**Evidence Table 1. Postmarketing studies: Adults**

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| **Author, Year, Study Design** | **Population studied** | **Vaccines included** | **Selection Bias** | **Attrition, non-response** | **Participation bias** | **Ascertainment of vaccination status** | **Ascertainment of health outcome** | **Analysis conducted** | **Adjusted for these potential confounders** | **Period data collected** | **Study funder** | **Primary results regarding vaccine** | **Any risk factor findings** | **Comment** |
| Baxter, 2012, Retrospective cohort[73](#_ENREF_73) | Sample size: 60,996; Location: US; Age: 18-49; Setting: Kaiser Permanente Managed Care Health Plans | Ann Arbor Strain LAIV | Through Kaiser Permanente'simmunization registries, approximately 20,000 individuals 18–49 years of age who were immunized from the 2003–2004 to 2007–2008 influenza seasons with LAIV as part of routine clinicalpractice were identified. | NA | These were participants of a health plan (i.e. insured). | Medical record | Medical records, healthcare utilization database | Cox proportional hazards model | Adjusted for: Matching factors, seasonal changes in background rates | 2003-2008 | MedImmune | The rate of hospitalization or death dueto any condition within 180 days of vaccination with LAIV waslower than with TIV (1.46 vs 9.10; p < 0.01) or no vaccine (1.46vs 3.36; p < 0.01).The incidence rate for any serious adverse event (SAE) within 21 days and 42 days of vaccination with LAIV was lower compared to no vaccination. | NR |  |

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| Baxter, et al. 2012,[86](#_ENREF_86)Observational post-licensure (Phase IV) study; retrospective cohort | N=29,000;Location=California;Age=60+ years;Setting=Kaiser Permanente Northern California (KPNC), a US managed care organization | ZostavaxTM, a live, attenuated varicella-zoster virus vaccine | Entire population | Not really discussed. Study notes: From July 2006 through November 2007, 29,486 people 60 yearsof age or older were vaccinated with zoster vaccine at KPNC. Ofthem, 29,010 people had continuous KPNC membership for at least180 days after vaccination, and were included in the study population. | Not discussed | Medical records. Detailed vaccination data are tracked and captured by the KaiserImmunization Tracking System (KITS), one of the largest electronic tracking systems for immunization in the U.S. The KITS systemcollects, among other information, the patient’s medical record number, date of vaccination, type of vaccine, route of administration, facility in which the vaccine was administered, manufacturerand vaccine lot number, and can be linked to other data sources to get additional information | Medical records. Subjects were followed for all postvaccination hospitalization and ED visits identiﬁed by International Classiﬁcation of DiseasesandRelatedHealthProblems-9(ICD9) codes in the electronic medical records. | Exact conditional method with mid-probability adjustment | Self-controlled | 2006-2007 | This study was sponsored by Merck Sharp & Dohme, Corp. Trung Nam Tran and Patricia Saddier were full time employees of Merck Sharp& Dohme, Corp. at the time of the study. | Table 2. Health outcomes with elevated RR and statistically signiﬁcant unadjusted p-value (p<0.05)(N=29,010).Coronary atherosclerosis and other heart disease1.86 (1.09–3.15); p=0.02Coronary atherosclerosis (ATS)1.97 (1.11–3.49); p=0.02Percutaneous transluminal coronary angioplasty(PTCA)2.26 (1.19–4.27); p=0.01Systemic lupus, erythematosus and connective tissuedisorders8.57 (1.08–212.11); p=0.04 | None | Table 3 shows RR for subsets of individuals: diabetics, people with CHD, and people 80+ years. |
| Duderstadt et al. 2012, Retrospective cohort[92](#_ENREF_92) | N=2,385,102 active military personnel, including 1,074 cases of type 1 diabetes;Location=US;Age=17-35 years; | Hepatitis B, MMR, smallpox, typhoid, yellow fever | Entire population of Defense Medical Surveillance System. A total of 17,874 were excluded; if these exclusions differed systematically from those included, bias would be introduced into the study | Not applicable | Not discussed | Defense Medical Surveillance System | Defense Medical Surveillance System | Poisson regression | Receipt of multiple vaccines, age, race, sex, service branch, military grade, occupation, deployment, and calendar year | January 1 2002 to December 31 2008 | Department of Defense | Risk Ratios for Diabetes Type 1Hepatitis B: 0.83 (0.72, 0.95)MMR: 0.71 (0.61, 0.83) | Not reported |  |
| Eder et al. 2011, Case-control[91](#_ENREF_91) | N=318 (159 Cases, 159 Controls);Location=Toronto;Age=Case/control, Mean (SD): 44.9 (13.1)/48.4 (13.3);Setting=Cases taken from University of Toronto Psoriatic Arthritis (PsA) cohort, clinic-based. Controls from Toronto Psoriasis Cohort | Hepatitis A and B, influenza, pneumococcus | Cases and controls selected from different populations. Cases were from a clinic-based group (PsA cohort) while controls were from another cohort of non-arthritic psoriasis patients. Study notes, "In order to minimize selection bias, psoriasis patients wererecruited from several sources: dermatology clinics at Toronto Western Hospital and Women’s College Hospital,community dermatologists, family medicine clinics in Toronto, and the general public in the greater Toronto area byadvertising in local newspapers." However there are no details given for the recruitment of the two cohorts to determine if systematic biases resulted in non-comparable populations | No attrition mentioned. In terms of recruitment, 190 PsA patients (cases) were identified, authors were unable to contact 29 (6 deceased), and 2 were excluded due to poor English language skills. Overall, 159 PsA patients (83.6%) were included in the study. 