Supplemental Table 4. Baseline characteristics of children hospitalized with asthma from 2010 to 2018

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Year pf admission** | **2010** | **2011** | **2012** | **2013** | **2014** | **2015** | **2016** | **2017** | **2018** | **%Increase** |
| N | 5560 | 7338 | 6517 | 7811 | 6374 | 8839 | 5759 | 6147 | 636 |  |
| Age, mean year | 5.0 | 4.6 | 4.6 | 4.6 | 4.4 | 4.7 | 4.4 | 4.4 | 4.2 |  |
| (SE) | (3.3) | (3.5) | (3.5) | (3.4) | (3.4) | (3.3) | (3.4) | (3.3) | (3.4) |  |
| Male, N | 3478 | 4595 | 4096 | 4890 | 3932 | 5504 | 3563 | 3766 | 397 |  |
| (%) | (62.6) | (62.6) | (62.9) | (62.6) | (61.7) | (52.4) | (61.9) | (61.3) | (64.2) |  |
| Atopic dermatitis, N | 129 | 173 | 198 | 226 | 215 | 279 | 183 | 243 | 24 |  |
| (%) | (2.3) | (2.4) | (3.0) | (2.9) | (3.4) | (3.2) | (3.2) | (4.0) | (3.8) |  |
| Allergic rhinitis, N | 189 | 299 | 324 | 396 | 376 | 534 | 378 | 434 | 45 |  |
| (%) | (3.4) | (4.1) | (5.0) | (5.0) | (5.9) | (6.0) | (6.6) | (7.1) | (7.1) |  |
| Food allergy, N | 55 | 74 | 68 | 105 | 106 | 132 | 72 | 115 | 9 |  |
| (%) | (1.0) | (1.0) | (1.0) | (1.3) | (1.7) | (1.5) | (1.3) | (1.9) | (1.4) |  |
| Obesity, N | 419 | 547 | 514 | 621 | 573 | 730 | 485 | 484 | 63 |  |
| (%) | (7.5) | (7.5) | (7.9) | (8.0) | (9.0) | (8.3) | (8.4) | (7.9) | (9.9) |  |
| Ambulance use, N | 252 | 264 | 299 | 396 | 313 | 572 | 346 | 454 | 42 |  |
| (%) | (4.5) | (3.6) | (4.6) | (5.1) | (4.9) | (6.5) | (6.0) | (7.4) | (6.6) |  |
| Academic hospital, N | 442 | 527 | 604 | 764 | 563 | 760 | 470 | 444 | 57 |  |
| (%) | (8.0) | (7.2) | (9.3) | (9.8) | (8.8) | (8.6) | (8.2) | (7.2) | (9.0) |  |
| Season, N |  |  |  |  |  |  |  |  |  |  |
| Spring | – | 1567 | 1666 | 1866 | 1542 | 1678 | 1584 | 1416 | 293 |  |
| (%) | – | (21.4) | (25.6) | (23.9) | (24.2) | (19.0) | (27.5) | (23.0) | – |  |
| Summer | 1657 | 1654 | 1445 | 1757 | 1268 | 1892 | 1362 | 1366 | – |  |
| (%) | – | (22.5) | (22.2) | (22.5) | (22.5) | (21.4) | (23.7) | (22.2) | – |  |
| Fall | 3457 | 2972 | 2368 | 3087 | 2634 | 4195 | 2000 | 2440 | – |  |
| (%) | – | (40.5) | (36.3) | (39.5) | (41.3) | (47.5) | (34.7) | (39.7) | – |  |
| Winter | 446 | 1145 | 1038 | 1101 | 930 | 1074 | 813 | 925 | 343 |  |
| (%) | – | (15.6) | (15.9) | (14.1) | (14.6) | (12.2) | (14.1) | (15.1) | – |  |

Supplemental Table 5. Trends in adjunctive treatments for children hospitalized with asthma

