Report for the Standardized First Kidney Transplant Waitlist Ratio for Incident Dialysis Patients (SWR)

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Introduction

A measure focusing on the wait listing process is appropriate for improving access to kidney transplantation for several reasons. First, wait listing is a necessary step prior to potential receipt of a deceased donor kidney (receipt of a living donor kidney is also accounted for in the measure). Second, dialysis facilities exert substantial control over the process of waitlisting. This includes proper education of dialysis patients on the option for transplant, referral of appropriate patients to a transplant center for evaluation, assisting patients with completion of the transplant evaluation process, and optimizing the health and functional status of patients in order to increase their candidacy for transplant wait listing. These types of activities are included as part of the conditions for coverage for Medicare certification of ESRD dialysis facilities. Finally, wide regional variations in wait listing rates highlight substantial room for improvement for this process measure [1,2,3].

This measure additionally focuses specifically on the population of patients incident to dialysis, examining for waitlist or living donor transplant events occurring within a year of dialysis initiation. This will evaluate and encourage rapid attention from dialysis facilities to waitlisting of patients to ensure early access to transplantation, which has been demonstrated to be particularly beneficial [4,5]. This measure contrasts with the other waitlisting measure, the Percentage of Prevalent Patients Waitlisted (PPPW), which focuses on a prevalent population of dialysis patients and is primarily designed to additionally capture listing that occurs beyond the first year of dialysis initiation, as well as also maintenance of patients on the waitlist.

Methods

Overview

The Centers for Medicare & Medicaid Services (CMS) has contracted with the University of Michigan's Kidney Epidemiology and Cost Center (UM-KECC) to develop access to kidney transplantation measures for ESRD patients, including Standardized First Kidney Transplant Waitlist Ratio for Incident Dialysis Patients (SWR) for new patients and the Percentage of Prevalent Patients Waitlisted (PPPW) for the prevalent population.

The SWR measure tracks the number of incident patients at the dialysis facility under the age of 75 listed on the kidney or kidney-pancreas transplant waitlist or who received a living donor transplant within the first year of initiating dialysis. For each facility, we calculated the Standardized Waitlist Ratio (SWR) to compare the observed waitlisting rate in the facility to the waitlisting rate that was expected. The SWR uses expected waitlisting calculated from a Cox model (SAS Institute Inc., 2004; Andersen, 1993; Collett, 1994), adjusting for age and patient comorbidities at incidence.

Data Sources

CROWNWeb (including CMS Medical Evidence Form (Form CMS-2728)) is the primary data source used for placing patients at dialysis facilities, age and incident comorbidities adjustments and exclusion of patients => 75 year-old (see information provided under "denominator details"). Organ Procurement and Transplant Network (OPTN) is the data source for waitlist or living donor transplant events. The Nursing Home Minimum Dataset and the CMS Medical Evidence Form (Form CMS-2728) are used to identify SNF patients. A separate CMS file that contains final action claims submitted by Hospice providers was used to determine the hospice status.

Outcome Definition

The numerator for the SWR for a given facility is the observed number of patients on the Waitlist (i.e., waitlisting or receipt of a living-donor transplant) within the first year following initiation of dialysis. To be included in the numerator for a particular facility, the patient must meet one of the two criteria:

- The patient is on the kidney or kidney-pancreas transplant waitlist or
- The patient has received a living donor transplant

Denominator Definition

The denominator for the SWR for a given facility is the expected number of waitlisting or living donor transplant events at the facility according to each patient's treatment history for patients within the first year following initiation of dialysis, adjusted for age and incident comorbidities, among patients under 75 years of age who were not already waitlisted prior to dialysis. The risk profile is quantified through covariate effects estimated through Cox regression (Cox, 1972; SAS Institute Inc., 2004; Kalbfleisch and Prentice, 2002; Collett, 1994). Please see the estimates in SWR model at the Appendix.

Risk Adjustment

Choosing Adjustment Factors

Age adjustment was deemed necessary on clinical grounds. Although age alone is not a contraindication to transplantation, older patients are likely to have more comorbidities and be generally more frail thus making them potentially less suitable candidates for transplantation and therefore some may be appropriately excluded from waitlisting for transplantation. This may affect waitlisting rates for facilities with a substantially older age composition than the average.

In addition, incident comorbidities were selected for adjustment into the SWR model based on demonstration of a higher associated mortality (hazard ratio above 1.0) and statistical significance (p-value <0.01) in first year mortality model.

