

CBE 2979: Standardized Transfusion Ratio for Dialysis Facilities

2.2 Evidence of Measure Importance

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Summarize evidence of the measure's importance from the literature, expert panel, or internal data analyses, linking the structure/process/intermediate outcome to the desired health outcome. Please provide references for supporting evidence. For instrument submissions, this evidence should include aspects of importance that apply across associated IDMs, such as evidence associated with the surveyed population or accountable entity, etc.

Note - This Evidence Summary was modified from the 2019-2020 Evidence Form submitted to the CBE. We performed an updated PUBMED Literature search using multiple search strategies for the years 2017-present. The search results were initially reviewed by one investigator to remove duplicates and off-topic citations. The resulting set of citations was independently reviewed by three investigators with clinical dialysis training or ESRD quality measure development expertise and experience. Of the approximately 1500 references reviewed, 23 were identified with consensus agreement. We have included selected recent references and updated the Evidence Summary with these additional citations in the summary and reference list below.

The Medicare ESRD Program requires Medicare certified dialysis facilities to manage the anemia of CKD as one of their responsibilities under the Conditions for Coverage [1]. In addition, the Medicare ESRD Program has included payment for ESAs in dialysis facility reimbursement since 1989. It is notable that initial inclusion of ESAs in dialysis program payment was associated with a dramatic reduction in the use of blood transfusions in the US chronic dialysis population [2] [3]. Changes to the Medicare Chronic Dialysis Prospective Payment System (Expanded PPS) in 2011, resulted in major changes in anemia management in US dialysis facilities and an initial increase in transfusion events in this population [19] [21] [22] [27] [28]. At approximately the same time, the US FDA revised their ESA package insert to emphasize the risks associated with ESA use and to de-emphasize achieved hemoglobin targets while strengthening their emphasis on transfusion-avoidance as the principal goal of ESA use. Recently, reliance on achieved hemoglobin concentration as an indicator of successful anemia management in this population has been de-emphasized. Use of other clinically meaningful outcomes, such as transfusion avoidance, have been recommended as alternate measures of anemia management [4-7] [28-30].

Best dialysis provider practice should include effective anemia management algorithms that focus on 1) prevention and treatment of iron deficiency, inflammation, and other causes of ESA resistance, 2) use of the lowest dose of ESAs that achieves an appropriate, individualized target hemoglobin that is consistent with FDA guidelines and current best practices, and 3) education of patients, their families, and medical providers to avoid unnecessary blood transfusion, to protect a valuable limited healthcare resource (banked blood products), and to minimize the risk of allosensitization as a result of unnecessary blood transfusion, eliminating or reducing one preventable barrier to successful kidney transplantation.

The decision to transfuse blood is intended to improve or correct the pathophysiologic consequences of severe anemia, defined by achieved hemoglobin or hematocrit, in a specific clinical context for each patient situation [9]. Consensus guidelines in the U.S. and other consensus guidelines defining appropriate use of blood transfusions are based, in large part, on the severity of anemia [10-12]. Given

the role of hemoglobin as a clinical outcome that defines anemia, as well as, forms a basis for consensus recommendations regarding use of blood transfusion, it is not surprising that the presence of decreased hemoglobin concentration is a strong predictor of subsequent risk for blood transfusion in multiple settings, including chronic dialysis [13-22] [31-33]. For example, researchers found a nearly four-fold higher risk-adjusted transfusion rate in dialysis patients with achieved hemoglobin <10 gm/dl compared to those with >10 gm/dl hemoglobin [20]. In addition to achieved hemoglobin, other factors related to dialysis facility practices, including the facility's response to their patients' achieved hemoglobin, may influence blood transfusion risk in the chronic dialysis population [23] [26]. In an observational study [23] comparing different facility level titration practices, among patients with hemoglobin <10 and those with hemoglobin >11, they found increased transfusion risk in patients with larger ESA dose reductions and smaller dose escalations, and reduced transfusion risk in patients with larger ESA dose increases and smaller dose reductions [26]. The authors reported no clinically meaningful differences in all-cause or cause-specific hospitalization events across groups.

