Supplementary Material

Supplementary Methods

**Study protocol:**

Attached.

**PRISMA Checklist:**

Attached.
Supplementary Figures

Figure S1. NRM cumulative incidence rates are comparable to NRM point estimates. A Left: Paired comparison of reported cumulative incidence rates of NRM and the calculated NRM point estimates. Mann-Whitney test was used to explore statistical significance. Right: Difference between NRM measures in %. B Correlation between NRM point estimates and cohort follow up times, which was primarily driven by clinical trial cohorts (light grey = clinical trials, dark grey = real-world studies). Pearson correlation was calculated and linear regression with 95% confidence interval is shown (orange line). Abbreviations: CT = clinical trial, NRM = non-relapse mortality, RW = real-world.
Figure S2. Subgroup analysis of NRM point estimates stratified for disease entity. Forest plot illustrating NRM point estimates and 95% confidence intervals for CAR-T cohorts separated by disease entity. Abbreviation: IL = indolent lymphoma, LBCL = large B-cell lymphoma, MCL = mantle cell lymphoma, MM = multiple myeloma, NRM = non-relapse mortality.
### Figure S3. Subgroup analysis of NRM point estimates stratified for CAR-T products.

Forest plot illustrating NRM point estimates and 95% confidence intervals for CAR-T cohorts separated by administered CAR-T product. NRM = non-relapse mortality.
Figure S4. Funnel plots.
Reporting bias was analyzed by funnel plots for all studies (A), separate entities (B) and treatment settings (C). Asymmetry was tested using linear regression test of funnel plot asymmetry.
Figure S5. Follow-up times are similar between different entity and treatment cohorts. Comparison of cohort follow-up times stratified by A tumor entities, B entity-specific CAR-T products (blue = IL, yellow = LBCL, grey = MM, red = MCL), and C costimulatory domains. Kruskal-Wallis test was used for comparisons of > 2 groups and Mann-Whitney test for comparing two groups. Abbreviations: FU = follow-up, IL = indolent lymphoma, LBCL = large B-cell lymphoma, MCL = mantle cell lymphoma, MM = multiple myeloma, NRM = non-relapse mortality.
Figure S6. NRM point estimates and follow-up times of axi-cel, tisa-cel and liso-cel separately stratified for indolent lymphoma and large B-cell lymphoma cohorts. Comparison of cohort NRM point estimates and follow-up times stratified for A indolent lymphoma and B large B-cell lymphoma. Chi-square test was used for statistical testing of NRM-related deaths across products. Mann-Whitney test was used for comparing FU times between products. Abbreviations: FU = follow-up, MCL = mantle cell lymphoma, MM = multiple myeloma, NRM = non-relapse mortality.
Figure S7. Reported cumulative incidence NRM rates vary between tumor entities and CAR-T products.

**Left:** NRM cumulative incidence rates are higher in studies reporting on patients with MCL compared to LBCL. **Right:** NRM cumulative incidence rates are higher in the LBCL-specific CAR-T product (yellow) axi-cel compared to tisa-cel. The MCL-specific CAR-T product (red) brexu-cel has the highest NRM rates. Mann-Whitney test was used for statistical testing.

Abbreviations: LBCL = large B-cell lymphoma, MCL = mantle cell lymphoma, NRM = non-relapse mortality.
Figure S8. CD28z-harboring CAR products are associated with increased NRM point estimates.
Bubble plot demonstrating NRM point estimates in relation to follow-up times for 4-1BB containing CAR products (dark blue) and CD28z containing CAR products (dark green). Each bubble represents one cohort. Bubble size indicates the total number of patients per cohort. The aggregated NRM point estimate for all cohorts treated with CAR products with the same costimulatory domain is encircled in black.
Figure S9. Subgroup analysis of NRM point estimates stratified for CAR-T costimulatory domain.

Forest plot illustrating NRM point estimates and 95% confidence intervals for CAR-T cohorts separated by CAR-T products containing either CD28z or 41BB costimulatory domains. NRM = non-relapse mortality.
Figure S10. NRM point estimates are associated with treatment settings but confounded by follow-up times.

A Bubble plot demonstrating NRM point estimates in relation to follow-up times for cohorts treated in clinical trials (light blue) or in real-world setting (dark grey). Each bubble represents one cohort. Bubble size indicates the total number of patients per cohort. The aggregated NRM point estimate for all cohorts within each treatment setting is encircled in black.

B NRM point estimates and 95%CI between 41BB- and CD28z containing CAR-T products (left) as well as FU times are shown. Fisher’s exact test was used for statistical testing of NRM-related deaths across cohorts within each treatment setting. Mann-Whitney test was used for statistical testing of FU times. Abbreviations: CT = clinical trial, NRM = non-relapse mortality, RW = real-world.
Figure S11. Subgroup analysis of NRM point estimates stratified for treatment setting. Forest plot illustrating NRM point estimates and 95% confidence intervals for CAR-T cohorts separated by treatment setting into clinical trials (CT) and real-world studies (RW). NRM = non-relapse mortality.
Figure S12. Exclusion of COVID-19 related deaths does not change distribution differences of causes of death between treatment settings. Causes of death compared between CAR-T cohorts treated in either a clinical trial (CT) or real-world setting (RW) with exclusion of COVID-19 related deaths. Chi-square distribution test was used for statistical testing.
Figure S13. Causes of death are similar between different CAR-T products. Causes of death compared between A CAR-T products harboring 41BB or CD28z costimulatory domains, and B between different entity-specific CAR-T products. Chi-square distribution test was used for statistical testing.