Adjustment in SWR

The denominator represents a facility's expected number of events (waitlistings or living-donor transplants), and is calculated based on a two-stage Cox model (Cox, 1972; SAS Institute Inc., 2004; Kalbfleisch and Prentice, 2002; Collett, 1994). The SWR is adjusted for incident comorbidities and age, using a linear spline with knots at 12, 18 and 64. Knot placements were determined empirically based on a preliminary model that categorized age. In addition, incident comorbidities were selected for adjustment into the SWR model based on demonstration of a higher associated mortality (hazard ratio above 1.0) and statistical significance (p-value <0.01) in first year mortality model.

Exclusions

Exclusions that are implicit in the denominator definition include:

- Patients who were 75 years of age or older at the initiation of dialysis;
- Preemptive patients: patients at the facility who had the first transplantation prior to the start of ESRD treatment; or were listed on the kidney or kidney-pancreas transplant waitlist prior to the start of dialysis;
- Patients who were admitted to a hospice at the time of initiation of dialysis;

- Patients who were admitted to a skilled nursing facility (SNF) at incidence or previously according to Form CMS-2728.

The CMS Medical Evidence Form and the CMS Long Term Care Minimum Data Set (MDS) were the data sources used for determining skilled nursing facility (SNF) patients. Patients who were identified in Questions 17u and 22 on the CMS Medical Evidence Form as institutionalized and SNF/Long Term Care Facility, respectively, or who had evidence of admission to a skilled nursing facility based on the MDS before their first service date and were not discharged prior to initiation of dialysis were identified as SNF patients. For hospice patients, a separate CMS file that contains final action claims submitted by Hospice providers was used to determine the hospice status.

Calculating SWR

The event was defined as waitlisting or living-donor transplantation. Time zero was defined as the first initiation of dialysis. Patients were followed until waitlisting, living donor transplantation, death, or one year anniversary since first dialysis (i.e., the earliest thereof). A two-stage Cox model was fitted to calculate the expected number of events. At the first stage, a Cox model stratified on facility was fitted in order to obtain an estimate of the age and comorbidities effects (unconfounded by facility) to be used as an offset. At the second stage, a national average baseline hazard was estimated. The national average baseline (from the second stage), age and comorbidities adjustments (from the first stage) were then used to compute the probability of an event for each patient, followed by the total expected number of events at each facility.

Let p denote the number of patient characteristics in the model and x_{ij} be the specific value of the j^{th} characteristic for the i^{th} patient-record. At the first stage, for patient-record i, we denote the measured characteristics or covariates as

$$\mathbf{X_i} = (x_{i1}, x_{i2}, \ldots, x_{ip}),$$

and use this to define the regression portion of a Cox model in which facilities define the strata. Note that for a categorical characteristic, the x_{ij} value is 1 if the patient falls into the category and 0 otherwise. The output of the first stage is a set of regression coefficients, $ß_1, ß_2, \ldots, ß_p$ and the corresponding predicted value for the i^{th} patient-record is given by

$$\mathbf{X_i ß} = ß_1 x_{i1} + ß_2 x_{i2} + \ldots + ß_p x_{ip}. \quad (1)$$

At the second stage, the relative risk estimates from the first stage were used as an offset, without stratification. . After the second stage, the linear prediction is

$$\mathbf{A_i} = ß_0 x_{i0} + \mathbf{X_i ß} = ß_0 x_{i0} + ß_1 x_{i1} + ß_2 x_{i2} + \ldots + ß_p x_{ip} \quad (2)$$

Suppose that t_i is the end of follow-up time for patient-record i, so that $S_0(t_i)$ is the baseline survival probability at time t_i. The survival probability for this patient-record i at time t_i is:

$$S_i(t_i) = [S_0(t_i)]^{\exp(A_i)}. \quad (3)$$

The expected number of waitlisting for this patient-record during follow-up time t_i arises from considerations in the Cox model and can be written as

$$-\ln(S_i(t_i)) = -e^{A_i} \ln [S_0(t_i)]. \quad (4)$$

The expected number of waitlisting at a given facility can now be computed simply by summing these expected values over the totality of patient-records in that facility. Specifically, the expected value is the sum over the N patient-records at the facility giving

$$E = \sum_{i=1}^{N} -\ln[S_i(t_i)] = -\sum_{i=1}^{N} e^{A_i} \ln[S_0(t_i)]. \quad (5)$$

Let O be the total number of waitlisting observed at the facility during the total four year follow up period. As stated above, the SWR is the ratio of the total number of observed waitlisting to the expected number

$$SWR = O/E. \quad (6)$$

Missing Data

Covariates of SWR includes incident patient's age at the date of first ESRD service and incident comorbidities on CMS Medical Evidence Form (CMS 2728 form). Since age was calculated using the date of first service from CMS Medical Evidence Form and date of birth, and date of birth was required in our Standard Analysis Data Files, no missing value in age was identified in the patient population. For incident comorbidities, data was obtained from item 17 (checkbox question) on CMS Medical Evidence Form. All co-morbid conditions that apply should have been checked by the attending physician. Therefore, there is no missing data in the adjustments for SWR.

