Online Supplementary Material

**TABLE S1** Number of exacerbations recorded during the study (full cohort, year 1 or year 2).

| Number of exacerbations | Year 1: acute exacerbation severity |          | Year 2: acute exacerbation severity |          |
|------------------------|-----------------------------------|----------|-----------------------------------|----------|
|                        | Any                               | Mild     | Moderate                          | Severe   | Any                               | Mild     | Moderate                          | Severe   |
|                        | 355                               | 31       | 304                               | 20       | 223                               | 20       | 191                               | 12       |
| Exacerbation rate per year*, mean (95% confidence interval) | 3.0 (2.6–3.5) | 0.3 (0.2–0.4) | 2.6 (2.2–3.0) | 0.2 (0.1–0.4) | 2.3 (2.0–2.7) | 0.2 (0.1–0.3) | 2.0 (1.7–2.4) | 0.1 (0.1–0.2) |

| Number of exacerbations | Number of subjects (N=127) |          | Number of subjects (N=103) |          |
|------------------------|---------------------------|----------|---------------------------|----------|
|                        | 0                         | 19 (15.0%) | 99 (78.0%) | 27 (21.3%) | 113 (89.0%) | 18 (17.5%) | 84 (81.6%) | 22 (21.4%) | 93 (90.3%) |
|                        | 1                         | 30 (23.6%) | 25 (19.7%) | 29 (22.8%) | 11 (8.7%) | 23 (22.3%) | 18 (17.5%) | 30 (29.1%) | 8 (7.8%) |
|                        | 2                         | 18 (14.2%) | 3 (2.4%) | 20 (15.7%) | 1 (0.8%) | 26 (25.2%) | 1 (1.0%) | 22 (21.4%) | 2 (1.9%) |
|                        | 3                         | 18 (14.2%) | 0 (0%) | 18 (14.2%) | 1 (0.8%) | 16 (15.5%) | 0 (0%) | 12 (11.7%) | 0 (0%) |
|                        | 4                         | 9 (7.1%) | 0 (0%) | 8 (6.3%) | 1 (0.8%) | 10 (9.7%) | 0 (0%) | 9 (8.7%) | 0 (0%) |
|                        | 5                         | 15 (11.8%) | 0 (0%) | 12 (9.4%) | 0 (0%) | 5 (4.9%) | 0 (0%) | 4 (3.9%) | 0 (0%) |
|                        | 6                         | 8 (6.3%) | 0 (0%) | 4 (3.1%) | 0 (0%) | 1 (1.0%) | 0 (0%) | 3 (2.9%) | 0 (0%) |
|                        | 7                         | 5 (3.9%) | 0 (0%) | 8 (6.3%) | 0 (0%) | 3 (2.9%) | 0 (0%) | 1 (1.0%) | 0 (0%) |
|                        | >7                        | 5 (3.9%) | 0 (0%) | 1 (0.8%) | 0 (0%) | 1 (1.0%) | 0 (0%) | 0 (0%) | 0 (0%) |

N, total number of subjects.

* Binomial negative model. Total exposure time was 117 years in year 1 and 96 years in year 2.
TABLE S2 Bacterial and viral pathogen incidence in stable-state and exacerbation-state sputum samples (full cohort, year 1 or year 2).