196 patients with psoriasis (controls) were approached for enrollment, of whom 159 (81.1%) completed the questionnaire. | Study did not note whether participants differed from nonparticipants. | Self-report through questionnaire | Clinical data were available from the cohorts’ computerized databases | Logistic regression | Age, sex, duration and severity of psoriasis, and level of education. | Not reported | Krembil Foundation, Arthritis Society Spondyloarthritis Research Consortium of Canada National Research Initiative. Dr. Eder’s work was supported by a fellowship grant from the Canadian Arthritis Network and by an Abbott Psoriatic Arthritis Fellowship. Ms. Law’s work was supported by a scholarship from the Canadian Arthritis Network. Dr. Chandran’s work was supported by a Canadian Institutes of Health Research and Krembil Foundation. | OR (95% CI) of PsA:Hepatitis A: 0.70 (0.14–2.99), p=0.58 Hepatitis B: 1.50 (0.76–2.81), p=0.25Pneumococcus: 1.40 (0.75–2.72), p=0.28Flu: 1.0 (0.58–1.57), p=0.87 | Not reported | Recall bias was a concern; those with arthritis may show higher recall of triggers. By approaching patients with a recent onset of arthritis, the study population had a short interval from the onset of PsA of approximately 3 years. Authors avoided linking environmental exposures and arthritis in the questionnaire, and requested information about events that occurred in the past 10 years. They also assessed recall bias by comparing reported information about exposure to infections and injuries with available data from a computerized database that stores medical records from 6 medical centers and outpatient clinics. The aim was to assess whether there has been underreporting of events by psoriasis patients. Overall, 3 of 3 patients with psoriasis reported a previous injury and 0 of 2 reported an infection. In the PsA group, only 1 of 3 reported an injury and 1 of 6 reported an infection. Therefore, although these ﬁgures are small, it seems that recall bias is not a threat to the validity of the study, as the rates of reporting were not lower in the psoriasis group." |
| Eurich et al. 2012, Prospective cohort[75](#_ENREF_75) | N=6171;Location=Edmonton (Alberta, Canada);Age=mean age 59 years;Setting=Population-based cohort of adults presenting with community-acquired pneumonia (CAP) in Edmonton | Pneumococcal polysaccharide vaccination (PPV) | Authors note a large protective effect against ACS events among patients receiving PPV during the acute pneumonia event was observed. Although this in itself is not improbable, the fact that no ACS events occurred within theﬁrst 2-4 weeks post discharge in this group suggests someselection bias was occurring, as PPV generally requires2-4 weeks to initiate a reasonable response.Also the majority of the cohort were older and antibody response isknown to be poor in older populations with comorbiditiesFinally there may have been confounding by the healthy-user or healthy-vaccine effect, whereby more healthy or health-seeking patients are administered PPV compared with non-PPV patients | Of the 6874 cohort patients with CAP, authors excluded 310 (5%)who had PPV ﬁrst administered during their initial CAP presentation and 393 (6%) who could not be linked to theadministrative databases, resulting in a ﬁnal study cohort of 6171 patients | Not discussed | PPV status was collected by trained staff masked to all study hypotheses.Receipt of vaccination was ascertained throughmultiple avenues including patient and proxy interview, medicalrecord review, contact with primary care physicians and recordsfrom regional ofﬁce of community health | Research nurses prospectively collected all clinically diagnosed ACS events in the emergency department and during hospitalization. Thereafter, ACS events were ascertained by linking patients tocomprehensive provincial healthcare administrative databases | Multivariable Cox proportional hazard model | Pneumonia severity based on the PSI; comorbidities including chronic obstructive pulmonary disease, diabetes, ischemic heart disease (IHD); functional status, smoking status andcardiovascular and other medicationsAuthors also completed a propensity (to receive PPV) score analysis | 2000 to 2002 | DTE receives salary support from Alberta Heritage Foundation for Medical Research (AHFMR) and the Canadian Institutes for Health Research (CIHR). SRMreceives salary support from AHFMR and holds an endowed chair in patient health management. TJM received Grants-in-aid from Capital Health; and unrestricted grantsfrom Abbott Canada, Pﬁzer Canada and Janssen-Ortho Canada. | Adjusted HRs for fatal and non-fatal ACS events within 90 days according to pneumococcal vaccination statusPrimary analysisDeath or ACS-related hospitalization:0.42 (0.27 to 0.66), p=<0.001Death: 0.92 (0.32 to 2.63), p=0.88Hospitalization due to ACS:0.35 (0.21 to 0.57), p=<0.001Propensity score analysisDeath or ACS-related hospitalization: 0.46 (0.28 to 0.73), p=0.001Death: 1.51 (0.42 to 5.34), p=0.53Hospitalization due to ACS: 0.36 (0.21 to 0.61), p=<0.001 | None |  |
| Farez et al. 2012, Self-controlled case series[62](#_ENREF_62) | N=137 Multiple Sclerosis patients;Location=Argentina;Age=37 +/-8 years (mean) | Influenza (monovalent Focetria, Novartis SRL, Italy or trivalent Istivac, Sanofi Pasteur, France) | Bias if cases differed from the general population in systematic ways (e.g., more or less likely to be vaccinated, doctors more likely to recommend vaccinations) | 161 relapsing–remitting MS patients were identified from the database. 23 patients refused to participate and 2 had received other immunizations, leaving 137 | Study notes patients excluded did not differ significantly from those included | Self-report | Database review | Poisson regression model | None given | 1 January and 31 December 2010 | Raul Carrea Institute for Neurological Research | 30-day risk period: 0.86 (95% CI 0.20–3.62, p=0.836)60-day risk period: 0.61 (95% CI 0.18–2.02, p=0.419)90-day risk period: 0.51 (95% CI 0.18–1.47, p=0.211) | Not reported |  |
