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## S1: Supplementary Methods

**1:1 Matching:** Matches one or more controls to cases with similar propensity scores (PS) based on a prespecified caliper and using numerical matching algorithms including exact, greedy, optimal, and full matching. In the scenario of 1:1 matching, one treated unit is matched with one non-treated unit in terms of similar characteristics.

**1:2 Matching:** Similar to 1:1 matching, except that one treated unit is matched with two non-treated units in terms of similar characteristics.

**Stratification (subclass):** Sample is divided into strata based on rank-ordered PSs and comparisons between groups are performed within each stratum.

**Inverse probability of treatment weighting:** Weights cases by the inverse of the PS. It is a technique similar to survey sampling, where weights are used to ensure that samples are representative of specific populations by creating pseudo-populations, thus retaining the whole sample size.

**Overlap weighting:** Each subject is weighted by its probability of being assigned to the opposite treatment group. Compared with IPTW ATE or ATT, overlap weights are restricted between 0 and 1, and consequently, the effect of extreme weights is eliminated. It up-weights patients whose PS are close to 0.5 and smoothly down-weights the patients in the tails of the PS distribution.

**Bayesian additive regression trees:** It is comprised of a sum-of-trees model and a regularization prior on the parameters of that model.

**Generalized boosted modeling:** It is a nonparametric technique that predicts the intervention by performing piecewise constant model, constructed as combination of simple regression trees. An iterative additive algorithm is applied in which firstly a simple regression tree predicts the intervention given covariates, and then additional trees are added without altering the previous fit. With too many iterations, the GBM over-fits the data, whereas with too few, important features of the data are not captured. Therefore, it is advised that the user selects the number of iterations that balances between under and over-fitting the data.

## S2: Supplementary R packages

**MatchIt:** Performs matching and Stratification. Available matching algorithms: nearest neighbor, Mahalanobis, caliper, exact, full, optimal, subclassification and includes built-in numeric and graphical diagnostics.

**tableone:** Creates ’table’ to describe Baseline Characteristics with or without Propensity Score Weights.

**survey:** Used to conduct the weighted analysis (IPTW).

**PSW:** Used to conduct the overlap weighting method.

**sandwich:** Provides robust and cluster robust standard errors through the vcovHC() and vcovCL() functions, respectively

**WeightIt:** Weighting for Covariate Balance in Observational Studies. An extended method- ological framework including Generalized boosted modeling PS (”gbm”), Bayesian additive regression trees PS (”bart”), SuperLearner PS (”super”) and more.

**riskCommunicator:** riskCommunicator estimates risk and rate differences, in addition to risk and rate ratios. The package estimates these effects using g-computation with the appropriate parametric model depending on the outcome (logistic regression for binary out- comes, Poisson regression for rate or count outcomes, and linear regression for continuous outcomes)

**mice:** Multiple imputation using Fully Conditional Specification (FCS) implemented by Chained Equations algorithm.

**MatchThem:** Calculates the causal effect estimate in each matched or weighted dataset (from m impute) using parametric or non-parametric statistical models and pools the obtained estimates from these models according to Rubin’s rules.

## S3: Supplementary Tables

### Table S1: Risk factors of LRTIs

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** |  | | |
| **Baseline Characteristics** |  | **Coding** | **Missingness** |
| Gender |  | M=Male, F=Female  above 16 years old  -  -  0 = ex-smoker, 1 = non-smoker, 2 = smoker  0 = compensation, 1 = no compensation  0 = ≤ 30, 1 = > 30  0 = low, 1 = medium, 2 = high | Complete  Complete  51%  52%  65%  Complete  82%  Complete |
| Age |
| Systolic BP |
| Diastolic BP |
| Smoking status |
| Socioeconomic Status |
| BMI Category |
| Risk status |
| **Lab results** |  | | |
| eGFR category |  | 0-15 = Stage 5, 15-30 = Stage 4,  30-60 = Stage 3, 60-90 = Stage 2,  90 = Stage 1 | 56% |
| **Vaccines** | **ATC** | | |
| Flu vaccination in 2018 | J07BB | 0 = not received, 1 = received | Complete |
| **Comorbidities** | **ICPC-2** | | |
| Chronic liver disease | D97 | 0 = not diagnosed, 1 = diagnosed | Complete |
| Heart failure | K77 | 0 = not diagnosed, 1 = diagnosed | Complete |
| Atrial fibrillation | K78 | 0 = not diagnosed, 1 = diagnosed | Complete |
| Heart valve disease | K83 | 0 = not diagnosed, 1 = diagnosed | Complete |
| Atherosclerosis | K92 | 0 = not diagnosed, 1 = diagnosed | Complete |
| Chronic obstructive pulmonary disease | R95 | 0 = not diagnosed, 1 = diagnosed | Complete |
| Asthma | R96 | 0 = not diagnosed, 1 = diagnosed | Complete |
| Diabetes | T89, T90 | 0 = not diagnosed, 1 = diagnosed | Complete |
| Hypertension | K86, K87 | 0 = not diagnosed, 1 = diagnosed | Complete |
| Ischemic disease | K74, K75, K76 | 0 = not diagnosed, 1 = diagnosed | Complete |
| Stroke | K90, K90 | 0 = not diagnosed, 1 = diagnosed | Complete |
| Cancer | Full list\* | 0 = not diagnosed, 1 = diagnosed | Complete |

\* Cancer variable refers to the following code: A79, B72, B73, B74, D74, D75, D76, D77, F74, H75, K72, L71, N74, N76, R84, R85, R92, S77, T71, T73, U75, U76, U77, U79, W72, X75, X76, X77, X81, Y77, Y78