|                     | Number stable-state samples/total number samples | Number exacerbation-state samples/total number samples | Yearly rate of exacerbations with samples containing pathogen* (95% CI) |
|---------------------|-----------------------------------------------|------------------------------------------------------|-----------------------------------------------------------------------|
|                     | Year 1                                      | Year 2                                              | Year 1                                                | Year 2                                                                 |
|                     |                  |                  | Year 1                                      | Year 2                                               |
| **Bacteria: culture-positive** | | | | |
| Any                 | 466/952 (48.9%) | 289/676 (42.8%) | 188/320 (58.8%) | 100/194 (51.5%) | 1.59 (1.30–1.95) | 1.04 (0.82–1.32) |
| H. influenzae       | 287/952 (30.1%) | 152/676 (22.5%) | 129/320 (40.3%) | 53/194 (27.3%) | 1.10 (0.84–1.43) | 0.55 (0.39–0.77) |
| M. catarrhalis      | 50/952 (5.3%)   | 23/676 (3.4%)   | 40/320 (12.5%) | 19/194 (9.8%)  | 0.34 (0.24–0.48) | 0.20 (0.12–0.33) |
| S. pneumoniae       | 177/952 (18.6%) | 108/676 (16.0%) | 47/320 (14.7%) | 29/194 (14.9%) | 0.39 (0.27–0.58) | 0.30 (0.19–0.46) |
| S. aureus           | 40/952 (4.2%)   | 43/676 (6.4%)   | 18/320 (5.6%)  | 9/194 (4.6%)   | 0.16 (0.07–0.36) | 0.10 (0.04–0.22) |
| P. aeruginosa       | 49/952 (5.1%)   | 32/676 (4.7%)   | 21/320 (6.6%)  | 16/194 (8.2%)  | 0.18 (0.09–0.35) | 0.17 (0.06–0.45) |
| **Bacteria: PCR-positive** | | | | | |
| Any                 | 515/910 (56.6%) | 310/590 (52.5%) | 204/307 (66.4%) | 103/177 (58.2%) | 1.74 (1.42–2.12) | 1.07 (0.65–1.35) |
| H. influenzae       | 405/910 (44.5%) | 232/566 (41.0%) | 165/306 (53.9%) | 69/177 (39.0%)  | 1.41 (1.12–1.77) | 0.72 (0.53–0.96) |
| M. catarrhalis      | 102/910 (11.2%) | 71/566 (12.5%)  | 60/306 (19.6%) | 31/177 (17.5%)  | 0.50 (0.37–0.69) | 0.32 (0.23–0.46) |
| S. pneumoniae       | 120/910 (13.2%) | 55/566 (9.7%)   | 26/306 (8.5%)  | 19/177 (10.7%)  | 0.22 (0.14–0.35) | 0.20 (0.13–0.31) |
| S. aureus           | 40/910 (4.4%)   | 29/590 (4.9%)   | 12/281 (4.3%)  | 8/177 (4.5%)    | 0.10 (0.03–0.32) | 0.08 (0.04–0.18) |
| P. aeruginosa       | 52/910 (5.7%)   | 42/590 (7.1%)   | 18/281 (6.4%)  | 17/177 (9.6%)   | 0.15 (0.07–0.35) | 0.18 (0.06–0.46) |
| **Virus**           | | | | | |
| Any                 | 124/910 (13.6%) | 65/590 (11.0%)  | 126/305 (41.3%) | 59/177 (33.3%)  | 1.07 (0.86–1.32) | 0.61 (0.47–0.79) |
| Enterovirus         | 83/910 (9.1%)   | 50/590 (8.5%)   | 80/305 (26.2%) | 34/177 (19.2%)  | 0.68 (0.51–0.89) | 0.35 (0.25–0.49) |
| Human rhinovirus    | 56/908 (6.2%)   | 38/590 (6.4%)   | 70/305 (23.0%) | 32/177 (18.1%)  | 0.59 (0.45–0.78) | 0.33 (0.23–0.47) |
| Human coronavirus   | 22/910 (2.4%)   | 5/590 (0.8%)    | 21/305 (6.9%)  | 8/177 (4.5%)    | 0.18 (0.11–0.29) | 0.08 (0.04–0.17) |
| Influenza virus     | 5/910 (0.5%)    | 1/950 (0.2%)    | 15/305 (4.9%)  | 7/177 (4.0%)    | 0.07 (0.03–0.14) | 0.05 (0.02–0.12) |
| Human metapneumovirus | 2/910 (0.2%) | 0 | 6/305 (2.0%) | 3/177 (1.7%) | 0.05 (0.02–0.11) | 0.03 (0.01–0.10) |
| Parainfluenza virus | 5/910 (0.5%)    | 6/590 (1.0%)    | 6/305 (2.0%)  | 4/177 (2.3%)    | 0.05 (0.02–0.11) | 0.04 (0.02–0.11) |
| Adenovirus          | 6/910 (0.7%)    | 0               | 3/305 (1.0%)  | 1/177 (0.6%)    | 0.03 (0.01–0.08) | 0.01 (0.00–0.07) |
| Respiratory syncytial virus | 2/910 (0.2%) | 3/590 (0.5%) | 3/305 (1.0%) | 5/177 (2.8%) | 0.03 (0.01–0.08) | 0.05 (0.02–0.12) |
| Human bocavirus     | 2/910 (0.2%)    | 0               | 3/305 (1.0%)  | 1/177 (0.6%)    | 0.02 (0.00–0.12) | 0.01 (0.00–0.07) |

