**Direct Standardized Cumulative-Hazard Ratio (DS-CMRR)**  
*Model-free,* fixed cohorts, and **no slope normalization**.  
We build vaccinated (dose ≥1) vs unvaccinated (dose 0) cohorts **as of the enrollment sheet**, compute **age-specific cumulative hazards** over time, then **direct-standardize** both cohorts to a **baseline reference distribution** (you can pick vax\_pt or expected\_deaths). Finally we form a **cumulative ratio** and a **delta-method CI** (Poisson counts, age-wise independence) with baseline anchoring to 1 at week ANCHOR\_WEEKS.

Here’s a clean, end-to-end recipe for how **KCOR** is computed. I’ll write it in “engineering steps” so you can map each step to code.

**Inputs**

* A weekly panel with columns like:
  + week (calendar time, e.g., ISO week start date)
  + YearOfBirth (or age bands)
  + dose (0,1,2,3,…)
  + Alive (person-time at risk that week; person-weeks)
  + Dead (deaths in that week)
* One or more **enrollment sheets** (e.g., 2021\_24) that define fixed cohorts “as of” a start week.

**0) Fix the cohorts (intention-to-t₀)**

For an enrollment sheet E (e.g., 2021\_24):

* **Treated** cohort = everyone vaccinated by week E (dose ≥ 1 at E).
* **Control** cohort = everyone unvaccinated by week E (dose = 0 at E).

From week E onward, keep each person in their **original cohort** (fixed cohorts). If you only have aggregated tables, construct cohort-specific Alive and Dead for each age×week by summing appropriate rows.

This step removes **dynamic HVE** artifacts tied to “time since vaccination.”

**1) Build weekly mortality rates per cohort and age**

For each age stratum a and week t:

* MR\_num[a,t] = Dead\_num[a,t] / Alive\_num[a,t]
* MR\_den[a,t] = Dead\_den[a,t] / Alive\_den[a,t]

(“num” = treated cohort; “den” = control cohort.)

If you prefer exact hazards, use:

* h[a,t] = -ln(1 - MR[a,t]) (for small MR, h ≈ MR)

**2) Estimate the aging slope (Gompertz) and detrend (slope-neutralize)**

Aging makes mortality drift upward over calendar time even with no treatment effect. KCOR removes that drift **within each cohort**, so any remaining shape reflects treatment differences rather than age drift.

For each cohort separately (or jointly—details vary by KCOR version):

1. Pick a **baseline window** well after the initial transients (e.g., a K-week window).
2. Fit a **slope** b in (log rate) space across that window, per cohort or pooled:
   * Option A (simple): fit log(MR[a,t]) = α[a] + b\*t with an **exponential** (WLS/OLS in log space).
   * Option B (robust): **quantile regression** on log(MR[a,t]) at τ≈0.10 to down-weight wave peaks.
3. Define the **detrend factor** relative to a reference week t\_ref inside the baseline window:
   * f[t] = exp(-b \* (t - t\_ref))
4. Apply detrending to each cohort’s weekly rates (per age):
   * MR\*\_num[a,t] = MR\_num[a,t] \* f\_num[t]
   * MR\*\_den[a,t] = MR\_den[a,t] \* f\_den[t]  
     (If you estimated one common slope b, then use the same f[t] for both.)

Intuition: if aging induces a smooth exponential rise, multiplying by f[t] flattens it. Now the **residual** curvature should be attributable to differences between cohorts, not Gompertz drift.

**3) Aggregate across age (optional but recommended)**

To minimize static HVE from different age mixes, combine age strata with a **fixed reference weighting** (direct standardization). Two common choices:

* **PT weights**: weights ∝ person-time in a short baseline window.
* **Expected-deaths weights**: weights ∝ (baseline mean MR across all doses) × (baseline PT).

For each week t, compute standardized rates:

* MR\*\_num\_std[t] = Σ\_a w[a] \* MR\*\_num[a,t]
* MR\*\_den\_std[t] = Σ\_a w[a] \* MR\*\_den[a,t]

(If you prefer to compute KCOR by age first, you can combine **after** the cumulative step; both are fine if you keep weights fixed.)

**4) Form cumulative curves**

KCOR uses cumulative outcomes over calendar time.

Using detrended **rates**:

* CMR\_num[t] = Σ\_{s ≤ t} MR\*\_num\_std[s]
* CMR\_den[t] = Σ\_{s ≤ t} MR\*\_den\_std[s]

(Using hazards is the exact variant: replace MR\* by h\* and “CMR” by cumulative hazard.)

**5) Compute the KCOR curve and anchor**

* KCOR\_raw[t] = CMR\_num[t] / CMR\_den[t]
* Choose an **anchor index** t0 (e.g., 4) and re-scale:
  + KCOR[t] = KCOR\_raw[t] / KCOR\_raw[t0]
  + So KCOR[t0] = 1.0 by definition.

Interpretation:

* KCOR > 1 ⇒ higher cumulative mortality in the vaccinated cohort (harm).
* KCOR < 1 ⇒ lower cumulative mortality in the vaccinated cohort (benefit).

**6) Uncertainty (CIs)**

Several options:

* **Delta on log scale (quick, conservative):** treat weekly deaths as Poisson, propagate via cumulative sums and ratio.
* **Age-wise exact/MOVER:** get age-specific cumulative CIs then combine with fixed weights.
* **Block bootstrap:** resample weeks in blocks (preserve serial structure), recompute KCOR, and take percentile CIs of log(KCOR).

Report CIs on the ratio scale by exponentiating.