### Table S2: Risk group definition according to diagnoses and medications

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| High risk | Diagnoses | HIV/AIDS | ICPC-2: B90 | Chronic |
|  |  | Lymphoma | ICPC-2: B72 | Chronic |
|  |  | Leukemia | ICPC-2: B73 | Chronic |
|  |  | Malignant neoplasm blood, other | ICPC-2: B74 | Chronic |
|  |  | Asplenia | ICD-10: D73.0 | Chronic |
|  |  | Sickle-cell disease or hemoglobinopathy | ICPC-2: B78 | Chronic |
|  |  | Cerebrospinal fluid leak | ICD-10: G96.0 | 1 year |
|  |  | Cochlear implant | ICD-10: Z96.2 | Chronic |
|  | Medication | Immunosuppressants | ATC: L04 | In 2019 or 2018, 1 prescription |
|  |  | Glucocorticoids | ATC: H02AB | 2 prescriptions in 2019 |
| Intermediate risk | Diagnoses | Chronic bronchitis | ICPC-2: R79 | Chronic |
|  |  | Congenital respiratory anomaly | ICPC-2: R89 | Chronic |
|  |  | COPD | ICPC-2: R95 | Chronic |
|  |  | Asthma | ICPC-2: R96 | Chronic |
|  |  | Congenital cardiovascular anomaly | ICPC-2: K73 | Chronic |
|  |  | Angina pectoris | ICPC-2: K74 | Chronic |
|  |  | Acute myocardial infarction | ICPC-2: K75 | Chronic |
|  |  | Chronic ischaemic heart disease | ICPC-2: K76 | Chronic |
|  |  | Heart failure | ICPC-2: K77 | Chronic |
|  |  | Atrial fibrillation | ICPC-2: K78 | Chronic |
|  |  | Pulmonary heart disease | ICPC-2: K82 | Chronic |
|  |  | Heart valve disease | ICPC-2: K83 | Chronic |
|  |  | TIA | ICPC-2: K89 | Chronic |
|  |  | CVA | ICPC-2: K90 | Chronic |
|  |  | Peripheral arterial disease | ICPC-2: K92 | Chronic |
|  |  | Chronic liver disease | ICPC-2: D97 | Chronic |
|  |  | Chronic alcohol abuse | ICPC-2: P15 | Chronic |
|  |  | Chronic kidney disease | Based on eGFR | 1x <60ml/min in 2017 or 2018 |
|  |  | Diabetes mellitus | ICPC-2: T89 or T90 | Chronic |
|  |  | Multiple sclerosis | ICPC-2: N86 | Chronic |
|  |  | Parkinson’s disease | ICPC-2: N87 | Chronic |
|  |  | Muscular dystrophy | ICD-10: G71.0 | Chronic |
|  |  | Myasthenia gravis | ICD-10: G70.0 | Chronic |
|  |  | Lambert-Eaton syndrome | ICD-10: G73.1 | Chronic |
|  |  | Myopathy | ICD-10: G70, G71, G72, G73 | Chronic |
|  |  | Motor neuron disease | ICD-10: G12.2 | Chronic |
|  |  | Charcot-Marie-Tooth disease | ICD-10: G60.0 | Chronic |
| Low risk | All other patients |  |  |  |

### Table S3: Balance covariates before and after 1:1 & 2:1 PS matching for PPV23 & PCV13 (0-5 years)

Original sample PS matching 1:1 PS matching 2:1

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variables | Not vaccinated | Vaccinated | SMD/  SPD |  | Not vaccinated | Vaccinated | SMD |  | Not vaccinated | Vaccinated | SMD/  SPD |
|  | (N = 188815) | (N = 6310) |  |  | (N = 6022) | (N = 6022) |  |  | (N = 11412) | (N = 6022) |  |
| Sex, Male (%) | 86893 (46.0) | 3029 (48.0) | 0.040 |  | 2875 (47.7) | 2875 (47.7) | <0.001 |  | 5360 (47.0) | 2875 (47.7) | 0.015 |
| Age, mean (SD) | 46.66 (18.99) | 69.41 (12.26) | 1.424 |  | 69.47 (12.61) | 69.34 (12.26) | 0.011 |  | 69.40 (12.78) | 69.34 (12.26) | 0.005 |
| Socioeconomic status | 160856 (85.2) | 5125 (81.2) | 0.106 |  | 4922 (81.7) | 4922 (81.7) | <0.001 |  | 9323 (81.7) | 4922 (81.7) | 0.001 |
| Risk status |  |  | 1.071 |  |  |  | <0.001 |  |  |  | 0.060 |
| High risk (%) | 4336 (2.3) | 920 (14.6) |  |  | 735 (12.2) | 735 (12.2) |  |  | 1190 (10.4) | 735 (12.2) |  |
| Low risk (%) | 139375 (73.8) | 1725 (27.3) |  |  | 1723 (28.6) | 1723 (28.6) |  |  | 3443 (30.2) | 1723 (28.6) |  |
| Intermediate risk, yes (%) | 45104 (23.9) | 3665 (58.1) |  |  | 3564 (59.2) | 3564 (59.2) |  |  | 6779 (59.4) | 3564 (59.2) |  |
| Smoking status |  |  | 0.317 |  |  |  | <0.001 |  |  |  | 0.018 |
| Ex-smoker (%) | 50625 (26.8) | 2585 (41.0) |  |  | 2455 (40.8) | 2455 (40.8) |  |  | 4572 (40.1) | 2455 (40.8) |  |
| Smoker (%) | 48780 (25.8) | 1111 (17.6) |  |  | 1023 (17.0) | 1023 (17.0) |  |  | 1917 (16.8) | 1023 (17.0) |  |
| Never-smoker (%) | 89410 (47.4) | 2614 (41.4) |  |  | 2544 (42.2) | 2544 (42.2) |  |  | 4923 (43.1) | 2544 (42.2) |  |
| Body mass index, obese (%) | 32792 (17.4) | 1317 (20.9) | 0.089 |  | 1323 (22.0) | 1259 (20.9) | 0.026 |  | 2487 (21.8) | 1259 (20.9) | 0.022 |
| Systolic pressure, mean (SD) | 124.65 (14.88) | 128.84 (14.54) | 0.285 |  | 129.55 (14.88) | 129.02 (14.43) | 0.037 |  | 129.62 (14.80) | 129.02 (14.43) | 0.041 |
| Diastolic pressure, mean (SD) | 76.69 (9.19) | 75.49 (8.49) | 0.135 |  | 76.10 (8.66) | 75.58 (8.47) | 0.060 |  | 76.15 (8.66) | 75.58 (8.47) | 0.067 |
| Liver disease, yes (%) | 4049 (2.1) | 386 (6.1) | 0.201 |  | 348 (5.8) | 370 (6.1) | 0.015 |  | 654 (5.7) | 370 (6.1) | 0.017 |
| Heart failure, yes (%) | 1771 (0.9) | 298 (4.7) | 0.230 |  | 244 (4.1) | 276 (4.6) | 0.026 |  | 436 (3.8) | 276 (4.6) | 0.038 |
| Atrial fibrillation, yes (%) | 4349 (2.3) | 711 (11.3) | 0.362 |  | 606 (10.1) | 678 (11.3) | 0.039 |  | 1120 (9.8) | 678 (11.3) | 0.047 |
| Heart valve, yes (%) | 2206 (1.2) | 360 (5.7) | 0.251 |  | 298 (4.9) | 334 (5.5) | 0.027 |  | 567 (5.0) | 334 (5.5) | 0.026 |
| Atherosclerosis, yes (%) | 2502 (1.3) | 327 (5.2) | 0.219 |  | 296 (4.9) | 304 (5.0) | 0.006 |  | 530 (4.6) | 304 (5.0) | 0.019 |
| COPD, yes (%) | 3976 (2.1) | 1012 (16.0) | 0.500 |  | 830 (13.8) | 820 (13.6) | 0.005 |  | 1305 (11.4) | 820 (13.6) | 0.066 |
| Asthma, yes (%) | 16310 (8.6) | 1226 (19.4) | 0.315 |  | 1035 (17.2) | 1093 (18.2) | 0.025 |  | 1859 (16.3) | 1093 (18.2) | 0.049 |
| Diabetes, yes (%) | 10674 (5.7) | 1155 (18.3) | 0.397 |  | 1148 (19.1) | 1100 (18.3) | 0.020 |  | 2162 (18.9) | 1100 (18.3) | 0.017 |
| Hypertension, yes (%) | 29216 (15.5) | 2746 (43.5) | 0.646 |  | 2612 (43.4) | 2596 (43.1) | 0.005 |  | 4853 (42.5) | 2596 (43.1) | 0.012 |
| Ischemic disease, yes (%) | 5347 (2.8) | 746 (11.8) | 0.350 |  | 672 (11.2) | 708 (11.8) | 0.019 |  | 1259 (11.0) | 708 (11.8) | 0.023 |
| Stroke, yes (%) | 4152 (2.2) | 500 (7.9) | 0.263 |  | 415 (6.9) | 469 (7.8) | 0.034 |  | 818 (7.2) | 469 (7.8) | 0.024 |
| Cancer, yes (%) | 30740 (16.3) | 2402 (38.1) | 0.505 |  | 2216 (36.8) | 2223 (36.9) | 0.002 |  | 4104 (36.0) | 2223 (36.9) | 0.020 |
| Egfr |  |  | 0.370 |  |  |  | 0.021 |  |  |  | 0.023 |
| Stage 1 (%) | 46271 (24.5) | 845 (13.4) |  |  | 829 (13.8) | 812 (13.5) |  |  | 1525 (13.4) | 812 (13.5) |  |
| Stage 2 (%) | 98308 (52.1) | 3118 (49.4) |  |  | 3039 (50.5) | 3005 (49.9) |  |  | 5729 (50.2) | 3005 (49.9) |  |
| Stage 3 (%) | 40743 (21.6) | 2094 (33.2) |  |  | 1929 (32.0) | 1963 (32.6) |  |  | 3748 (32.8) | 1963 (32.6) |  |
| Stage 4 (%) | 2948 (1.6) | 201 (3.2) |  |  | 176 (2.9) | 191 (3.2) |  |  | 323 (2.8) | 191 (3.2) |  |
| Stage 5 (%) | 545 (0.3) | 52 (0.8) |  |  | 49 (0.8) | 51 (0.8) |  |  | 87 (0.8) | 51 (0.8) |  |
| Flu vaccine in 2018, yes (%) | 33034 (17.5) | 5203 (82.5) | 1.709 |  | 4923 (81.8) | 4932 (81.9) | 0.004 |  | 9231 (80.9) | 4932 (81.9) | 0.026 |