| Garbe et al. 2012, Case-control[68](#_ENREF_68) | N=1,200 (outpatient + inpatient). Influenza results presented just for outpatients where N=861;Location=Berlin, Germany;Age=18-92;Setting=Berlin hospitals, hematological practices, and laboratories | Influenza vaccine (Pneumococcal and poliomyelitis vaccine also assessed as causing 1 case each but ORs were Not reported.) | Cases and controls selected from the same hospitals using the same general procedures for interviews reducing the chance of selection bias occurring. Vaccines were not the only drugs study was interested in so diagnostic or surveillance biases lessened. Exposure misclassification was aminor concern because drug exposures were assessed 1 week before the index date | None | Study did not address | Self-report through face-to-face interviews and physician-provided information | Patients with ITP were identified through regular active inquiry in 2- to 3-week intervals in hospitals, hematological practices and laboratories. Diagnosis was additionally based on a face-to-face interview and physician-provided information. An advisory board assessed ambiguous cases. | Unconditional logistic regression | Model 1: age and sex (“single drug assessment”) Model 2: age, sex and all drugs that were significant in the single drug assessment (“joint drug assessment”) | October 2000 until March 2009 | Cases were collected within the study “Berlin Case–Control Surveillance (FAKOS) of Serious Blood Dyscrasias”,which was supported by a grant from the Federal Institute for Drugs andMedical Devices (Bonn, Germany). | OR (95% CI) of ITP Influenza, outpatient cases and controls:Model 1: 3.8 (1.5–9.1) Model 2: 4.0 (1.5–9.6) | Not reported |  |
| Glanz et al. 2011, Self-controlled case series[115](#_ENREF_115) | N=66,283 who received trivalent inactivated influenza vaccine (TIV);Location=US;Age=24-59 months;Setting=Seven US managed care organizations (Vaccine Safety Datalink) | TIV | No info on systematic differences between sites in vaccine or outcome administration or ascertainment | Not discussed | Not discussed | VSD records review | Medical record review | Conditional Poisson regression | Calendar month (season) and age | 2002-2006 | Centers for Disease Control and Prevention | Medically Attended Events That Met the Screening Criteria in Risk Windows of 0 to 2, 1 to 14, and 1 to 42 Days After VaccinationNon-confirmed Cases From Electronic Data AnalysisPotentially seriousNervous system disorder: 6.32 (0.96-41.65), p=0.06 Cardiac event: 3.56 (0.55-22.89), p=0.18Hypotension: 5.52 (0.71-43.07), p=0.10Gastrointestinal tract disorder: 2.75 (1.07-7.09), p=0.04 Cellulitis and skin reaction: 3.06 (0.89-10.53), p=0.08 Potentially less serious and commonRash: 2.33 (0.68-7.93), p=0.18 Limb soreness: 3.56 (1.30-9.75), p=0.01Fever: 1.40 (1.09-1.80), p=0.01 Gastrointestinal tract symptoms (vomiting and diarrhea): 1.52 (1.18-1.95), p=0.001 Medical Record–Confirmed CasesPotentially seriousGastrointestinal tract disorder: 7.70 (1.11-53.52), p=0.04Cellulitis and skin reaction: 3.27 (0.36-29.70), p=0.29Potentially less serious and commonRash: 1.94 (0.44-8.63), p=0.38Fever: 1.71 (1.64-1.80)Gastrointestinal tract symptoms (vomiting and diarrhea): 1.18 (1.10-1.25) | None given |  |
| Greene et al. 2012, Self-controlled risk interval and case-centered analysis[56](#_ENREF_56) | N=1.48 million doses Monovalent inactivated H1N1 and 1.72 million doses TIV; 8 US MCOs | Monovalent inactivated influenza vaccine (MIV) and seasonal trivalent inactivated influenza vaccine (TIV) during the 2009-2010 season | Differences across sites in study participants and entry into medical care organizations may be relevant in terms of sampling bias | Not reported | Not reported | Electronic data and medical record review | Electronic data and medical chart review | Conditional Poisson regression for self-controlled analysis and logistic regression for case-centered analysis | Case-centered analyses by stratum of onset date, age, sex, site | 2009–2010 | Centers for Disease Control and Prevention | Relative Risk (self-controlled risk analysis) of Guillain-Barré Syndrome (GBS, RR, 95% CIMIVConfirmed GBS 4.4 (1.3, 14.2)TIVConfirmed GBS: 1.3 (0.5, 3.8)Case-centered:The odds ratio for illness onset inside of the 42-day risk period versus outside of that period was 2.0 (95% CI: 0.5, 8.1). | None |  |
| Grimaldi-Bensouda et al. 2011, Prospective case-control[58](#_ENREF_58" \o "Grimaldi-Bensouda, 2011 #5285) | N=1225;Location=France;Age=Cases/Controls, Mean (SD): 48.6 (18.0)/50.7 (18.1);Setting=Cases drawn from all university and major regional hospital centers in metropolitan France known to have a large neurology clinic and centers treating neurologic disease in children; Controls from registry of general practice patients across France | Influenza vaccines (seasonal and A/H1N1) | Hospital-based cases and controls from general practitioner lists. Diagnostic and surveillance approaches may differ such that hospital cases may have had better ascertainment of risk factors. Authors note that exposure misclassification may have occurred. | None | Not discussed | Self-report and objective confirmation obtained in a sample of 40% of cases and controls for the seasonal vaccination. The proportion was raised to 100% during the A/H1N1 vaccination program. Confirmation included copies of vaccination sheets, certificates, and other documentation. | A neurologist completed a detailed medical form - cases ascertained using an algorithm considering clinical, electrophysiologic, and cerebrospinal fluid data. Borderline cases were reviewed by independent and blinded experts | Conditional logistic regression | Cases/controls matched by age, gender, index date (calendar month), and regionReceipt of other vaccines during the same time window, receipt of influenza vaccine in the past (before the time window considered), family history of autoimmune diseases, number of physician consultations in the previous year (0–2, 3–6, 7–12, or >=13), antibiotic or antiviral treatment in the previous 2 months, use of antipyretic agents in the previous 2 months. | March 2007 and June 2010. For the influenza A/H1N1 vaccine, analysis was restricted to the GBS cases that had occurred from commencement of the French national vaccination program on October 20, 2009, to 6 weeks after the end of the vaccination campaign on March 31, 2010 | LA-SER, GSK Biologicals, and Sanofi-Pasteur | All influenza vaccines (A/H1N1 + seasonal)First 6 weeks: 1.22 (0.45-3.32) 7 weeks to 3 months: 0.66 (0.27-1.65)4 months to 6 months: 0.80 (0.34-1.88)Seasonal influenza vaccine only First 6 weeks: 1.30 (0.41-4.12)7 weeks to 3 months: 0.60 (0.23-1.60)4 months to 6 months: 0.69 (0.29-1.66)Influenza A/H1N1 vaccine only First 6 weeks: 0.92 (0.11-7.55)7 weeks to 3 months: 1.08 (0.09-13.15) | Not reported |  |
