

**Appendix 2 (as supplied by the authors): Further details on characteristics of studies included in the meta-analysis**

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| Author                          | Alfageme 2006 <sup>1</sup>   |
| Approximate year of trial start | 2003   |
| Study population                | Spanish COPD patients, excluding those with specified co-morbidities.<br>95% male. Mean 68.5 years old, range 61-73 years  |
| Maximum follow up time          | 2.7 years  |
| Interventions                   | 23-valent PPV. No intervention in control group other than follow up checks, as in vaccine group   |
| Quality                         | Described as randomised. Generation of allocation sequence described and adequate but concealment of allocation not described<br>Not described as double-blind but outcome assessors are blinded   |
| Outcomes                        | Presumptive pneumococcal pneumonia (radiographic and bacteriologic)<br>All-cause pneumonia (radiographic)<br>All-cause mortality<br>Mortality due to pneumonia (method of assessment of this outcome not clearly explained)  |
| Author                          | Austrian 1976 <sup>2</sup>   |
| Approximate year of trial start | 1972   |
| Study population                | Young gold-miners in South Africa<br>100% male. Age not well defined   |
| Maximum follow up time          | Not reported   |
| Interventions                   | 13 valent PPV. 2 control groups : saline placebo and Meningococcal A vaccine   |
| Quality                         | Described as randomised. Generation of allocation sequence described and adequate but concealment of allocation not described<br>Not reported as double-blind and no description of who, if anyone, was blinded  |
| Outcomes                        | Presumptive pneumococcal pneumonia (radiographic and is suggestive that culture performed but not explicitly stated)<br>All-cause pneumonia (radiographic)   |
| Author                          | Austrian 1980 <sup>3</sup>   |
| Approximate year of trial start | 1973   |
| Study population                | a) US psychiatric hospital patients (resident for over 3m)<br>b) clients (>45yo) of a health insurance plan<br>Sex and age distribution not well defined for either trial  |
| Maximum follow up time          | a) 3.0 years b) 2.8 years  |
| Interventions                   | 12v PPV with saline placebo in controls  |
| Quality                         | a) Not described as randomised. Neither generation of allocation sequence nor concealment of allocation described.<br>Described as double-blind but not possible to determine who is truly blinded<br>b) Described as randomised. Generation of allocation sequence and concealment of allocation described and adequate   |
| Outcomes                        | Not described as double-blind. Some trial staff blinded but unclear regarding outcome assessors<br>a) All-cause pneumonia (radiographic)<br>All-cause mortality<br>Mortality due to pneumonia (method of assessment of this outcome not clearly explained)<br>Bacteraemia/septicaemia<br>b) All-cause pneumonia (radiographic)<br>All-cause bronchitis<br>All-cause mortality<br>Mortality due to pneumonia (from death certificates)<br>Mortality due to pneumococcal infection ("death associated with the isolation from respiratory secretions of a pneumococcal type in the vaccine") |

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| Author                          | Davis 1987 <sup>4</sup>  |
| Approximate year of trial start | 1978   |
| Study population                | US COPD patients<br>Mean age 62.5 years. Sex distribution not defined  |
| Maximum follow up time          | Not reported   |
| Interventions                   | 14-valent PPV. Control group given saline placebo  |
| Quality                         | Described as randomized. Generation of allocation sequence described and adequate but concealment of allocation not described  |
| Outcomes                        | Described as double-blind. Participants are blinded. Outcome assessors are blinded.<br>Definitive pneumococcal pneumonia (radiographic and bacteriologic)<br>Presumptive pneumococcal pneumonia (radiographic and bacteriologic)<br>All-cause pneumonia (radiographic)<br>All-cause mortality<br>Mortality due to pneumonia (method of assessment of this outcome not clearly explained) |
| Author                          | French 2000 <sup>5</sup>   |
| Approximate year of trial start | 1995   |
| Study population                | Ugandan HIV+ 15-55yo, not pregnant, not on rifampicin, not stage 4, no acute febrile illnesses<br>29% male. Mean age 31 years. Minimum age 15 years.   |
| Maximum follow up time          | 2.7 years  |
| Interventions                   | 23-valent PPV. Controls received sodium phosphate carrier (placebo)  |
| Quality                         | Described as randomised but neither generation of allocation sequence nor allocation concealment described.<br>Described as double-blind. Participants are blinded. Some trial staff blinded but unclear if outcome assessors are blinded.   |
| Outcomes                        | All-cause pneumonia (radiographic)<br>All-cause mortality<br>Invasive pneumococcal disease   |
| Author                          | Gaillat 1985 <sup>6</sup>  |
| Approximate year of trial start | 1980   |
| Study population                | French elderly in hospitals or nursing homes<br>34% male. Mean age 74 years  |
| Maximum follow up time          | 2.0 years  |
| Interventions                   | 14-valent PPV. No intervention in control group  |
| Quality                         | Described as randomized. Generation of allocation sequence not described. Concealment of randomization described but not adequate.<br>Not apparently blinded   |
| Outcomes                        | All-cause pneumonia (appears not all cases had radiographic confirmation but percentage unclear)<br>All-cause mortality  |
| Author                          | Honkanen 1999 <sup>7</sup>   |
| Approximate year of trial start | 1992   |
| Study population                | Finnish older than 65yo<br>Mean age 73.5 years   |
| Maximum follow up time          | 3.2yrs   |
| Interventions                   | 23-valent PPV and influenza vaccine in pneumococcal vaccine group. Influenza vaccine in control group.   |
| Quality                         | Not described as randomized. Method of allocation by odd or even year of birth.<br>Not described as double-blind. Unclear if outcome assessors blind   |
| Outcomes                        | Presumptive pneumococcal pneumonia (radiographic and presence of circulating pneumolysin specific immune complexes)<br>All-cause pneumonia (radiographic)<br>Bacteraemia/septicaemia   |

