Supplemental Digital Content 3a. Year-by-year resistance rates in invasive (blood/CSF) bacterial isolates for children (0-18 years) and adults from the Norwegian Surveillance System for Antimicrobial Drug Resistance (NORM).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **2013** | **2014** | **2015** | **2016** | **2017** | **P\*** |
|  | **Total n** | **Resistantn(%)** | **Total n**  | **Resistant n(%)** | **Total, n** | **Resistant****n(%)** | **Total n** | **Resistant****n(%)** | **Total n** | **Resistant****n(%)** |  |
| **Children** |  |  |  |  |  |  |  |  |  |  |  |
| ***S. pneumoniae*** |  |  |  |  |  |  |  |  |  |  |  |
| Penicillin NS | 33 | 2 (6.1) | 28 | 5 (17.9) | 27 | 3 (11.1) | 39 | 1 (2.6) | 24 | 7 (29.2) | ***0.017*** |
| Erythromycin | 33 | 0 (0.0) | 28 | 5 (17.9) | 27 | 1 (3.7) | 39 | 3 (7.7) | 24 | 8 (33.3) | ***0.001*** |
| Clindamycin | 33 | 0 (0.0) | 28 | 4 (14.3) | 27 | 1 (3.7) | 39 | 1 (2.6) | 24 | 8 (33.3) | ***0.000*** |
| SXT | 33 | 3 (9.1) | 28 | 5 (17.9) | 27 | 8 (29.6) | 39 | 5 (12.8) | 24 | 6 (25.0) | 0.215 |
| ***S. pyogenes*** |  |  |  |  |  |  |  |  |  |  |  |
| Erythromycin | 13 | 0 (0.0) | 20 | 0 (0.0) | 18 | 2 (11.1) | 16 | 1 (6.3) | 26 | 2 (7.7) | 0.572 |
| ***S. agalactiae*** |  |  |  |  |  |  |  |  |  |  |  |
| Erythromycin | n/a | n/a | 47 | 10 (21.3) | 50 | 12 (24.0) | 14 | 6 (42.9) | 32 | 14 (43.8) | 0.079 |
| Clindamycin | n/a | n/a | 47 | 9 (19.2) | 50 | 9 (18.0) | 14 | 7 (50.0) | 32 | 11 (34.4) | ***0.040*** |
| ***E. faecalis*** |  |  |  |  |  |  |  |  |  |  |  |
| High level gentamicin | 12 | 3 (25.0) | 12 | 0 (0.0) | 15 | 1 (6.7) | 12 | 2 (16.7) | 13 | 2 (15.4) | 0.396 |
| ***S. aureus*** |  |  |  |  |  |  |  |  |  |  |  |
| Beta-lactamase | 81 | 61 (75.3) | 62 | 43 (69.4) | 70 | 51 /72.9) | 45 | 33 (73.3) | 72 | 53 (73.6) | 0.957 |
| Erythromycin | 81 | 4 (4.9) | 62 | 0 (0.0) | 70 | 3 (4.3) | 45 | 5 (11.1) | 72 | 3 (4.2) | 0.099 |
| Ciprofloxacin | 81 | 0 (0.0) | 62 | 1 (1.6) | 70 | 1 (1.4) | 45 | 1 (2.2) | 72 | 3 (4.2) | 0.376 |
| ***E.coli*** |  |  |  |  |  |  |  |  |  |  |  |
| Gentamicin | 33 | 3 (9.1) | 35 | 2(5.7) | 46 | 2(4.3) | 47 | 2(4.3) | 51 | 4(7.8) | 0.870 |
| Ampicillin | 33 | 18(54.6) | 35 | 16(45.7) | 46 | 22(47.8) | 47 | 13(27.7) | 51 | 27 (52.9) | 0.079 |
| Cefotaxime | 33 | 1(3.0) | 35 | 0(0.0) | 46 | 0(0.0) | 47 | 1(2.1) | 51 | 3 (5.9) | 0.368 |
| Ciprofloxacin | 33 | 3(9.1) | 35 | 1(2.9) | 46 | 2(4.4) | 47 | 2(4.3) | 51 | 8(15.7) | 0.160 |
| SXT | 33 | 13(39.4) | 35 | 10(28.6) | 46 | 16(34.8) | 47 | 5(10.6) | 51 | 13(25.5) | ***0.033*** |
| ESBL | 33 | 1(3.0) | 35 | 0(0.0) | 46 | 0(0.0) | 47 | 1(2.1) | 51 | 3(5.9) | 0.368 |
| ***Klebsiella spp*.** |  |  |  |  |  |  |  |  |  |  |  |
| SXT | 10 | 5 (50.0) | 9 | 1 (11.1) | 12 | 0 (0.0) | 25 | 2 (8.0) | 15 | 4 (26.7) | ***0.012*** |
| ESBL | 10 | 1 (10.0) | 9 | 0 (0.0) | 12 | 0 (0.0) | 25 | 1 (4.0) | 15 | 2 (13.3) | 0.479 |
| Ciprofloxacin | 10 | 0 (0.0) | 9 | 0 (0.0) | 12 | 0 (0.0) | 25 | 3 (12.0) | 15 | 3 (20.0) | 0.286 |
| **Adults** |  |  |  |  |  |  |  |  |  |  |  |
| ***S. pneumoniae*** |  |  |  |  |  |  |  |  |  |  |  |
| Penicillin NS | 575 | 17 (3.0) | 533 | 26 (4.9) | 492 | 36 (7.3) | 555 | 31 (5.6) | 512 | 45 (8.8) | ***0.001*** |
| Erythromycin | 575 | 22 (3.8) | 533 | 20 (3.8) | 492 | 24 (4.9) | 555 | 30 (5.4) | 512 | 34 (6.6) | 0.159 |
| Clindamycin | 575 | 15 (2.6) | 533 | 14 (2.6) | 492 | 18 (3.7) | 555 | 24 (4.3) | 512 | 25 (4.9) | 0.174 |