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Year of admission** | **2010** | **2011** | **2012** | **2013** | **2014** | **2015** | **2016** | **2017** | **2018** | **%Increase** |
| Total, N | 5560 | 7338 | 6517 | 7811 | 6374 | 8839 | 5759 | 6147 | 636 |  |
| Adjunctive treatments, N |  |  |  |  |  |  |  |  |  |  |
| Antitussives | 1951 | 2605 | 2199 | 2554 | 2132 | 2812 | 1692 | 1661 | 174 | -8.7% |
| (%) | (35.1) | (35.5) | (33.7) | (32.7) | (33.5) | (31.8) | (29.4) | (27.0) | (27.4) | (-9.2%, -7.6%) |
|  Dextromethorphan | 170 | 158 | 135 | 125 | 93 | 207 | 86 | 73 | 8 | -5.4% |
|  (%) | (3.1) | (2.2) | (2.1) | (1.6) | (1.5) | (2.3) | (1.5) | (1.2) | (1.3) | (-8.9%, -2.7%) |
|  Tipepidine | 1651 | 2185 | 1827 | 2168 | 1872 | 2374 | 1452 | 1472 | 152 | -8.4% |
|  (%) | (29.1) | (29.8) | (28.0) | (27.8) | (29.4) | (26.9) | (25.2) | (24.0) | (23.9) | (-8.5%, -6.2%) |
| Mucolytics | 3761 | 4948 | 4562 | 5450 | 4517 | 6314 | 4151 | 4543 | 482 | 6.0% |
| (%) | (67.6) | (67.4) | (70.0) | (69.8) | (70.9) | (71.4) | (72.1) | (73.9) | (75.8) | (4.8%, 7.1%) |
| Ambroxol | 2110 | 2727 | 2504 | 3183 | 2574 | 3822 | 2442 | 2721 | 285 | 5.9% |
| (%) | (38.0) | (37.2) | (38.4) | (40.8) | (40.4) | (43.2) | (42.4) | (44.3) | (44.8) | (4.7%, 7.2%) |
| Antihistamines | 963 | 1279 | 1000 | 1021 | 790 | 977 | 602 | 677 | 74 | -15.0% |
| (%) | (17.3) | (17.4) | (15.3) | (13.1) | (12.4) | (11.1) | (10.5) | (11.0) | (11.6) | (-16.2%, -13.7%) |
|  FGAHs | 576 | 719 | 497 | 433 | 328 | 323 | 152 | 152 | 17 | -29.1% |
|  (%) | (10.4) | (9.8) | (7.6) | (5.5) | (5.2) | (5.7) | (3.7) | (2.6) | (2.7) | (-30.8%, -27.4%) |
|  Sedative SGAHs | 230 | 301 | 233 | 270 | 168 | 169 | 105 | 90 | 7 | -22.0% |
|  (%) | (4.1) | (4.1) | (3.6) | (3.5) | (2.6) | (1.9) | (1.8) | (1.5) | (1.1) | (-24.3%, -19.6%) |
|  Non-sedative SGAHs | 191 | 289 | 291 | 345 | 314 | 514 | 354 | 457 | 53 | 11.1% |
| (%) | (3.4) | (3.9) | (4.5) | (4.4) | (4.9) | (5.8) | (6.2) | (7.4) | (8.3) | (8.7%, 13.5%) |
| LTRA | 3784 | 4884 | 4510 | 5601 | 4540 | 6288 | 4186 | 4691 | 499 | 9.0% |
| (%) | (68.1) | (66.6) | (69.2) | (71.7) | (71.2) | (71.1) | (72.7) | (76.3) | (78.5) | (7.8%, 10.1%) |
| Mediator release inhibitors | 2242 | 2986 | 2628 | 3095 | 2713 | 3695 | 2357 | 2580 | 266 | 1.6% |
| (%) | (40.3) | (40.7) | (40.3) | (39.6) | (42.6) | (41.8) | (40.9) | (42.0) | (41.8) | (-0.2%, 3.5%) |
| Xanthine | 912 | 949 | 641 | 640 | 427 | 543 | 228 | 211 | 15 | -30.6% |
| (%) | (16.4) | (12.9) | (9.8) | (8.2) | (6.7) | (6.1) | (4.0) | (3.4) | (2.4) | (-32.1%, -29.2%) |
| Inhaled corticosteroids | 574 | 860 | 755 | 884 | 671 | 927 | 592 | 688 | 81 | -1.8% |
| (%) | (10.3) | (11.7) | (11.6) | (11.3) | (10.5) | (10.5) | (10.3) | (11.2) | (12.7) | (-3.3%, -0.2%) |