### Table S4: Balance covariates before and after IPTW & overlap for PPV23 & PCV13 (0-5 years)

Original sample Inverse Probability Treatment Weighted Overlap Weights

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variables | Not vaccinated | Vaccinated | SMD/  SPD |  | Not vaccinated | Vaccinated | SMD |  | Not vaccinated | Vaccinated | SMD/  SPD |
|  | (N = 188815) | (N = 6310) |  |  | (N = 6526.5) | (N = 6310.0) |  |  | (N = 5222.0) | (N = 5222.0) |  |
| Sex, Male (%) | 86893 (46.0) | 3029 (48.0) | 0.040 |  | 3139.2 (48.1) | 3029.0 (48.0) | 0.002 |  | 2457.9 (47.1) | 2457.9 (47.1) | <0.001 |
| Age, mean (SD) | 46.66 (18.99) | 69.41 (12.26) | 1.424 |  | 70.29 (15.38) | 69.41 (12.26) | 0.063 |  | 68.73 (15.86) | 68.73 (12.63) | <0.001 |
| Socioeconomic status | 160856 (85.2) | 5125 (81.2) | 0.106 |  | 5263.7 (80.7) | 5125.0 (81.2) | 0.014 |  | 4217.8 (80.8) | 4217.8 (80.8) | <0.001 |
| Risk status |  |  | 1.071 |  |  |  | 0.056 |  |  |  | <0.001 |
| High risk (%) | 4336 (2.3) | 920 (14.6) |  |  | 1081.7 (16.6) | 920.0 (14.6) |  |  | 630.0 (12.1) | 630.0 (12.1) |  |
| Low risk (%) | 139375 (73.8) | 1725 (27.3) |  |  | 1707.5 (26.2) | 1725.0 (27.3) |  |  | 1598.7 (30.6) | 1598.7 (30.6) |  |
| Intermediate risk, yes (%) | 45104 (23.9) | 3665 (58.1) |  |  | 3737.3 (57.3) | 3665.0 (58.1) |  |  | 2993.3 (57.3) | 2993.3 (57.3) |  |
| Smoking status |  |  | 0.317 |  |  |  | 0.009 |  |  |  | <0.001 |
| Ex-smoker (%) | 50625 (26.8) | 2585 (41.0) |  |  | 2692.5 (41.3) | 2585.0 (41.0) |  |  | 2079.0 (39.8) | 2079.0 (39.8) |  |
| Smoker (%) | 48780 (25.8) | 1111 (17.6) |  |  | 1128.3 (17.3) | 1111.0 (17.6) |  |  | 920.4 (17.6) | 920.4 (17.6) |  |
| Never-smoker (%) | 89410 (47.4) | 2614 (41.4) |  |  | 2705.7 (41.5) | 2614.0 (41.4) |  |  | 2222.5 (42.6) | 2222.5 (42.6) |  |
| Body mass index, obese (%) | 32792 (17.4) | 1317 (20.9) | 0.089 |  | 1357.1 (20.8) | 1317.0 (20.9) | 0.002 |  | 1090.7 (20.9) | 1090.7 (20.9) | <0.001 |
| Systolic pressure, mean (SD) | 124.65 (14.88) | 128.84 (14.54) | 0.285 |  | 128.85 (15.02) | 128.84 (14.54) | 0.001 |  | 128.27 (15.00) | 128.27 (14.49) | <0.001 |
| Diastolic pressure, mean (SD) | 76.69 (9.19) | 75.49 (8.49) | 0.135 |  | 75.31 (8.85) | 75.49 (8.49) | 0.021 |  | 75.12 (8.88) | 75.12 (8.52) | <0.001 |
| Liver disease, yes (%) | 4049 (2.1) | 386 (6.1) | 0.201 |  | 412.9 (6.3) | 386.0 (6.1) | 0.009 |  | 303.0 (5.8) | 303.0 (5.8) | <0.001 |
| Heart failure, yes (%) | 1771 (0.9) | 298 (4.7) | 0.230 |  | 334.5 (5.1) | 298.0 (4.7) | 0.019 |  | 234.5 (4.5) | 234.5 (4.5) | <0.001 |
| Atrial fibrillation, yes (%) | 4349 (2.3) | 711 (11.3) | 0.362 |  | 783.0 (12.0) | 711.0 (11.3) | 0.023 |  | 559.2 (10.7) | 559.2 (10.7) | <0.001 |
| Heart valve, yes (%) | 2206 (1.2) | 360 (5.7) | 0.251 |  | 389.2 (6.0) | 360.0 (5.7) | 0.011 |  | 272.6 (5.2) | 272.6 (5.2) | <0.001 |
| Atherosclerosis, yes (%) | 2502 (1.3) | 327 (5.2) | 0.219 |  | 362.6 (5.6) | 327.0 (5.2) | 0.017 |  | 249.9 (4.8) | 249.9 (4.8) | <0.001 |
| COPD, yes (%) | 3976 (2.1) | 1012 (16.0) | 0.500 |  | 1123.7 (17.2) | 1012.0 (16.0) | 0.032 |  | 675.4 (12.9) | 675.4 (12.9) | <0.001 |
| Asthma, yes (%) | 16310 (8.6) | 1226 (19.4) | 0.315 |  | 1308.3 (20.0) | 1226.0 (19.4) | 0.015 |  | 922.4 (17.7) | 922.4 (17.7) | <0.001 |
| Diabetes, yes (%) | 10674 (5.7) | 1155 (18.3) | 0.397 |  | 1205.6 (18.5) | 1155.0 (18.3) | 0.004 |  | 927.9 (17.8) | 927.9 (17.8) | <0.001 |
| Hypertension, yes (%) | 29216 (15.5) | 2746 (43.5) | 0.646 |  | 2897.9 (44.4) | 2746.0 (43.5) | 0.018 |  | 2195.5 (42.0) | 2195.5 (42.0) | <0.001 |
| Ischemic disease, yes (%) | 5347 (2.8) | 746 (11.8) | 0.350 |  | 821.0 (12.6) | 746.0 (11.8) | 0.023 |  | 593.2 (11.4) | 593.2 (11.4) | <0.001 |
| Stroke, yes (%) | 4152 (2.2) | 500 (7.9) | 0.263 |  | 536.4 (8.2) | 500.0 (7.9) | 0.011 |  | 402.1 (7.7) | 402.1 (7.7) | <0.001 |
| Cancer, yes (%) | 30740 (16.3) | 2402 (38.1) | 0.505 |  | 2535.6 (38.9) | 2402.0 (38.1) | 0.016 |  | 1874.0 (35.9) | 1874.0 (35.9) | <0.001 |
| Egfr |  |  | 0.370 |  |  |  | 0.013 |  |  |  | <0.001 |
| Stage 1 (%) | 46271 (24.5) | 845 (13.4) |  |  | 853.6 (13.1) | 845.0 (13.4) |  |  | 723.5 (13.9) | 723.5 (13.9) |  |
| Stage 2 (%) | 98308 (52.1) | 3118 (49.4) |  |  | 3224.5 (49.4) | 3118.0 (49.4) |  |  | 2599.7 (49.8) | 2599.7 (49.8) |  |
| Stage 3 (%) | 40743 (21.6) | 2094 (33.2) |  |  | 2175.0 (33.3) | 2094.0 (33.2) |  |  | 1691.6 (32.4) | 1691.6 (32.4) |  |
| Stage 4 (%) | 2948 (1.6) | 201 (3.2) |  |  | 215.8 (3.3) | 201.0 (3.2) |  |  | 164.8 (3.2) | 164.8 (3.2) |  |
| Stage 5 (%) | 545 (0.3) | 52 (0.8) |  |  | 57.6 (0.9) | 52.0 (0.8) |  |  | 42.4 (0.8) | 42.4 (0.8) |  |
| Flu vaccine in 2018, yes (%) | 33034 (17.5) | 5203 (82.5) | 1.709 |  | 5425.5 (83.1) | 5203.0 (82.5) | 0.018 |  | 4142.6 (79.3) | 4142.6 (79.3) | <0.001 |