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| Author                          | Kaufman 1947 <sup>8</sup>  |
| Approximate year of trial start | 1937   |
| Study population                | Elderly in New York City Home<br>Mean 67 years. Sex distribution not defined   |
| Maximum follow up time          | 1.5 years  |
| Interventions                   | 3-valent PPV. No intervention in control group   |
| Quality                         | Described as randomised. Randomization not adequate.<br>Not described as double-blind and no further description of any blinding in paper  |
| Outcomes                        | All-cause pneumonia (unclear diagnostic criteria)<br>All-cause mortality   |
| Notes                           | Results from Kaufman 1941 <sup>9</sup> are summarized in Kaufman 1947 – only these data were extracted. A randomization process is reported starting in the trial's second year (alternation; volunteers taken in first year), results were extracted from second year on. |
| Author                          | Klustersky 1986 <sup>10</sup>  |
| Approximate year of trial start | 1987   |
| Study population                | Belgian bronchogenic carcinoma patients, most with no radiotherapy or chemotherapy prior to vaccination<br>96% male. Mean age 61 years, range 42-78 years  |
| Maximum follow up time          | Not reported   |
| Interventions                   | 17v PPV. Saline placebo in control group   |
| Quality                         | Described as randomized. No description of generation of allocation sequence but concealment described and adequate<br>Not reported as double-blind but participants blind and at least some trial staff. Unclear if outcome assessors blind                               |
| Outcomes                        | Presumptive pneumococcal pneumonia (radiographic and bacteriologic)<br>Mortality due to pneumococcal infection (deaths from pneumococcal septicaemias)<br>Bacteraemia/septicaemia  |
| Author                          | Koivula 1997 <sup>11</sup>   |
| Approximate year of trial start | 1982   |
| Study population                | Finnish elderly (over 60yo)  |
| Maximum follow up time          | 3.0 years  |
| Interventions                   | 14-valent PPV and influenza vaccine in intervention group. Influenza vaccine in control group<br>37% male.   |
| Quality                         | Described as randomized. Generation of allocation sequence described and adequate.<br>Concealment described and but difficult to determine if adequate.<br>Not reported as double-blind but outcome assessors blinded.   |
| Outcomes                        | Presumptive pneumococcal pneumonia (radiographic and two-fold rise of pneumolysin antibodies)<br>All-cause pneumonia (radiographic)<br>All-cause mortality<br>Mortality due to pneumonia (from death certificates)   |
| Notes                           | Database of elderly residents randomised prior to recruitment. Outcomes also reported for non-responders   |
| Author                          | Leech 1987 <sup>12</sup>   |
| Approximate year of trial start | 1981   |
| Study population                | Canadian COPD patients<br>71% male. Mean age 67 years, range 40-89 years   |
| Maximum follow up time          | 2.2 years  |
| Interventions                   | 14-valent PPV. Saline placebo in control group. Both groups given influenza vaccine at 0, 1 and 2 years  |
| Quality                         | Described as randomised but neither generation of allocation sequence nor allocation concealment described.<br>Described as double-blind. At least some trial staff blinded but unclear if outcome assessors blind   |
| Outcomes                        | All-cause mortality<br>Bacteraemia/septicaemia   |