Supplemental Table 6. Trends in patient characteristics, healthcare utilization, and antiepileptic drug use among children aged > 5 years

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Year pf admission** | **2010** | **2011** | **2012** | **2013** | **2014** | **2015** | **2016** | **2017** | **2018** | **%Increase** |
| N | 2277 | 2584 | 2349 | 2791 | 2133 | 3336 | 1923 | 1994 | 190 |  |
| Age, mean year | 8.3 | 8.6 | 8.6 | 8.5 | 8.5 | 8.3 | 8.5 | 8.3 | 8.7 |  |
| (SE) | (2.5) | (2.6) | (2.6) | (2.6) | (2.6) | (2.5) | (2.6) | (2.6) | (2.6) |  |
| Male, N | 1364 | 1498 | 1356 | 1682 | 1252 | 1984 | 1127 | 1169 | 110 |  |
| (%) | (59.9) | (58.0) | (57.7) | (60.3) | (58.7) | (59.5) | (58.6) | (58.6) | (57.9) |  |
| Atopic dermatitis, N | 47 | 51 | 68 | 90 | 68 | 108 | 62 | 89 | 7 |  |
| (%) | (2.3) | (2.0) | (2.9) | (3.2) | (3.2) | (3.2) | (3.2) | (4.5) | (3.7) |  |
| Allergic rhinitis, N | 91 | 127 | 165 | 197 | 162 | 261 | 162 | 163 | 14 |  |
| (%) | (4.0) | (4.9) | (7.0) | (7.1) | (7.6) | (7.8) | (8.4) | (8.2) | (7.4) |  |
| Food allergy, N | 14 | 26 | 16 | 37 | 26 | 42 | 20 | 28 | 3 |  |
| (%) | (0.6) | (1.0) | (0.7) | (1.3) | (1.2) | (1.3) | (1.0) | (1.4) | (1.6) |  |
| Obesity, N | 216 | 254 | 204 | 262 | 248 | 348 | 221 | 210 | 25 |  |
| (%) | (9.5) | (9.8) | (8.7) | (9.4) | (11.6) | (10.4) | (10.5) | (10.5) | (13.2) |  |
| Ambulance use, N | 121 | 125 | 150 | 195 | 137 | 261 | 152 | 185 | 19 |  |
| (%) | (5.3) | (4.8) | (6.4) | (7.0) | (6.4) | (7.8) | (7.9) | (9.3) | (10) |  |
| Academic hospital, N | 190 | 145 | 193 | 284 | 178 | 278 | 165 | 160 | 20 |  |
| (%) | (8.4) | (5.6) | (8.2) | (10.2) | (8.4) | (8.3) | (8.6) | (8.0) | (10.5) |  |
| Season, N |  |  |  |  |  |  |  |  |  |  |
| Spring | – | 506 | 611 | 606 | 495 | 596 | 539 | 473 | 100 |  |
| (%) | – | (19.6) | (26.0) | (21.7) | (23.2) | (17.9) | (28.0) | (23.7) | – |  |
| Summer | 655 | 531 | 460 | 540 | 374 | 641 | 424 | 355 | – |  |
| (%) | – | (20.6) | (19.6) | (19.4) | (17.5) | (19.2) | (22.5) | (17.8) | – |  |
| Fall | 1486 | 1140 | 944 | 1256 | 964 | 1743 | 679 | 842 | – |  |
| (%) | – | (44.1) | (40.2) | (45.0) | (45.2) | (52.3) | (35.3) | (42.2) | – |  |
| Winter | 136 | 407 | 334 | 389 | 300 | 356 | 281 | 324 | 90 |  |
| (%) | – | (15.8) | (14.2) | (13.9) | (14.1) | (10.7) | (14.6) | (16.3) | – |  |
| Healthcare cost, mean JPY | 215.681 | 210,307 | 218,670 | 222,825 | 222,053 | 226,107 | 227,400 | 227,682 | 223,079 | 0.6% |
| (SE) | (2139) | (2113) | (2290) | (2008) | (2268) | (1696) | (2407) | (2424) | (7453) | (0.3%, 0.8%) |
| Length of stay, mean days | 5.6 | 5.5 | 5.5 | 5.6 | 5.5 | 5.5 | 5.5 | 5.5 | 5.3 | -0.6% |
| (SE) | (0.1) | (0.1) | (0.1) | (0.1) | (0.1) | (0.1) | (0.1) | (0.1) | (0.1) | (-0.9%, -0.4%) |
| Mechanical ventilation, N | 23 | 15 | 12 | 19 | 26 | 24 | 20 | 13 | 2 | -0.3% |
| (%) | (1.0) | (0.6) | (0.5) | (0.7) | (1.2) | (0.7) | (1.0) | (0.6) | (1.1) | (-10%, 10.1%) |

