| **Evidence Table 2. Vaccinated versus unvaccinated: Adults** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Author- Year- Country** | **Study Design** | **McHarm Score** | **Population** | **Vaccine1** | **Timing1** | **Adverse Event1** | **OR, 95% CI, versus unvaccinated group** |
| Barrett P. N. et al, 2011 US[47](#_ENREF_47) | Controlled Clinical Trial | 4 | Sample size: 7250, Mean age: NR, Age range: 18 - 49 | Influenza (inactivated), Baxter, Austria, contain 15 µg of haemagglutinin antigen from each of the three virus strains - A/Brisbane/59/2007 (A/H1N1), A/Uruguay/716/2007(A/Brisbane/10/2007-like) (A/H3N2), and B/Florida/4/2006 (B). The three virus strains were egg-derived wild-type strains provided by the National Institute for Biological Standards and Control (Potters Bar, UK)., Adjuvant: Not Reported, Preservative: Not reported, Delivery: Intramuscular | Dose1: 0 Days | Any adverse event: 35% Any SAE: 0.8%, Sev: 3-5 Event: Arthralgia: 6%, Syscat: 15, Sev: 1-3 Event: Chills: 6%, Syscat: 8, Sev: 1-3 Event: Cough: 1%, Syscat: 22, Sev: 1-3 Event: Fatigue: 18%, Syscat: 8, Sev: 1-3 Event: Headache: 18%, Syscat: 8, Sev: 1-3 Event: Hyperhidrosis: 5%, Syscat: 8, Sev: 1-3 Event: Malaise: 14%, Syscat: 8, Sev: 1-3 Event: Myalgia: 18%, Syscat: 8, Sev: 1-3 Event: Oropharyngeal pain: 2%, Syscat: 7, Sev: 1-3 Event: Pyrexia: 2%, Syscat: 8, Sev: 1-3 Event: Death: 0.05%, Sev: 5 | Arthralgia: OR 2.103 (1.666-2.655)\*\* Chills: OR 2.239 (1.766-2.838)\*\* Cough: OR 1.427 (0.862-2.361) Fatigue: OR 1.577 (1.382-1.8)\*\* Headache: OR 1.396 (1.229-1.587)\*\* Hyperhidrosis: OR 1.678 (1.306-2.155)\*\* Malaise: OR 2.024 (1.736-2.36)\*\* Myalgia: OR 3.281 (2.799-3.846)\*\* Oropharyngeal pain: OR 1.626 (1.058-2.5)\*\* Pyrexia: OR 2.271 (1.537-3.355)\*\* |
| Bhatla N. et al.,2010 India[89](#_ENREF_89) | Controlled Clinical Trial | 7 | Sample size: 337, Mean age: 28.4, Age range: 18 - 35, Percent female: 100% | Human papillomavirus (HPV), HPV-16/18 L1 virus-like particle (VLP) cervical ca, GlaxoSmithKline, HPV-16/18 L1 virus-like particle (VLP) cervical cancer vaccine containing the proprietary ASO4 (3-O-desacyl-4(1)-monophosphoryl lipid [MPL] [0 mcg MPL] adsorbed on aluminum [Al] hydroxide [500 mcg AL(+3)]) adjuvant system, Adjuvant: ASO 4-Aluminum, Preservative: Not reported, Delivery: Intramuscular | Dose1: 0 Month Dose2: 1 Month Dose3: 6 Month | Any adverse event: 7.4% Any SAE: 1.1% Event: Acute appendicitis: 0.6%, Syscat: 7 Event: Lymph node tuberculosis: 0.6%, Syscat: 11 Event: Pain (Grade 3): 20.5%, Syscat: 17, Sev: 3 Event: Redness (>50 mm): 0.6%, Syscat: 23, Sev: 3 Event: Swelling (>50 mm): 2.9%, Syscat: 23, Sev: 3 | Pain (Grade 3): OR 6.189 (2.634-14.54)\*\* Redness (>50 mm): OR 1 (0.063-15.882) |
| Frey S. et al,2010 US, Finland, Poland[48](#_ENREF_48) | Controlled Clinical Trial | 4 | Sample size: 11404, Mean age: 33, Age range: 18 - 49, Percent female: 55% | Influenza (inactivated), Agrippal, Novartis, 15 mg of hemagglutinin per 0.5-mL dose of each virus strain recommended for the 2007–2008 Northern Hemisphere influenza season: A/Solomon Islands/3/2006 (H1N1)–like, A/Wisconsin/67/2005 (H3N2)–like, and B/Malaysia/2506/2004–like, Adjuvant: Not Reported, Preservative: Not reported, Delivery: Intramuscular | Dose1: 1 Days | Any SAE: 0.95% Event: Chills (mild-moderate): 5%, Syscat: 8, Sev: 1-2 Event: Malaise (mild-moderate): 7.5%, Syscat: 8, Sev: 1-2 Event: Myalgia (mild-moderate): 9%, Syscat: 8, Sev: 1-2 Event: Arthralgia (mild-moderate): 2.5%, Syscat: 15, Sev: 1-2 Event: Headache (mild-moderate): 15%, Syscat: 8, Sev: 1-2 Event: Sweating (mild-moderate): 2.5%, Syscat: 8, Sev: 1-2 Event: Fatigue (mild-moderate): 11%, Syscat: 8, Sev: 1-2 Event: Fever (mild-moderate): 1%, Syscat: 8, Sev: 1-2 Event: Withdrawal after AE: 0.03%, Sev: 1-2 Event: Death: 0.03%, Sev: 5 | Headache (mild-moderate): OR 1 (0.881-1.134) Arthralgia (mild-moderate): OR 0.961 (0.722-1.279) Chills (mild-moderate): OR 1 (0.813-1.23) Death: OR 1.061 (0.066-16.969) Fatigue (mild-moderate): OR 1.112 (0.96-1.289) Fever (mild-moderate): OR 2.01 (1.159-3.487)\*\* Malaise (mild-moderate): OR 1.27 (1.061-1.521)\*\* Myalgia (mild-moderate): OR 1.314 (1.112-1.553)\*\* Sweating (mild-moderate): OR 1 (0.749-1.335) Withdrawal after AE: OR 1.061 (0.066-16.969) |
| Iorio V et al.,2010 Italy[49](#_ENREF_49) | Controlled Clinical Trial | 4 | Sample size: 104, Mean age: 71, Age range: 18 - NR, Percent female: 45.1% | Influenza (inactivated), Fluad, Novartis, Fujian/411/02 (influenza A[H3N2]),New Caledonia/20/99 (influenza A[H1N1]), and Shanghai/361/02 (influenzaB), Adjuvant: Other adjuvant, Preservative: Not reported, Delivery: Intramuscular | Dose1: 0 Days Dose2: 42 Days | Any SAE: 0%, Syscat: 0 Event: Posttraumatic elbow hematoma: 0.96%, Syscat: 26, Sev: 1-3 Event: Gingival bleeding: 0.96%, Syscat: 7, Sev: 1-3 Event: Nosebleeds: 2.88%, Syscat: 22, Sev: 1-3 Event: Conjunctival hemorrhage: 0.96%, Syscat: 6, Sev: 1-3 Event: Bruising: 0%, Syscat: 12 | Nosebleeds: OR 0.743 (0.162-3.403) |