### Table S5: Balance covariates before and after BART & GBM for PPV23 & PCV13 (0-5 years)

Original sample Bayesian Additive Regression Trees Generalized Boosted Models

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variables | Not vaccinated | Vaccinated | SMD/  SPD |  | Not vaccinated | Vaccinated | SMD |  | Not vaccinated | Vaccinated | SMD/  SPD |
|  | (N = 188815) | (N = 6310) |  |  | (N = 6309.3) | (N = 6310.0) |  |  | (N = 6290.7) | (N = 6310.0) |  |
| Sex, Male (%) | 86893 (46.0) | 3029 (48.0) | 0.040 |  | 2990.9 (47.4) | 3029.0 (48.0) | 0.012 |  | 3014.4 (47.9) | 3029.0 (48.0) | 0.002 |
| Age, mean (SD) | 46.66 (18.99) | 69.41 (12.26) | 1.424 |  | 69.51 (12.40) | 69.41 (12.26) | 0.008 |  | 69.32 (12.45) | 69.41 (12.26) | 0.008 |
| Socioeconomic status | 160856 (85.2) | 5125 (81.2) | 0.106 |  | 5087.3 (80.6) | 5125.0 (81.2) | 0.015 |  | 5080.7 (80.8) | 5125.0 (81.2) | 0.012 |
| Risk status |  |  | 1.071 |  |  |  | 0.009 |  |  |  | 0.009 |
| High risk (%) | 4336 (2.3) | 920 (14.6) |  |  | 940.3 (14.9) | 920.0 (14.6) |  |  | 899.6 (14.3) | 920.0 (14.6) |  |
| Low risk (%) | 139375 (73.8) | 1725 (27.3) |  |  | 1712.8 (27.1) | 1725.0 (27.3) |  |  | 1736.4 (27.6) | 1725.0 (27.3) |  |
| Intermediate risk, yes (%) | 45104 (23.9) | 3665 (58.1) |  |  | 3656.1 (57.9) | 3665.0 (58.1) |  |  | 3654.6 (58.1) | 3665.0 (58.1) |  |
| Smoking status |  |  | 0.317 |  |  |  | 0.018 |  |  |  | 0.010 |
| Ex-smoker (%) | 50625 (26.8) | 2585 (41.0) |  |  | 2534.8 (40.2) | 2585.0 (41.0) |  |  | 2545.0 (40.5) | 2585.0 (41.0) |  |
| Smoker (%) | 48780 (25.8) | 1111 (17.6) |  |  | 1106.5 (17.5) | 1111.0 (17.6) |  |  | 1120.1 (17.8) | 1111.0 (17.6) |  |
| Never-smoker (%) | 89410 (47.4) | 2614 (41.4) |  |  | 2668.0 (42.3) | 2614.0 (41.4) |  |  | 2625.6 (41.7) | 2614.0 (41.4) |  |
| Body mass index, obese (%) | 32792 (17.4) | 1317 (20.9) | 0.089 |  | 1329.1 (21.1) | 1317.0 (20.9) | 0.005 |  | 1336.8 (21.3) | 1317.0 (20.9) | 0.009 |
| Systolic pressure, mean (SD) | 124.65 (14.88) | 128.84 (14.54) | 0.285 |  | 128.95 (14.72) | 128.84 (14.54) | 0.008 |  | 128.79 (14.43) | 128.84 (14.54) | 0.003 |
| Diastolic pressure, mean (SD) | 76.69 (9.19) | 75.49 (8.49) | 0.135 |  | 75.72 (8.56) | 75.49 (8.49) | 0.026 |  | 75.54 (8.44) | 75.49 (8.49) | 0.006 |
| Liver disease, yes (%) | 4049 (2.1) | 386 (6.1) | 0.201 |  | 389.5 (6.2) | 386.0 (6.1) | 0.002 |  | 383.2 (6.1) | 386.0 (6.1) | 0.001 |
| Heart failure, yes (%) | 1771 (0.9) | 298 (4.7) | 0.230 |  | 305.7 (4.8) | 298.0 (4.7) | 0.006 |  | 290.3 (4.6) | 298.0 (4.7) | 0.005 |
| Atrial fibrillation, yes (%) | 4349 (2.3) | 711 (11.3) | 0.362 |  | 722.9 (11.5) | 711.0 (11.3) | 0.006 |  | 694.8 (11.0) | 711.0 (11.3) | 0.007 |
| Heart valve, yes (%) | 2206 (1.2) | 360 (5.7) | 0.251 |  | 357.6 (5.7) | 360.0 (5.7) | 0.002 |  | 339.1 (5.4) | 360.0 (5.7) | 0.014 |
| Atherosclerosis, yes (%) | 2502 (1.3) | 327 (5.2) | 0.219 |  | 329.1 (5.2) | 327.0 (5.2) | 0.002 |  | 320.7 (5.1) | 327.0 (5.2) | 0.004 |
| COPD, yes (%) | 3976 (2.1) | 1012 (16.0) | 0.500 |  | 1003.1 (15.9) | 1012.0 (16.0) | 0.004 |  | 1014.7 (16.1) | 1012.0 (16.0) | 0.003 |
| Asthma, yes (%) | 16310 (8.6) | 1226 (19.4) | 0.315 |  | 1227.2 (19.5) | 1226.0 (19.4) | 0.001 |  | 1219.6 (19.4) | 1226.0 (19.4) | 0.001 |
| Diabetes, yes (%) | 10674 (5.7) | 1155 (18.3) | 0.397 |  | 1168.8 (18.5) | 1155.0 (18.3) | 0.006 |  | 1155.1 (18.4) | 1155.0 (18.3) | 0.001 |
| Hypertension, yes (%) | 29216 (15.5) | 2746 (43.5) | 0.646 |  | 2752.4 (43.6) | 2746.0 (43.5) | 0.002 |  | 2713.3 (43.1) | 2746.0 (43.5) | 0.008 |
| Ischemic disease, yes (%) | 5347 (2.8) | 746 (11.8) | 0.350 |  | 760.4 (12.1) | 746.0 (11.8) | 0.007 |  | 746.9 (11.9) | 746.0 (11.8) | 0.002 |
| Stroke, yes (%) | 4152 (2.2) | 500 (7.9) | 0.263 |  | 506.1 (8.0) | 500.0 (7.9) | 0.004 |  | 502.3 (8.0) | 500.0 (7.9) | 0.002 |
| Cancer, yes (%) | 30740 (16.3) | 2402 (38.1) | 0.505 |  | 2391.8 (37.9) | 2402.0 (38.1) | 0.003 |  | 2382.2 (37.9) | 2402.0 (38.1) | 0.004 |
| Egfr |  |  | 0.370 |  |  |  | 0.016 |  |  |  | 0.022 |
| Stage 1 (%) | 46271 (24.5) | 845 (13.4) |  |  | 875.6 (13.9) | 845.0 (13.4) |  |  | 885.6 (14.1) | 845.0 (13.4) |  |
| Stage 2 (%) | 98308 (52.1) | 3118 (49.4) |  |  | 3121.1 (49.5) | 3118.0 (49.4) |  |  | 3106.7 (49.4) | 3118.0 (49.4) |  |
| Stage 3 (%) | 40743 (21.6) | 2094 (33.2) |  |  | 2059.4 (32.6) | 2094.0 (33.2) |  |  | 2048.3 (32.6) | 2094.0 (33.2) |  |
| Stage 4 (%) | 2948 (1.6) | 201 (3.2) |  |  | 199.9 (3.2) | 201.0 (3.2) |  |  | 196.4 (3.1) | 201.0 (3.2) |  |
| Stage 5 (%) | 545 (0.3) | 52 (0.8) |  |  | 53.2 (0.8) | 52.0 (0.8) |  |  | 53.6 (0.9) | 52.0 (0.8) |  |
| Flu vaccine in 2018, yes (%) | 33034 (17.5) | 5203 (82.5) | 1.709 |  | 5201.0 (82.4) | 5203.0 (82.5) | 0.001 |  | 5172.9 (82.2) | 5203.0 (82.5) | 0.006 |