| Gwini et al. 2011, Self-controlled case series[67](#_ENREF_67) | N=8,180 cases of first acute myocardial infarction;Location=UK;Age=>=40 years; | Influenza | Population of study may differ from population as a whole in systematic ways that decrease generalizability | None | Not discussed | General Practice Research Database (GPRD) | General Practice Research Database (GPRD) | Conditional Poisson regression | Seasonality | 2002-2007 | Research for Patient Benefit Program of the National Institute for Health Research, United Kingdom | Incidence Rate RatioPost-vaccination intervals1-14 days: 0.68 (0.6–0.78)15-28 days: 0.75 (0.66–0.86)29-59 days: 0.82 (0.75–0.90)60-90 days: 0.96 (0.87–1.07)91-120 days: 0.98 (0.89–1.09)121-180 days: 1.02 (0.95–1.10) |  |  |
| Hambidge et al. 2011, Self-controlled case series[69](#_ENREF_69) | N=348 adults with sickle cell disease in8 MCOs in the US;(Vaccine Safety Datalink (VSD) cohort) | Influenza | Unclear about differences between sites in population selection, case and exposure ascertainment; differences between cases and other populations (e.g., cases may have been more likely to be vaccinated) | Not discussed | Not discussed | Medical record | Medical record | Conditional Poisson regression | Stratification by sex and age, adjustment for month within season | 1991-2006 | Centers for Disease Control and Prevention | Incidence rate ratios for sickle cell hospitalizationAll: 0.92 (0.66, 1.28), p=0.6 | Males: 1.00 (0.59, 1.72), p=1.0Females 0.87 (0.57, 1.31), p=0.518-49 yrs: 0.84 (0.57, 1.22), p=0.850-64 yrs: 1.51 (0.72, 3.18), p=0.3>=65 yrs: 0.94 (0.10, 8.55), p=1.0 |  |
| Hedlund et al. 2003, Prospective cohort[66](#_ENREF_66) | N=100,242;Location=Stockholm County, Sweden;Age=>=65 years;Setting=All individuals in Stockholm County aged 65 years or older were invited to take part in a vaccination campaign against inﬂuenza and pneumococcal infection during 3 consecutive years, 1998–2000 | Influenza and 23-valent pneumococcal vaccine (PV) | No randomization - vaccinated group may differ systematically in some fashion that makes them more likely to show adverse (or non-adverse) effects that are not related to the vaccine | Not discussed | Not discussed | Department of CommunicableDisease Control and Prevention for Stockholm County database | Data on discharge diagnoses and mortality were obtained from the administrative database of Stockholm CountyCouncil | Poisson regression | Age and gender | 1998-1999 | Financial supported for this study was received from The Stockholm City Council, The Swedish Heart-Lung Foundation, The Swedish Society of Medicine, and KarolinskaInstitute. | Hospital admissions/100 000 individuals between 1 December 1998 and 30 November 1999Inﬂuenza 0.68 (0.53-0.88), p=0.002Pneumonia 0.78 (0.71-0.86), p=<0.0001IPD: 0.46 (0.25-0.87), p=0.007COPD: 1.04 (0.92-1.17), p=0.55Cardiac failure: 0.95 (0.87-1.05), p=0.34In-hospital mortality due to investigated diagnoses/100 000 individuals between 1 December 1998 and 30 November 1999Inﬂuenza 1.20 (0.39-3.70), p=0.75Pneumonia 0.55 (0.43-0.71), p=<0.0001IPD: 0.53 (0.06-5.10), p=0.58COPD: 0.53 (0.29-0.98), p=0.034Cardiac failure: 0.72 (0.59-0.87), p=0.0007Hospital admissions/100 000 individuals per year between 1 December 1998 and 31 May 1999Inﬂuenza: 0.66 (0.52-0.82), p=0.0002Pneumonia: 0.72 (0.65-0.79), p=<0.0001IPD: 0.47 (0.24-0.93), p=0.02COPD: 1.07 (0.94-1.23), p=0.32Cardiac failure: 0.90 (0.80-1.01), p=0.08Hospital admissions/100 000 individuals per year between 1 June and 30 November 1999Inﬂuenza: 1.36 (0.58-3.17), p=0.48Pneumonia: 0.88 (0.77-1.00), p=0.05IPD: 0.45 (0.15-1.32), p=0.20COPD: 1.00 (0.87-1.15), p=0.98Cardiac failure: 1.02 (0.93-1.11), p=0.69 | None |  |
| Hurst et al. 2011, Retrospective cohort[71](#_ENREF_71) | N=51,730 adult Medicare patients with renal transplant;Location=US;Age=>=65 years;9,678 had claims for influenza vaccine in the first year post transplant | Influenza | Entire population | Not reported | Not discussed | Medicare claims data | US Renal Data System (RDS) record review | Cox non-proportional hazards regression | Factors known to beindependently associated with allograft loss (recipient age, black race, PRA 20%, dialysis vintage, diabetes mellitus, congestive heart failure, ischemic heart disease, tobacco use, HLA matching, donor age of 50 years, donor black race, deceased-donor transplant, expanded criteria donor,delayed graft function, cold ischemic time of 24 hours,year of transplant, and induction/discharge immunosuppression). Others not specified for the relevant model but could include: older age, diabetes, later year of transplant, and tacrolimus or mycophenolate at discharge | 2000-2006 | Not specified | Vaccination in the first year after transplant was associated with lower risk of subsequent allograft loss and deathAdjusted hazard ratio Allograft loss: 0.77 (0.69-0.85), p=0.001Death: 0.82 (0.76-0.89), p=0.001Acute rejection in the first year was not associated with vaccination in the first 6 or 12 months after transplantAdjusted odds ratio Rejection in first 6 mo: 1.00 (0.88-1.14), p=0.965Rejection in first 12 mo: 0.97 (0.89-1.07), p=0.569 | Not reported |  |
