

| Number | Query results | Results |
|--------|---|---------|
| #27 | 'cytomegalovirus infection'/exp AND 'influenza vaccine'/exp OR ('cytomegalovirus infection'/exp AND 'influenza vaccination'/exp) OR ('cytomegalovirus infection'/exp AND ('influenza virus'/exp AND 'vaccine'/exp OR ('influenza virus'/exp AND 'vaccination'/exp))) OR ('cytomegalovirus'/exp AND 'influenza vaccine'/exp) OR ('cytomegalovirus'/exp AND 'influenza vaccination'/exp) OR ('cytomegalovirus'/exp AND ('influenza virus'/exp AND 'vaccine'/exp OR ('influenza virus'/exp AND 'vaccination'/exp))) OR ('cytomegalovirus'/exp/mj AND ('immune response'/exp/mj OR 'immune status'/exp/mj)) OR ('cytomegalovirus infection'/exp/mj AND ('immune response'/exp/mj OR 'immune status'/exp/mj)) AND 'human'/de | 689 |
| #26 | 'cytomegalovirus infection'/exp AND 'influenza vaccine'/exp OR ('cytomegalovirus infection'/exp AND 'influenza vaccination'/exp) OR ('cytomegalovirus infection'/exp AND ('influenza virus'/exp AND 'vaccine'/exp OR ('influenza virus'/exp AND 'vaccination'/exp))) OR ('cytomegalovirus'/exp AND 'influenza vaccine'/exp) OR ('cytomegalovirus'/exp AND 'influenza vaccination'/exp) OR ('cytomegalovirus'/exp AND ('influenza virus'/exp AND 'vaccine'/exp OR ('influenza virus'/exp AND 'vaccination'/exp))) OR ('cytomegalovirus'/exp/mj AND ('immune response'/exp/mj OR 'immune status'/exp/mj)) OR ('cytomegalovirus infection'/exp/mj AND ('immune response'/exp/mj OR 'immune status'/exp/mj)) | 837 |
| #25 | 'cytomegalovirus'/exp/mj AND ('immune response'/exp/mj OR 'immune status'/exp/mj) OR ('cytomegalovirus infection'/exp/mj AND ('immune response'/exp/mj OR 'immune status'/exp/mj)) | 429 |
| #24 | 'cytomegalovirus infection'/exp/mj AND ('immune response'/exp/mj OR 'immune status'/exp/mj) | 227 |
| #23 | 'cytomegalovirus'/exp/mj AND ('immune response'/exp/mj OR 'immune status'/exp/mj) | 238 |
| #22 | 'immune response'/exp/mj OR 'immune status'/exp/mj | 92,574 |
| #21 | 'cytomegalovirus'/exp/mj | 14,375 |
| #20 | 'cytomegalovirus infection'/exp/mj | 16,489 |
| #19 | 'immune status'/exp/mj | 932 |
| #18 | 'immune response'/exp/mj | 91,662 |
| #17 | 'cytomegalovirus infection'/exp AND 'influenza vaccine'/exp OR ('cytomegalovirus infection'/exp AND 'influenza vaccination'/exp) OR ('cytomegalovirus infection'/exp AND ('influenza virus'/exp AND 'vaccine'/exp OR ('influenza virus'/exp AND 'vaccination'/exp))) OR ('cytomegalovirus'/exp AND 'influenza vaccine'/exp) OR ('cytomegalovirus'/exp AND 'influenza vaccination'/exp) OR ('cytomegalovirus'/exp AND ('influenza virus'/exp AND 'vaccine'/exp OR ('influenza virus'/exp AND 'vaccination'/exp))) | 414 |
| #16 | 'cytomegalovirus'/exp AND ('influenza virus'/exp AND 'vaccine'/exp OR ('influenza virus'/exp AND 'vaccination'/exp)) | 122 |
| #15 | 'cytomegalovirus'/exp AND 'influenza vaccination'/exp | 41 |
| #14 | 'cytomegalovirus'/exp AND 'influenza vaccine'/exp | 134 |
| #13 | 'cytomegalovirus infection'/exp AND ('influenza virus'/exp AND 'vaccine'/exp OR ('influenza virus'/exp AND 'vaccination'/exp)) | 47 |
| #12 | 'cytomegalovirus infection'/exp AND 'influenza vaccination'/exp | 72 |
| #11 | 'cytomegalovirus infection'/exp AND 'influenza vaccine'/exp | 203 |
| #10 | 'influenza virus'/exp AND 'vaccine'/exp OR ('influenza virus'/exp AND 'vaccination'/exp) | 13,079 |
| #9 | 'influenza virus'/exp AND 'vaccination'/exp | 6,925 |
| #8 | 'influenza virus'/exp AND 'vaccine'/exp | 11,990 |
| #7 | 'vaccine'/exp | 286,298 |
| #6 | 'vaccination'/exp | 143,378 |
| #5 | 'influenza virus'/exp | 54,474 |
| #4 | 'influenza vaccination'/exp | 13,281 |
| #3 | 'influenza vaccine'/exp | 30,951 |
| #2 | 'cytomegalovirus'/exp | 34,775 |
| #1 | 'cytomegalovirus infection'/exp | 34,353 |

Supplementary Table 1. Literature search strategy for the effect of CMV-infection on the immune response to influenza vaccination. Results represent the number of articles. Search was performed on 27 June 2017.