**7) Diagnostics you should always check**

* **Baseline window choice** (different K, different t\_ref) — the shape should be stable.
* **Slope method** (exponential vs τ-quantile) — curves shouldn’t flip sign.
* **Age weighting** (PT vs expected-deaths) — shouldn’t change the story.
* **Placebo pre-period** (if available) — should hover ~1 after detrending.
* **Zero/near-zero cells** — guard with small epsilons and/or smoothing.
* **Denominator integrity** — Alive must be person-time for that week, not cumulative headcount.

**Minimal pseudocode**

for each enrollment E:

define cohorts at E (fixed membership)

build weekly MR\_num[a,t], MR\_den[a,t]

estimate slope(s) b over baseline window

f[t] = exp(-b\*(t - tref))

MR\*\_num[a,t] = MR\_num[a,t]\*f\_num[t]

MR\*\_den[a,t] = MR\_den[a,t]\*f\_den[t]

MR\*\_num\_std[t] = sum\_a w[a]\*MR\*\_num[a,t]

MR\*\_den\_std[t] = sum\_a w[a]\*MR\*\_den[a,t]

CMR\_num[t] = cumsum\_t MR\*\_num\_std[t]

CMR\_den[t] = cumsum\_t MR\*\_den\_std[t]

KCOR\_raw[t] = CMR\_num[t]/CMR\_den[t]

KCOR[t] = KCOR\_raw[t]/KCOR\_raw[t0]

(compute CI via chosen method)

**Relationship to your GLM and DS-CMRR**

* **GLM (dose×week, offset=log(Alive), age factors)**: model-based weekly rates; when cumulatively integrated, it tends to produce the **same shape** as KCOR when you’ve controlled age and exposure well — which you observed.
* **DS-CMRR**: a model-light cross-check that skips slope-neutralization by standardizing age directly and cumulating hazards/rates; you saw it tracks KCOR’s shape too.

When **all three** (KCOR, GLM, DS-CMRR) align across enrollment dates and sensitivity choices, you have a very robust signal.

# Comparison with KCOR

here’s the quick, side-by-side of **this method** (the fixed-cohort, direct-standardized cumulative-hazard ratio from DS\_CMRR) vs **KCOR**.

**Key differences**

* **Design / cohorts**
  + **DS\_CMRR:** Fixed cohorts at enrollment t0t₀t0​. “Vaccinated” = dose≥1 by t0t₀t0​ (configurable); “unvaccinated” = dose0 by t0t₀t0​. No people move between arms afterward.
  + **KCOR:** Same fixed-cohort idea, but framed explicitly as a cumulative outcome ratio between pre-chosen arms (e.g., dose2 vs dose0, dose1 vs dose0).
* **How aging / secular drift is handled**
  + **DS\_CMRR:** Controls *composition* by **direct age standardization** to a fixed reference distribution (e.g., expected\_deaths or vax\_pt). **No slope neutralization.**
  + **KCOR:** Explicit **slope neutralization** (exponential or τ-quantile fit) to remove Gompertz-like upward drift and wave structure within each arm, then compare.
  + **Implication:** KCOR is less sensitive to long-run trend mis-matches; DS\_CMRR is less model-dependent but can show residual trend if age-standardization doesn’t fully soak it up.
* **What’s actually cumulated**
  + **DS\_CMRR:** Aggregates **Dead** and **PT** within each age×week, converts to **hazard** −ln⁡(1 ⁣− ⁣MR)-\ln(1\!-\!MR)−ln(1−MR), **then** cumsums hazards to a cumulative hazard and **then** standardizes (or standardizes first, depending on implementation). Output is a **cumulative hazard ratio** (anchored), labeled “KCOR” for easy overlay.
  + **KCOR:** Works with **detrended mortality rates** (or their hazards) and cumulates to a **cumulative rate**; takes the **ratio** and anchors.
  + **Practical:** When weekly rates are small, hazard vs rate differences are tiny; curves should look the same if everything is wired correctly.
* **Adjustment knobs**
  + **DS\_CMRR:** Only the **weighting scheme** (e.g., expected\_deaths vs vax\_pt), the **anchor**, and which **doses** are pooled as “vaccinated”.
  + **KCOR:** The **slope model** (exp vs τ-quantile), the **baseline window** and reference week, plus the same **anchor** and **dose pairing** choices.
* **Stat inference**
  + **DS\_CMRR:** Model-light; the simple CI I shipped is conservative. Prefer **block bootstrap** or age-wise exact/MOVER then combine by weights.
  + **KCOR:** Usually delta or bootstrap; similar guidance—bootstrap is easiest to trust.
* **Bias handling**
  + **Both:** Fixed cohorts → no “time-since-vax” (dynamic HVE) artifact.
  + **DS\_CMRR:** Addresses **static HVE** mainly via **age standardization** (pick a sensible reference).
  + **KCOR:** Addresses static HVE via age handling **plus** removes **secular slope** differences; a bit more robust to residual demographic drift that shows up as slow trends.
* **Failure modes**
  + **DS\_CMRR:** (i) wrong vaccinated aggregation (must sum Dead and PT first, then compute MR→hazard), (ii) changing weights mid-series, (iii) stitching multiple enrollments into one line, (iv) sparse/zero cells causing spikes.
  + **KCOR:** (i) bad slope window or mis-specified detrending, (ii) anchoring mishaps, (iii) sensitivity if detrending overfits waves.

**When to favor which**

* **Use KCOR** when you’re spanning long periods with obvious secular aging/wave drift—you want that **slope neutralization**.
* **Use DS\_CMRR** when you want **minimal modeling**, emphasize **age-mix control**, and keep cohorts fixed—great as an independent cross-check.
* If **KCOR ≈ DS\_CMRR** (and matches **GLM**), you’ve got strong triangulation.