Emergency Department Utilization Among Maintenance Hemodialysis Patients: A Systematic Review

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Rationale & Objective: To evaluate predictors of emergency department (ED) utilization by adult patients receiving hemodialysis (HD) and interventions to reduce ED utilization by HD patients.

Study Design: We searched Ovid MEDLINE, Ovid Embase, and the Cochrane Library for randomized controlled trials and observational studies published until April 2020.

Setting & Participants: We included studies that investigated predictors of ED utilization and/or interventions to reduce ED utilization in HD patients. We extracted data regarding the study design and study population and results regarding ED utilization from 38 studies using Excel software.

Analytical Approach: We performed a narrative synthesis to group articles that investigated similar themes.

Results: 1,060 titles and abstracts were screened, of which 98 were selected for full-text review. In total, 38 studies met the inclusion criteria and underwent data extraction. Quality was high according to the Downs and Black tool, with 11 studies rated as good, 22 as fair, and 5 as poor.

he United States end-stage kidney disease (ESKD) population has increased by 91% since 2000, totaling 746,557 patients in 2017.¹ Current Medicare expenditures for these patients has reached \$35.9 billion a year, accounting for 7.2% of all Medicare spending.¹ This evolving burden of kidney failure is largely due to the combination of an aging population, the increasing prevalence of obesity and diabetes mellitus, and the improving survival of patients with ESKD.¹ Increased survival likely reflects improvements in ESKD care during the past 20 years, which are associated with a concomitant decline in hospitalization rates.¹⁻³ Despite this, patients with ESKD continue to have the highest risk for hospitalization among patients with other chronic medical conditions like heart failure, pulmonary disease, and cancer and are at higher risk of adverse safety events.^{4,5}

Although hospitalization rates for patients with ESKD are declining, emergency department (ED) visits are increasing.^{1–3} This reduction in admissions may be in part due to the increase of observational stays in lieu of admission, but hemodialysis (HD) patients are still presenting to the ED 8.5 times more frequently than the general population.^{2,6,7} In-center HD patients use the ED more than those on home HD or peritoneal dialysis, emphasizing the particular challenges that in-center HD

34 studies described predictors of ED utilization, whereas 4 studies investigated interventions in which ED utilization was studied. Our narrative synthesis produced 8 concept subgroups in the core concepts of access to care, comorbid condition burden, and new health care models. Poor access to care and a high comorbid condition burden are associated with increased ED use. No ED-based interventions designed to reduce ED utilization were identified, but recent changes in health care systems, like the formation of End-Stage Renal Disease Seamless Care Organizations and greater involvement of palliative care services, are associated with improved outcomes.

Limitations: Clinical heterogeneity and variability in the included studies precluded a meta-analysis.

Conclusions: HD patients' high ED use is multifactorial. Further research is required to understand and predict ED utilization in this vulnerable population, which will facilitate the development of interventions to reduce avoidable ED use.

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patients face compared with those of the overall ESKD population.⁸ However, many ED visits by patients with ESKD are for complaints seemingly unrelated to kidney disease, suggesting that comorbid conditions and other health care needs contribute to their high ED utilization.^{3,9,10}

To reduce health care utilization by patients with ESKD, the Centers for Medicare and Medicaid Services launched the Comprehensive End-Stage Renal Disease (ESRD) Care Model in 2015, under which nephrologists, dialysis facilities, and other providers formed ESRD Seamless Care Organizations.^{11,12} Similarly, the ESRD network programs, which are supported by the Centers for Medicare and Medicaid Services, have recently designated the reduction of ED utilization as a priority for quality improvement.¹³ Because HD patients appear to be the greatest ED utilizers among patients with ESKD and are the largest subset of the ESKD patient population, understanding ED utilization by HD patients is a critical step toward reaching these initiatives' goals.^{1,8}

This study is a systematic review designed to identify predictors and interventions for ED utilization in HD patients. While a narrative review was performed in the early 2000s, our systematic review is of much greater scope and includes many papers from the past 15 years.¹⁰ We also

Complete author and article information provided before references.