| SXT | 575 | 20 (3.5) | 533 | 30 (5.6) | 492 | 41 (8.3) | 555 | 42 (7.6) | 512 | 38 (7.4) | ***0.008*** |
| ***S. pyogenes*** |  |  |  |  |  |  |  |  |  |  |  |
| Erythromycin | 149 | 3 (2.0) | 168 | 7 (4.2) | 182 | 5 (2.8) | 171 | 6 (3.5) | 213 | 8 (3.8) | 0.829 |
| Clindamycin | 149 | 1 (0.7) | 168 | 4 (2.4) | 182 | 3 (1.7) | 171 | 3 (1.8) | 213 | 6 (2.8) | 0.690 |
| SXT | 149 | 5 (3.4) | 168 | 5 (3.0) | 182 | 2 (1.1) | 171 | 3 (1.8) | 213 | 2 (0.9) | 0.356 |
| **S. agalactiae** |  |  |  |  |  |  |  |  |  |  |  |
| Erythromycin | n/a | n/a | 196 | 34 (17.4) | 229 | 38 (16.6) | 267 | 42 (15.7) | 203 | 39 (19.2) | 0.791 |
| Clindamycin | n/a | n/a | 196 | 22 (11.2) | 229 | 30 (13.1) | 267 | 28 (10.5) | 203 | 24 (11.8) | 0.835 |
| ***E. faecalis*** |  |  |  |  |  |  |  |  |  |  |  |
| High level gentamicin | 401 | 94 (23.4) | 395 | 76 (19.2) | 368 | 49 (13.3) | 409 | 77 (18.8) | 440 | 68 (15.5) | ***0.003*** |
| ***S. aureus*** |  |  |  |  |  |  |  |  |  |  |  |
| Beta-lactamase | 1074 | 772 (71.9) | 1101 | 805 (73.1) | 1207 | 881 (73.0) | 1210 | 879 (72.6) | 1240 | 869 (70.1) |  |
| MRSA | 1074 | 3 (0.3) | 1101 | 9 (0.8) | 1207 | 8 (0.7) | 1210 | 13 (1.1) | 1240 | 10 (0.8) | 0.265 |
| Erythromycin | 1070 | 41 (3.8) | 1101 | 47 (4.3) | 1207 | 66 (5.5) | 1210 | 59 (4.9) | 1240 | 37 (3.0) | ***0.029*** |
| Clindamycin | 1074 | 17 (1.6) | 1101 | 9 (0.8) | 1207 | 20 (1.7) | 1210 | 16 (1.3) | 1240 | 8 (0.7) | 0.085 |
| SXT | 1074 | 6 (0.6) | 1101 | 0 (0.0) | 1207 | 4 (0.3) | 1210 | 3 (0.3) | 1240 | 3 (0.2) | 0.132 |
| Ciprofloxacin | 1074 | 33 (3.1) | 1101 | 32 (2.9) | 1207 | 28 (2.3) | 1210 | 86 (7.1) | 1240 | 44 (3.6) | ***0.000*** |
| Gentamicin | 1074 | 3 (0.3) | 1101 | 5 (0.5) | 1207 | 2 (0.2) | 1210 | 5 (0.4) | 1240  | 8 (0.7) | 0.404 |
| ***E. coli*** |  |  |  |  |  |  |  |  |  |  |  |
| Gentamicin | 1579 | 87(5.6) | 1610 | 125(7.8) | 1906 | 113(5.9) | 1893 | 120(6.3) | 2085 | 146(7.0) | 0.068 |
| Ampicillin | 1579 | 670(42.4) | 1610 | 685(42.6) | 1906 | 839(44.0) | 1893 | 831(43.9) | 2085 | 915(43.9) | 0.779 |
| Cefotaxime | 1579 | 86(5.5) | 1610 | 100(6.2) | 1906 | 127(6.7) | 1893 | 115(6.1) | 2085 | 140(6.7) | 0.531 |
| Piperacillin/tazobactam | 1579 | 34(2.2) | 1610 | 47(2.9) | 1906 | 29(1.5) | 1893 | 37(2.0) | 2085 | 32(1.5) | ***0.019*** |
| Ciprofloxacin | 1579 | 187(11.8) | 1610 | 206(12.8) | 1906 | 222(11.7) | 1893 | 243(12.8) | 2085 | 317(15.2) | ***0.007*** |
| SXT | 1579 | 397(25.1) | 1610 | 447(27.8) | 1906 | 509(26.7) | 1893 | 495(26.2) | 2085 | 527(25.3) | 0.389 |
| ESBL  | 1579 | 80(5.1) | 1610 | 95(5.9) | 1906 | 127(6.7) | 1893 | 112(5.9) | 2085 | 138(6.6) | 0.266 |
| ***Klebsiella spp*.** |  |  |  |  |  |  |  |  |  |  |  |
| Gentamicin | 642 | 7 (1.1) | 745 | 19 (2.6) | 811 | 22 (2.7) | 830 | 29 (3.5) | 869 | 27 (3.1) | 0.061 |
| Cefotaxime | 642 | 15 (2.3) | 745 | 27 (3.6) | 811 | 24 (3.0) | 830 | 40 (4.8) | 869 | 46 (5.3) | ***0.013*** |
| ESBL | 642 | 17 (2.7) | 745 | 26 (3.5) | 811 | 24 (3.0)  | 830 | 38 (4.6) | 869 | 45 (5.2) | ***0.043*** |
| Piperacillin/tazobactam | 642 | 23 (3.6) | 745 | 29 (3.9) | 811 | 27 (3.3) | 830 | 34 (4.1) | 869 | 35 (4.0) | 0.922 |
| SXT | 64 | 64 (10.0) | 745 | 71 (9.5) | 811 | 80 (9.9) | 830 | 91 (11.0) | 869 | 120 (13.8) | ***0.033*** |
| Ciprofloxacin | 642 | 19 (3.0) | 745 | 30 (4.0) | 811 | 29 (3.6) | 830 | 93 (11.2) | 869 | 106 (12.2) | ***0.000*** |