Data extraction form per study

Characteristics of studies (Summarized in Table 1)

| | | | | | | | |
|----------------------|------------------------------|--------------------|--------------------|----------------------------------|--------------------|-----------------------|----------|
| Primary study design | Design for research question | Original paper URL | Conclusion/summary | Population (sample size and age) | Exclusion criteria | Setting (country etc) | Timeline |
|----------------------|------------------------------|--------------------|--------------------|----------------------------------|--------------------|-----------------------|----------|

Influenza vaccine outcomes (Summarized in Table 2)

| | | | | | |
|--------------------------|----------------------|-------------------------|--------------------------|-------------------|----------|
| Increase GMT (outcome 1) | Response (outcome 2) | Correlation (outcome 3) | Antibodies (another way) | Model (corrected) | Cellular |
|--------------------------|----------------------|-------------------------|--------------------------|-------------------|----------|

Conclusion articles (Summarized in Figure 3, and Supplementary table 3)

| | | | |
|---|--|--|--------------------|
| Influenza virus strain(s) antibodies measured | Reported effect of CMV Young study group | Reported effect of CMV Old study group | Statistical method |
|---|--|--|--------------------|

Risk of bias and study quality of studies included for systematic assessment (summarized in Table 3)

| | | | | | |
|--------------------|--------------------------------|--------------------|------------------------|------------------|---------------------|
| Study controls for | Statistical method appropriate | Selection (max 4*) | Comparability (max 2*) | Outcome (max 3*) | Overall score (+/-) |
|--------------------|--------------------------------|--------------------|------------------------|------------------|---------------------|

Influenza vaccination (summarized in Supplementary table 4)

| | | | | |
|--------------|-------------------------------|------|---------------------------|---------|
| Type vaccine | year and pandemic or seasonal | Dose | influenza virus strain(s) | Booster |
|--------------|-------------------------------|------|---------------------------|---------|

Time and type of measurement of influenza and CMV antibodies (summarized in Supplementary table 5)

| | | | | | |
|--------------------------------|----------------------|---------------------|--------------------------|--------------------------|---------------------|
| Influenza antibody measurement | | | CMV antibody measurement | | |
| Time after vaccination | Assay of measurement | Vaccination history | Assay of measurement | Cut-off CMV-seropositive | Borderline handling |

Supplementary Table 2. Data extraction form per study.

| Study | Influenza virus strain(s) antibodies measured | Reported effect of CMV | |
|---------------------------------|--|--|---|
| | | Young | Old |
| Turner et al, 2014 | A/H3N2 A/H1N1 A/H1N1 B Vic | Negative Brisbane H1N1 or H3N2* No effect Brisbane H1N1 or H3N2* B Vic | - |
| Den Elzen et al, 2011 | A/H3N2 | - | No effect A/H3N2 |
| Derhovanessian et al, 2012 | A/H1N1 A/H3N2 B Vic | No effect A/H1N1 A/H3N2 B Vic | Negative A/H3N2 No effect A/H1N1 B Vic |
| Nielsen et al, 2015 | A/H1N1 | No effect A/H1N1 (age range 21-77) | |
| Furman et al, 2015 – study 1 ** | A/H1N1 A/H3N2 B Vic | Positive GM of the strains A/H1N1, A/H3N2, B Vic | No effect GM of the strains A/H1N1, A/H3N2, B Vic |
| Furman et al, 2015 – study 2 ** | A/H1N1 A/H3N2 B Vic | Positive GM of the strains A/H1N1, A/H3N2, B Vic | No effect GM of the strains A/H1N1, A/H3N2, B Vic |
| Furman et al, 2015 – study 3 ** | A/H1N1 A/H3N2 B Vic | Positive GM of the strains A/H1N1, A/H3N2, B Vic | No effect GM of the strains A/H1N1, A/H3N2, B Vic |
| Haq et al, 2016 | A/H3N2 | - | No effect A/H3N2 |
| McElhaney et al, 2015 | Unkown which strain was measured | - | Positive Unkown which strain |
| Frasca et al, 2015 | A/H1N1 A/H3N2 B Vic | Negative A/H1N1 Others were not shown 'because low titers' | Negative A/H1N1 Others were not shown 'because low titers' |
| Trzonkowski et al, 2003 | A/H1N1 A/H3N2 B Yam | Negative H1N1 No effect A/H3N2 B Yam (not significant: P=0.07 and P=0.08) | Negative A/H1N1 A/H3N2 B Yam 1 |
| Strindhall et al, 2015 | A/H1N1 A/H3N2 B Vic | - | No effect A/H1N1 A/H3N2 B Vic |
| Reed et al, 2016 | A/H1N1 A/H3N2 B (For each year performed) | - | Negative Averaged strains per year. On persistence and on peak in combination with other factors. |
| Wald et al, 2013 | A/H1N1pdm | Positive A/H1N1pdm | No effect A/H1N1pdm |

| | | | |
|--------------------------------|----------------------------------|---|---|
| Arias et al, 201 | Unkown which strain was measured | - | Negative Unkown |
| Moro-Garcia et al, 2011 | Unkown which strain was measured | - | Negative Unkown |
| Guidi et al, 2014 | A/H1N1 or A/H1N1pdm | - | No effect A/H1N1 or A/H1N1pdm |

* Unkown for which influenza A/Brisbane strain a negative effect respectively no effect was found in this study (H1N1 or H3N2)

- not investigated in this study for this age group.

** Studies from Furman et al (1) reported a geometric mean of three influenza strains, no data of individual strains was reported.

Supplementary Table 3. Conclusion reported by articles.