The Food and Drug Administration position defining the primary indication of ESA use in the CKD population is for transfusion avoidance, reflecting the assessment of the relative risks and benefits of ESA use versus blood transfusion. Several historical studies, and one recent research study [21] document the specific risks of allosensitization after blood transfusion and the potential for transfusion-associated allosensitization to interfere with timely kidney transplantation [24]. A recent analysis demonstrated increased odds ratios for allosensitization associated with transfusion, particularly for men and parous women. That study also demonstrated a 28% reduction in likelihood of transplantation in transfused individuals, based on a multivariate risk-adjusted statistical model [25].

New Anemia Treatment- ESA Biosimilars and HIF protease inhibitors

In the interval since our last submission of STrR for consensus-body review, additional erythropoiesis stimulating pharmacologic agents have been approved for the treatment of ESRD-associated anemia, including ESA-biosimilars and HIF protease inhibitors. Our updated literature search reflects on the clinical effects on anemia management in the chronic dialysis population [34-38]. Several agents have been shown to be non-inferior to traditional ESAs in use prior to 2019. Importantly, there have been no consistent identification of increased transfusion-avoidance in the chronic dialysis population. Based on these reports, we do not believe the newer pharmacologic options fundamentally change the importance of the current transfusion avoidance objective underpinning the current STrR quality measure.

Changes to Predictive Model Risk Mitigation Strategy

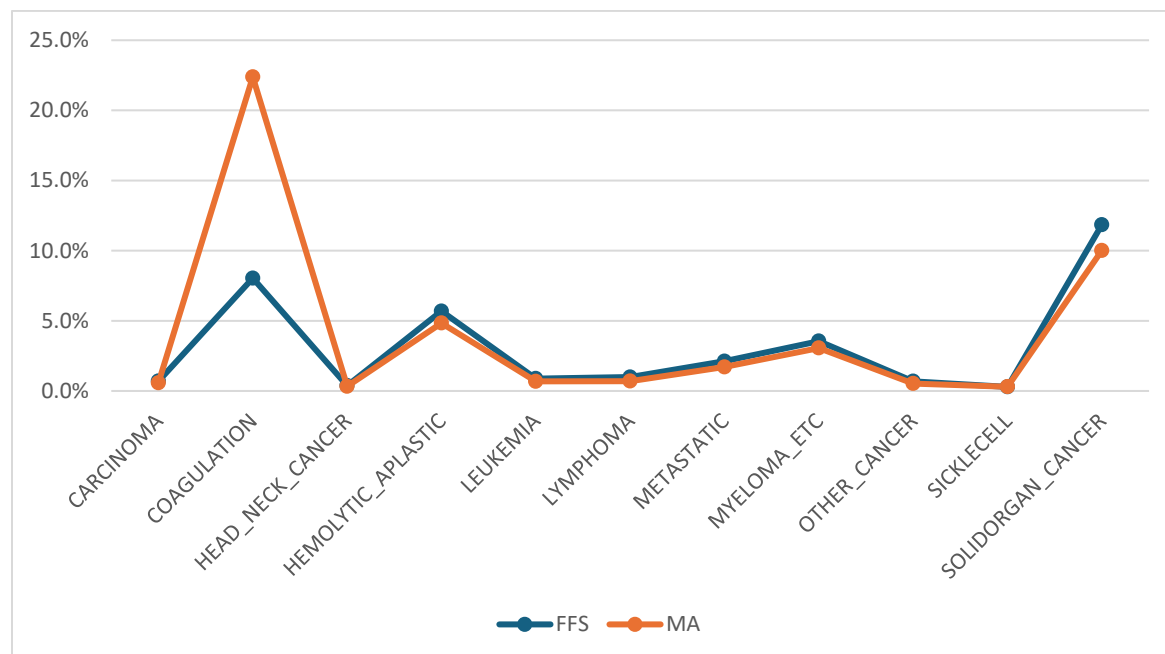
Based on concerns by the initial Technical Expert Panel (TEP) that recommended development of STrR, and US FDA concerns about unintended negative consequences of ESA use in patients with active malignancy, reflected in their package insert for ESAs, the current endorsed version of STrR excludes individual patients with history of either hematologic or solid organ malignancies (and assorted coagulopathies and hereditary anemias) from the measure. During our current comprehensive review, we evaluated whether this broad claims-based exclusion strategy was supported by clinical practice in the U.S. Medicare chronic dialysis population. Specifically, we were curious about whether clinical practice included residual prohibitions against use of ESAs in chronic dialysis patients with history of malignancy [39]. We compared ESA use, achieved hemoglobin, and transfusion event rates between those populations excluded and included in the STrR quality measure in 2023. Table 1 includes results of