### Table S6: RR of PPV23 & PCV13 for all age & risk groups

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **age risk** | **Patients** | **Crude** | **Adjusted** | **PS 1\_1** | **PS 1\_2** | **Strata** | **IPTW** | **Overlap** | **BART** | **GBM** |
| 16\_49 | 442 | 2.57 [1.83, 3.59] | 1.27 [0.92, 1.67] | 1.1 [0.47, 2.56] | 1.07 [0.52, 2.22] | 1.24 [0.71, 2.19] | 1.05 [0.59, 1.84] | 1.02 [0.58, 1.8] | 0.94 [0.53, 1.67] | 1.01 [0.57, 1.79] |
| 16\_49 high | 150 | 0.99 [0.51, 1.92] | 0.83 [0.5, 1.39] | 1 [0.3, 3.37] | 1.34 [0.43, 4.13] | 1.3 [0.49, 3.46] | 1.29 [0.52, 3.18] | 1.22 [0.5, 2.99] | 1.28 [0.53, 3.11] | 1.34 [0.53, 3.4] |
| 16\_49 intermediate | 123 | 2.15 [1.28, 3.61] | 1.48 [0.85, 1.83] | 0.67 [0.11, 3.92] | 0.56 [0.12, 2.68] | 0.46 [0.11, 1.84] | 0.44 [0.11, 1.74] | 0.44 [0.11, 1.75] | 0.41 [0.1, 1.65] | 0.43 [0.11, 1.7] |
| 16\_49 low | 169 | 2.42 [1.33, 4.42] | 2.04 [1.22, 2.67] | 2 [0.37, 10.77] | 1.33 [0.38, 4.66] | 1.33 [0.51, 3.51] | 1.21 [0.46, 3.2] | 1.2 [0.46, 3.18] | 1.17 [0.44, 3.11] | 1.2 [0.45, 3.17] |
| 16\_84 | 5882 | 1.63 [1.45, 1.83] | 0.75 [0.67, 0.89] | 0.75 [0.64, 0.88] | 0.78 [0.67, 0.89] | 0.85 [0.75, 0.96] | 0.76 [0.66, 0.87] | 0.79 [0.7, 0.9] | 0.77 [0.67, 0.87] | 0.76 [0.67, 0.86] |
| 16\_84 high | 887 | 1.12 [0.84, 1.49] | 0.81 [0.63, 1.05] | 0.81 [0.54, 1.22] | 0.94 [0.64, 1.38] | 0.84 [0.61, 1.16] | 0.73 [0.52, 1.04] | 0.77 [0.56, 1.07] | 0.86 [0.62, 1.18] | 0.8 [0.58, 1.12] |
| 16\_84 intermediate | 3344 | 1.08 [0.93, 1.25] | 0.71 [0.61, 0.77] | 0.68 [0.56, 0.82] | 0.69 [0.58, 0.82] | 0.74 [0.63, 0.87] | 0.72 [0.61, 0.85] | 0.74 [0.63, 0.87] | 0.72 [0.61, 0.85] | 0.72 [0.61, 0.84] |
| 16\_84 low | 1651 | 1.5 [1.16, 1.94] | 0.83 [0.73, 0.96] | 1.02 [0.71, 1.46] | 0.96 [0.7, 1.3] | 1.03 [0.79, 1.34] | 0.94 [0.72, 1.22] | 0.96 [0.74, 1.24] | 0.83 [0.64, 1.09] | 0.85 [0.65, 1.11] |
| 50\_64 | 1113 | 2.05 [1.73, 2.44] | 1.11 [0.94, 1.19] | 0.98 [0.68, 1.41] | 1.04 [0.75, 1.43] | 1.06 [0.8, 1.39] | 1.03 [0.79, 1.36] | 1.06 [0.81, 1.39] | 0.99 [0.75, 1.3] | 1.01 [0.76, 1.33] |
| 50\_64 high | 253 | 1.07 [0.76, 1.51] | 0.84 [0.58, 1.24] | 1.08 [0.51, 2.32] | 1.47 [0.71, 3.03] | 1.08 [0.59, 1.99] | 1.11 [0.6, 2.03] | 1.06 [0.59, 1.92] | 1.09 [0.61, 1.93] | 1.11 [0.6, 2.04] |
| 50\_64 intermediate | 550 | 1.55 [1.21, 1.98] | 1.12 [0.97, 1.27] | 0.78 [0.48, 1.26] | 0.83 [0.54, 1.28] | 0.89 [0.6, 1.31] | 0.88 [0.6, 1.3] | 0.92 [0.63, 1.35] | 0.86 [0.58, 1.26] | 0.87 [0.6, 1.28] |
| 50\_64 low | 310 | 2.14 [1.51, 3.04] | 1.82 [1.37, 2.24] | 1.75 [0.74, 4.11] | 1.33 [0.69, 2.59] | 1.36 [0.8, 2.31] | 1.27 [0.75, 2.14] | 1.29 [0.76, 2.17] | 1.23 [0.73, 2.08] | 1.26 [0.75, 2.12] |
| 50\_84 | 5440 | 1.15 [1.02, 1.3] | 0.75 [0.64, 0.83] | 0.74 [0.63, 0.87] | 0.76 [0.66, 0.88] | 0.78 [0.68, 0.88] | 0.73 [0.64, 0.84] | 0.76 [0.67, 0.86] | 0.76 [0.67, 0.86] | 0.75 [0.66, 0.86] |
| 50\_84 high | 737 | 0.92 [0.67, 1.24] | 0.75 [0.57, 0.88] | 0.79 [0.51, 1.22] | 0.88 [0.59, 1.33] | 0.85 [0.61, 1.19] | 0.74 [0.52, 1.07] | 0.79 [0.56, 1.11] | 0.85 [0.61, 1.18] | 0.8 [0.57, 1.14] |
