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**Supplemental Methods 1.** Methods for identifying antibiotics.

The National Hospital Ambulatory Medical Care Survey (NHAMCS) uses the Cerner Multum Lexicon Plus database to convert information on drugs described to therapeutic drug classes and agents. To identify eligible antibiotics in our study, we used Multum codes as shown below.

|  |  |
| --- | --- |
| **Antibiotic agents** | **Multum code** |
| Metronidazole | d00108 |
| Tinidazole | d04935 |
| Atovaquone | d01120 |
| Rifampin | d00047 |
| Cefaclor | d00081 |
| Cefadroxil | d00080 |
| Cefdinir | d04256 |
| Cefixime | d00072 |
| Cefpodoxime | d00095 |
| Cefprozil | d00073 |
| Cefuroxime | d00056 |
| Cephalexin | d00096 |
| Vancomycin | d00125 |
| Clindamycin | d00043 |
| Azithromycin | d00091 |
| Clarithromycin | d00097 |
| Erythromycin | d00046 |
| Rifaximin | d05294 |
| Linezolid | d04534 |
| Amoxicillin | d00088 |
| Amoxicillin-clavulanate | d00089 |
| Ampicillin | d00003 |
| Dicloxacillin | d00153 |
| Penicillin | d00116 |
| Ciprofloxacin | d00011 |
| Fluoroquinolones, miscellaneous | n08223 |
| Gatifloxacin | d04504 |
| Levofloxacin | d04109 |
| Moxifloxacin | d04500 |
| Ofloxacin | d00114 |
| Sulfamethoxazole | d00119 |
| Sulfamethoxazole-trimethoprim | d00124 |
| Sulfonamides, miscellaneous | c00015 |
| Doxycycline | d00037 |
| Minocycline | d00110 |
| Sarecycline | d09003 |
| Tetracycline | d00041 |
| Demeclocycline | d01068 |
| Oxytetracycline | d01070 |
| Fosfomycin | d04106 |
| Methenamine | d00106 |
| Nitrofurantoin | d00112 |
| Trimethoprim | d00123 |

**Supplemental Methods 2.** Subclassifications of “never” diagnosis codes.

Among all visits with inappropriate antibiotic prescriptions (i.e., only associated with “never” codes) in the sample, there were 2,698 unique “never” diagnosis codes. We further subclassified these codes as plausible indications for antibiotics or not (“Never, plausible” versus “Never, not plausible”). For those deemed plausible, we also include diagnosis subcategories, such as skin and soft tissue infection, potential signs and symptoms of infection, and upper respiratory infection, among others. We included these subclassifications in an attachment (see file entitled “ICD-10-CM\_NHMACS\_never\_2016\_2017\_2018\_2019\_2020\_2021.xlsx”). This file also contains the classification decisions used for the sensitivity analysis, in addition to those used for the main analysis.

