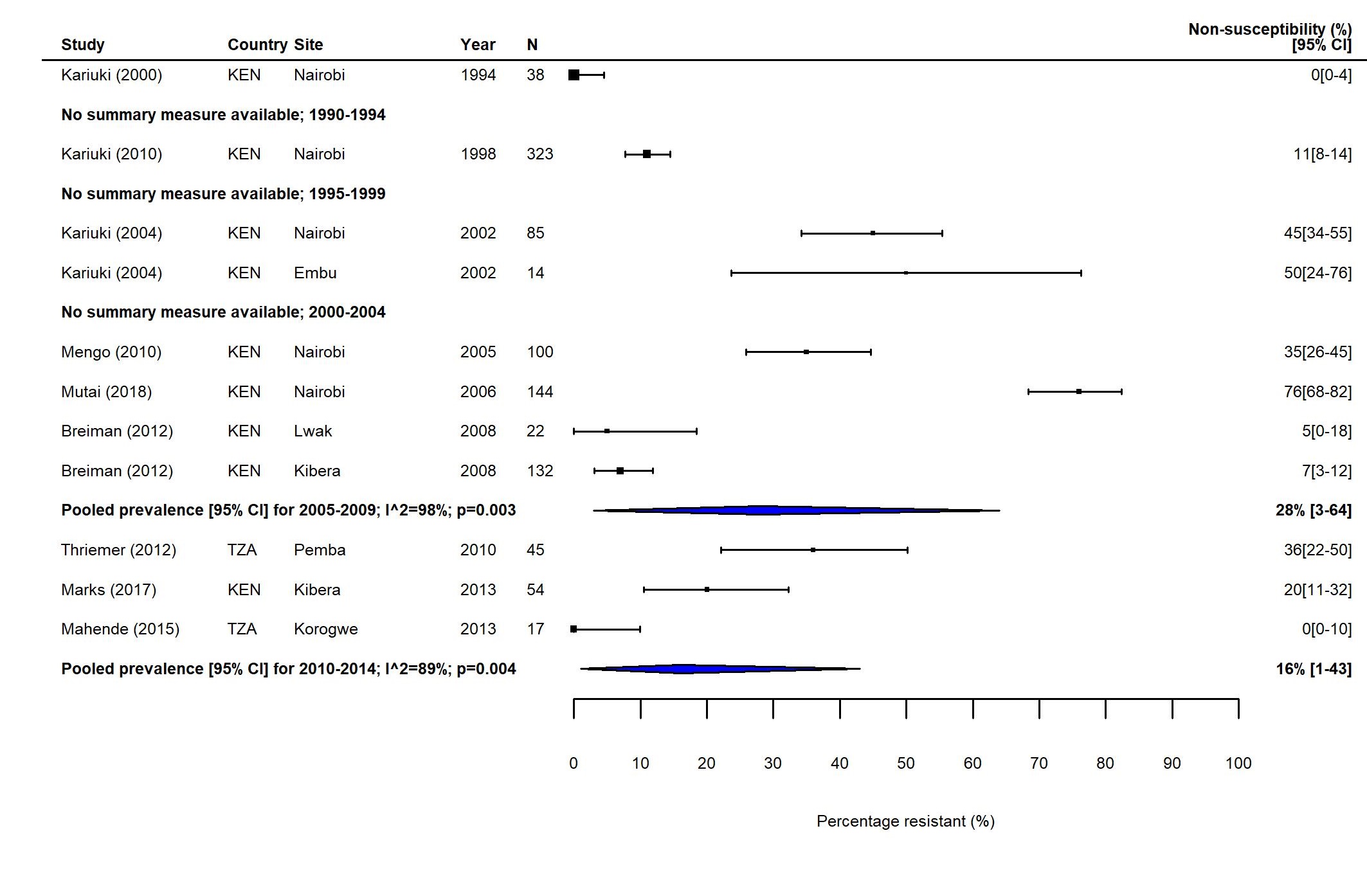
**Figure S5. MDR *S.* Typhi in East Asia:** Forest plots illustrating the prevalence of MDR amongst *S.* Typhi isolates in East Asia, grouped by five-year time-periods. Individual study results are displayed with 95% confidence intervals, the pooled prevalence [95%CI] for each subgroup is represented by the blue diamond. Multidrug resistance is defined as concurrent resistance against ampicillin, chloramphenicol and co-trimoxazole. ****