| Jackson L. A. et al.,2010 US[50](#_ENREF_50) | Controlled Clinical Trial | 7 | Sample size: 7611, Mean age: 32.7, Age range: 18 - 49, Percent female: 60%, Percent pregnant: Percent Pregnant: 0.7% | Influenza (inactivated), Flulaval, ID Biomedical Corporation of Quebec (trademarked b, 15 ìg of hemagglutinin(HA) antigen of each recommended influenza strain. Antigens for Season 1 (2005-2006) were A/New Caledonia/20/1999 (H1N1), A/New York/55/2004 (H3N2, A/California/7/2004-like), and B/Jiangsu/10/2003 (B/Shanghai/361/2002-like). Antigens for Season 2 (2006-2007) were A/New Caledonia/20/1999 (H1N1) virus, A/Wisconsin/67/2005 (H3N2), and B/Malaysia/2506/2004., Adjuvant: Not Reported, Preservative: Not reported, Delivery: Not reported | Dose1: 0 Days | Any adverse event: 66% Any SAE: 1.1% Event: Fever: 3%, Syscat: 8, Sev: 1-3 Event: Myalgia/arthralgia: 18%, Syscat: 15, Sev: 1-3 Event: Malaise: 9%, Syscat: 8, Sev: 1-3 Event: Swelling of the face: 1%, Syscat: 8, Sev: 1-3 Event: Cough: 8%, Syscat: 22, Sev: 1-3 Event: Chest tightness or difficulty breathing: 3%, Syscat: 22, Sev: 1-3 Event: Sore throat, hoarseness, or pain swallowing: 9%, Syscat: 7, Sev: 1-3 Event: Death: 0%, Sev: 5 | Chest tightness or difficulty breathing: OR 1.218 (0.938-1.581) Cough: OR 1.17 (0.982-1.396) Fever: OR 1.786 (1.278-2.496)\*\* Myalgia/arthralgia: OR 1.979 (1.732-2.262)\*\* Sore throat, hoarseness, or pain swallowing: OR 0.949 (0.809-1.112) Swelling of the face: OR 1.4 (0.915-2.143) |
| Johnstone, J. et al. 2012[240](#_ENREF_240) 40 countries | Cohort | 2 | Sample size : 31546, Mean age: 66 (approx), Age range: 55 - NR, Percent female: 29.9% | Influenza (inactived) , NR , Adjuvant: Not Reported , Preservative: Not reported , Delivery: Not reported | Dose1: NR | Event: Any major cardiovascular event (during flu season) : 1.1% , Syscat: 2 , Sev: 3-4 Event: Any major cardiovascular event (non flu season) : 0.94% , Syscat: 2 , Sev: 3-4 Event: Non cardiovascular deaths : 0.01% , Syscat: 2 , Sev: 4 Event: Cancer deaths : 0% , Sev: 4 Event: Deaths from other causes : 0.05% , Sev: 4 | Any major cardiovascular event (during flu season): OR 1.082 (0.834-1.404) Any major cardiovascular event (during flu season): OR 1.082 (0.834-1.404) Any major cardiovascular event (non flu season): OR 0.887 (0.674-1.168) Any major cardiovascular event (non flu season): OR 0.887 (0.674-1.168) Deaths from other causes: OR 0.228 (0.028-1.856) Deaths from other causes: OR 0.228 (0.028-1.856) Non cardiovascular deaths: OR 0.133 (0.017-1.024) Non cardiovascular deaths: OR 0.133 (0.017-1.024) |
| Langley J. M., et al,2011 Canada[46](#_ENREF_46) | Controlled Clinical Trial | 4 | Sample size: 1348, Mean age: 37.1, Age range: 18 - 64, Percent female: 54.2% | Influenza (inactivated), NR, Contains equal parts of three monovalent egg-grown, formalin-inactivated influenza antigens formulated with OMPs of N. meningitidis serogroup B strain 8047 at an initial ratio of OMP to haemagglutinin (HA) of 4:1. After diafiltration to remove detergents necessary to keep the OMPs in stable solution in the absence of antigen, the overall total protein to HA ratio in the final vaccine product is 2.5 to 5:1. The trivalent vaccine stock contained HA from each of A/New Caledonia/20/99 [H1N1], A/Panama/2007/99 [H3N2] and B/Shangdong/7/97 [H1N1, Adjuvant: Not Reported, Preservative: Thimerisol, Delivery: Intranasal | Dose1: 0 Days Dose2: 14 Days | Any SAE: 0.219%, Syscat: 10, Sev: 3,4 Event: Shortness of breath (Grade 2/3): 0%, Syscat: 22, Sev: 3-5 Event: Lightheadedness/Dizziness (Grade2/3): 0%, Syscat: 17, Sev: 3-5 Event: New rash/itchy rash (Grade 2/3): 0%, Syscat: 10, Sev: 3-5 Event: Feverishness (Grade2/3): 0%, Syscat: 8, Sev: 3-5 Event: Burning/stinging nose (Grade2/3): 0%, Syscat: 8, Sev: 3-5 Event: Burning/stinging throat (Grade 2/3): 0%, Syscat: 8, Sev: 3-5 Event: Itching nose/throat/eyes (Grade 2/3): 0%, Syscat: 8, Sev: 3-5 Event: Temp >39C: 0%, Syscat: 8, Sev: 3-5 |  |
| Lee S. et al,2011 Korea[90](#_ENREF_90) | Controlled Clinical Trial | 5 | Sample size: 20, Mean age: 28.1, Age range: NR, Percent female: 0% | Td, SK Td Vaccine Inj, SK Chemicals, Seongnam, Korea, >= 2 IU of diphtheria toxoid and >=20 IU of tetanus toxoid, Adjuvant: Not Reported, Preservative: Not reported, Delivery: Intramuscular | Dose1: 0 Days | Any adverse event: 80% Event: Serious adverse events: 0% Event: Hypoaesthesia: 30%, Syscat: 17 Event: Hypoaesthesia (vaccine-related): 20%, Syscat: 17 | Hypoaesthesia: OR 3.857 (0.326-45.572) |
| Macaladad N. et al.,2007 Brazil, Costa Rica, Colombia, Mexico, Peru and Venezuela and the Philippines[78](#_ENREF_78" \o "Macaladad, 2007 #20162) | Controlled Clinical Trial | 2 | Sample size: 21, Mean age: 38.1, Age range: 27 - 69, Percent female: 66.7% | Zoster, NR, 50,000 PFU/0.5 mL, Adjuvant: Not Reported, Preservative: Not reported, Delivery: injected | Dose1: 0 NR | Any adverse event: 37.5% Any SAE: 0% Event: Injection-site: 25.0%, Syscat: 8 Event: Systemic: 12.5% Event: Vaccine-related (Related to injection-site AE): 25.0%, Syscat: 8 Event: Injection-site (mild burning, erythema and pruritus): 25.0%, Syscat: 8, Sev: 2 Event: Serious vaccine-related AE: 0% |  |