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| Author                          | MacLeod 1945 <sup>13</sup>  |
| Approximate year of trial start | 1944  |
| Study population                | US trainees at the Army Airforce Technical School   |
| Maximum follow up time          | Not reported  |
| Interventions                   | 4V PPV. Saline placebo in control group   |
| Quality                         | 100% male. Mean age 23.3 years. Minimum age 18 years<br>Described as randomised. Both generation of allocation sequence and allocation concealment described but neither are adequate.<br>Not described as double-blind and no further description of any blinding in paper   |
| Outcomes                        | Presumptive pneumococcal pneumonia (clinical and bacteriologic)   |
| Author                          | Örtqvist 1998 <sup>14</sup>   |
| Approximate year of trial start | 1991  |
| Study population                | Swedish non-immunocompromised middle aged and elderly (50yo and over) who had previously been hospitalised for community acquired pneumonia<br>48% male. Mean age 69.2 years, range 50-85 years   |
| Maximum follow up time          | Not reported  |
| Interventions                   | 23-valent PPV. Control group received saline placebo  |
| Quality                         | Described as randomised and both generation of allocation sequence and allocation concealment are adequate.<br>Described as double-blind and both participants and outcome assessors are blinded  |
| Outcomes                        | Definitive pneumococcal pneumonia<br>Presumptive pneumococcal pneumonia (radiographic and bacteriologic/two-fold rise of pneumolysin antibodies)<br>All-cause pneumonia (radiographic)<br>All-cause mortality<br>Mortality due to pneumonia (method of assessment of this outcome not clearly explained)<br>Bacteraemia/septicaemia |
| Author                          | Riley 1977 <sup>15</sup>  |
| Approximate year of trial start | 1974  |
| Study population                | Highlanders over 10 yo in Papua New Guinea<br>Sex distribution not defined  |
| Maximum follow up time          | Not reported  |
| Interventions                   | 14-valent PPV. Control received placebo   |
| Quality                         | Described as randomized. Generation of allocation sequence not described. Concealment of allocation described and adequate<br>Described as double-blind. Participants are blinded. Outcome assessors are blinded.   |
| Outcomes                        | All-cause pneumonia (radiographic where possible, percentage unclear)<br>All-cause mortality<br>Mortality due to pneumonia (from questioning relatives)<br>Acute lower respiratory tract infections   |
| Notes                           | 540 records were lost.  |

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| Author                          | Simberkoff 1986 <sup>16</sup>   |
| Approximate year of trial start | 1981  |
| Study population                | US "high-risk" patients i.e. those 55yo or older, or with chronic disease   |
| Maximum follow up time          | Not reported  |
| Interventions                   | 14-valent PPV. Saline placebo in control group  |
| Quality                         | Described as randomized. No description of generation of allocation sequence but concealment described and adequate   |
| Outcomes                        | Described as double-blind but no description of who is blinded<br>Presumptive pneumococcal pneumonia (radiographic and bacteriologic)<br>All-cause pneumonia (radiographic)<br>All-cause bronchitis<br>All-cause mortality<br>Mortality due to pneumonia (deaths following radiographically positive pneumonia)<br>Mortality due to pneumococcal infection (appears to be from death certificates, "listed as primary or contributory cause of death")<br>Bacteraemia/septicaemia |
| Author                          | Smit 1977 <sup>17</sup>   |
| Approximate year of trial start | a) 1973 b) 1974   |
| Study population                | Young gold-miners in South Africa   |
| Maximum follow up time          | 100% male. Age distribution not well defined<br>a) 2.3 years b) 1.6 years   |
| Interventions                   | a) 6v PPV. Two control groups: saline placebo and Meningococcal A and C vaccine<br>b) 12v PPV. Two control groups: saline placebo and Meningococcal A and C vaccine   |
| Quality                         | a) and b) Described as randomized but neither generation of allocation sequence nor allocation concealment described.<br>Not described as double-blind but outcome assessors appear to be blinded   |
| Outcomes                        | a) and b)<br>Presumptive pneumococcal pneumonia (radiographic and bacteriologic)<br>All-cause pneumonia (radiographic), results only available for both control groups combined<br>All-cause bronchitis, results only available for both control groups combined  |
| Author                          | Steentoft 2006 <sup>18</sup>  |
| Approximate year of trial start | 2005  |
| Study population                | Danish COPD patients<br>55% male. Age range 47-86 years   |
| Maximum follow up time          | Not reported  |
| Interventions                   | 23-valent PPV and combinations of steroid treatments in vaccine groups (3). Control group only has the steroid combinations   |
| Quality                         | Described as randomized. No description of generation of allocation sequence but concealment described and adequate<br>No blinding reported   |
| Outcomes                        | All-cause pneumonia (radiographic)  |
| Notes                           | Three vaccine groups combined as this reflects the steroid treatment patterns in the control group  |
| Author                          | Zhogolev 2003 <sup>19</sup>   |
| Approximate year of trial start | 2001  |
| Study population                | Russian soldiers in a) North-west Russia, b) Central Russia, c) East Russia<br>100% male. Age range not defined   |
| Maximum follow up time          | Not reported  |
| Interventions                   | 23-valent polysaccharide, control group received no intervention  |
| Quality                         | No description of generation of allocation sequence, concealment of allocation or blinding  |
| Outcomes                        | a, b and c) All cause pneumonia (diagnostic criteria unclear)   |
| Notes                           | 4 trials are reported in three Russian regions with differing risk settings. Incidence of pneumonia in controls was much higher in the "central" region, compared to the others. One trial not included due to confounding.   |

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## References

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