95% CI, 95% confidence interval.

*a* Binomial negative model. Total exposure time was 117 years in year 1 and 96 years in year 2.
TABLE S3  Average presence of bacterial or viral pathogens or eosinophil rate >3% in sputum samples at exacerbation or stable state by frequency of exacerbation (completer cohort, year 1 or year 2).

Exacerbation samples, year 1

| Type                        | Exacerbation frequency during year 1 | N  | %   | 95% CI LL | 95% CI UL |
|-----------------------------|--------------------------------------|----|-----|-----------|-----------|
| Presence of Hi (culture)    | >4                                   | 24 | 40.0| 31.2      | 49.3      |
|                             | 2–4                                  | 30 | 35.4| 24.5      | 47.4      |
|                             | 1                                    | 17 | 52.9| 30.1      | 75.0      |
|                             | Total                                 | 71 | 39.6| 32.8      | 46.6      |
| Presence of Hi (PCR)        | >4                                   | 24 | 47.7| 38.5      | 57.1      |
|                             | 2–4                                  | 30 | 47.7| 35.8      | 59.7      |
|                             | 1                                    | 15 | 73.3| 48.5      | 90.8      |
|                             | Total                                 | 69 | 49.7| 42.6      | 56.8      |
| Presence of Mcat (culture)  | >4                                   | 24 | 14.5| 8.8       | 21.9      |
|                             | 2–4                                  | 30 | 21.5| 12.8      | 32.5      |
|                             | 1                                    | 17 | 11.8| 2.1       | 32.1      |
|                             | Total                                 | 71 | 14.6| 10.1      | 20.0      |
| Presence of Mcat (PCR)      | >4                                   | 24 | 23.9| 16.5      | 32.4      |
|                             | 2–4                                  | 30 | 21.5| 12.8      | 32.5      |
|                             | 1                                    | 15 | 26.7| 9.2       | 51.5      |
|                             | Total                                 | 69 | 23.3| 17.6      | 29.6      |
| Presence of bacteria (culture) | >4                                  | 24 | 55.5| 46.1      | 64.5      |
|                             | 2–4                                  | 30 | 60.0| 47.9      | 71.4      |
|                             | 1                                    | 17 | 76.5| 53.5      | 92.0      |
|                             | Total                                 | 71 | 58.9| 51.8      | 65.7      |
| Presence of bacteria (PCR)  | >4                                   | 24 | 63.3| 54.0      | 72.0      |
|                             | 2–4                                  | 30 | 63.1| 51.0      | 74.1      |
|                             | 1                                    | 15 | 86.7| 64.2      | 97.7      |
|                             | Total                                 | 69 | 65.1| 58.1      | 71.8      |
| Presence of bacteria (PCR) and virus | >4                                  | 24 | 24.8| 17.3      | 33.4      |
|                             | 2–4                                  | 30 | 28.1| 18.1      | 39.9      |
|                             | 1                                    | 15 | 46.7| 23.5      | 70.9      |
|                             | Total                                 | 69 | 27.7| 21.6      | 34.3      |
| Presence of virus           | >4                                   | 24 | 39.4| 30.6      | 48.8      |
|                             | 2–4                                  | 30 | 43.8| 32.0      | 56.0      |
|                             | 1                                    | 15 | 60.0| 35.1      | 81.7      |
|                             | Total                                 | 69 | 42.6| 35.6      | 49.7      |
| Presence of eosinophils >3% | >4                                   | 24 | 25.5| 17.9      | 34.1      |
|                             | 2–4                                  | 30 | 27.7| 17.8      | 39.3      |
|                             | 1                                    | 17 | 17.6| 4.7       | 39.6      |
|                             | Total                                 | 71 | 25.5| 19.7      | 32.0      |
| Absence of bacteria/virus/eosinolphils | >4                                  | 24 | 15.6| 9.6       | 23.2      |
| Type | Exacerbation frequency during year 1 | N  | %   | 95% CI LL | 95% CI UL |
|------|-------------------------------------|----|-----|-----------|-----------|
| 2-4  |                                     | 30 | 6.3 | 2.0       | 13.9      |
| 1    |                                     | 15 | 0.0 | 0.0       | 1.0       |
| Total|                                     | 69 | 11.2| 7.2       | 16.2      |