this analysis, demonstrating nearly identical ESA use, and achieved hemoglobin levels in the two groups. Of note, there was an increased transfusion event rate in the “excluded” population, despite similar ESA use and achieved hemoglobin patterns. In addition, Figure 1 demonstrates striking increased reporting of one specific ICD-10 code in Medicare Advantage patients. The presence of this one code has a much weaker association with the dependent variable in fully risk-adjusted models in Medicare Advantage patients compared with Medicare Fee for Service (FFS) individuals. In addition, prior literature suggests a possible financial incentive for increased reporting of this specific coagulation code in MA beneficiaries [27].

Table 1. Anemia Treatment and Outcomes in Patients with and without Excluding Comorbidities

	Patient Months	
	Excluded (33%)	No excluding comorbidity (67%)
%transfusion	6.4%	2.5%
%ESA	67.1%	68.7%
HGB	10.6	10.8

Figure 1. Percent of Patient-Months with a Potential Comorbidity Exclusion by Comorbidity Category



These observations led us to the conclusion that our risk exclusion strategy, based on the assumption that clinical providers would follow FDA recommendations regarding avoidance of ESA use in patients with malignancies was not supported by evidence. Since the treatment options available for patients with these previously-excluding conditions are apparently actively in use in the population, we have revised our risk mitigation strategy to one that risk adjusts for the presence of the coagulation,

hereditary anemia, and malignancy categories, rather than excluding these individuals. We have adjusted for Medicare Advantage insurance as a protection against potential bias from any reporting biases that might be present related to Medicare insurance type.

In addition, during public comment periods included as part of prior consensus review and, more recently received during public comment periods related to Medicare’s ESRD QIP inclusion of the STrR quality measure, some in the dialysis community have called for risk adjustment for history of gastrointestinal (GI) bleeding, given the potential limited dialysis facility control over GI bleeding and a small amount of recent evidence suggesting that dialysis facility anticoagulation use may not influence the risk of hospitalization for GI bleeding [38]. Inclusion of ICD10 diagnoses codes that reflect GI bleeding related to a broad group of gastrointestinal and systemic conditions (Table 2) is associated with increased transfusion risk in a fully adjusted predictive model. Based on these analyses and the previously mentioned dialysis community feedback, we have included risk adjustment for GI bleeding in the STrR submitted for consensus review.

Table 2. ICD10 codes for Gastrointestinal and Genitourinary Bleeding

Comorbidity Category	code	Description
GI/GU bleeding	K2211	Ulcer of esophagus with bleeding
GI/GU bleeding	K226	Gastro-esophageal laceration-hemorrhage syndrome
GI/GU bleeding	K2901	Acute gastritis with bleeding
GI/GU bleeding	K2931	Chronic superficial gastritis with bleeding
GI/GU bleeding	K2941	Chronic atrophic gastritis with bleeding
GI/GU bleeding	K2951	Unspecified chronic gastritis with bleeding
GI/GU bleeding	K2961	Other gastritis with bleeding
GI/GU bleeding	K2971	Gastritis, unspecified, with bleeding
GI/GU bleeding	K2981	Duodenitis with bleeding
GI/GU bleeding	K2991	Gastroduodenitis, unspecified, with bleeding
GI/GU bleeding	K31811	Angiodysplasia of stomach and duodenum with bleeding
GI/GU bleeding	K3182	Dieulafoy lesion (hemorrhagic) of stomach and duodenum
GI/GU bleeding	K50011	Crohn's disease of small intestine with rectal bleeding
GI/GU bleeding	K50111	Crohn's disease of large intestine with rectal bleeding
GI/GU bleeding	K50811	Crohn's disease of both small and large intestine with rectal bleeding
GI/GU bleeding	K50911	Crohn's disease, unspecified, with rectal bleeding