| Johnstone et al. 2012, Prospective cohort[65](#_ENREF_65) | N=31,546;Location=40 countries;Setting=Participants in the ONTARGET /TRANSCEND trials: at least 55 years old and a history of vascular disease or diabetes with document end-organ damage | Influenza, pneumococcal | Difficult to determine without more details on the original studies through which population drawn from | In total, 99.8% of participants were followed up until the primary outcome occurred or the end of study | Not discussed | Self-report | All study outcomes were prospectively adjudicated by a central committee blinded to study medication allocation and influenza vaccination status with the use of standardized criteria | Logistic regression | Adjusted by propensity score for influenza vaccination (body mass index, age, sex, ethnicity, education, vitamin use, smoking history, alcohol use, history of pneumococcal vaccination), history of coronary artery disease, diabetes mellitus, hypertension, stroke, admission to a nursing home, or use of aspirin, beta-blocker, lipid-lowering drug, angiotensin-converting enzyme inhibitor, or angiotensin II inhibitor | 2004 to 2007 | This study was supported by a grant from Boehringer Ingelheim. Dr Yusuf was supported by the Heart and Stroke Foundation of Ontario and a Senior Scientist Award from the Canadian Institutes of Health Research (CIHR). Dr Johnstone receives salary support from CIHR. Dr Loeb holds the Michael G. DeGroote Chair in Infectious Diseases at McMaster University | Association Between Influenza Vaccination and Risk of Major Adverse Vascular Events During the Influenza SeasonCohort2003-2004: 0.96 (0.73–1.27), p=0.792004-2005: 0.62 (0.50–0.77), p=<0.00012005-2006: 0.69 (0.53–0.91), p=0.0092006-2007: 0.52 (0.42–0.65), p=<0.0001Association Between Influenza Vaccination and Risk of the Major Adverse Vascular Events During the Non-influenza SeasonCohort2003-2004: 0.81 (0.61–1.09), p=0.162004-2005: 0.64 (0.50–0.83), p=0.00052005-2006: 0.74 (0.56–0.98), p=0.042006-2007: 0.50 (0.38–0.67), p=<0.0001Association Between Influenza Vaccination and Risk of Non-cardiovascular Death During the Influenza SeasonCohort2004-2005Non-cardiovascular deaths: 0.26 (0.16–0.40), p=<0.0001Cancer deaths: 0.20 (0.10–0.39), p=<0.0001Deaths resulting from other causes: 0.33 (0.18–0.60), p=0.00042005–2006Non-cardiovascular deaths: 0.21 (0.10–0.46), p=0.0001Cancer deaths: 0.27 (0.10–0.69), p=0.0065Deaths resulting from other causes: 0.14 (0.03–0.58), p=0.00702006-2007Non-cardiovascular deaths: 0.27 (0.18–0.41), p=<0.0001Cancer deaths: 0.17 (0.10–0.31), p=<0.0001Deaths resulting from other causes: 0.47 (0.25–0.86), p=0.0137 | Not reported | There was no association between pneumococcal vaccination and the primary outcome during any of the influenza seasons |
| Siriwardena et al. 2010, Matched case-control[64](#_ENREF_64) | N=78,706 (16,012 cases of myocardial infarction (MI), 62,964 controls);Location=UK;Age=40 to >=65;Setting=United Kingdom General Practice ResearchDatabase (GPRD), an extensively validated computerized database, representative of and comprising 5% of the population of England and Wales. | Influenza; pneumococcal (study didn't specify types) | Possible biases in that those with risk factor for outcome may be more likely to be vaccinated, but confounders related to this were controlled for in multivariate analyses | Regression analyses dropped some participants due to missing data on risk factors such as smoking. | Not discussed | Data were extracted from the GPRD (assume by researchers). Virtually all patients in the database are registered with a general practitioner, and all health care attendances are recorded in the database. The database contains anonymized patient data that includes demographic information, diagnoses, medication, health-related behaviors, referrals and treatment outcomes.Influenza vaccination was defined as vaccination given in the year preceding the index date. Other exposures to influenza vaccination considered were influenza vaccination within the current vaccination season and early (i.e., between Sept. 1 and Nov. 15) or late vaccination (i.e., between Nov. 16 and Feb. 28 or 29, depending on the year). Patients were considered to have had a pneumococcal vaccination if they had ever received the pneumococcal vaccine before the index date. Combined vaccination was defined as pneumococcal vaccination ever combined with influenza vaccination in the year preceding the index date. | Data were extracted from the GPRD (assume by researchers). Cases were at least 40 years at the time of first acute myocardial infarction (fatal or nonfatal) had clinical records for over five and a half years(between Nov. 1, 2001, to May 31, 2007) and were identified using standardized (Read and Oxford Medical InformationSystems [OXMIS]) codes. | Conditional logistic regression | Model 1 adjusted for asthma or chronic obstructive pulmonary disease, chronic heart disease, stroke or transient ischemic attack, diabetes, splenectomy, chronic liver disease, chronic renal failure, immunosuppression and HIV, hyperlipidemia, family history of acute myocardial infarction, peripheral vascular disease, hypertension, smoking status, treatment with acetylsalicylic acid, treatment with statins, treatment with antihypertensives, and general practice consultations. Each type of vaccination was adjusted for the other type. Second set of models (Model 2) adjusted for all of the above variables as well as for body mass index, systolic blood pressure and total cholesterol using 10 multiply imputed data sets. (Systolic blood pressure, body mass index, and total cholesterol were not included in the main adjusted analyses owing to missing data (63%, 45% and 15% completeness respectively). Matched case-control, matched for: age, sex, general practice attended and calendar time (i.e., month corresponding to index date of acute myocardial infarction) | Cases identified from incident occurring between Nov.1, 2001, to May 31, 2007. | This study was supported by funding from the Research for Patient Benefit Program of the National Institute for Health Research, United Kingdom | OR (95% CI) of acute MIInfluenza vaccination within previous year:Model 1: 0.81 (0.77-0.85), p<0.001Model 2: 0.83 (0.80–0.88)Pneumococcal vaccination within previous year:Model 1: 0.96 (0.91–1.02)Model 2: 0.98 (0.93-1.04)Pneumococcal vaccination results included in Appendix (www.cmaj.ca/cgi/content/full/cmaj.091891/DC1) | None given, but subgroup results shows for the following categories:InfluenzaVaccination in preceding yr: < 65 yr: Model 1: 0.81 (0.73–0.90) Model 2: 0.83 (0.75–0.92) ≥ 65 yr: Model 1: 0.79 (0.75–0.83) Model 2: 0.82 (0.78–0.86)Time since last vaccination at index date, months: 0–3 months: Model 1: 0.80 (0.74–0.86) Model 2: 0.84 (0.80–0.94) 3–6 months: Model 1: 0.82 (0.76–0.89) Model 2: 0.86 (0.85–0.99) 6–12 months: Model 1: 0.87 (0.81–0.94) Model 2: 0.91 (1.06–1.24) 12–60 months: Model 1: 1.12 (1.03–1.21) Model 2: 1.15 (0.88–1.20) ≥ 60 months: Model 1: 0.96 (0.82–1.13) Model 2: 1.03Within-season vaccination Yes: Model 1: 0.80 (0.76–0.84) Model 2: 0.83 (0.79–0.87) Early within-season (Sept. to mid-Nov.):Model 1: 0.79 (0.75–0.83) Model 2: 0.82 (0.78–0.86) Late within-season (mid-Nov. to Feb.):Model 1: 0.88 (0.79–0.97) Model 2: 0.90 (0.82–1.00)Vaccination in previous yr, by month of index date: Sept. to Nov.:Model 1: 0.75 (0.68–0.83) Model 2: 0.77 (0.70–0.85) Dec. to Mar.: Model 1: 0.86 (0.79–0.93) Model 2: 0.88 (0.82–0.95) Apr. to Aug.:Model 1: 0.80 (0.73–0.86) Model 2: 0.84 (0.77–0.90)Pneumococcal< 65:Model 1: 0.83 (0.73–0.95) Model 2: 0.91 (0.79–1.05) ≥ 65:Model 1: 0.88 (0.83–0.93) Model 2: 0.97 (0.91–1.03) |  |
