KHI KIDNEY HEALTH INITIATIVE

| DATA STANDARD | **Mortality Rate** |
|---|---|
| DESCRIPTION | Mortality rate is defined by the count of deaths divided by the cumulative length of follow-up time (e.g., person-years) among a defined cohort of dialysis patients. The mortality rate is based on cumulative cohort patient-time of observation so that comparisons can be made between cohorts with varying lengths of follow-up among patients.<br><br>Maintenance dialysis is defined by hemodialysis or peritoneal dialysis performed routinely as kidney replacement therapy (KRT) for individuals with ESKD. |
| RATIONALE | Prevention of death or at least prolongation of survival is one of the primary goals of healthcare. Mortality is an important outcome in observational studies or clinical trials and may be a particularly important measure in the dialysis population due to the high mortality associated with ESKD requiring KRT. |
| DATA SOURCE(S) | Patient-level data |
| REQUIRED DATA ELEMENTS | • Number of deaths (Count): Defined by the number of patients who die during the time period under consideration (e.g., follow-up period or evaluation period). Although death is a well-defined outcome, there are circumstances in which incomplete information may be necessary to adjudicate specific cases. The follow-up period should be defined *a priori* by the investigators as a calendar start date and end date of the observation.<br>• Start date of individual's follow-up time: Date within the study observation period at which the patient joins the cohort and is "at risk." |

*The Kidney Health Initiative is a public-private partnership between the American Society of Nephrology, US Food and Drug Administration and over 100 companies and organizations in the kidney community. KHI leadership acknowledges and thanks the workgroup that developed these data standards to support research and development in kidney disease. To learn more about KHI or this project, please visit www.kidneyhealthinitiative.org.*

*Data Standard Published: October 2021*

| | |
|---|---|
| **REQUIRED DATA ELEMENTS (Cont'd)** | • End date of individual's follow-up time: Earliest of: (a) last date of observations (e.g., for loss of follow-up), (b) the end date of the study's observation period, (c) censoring event, or (d) date of death.<br>• Determine *a priori* the censoring events, depending on the goal of the analysis, to include or exclude events such as recovery of kidney function, or kidney transplantation |
| **DERIVED DATA ELEMENTS** | • Individual Follow-up Time: time under observation (e.g., days, months, years, etc.) for each individual included in the cohort.<br><br>Individual Patient Follow-up Time = (End Date – Start Date)<br><br>• Cumulative follow-up time: sum of the follow-up time for all individuals in the cohort, expressed as person-years (or other time units as applicable); of note, if the follow-up time for individuals in the cohort is available in days, consider dividing by 365.25 to account for leap years when converting into patient-years.<br><br>Cumulative Follow-up Time = Σ Individual Patient Follow-up Time |
| **CALCULATION METHOD** | $\text{Mortality Rate} = \frac{\text{Number of Deaths}}{\text{Cumulative Follow-up Time}}$ |
| **EXCLUSIONS** | • Current diagnosis of acute kidney injury (individuals who transition from AKI to ESKD should be included after transition to ESKD) |
| **ADDITIONAL DESIRABLE DATA ELEMENTS FOR COLLECTION** | The following additional data elements are not required to calculate the measure, but may be necessary for providing context, comparing populations and/or interpretation of findings:<br>• Demographics (age, sex, race, ethnicity)<br>• Dialysis modality ascertained as modality preceding death<br>• Time on dialysis<br>• Comorbid conditions, including diabetes mellitus<br>• Primary cause of ESKD<br>• Type of dialysis access |