Comorbidity Category	code	Description
GI/GU bleeding	K51011	Ulcerative (chronic) pancolitis with rectal bleeding
GI/GU bleeding	K51211	Ulcerative (chronic) proctitis with rectal bleeding
GI/GU bleeding	K51311	Ulcerative (chronic) rectosigmoiditis with rectal bleeding
GI/GU bleeding	K51411	Inflammatory polyps of colon with rectal bleeding
GI/GU bleeding	K51511	Left sided colitis with rectal bleeding
GI/GU bleeding	K51811	Other ulcerative colitis with rectal bleeding
GI/GU bleeding	K51911	Ulcerative colitis, unspecified with rectal bleeding
GI/GU bleeding	K5701	Diverticulitis of small intestine with perforation and abscess with bleeding
GI/GU bleeding	K5711	Diverticulosis of small intestine without perforation or abscess with bleeding
GI/GU bleeding	K5713	Diverticulitis of small intestine without perforation or abscess with bleeding
GI/GU bleeding	K5721	Diverticulitis of large intestine with perforation and abscess with bleeding
GI/GU bleeding	K5731	Diverticulosis of large intestine without perforation or abscess with bleeding
GI/GU bleeding	K5733	Diverticulitis of large intestine without perforation or abscess with bleeding
GI/GU bleeding	K5741	Diverticulitis of both small and large intestine with perforation and abscess with bleeding
GI/GU bleeding	K5751	Diverticulosis of both small and large intestine without perforation or abscess with bleeding
GI/GU bleeding	K5753	Diverticulitis of both small and large intestine without perforation or abscess with bleeding
GI/GU bleeding	K5781	Diverticulitis of intestine, part unspecified, with perforation and abscess with bleeding
GI/GU bleeding	K5791	Diverticulosis of intestine, part unspecified, without perforation or abscess with bleeding

Comorbidity Category	code	Description
GI/GU bleeding	K5793	Diverticulitis of intestine, part unspecified, without perforation or abscess with bleeding
GI/GU bleeding	I8501	Esophageal varices with bleeding
GI/GU bleeding	I8511	Secondary esophageal varices with bleeding
GI/GU bleeding	K250	Acute gastric ulcer with hemorrhage
GI/GU bleeding	K252	Acute gastric ulcer with both hemorrhage and perforation
GI/GU bleeding	K254	Chronic or unspecified gastric ulcer with hemorrhage
GI/GU bleeding	K256	Chronic or unspecified gastric ulcer with both hemorrhage and perforation
GI/GU bleeding	K260	Acute duodenal ulcer with hemorrhage
GI/GU bleeding	K262	Acute duodenal ulcer with both hemorrhage and perforation
GI/GU bleeding	K264	Chronic or unspecified duodenal ulcer with hemorrhage
GI/GU bleeding	K266	Chronic or unspecified duodenal ulcer with both hemorrhage and perforation
GI/GU bleeding	K270	Acute peptic ulcer, site unspecified, with hemorrhage
GI/GU bleeding	K272	Acute peptic ulcer, site unspecified, with both hemorrhage and perforation
GI/GU bleeding	K274	Chronic or unspecified peptic ulcer, site unspecified, with hemorrhage
GI/GU bleeding	K276	Chronic or unspecified peptic ulcer, site unspecified, with both hemorrhage and perforation
GI/GU bleeding	K280	Acute gastrojejunal ulcer with hemorrhage
GI/GU bleeding	K282	Acute gastrojejunal ulcer with both hemorrhage and perforation
GI/GU bleeding	K284	Chronic or unspecified gastrojejunal ulcer with hemorrhage
GI/GU bleeding	K286	Chronic or unspecified gastrojejunal ulcer with both hemorrhage and perforation
GI/GU bleeding	K625	Hemorrhage of anus and rectum