| Madhi S. A. e t al.,2011 South Africa[53](#_ENREF_53) | Controlled Clinical Trial | 3 | Sample size: 189, Mean age: 36.3, Percent female: 84%, Conditions: HIV | Influenza (inactivated), Mutagrip, Sanofi, 15ugm each (per 0.5 ml) A/Solomon Islands/3/2006 (IVR-145), A/Brisbane/10/2007(IVR-147),B/Florida/4/2006, Adjuvant: Not Reported, Preservative: Not reported, Delivery: Intramuscular | Dose1: NR Dose2: NR Dose3: NR | Any adverse event: 14.4% Event: Pain: 8.3% Event: Redness: 2.1% Event: Swelling: 2.1% Event: Lump formation: 1.0% Event: Bruising: 0% Event: Itching: 3.1% Event: Rigors (muscle cramp): 0% Event: Fatigue: 1.0% Event: Headache: 3.1% Event: Fits (seizures): 0% Event: Myalgia: 3.1% Event: Arthralgia: 3.1% Event: Fever: 0% | Arthralgia: OR 0.694 (0.151-3.19) Fatigue: OR 0.179 (0.021-1.564) Headache: OR 0.936 (0.184-4.762) Itching: OR 2.872 (0.293-28.127) Lump formation: OR 0.464 (0.041-5.201) Myalgia: OR 1.42 (0.232-8.7) Pain: OR 1.955 (0.568-6.73) Redness: OR 1.895 (0.169-21.26) |
| Mills R. et a.,2010 US[81](#_ENREF_81) | Controlled Clinical Trial | 5 | Sample size: 101, Mean age: 67.8 (approx.), Age range: 50 - 93, Percent female: 59.4% | Zoster, Zostavax, Merck, Lyophilized zoster vaccine (~89,000 plaque-forming units[PFU]/dose at release), Adjuvant: Not Reported, Preservative: Not reported, Delivery: Subcutaneous | Dose1: 0 Days Dose2: 28 Days | Any adverse event: 52.0%, Syscat: 8 Any SAE: 0%, Sev: 3,4,5 Event: Overall - Injection site AEs: 45.9%, Syscat: 8 Event: Overall - Systemic AEs: 15.3%, Syscat: 8 Event: Overall - Vaccine related AEs: 2.0%, Syscat: 8 Event: Deaths: 0% Event: Stratum 1: 1 or more AEs: 54.4%, Syscat: 8 Event: Stratum 1: Injection site AEs: 47.1%, Syscat: 8 Event: Stratum 1: Systemic AEs: 13.2%, Syscat: 8 Event: Stratum 1: Vaccine related AEs: 1.5%, Syscat: 8 Event: Stratum 2: 1 or more AEs: 46.7%, Syscat: 8 Event: Stratum 2: Injection site AEs: 43.3%, Syscat: 8 Event: Stratum 2: Systemic AEs: 20.0%, Syscat: 8 Event: Stratum 2: Vaccine related AEs: 3.3%, Syscat: 8 Event: 50-59y: 1 or more AE: 47.4%, Syscat: 8 Event: 50-59y: Systemic AE: 5.3%, Syscat: 8 Event: 50-59y: Vaccine related AE: 0%, Syscat: 8 Event: >=60y: 1 or more AE: 53.2%, Syscat: 8 Event: >=60y: Systemic AE: 17.7%, Syscat: 8 Event: >=60y: Vaccine related AE: 2.5%, Syscat: 8 | 50-59y: Systemic AE: OR 0.245 (0.027-2.231) 50-59y: 1 or more AE: OR 1.899 (0.613-5.88) >=60y: Systemic AE: OR 1.664 (0.685-4.042) >=60y: 1 or more AE: OR 5.371 (2.609-11.054)\*\* Overall - Injection site AEs: OR 19.841 (6.773-58.123)\*\* Overall - Systemic AEs: OR 1.195 (0.537-2.659) Stratum 1: 1 or more AEs: OR 19.185 (5.673-64.881)\*\* Stratum 1: Injection site AEs: OR 3.49 (1.674-7.277)\*\* Stratum 1: Systemic AEs: OR 0.567 (0.236-1.364) Stratum 2: Injection site AEs: OR 14.943 (1.916-116.559)\*\* Stratum 2: Systemic AEs: OR 6.383 (0.754-54.018) Stratum 2: 1 or more AEs: OR 8.058 (1.781-36.46)\*\* |
| Murray A. V. et al.,2011 US, Canada, Spain, Germany, UK[83](#_ENREF_83) | Controlled Clinical Trial | 4 | Sample size: 11999, Mean age: 70.4, Age range: 60 - 99, Percent female: 58.6% | Zoster, Zostovax, Merck, Lyophilized ZV, Adjuvant: Not Reported, Preservative: Not reported, Delivery: Subcutaneous | Dose1: 0 | Any SAE: 5.7% Event: Blood/Lymphatic disorders(1-42d): 0%, Syscat: 1 Event: Cardiac disorders(1-42d): 0.3%, Syscat: 2 Event: GI disorders(1-42d): 0.1%, Syscat: 7 Event: Respiratory/Thoracic (1-42d): 0.1%, Syscat: 22 Event: Neoplasms(1-42d): 0.3%, Syscat: 16 Event: Nervous system (1-42d): 0.1%, Syscat: 17 Event: Psychiatric (1-42d): 0.0%, Syscat: 19 Event: Vaccine related SAEs (1-42d): 0.0%, Syscat: 6,15 Event: Death (1-42d): 0.1% Event: Blood/Lymphatic disorders(1-182d): .1%, Syscat: 1 Event: Cardiac disorders (1-182d): 1.2%, Syscat: 2 Event: GI disorders (1-182d): 0.6%, Syscat: 7 Event: Respiratory/Thoracic (1-182d): 0.5%, Syscat: 22 Event: Neoplasms (1-182d): 1.3%, Syscat: 16 Event: Nervous system(1-182d): 0.4%, Syscat: 17 Event: Psychiatric (1-182d): 0.1%, Syscat: 19 Event: Vaccine related SAEs(1-182d): 0.0% Event: Death (1-182d): 0.4% | Blood/Lymphatic disorders(1-182d): OR 1.253 (0.336-4.669) Cardiac disorders (1-182d): OR 1.016 (0.733-1.41) Cardiac disorders(1-42d): OR 1.002 (0.53-1.895) Death (1-182d): OR 1.417 (0.76-2.64) Death (1-42d): OR 1.203 (0.367-3.944) GI disorders (1-182d): OR 1.281 (0.787-2.085) GI disorders(1-42d): OR 1.337 (0.464-3.855) Neoplasms (1-182d): OR 1.317 (0.934-1.858) Neoplasms(1-42d): OR 1.672 (0.731-3.824) Nervous system(1-182d): OR 0.808 (0.476-1.369) Nervous system (1-42d): OR 0.716 (0.227-2.256) Psychiatric (1-182d): OR 60.2 (0.116-31171.904) Psychiatric (1-42d): OR 1.002 (0.141-7.118) Respiratory/Thoracic (1-182d): OR 1.123 (0.654-1.928) Respiratory/Thoracic (1-42d): OR 1.504 (0.424-5.333) |
| Ngan H. Y. S. et al., 2010 Hong Kong[88](#_ENREF_88) | Controlled Clinical Trial | 7 | Sample size: 300, Age range: 18 - 35, Percent female: 100% | Human papillomavirus (HPV), Cevarix, GlaxoSmithKline, Each dose (0.5 mL) of the HPV-16/18 vaccine contained20 µg each of HPV-16 and -18 L1 (structural protein of HPV) virus-like particle (VLP) and adjuvant with a proprietary AS04 (3-O-desacyl-4’-monophosphoryllipid [50 µg] adsorbed on aluminium hydroxide [Al(OH)3, 500 µg], Adjuvant: ASO 4, Preservative: Not reported, Delivery: Intramuscular | Dose1: 0 Month Dose2: 1 Month Dose3: 6 Month | Any adverse event: 90% Any SAE: 2% Event: Arthralgia: 8%, Syscat: 15, Sev: 1-3 Event: Fatigue: 42%, Syscat: 8, Sev: 1-3 Event: Fever: 6%, Syscat: 8, Sev: 1-3 Event: GI symptoms: 16%, Syscat: 7, Sev: 1-3 Event: Headache: 24%, Syscat: 8, Sev: 1-3 Event: Myalgia: 35%, Syscat: 8, Sev: 1-3 Event: Rash: 3%, Syscat: 10, Sev: 1-3 Event: Urticaria: 2%, Syscat: 10, Sev: 1-3 | Arthralgia: OR 1.362 (0.556-3.336) Fatigue: OR 1.69 (1.049-2.721)\*\* Fever: OR 0.734 (0.3-1.797) GI symptoms: OR 1.714 (0.86-3.415) Headache: OR 1.439 (0.822-2.519) Myalgia: OR 1.705 (1.031-2.82)\*\* Rash: OR 3.062 (0.476-19.708) Urticaria: OR 1 (0.199-5.036) |