| Tanner et al. 2012, Case-control[63](#_ENREF_63) | N=286;Location=Utah;Age=20.4 to 92.5;Setting=The University of Utah Voice Disorders Center | Swine flu(Also assessed measles, mumps, and rubella separately - unsure if any of these are MMR) | Selected segment - University of Utah Voice Disorders Center | No details about dropping out over the course of the study, but study notes in the recruitment phase:Of the 192 patients approached and invited to participate, 150 individualswith SD completed the study(cases)Of the 160 patients approached and invitedto participate, 136 VC individuals completed the study (controls) | Not reported | Self-report through questionnaire. Trained examiners administered the questionnaire to each participant and were periodically audited to ensure accuracy. | Voice disorder diagnosis was confirmed by a multidisciplinary team of professionals including a laryngologist and one of four speech-language pathologists. Diagnosis was assigned following a thorough evaluation including a detailed case history, auditory-perceptual evaluation, and videolaryngostroboscopy, employing diagnostic criteria previously established and reported. | Logistic regression | Age, sex, race/ethnicity | Not reported | The work was supported inpart by a University of Utah College of Health Researchand Creative Grant | Vacc v. Nonvacc:2.1 (0.9-5.0)Don't Know v. Nonvacc:2.3 (1.3-4.1) | Not reported |  |
| Ting et al. 2011, Retrospective matched cohort (each pair included 1 vaccinated and 1 non-vaccinated COPD patient)[72](#_ENREF_72) | 586 patients with moderate to severe COPD identified in COPD Registers of 6 general practices in North Derbyshire UK.Age range 37-89 (median 68) | influenza | entire population of COPD patients in these 6-practices | n/a | n/a | medical record | medical record (spirometry records) | McNemar's test | controlled for environmental factors (weather, prevalence of respiratory viral pathogens) | 10/2005-12/2005 | NR | In the 14 days following vaccination, the control group had 21 COPD exacerbations cf. 11 in the vaccinated group (McNemar's p=0.11, not significant; OR 0.52 [95% CI 0.29, 1.14]) |  | Study did NOT look at exacerbations by COPD stage or other risk factors. |
| Tseng et al. 2010, Prospective cohort[74](#_ENREF_74) | N=84,170;Location=CA;Age=45-69 years;Setting=Kaiser Permanente Northern and Southern California health plans (California Men's Health Study) | Pneumococcal | Should be noted, participants who were vaccinated were significantly older than participants who were not vaccinated. Region, race/ethnicity, household income, education, andBMI also were associated significantly with vaccination status. | Study notes themean (SD) length of follow-up was 4.7 (1.36) years. The unvaccinated group had relatively shorter length of followup | Not discussed | Immunization records were tracked by the Kaiser Immunization Tracking System | Electronic health records | Cox proportional hazards regression | Propensity score was created: age, race/ethnicity, region (northern vs southern California Kaiser Permanente), household income, education,BMI, cigarette smoking, physical activity level, sedentary for more than 6.5 hours per day outside of work, alcohol consumption, number of influenza vaccines received, calorie intake, fat intake, fruit and vegetable consumption, history of diabetes, history of high blood pressure, history of high cholesterol, history of peripheral artery disease, history of other heart diseases, history of stroke, history of acute MI, and the log scale transformed number of outpatient visits during the 5 years before baseline. Cigarette smoking was modeled through smoking status  | 2002-2007 | This study was funded by California Cancer Research Program and Kaiser Permanente. | Association of Pneumococcal Vaccination and Incidence of MI and StrokeAcute MIAll men: 1.09 (0.98-1.21), p=0.13StrokeAll men: 1.14 (1.00-1.31), p=0.05 | Association of Pneumococcal Vaccination and Incidence of MI and StrokeAge, y<65: 1.23 (1.08-1.40), p=0.001>=65: 0.89 (0.80-1.01), p=0.10High-risk groupsCurrent smokers: 1.11 (0.83-1.47), p=0.48Diabetes: 1.04 (0.87-1.24), p=0.51Hypertension: 1.10 (0.97-1.25), p=0.16Low-risk group: 0.98 (0.35-2.73), p=0.97Influenza vaccine0: 1.10 (0.70-1.72), p=0.691-10: 1.10 (0.97-1.26), p=0.14>10: 1.00 (0.83-1.21), p=0.97 |  |