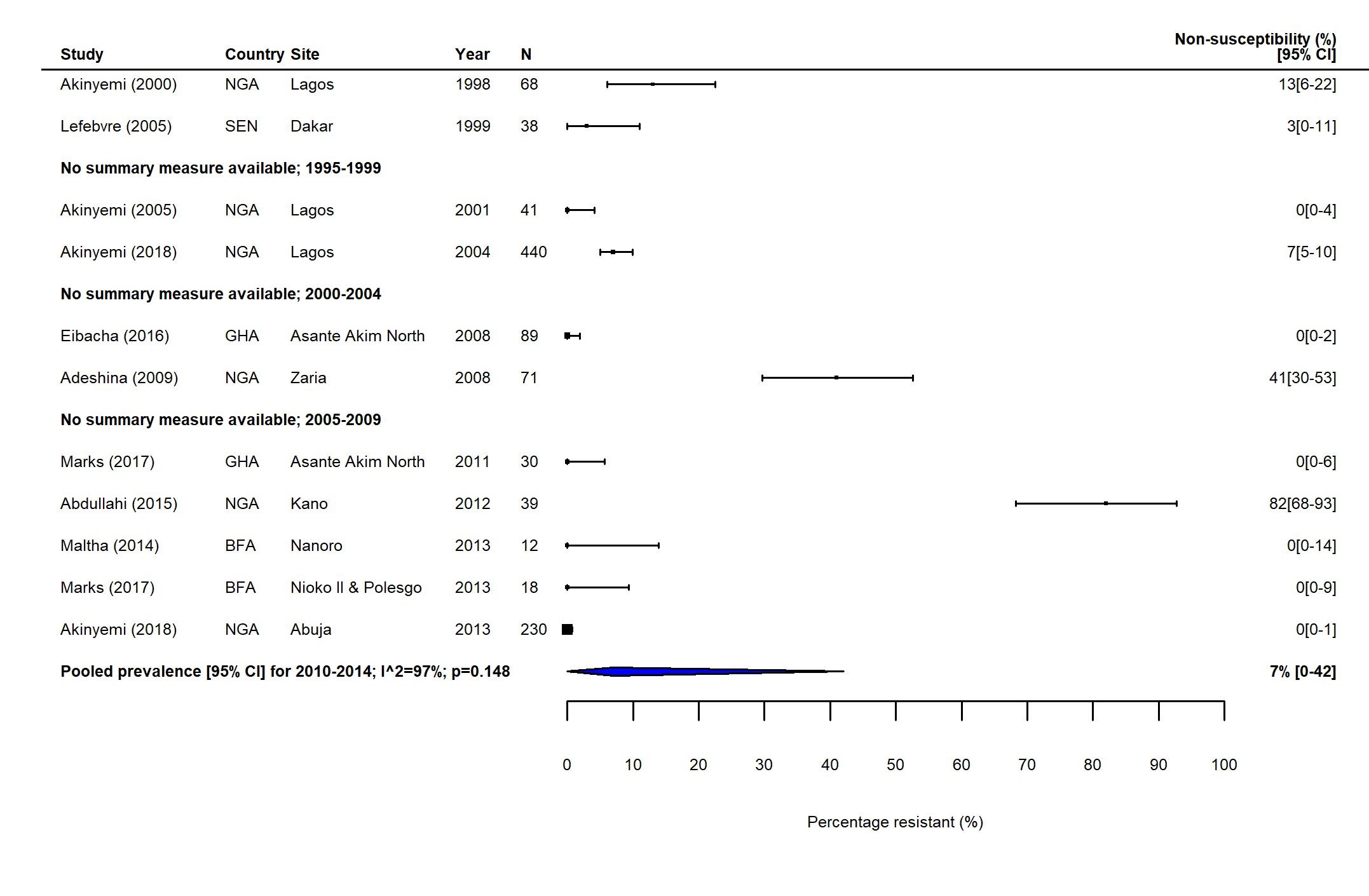
**Figure S6.** **FQNS *S.* Typhi in sub-Saharan Africa:** Forest plots illustrating the prevalence of FQNS amongst *S.* Typhi in sub-Saharan Africa, grouped by five-year time-periods. Individual study results are displayed with 95% confidence intervals, the pooled prevalence [95%CI] for each subgroup are represented by the blue diamonds: (a) Central sSA; (b) Eastern sSA; (c) Western sSA.

To allow the analysis of resistance trends over time despite typhoid-specific breakpoint changes for ciprofloxacin (CLSI, 2012) coming into effect during our study (1990-2018), we categorised intermediate (ciprofloxacin MIC 0.12–0.5 μg/ml) and resistant isolates (≥ 1 μg/ml) according to the updated breakpoints, as well as isolates with 'decreased ciprofloxacin (or fluoroquinolone) susceptibility' (ciprofloxacin MIC 0.125–1.0 μg/ml) and nalidixic acid resistant isolates (as proxy marker for 'decreased ciprofloxacin (or fluoroquinolone) susceptibility') as fluoroquinolone non-susceptible (FQNS).

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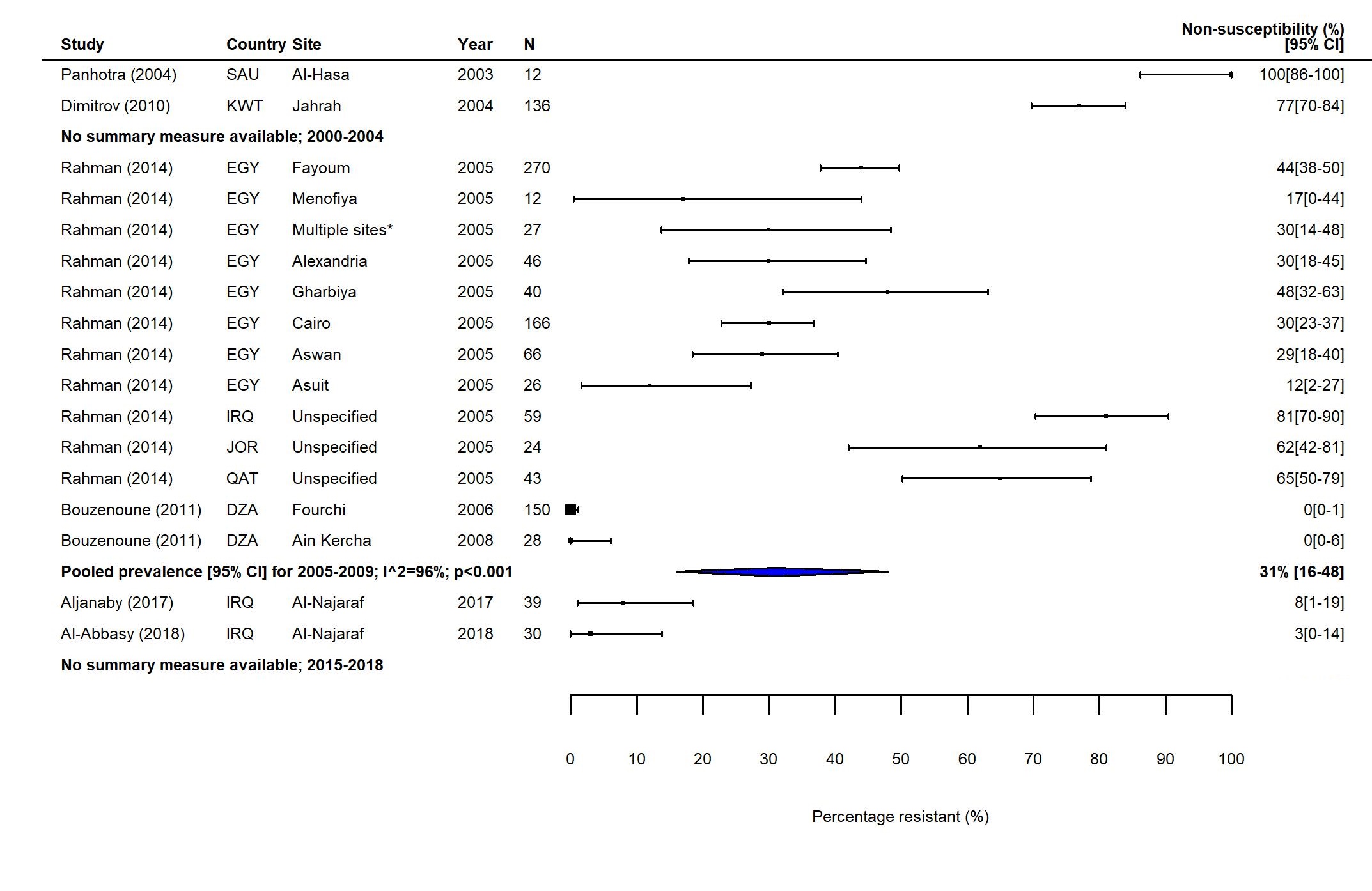
(a)