SE, standard error; %Increase, %increase of proportion per year for health resource utilization in ratio scale

Supplemental Table 7. Trends in early antibiotic use among children aged > 5 years

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Fiscal year** | **2010** | **2011** | **2012** | **2013** | **2014** | **2015** | **2016** | **2017** | **2018** | **%Increase** |
| N | 2277 | 2584 | 2349 | 2791 | 2133 | 3336 | 1923 | 1994 | 190 |  |
| Total, N | 959 | 972 | 871 | 938 | 677 | 1082 | 619 | 525 | 29 | -11.1% |
| (%) | (42.1) | (37.6) | (37.1) | (33.6) | (31.7) | (32.4) | (32.2) | (26.3) | (15.3) | (-12.6%, -10.6%) |
| Macrolide, N | 563 | 585 | 479 | 492 | 303 | 520 | 300 | 284 | 15 | -12.4% |
| (%) | (24.7) | (22.6) | (20.4) | (17.6) | (14.2) | (15.6) | (15.6) | (14.2) | (7.9) | (-14.2%, -11.6%) |
| Cephalosporin, N | 222 | 185 | 132 | 161 | 117 | 192 | 100 | 81 | 3 | -15.9% |
| (%) | (9.8) | (7.2) | (5.6) | (5.8) | (5.5) | (5.8) | (5.2) | (4.1) | (1.6) | (-17.6%, -11.8%) |
|  3rd generation, N | 112 | 91 | 75 | 106 | 63 | 131 | 67 | 49 | 1 | -9.1% |
|  (%) | (4.9) | (3.5) | (3.2) | (3.8) | (3.0) | (3.9) | (3.5) | (2.5) | (0.5) | (-11.9%, -4.2%) |
| Penicillin, N | 107 | 104 | 102 | 140 | 106 | 217 | 90 | 95 | 5 | 2.2% |
| (%) | (4.1) | (4.0) | (4.3) | (5.0) | (5.0) | (6.5) | (4.7) | (4.8) | (2.6) | (-1.4%, 6.0%) |
| Quinolone, N | 3 | 5 | 36 | 25 | 17 | 41 | 40 | 15 | 1 | 15.0% |
| (%) | (0.1) | (0.2) | (1.5) | (0.9) | (0.8) | (1.2) | (2.1) | (0.8) | (0.5) | (6.5%, 24.1%) |
| Tetracycline, N | 17 | 49 | 72 | 45 | 18 | 40 | 35 | 13 | 0 | -7.1% |
| (%) | (0.8) | (1.9) | (3.1) | (1.6) | (0.8) | (1.2) | (1.8) | (0.7) | (0) | (-12.8%, -0.1%) |

%Increase, %increase of proportion per year for health resource utilization in ratio scale

Supplemental Table 8. Trends in adjunctive treatments among children aged > 5 years