Testing Results

Table 1. Coefficients and p-value in model (note:a_+=max(a,0))

Covariate	Coefficient	p-value	Hazard Ratio
Age	0.08	<.001	1.09
$(age-12)_+$	-0.14	<.001	0.87
$(age-18)_+$	0.03	0.046	1.03
$(age-64)_+$	-0.10	<.001	0.91
Heart disease (atherosclerotic heart disease or congestive heart failure or other cardiac disease)	-0.50	<.001	0.61
Inability to ambulate	-0.89	<.001	0.41
Chronic obstructive pulmonary disease	-0.93	<.001	0.39
Inability to transfer	-0.45	0.017	0.64
Malignant neoplasm, Cancer	-0.58	<.001	0.56
Peripheral vascular disease	-0.39	<.001	0.68
Cerebrovascular disease, CVA, TIA	-0.38	<.001	0.68
Alcohol dependence	-0.29	<.001	0.75

Covariate	Coefficient	p-value	Hazard Ratio
Drug dependence	-1.69	<.001	0.19
Amputation	-0.58	<.001	0.56
Needs assistance with daily activities	-0.62	<.001	0.54

The c-index is 0.67, which suggests relatively good discrimination ability (e.g., differentiating high from low risk patients) of the risk model. In particular, among all pairs of patients where the ordering of time-to-event is known, the model correctly predicted the ordering 67% of the time.

Reliability Testing

The reliability of the Standardized Waitlist Ratio (SWR) was assessed using data among incident dialysis patients during 2013-2015. If the measure were a simple average across individuals in the facility, the usual approach for determining measure reliability would be a one-way analysis of variance (ANOVA), in which the between and within facility variation in the measure is determined. The inter-unit reliability (IUR) measures the proportion of the total variation of a measure that is attributable to the between-facility variation.

The SWR, however, is not a simple average and we instead estimate the IUR using a bootstrap approach, which uses a resampling scheme to estimate the within facility variation that cannot be directly estimated by ANOVA. A small IUR (near 0) reveals that most of the variation of the measures between facilities is driven by random noise, indicating the measure would not be a good characterization of the differences among facilities, whereas a large IUR (near 1) indicates that most of the variation between facilities is due to the real difference between facilities.

Here we describe our approach to calculating IUR. Let $T_1,\ldots,T_N$ be the SWR for these facilities. Within each facility, select at random and with replacement B (say 100) bootstrap samples. That is, if the ith facility has n_i subjects, randomly draw with replacement n_i subjects from those in the same facility, find their corresponding SWR_i and repeat the process B times. Thus, for the ith facility, we have bootstrapped SWRs of $T^*_{i1},\ldots, T^*_{i200}$. Let S^*_i be the sample variance of this bootstrap sample. From this it can be seen that

$$s^2_{t,w} = \frac{\sum_{i=1}^{N}[(n_i - 1)S_i^{*2}]}{\sum_{i=1}^{N}(n_i - 1)}$$

is a bootstrap estimate of the within-facility variance in the SWR, namely, $\sigma^2_{t,w}$. Calling on formulas from the one way analysis of variance, an estimate of the overall variance of T_i is

$$s^2_t = \frac{1}{n'(N-1)}\sum_{i=1}^{N} n_i(T_i - \bar{T})^2$$

where

$$\bar{T} = \sum n_i T_i / \sum n_i$$

is the weighted mean of the observed SWR and

$$n' = \frac{1}{N-1}\left(\sum n_i - \sum n_i^2 \Big/ \sum n_i\right)$$

is approximately the average facility size (number of patients per facility). Note that s_t^2 is the total variation of SWR and is an estimate of $\sigma_b^2 + \sigma_{t,w}^2$, where σ_b^2 is the between-facility variance, the true signal reflecting the differences across facilities. Thus, the estimated IUR, which is defined by

$$IUR = \frac{\sigma_b^2}{\sigma_b^2 + \sigma_{t,w}^2},$$

can be estimated with $(s_t^2 - s_{t,w}^2)/s_t^2$.