| Schmader K. E. et al.,2012 North America and Europe[79](#_ENREF_79) | Controlled Clinical Trial | 4 | Sample size: 22439, Mean age: 54.8, Age range: 50 - 59, Percent female: 61.9% | Zoster, Zostavax, Merck, lyophilized ZV with stabilizers, Adjuvant: Not Reported, Preservative: Not reported, Delivery: Subcutaneous | Dose1: 0 (Baseline) | Any adverse event: 72.8% Any SAE: 0.6% Event: 1 or more Injection-site AEs: 63.9% Event: 1 or more Systemic AEs: 35.4% Event: With vaccine-related AEs: 65.0% Event: Vaccine Related Injection site AEs: 63.9% Event: Vaccine relate systemic AEs: 6.7% Event: With vaccine related SAE: 0% Event: SAE with death: 0% | 1 or more Injection-site AEs: OR 10.379 (9.722-11.081)\*\* SAE with death: OR 0.334 (0.035-3.209) With vaccine-related AEs: OR 8.385 (7.882-8.922)\*\* Vaccine relate systemic AEs: OR 0.43 (0.393-0.471)\*\* With vaccine related SAE: OR 0.002 (0-0.013)\*\* 1 or more Systemic AEs: OR 1.089 (1.031-1.151)\*\* |
| Simberkoff M. S. et al.,2010 US[82](#_ENREF_82) | Controlled Clinical Trial | 7 | Sample size: 38546, Mean age: NR, Age range: 60 - NR | Zoster, Merck, Median potency, 24600 plaque-forming units per dose, Adjuvant: Not Reported, Preservative: Not reported, Delivery: Subcutaneous | Dose1: 0 Days | Any adverse event: 1.4%, Sev: 1-5 Any SAE: 1.68%, Sev: 3-5 Event: # of SAE (60-69y): 0.7%, Sev: 3-5 Event: # of SAE (>=70y): 0.98%, Sev: 3-5 Event: # of SAE (70-80y): 0.78%, Sev: 3-5 Event: # of SAE (>=80y): 0.2%, Sev: 3-5 Event: COSTART - Cardiovascular: 0.5%, Syscat: 2, Sev: 3-5 Event: COSTART - Digestive: 0.21%, Syscat: 7, Sev: 3-5 Event: COSTART - Musculoskeletal: 0.08%, Syscat: 15, Sev: 3-5 Event: COSTART - Nervous Sys: 0.18%, Syscat: 17, Sev: 3-5 Event: COSTART - Respiratory: 0.16%, Syscat: 22, Sev: 3-5 Event: COSTART - Sight/Sense: 0.02%, Syscat: 5,6, Sev: 3-5 Event: COSTART - Skin: 0.15%, Syscat: 23, Sev: 3-5 Event: COSTART - Genitourinary: 0.08%, Syscat: 20, Sev: 3-5 Event: COSTART - Endocrine: 0.01%, Syscat: 5, Sev: 3-5 Event: COSTART - Hemic/Lymphatic: 0.03%, Syscat: 1, Sev: 3-5 Event: COSTART - Metabolic/Nutritional: 0.03%, Syscat: 14, Sev: 3-5 Event: Diagnostic grp - Cancer: 0.27%, Syscat: 16, Sev: 3-5 Event: Diagnostic grp - Vascular (pathological)): 0.41%, Syscat: 26, Sev: 3-5 Event: Diagnostic grp - Vascular (functional): .23%, Syscat: 26 Sev: 3-5 | # of SAE (60-69y): OR 1.081 (0.847-1.38) # of SAE (70-80y): OR 0.909 (0.728-1.135) # of SAE (>=70y): OR 0.969 (0.793-1.185) # of SAE (>=80y): OR 1.301 (0.808-2.095) COSTART - Cardiovascular: OR 1.117 (0.835-1.496) COSTART - Digestive: OR 0.719 (0.481-1.075) COSTART - Endocrine: OR 0.25 (0.028-2.237) COSTART - Genitourinary: OR 0.941 (0.476-1.864) COSTART - Hemic/Lymphatic: OR 2.501 (0.485-12.894) COSTART - Metabolic/Nutritional: OR 1.667 (0.398-6.978) COSTART - Musculoskeletal: OR 1 (0.489-2.047) COSTART - Nervous Sys: OR 1.03 (0.642-1.652) COSTART - Respiratory: OR 0.973 (0.588-1.609) COSTART - Skin: OR 0.903 (0.542-1.506) Diagnostic grp - Cancer: OR 1.131 (0.76-1.683) |
| Talaat K. R. et al.,2010 United States[52](#_ENREF_52) | Controlled Clinical Trial | 5 | Sample size: 1313, Mean age: 56.5, Age range: 18 - 93, Percent female: 57.1% | Influenza - monovalent H1N1, CSL Limited, The 7.5-mgdoses were supplied in prefilled syringes that contained 7.5 mg of HA in 0.25 mL of thimerosal-free diluent., Adjuvant: Adjuvant Free, Preservative: Other, Delivery: Intramuscular | Dose1: NR Dose2: 21 Days | Event: Any systemic AE (Dose 1): 26%, Syscat: 8, Sev: 1-3 Event: Any systemic AE (Dose 2): 13%, Syscat: 8, Sev: 1-3 Event: Headache (Dose 1): 15%, Syscat: 8, Sev: 1-3 Event: Headache (Dose 2): 9%, Syscat: 8, Sev: 1-3 Event: Myalgia (Dose 1): 12%, Syscat: 8, Sev: 1-3 Event: Myalgia (Dose 2): 6%, Syscat: 8, Sev: 1-3 Event: Malaise (Dose 1): 8%, Syscat: 8, Sev: 1-3 Event: Malaise (Dose 2): 8%, Syscat: 8, Sev: 1-3 Event: Nausea (Dose 1): 4%, Syscat: 8, Sev: 1-3 Event: Nausea(Dose 2): 3%, Syscat: 8, Sev: 1-3 Event: Chills(Dose 1): 2%, Syscat: 8, Sev: 1-3 Event: Chills(Dose 2): 2%, Syscat: 8, Sev: 1-3 Event: Vomiting(Dose 1): 1%, Syscat: 8, Sev: 1-3 Event: Vomiting(Dose 2): 0.5%, Syscat: 8, Sev: 1-3 Event: Fever (Dose 1): 1%, Syscat: 8, Sev: 1-3 Event: Fever(Dose 2): 0.5%, Syscat: 8, Sev: 1-3 | Any systemic AE (Dose 1): OR 1.176 (0.701-1.974) Any systemic AE (Dose 2): OR 0.562 (0.32-0.987)\*\* Chills(Dose 1): OR 1 (0.208-4.801) Fever (Dose 1): OR 0.99 (0.11-8.922) Headache (Dose 1): OR 1.428 (0.719-2.835) Headache (Dose 2): OR 1 (0.464-2.154) Malaise (Dose 1): OR 1 (0.445-2.247) Malaise (Dose 2): OR 0.704 (0.341-1.452) Myalgia (Dose 1): OR 2.136 (0.885-5.159) Myalgia (Dose 2): OR 0.645 (0.29-1.437) Nausea (Dose 1): OR 1 (0.326-3.067) Nausea(Dose 2): OR 3.062 (0.39-24.025) Vomiting(Dose 1): OR 0.495 (0.089-2.744) Vomiting(Dose 2): OR 0.497 (0.045-5.549) |