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Year of admission** | **2010** | **2011** | **2012** | **2013** | **2014** | **2015** | **2016** | **2017** | **2018** | **%Increase** |
| Total, N | 2277 | 2584 | 2349 | 2791 | 2133 | 3336 | 1923 | 1994 | 190 |  |
| Adjunctive treatments, N |  |  |  |  |  |  |  |  |  |  |
| Antitussives | 685 | 773 | 697 | 793 | 574 | 934 | 467 | 468 | 35 | -6.9% |
| (%) | (30.1) | (29.9) | (29.7) | (28.4) | (26.9) | (28.0) | (24.3) | (23.47) | (18.4) | (-8.6%, -4.9%) |
|  Dextromethorphan | 76 | 73 | 67 | 76 | 52 | 113 | 57 | 46 | 3 | 3.7% |
|  (%) | (3.3) | (2.8) | (2.9) | (2.7) | (2.4) | (3.4) | (3.0) | (2.3) | (1.6) | (-1.4%, 9.1%) |
|  Tipepidine | 501 | 549 | 490 | 561 | 431 | 664 | 324 | 351 | 22 | -6.6% |
|  (%) | (22.0) | (21.3) | (20.9) | (20.1) | (20.2) | (19.9) | (16.9) | (17.6) | (11.6) | (-8.7%, -4.5%) |
| Mucolytics | 1427 | 1601 | 1493 | 1760 | 1354 | 2220 | 1229 | 1375 | 132 | 4.7% |
| (%) | (62.7) | (62.0) | (63.6) | (63.1) | (63.5) | (66.6) | (63.9) | (68.9) | (69.5) | (2.9%, 6.5%) |
| Ambroxol | 823 | 880 | 792 | 999 | 756 | 1264 | 704 | 789 | 71 | 3.8% |
| (%) | (36.1) | (34.1) | (33.7) | (35.8) | (35.4) | (37.9) | (36.6) | (39.6) | (37.4) | (1.8%, 5.8%) |
| Antihistamines | 316 | 358 | 321 | 374 | 249 | 388 | 221 | 275 | 21 | -7.2% |
| (%) | (13.9) | (13.9) | (13.7) | (13.4) | (11.7) | (11.6) | (11.5) | (13.8) | (11.1) | (-9.4%, -5.0%) |
|  FGAHs | 151 | 144 | 105 | 103 | 62 | 88 | 36 | 36 | 2 | -25.2% |
|  (%) | (6.6) | (5.6) | (4.5) | (3.7) | (2.9) | (2.6) | (1.9) | (1.8) | (1.1) | (-28.4%, -21.7%) |
|  Sedative SGAHs | 65 | 65 | 63 | 69 | 33 | 32 | 12 | 19 | 2 | -23.9% |
|  (%) | (2.9) | (2.5) | (2.7) | (2.5) | (1.6) | (1.0) | (0.6) | (1.0) | (1.1) | (-28.4%, -19.0%) |
|  Non-sedative SGAHs | 114 | 157 | 163 | 215 | 160 | 284 | 177 | 230 | 18 | 10.1% |
| (%) | (5.0) | (6.1) | (6.9) | (7.7) | (7.5) | (8.5) | (9.2) | (11.5) | (9.5) | (6.9%, 13.4%) |
| LTRA | 1531 | 1710 | 1588 | 1963 | 1463 | 2354 | 1339 | 1539 | 148 | 8.6% |
| (%) | (67.2) | (66.2) | (67.6) | (70.3) | (68.6) | (70.6) | (69.6) | (77.2) | (77.9) | (6.8%, 10.5%) |
| Mediator release inhibitors | 907 | 1055 | 951 | 1106 | 905 | 1394 | 793 | 784 | 81 | 1.6% |
| (%) | (39.8) | (40.8) | (40.5) | (39.6) | (42.4) | (41.8) | (41.2) | (39.3) | (42.6) | (-0.2%, 3.5%) |
| Xanthine | 575 | 592 | 415 | 406 | 280 | 333 | 138 | 113 | 10 | -30.2% |
| (%) | (25.3) | (22.9) | (17.7) | (14.6) | (13.1) | (10.0) | (7.2) | (6.7) | (5.3) | (-32.1%, -29.2%) |
| Inhaled corticosteroids | 263 | 355 | 312 | 381 | 249 | 384 | 229 | 261 | 32 | -1.0% |
| (%) | (11.6) | (13.7) | (13.3) | (13.7) | (11.7) | (11.5) | (11.9) | (13.1) | (16.8) | (-3.4%, 1.5%) |

FGAHs, first-generation antihistamines; SGAHs, second-generation antihistamines; LTRA, leukotriene receptor antagonists; %Increase, %increase of proportion per year for health resource utilization in ratio scale