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PLAIN-LANGUAGE SUMMARY

Patients with kidney failure, especially those on hemodialysis, visit the emergency department much more frequently than the general population. This contributes to hemodialysis patients' increasingly high health care utilization over the last 20 years. In this article, we propose a conceptual framework that summarizes the existing literature on emergency department use by the hemodialysis patient population and associated interventions. Many variables have been shown to predict emergency department use by hemodialysis patients, including access to care, their comorbid condition burden, and the evolving health care models. However, few interventions have demonstrated an impact on emergency department use by this vulnerable population.

produced a conceptual framework through narrative synthesis to codify how these predictors and interventions affect ED use.¹⁴

METHODS

This systematic review was constructed using Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines.¹⁵ A protocol titled "The Need for Accessible Emergency Care for Patients with End-Stage Renal Disease" was registered in PROSPERO, an international prospective register of systematic reviews (https://www.crd.york.ac. uk/prospero/display_record.php?RecordID=196569). The Preferred Reporting Items for Systematic Reviews and Meta-Analysis checklist can also be found in items S1 and S2.

Search Strategy

Comprehensive literature searches were performed to identify predictors of ED utilization and interventions with ED utilization as a measured outcome among adult HD patients. All searches were developed and performed by experienced medical librarians (KM, CJ), in consultation with the lead investigators (GH, PS).

The search was run on April 15, 2020, using Ovid MEDLINE ALL (from 1946 to April 14, 2020), Ovid Embase (from 1974 to April 14, 2020), and the Cochrane Library (Cochrane Reviews, Cochrane Protocols, Cochrane Trials, and Cochrane Editorials). Search terms in each database included all appropriate subject headings and/or keywords associated with our research question, including the following: renal dialysis, renal insufficiency/therapy, chronic kidney failure/therapy, hospital emergency service, emergency medical services, emergency medicine, utilization review, facilities and services utilization, and patient acceptance of health care.

The search terms were joined using Boolean operators "OR" and "AND," as appropriate. There were no language, publication date, or article-type restrictions implemented. Our search strategies can be found in items \$3-\$5.

Study Selection

After excluding duplicates, GH and HS independently screened the titles and abstracts using Covidence, a systematic review screening tool. Discrepancies were resolved by consensus, with PS serving as tiebreaker. All citations were reviewed against predefined inclusion/exclusion criteria.

The inclusion criteria were as follows: described ED utilization by HD patients, patient age >18 years, and identification of ED utilization predictors or testing of interventions with ED utilization as an outcome measure.

The exclusion criteria were as follows: HD patients not stratified from other dialysis modalities, ED utilization not reported, no quantitative data for analysis, systematic reviews, scoping reviews, meta-analyses, and duplicate publications.

A full-text review followed the initial title and abstract screening phase. Studies were selected for inclusion using the criteria outlined above. GH, HS, and PS extracted data using a predetermined extraction tool (Table S1). A metaanalysis was precluded by heterogeneity in the reporting of outcomes. A narrative synthesis approach, as described by Snilstveit et al,¹⁴ was used to group articles with similar ED utilization–associated factors thematically.

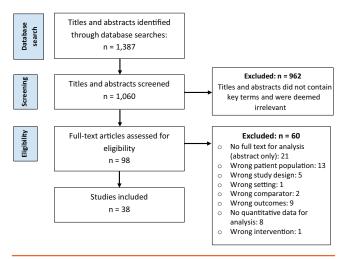
Quality Assessment

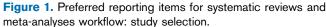
The included studies were assessed for quality using the Downs and Black checklist.¹⁶ This checklist consists of 27 questions designed to evaluate both randomized and nonrandomized studies for the overall quality of reporting and for internal and external validity. Quality levels were assigned to each included study, using the categories proposed by Hooper et al¹⁷: excellent (Downs and Black score \geq 26), good (20-25), fair (15-19), and poor (\leq 14). GH, HS, KM, and PS scored each included study individually, with quality levels assigned after consensus was reached (Table S2).

RESULTS

The initial electronic database search yielded 1,060 unique titles and abstracts. Of these, 98 appeared to meet the inclusion criteria and were imported for full-text review. Of the excluded texts, 21 were potentially relevant abstracts without an associated article (Fig 1). In total, 38 articles were included. They were published between 2007 and 2020; 74% were published in US cohorts, and the majority were retrospective cohort studies (71%). Thirty-four papers investigated predictors of ED utilization, whereas 4 evaluated an intervention's effect on ED utilization. The study populations ranged from 12 to 9,672,413 (Table S1).

With respect to the quality assessment, 10 studies were rated as good, 22 as fair, and 5 as poor using the Downs and Black tool. Although none achieved an excellent score, the Downs and Black tool is designed to award only randomized controlled trials such a score. Only 1 randomized





controlled trial met the inclusion criteria, so our included studies achieved a high level of quality for our chosen quality assessment tool.

