**Supplementary Table 1**

Evidence summary of systematic literature review (O’Brien et al. [26])

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| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Studies** | **Baseline measure-ments** | **Single MDA** | **Multiple MDA** | **Outcome Macrolide** | **Outcome Non-Macrolides** |
| **Gut bacteria** | **Treated children** | Seidman JC, Int J epidemiol, 2014[39](#_ENREF_39) | Yes | X |  | Increase in AZM-resistant *E. coli* from 21% (bl) to 61% (1m), 42% (3m), 23% (6m) and higher at each time point c/w controls. | No data. |
| Doan T, NEJM, 2019[19](#_ENREF_19) | No |  | X | Determinants of MLSB-resistance more prevalent in the communities that received azithromycin (68%) than in those that did not (46%). | No evidence of a significant between-group difference. |
| **Household contacts** | Bloch EM, Am J Trop Med Hyg, 2017[40](#_ENREF_40) | No |  | X | Moderate rates of AZM-resistant *E. coli* (17%) among children born after the last MDA. | No data. |
| **Naso-pharyngeal bacteria** | **Treated children** | Leach AJ, Clin Inf Dis, 1997[41](#_ENREF_41) | Yes | X |  | Increase in AZM-resistant *S. pneumoniae* from 1.9% (bl) to 55% (2-3w), 35% (2m), and 5.9% (6m). | No data. |
| Coles CL, Clin Inf Dis, 2013[42](#_ENREF_42) | Yes | X |  | Increase in AZM-resistant *S. pneumoniae* from 36% (bl) to 82% (6m). | No consistent pattern for *S. pneumoniae* resistance to COT or PEN. |
| Gaynor BD, BJO, 2003[43](#_ENREF_43) | No | X |  | No AZM-resistant *S. pneumoniae.* | No data. |
| Batt SL, Antimicr agents Chemother, 2003[44](#_ENREF_44) | Yes | X |  | No increase in ERY-resistant *S. pneumoniae*. | No consistent pattern for *S. pneumoniae* resistance to COT or PEN. |
| Fry AM, Clin Inf Dis, 2002[45](#_ENREF_45) | Yes | X |  | Increase in AZM-resistant S*. pneumoniae* from 0% (10d) to 4.5% (6m) | No consistent pattern for *S. pneumoniae* resistance to PEN, CLI, SULF or CHLOR |
| Burr SE, WHO Bulletin, 2014[46](#_ENREF_46) | No | X | X | No relevant increase in AZM-resistant *S. pneumoniae* until 6m after MDA (0% to 0.9%). No difference of AZM-resistant *S. pneumoniae* after 3 versus 1 MDA round (0.9% vs. 0.3%, 6m vs. 30m). | No data. |
| Doan T, NEJM, 2019[19](#_ENREF_19) | No |  | X | Increase in ERY-resistant *S. pneumoniae* in treatment (12%) vs. placebo (3%) group (6m) | No difference in PEN, COT or DOXY-resistant *S. pneumoniae* in the treatment vs. placebo group. No MERO, LEVO, CEF, VANCO, LIN-resistant pneumococcus in either treatment group. |
| Skalet AH, PLoS med, 2010[27](#_ENREF_27) | Yes |  | X | Increase in AZM-resistant *S. pneumoniae* from 3.6% (bl) to 47% (12m), vs. 9% (12m) in the untreated group. | Increase in *S. pneumoniae* resistant to CLI and TET both in the treatment and non-treatment group (without significant difference). No PEN-resistant pneumococcus in both groups. |
| Keenan JD, J Infect Dis, 2015[29](#_ENREF_29) | Yes |  | X | Increase in AZM-resistant *S. pneumoniae* from 5% (bl) to 15% (3m). | No increase in the proportion of TET or PEN resistant *S. pneumoniae*. |
| Maher MC, PloS one, 2012[47](#_ENREF_47) | Yes |  | X | Increase in AZM-resistant *S. pneumoniae* from 1% (bl) to 77% (directly after 6th MDA) and 21% (24m) | No data. |
| Keenan JD, Pediatr Infect Dis J, 2016[48](#_ENREF_48) | No |  | X | 58% of AZM-resistant *S. pneumoniae* (3m) | 35% TET-resistant *S.* *pneumoniae*, no PEN resistance. |
| Haug S, Clin Inf Dis, 2010[49](#_ENREF_49) | No |  | X | Increase in AZM-resistant *S. pneumoniae* to 77% (6m), 31% (12m), and 21% (24m). No resistance in control group isolates except one single resistant isolate (24m). | Increase in CLI-resistant *S. pneumoniae* from 35% (6m) to 60% (24m, not significant). No consistent change of TET, PEN-, and COT-resistant *S. pneumoniae* during study course in treated or untreated group. |
| **Household contacts** | Bloch EM, Am J Trop Med Hyg, 2017[40](#_ENREF_40) | No |  | X | 14% AZM-resistant *S. pneumoniae*. | No data. |

Footnotes:

Abbreviations: bl, baseline; 1m, 1 month; CEF, ceftriaxone; CHLOR, chloramphenicol; CLI, clindamycin; COT, cotrimoxazole; DOXY, doxycycline; LEVO, levofloxacine; LIN, linezolid; MERO, meropenem; PEN, penicillin; SULF, sulfamethoxazole; VANCO, vancomycin