**** (b)

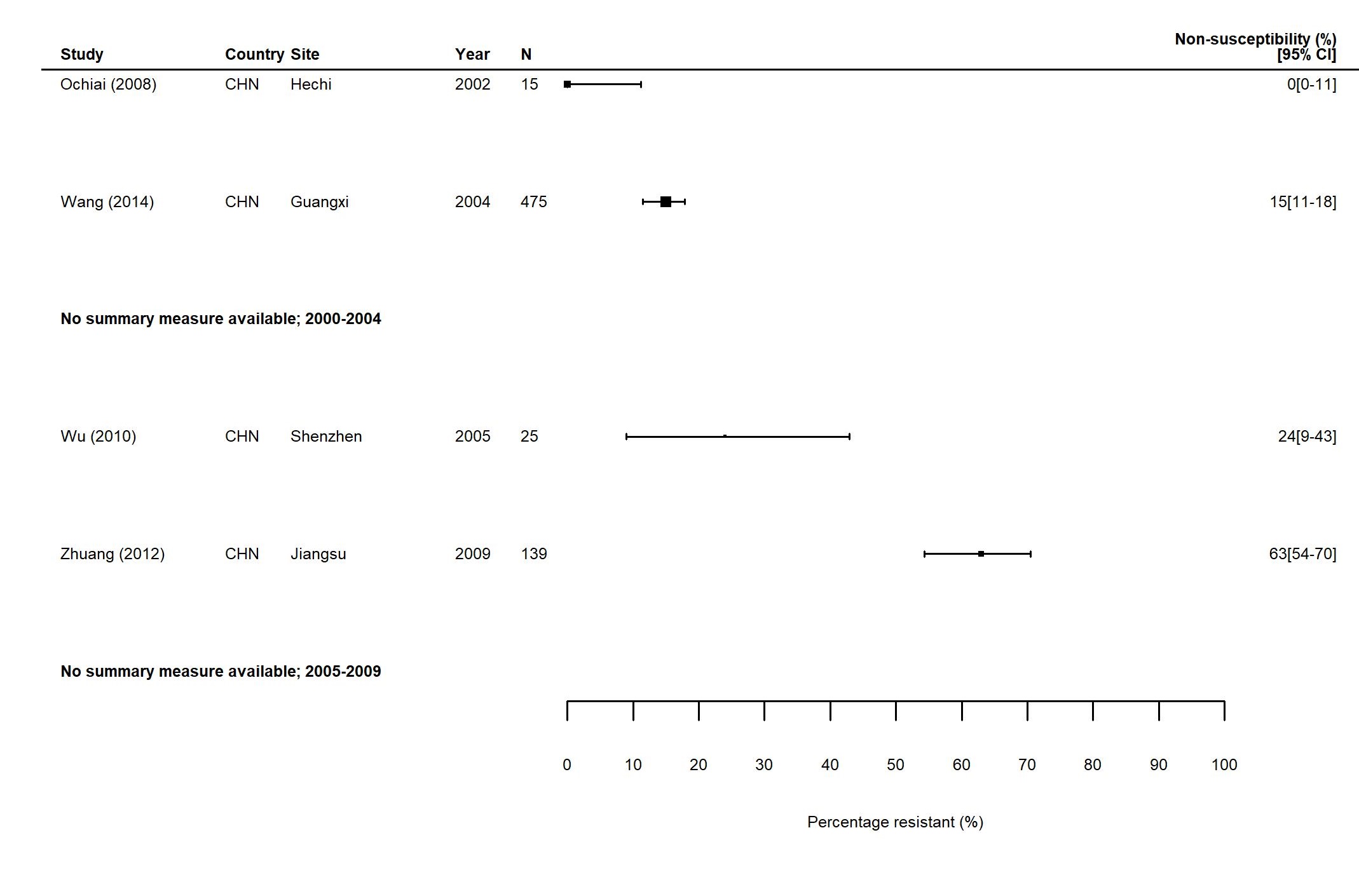


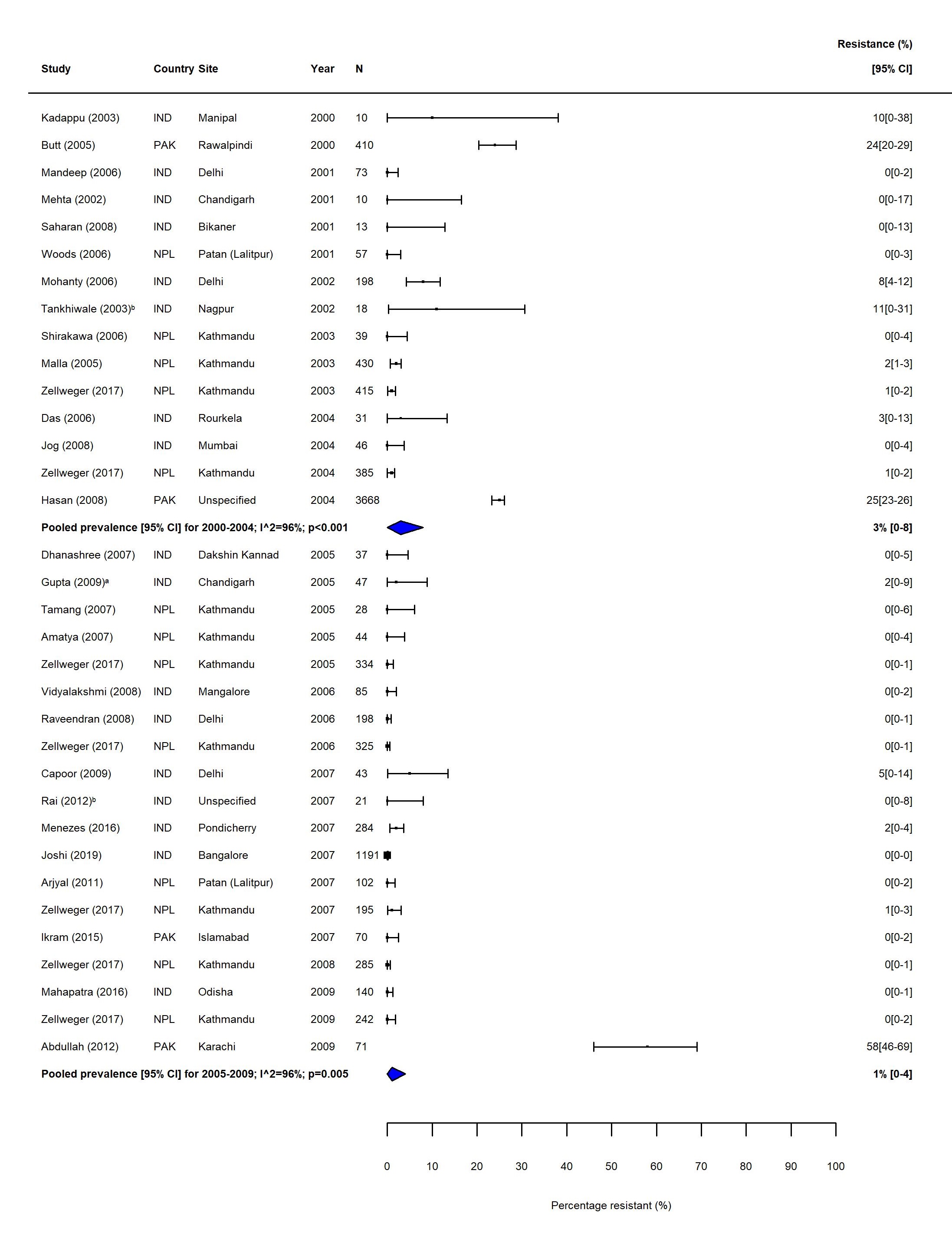
(c)

**Figure S7.** **FQNS *S.* Typhi in North Africa and the Middle East (NAME):** Forest plots illustrating the prevalence of FQNS amongst *S.* Typhi in NAME, grouped by five-year time-periods. Individual study results are displayed with 95% confidence intervals, the pooled prevalence [95%CI] for each subgroup are represented by the blue diamonds.

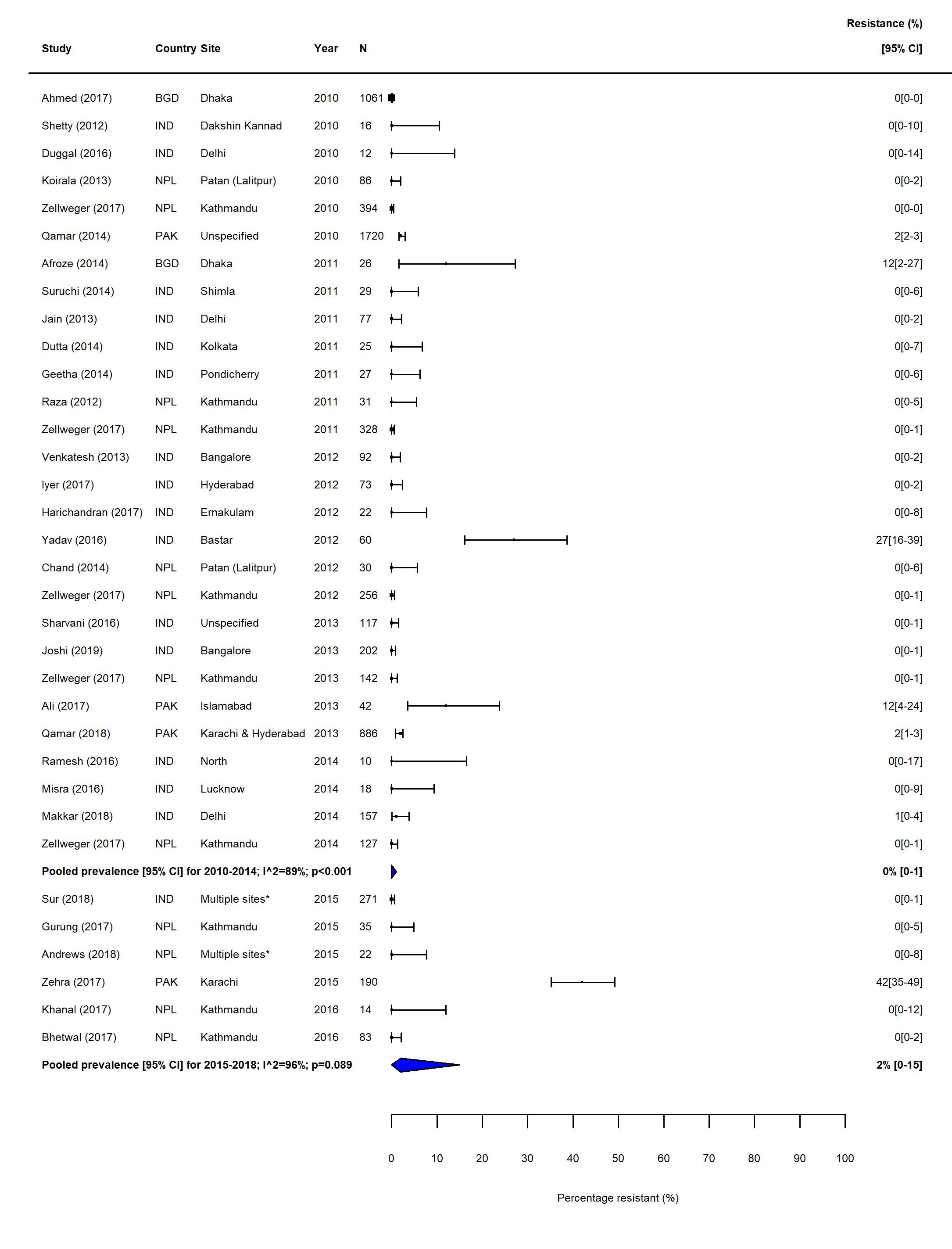
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**Figure S8.** **FQNS *S.* Typhi in East Asia:** Forest plots illustrating the prevalence of FQNS amongst *S.* Typhi in East Asia, grouped by five-year time-periods. Individual study results are displayed with 95% confidence intervals, the pooled prevalence [95%CI] for each subgroup are represented by the blue diamonds.