The reliability of SWR calculation only included facilities with at least 11 patients and at least 2 expected waitlisting events during the reporting period. The IUR value is 0.60 for 4,276 facilities. Facilities with <11 eligible patients or <2 expected events were excluded from this calculation.

Validity Testing

Systematic Assessment of Face Validity

The primary purpose of this measure is to increase access to kidney transplantation for patients on chronic dialysis. Because waitlisting is a crucial, necessary step prior to potential receipt of a deceased donor kidney, a measure which assesses waitlisting of patients by dialysis facilities has face validity as a measure of access to transplantation. Furthermore, a Technical Expert Panel (TEP), of 11 members consisting of transplant nephrologists, social workers, administrators and nurses with transplant process, policy and research expertise was convened. The TEP was charged with development of potential dialysis facility measures directed at improving access to transplantation. Although not unanimous, there was majority (by formal vote of 8-3) support for a dialysis facility measure related to waitlisting, on the basis that dialysis facilities importantly contribute to waitlisting of patients by helping them to navigate the process from referral through completion of the transplant evaluation, ensuring that all necessary testing as part of the evaluation process is done in a timely manner, and contributing to their overall health and therefore suitability for transplantation.

Empirical Validity Testing

We assessed empirical validity of the measure by calculating Spearman correlations. Spearman correlation was selected because the data are rank-ordered (non-parametric data). Correlations were calculated to assess the association of the SWR with other outcome quality measures. First, to demonstrate the relationship between SWR and the anticipated outcome of increasing transplantation rates for patients at the facility, we examined the correlation of facility ranking with respect to the measure and the Standardized Transplant Ratio (STR, 2013-2016). The STR is the ratio of the actual number of first transplants to the expected number of first transplants for the facility in 2013-2016, given the age composition of the facility's patients. There are 4,092 facilities available for comparison. We expected to find that the SWR and STR would be positively correlated.

We further examined the relationship between SWR and First Year Standardized Mortality Ratio (SMR) in 2013-2015, a measure reflecting the quality of overall health care delivered to incident dialysis patients by facilities. We anticipated that facilities with higher SWR would also have lower rates of adverse health outcomes, reflecting that maintenance of good health status by dialysis facilities increases the likelihood of waitlisting. Therefore we expected to find that SWR and SMR would be negatively correlated.

The Spearman correlation coefficient between facility SWR and STR was highly significant: rho=0.52, p<.001. SWR was negatively correlated with First Year Standardized Mortality Ratio in 2013-2015 (r=-0.19, p<.001). The negative correlation between SWR and First Year Standardized Mortality Ratio indicates that facility with higher waitlisting rate have lower mortality rate among incident patients.