| Tseng et al. 2012, Case-centered and Self-controlled case series[85](#_ENREF_85) | N=193,083 recipients of zoster vaccine in 8 US MCOs;Age=50 and older; | Zoster | VSD population - might be differences in case and exposure ascertainment across sites | Not discussed | Not discussed | Medical records | Authors used computerized data to identify any adultwith a pre-speciﬁed event of interest or death | Case-centered: logistic regressionSCCS: conditional Poisson regression | No additional confounders controlled for in models | 1 January 2007 to 31 December 2008 | Contract from the Centers for DiseaseControl and Prevention | Relative risk (RR) and 95% conﬁdence interval (CI) of pre-speciﬁed adverse events within predeﬁned risk windows following vaccination with a zoster vaccineCase-centeredDay 1-14Stroke: 1.03 (0.83–1.28)Acute myocardial infarction: 1.17 (0.92–1.48)Cardiomyopathy: 0.73 (0.51–1.03) Heart failure: 0.76 (0.46–1.24) Meningitis, encephalitis and encephalopathy: 0.54 (0.19–1.52) Ramsey-Hunt syndromes and Bell’s palsy: 0.63 (0.29–1.38)Day 15-28Stroke: 0.92 (0.73–1.16)Acute myocardial infarction: 1.04 (0.81–1.34) Acute Myocarditis: 8.98 (1.67–46.36)Cardiomyopathy: 1.11 (0.83–1.48) Heart failure: 1.08 (0.70–1.65) Meningitis, encephalitis and encephalopathy: 0.90 (0.40–2.05) Day 29-42Stroke: 1.06 (0.85–1.31) Acute myocardial infarction: 0.97 (0.75–1.26)Acute pericarditis: 1.04 (0.13–8.05)Acute Myocarditis: 17.18 (3.71–79.67) Cardiomyopathy: 1.00 (0.74–1.36) Heart failure: 0.95 (0.60–1.49) Meningitis, encephalitis and encephalopathy: 0.62 (0.23–1.69)Day 1-42Stroke: 1.00 (0.87–1.15)Acute myocardial infarction: 1.07 (0.92–1.26)Acute pericarditis: 0.27 (0.03–2.22)Acute Myocarditis: 19.44 (3.58–105.68)Cardiomyopathy: 0.94 (0.77–1.14)Heart failure: 0.91 (0.68–1.21)Meningitis, encephalitis and encephalopathy: 0.66 (0.37–1.16)Mortality: 0.31 (0.23–0.40)Day 1-7Cellulitis and infection: 1.30 (1.18–1.44)Allergic Reaction: 2.13 (1.87–2.40)SCCSDay 1-14Cerebrovascular diseases: 0.94 (0.70–1.28)Acute myocardial infarction: 1.22 (0.87–1.73)Cardiomyopathy: 0.70 (0.45–1.10) Heart failure: 0.77 (0.41–1.46) Meningitis, encephalitis and encephalopathy: 0.80 (0.21–2.98) Ramsey-Hunt syndromes and Bell’s palsy: 0.78 (0.29–2.09)Day 15-28Cerebrovascular diseases: 1.03 (0.74–1.42) Acute myocardial infarction: 1.24 (0.85–1.79) Cardiomyopathy: 1.05 (0.69–1.59) Heart failure: 0.92 (0.51–1.63) Meningitis, encephalitis and encephalopathy: 0.86 (0.29–2.55) Day 29-42Cerebrovascular diseases: 0.97 (0.71–1.30)Acute myocardial infarction: 0.97 (0.67–1.39)Acute pericarditis: 1.00 (0.06–15.99) Acute Myocarditis: 3.00 (0.31–28.84) Cardiomyopathy: 0.86 (0.57–1.29) Heart failure: 0.64 (0.36–1.16) Meningitis, encephalitis and encephalopathy: 0.80 (0.21–2.98) Day 1-42Cerebrovascular diseases: 0.99 (0.83–1.19)Acute myocardial infarction: 1.05 (0.86–1.29)Acute pericarditis: 0.50 (0.05–5.51)Acute Myocarditis: 5.00 (0.58–42.80)Cardiomyopathy: 0.94 (0.73–1.20)Heart failure: 0.88 (0.61–1.25)Meningitis, encephalitis and encephalopathy: 0.78 (0.39–1.56)Day 1-7Cellulitis and infection: 1.10 (0.95–1.26)Allergic Reaction: 2.32 (1.85–2.91) | Not reported |  |
| Uno et al. 2012, Case-control[145](#_ENREF_145" \o "Uno, 2012 #96) | N=413 (189 ASD cases, 224 controls);Location=Kanto area, Japan;Age=22.6 years (mean);Setting=Cases were patients of the YokohamaPsycho-Developmental Clinic (YPDC). Controls were volunteers from area schools. | MMR, diphtheria–pertussis–tetanus vaccine (DPT); the polio vaccine. Study did not specify whether DPT was acellular and did not specify whether polio was inactivated.Only MMR was included in controlled analyses. | Selected segment - Kanto, Japan. Also, cases were patients of psycho-developmental clinic (may differ from cases that don't go to clinic) | 89 of 1875 cases excluded because missing vaccine records. Additional 3 excluded because received vaccines overseas. 1429 cases born before 3/84 or after 5/92, leaving 354 cases. 189 cases could be matched to a control. | Not reported | Study notes that "vaccination history...collected based on the MCH handbook,which was routinely attached to each patient’s ﬁle, were examined." Study did not note exactly who did the examining, but I assume it was the researchers. | Patients were diagnosed based on the (DSM-IV) and standardized criteria using the Diagnostic Interview for Social and Communication Disorder (DISCO). Another child psychiatrist or clinical psychologist conducted intellectual or developmental tests, such as the Psycho-Educational Proﬁle-Revised and Wechsler Intelligence Scale for Children-Third Edition. After the interview and testing, the diagnosis was made by the team according to the DSM-IV criteria.  | Conditional logistic regression | Maternal hypertension, low Apgar score, obstetrical vacuum extraction or forceps delivery (Table 4 displays results with control variables. Tables 1-3 display crude ORs. Authors only controlled for those risk factors that displayed high crude ORs.)Cases/controls matched by sex and year of birth | Study doesn't note when researchers collected data, but the universe of eligible participants included patients visiting the clinic between April 1997 (when the clinic opened) and March 2011. | A part of the study is the result of research grants from the Ministry of Health, Labor and Welfare of Japan, and “Integrated researchon neuropsychiatric disorders” carried out under the Strategic Research Program for Brain Sciences by the Ministry of Education, Culture, Sports, Science and Technology of Japan | MMR: 1.10 (0.64–1.90), p=0.72 | Maternal hypertension:4.19 (0.46–38.57), p=0.21Low Apgar score:2.06 (0.18–22.12), p=0.57Obstetrical vacuum extraction or forcepsdelivery:0.98 (0.50–1.92), p=0.96 |  |
| Vila-Corcoles et al. 2012, Prospective cohort[76](#_ENREF_76) | N=27,204 (8,981 vaccinated, 18,223 unvaccinated);Location=Spain;Age=71.7 (mean at study start);Setting=nine primary care centers in the HealthRegion of Tarragona (a mixed residential-industrialurban area in the Mediterranean coast of Catalonia, Spain) | Pneumococcal (PPV23) | Paper did not provide details on recruitment - referred reader to another paper | None discussed | Not discussed | Review of the primary care centers’ electronic clinicalrecords | Computerized clinical record systemOutcomes identified bases on ICD-9 codes with physician verification based on medical record review | Cox proportional hazards models | The following variables were considered in all the initial models: age, sex, number of outpatient visits to family physician in 12-months before study start, influenza vaccination in prior autumn, history of coronary artery disease, history of stroke, history of chronic heart disease, chronic pulmonary disease, hypertension, hypercholesterolemia, obesity, diabetes mellitus, smoking status, alcoholism, chronic severe liver disease, chronic severe nephropathy, cancer, dementia and nursing-home residence. Age, sex and influenza vaccine status were judged epidemiologically relevant variables, being