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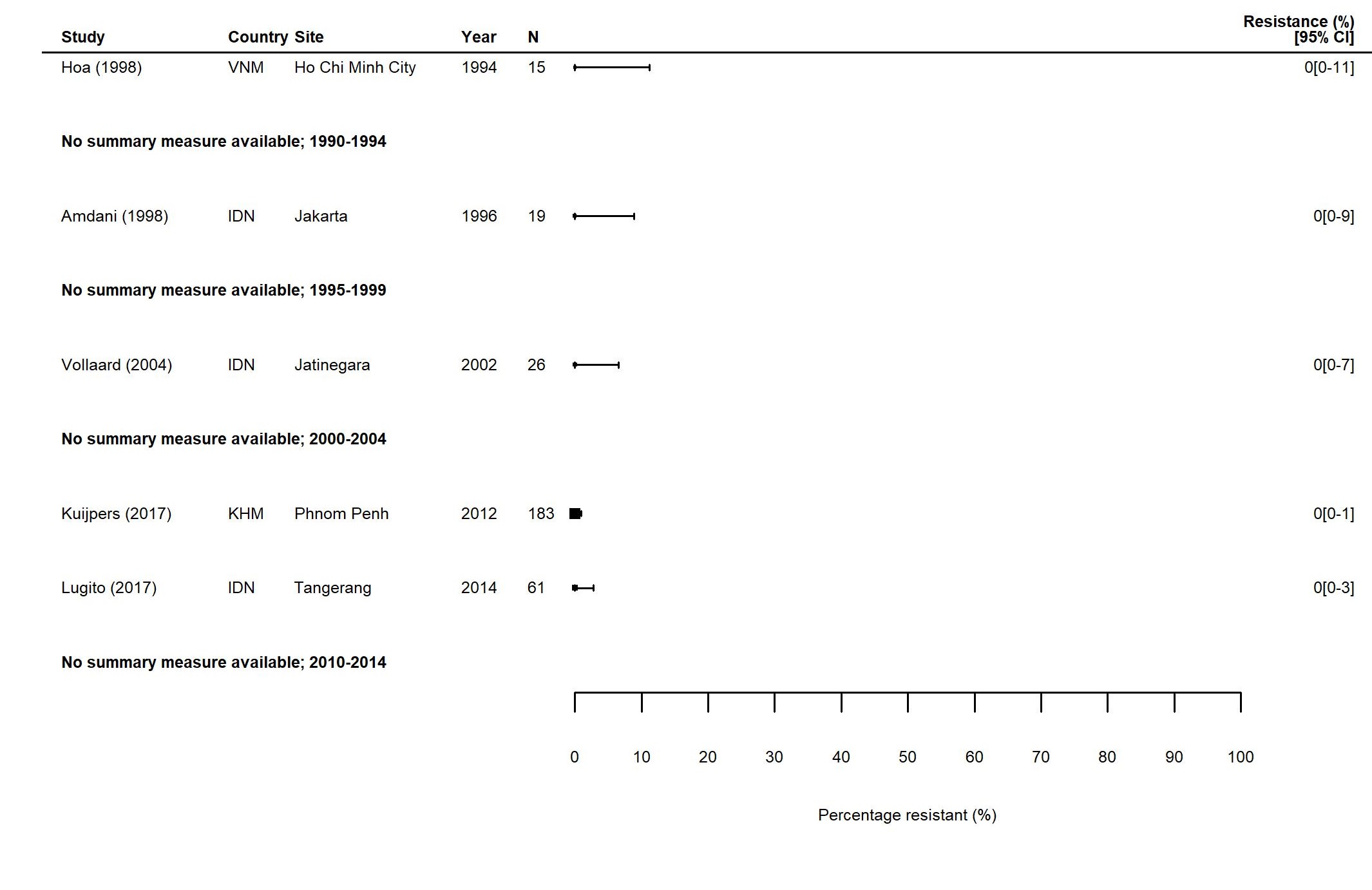
**Figure S9. MDR *S.* Paratyphi in South Asia:** Forest plots illustrating the prevalence of MDR amongst *S.* Paratyphi isolates in South Asia, grouped by five-year time-periods. Individual study results are displayed with 95% confidence intervals, the pooled prevalence [95%CI] for each subgroup is represented by the blue diamond: (a) 1990-1999; (b) 2000-2009; (c) 2010-2018. Multidrug resistance is defined as concurrent resistance against ampicillin, chloramphenicol and co-trimoxazole.  (a) 