N, number of patients; 95% CI LL/UL, 95% confidence interval lower limit/upper limit; Hi, *Haemophilus influenzae*; Mcat, *Moraxella catarrhalis*. 
## Exacerbation samples, year 2

| Type                          | Exacerbation frequency during year 2 | N  | %   | 95% CI LL | 95% CI UL |
|-------------------------------|--------------------------------------|----|-----|-----------|-----------|
| Presence of Hi (culture)      | >4                                   | 9  | 23.5| 11.5      | 39.4      |
|                               | 2–4                                  | 42 | 28.4| 19.7      | 38.4      |
|                               | 1                                    | 16 | 18.8| 5.0       | 41.7      |
|                               | Total                                 | 67 | 26.1| 19.2      | 33.8      |
| Presence of Hi (PCR)          | >4                                   | 8  | 29.0| 15.2      | 46.2      |
|                               | 2–4                                  | 41 | 42.2| 31.9      | 52.9      |
|                               | 1                                    | 14 | 35.7| 14.6      | 61.7      |
|                               | Total                                 | 63 | 38.3| 30.2      | 46.9      |
| Presence of Mcat (culture)    | >4                                   | 9  | 8.8 | 2.3       | 21.3      |
|                               | 2–4                                  | 42 | 9.1 | 4.3       | 16.3      |
|                               | 1                                    | 16 | 12.5| 2.2       | 33.8      |
|                               | Total                                 | 67 | 9.4 | 5.3       | 15.0      |
| Presence of Mcat (PCR)        | >4                                   | 8  | 9.7 | 2.5       | 23.2      |
|                               | 2–4                                  | 41 | 19.3| 11.8      | 28.6      |
|                               | 1                                    | 14 | 35.7| 14.6      | 61.7      |
|                               | Total                                 | 63 | 18.8| 12.6      | 26.1      |
| Presence of bacteria (culture)| >4                                   | 9  | 44.1| 28.3      | 60.8      |
|                               | 2–4                                  | 42 | 52.3| 41.9      | 62.5      |
|                               | 1                                    | 16 | 50.0| 26.9      | 73.1      |
|                               | Total                                 | 67 | 50.0| 41.7      | 58.3      |
| Presence of bacteria (PCR)    | >4                                   | 8  | 51.6| 34.4      | 68.5      |
|                               | 2–4                                  | 41 | 60.2| 49.5      | 70.3      |
|                               | 1                                    | 14 | 57.1| 31.7      | 80.2      |
|                               | Total                                 | 63 | 57.8| 49.2      | 66.2      |
| Presence of bacteria (PCR)    | >4                                   | 8  | 3.2 | 0.2       | 13.4      |
|                               | 2–4                                  | 41 | 24.1| 15.8      | 34.0      |
|                               | 1                                    | 14 | 42.9| 19.8      | 68.3      |
|                               | Total                                 | 63 | 21.1| 14.6      | 28.7      |
| Presence of bacteria (PCR)    | >4                                   | 8  | 12.9| 4.2       | 27.5      |
|                               | 2–4                                  | 41 | 42.2| 31.9      | 52.9      |
|                               | 1                                    | 14 | 78.6| 53.4      | 94.2      |
|                               | Total                                 | 63 | 39.1| 30.9      | 47.7      |
| Presence of eosinophils >3%   | >4                                   | 9  | 38.2| 23.2      | 55.0      |
|                               | 2–4                                  | 42 | 21.6| 13.9      | 30.9      |
|                               | 1                                    | 16 | 18.8| 5.0       | 41.7      |
|                               | Total                                 | 67 | 25.4| 18.6      | 33.0      |
| Absence of bacteria/virus/eosinophils | >4 | 8  | 16.1| 6.1       | 31.5      |
|                               | 2–4                                  | 41 | 12.0| 6.2       | 20.2      |
|                               | 1                                    | 14 | 0.0 | 0.0       | 0.0       |
|                               | Total                                 | 63 | 11.7| 6.9       | 18.0      |