**Supplemental Table 1.** Demographic characteristics of sample by age group. Subcategories may not sum up to total sample size due to rounding errors after use of survey weights and design-based variance estimators to account for the complex survey design.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristic** | **Overall, No. (%)**(n = 152,449,442) | **Children, No. (%)**(n = 31,714,726) | **Adults, No. (%)**(n = 94,016,603) | **Older adults, No. (%)**(n = 26,718,112) |
| **Female sex** | 87,737,545 (57.6%) | 15,702,068 (49.5%) | 56,638,335 (60.2%) | 15,397,141 (57.6%) |
| **Age group, years** |  |
|  0-1 | ··· | 6,631,523 (20.9%) | ··· | ··· |
|  2-5 | ··· | 9,857,892 (31.1%) | ··· | ··· |
|  6-11 | ··· | 8,583,401 (27.1%) | ··· | ··· |
|  12-17 | ··· | 6,641,908 (20.9%) | ··· | ··· |
|  18-25 | ··· | ··· | 20,222,873 (21.5%) | ··· |
|  26-34 | ··· | ··· | 21,959,043 (23.4%) | ··· |
|  35-44 | ··· | ··· | 19,096,807 (20.3%) | ··· |
|  45-54 | ··· | ··· | 17,037,165 (18.1%) | ··· |
|  55-64 | ··· | ··· | 15,700,713 (16.7%) | ··· |
|  65-74 | ··· | ··· | ··· | 12,569,714 (47.0%) |
|  75-84 | ··· | ··· | ··· | 8,825,326 (33.0%) |
|  ≥85 | ··· | ··· | ··· | 5,323,071 (19.9%) |
| **Race and ethnicity** |  |
|  Hispanic, any race | 23,919,528 (15.7%) | 8,334,426 (26.3%) | 13,228,368 (14.1%) | 2,356,733 (8.8%) |
|  Non-Hispanic, Black | 35,632,730 (23.4%) | 8,374,515 (26.4%) | 24,175,496 (25.7%) | 3,082,719 (11.5%) |
|  Non-Hispanic Other | 4,472,256 (2.9%) | 1,200,030 (3.8%) | 2,294,975 (2.4%) | 977,250 (3.7%) |
|  Non-Hispanic, White | 88,424,926 (58.0%) | 13,805,754 (43.5%) | 54,317,762 (57.8%) | 20,301,409 (76.0%) |
| **Geographic census region** |  |
|  Northeast | 21,295,859 (14.0%) | 4,217,838 (13.3%) | 12,695,069 (13.5%) | 4,382,952 (16.4%) |
|  Midwest | 33,528,031 (22.0%) | 7,079,006 (22.3%) | 20,382,776 (21.7%) | 6,066,249 (22.7%) |
|  South | 67,065,134 (44.0%) | 14,693,094 (46.3%) | 41,778,892 (44.4%) | 10,593,148 (39.6%) |
|  West | 30,560,415 (20.0%) | 5,724,787 (18.1%) | 19,159,865 (20.5%) | 5,675,762 (21.2%) |
| **Residence in metropolitan statistical area** | 127,965,999 (83.9%) | 26,991,719 (85.1%) | 79,395,431 (84.4%) | 21,578,848 (80.8%) |

**Supplemental Table 2.** Most frequent indications among visits with inappropriate antibiotic prescribing and a plausible antibiotic indication.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Indication** | **Overall, No. (%)**(n = 22,736,645) | **Children, No. (%)**(n = 5,289,605) | **Adults, No. (%)**(n = 14,078,131) | **Older adults, No. (%)**(n = 3,368,909) |
| Acute serous or nonsuppurative otitis media | 674,203 (3.0%) | 557,313 (10.5%) | 113,357 (0.8%) | 3,532 (0.1%) |
| Asthma | 1,316,811 (5.8%) | 168,216 (3.2%) | 1,061,136 (7.5%) | 87,458 (2.6%) |
| Bronchitis | 3,967,168 (17.4%) | 637,318 (12.0%) | 2,742,513 (19.5%) | 587,336 (17.4%) |
| Conjunctivitis, scleritis, and other ophthalmologic conditions | 691,978 (3.0%) | 360,901 (6.8%) | 279,095 (2.0%) | 51,981 (1.5%) |
| Fungal infection | 183,021 (0.8%) | 56,194 (1.1%) | 108,047 (0.8%) | 18,779 (0.6%) |
| Other viral infection | 1,112,529 (4.9%) | 290,852 (5.5%) | 641,537 (4.6%) | 180,138 (5.3%) |
| Parasitic infection | 72,720 (0.3%) | 47,207 (0.9%) | 25,512 (0.2%) | 0 (0.0%) |
| Potential signs and symptoms of infection | 12,287,509 (54.0%) | 2,388,468 (45.2%) | 7,703,768 (54.7%) | 2,195,272 (65.2%) |
| Skin and soft tissue infection | 73,196 (0.3%) | 15,982 (0.3%) | 40,677 (0.3%) | 16,536 (0.5%) |
| Toxic gastroenteritis and colitis | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Upper respiratory infection | 2,357,505 (10.4%) | 767,149 (14.5%) | 1,362,484 (9.7%) | 227,872 (6.8%) |

**Supplemental Table 3.** Most frequent diagnosis codes among visits with inappropriate antibiotic prescribing in which the indication was potential signs and symptoms of infection.