SXT: trimethoprim*/*sulfamethoxazole; Penicillin NS: penicillin non-susceptibility

\* Chi squared test comparing proportion of resistance. Fisher`s exact test was used if any expected frequency <5.

Supplemental Digital Content 3b. Susceptibility pattern for selected bacteria in invasive (blood/CSF) isolates in children (0-18 years) from the Norwegian Surveillance System for Antimicrobial Drug Resistance (NORM) 2013-2017

|  |  |  |  |
| --- | --- | --- | --- |
|  | **S**\***, n (%)** | **I, n (%)** | **R, n (%)** |
| ***E. faecium* (n=9)** |  |  |  |
| Ampicillin | 2 (22.2) | 0 (0.0) | 7 (77.8) |
| Gentamicin | 9 (100.0) | - | 0 (0.0) |
| Imipenem | 1 (11.1) | 1 (11.1) | 7 (88.8) |
| Vancomycin | 9 (100.0) | - | 0 (0.0) |
| ***H. influenzae* (n=34)** |  |  |  |
| Beta-lactamase | 32 (94.1) | - | 2 (5.9) |
| Ampicillin | 31 (91.2) | - | 3 (8.8) |
| Cefotaxime | 34 (100.0) | - | 0 (0.0) |
| Ciprofloxacin | 34 (100.0) | - | 0 (0.0) |
| Trimethoprim/sulfamethoxazole | 30 (88.2) | - | 4 (11.8) |
| ***N. meningitidis* (n=12)** |  |  |  |
| Penicillin G | 6 (50.0) | 5 (41.7) | 1 (8.3) |
| Ceftriaxone | 12(100.0) | - | 0 (0.0) |
| Azithromycin | 12 (100.0) | - | 0 (0.0) |
| ***P. aeruginosa* (n=5)** |  |  |  |
| Gentamicin | 5 (100.0) | - | 0 (0.0) |
| Tobramycin | 5 (100.0) | - | 0 (0.0) |
| Ceftazidime | 4 (80.0) | - | 1 (20.0) |

\* S: sensitive; I: intermediate resistant; R: resistant