N, number of patients; 95% CI LL/UL, 95% confidence interval lower limit/upper limit; Hi, *Haemophilus influenzae*; Mcat, *Moraxella catarrhalis*.
## Stable-state samples, year 1

| Type                                    | Exacerbation frequency during year 1 | N  | %  | 95% CI LL | 95% CI UL |
|-----------------------------------------|-------------------------------------|----|----|-----------|-----------|
| Presence of Hi (culture)                |                                     |    |    |           |           |
| >4                                      | 24                                  |    | 30.0 | 23.0 | 37.6     |
| 2–4                                     | 30                                  |    | 24.4 | 18.4 | 31.2     |
| 0–1                                     | 27                                  |    | 38.0 | 31.3 | 45.0     |
| Total                                   | 81                                  |    | 31.1 | 27.2 | 35.2     |
| Presence of Hi (PCR)                    |                                     |    |    |           |           |
| >4                                      | 24                                  |    | 43.9 | 36.1 | 52.0     |
| 2–4                                     | 30                                  |    | 39.0 | 31.9 | 46.4     |
| 0–1                                     | 27                                  |    | 55.0 | 47.9 | 62.0     |
| Total                                   | 81                                  |    | 46.4 | 42.1 | 50.7     |
| Presence of Mcat (culture)              |                                     |    |    |           |           |
| >4                                      | 24                                  |    | 6.0  | 2.9  | 10.6     |
| 2–4                                     | 30                                  |    | 8.1  | 4.7  | 12.8     |
| 0–1                                     | 27                                  |    | 3.1  | 1.3  | 6.2      |
| Total                                   | 81                                  |    | 5.6  | 3.9  | 7.9      |
| Presence of Mcat (PCR)                  |                                     |    |    |           |           |
| >4                                      | 24                                  |    | 12.2 | 7.6  | 18.1     |
| 2–4                                     | 30                                  |    | 11.6 | 7.4  | 17.0     |
| 0–1                                     | 27                                  |    | 10.6 | 6.7  | 15.5     |
| Total                                   | 81                                  |    | 11.4 | 8.8  | 14.3     |
| Presence of bacteria (culture)          |                                     |    |    |           |           |
| >4                                      | 24                                  |    | 50.7 | 42.7 | 58.6     |
| 2–4                                     | 30                                  |    | 50.6 | 43.1 | 58.0     |
| 0–1                                     | 27                                  |    | 53.1 | 46.1 | 60.1     |
| Total                                   | 81                                  |    | 51.6 | 47.2 | 55.9     |
| Presence of bacteria (PCR)              |                                     |    |    |           |           |
| >4                                      | 24                                  |    | 56.1 | 48.0 | 63.9     |
| 2–4                                     | 30                                  |    | 55.2 | 47.8 | 62.5     |
| 0–1                                     | 27                                  |    | 64.0 | 57.0 | 70.6     |
| Total                                   | 81                                  |    | 58.7 | 54.4 | 63.0     |
| Presence of bacteria (PCR) and virus    |                                     |    |    |           |           |
| >4                                      | 24                                  |    | 6.8  | 3.4  | 11.5     |
| 2–4                                     | 30                                  |    | 5.2  | 2.5  | 9.2      |
| 0–1                                     | 27                                  |    | 9.6  | 5.9  | 14.3     |
| Total                                   | 81                                  |    | 7.3  | 5.2  | 9.8      |
| Presence of virus                       |                                     |    |    |           |           |
| >4                                      | 24                                  |    | 14.2 | 9.2  | 20.4     |
| 2–4                                     | 30                                  |    | 12.2 | 7.9  | 17.6     |
| 0–1                                     | 27                                  |    | 13.3 | 9.0  | 18.6     |
| Total                                   | 81                                  |    | 13.2 | 10.4 | 16.3     |
| Presence of eosinophils >3%             |                                     |    |    |           |           |
| >4                                      | 24                                  |    | 33.3 | 26.1 | 41.1     |
| 2–4                                     | 30                                  |    | 36.0 | 29.1 | 43.4     |
| 0–1                                     | 27                                  |    | 33.9 | 27.4 | 40.7     |
| Total                                   | 81                                  |    | 34.4 | 30.4 | 38.6     |
| Absence of bacterial/virus/eosinophils  |                                     |    |    |           |           |
| >4                                      | 24                                  |    | 25.0 | 18.5 | 32.4     |
| 2–4                                     | 30                                  |    | 19.8 | 14.3 | 26.1     |
| 0–1                                     | 27                                  |    | 28.2 | 22.1 | 34.9     |
| Total                                   | 81                                  |    | 24.4 | 20.8 | 28.3     |