included in all the final models.Final Models: CAP: Adjusted for age, sex, number of outpatient visits in prior year, influenza vaccination in prior year, chronic pulmonary disease, chronic heart disease, smoking and nursing-home resident AMI: Adjusted for age, sex, number of outpatient visits in prior year, influenza vaccination in prior year, history of coronary artery disease, chronic heart disease, diabetes mellitus, hypercholesterolemia, smoking (confounder) and nursing-home resident Ischemic Heart Disease: Adjusted for age, sex, number of outpatient visits in prior year, influenza vaccination in prior year, history of coronary artery disease, history of stroke, smoking (confounder) and nursing-home resident Death from any cause: Adjusted for age, sex, number of outpatient visits in prior year, influenza vaccination in prior year, chronic pulmonary disease, chronic heart disease, diabetesmellitus, cancer, chronic nephropathy, dementia, hypertension, hypercholesterolemia, obesity, smoking, and nursing home-resident | Cohort members were followed from the start ofthe study (December 1, 2008) until the occurrence of any event, change in pneumococcal vaccination status, disenrollment from the primary care center, death, or until the end of first 12-month follow-up (November 30, 2009). | This work was supported by a grant from the “Fondo de Investigación Sanitaria” of the Instituto de Salud Carlos III [FIS 09/00043] of the Spanish Health Ministry | Multivariate hazard ratio (95% CI)CAP: 0.85 (0.62-1.15), p=0.287AMI: 0.83 (0.56-1.22), p=0.347Ischemic Stroke: 0.65 (0.42-0.99), p=0.048Death from any cause: 0.88 (0.75-1.03), p=0.12 | Not reported |  |
| Yu et al. 2007, Case-control[93](#_ENREF_93) | N=1,875 (355 Graves' disease cases, 418 Hashimoto's thyroiditis cases, 1,102 controls);Location=Vaccine Safety Datalink Project:Group Health Cooperative, Seattle, WA; NorthwestKaiser Permanente, Portland, OR; and Kaiser Permanente of Northern California, Oakland, CA;Age=18–69 years;Setting=Three health maintenance organizations (HMOs) | Hepatitis B vaccine, influenza, MMR, Hepatitis A, polio | Potential for those with disease to be more likely to receive vaccination or more likely to be assessed for vaccination. Also possible recall bias and exposure misclassification. Authors noted that case groups may have included some subjects with thyroid conditions other thanGraves’ disease or Hashimoto’s thyroiditis. | None | Not discussed | Vaccine information was collected from administrative immunization records, chart review, and telephone interviews with study subjects | Medical record review. Identiﬁed cases of Graves’ disease and Hashimoto’s thyroiditis on the basis of International Classiﬁcation of Diseases, Ninth Revision(ICD-9) codes for thyroid disease, associated withinpatient and outpatient medical encounters that were recorded in HMO administrative data systems. | Logistic regression | Controls were frequency-matched to cases by birth year, sex, and study site (HMO)All models adjusted for frequency-matching variables (age groups, sex, site, and index year), personal and family history of autoimmune disease, smoking status, race, and education | January 1, 1999 through June 30, 2002 | ID Biomedical, Chiron Therapeutics and Vaccines, and Sanoﬁ Pasteur; Studysupported by the Vaccine Safety Datalink contractwith America’s Health Insurance Plans, funded by the CDC | OR (95% CI) for Graves’ diseaseMain analysisHepatitis B: 0.90 (0.62–1.32)Inﬂuenza: 1.07 (0.80–1.42)MMR: 0.59 (0.29–1.20)Hepatitis A: 0.70 (0.43–1.13)Polio: 1.29 (0.76–2.17)OR (95% CI) for Hashimoto’s thyroiditisMain analysisHepatitis B: 1.23 (0.87–1.73)Inﬂuenza: 1.15 (0.89–1.48)MMR: 1.50 (0.79–2.86)Hepatitis A: 0.97 (0.64–1.46)Polio: 1.17 (0.73–1.86) | Not reported |  |
| Zhang et al. 2012, Retrospective cohort[84](#_ENREF_84) | N=463,541(4,026 with ankylosing spondylitis, 66,751 with inflammatory bowel disease, 11,030 with psoriatic arthritis, 89,565 with psoriasis, and 292,169 with RA);Location=US;Age=74 years (mean at study start);Setting=US Medicare beneficiaries | Zoster Herpes | Could not control for differences between those who received vaccinations and those who did not (e.g., those receiving vaccines may be a healthier population).Misclassification of medication exposure | Actual vaccine administrationdates were unknown for 59% of patients, which resulted in the exclusionof these patients from safety analyses potentially introducing bias | Did not discuss | Database review | Database review (administrative claims fromphysicians or hospitalizations) | Proportional hazard regression | Sex, race, immune-mediated disease, time varying concurrent medications, andtime-varying health care utilization (hospitalization and physician visits) | January 1, 2006, through December 31, 2009 | Agency for Healthcare Research and Quality | HR (95% CI) for Herpes Zoster IncidenceUsing ICD-9-CM diagnosis code+pharmacy claim definition for HZ case (Def 1)HZ vaccination: 0.61 (0.52-0.71) Using ICD-9-CM diagnosis code only for HZ case (Def 2)HZ vaccination: 0.67 (0.59-0.75) | SexMen [Reference]Women Def 1: 1.22 (1.17-1.28) Def 2: 1.21 (1.17-1.26)RaceWhite [Reference] Black Def 1: 0.67 (0.62-0.73) Def 2: 0.69 (0.64-0.74)Other Def 1: 0.89 (0.81-0.97) Def 2: 0.89 (0.83-0.95)Immune-mediated diseaseRheumatoid arthritis [Reference] Ankylosing spondylitis Def 1: 0.98 (0.77-1.25) Def 2: 0.94 (0.77-1.13)Inflammatory bowel diseases Def 1: 1.03 (0.97-1.10) Def 2: 1.02 (0.97-1.07)Psoriatic arthritis Def 1: 0.92 (0.80-1.05) Def 2: 0.92 (0.83-1.02)Psoriasis Def 1: 0.99 (0.93-1.05) Def 2: 0.97 (0.93-1.02)Hospitalized in the previous 6 moNo [Reference] Yes Def 1: 1.00 (0.95-1.05) Def 2: 1.25 (1.20-1.29)No. of physician visits in the previous 6 moDef 1: 1.04 (1.04-1.04) Def 2: 1.04 (1.04-1.04)DMARDs, exclusive groupsNon-biologic DMARDs [Reference] Anti-TNF biologics Def 1: 1.15 (1.08-1.23) Def 2: 1.10 (1.04-1.16)Non-TNF biologics Def 1: 0.99 (0.86-1.13) Def 2: 1.05 (0.94-1.16)None Def 1: 0.84 (0.80-0.88) Def 2: 0.86 (0.82-0.89)Oral glucocorticoid useNo [Reference] Yes Def 1: 1.79 (1.71-1.86) Def 2: 1.69 (1.64-1.75) |  |