**Identification of studies via databases and registers**

**Identification of studies via other methods**

Records removed *before screening*:

Duplicate records removed

(n = 7,051)

Records published before 2020 (n = 16)

Records identified from:

Personal communication (n = 38)

Records identified from:

Pubmed (n = 16,159)

ScienceDirect (n = 3,613)

Google Scholar (n = 600)

References from meta-analyses (n = 87)

**Identification**

Records excluded

Not about (excess) mortality, vaccine, or Covid-19 (n = 12,319)

Duplicates (n = 44)

Retracted (n = 1)

Records screened

(n = 13,392)

Reports not retrieved (n = 0)

Reports sought for retrieval

Personal communication (n = 38)

Reports not retrieved (n = 8)

Reports sought for retrieval

(n = 1,028)

**Screening**

Reports excluded:

Animal study (n = 2)

No statistical analysis (n = 111)

No vaccination data included (n= 98)

Not about adverse events or mortality (n = 119)

Not about Covid-19 (n = 5)

Reports excluded:

No statistical analysis (n = 4)

No vaccination data included (n= 5)

Not about adverse events or mortality (n = 2)

Not about Covid-19 (n = 1)

Duplicate (n=2)

Reports assessed for eligibility

(n = 1,020)

Reports assessed for eligibility

(n = 38)

Reports of included studies

(n = 685)

Total reports of included studies

(n = 709)

**Included**

Reports of included studies

(n = 24)

**Defining the landscape of studies included by primary outcome assessed, study design, and definitions wielded for mortality and being vaccinated**

Total reports of included studies

(n = 709)

Includes studies in methodological review

(n = 83)

Inclusion for methodological review (n = 62)

Inclusion for methodological review (n = 20)

Inclusion for methodological review (n = 1)

**Definitions clear**

**Study design**

Meta-analysis / Systematic review (n = 2)

Randomized Controlled Trial (n = 1)

Prospective observational cohort (n = 4)

Retrospective observational cohort (n =16)

Cross-sectional (n = 8)

Case-control / matched (n =1)

Vaccination (n = 2)

Infection (n = 4)

Mortality (n = 6)

Vaccination (n = 43)

Infection (n = 73)

Mortality (n = 101)

Mortality (n = 176)

Adverse events (n = 32)

Unclear or other (n = 501)

Meta-analysis / Systematic review (n = 3)

Randomized Controlled Trial (n = 1)

Prospective observational cohort (n = 10)

Retrospective observational cohort (n =140)

Cross-sectional (n = 2)

Case-control / matched (n =12)

Modelling study (n = 5)

Unclear (n = 3)

Vaccination (n = 138)

Infection (n = 253)

Mortality (n = 201)

Meta-analysis / Systematic review (n = 48)

Rapid review (n = 1)

Randomized Controlled Trial (n = 8)

Prospective observational cohort (n = 47)

Retrospective observational cohort (n = 267)

Case-series (n = 2)

Cross-sectional (n = 20)

Case-control / matched (n = 28)

Propensity score-matched (n = 4)

Test-negative design (n = 17)

Modelling study (n = 53)

Unclear (n = 6)

**Inclusion (RoB)**

**Primary outcome**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **No of studies** | **Design** | **Risk of bias** | | **Inconsistency** | | **Indirectness[[1]](#footnote-1)** | | **Imprecision** | | **Other[[2]](#footnote-2)** | **Certainty**  **(overall score)[[3]](#footnote-3)** |
| **Outcome:** | | | | | | | | | | | |
| All-cause mortality |  |  | |  | |  | |  | |  |  |
| **Outcome:** | | | | | | | | | | | |
| Covid-19 mortality |  |  | |  | |  | |  | |  |  |
| **Outcome:** | | | | | | | | | | | |
| Vaccine mortality |  |  | |  | |  | |  | |  |  |
| **Outcome:** | | | | | | | | | | | |
| Excess mortality |  |  | |  | |  | |  | |  |  |
| **Example:** The use of lay health workers compared to usual health care services  **Outcome:** Immunisation uptake in children | | | | | | | | | | | |
| 4 | Randomised trials  (4) | | Serious risk of bias  (-0.5) | | Important inconsistency  (-0.5) | | No serious indirectness | | No serious imprecision | None | Moderate   (3) |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **[[4]](#footnote-4)** | | | | | |
| **People:[[5]](#footnote-5)**  **Settings:Error! Bookmark not defined.**  **Intervention:Error! Bookmark not defined.**  **Comparison:Error! Bookmark not defined.** | | | | | |
| **Outcomes** | **Absolute Effect\*** | | **Relative effect**  **(95% CI)** | **Number of studies** | **Certainty of the evidence (GRADE)†** |
| Without | With |
| All-cause mortality | per | per | RR  (to ) |  | ⊕⊕⊕⊕High |
| Difference: per  (95% CI: to ) | |
| Covid-19  mortality | per | per | RR  (to ) |  | ⊕⊕⊕⊖Moderate |
| Difference: per  (95% CI: to ) | |
| Vaccine  mortality | per | per | RR  (to ) |  | ⊕⊕⊖⊖Low |
| Difference: per  (Margin of error: to ) | |
| Excess  mortality | per | per | RR  (to ) |  | ⊕⊖⊖⊖Very low |
| Difference: per  (Margin of error: to ) | |
|  |  | | - | - | - |
| 95% CI: 95% Confidence interval; RR: Risk ratio  \* The risk WITHOUT the intervention is based on . The corresponding risk WITH the intervention (and the 95% confidence interval for the difference) is based on the overall relative effect (and its 95% confidence interval).  **†** GRADE Working Group grades of evidence  **High** = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different‡ is low.  **Moderate** = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different‡ is moderate.  **Low** = This research provides some indication of the likely effect. However, the likelihood that it will be substantially different‡ is high.  **Very low** = This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different‡ is very high.  ‡ Substantially different = a large enough difference that it might affect a decision | | | | | |

1. Indirectness includes consideration of

   * Indirect (between study) comparisons
   * Indirect (surrogate) outcomes
   * Applicability (study populations, interventions or comparisons that are different than those of interest)

   [↑](#footnote-ref-1)
2. Other considerations for downgrading include publication bias. Other considerations for upgrading include a strong association with no plausible confounders, a dose response relationship, and if all plausible confounders or biases would decrease the size of the effect (if there is evidence of an effect), or increase it if there is evidence of no harmful effect (safety) [↑](#footnote-ref-2)
3. 4  **High** = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different\*\* is low.

   3  **Moderate** = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different\*\* is moderate.

   2  **Low** = This research provides some indication of the likely effect. However, the likelihood that it will be substantially different\*\* is high.

   1  **Very low** = This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different\*\* is very high.

   \*\* Substantially different = a large enough difference that it might affect a decision [↑](#footnote-ref-3)
4. A title indicating the comparison summarised in the table [↑](#footnote-ref-4)
5. The characteristics of the evidence, including the types of participants (patients or populations), types of settings (e.g. countries) where the studies were done, the intervention and what the intervention was compared to [↑](#footnote-ref-5)