| 50\_84 intermediate | 3221 | 0.95 [0.82, 1.11] | 0.73 [0.62, 0.83] | 0.68 [0.56, 0.82] | 0.69 [0.58, 0.83] | 0.73 [0.62, 0.86] | 0.71 [0.61, 0.84] | 0.73 [0.62, 0.86] | 0.73 [0.62, 0.86] | 0.72 [0.61, 0.85] |
| 50\_84 low | 1482 | 1.05 [0.8, 1.37] | 0.81 [0.68, 1.09] | 0.98 [0.68, 1.42] | 0.94 [0.68, 1.29] | 0.84 [0.64, 1.11] | 0.85 [0.65, 1.12] | 0.86 [0.65, 1.13] | 0.81 [0.61, 1.06] | 0.81 [0.62, 1.07] |
| 50\_plus | 5868 | 1.53 [1.41, 1.66] | 0.92 [0.87, 0.97] | 0.78 [0.67, 0.91] | 0.79 [0.69, 0.91] | 0.78 [0.69, 0.88] | 0.73 [0.65, 0.83] | 0.75 [0.66, 0.85] | 0.78 [0.69, 0.89] | 0.78 [0.69, 0.88] |
| 50\_plus high | 770 | 1.16 [0.97, 1.4] | 0.95 [0.85, 1.04] | 0.89 [0.58, 1.34] | 0.97 [0.66, 1.42] | 0.94 [0.69, 1.28] | 0.86 [0.61, 1.21] | 0.85 [0.61, 1.17] | 0.93 [0.68, 1.28] | 0.88 [0.63, 1.23] |
| 50\_plus intermediate | 3542 | 1.2 [1.08, 1.33] | 0.92 [0.84, 0.98] | 0.71 [0.59, 0.85] | 0.72 [0.61, 0.85] | 0.72 [0.62, 0.84] | 0.7 [0.6, 0.81] | 0.72 [0.62, 0.83] | 0.74 [0.64, 0.86] | 0.74 [0.64, 0.86] |
| 50\_plus low | 1556 | 1.22 [1, 1.5] | 0.95 [0.84, 1.19] | 1 [0.7, 1.43] | 0.96 [0.7, 1.3] | 0.86 [0.66, 1.13] | 0.87 [0.67, 1.13] | 0.87 [0.67, 1.14] | 0.83 [0.64, 1.08] | 0.83 [0.64, 1.09] |
| 65\_74 | 2551 | 1.18 [1.03, 1.35] | 0.8 [0.72, 0.89] | 0.69 [0.53, 0.88] | 0.71 [0.57, 0.89] | 0.71 [0.57, 0.87] | 0.68 [0.55, 0.84] | 0.67 [0.54, 0.82] | 0.7 [0.57, 0.86] | 0.67 [0.54, 0.83] |
| 65\_74 high | 299 | 1.13 [0.83, 1.56] | 1 [0.77, 1.34] | 0.86 [0.4, 1.81] | 0.82 [0.41, 1.64] | 0.85 [0.49, 1.45] | 0.81 [0.46, 1.45] | 0.73 [0.42, 1.28] | 0.84 [0.49, 1.46] | 0.75 [0.42, 1.32] |
| 65\_74 intermediate | 1496 | 1 [0.84, 1.2] | 0.79 [0.61, 0.9] | 0.62 [0.45, 0.85] | 0.62 [0.47, 0.83] | 0.65 [0.5, 0.85] | 0.64 [0.49, 0.84] | 0.63 [0.48, 0.82] | 0.64 [0.49, 0.84] | 0.63 [0.48, 0.82] |
| 65\_74 low | 756 | 0.87 [0.63, 1.21] | 0.78 [0.65, 0.96] | 0.81 [0.49, 1.35] | 0.93 [0.59, 1.47] | 0.76 [0.51, 1.14] | 0.78 [0.52, 1.16] | 0.78 [0.52, 1.16] | 0.77 [0.52, 1.15] | 0.77 [0.52, 1.15] |
| 65\_84 | 4327 | 0.93 [0.81, 1.06] | 0.73 [0.63, 0.88] | 0.69 [0.58, 0.83] | 0.71 [0.6, 0.84] | 0.7 [0.61, 0.82] | 0.65 [0.56, 0.76] | 0.67 [0.58, 0.78] | 0.72 [0.62, 0.83] | 0.7 [0.6, 0.81] |
| 65\_84 high | 484 | 0.81 [0.56, 1.19] | 0.73 [0.5, 1.17] | 0.68 [0.4, 1.16] | 0.69 [0.42, 1.14] | 0.78 [0.53, 1.16] | 0.68 [0.44, 1.04] | 0.71 [0.47, 1.07] | 0.79 [0.53, 1.18] | 0.73 [0.48, 1.11] |
| 65\_84 intermediate | 2671 | 0.84 [0.7, 0.99] | 0.71 [0.61, 0.85] | 0.66 [0.53, 0.82] | 0.67 [0.55, 0.81] | 0.69 [0.58, 0.83] | 0.67 [0.56, 0.81] | 0.68 [0.57, 0.82] | 0.71 [0.59, 0.84] | 0.7 [0.58, 0.84] |
| 65\_84 low | 1172 | 0.82 [0.6, 1.12] | 0.71 [0.56, 0.9] | 0.85 [0.56, 1.29] | 0.85 [0.59, 1.22] | 0.7 [0.51, 0.97] | 0.72 [0.52, 0.99] | 0.72 [0.52, 1] | 0.72 [0.52, 0.99] | 0.72 [0.52, 0.99] |
| 65\_plus | 4755 | 1.21 [1.11, 1.33] | 0.9 [0.79, 1.01] | 0.74 [0.63, 0.88] | 0.75 [0.64, 0.87] | 0.72 [0.63, 0.82] | 0.68 [0.59, 0.78] | 0.68 [0.59, 0.78] | 0.75 [0.66, 0.86] | 0.74 [0.64, 0.85] |