References

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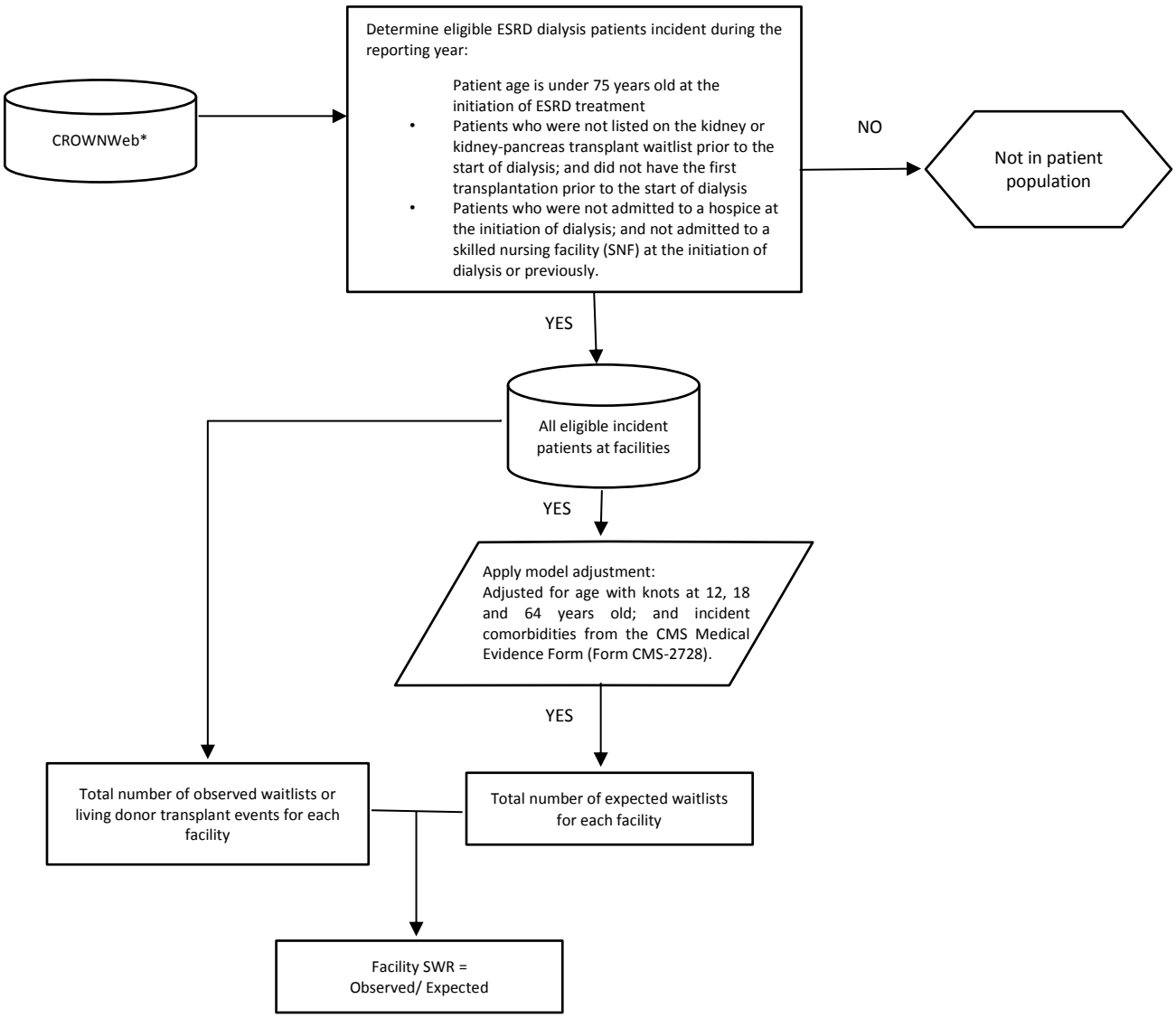
Appendix

Measure Calculation Flow Chart



*CROWNWeb (including CMS Medical Evidence Form (Form CMS-2728)) is the primary data source used for placing patients at dialysis facilities, age and incident comorbidities adjustments and exclusion of patients ≥75 year-old. Organ Procurement and Transplant Network (OPTN) is the data source for waitlist or living donor transplant events. The Nursing Home Minimum Dataset and the CMS Medical Evidence Form (Form CMS-2728) are used to identify SNF patients. A separate CMS file that contains final action claims submitted by Hospice providers was used to determine the hospice status.

Data Dictionary

Variable	Primary Data Source
Facility CCN #	CMS data sources[*1]
Reporting year	CROWNWeb
Waitlist status	Organ Procurement and Transplant Network (OPTN)
Date of Birth	CMS data sources[*1]
Date of First ESRD	Medical Evidence Form (CMS-2728)
Heart disease	Medical Evidence Form (CMS-2728)
Inability to ambulate	Medical Evidence Form (CMS-2728)
Chronic obstructive pulmonary disease	Medical Evidence Form (CMS-2728)
Inability to transfer	Medical Evidence Form (CMS-2728)
Malignant neoplasm, Cancer	Medical Evidence Form (CMS-2728)
Peripheral vascular disease	Medical Evidence Form (CMS-2728)
Cerebrovascular disease, CVA, TIA	Medical Evidence Form (CMS-2728)
Alcohol dependence	Medical Evidence Form (CMS-2728)
Drug dependence	Medical Evidence Form (CMS-2728)
Amputation	Medical Evidence Form (CMS-2728)
Needs assistance with daily activities	Medical Evidence Form (CMS-2728)
Nursing home status[*1*2]	Medical Evidence Form (Form CMS-2728) Question 17u and 22
Nursing home status on the first service date [*1*2]	CMS Long Term Care Minimum Data Set (MDS)
Hospice status on the first service date [*1*2]	CMS Hospice file

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Unique patients are identified by using a combination of SSN, first name, surname, gender, Medicare claim number and birth date. A matching process is performed to ensure that minor typos and misspellings do not cause a patient record to fall out of their history. The matching process is able to successfully match 99.5% of patients. The remaining patients have incomplete or incorrect data that does not allow them to be matched.

*2. Exclusion factors