| Treanor J. J. et al.,2011 USA[51](#_ENREF_51) | Controlled Clinical Trial | 3 | Sample size: 4648, Mean age: 32.5, Age range: 18 - 55, Percent female: 59%, Percent pregnant: Percent Pregnant: 0.8% | Influenza (inactivated), FluBlok, NR, The trivalent vaccine contained 45 mcg of each purified rHA0 derived from the A/Solomon Islands/3/2006 (H1N1), A/Wisconsin/67/2005 (H3N2), and B/Malaysia/2506/2004 influenza viruses recommended for the 2007–2008 influenza season formulated with 0.005% Tween®-20 in 10mM sodiumphosphate buffer pH 7.0 ± 0.4 without a preservative, Adjuvant: Not Reported, Preservative: Preservative Free, Delivery: Intramuscular | Dose1: 0 Days | Any adverse event: 51.1% Any SAE: 1.5% Event: Fever (=100.4): 0.7%, Syscat: 8, Sev: 1-5 Event: Fatigue or lack of energy: 14.5%, Syscat: 8 Event: Shivering or chills: 3.0%, Syscat: 8 Event: Joint pain: 3.8%, Syscat: 15 Event: Muscle pain: 10.2%, Syscat: 15 Event: Headache: 14.9%, Syscat: 8 Event: Nausea: 5.5%, Syscat: 7 Event: Pain: 36.3%, Syscat: 8 Event: Bruising: 3.2%, Syscat: 12 | Bruising: OR 1.258 (0.89-1.778) Fatigue or lack of energy: OR 1.004 (0.853-1.182) Fever (=100.4): OR 1.395 (0.665-2.928) Headache: OR 0.964 (0.821-1.131) Joint pain: OR 1.056 (0.779-1.432) Muscle pain: OR 1.585 (1.283-1.958)\*\* Nausea: OR 1.173 (0.903-1.524) Pain: OR 6.686 (5.62-7.953)\*\* Shivering or chills: OR 0.968 (0.692-1.354) |
| Vermeulen J. N. et al.,2012 US and Netherlands[80](#_ENREF_80) | Controlled Clinical Trial | 5 | Sample size: 210, Mean age: 68.7 (Tx); 70.7 (Placebo), Age range: 58 - 90, Percent female: 62.85% | Zoster, Zostavax, Merck, lyophilized ZV (~23,000 plaque forming unit [PFU]/0.5 mL), Adjuvant: Not Reported, Preservative: Not reported, Delivery: Subcutaneous | Dose1: 0 Days Dose2: 42 Days | Event: 1 or more AEs (Post Dose 1): 71.2% Event: With vaccine-related AEs (Post Dose 1): 52.9% Event: Systemic AEs (Post Dose 1): 12.5% Event: SAE (Post Dose 1): 0% Event: Discontinued due to a vaccine-related AE (Post dose 1): 1.9% Event: 1 or more AEs (Post dose 2): 76.5% Event: With vaccine-related AEs (Post Dose 2): 63.3% Event: Systemic AEs (Post Dose 2): 5.1% Event: Systemic AEs (PD #2) -Rash: 2.0%, Syscat: 10 Event: SAEs (Post dose 2): 5.1% Event: Discontinued due to vaccine related AE (Dose 2): 0% | 1 or more AEs (Post Dose 1): OR 3.062 (1.732-5.412)\*\* Systemic AEs (PD #2) -Rash: OR 2.019 (0.18-22.617) Systemic AEs (Post Dose 2): OR 0.825 (0.244-2.791) Systemic AEs (Post Dose 1): OR 14.696 (1.886-114.525)\*\* 1 or more AEs (Post dose 2): OR 4.063 (2.278-7.243)\*\* With vaccine-related AEs (Post Dose 1): OR 8.525 (4.179-17.389)\*\* With vaccine-related AEs (Post Dose 2): OR 11.174 (5.461-22.867)\*\* |
| Wang, I.K. et al. 2013[54](#_ENREF_54) Taiwan | Cohort | 5 | Sample size : 4018, Mean age: 70/59 (vaccinated/nonvaccinate, Age range: 18 - 65+, Percent female: 51%, Conditions: ESRD | Influenza (inactived) , Not specified , NR , Not reported , Adjuvant: Not Reported , Preservative: Not reported , Delivery: Not reported | Dose1: Not reported | Event: Total hospitalization : 55% Event: Pneumonia/influenza-hospitalization : 17% , Syscat: 22 Event: Septicemia, bacteremia, and viremia-hospitalization : 12% , Syscat: 11 Event: Heart disease-hospitalization : 41% , Syscat: 2 Event: Respiratory Failure-hospitalization : 8% , Syscat: 22 Event: Intensive care unit admission-hospitalization : 2% Event: Mortality-hospitalization : 15% | Heart disease-hospitalization: OR 1.253 (1.072-1.465)\*\* Intensive care unit admission-hospitalization: OR 0.341 (0.206-0.564)\*\* Pneumonia/influenza-hospitalization: OR 1.238 (1.005-1.524)\*\* Respiratory Failure-hospitalization: OR 0.963 (0.727-1.276) Septicemia, bacteremia, and viremia-hospitalization: OR 1.158 (0.916-1.464) Total hospitalization: OR 1.096 (0.94-1.277) |
| Weinberg A. et al.,2010 US (No direct mentions)[87](#_ENREF_87) | Cohort | 1 | Sample size: 82, Mean age: NR, Age range: 18 - 65, Percent female: 35.3%, Conditions: HIV | Varicella, Varivax, Merck, Adjuvant: Not Reported, Preservative: Not reported, Delivery: Not reported | Dose1: 0 Weeks Dose2: 12 Weeks | Event: Dose1: Systemic rash (non-zosteriform): 3%, Syscat: 10, Sev: 1,2 Event: Dose 1: Pruritis: 3%, Syscat: 6, Sev: 1,2 Event: Dose 1: Adenopathy: 0%, Syscat: 26, Sev: 1,2 Event: Dose 1: Nose bleed: 0%, Sev: 1,2 Event: Dose 1: Influenza-like illness: 9%, Syscat: 8, Sev: 1,2 Event: Dose 1: Chest pain: 0%, Syscat: 2, Sev: 1,2 Event: Dose 1: Liver enzyme elevation: 0%, Syscat: 9, Sev: 1,2 Event: Dose 2: Systemic rash (non-zosteriform): 3%, Syscat: 10, Sev: 1,2 Event: Dose2: Pruritis: 0%, Syscat: 6, Sev: 1,2 Event: Dose2: Adenopathy: 0%, Syscat: 26, Sev: 1,2 Event: Dose2: Nose bleed: 3%, Sev: 1,2 Event: Dose2: Influenza-like illness: 0%, Syscat: 8, Sev: 1,2 Event: Dose2:Chest pain: 0%, Syscat: 2, Sev: 1,2 Event: Dose2: Liver enzyme elevation: 6%, Syscat: 9, Sev: 1,2 | Dose 1: Influenza-like illness: OR 1.55 (0.242-9.94) Dose 1: Pruritis: OR 0.484 (0.042-5.618) Dose1: Systemic rash (non-zosteriform): OR 0.484 (0.042-5.618) Dose2: Liver enzyme elevation: OR 2.065 (0.178-23.943) Dose 2: Systemic rash (non-zosteriform): OR 1 (0.06-16.69) |

| **Evidence Table 2. Vaccinated versus unvaccinated: Adults** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Author- Year- Country** | **Vaccine2** | **Timing2** | **Adverse Event2** | **Control group** | **Adverse Events Control** |