| 65\_plus high | 517 | 1.13 [0.91, 1.4] | 1 [0.8, 1.31] | 0.81 [0.49, 1.34] | 0.81 [0.51, 1.28] | 0.91 [0.63, 1.31] | 0.84 [0.57, 1.25] | 0.81 [0.55, 1.18] | 0.91 [0.62, 1.32] | 0.83 [0.56, 1.23] |
| 65\_plus intermediate | 2992 | 1.04 [0.93, 1.16] | 0.87 [0.81, 0.96] | 0.7 [0.57, 0.85] | 0.7 [0.59, 0.84] | 0.69 [0.59, 0.82] | 0.66 [0.56, 0.78] | 0.68 [0.57, 0.8] | 0.73 [0.62, 0.86] | 0.73 [0.62, 0.85] |
| 65\_plus low | 1246 | 0.9 [0.7, 1.16] | 0.8 [0.59, 0.98] | 0.88 [0.59, 1.31] | 0.88 [0.62, 1.24] | 0.74 [0.55, 1.01] | 0.76 [0.56, 1.03] | 0.75 [0.55, 1.02] | 0.75 [0.55, 1.02] | 0.75 [0.55, 1.02] |
| 75\_84 | 1776 | 1.31 [1.13, 1.51] | 0.99 [0.8, 1.13] | 0.7 [0.55, 0.91] | 0.71 [0.57, 0.9] | 0.72 [0.59, 0.89] | 0.66 [0.53, 0.83] | 0.71 [0.58, 0.88] | 0.73 [0.59, 0.9] | 0.73 [0.59, 0.91] |
| 75\_84 high | 185 | 1.07 [0.77, 1.49] | 0.89 [0.54, 1.16] | 0.53 [0.24, 1.15] | 0.59 [0.28, 1.22] | 0.74 [0.41, 1.33] | 0.61 [0.32, 1.15] | 0.74 [0.41, 1.36] | 0.73 [0.4, 1.32] | 0.71 [0.39, 1.3] |
| 75\_84 intermediate | 1175 | 1.17 [0.98, 1.39] | 0.92 [0.81, 1.06] | 0.7 [0.52, 0.94] | 0.72 [0.55, 0.93] | 0.76 [0.59, 0.97] | 0.73 [0.57, 0.93] | 0.76 [0.6, 0.97] | 0.77 [0.6, 0.98] | 0.77 [0.6, 0.98] |
| 75\_84 low | 416 | 0.96 [0.63, 1.47] | 0.79 [0.57, 0.98] | 0.93 [0.46, 1.91] | 0.74 [0.4, 1.34] | 0.61 [0.35, 1.05] | 0.64 [0.37, 1.1] | 0.64 [0.37, 1.1] | 0.63 [0.37, 1.09] | 0.64 [0.37, 1.09] |
| 75\_plus | 2204 | 1.24 [1.1, 1.41] | 1.01 [0.9, 1.12] | 0.79 [0.63, 0.99] | 0.78 [0.64, 0.95] | 0.78 [0.66, 0.93] | 0.73 [0.61, 0.88] | 0.75 [0.63, 0.9] | 0.8 [0.67, 0.95] | 0.8 [0.67, 0.95] |
| 75\_plus high | 218 | 1.16 [0.87, 1.56] | 1.05 [0.81, 1.43] | 0.78 [0.4, 1.51] | 0.81 [0.44, 1.5] | 1.03 [0.63, 1.69] | 0.95 [0.56, 1.62] | 0.97 [0.58, 1.63] | 0.99 [0.59, 1.65] | 0.94 [0.55, 1.58] |
| 75\_plus intermediate | 1496 | 1.09 [0.94, 1.26] | 0.95 [0.81, 1.07] | 0.76 [0.59, 0.98] | 0.76 [0.61, 0.96] | 0.77 [0.63, 0.95] | 0.73 [0.6, 0.9] | 0.76 [0.62, 0.94] | 0.79 [0.64, 0.97] | 0.8 [0.65, 0.98] |
| 75\_plus low | 490 | 0.94 [0.64, 1.39] | 0.86 [0.53, 1] | 1 [0.53, 1.9] | 0.82 [0.48, 1.4] | 0.73 [0.45, 1.18] | 0.75 [0.46, 1.2] | 0.74 [0.46, 1.19] | 0.72 [0.45, 1.16] | 0.73 [0.45, 1.17] |
| 85\_plus | 428 | 1.26 [0.99, 1.61] | 1.04 [0.74, 1.26] | 1.17 [0.73, 1.86] | 1.06 [0.71, 1.57] | 1.05 [0.76, 1.45] | 1.02 [0.73, 1.43] | 0.96 [0.69, 1.35] | 1.05 [0.75, 1.46] | 1.05 [0.76, 1.46] |
| 85\_plus high | 33 | 1.56 [0.83, 2.92] | 1.43 [0.88, 2.28] | 5 [0.64, 38.87] | 2.72 [0.73, 10.1] | 2.85 [1.16, 7] | 3.18 [1.25, 8.11] | 2.22 [0.85, 5.78] | 3.61 [1.38, 9.43] | 3.34 [1.24, 8.97] |
| 85\_plus intermediate | 321 | 1.08 [0.82, 1.43] | 1.04 [0.74, 1.3] | 1 [0.59, 1.68] | 0.92 [0.59, 1.43] | 0.9 [0.62, 1.31] | 0.85 [0.58, 1.24] | 0.87 [0.6, 1.28] | 0.86 [0.59, 1.27] | 0.88 [0.6, 1.29] |
| 85\_plus low | 74 | 0.91 [0.35, 2.4] | 0.91 [0.23, 1.59] | 1.33 [0.31, 5.75] | 1.32 [0.38, 4.52] | 1.3 [0.48, 3.55] | 1.25 [0.46, 3.39] | 1.18 [0.44, 3.2] | 1.35 [0.5, 3.69] | 1.4 [0.52, 3.78] |