|  |  |  |  |
| --- | --- | --- | --- |
| **Overall** | **Children** | **Adults** | **Older adults** |
| 1. R109: Unspecified abdominal pain2. R51: Headache3. R112: Nausea with vomiting, unspecified4. R060: Dyspnea5. R509: Fever, unspecified6. R111: Vomiting7. R197: Diarrhea, unspecified8. R101: Pain localized to upper abdomen9. R05: Cough10. R103: Pain localized to other parts of lower abdomen | 1. R509: Fever, unspecified2. R111: Vomiting3. R109: Unspecified abdominal pain4. R05: Cough5. R197: Diarrhea, unspecified6. R112: Nausea with vomiting, unspecified7. R51: Headache8. R21: Rash and other nonspecific skin eruption9. R103: Pain localized to other parts of lower abdomen10. R098: Other specified symptoms and signs involving the circulatory and respiratory systems | 1. R109: Unspecified abdominal pain2. R51: Headache3. R112: Nausea with vomiting, unspecified4. R101: Pain localized to upper abdomen5. R060: Dyspnea6. R103: Pain localized to other parts of lower abdomen7. R197: Diarrhea, unspecified8. R111: Vomiting9. R110: Nausea10. R05: Cough | 1. R060: Dyspnea2. R109: Unspecified abdominal pain3. R197: Diarrhea, unspecified4. R112: Nausea with vomiting, unspecified5. R51: Headache6. R101: Pain localized to upper abdomen7. R05: Cough8. R509: Fever, unspecified9. R111: Vomiting10. R110: Nausea |

**Supplemental Table 4.** Most frequent diagnosis codes among visits with inappropriate antibiotic prescribing and no plausible antibiotic indication.

|  |  |  |  |
| --- | --- | --- | --- |
| **Overall** | **Children** | **Adults** | **Older adults** |
| 1. I10: Essential (primary) hypertension2. R079: Chest pain, unspecified3. M255: Pain in joint4. R078: Other chest pain5. M796: Pain in limb, hand, foot, fingers and toes6. F419: Anxiety disorder, unspecified7. R55: Syncope and collapse8. M545: Low back pain9. F329: Major depressive disorder, single episode, unspecified10. R42: Dizziness and giddiness | 1. S099: Unspecified injury of face and head2. M255: Pain in joint3. K590: Constipation4. S934: Sprain of ankle5. R458: Other symptoms and signs involving emotional state6. K529: Noninfective gastroenteritis and colitis, unspecified7. S060: Concussion8. F329: Major depressive disorder, single episode, unspecified9. M796: Pain in limb, hand, foot, fingers and toes10. T148: Other injury of unspecified body region | 1. R079: Chest pain, unspecified2. I10: Essential (primary) hypertension3. M255: Pain in joint4. R078: Other chest pain5. F419: Anxiety disorder, unspecified6. M796: Pain in limb, hand, foot, fingers and toes7. M545: Low back pain8. F329: Major depressive disorder, single episode, unspecified9. R458: Other symptoms and signs involving emotional state10. F179: Nicotine dependence | 1. I10: Essential (primary) hypertension2. R079: Chest pain, unspecified3. M255: Pain in joint4. R55: Syncope and collapse5. I489: Unspecified atrial fibrillation and atrial flutter6. R42: Dizziness and giddiness7. E119: Type 2 diabetes mellitus without complications8. R531: Weakness9. I509: Heart failure, unspecified10. N179: Acute kidney failure, unspecified  |

**Supplemental Table 5.** Most frequent indications among visits with inappropriate antibiotic prescribing and a plausible antibiotic indication, main versus sensitivity analysis.

|  |  |  |
| --- | --- | --- |
| **Subcategory** | **Overall, Main Analysis, No. (%)**(n = 22,736,645) | **Overall, Sensitivity Analysis, No. (%)**(n = 22,736,645) |
| Acute serous or nonsuppurative otitis media | 674,203 (3.0%) | 625,618 (2.8%) |
| Asthma | 1,316,811 (5.8%) | 1,439,330 (6.3%) |
| Bronchitis | 3,967,168 (17.4%) | 3,778,622 (16.6%) |
| Conjunctivitis, scleritis, and other ophthalmologic conditions | 691,978 (3.0%) | 695,108 (3.1%) |
| Fungal infection | 183,021 (0.8%) | 167,607 (0.7%) |
| Other viral infection | 1,112,529 (4.9%) | 1,090,870 (4.8%) |
| Parasitic infection | 72,720 (0.3%) | 73,958 (0.3%) |
| Potential signs and symptoms of infection | 12,287,509 (54.0%) | 12,410,736 (54.6%) |
| Skin and soft tissue infection | 73,196 (0.3%) | 75,501 (0.3%) |
| Toxic gastroenteritis and colitis | 0 (0.0%) | 0 (0.0%) |
| Upper respiratory infection | 2,357,505 (10.4%) | 2,379,291 (10.5%) |

**Supplemental Figure 1.** Number of weighted visits with antibiotic prescriptions and inappropriate prescribing with or without a plausible antibiotic indication.