| | |
|---|---|
| **ADDITIONAL DESIRABLE DATA ELEMENTS FOR COLLECTION (Cont'd)** | **Optional Mortality Sub-Measures Requiring Additional Data Collection**<br>Calculation of sub-measures will require collection of additional data elements to be determined *a priori*<br>• Cause-specific death rate: To calculate cause-specific death rates (e.g., sudden cardiac death, cancer, infection, etc.), the data elements will need to include the cause of death.<br>• Subgroup-specific death rate: To calculate subgroup-specific death rates, the data elements will need to include the patient-specific data delineating subgroups of interest which may include demographics, co-morbidities or indicators of socioeconomic status. |
| **NOTES** | • In general, mortality rates for observational studies are often adjusted to facilitate comparisons[1,2] Adjustment variables may include demographics, time since starting dialysis (e.g., vintage), dialysis modality, and the presence/absence of diabetes. Ideally the model would further include additional patient factors such as additional co-morbidities (e.g., heart failure, coronary artery disease, etc.). Adjusting mortality rates may not be necessary, as in the setting of randomized clinical trials (particularly when randomization effectively balances confounding factors between comparator arms).<br>• Adjustment can be done using direct or indirect standardization, when standardization is done with a criterion of interest (e.g., age).[3]<br>- Direct standardization: A population standard is used – for example, age-specific structure of the United States prevalent hemodialysis population in 2018, may be used as the standard.<br>- Indirect standardization: A common set of criterion-specific rates may be utilized, for example, age-specific mortality rates derived from the United States prevalent hemodialysis population in 2018, utilized to compare observed rates that need to be standardized. This method encompasses calculation of a standardized mortality ratio.<br>• Statistical modeling or regression may be undertaken to understand the importance of covariates (e.g., demographics), to account for confounding, and to determine significant differences between groups.[2] There are a variety of modeling techniques available. Statistical modeling is preferred when the study design requires adjusting for multiple confounders and may be useful in randomized clinical trials when randomization fails to balance all measured confounders.<br>• Investigators should consider how to calculate time for follow-up in patients with gaps in follow-up (e.g., "snowbirds" who leave one facility |

| | |
|---|---|
| **NOTES (Cont'd)** | during the winter months to have dialysis in a warmer climate), which is particularly relevant when attributing deaths to providers of care.<br>• Researchers should also determine if there is a maximum amount of absence that will trigger a censor date for loss to follow-up (e.g., 30, 60, 90 days).<br>• To improve completeness of data capture, investigators can consider linking to national databases/registries to determine death status for patients who are lost to follow-up when feasible. |
| **EXAMPLE MEASURE CALCULATION** | Period: 1/1/18 to 12/31/18<br>Population: All hemodialysis patients treated in location A and location B<br>Number of Deaths: location A = 10; location B = 15<br><br>Follow-up Time:<br>A = 80 patients with 50 patient-years of cumulative follow-up<br>B = 180 patients with 150 patient-years of cumulative follow-up<br><br>Mortality Rate A = 10/50 = 1 death per 5 patient-years = 0.20 deaths/patient-year<br><br>Mortality Rate B = 15/150 = 1 death per 10 patient years = 0.10 deaths/patient-year<br><br>Adjustment of these rates based on cohort characteristics may provide additional insights as to other factors that may have influenced the difference in mortality rates observed. |
| **REFERENCES** | 1. Thadhani R, Tonelli M. Cohort studies: marching forward. Clin J Am Soc Nephrol. 2006 Sep;1(5):1117-23.<br>2. Jager KJ, Zoccali C, Macleod A, Dekker FW. Confounding: what it is and how to deal with it. Kidney Int. 2008; Feb;73(3):256-60.<br>3. Tripepi G, Jager KJ, Dekker FW, Zoccali C. Stratification for confounding--part 2: direct and indirect standardization. Nephron Clin Pract. 2010;116(4):c322-5. |

Our thanks to the ESKD Data Standards Workgroup for their tireless and diligent work.

Lorien S. Dalrymple, MD, MPH (Co-Chair)
Fresenius Medical Care North America

Eric W. Young, MD (Co-Chair)
Arbor Research Collaborative for Health

Youssef Farag, MD, PhD, MPH
Goldfinch Bio

Michael J. Fischer, MD, MSPH
Department of Veterans Affairs

Emel Hamilton, MSN/INF, RN, CNN
Fresenius Medical Care North America

Wael Hussein, MRCPI, MBBS, MSc
Satellite Healthcare

Eduardo Lacson Jr., MD, MPH, FASN
Tufts University School of Medicine

Norma J. Ofsthun, PhD
Fresenius Medical Care North America

Francesca Tentori, MD, MS
Davita Healthcare, Inc.

Mahesh Krishnan, MD, MPH, FASN (KHI Board Liaison)
Davita Healthcare, Inc.