### Table S7: Description of main and sensitivity analyses

|  |  |  |  |
| --- | --- | --- | --- |
| Type of analysis | Data source | Treatment | Outcome |
| Main | Vaccine & prescription file | PPV23 & PCV13 | LRTIs with antibiotics |
| Sensitivity | Vaccine & prescription file | PPV23 & PCV13 | LRTIs no antibiotics |
| Sensitivity | Vaccine file | PPV23 & PCV13 | LRTIs with antibiotics |
| Sensitivity | Vaccine file | PPV23 & PCV13 | LRTIs no antibiotics |
| Sensitivity | Vaccine & prescription file | PPV23 or PCV13 | LRTIs with antibiotics |
| Sensitivity | Vaccine & prescription file | PPV23 or PCV13 | LRTIs no antibiotics |
| Sensitivity | Vaccine file | PPV23 or PCV13 | LRTIs with antibiotics |
| Sensitivity | Vaccine file | PPV23 or PCV13 | LRTIs no antibiotics |

## S4: Supplementary Figures

### Figure S1: Forest plot of the RR of PPV23 & PCV13 on LRTIs treated with antibiotics (vaccine and prescription registration) in the 16-84 age group stratified by risk status.

Chart, box and whisker chart

Description automatically generated

### Figure S2: Forest plot of the RR of PPV23 & PCV13 on LRTIs treated with antibiotics (vaccine and prescription registration) in the 50-84 age group stratified by risk status.

Chart

Description automatically generated

### Figure S3. Forest plot of the RR of PPV23 or PCV13 on LRTIs without and with antibiotics for vaccines located in different data sources

Chart

Description automatically generated

### Figure S4: Forest plot of the RR of PPV23 & PCV13 on LRTIs without and with antibiotics for vaccines located in different data sources.

Chart

Description automatically generated

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