| Barrett P. N. et al.,2011 US[47](#_ENREF_47) |  |  |  | Placebo Buffered saline | Any adverse event: 22%, Sev: 1-5 Any SAE: 0.7%, Sev: 3-5 Event: Arthralgia: 3%, Syscat: 15, Sev: 1-3 Event: Chills: 3%, Syscat: 8, Sev: 1-3 Event: Cough: 0.7%, Syscat: 22, Sev: 1-3 Event: Fatigue: 12%, Syscat: 8, Sev: 1-3 Event: Headache: 13%, Syscat: 8, Sev: 1-3 Event: Hiperhidrosis: 3%, Syscat: 8, Sev: 1-3 Event: Malaise: 227%, Syscat: 8, Sev: 1-3 Event: Myalgia: 6%, Syscat: 8, Sev: 1-3 Event: Oropharyngeal pain: 0.9%, Syscat: 7, Sev: 1-3 Event: Pyrexia: 1%, Syscat: 8, Sev: 1-3 Event: Death: 0%, Sev: 5 Event: Potentially placebo related SAE: 0.05%, Syscat: 26, Sev: 3 |
| Bhatla N. et al.,2010 India[89](#_ENREF_89) |  |  |  | Aluminum hydroxide (placebo) Contains only the aluminum hydrozide, no ASO4 | Any adverse event: 13.4% Any SAE: 2.2% Event: Miscarriage: 0.6%, Syscat: 18, Sev: 5 Event: Bronchogenic cyst: 0.6%, Syscat: 22 Event: Cataract: 0.6%, Syscat: 6 Event: Pneumothorax of the left lung: 0.6%, Syscat: 22 Event: Pain (Grade 3): 4.0%, Syscat: 17, Sev: 3 Event: Redness (>50 mm): 0.6%, Syscat: 23, Sev: 3 Event: Swelling (>50 mm), Syscat: 23, Sev: 3 |
| Frey S. et al.,2010 US, Finland, Poland[48](#_ENREF_48) | Influenza (inactivated), Optaflu, Novartis, 15 mg of hemagglutinin per 0.5-mL dose of each virus strain recommended for the 2007–2008 Northern Hemisphere influenza season: A/Solomon Islands/3/2006 (H1N1)–like, A/Wisconsin/67/2005 (H3N2)–like, and B/Malaysia/2506/2004–like, Adjuvant: Not Reported, Preservative: Not reported, Delivery: Intramuscular | Dose1: 1 Days | Any SAE: 1.1% Event: Chills (mild-moderate), Syscat: 8, Sev: 1-2 Event: Malaise (mild-moderate): 7.5%, Syscat: 8, Sev: 1-2 Event: Myalgia (mild-moderate), Syscat: 8, Sev: 1-2 Event: Arthralgia (mild-moderate): 3.5%, Syscat: 15, Sev: 1-2 Event: Headache (mild-moderate): 15%, Sev: 1-2 Event: Sweating (mild-moderate), Sev: 1-2 Event: Fatigue (mild-moderate): 10%, Syscat: 8, Sev: 1-2 Event: Fever (mild-moderate): 1%, Syscat: 8, Sev: 1-2 Event: Withdrew after AE: .1%, Sev: 1-2 Event: Death: .1%, Sev: 5 AE: 0% | Placebo Unsure of adjuvants, preservatives and formulations | Any SAE: 0.97% Event: Chills (mild-moderate): 5%, Sev: 1-2 Event: Malaise (mild-moderate): 6%, Sev: 1-2 Event: Myalgia (mild-moderate): 7%, Sev: 1-2 Event: Arthalgia (mild-moderate): 2.6%, Sev: 1-2 Event: Headache (mild-moderate): 15%, Sev: 1-2 Event: Sweating (mild-moderate): 2.5%, Sev: 1-2 Event: Fatigue (mild-moderate), Sev: 1-2 Event: Fever (mild-moderate): 0.5%, Sev: 1-2 Event: Withdrew after AE (mild-moderate): 0.03%, Sev: 1-2 Event: Death (mild-moderate): .03%, Sev: 5 |
| Iorio A. et al.,2010 Italy[49](#_ENREF_49) |  |  |  | Placebo | Any SAE: 0%, Syscat: 0 Event: Nosebleeds: 3.85%, Syscat: 22, Sev: 1-3 Event: Bruising: 0.96%, Syscat: 12, Sev: 1-3 Event: Posttraumatic elbow hematoma: 0%, Syscat: 26 Event: Gingival bleeding: 0%, Syscat: 7 Event: Conjunctival hemorrhage: 0%, Syscat: 6 |
| Jackson L. A. et al.,2010 US[50](#_ENREF_50) |  |  |  | Placebo saline placebo injection | Any adverse event: 44% Any SAE: 1.0% Event: Fever: 1%, Syscat: 8, Sev: 1-3 Event: Myalgia/arthralgia: 10%, Syscat: 15, Sev: 1-3 Event: Swelling of the face: 1.0%, Syscat: 8, Sev: 1-3 Event: Cough: 7.0%, Syscat: 22, Sev: 1-3 Event: Chest Tightness/Difficulty breathing: 3.0%, Syscat: 22, Sev: 1-3 Event: Sore throat, hoarseness or pain on swallowing: 9.0%, Syscat: 7, Sev: 1-3 Event: Death (road accident): .03%, Sev: 5 AE: 0% |
| Johnstone, J. et al. 2012[240](#_ENREF_240) 40 countries | Influenza (inactived) , Adjuvant: Not Reported , Preservative: Not reported , Delivery: | Dose1: NR | Event: Any major cardiovascular event (during flu season) : 155% , Syscat: 2 , Sev: 3-4 Event: Any major cardiovascular event (non flu season) : 0.97% , Syscat: 2 , Sev: 3-4 Event: Non cardiovascular deaths : 0.23% , Sev: 4 Event: Cancer deaths : 0.1% , Sev: 4 Event: Deaths from other causes : 0.13% , Sev: 4 AE: 0.01% AE: 0% AE: 0% | Nothing | Event: Any major cardiovascular event (during flu season) : 1.0% , Syscat: 2 , Sev: 3-4 Event: Any major cardiovascular event (non flu season) : 1.05% , Syscat: 2 , Sev: 3-4 Event: Non cardiovascular deaths : 0.08% , Sev: 4 Event: Cancer deaths : 0.03% , Sev: 4 Event: Deaths from other causes : 0.01% , Sev: 4 |
| Langley J. M. et al.,2011 Canada[46](#_ENREF_46) | Influenza (inactivated), Contains equal parts of three monovalent egg-grown, formalin-inactivated influenza antigens formulated with OMPs of N. meningitidis serogroup B strain 8047 at an initial ratio of OMP to haemagglutinin (HA) of 4:1. After diafiltration to remove detergents necessary to keep the OMPs in stable solution in the absence of antigen, the overall total protein to HA ratio in the final vaccine product is 2.5 to 5:1. The trivalent vaccine stock contained HA from each of A/New Caledonia/20/99 [H1N1], A/Panama/2007/99 [H3N2] and B/Shangdong/7/97 [H1N1, Adjuvant: Not Reported, Preservative: Thimerisol, Delivery: | Dose1: 0 Days | Any SAE: 0% Event: Shortness of breath (Grade 2/3): 0%, Syscat: 22, Sev: 3-5 Event: Lightheadedness/Dizziness (Grade2/3): 0%, Syscat: 17, Sev: 3-5 