Comorbidity Category	code	Description
GI/GU bleeding	K920	Hematemesis
GI/GU bleeding	K921	Melena
GI/GU bleeding	K922	Gastrointestinal hemorrhage, unspecified
GI/GU bleeding	N924	Excessive bleeding in the premenopausal period
GI/GU bleeding	N950	Postmenopausal bleeding
GI/GU bleeding	N938	Other specified abnormal uterine and vaginal bleeding
GI/GU bleeding	N939	Abnormal uterine and vaginal bleeding, unspecified

Changes to Predictive Model re. Risk Mitigation

Finally, our current endorsed version of STrR has excluded patients enrolled in Medicare Advantage plans since it was initially developed in 2015. The rationale for exclusion of MA patients was twofold and based on the lack of MA encounter data availability for outpatient encounters. Previously, we had shown failure to account for approximately 15-20% of transfusion events in the MA population due to inability to use Medicare Advantage encounter data. In addition, a simple majority of diagnoses for malignancy, used to exclude patients from the endorsed version of STrR, arise from outpatient claim sources for Medicare FFS patients. Historically, lack of availability of outpatient Medicare Advantage encounter data created insurmountable biases when comparing patients with MA insurance to Medicare FFS patients. Within the last 2-3 years, MA encounter data have become available for use and we have extensively tested the outpatient MA encounter data against outpatient Medicare FFS sources for both frequency of transfusion events, as well as for frequency of specific categories of ICD10-based diagnoses (see STTr_Dic_Code_List_Final Draft_07-29-25.xlsx). Based on 2023 data, the frequency of outpatient transfusion reporting is very similar comparing MA and FFS patients. In addition, only relatively small differences in frequency of reporting for most comorbidity categories are present, with the exception of one acquired coagulation code, described above. Inclusion of MA patients in the new risk-adjusted predictive model used to define the STTrR denominator (expected transfusion events) results in only small differences in dialysis facility STTrR as evidenced by the MA risk covariate included in the model (MA covariate- from fully adjusted model; full model available in Section 5.4.4). Table 3 demonstrates dialysis facility flagging results with and without MA patient inclusion. (See section 5.4 for more results)

Table 3a. Flagging table of current endorsed STrR with or without MA patient time, 2023 (N=5,084)

	Current endorsed STrR including MA patient time		
Current endorsed STrR excluding MA patient time	Better than Expected	As Expected	Worse than Expected
Better than Expected	0 (0%)	4 (0.1%)	0 (0.0%)
As Expected	10 (0.2%)	4,580 (90.1%)	140 (2.8%)
Worse than Expected	0 (0.0%)	174 (3.4%)	176 (3.5%)

*The facilities with patient years at risk ≥ 10 applied in the both methods are reported in the table.

4,756 (93.6%) facilities do not change flagging

184 (3.6%) facilities get better while including MA patient time.

144 (2.9%) facilities get worse while including MA patient time.

Due to including patient time with MA, 6,927 facilities with patient years at risk ≥ 10 report STrR, compared to 5,084 facilities reporting STrR in current endorsed method (excluding patient time with MA). Please note that both methods exclude patient time with prior year prevalent comorbidities.

Table 3b. Flagging table of proposed vs. current endorsed STrR, 2023 (N=5,084)

	Proposed STrR		
Current endorsed STrR	Better than Expected	As Expected	Worse than Expected
Better than Expected	0 (0%)	4 (0.1%)	0 (0.0%)
As Expected	30 (0.6%)	4,489 (88.3%)	211 (4.1%)
Worse than Expected	0 (0.0%)	232 (4.6%)	118 (2.3%)

*The facilities with patient years at risk ≥ 10 applied in the both methods are reported in the table.

4,607 (90.6%) facilities do not change flagging

262 (5.2%) facilities get better while using the proposed STrR (including MA patient time and not excluding patient time with prior year prevalent comorbidities)

325 (4.2%) facilities get worse while using the proposed STrR

Due to including patient time with MA and not excluding patient time with prior year prevalent comorbidities, 7,268 facilities with patient years at risk ≥ 10 report STrR (proposed), compared to 5,084 facilities reporting STrR in current method (excluding patient time with MA or prior year prevalent comorbidities).

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