N, number of patients; 95% CI LL/UL, 95% confidence interval lower limit/upper limit; Hi, *Haemophilus influenzae*; Mcat, *Moraxella catarrhalis*.
## Stable-state samples, year 2

| Type                          | Exacerbation frequency during year 2 | N   | %   | 95% CI LL | 95% CI UL |
|-------------------------------|--------------------------------------|-----|-----|-----------|-----------|
| Presence of Hi (culture)      | >4                                   | 9   | 20.0| 10.2      | 33.2      |
|                               | 2–4                                  | 40  | 20.5| 15.6      | 26.1      |
|                               | 0–1                                  | 28  | 25.1| 19.4      | 31.5      |
|                               | Total                                 | 77  | 22.4| 18.8      | 26.4      |
| Presence of Hi (PCR)          | >4                                   | 9   | 26.3| 14.2      | 41.6      |
|                               | 2–4                                  | 40  | 42.1| 35.4      | 49.1      |
|                               | 0–1                                  | 27  | 43.7| 36.4      | 51.1      |
|                               | Total                                 | 76  | 41.3| 36.6      | 46.1      |
| Presence of Mcat (culture)    | >4                                   | 9   | 2.2 | 0.1       | 9.4       |
|                               | 2–4                                  | 40  | 3.1 | 1.4       | 6.0       |
|                               | 0–1                                  | 28  | 5.1 | 2.6       | 8.8       |
|                               | Total                                 | 77  | 3.9 | 2.4       | 5.9       |
| Presence of Mcat (PCR)        | >4                                   | 9   | 2.6 | 0.2       | 11.1      |
|                               | 2–4                                  | 40  | 7.6 | 4.5       | 11.9      |
|                               | 0–1                                  | 27  | 23.6| 17.7      | 30.2      |
|                               | Total                                 | 76  | 13.9| 10.8      | 17.5      |
| Presence of bacteria (culture)| >4                                   | 9   | 48.9| 34.7      | 63.2      |
|                               | 2–4                                  | 40  | 41.5| 35.2      | 48.0      |
|                               | 0–1                                  | 28  | 42.6| 35.8      | 49.6      |
|                               | Total                                 | 77  | 42.7| 38.2      | 47.2      |
| Presence of bacteria (PCR)    | >4                                   | 9   | 51.3| 35.9      | 66.5      |
|                               | 2–4                                  | 40  | 50.5| 43.6      | 57.4      |
|                               | 0–1                                  | 28  | 55.5| 48.2      | 62.6      |
|                               | Total                                 | 77  | 52.7| 48.0      | 57.4      |
| Presence of bacteria (PCR) and virus | >4 | 9 | 0.0 | . | . |
|                               | 2–4                                  | 40  | 2.5 | 0.9       | 5.2       |
|                               | 0–1                                  | 28  | 11.0| 7.0       | 16.1      |
|                               | Total                                 | 77  | 5.9 | 3.9       | 8.4       |
| Presence of virus             | >4                                   | 9   | 2.6 | 0.1       | 10.8      |
|                               | 2–4                                  | 40  | 6.4 | 3.6       | 10.4      |
|                               | 0–1                                  | 28  | 15.9| 11.1      | 21.7      |
|                               | Total                                 | 77  | 10.2| 7.5       | 13.3      |
| Presence of eosinophils >3%   | >4                                   | 9   | 46.7| 32.6      | 61.1      |
|                               | 2–4                                  | 40  | 33.9| 27.9      | 40.3      |
|                               | 0–1                                  | 28  | 26.7| 20.8      | 33.2      |
|                               | Total                                 | 77  | 32.1| 28.0      | 36.5      |
| Absence of bacterial virus/eosinophils | >4 | 9 | 25.6 | 13.8 | 40.6 |
|                               | 2–4                                  | 40  | 32.2| 26.0      | 38.8      |
|                               | 0–1                                  | 28  | 32.4| 25.9      | 39.4      |
|                               | Total                                 | 77  | 31.7| 27.4      | 36.2      |