Event: New rash/itchy rash (Grade 2/3): 0%, Syscat: 10, Sev: 3-5 Event: Feverishness (Grade2/3): 0%, Syscat: 8, Sev: 3-5 Event: Burning/stinging nose (Grade2/3): 0%, Sev: 3-5 Event: Burning/stinging throat (Grade 2/3): 0%, Sev: 3-5 Event: Itching nose/throat/eyes (Grade 2/3): 0%, Syscat: 8, Sev: 3-5 Event: Temp >39C: 0%, Syscat: 8, Sev: 3-5 AE: 0% AE: 0% AE: 0% |  | Event: Shortness of breath (Grade 2/3): 0%, Syscat: 22, Sev: 3-5 Event: Lightheadedness or dizziness (2/3): 0%, Syscat: 17, Sev: 3-5 Event: A new rash or a rash that has become itchy (2/3): 0%, Syscat: 10, Sev: 3-5 Event: Feverishness: 0%, Syscat: 8, Sev: 3-5 Event: Temperature (>39C): 0%, Syscat: 8, Sev: 3-5 Event: Burning or stinging in the nose (2/3): 0%, Syscat: 8, Sev: 3-5 Event: Burning or stinging in the throat (2/3): 0%, Syscat: 8, Sev: 3-5 Event: Itching nose/throat eyes (2/3): 0%, Syscat: 8, Sev: 3-5 |
| Lee S. et al.,2011 Korea[90](#_ENREF_90) |  |  |  | Placebo Unsure of adjuvants, preservatives and formulations | Any adverse event: 40% Event: Serious adverse events (any): 0% Event: Hypoaesthesia (any): 10%, Syscat: 17 Event: Hypoaesthesia (vaccine-related): 0%, Syscat: 17 |
| Macaladad N. et al.,2007 Brazil, Costa Rica, Colombia, Mexico, Peru and Venezuela and the Philippines[78](#_ENREF_78" \o "Macaladad, 2007 #20162) |  |  |  | Placebo Unsure of adjuvants, preservatives and formulations | Any adverse event: 0% Any SAE: 0% Event: Injection-site: 0%, Syscat: 8 Event: Systemic: 0% Event: Vaccine-related (Related to injection-site AE): 0%, Syscat: 8 Event: Injection-site (mild burning, erythema and pruritus): 0%, Syscat: 8, Sev: 2 Event: Serious vaccine-related AE: 0% |
| Madhi S. A. et al.,2011 South Africa[53](#_ENREF_53) |  |  |  | Placebo Unsure of adjuvants, preservatives and formulations | Any adverse event: 9.9% Event: Pain: 4.4% Event: Redness: 1.1% Event: Swelling: 0% Event: Lump formation: 2% Event: Bruising: 0% Event: Itching: 1.1% Event: Rigors: 5% Event: Fatigue: 5.5% Event: Headache: 3.3% Event: Fits: 0% Event: Myalgia: 2.2% Event: Arthralgia: 4.4% Event: Fever: 1.1% |
| Mills R. et al.,2010 US[81](#_ENREF_81) |  |  |  | Nothing | Any adverse event: 17.7%, Syscat: 8 Any SAE: 0%, Syscat: 8, Sev: 3,4,5 Event: Overall: Injection site AE: 4.3%, Syscat: 8 Event: Overall: Systemic: 13.5%, Syscat: 8 Event: Overall: Vaccine related: 0%, Syscat: 8 Event: Overall: Deaths: 0% Event: Stratum1: With one or more AE: 22.7%, Syscat: 8 Event: Stratum1:Injection AE: 4.5%, Syscat: 8 Event: Stratum1:Systemic AE: 0%, Syscat: 8 Event: Stratum1:Vaccine AE: 0%, Syscat: 8 Event: Stratum2:With one or more AE: 6.7%, Syscat: 8 Event: Stratum2:Injection AE: 3.3%, Syscat: 8 Event: Stratum2:Systemic AE: 3.3%, Syscat: 8 Event: Stratum2:Vaccine AE: 0%, Syscat: 8 Event: 50-59y:With one or more AE: 26.3%, Syscat: 8 Event: 50-59y:Systemic AE: 21.1%, Syscat: 8 Event: 50-59y:Vaccine AE: 0%, Syscat: 8 Event: >=60y:With one or more AE: 15.6%, Syscat: 8 Event: >=60y:Systemic AE: 11.7% Event: >=60y:Vaccine AE: 0%, Syscat: 8 |
| Murray A. V. et al.,2011 US, Canada, Spain, Germany, UK[83](#_ENREF_83) |  |  |  | Placebo Placebo includes same adjuvants, preservatives, formulations as the active group | Any SAE: 5.0% Event: Blood/Lymphatic (1-42d): 0%, Syscat: 1 Event: Cardiac(1-42d): 0.3%, Syscat: 2 Event: GI(1-42d): 0.1%, Syscat: 7 Event: Neoplasms(1-42d): 0.2%, Syscat: 16 Event: Nervous system(1-42d): 0.1%, Syscat: 17 Event: Psychiatric(1-42d): 0.0%, Syscat: 19 Event: Respiratory(1-42d): 0%, Syscat: 22 Event: Vaccine SAE(1-42d): 0% Event: Death(1-42d): 0.1% Event: Blood/Lymphatic (1-182d): 0.1%, Syscat: 1 Event: Cardiac(1-182d): 1.2%, Syscat: 2 Event: GI(1-182d): 0.5%, Syscat: 7 Event: Neoplasm(1-182d): 1.0%, Syscat: 16 Event: Nervous(1-182d): 0.5%, Syscat: 17 Event: Psychiatric(1-182d): 0.1%, Syscat: 19 Event: Respiratory(1-182d): 0.4%, Syscat: 22 Event: Vaccine SAE(1-182d): 0.0% Event: Death(1-182d): 0.3% |
| Ngan H. Y. S. et al.,2010 Hong Kong[88](#_ENREF_88) |  |  |  | Placebo Placebo includes same adjuvants, preservatives, formulations as the active group | Any adverse event: 77% Any SAE: 0.67%, Sev: 1-3 Event: Arthralgia: 6%, Syscat: 15, Sev: 1-3 Event: Fatigue: 30%, Syscat: 8, Sev: 1-3 Event: Fever: 8%, Syscat: 8, Sev: 1-3 Event: GI symptoms: 10%, Syscat: 7, Sev: 1-3 Event: Headache: 18%, Syscat: 8, Sev: 1-3 Event: Myalgia: 24%, Syscat: 8, Sev: 1-3 Event: Rash, Syscat: 10, Sev: 1-3 Event: Urticaria: 2%, Syscat: 10, Sev: 1-3 |
| Schmader K. E. et al.,2012 North America and Europe[79](#_ENREF_79) |  |  |  | Placebo Placebo includes same adjuvants, preservatives, formulations as the active group | Any adverse event: 41.5% Any SAE: 0.5% Event: With 1 or more injection site AEs: 14.4% Event: With 1 or more systemic AEs: 33.5% Event: Vaccine related AEs: 17.9% Event: Vaccine related injection site AEs: 14.4% Event: Vaccine related systemic AEs: 4.7% Event: Serious vaccine related AEs: 0% Event: SAE with death: .03% AE: 0% |