(b)

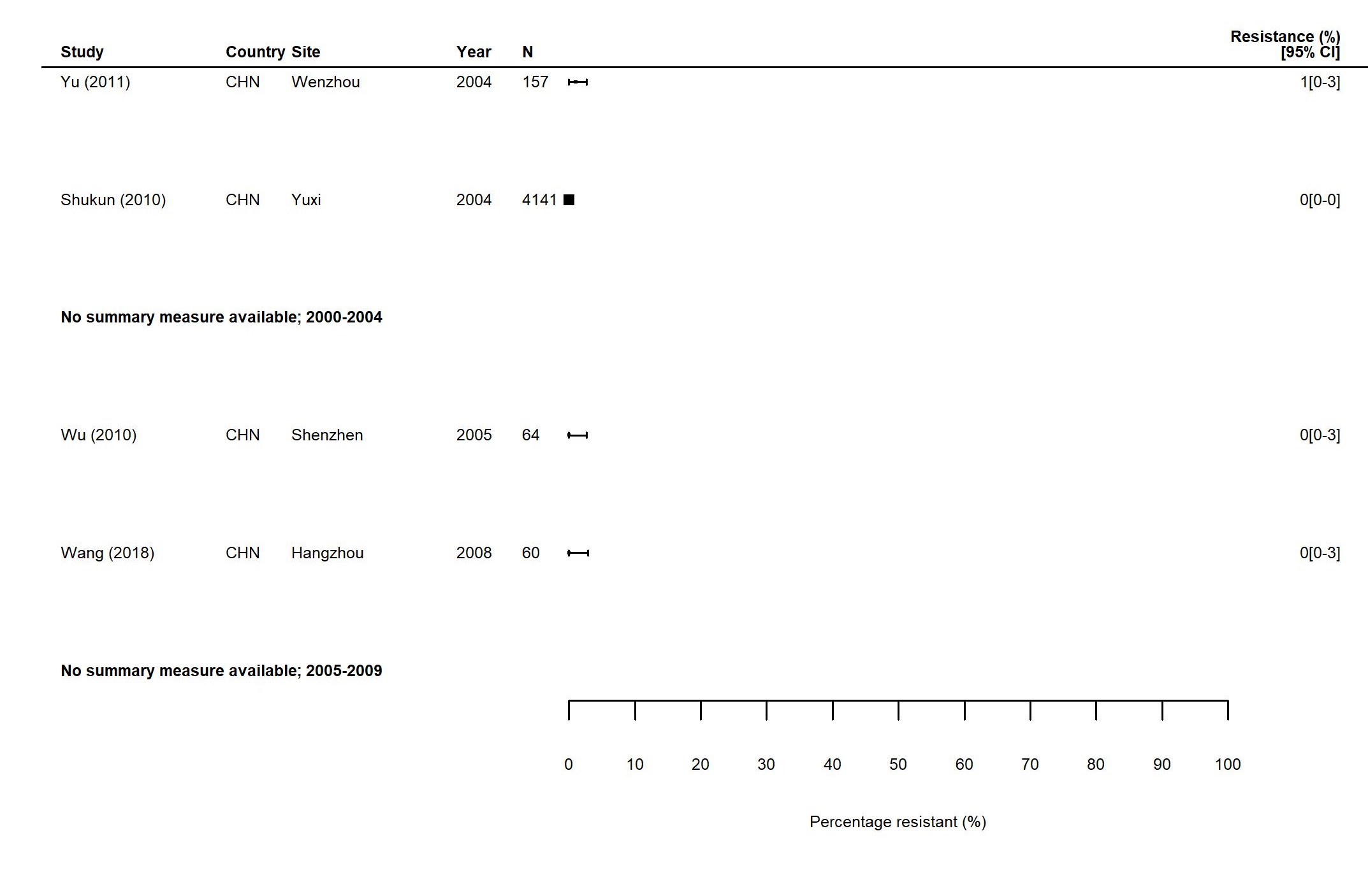


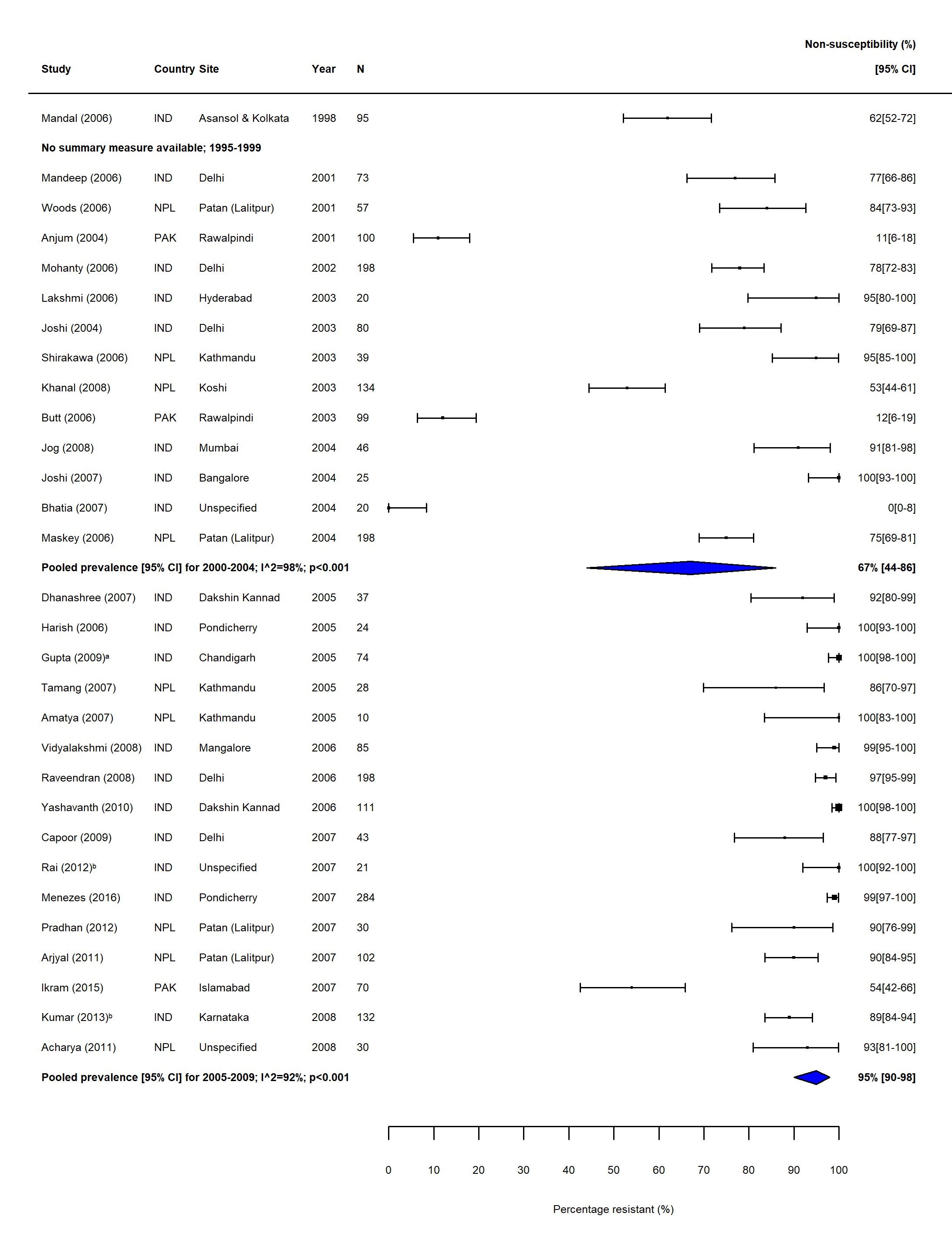
(c)

**Figure S10. MDR *S.* Paratyphi in Southeast Asia:** Forest plots illustrating the prevalence of MDR amongst *S.* Paratyphi isolates in Southeast Asia, grouped by five-year time-periods. Individual study results are displayed with 95% confidence intervals, the pooled prevalence [95%CI] for each subgroup is represented by the blue diamond. Multidrug resistance is defined as concurrent resistance against ampicillin, chloramphenicol and co-trimoxazole.