N, number of patients; 95% CI LL/LL, 95% confidence interval lower limit/upper limit; Hi, *Haemophilus influenzae*; Mcat, *Moraxella catarrhalis*. 
**TABLE S4** Percentage of visits in which patients were receiving chronic azithromycin treatment according to difference between number of exacerbations in year 2 versus number in year 1 (completer cohort, year 1 or year 2).

| Number of exacerbations in year 2 minus number in year 1 | Number of patients | Number of visits | Percentage of visits under azithromycin |
|----------------------------------------------------------|--------------------|-----------------|----------------------------------------|
|                                                          |                    | Year 1          | Year 2                                 |
| ≤ -2                                                     | 32                 | 449            | 382                                    |
|                                                          |                     |                |                                        |
| -1                                                       | 13                 | 171            | 160                                    |
|                                                          |                     |                |                                        |
| 0                                                        | 15                 | 200            | 187                                    |
|                                                          |                     |                |                                        |
| +1                                                       | 13                 | 177            | 160                                    |
|                                                          |                     |                |                                        |
| ≥ +2                                                     | 15                 | 198            | 193                                    |


**FIGURE S1** Effect of the presence of aetiological factors (bacterial or viral infection, or eosinophilic inflammation) at any visit on the odds of experiencing a change in number of exacerbations in year 2 relative to year 1 (completer cohort).

*Haemophilus influenzae* detected by PCR or culture

Comparison of ≤ -2 and ≥ +2 groups, *p*=0.001 (PCR) and 0.004 (culture).

*Moraxella catarrhalis* detected by PCR or culture

Comparison of ≤ -2 and ≥ +2 groups, *p*=0.211 (PCR) and 0.122 (culture).

Viruses and eosinophils

Comparison of ≤ -2 and ≥ +2 groups, *p*=0.492 (viruses) and *p*=0.988 (eosinophils).

≤ -2, at least two fewer exacerbations in year 2 than in year 1; -1, one fewer exacerbation; 0, no change; 1, one more exacerbation; ≥ +2, at least two more exacerbations. LL, 95% confidence interval lower limit; UL, 95% confidence interval upper limit. *P* values were estimated using the Wald test.