| Simberkoff M. S. et al.,2010 US[82](#_ENREF_82) |  |  |  | Placebo Unsure of adjuvants, preservatives and formulations | Any adverse event: 1.4%, Sev: 1-5 Any SAE: 1.66%, Sev: 3-5 Event: # of SAE (60-69y): 0.65%, Sev: 3-5 Event: # of SAE (>=70y): 1.01%, Sev: 3-5 Event: # of SAE (70-80y): 0.86%, Sev: 3-5 Event: # of SAE (>=80y): 0.16%, Sev: 3-5 Event: Diagnostic grp - Cancer: 0.24%, Syscat: 16, Sev: 3-5 Event: Diagnostic grp - Vascular (pathological): 0.4%, Syscat: 26, Sev: 3-5 Event: Diagnostic grp - Vascular (functional): 86%, Syscat: 26, Sev: 3-5 Event: COSTART - Cardiovascular: 0.45%, Syscat: 2, Sev: 3-5 Event: COSTART - Digestive: 0.3%, Syscat: 7, Sev: 3-5 Event: COSTART - Endocrine: .02%, Syscat: 5, Sev: 3-5 Event: COSTART - Hemic/Lymphatic: 0.01%, Syscat: 1, Sev: 3-5 Event: COSTART - Metabolic/nutritional: 0.02%, Syscat: 14, Sev: 3-5 Event: COSTART - Musculoskeletal: 0.08%, Syscat: 15, Sev: 3-5 Event: COSTART - Nervous system: 0.18%, Syscat: 17, Sev: 3-5 Event: COSTART - Respiratory, Syscat: 22, Sev: 3-5 Event: COSTART - Skin: 0.16%, Syscat: 23, Sev: 3-5 Event: COSTART - Sight/Sense: 0%, Sev: 3-5 Event: COSTART - Genitourinary: .09%, Syscat: 20, Sev: 3-5 |
| Talaat K. R. et al.,2010 United States[52](#_ENREF_52) | Influenza - monovalent H1N1, CSL Limited, The 15mg dose was supplied in multidose vials of 60 mg of HA per milliliter with thimerosal 0.01% (wt/vol)., Adjuvant: Adjuvant Free, Preservative: Thimerisol, Delivery: Intramuscular | Dose1: NR NR Dose2: 21 Days | Event: Any systemic AE (Dose 1), Syscat: 8, Sev: 1-3 Event: Any systemic AE (Dose 2): 18%, Syscat: 8, Sev: 1-3 Event: Headache (Dose 1), Syscat: 8, Sev: 1-3 Event: Headache(Dose 2): 11%, Syscat: 8, Sev: 1-3 Event: Malaise(Dose 1): 14%, Sev: 1-3 Event: Malaise(Dose 2), Sev: 1-3 Event: Myalgia(Dose 1): 15%, Syscat: 8, Sev: 1-3 Event: Myalgia(Dose 2): 8%, Syscat: 8, Sev: 1-3 Event: Nausea(Dose 1): 5%, Syscat: 8, Sev: 1-3 Event: Nausea(Dose 2): 5%, Syscat: 8, Sev: 1-3 Event: Chills(Dose 1): 3%, Syscat: 8, Sev: 1-3 Event: Chills(Dose 2): 3%, Syscat: 8, Sev: 1-3 Event: Vomiting(Dose 1): 1%, Syscat: 8, Sev: 1-3 Event: Vomiting(Dose 2): 3%, Syscat: 8, Sev: 1-3 Event: Fever(Dose 1): 1%, Syscat: 8, Sev: 1-3 Event: Fever(Dose 2): 1%, Sev: 1-3 AE: 4% | Placebo Placebo was supplied in multidose vials containing vaccine diluent and thimerosal 0.01% (wt/vol). The 7.5microgram vaccine did not have thimerosal. | Event: Any systemic AEs (Dose 1): 23%, Syscat: 8, Sev: 1-3 Event: Any systemic AEs (Dose 2): 21%, Syscat: 8, Sev: 1-3 Event: Headache (Dose 1): 11%, Syscat: 8, Sev: 1-3 Event: Headache (Dose 2): 9%, Syscat: 8, Sev: 1-3 Event: Malaise (Dose 1): 8%, Syscat: 8, Sev: 1-3 Event: Malaise (Dose 2): 11%, Syscat: 8, Sev: 1-3 Event: Myalgia (Dose 1), Syscat: 8, Sev: 1-3 Event: Myalgia (Dose 2): 9%, Syscat: 8, Sev: 1-3 Event: Nausea (Dose 1): 4%, Syscat: 8, Sev: 1-3 Event: Nausea (Dose 2): 2%, Syscat: 8, Sev: 1-3 Event: Chills (Dose 1): 1%, Syscat: 8, Sev: 1-3 Event: Chills (Dose 2): 2%, Syscat: 8, Sev: 1-3 Event: Vomiting (Dose 1): 0%, Syscat: 8, Sev: 1-3 Event: Vomiting (Dose 2): 2%, Syscat: 8, Sev: 1-3 Event: Fever (Dose 1): 1%, Syscat: 8, Sev: 1-3 Event: Fever (Dose 2): 1%, Syscat: 8, Sev: 1-3 |
| Treanor J. J. et al.,2011 USA[51](#_ENREF_51) |  |  |  | Placebo Saline injection | Any adverse event: 31.6% Any SAE: 1.3% Event: Fever (=100.4): 0.5%, Syscat: 8, Sev: 1-5 Event: Fatigue or lack of energy: 14.5%, Syscat: 8 Event: Shivering or chills: 3.1%, Syscat: 8 Event: Joint pain: 3.6%, Syscat: 15 Event: Muscle pain: 6.7%, Syscat: 15 Event: Headache: 15.4%, Syscat: 8 Event: Nausea: 181%, Syscat: 7 Event: Pain: 7.9%, Syscat: 8 Event: Bruising: 2.6%, Syscat: 12 |
| Vermeulen J. N. et al.,2012 US and Netherlands[80](#_ENREF_80) |  |  |  | Placebo Unsure of adjuvants, preservatives and formulations | Event: 1 or more AE (Dose 1): 43.8% Event: With vaccine-related AEs (Dose 1): 11.4% Event: Systemic AEs (Dose 1): 1.0% Event: SAEs (Dose 1): 0% Event: Discontinued due to vaccine AE (Dose 1): 0% Event: With one or more AE (Dose 2): 39.6% Event: With vaccine-related AEs (Dose 2): 6% Event: Systemic AE (Dose 2): 5.9% Event: Rash: 1%, Syscat: 10 Event: SAEs (Dose 2): 0% Event: Discontinued due to vaccine AE (Dose 2): 0% |
| Wang, I.K. et al. 2013[54](#_ENREF_54) Taiwan |  |  |  | Nothing | Event: Total hospitalization : 53% Event: Pneumonia/influenza-hospitalization : 14% , Syscat: 22 Event: Septicemia, bacteremia, and viremia : 11% , Syscat: 11 Event: Heart disease : 36% , Syscat: 2 Event: Respiratory Failure : 8% , Syscat: 22 Event: Intensive care unit admission : 6% Event: Mortality : 18% AE: .56% |
| Weinberg A. et al.,2010 US (No direct mentions)[87](#_ENREF_87) |  |  |  | Placebo Unsure of adjuvants, preservatives and formulations | Event: Dose 1: Systemic rash (non-zosteriform): 6%, Syscat: 10, Sev: 1,2 Event: Dose 1: Pruritis: 6%, Syscat: 6, Sev: 1,2 Event: Dose 1: Adenopathy: 3%, Syscat: 26, Sev: 1,2 Event: Dose 1: Nose bleed: 0%, Syscat: Not sure, Sev: 1,2 Event: Dose 1: Influenza-like illness: 6%, Syscat: 8, Sev: 1,2 Event: Dose 1: Chest pain: 3%, Syscat: 2, Sev: 1,2 Event: Dose 1: Liver enzyme elevation: 1%, Syscat: 9, Sev: 1,2 Event: Dose 2:Systemic rash (non-zosteriform): 3%, Syscat: 10, Sev: 1,2 Event: Dose 2: Pruritis: 3%, Syscat: 6, Sev: 1,2 Event: Dose 2: Adenopathy: 0%, Syscat: 26, Sev: 1,2 Event: Dose 2: Nose bleed: 0%, Syscat: Not sure, Sev: 1,2 Event: Dose 2: Influenza-like illness: 3%, Syscat: 8, Sev: 1,2 Event: Dose 2: Chest pain: 0%, Syscat: 2, Sev: 1,2 Event: Dose 2: Liver enzyme elevation: 3%, Syscat: 9, Sev: 1,2 |