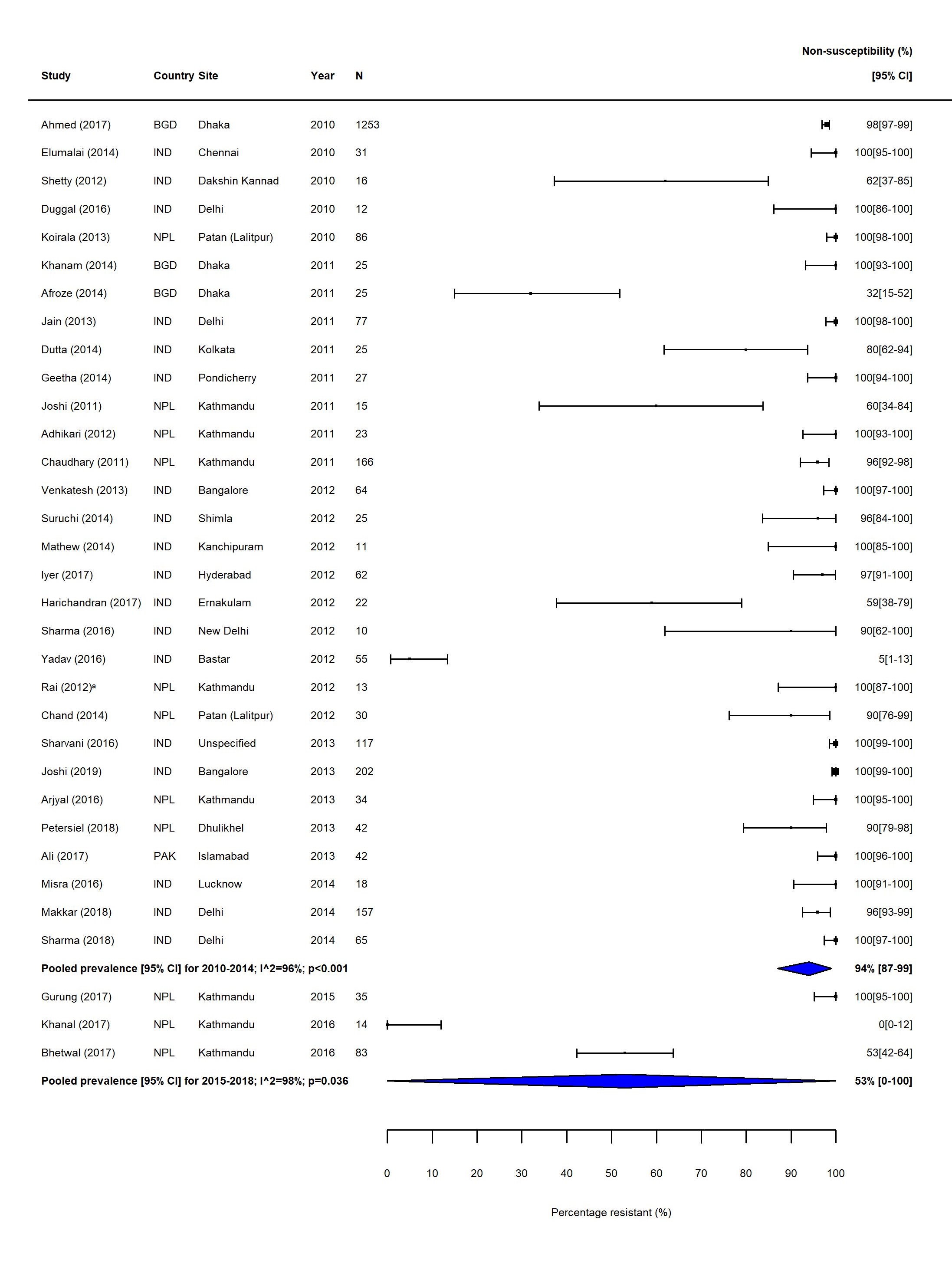


**Figure S11. MDR *S.* Paratyphi in East Asia:** Forest plots illustrating the prevalence of MDR amongst *S.* Paratyphi isolates in East Asia, grouped by five-year time-periods. Individual study results are displayed with 95% confidence intervals, the pooled prevalence [95%CI] for each subgroup is represented by the blue diamond. Multidrug resistance is defined as concurrent resistance against ampicillin, chloramphenicol and co-trimoxazole.

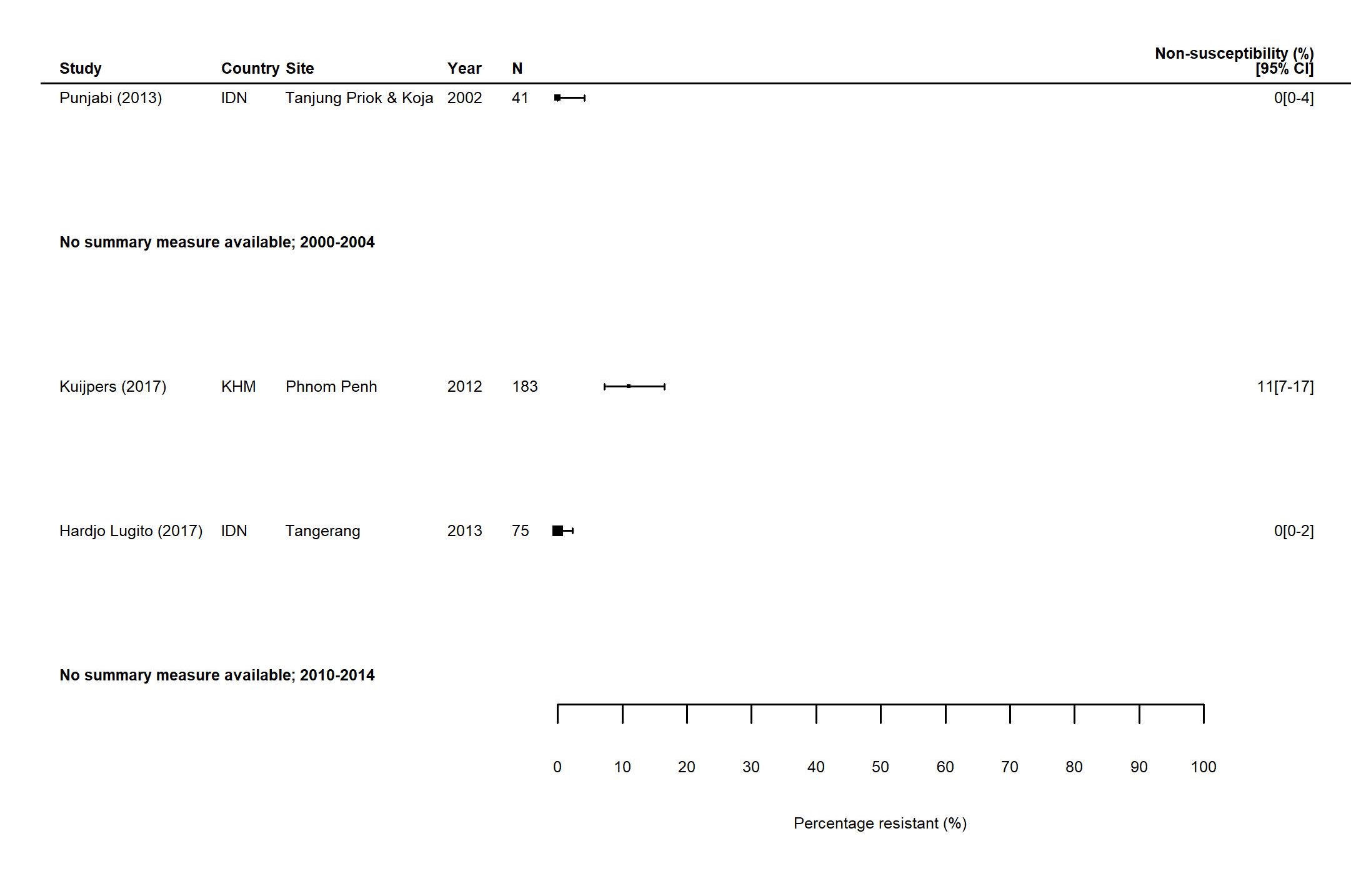
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**Figure S12. FQNS *S.* Paratyphi in South Asia:** Forest plots illustrating the prevalence of FQNS amongst *S.* Paratyphi in South Asia, grouped by five-year time-periods. Individual study results are displayed with 95% confidence intervals, the pooled prevalence [95%CI] for each subgroup are represented by the blue diamonds.: (a) 1990-2009; (b) 2010-2018.

(a)



(b)

**Figure S13. FQNS *S.* Paratyphi in Southeast Asia:** Forest plots illustrating the prevalence of FQNS amongst *S.* Paratyphi in Southeast Asia, grouped by five-year time-periods. Individual study results are displayed with 95% confidence intervals, the pooled prevalence [95%CI] for each subgroup are represented by the blue diamonds.

**Figure S14.** **FQNS *S.* Paratyphi in East Asia:** Forest plots illustrating the prevalence of FQNS amongst *S.* Paratyphi in East Asia, grouped by five-year time-periods. Individual study results are displayed with 95% confidence intervals, the pooled prevalence [95%CI] for each subgroup are represented by the blue diamonds. 