Using narrative synthesis as described by Snilstveit et al,¹⁴ we summarized ED utilization themes among the included papers to form 8 concept subgroups by consensus (GH, AB, HS, PS). The subgroups were as follows: dialysis, social determinants of health, undocumented immigrant

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populations, medications and adverse drug events, laboratory values and scoring forms, psychiatric illness, palliative care, and new financial models (Table 1).^{3,7,18–53} The main characteristics of these studies are provided in separate tables for each concept subgroup (Tables 2-9).^{3,7,18–53} By consensus (GH, PS), these concept subgroups were subsequently organized into 3 core concepts: access to care, comorbid condition burden, and new health care models (Fig 2). The number of studies in each concept subgroup is shown in Fig 3.

The access to care core concept included 20 papers. Higher ED utilization was predicted by missed dialysis, longer interdialytic intervals, dialysis through catheters instead of arteriovenous fistulas, dialysis initiation, frequent postdialysis weights above target, prior hospitalization for dialysis, and infrequent predialysis care.^{3,7,18-25} Higher ED utilization was also predicted by the following social determinants of health: racial segregation, lower community income, female sex, Black race, reliance on public transport, and lower health literacy.²⁶⁻³⁰ The undocumented and social determinants of health concept subgroups were treated separately to reflect the unique barriers to care that undocumented persons face in the United States, such as their ineligibility for Medicare.⁵⁴ Several studies demonstrated an association between undocumented status and higher rates of ED visits.³²⁻³⁴ The use of loop diuretics in appropriate undocumented

Concept Subgroups	Identified Factors	Targeted Intervention(s)	Included Studies
Dialysis	Interdialytic interval; missed dialysis; Frequency of nephrologic care; dialysis access type; history of hospitalization for dialysis; dialysis initiation; postdialysis weights above target	None identified	Assimon et al ¹⁸ (2018); Bartolacci et al ¹⁹ (2018); Chan et al, (2014) ²⁰ ; Chen et al ²¹ (2019); Coentrão et al ²² (2012); Cohen et al ²³ (2020); Harel et al ³ (2015); Komenda et al ⁷ (2018); Siracuse et al ²⁴ (2017); Zhang et al ²⁵ (2019)
Social determinants of health	Transportation; racial segregation; female sex; health literacy; Black race; community income	None identified	Balhara et al ²⁶ (2020); Golestaneh et al ²⁷ (2019); Golestaneh et al ²⁸ (2018); Green et al ²⁹ (2013); Thomas-Hawkins et al ³⁰ (2019)
Undocumented immigrant populations	Reliance on emergency-only HD; use of furosemide	Initiating emergency dialysis based on strict clinical and laboratory cutoffs	Ahmed et al ³¹ (2016); Cervantes et al ³² (2018); Nguyen et al ³³ (2019); Sheikh- Hamad et al ³⁴ (2007); Sher et al ³⁵ (2017)
Medications and adverse drug events	Anticoagulant use; initiation of LTBI treatment; anticholinergic medication use; gabapentin/pregabalin use; muscle relaxant use	None identified	Chan et al ³⁶ (2018); Hamadah et al ³⁷ (2016); Ishida et al ³⁸ (2019); Ishida et al ³⁹ (2018); Mina et al ⁴⁰ (2019)
Laboratory values and scoring forms	Serum potassium level; serum- dialysate potassium gradient; serum NT-proBNP level; severe frailty score (Edmonton Frail Score)	Home telemonitoring	Berman et al ⁴¹ (2011); Brunelli et al ⁴² (2017); Brunelli et al ⁴³ (2018); Chen et al ⁴⁴ (2019); Garcia-Canton et al ⁴⁵ (2019); Minatodani & Berman ⁴⁶ (2013)
Psychiatric illness	Depression (HADS scale); depression (PHQ-9); pain (SF-MPQ)	None identified	Abbas Tavallaii et al ⁴⁷ (2009); El-Majzoub et al ⁴⁸ (2019); Vork et al ⁴⁹ (2018); Weisbord et al ⁵⁰ (2014)
Palliative care	Home palliative care utilization	None identified	Nesrallah et al ⁵¹ (2018)
New financial models	ACO-governed health care delivery	Initiating a payer- provider partnership	Kindy et al ⁵² (2018); Marrufo et al ⁵³ (2020)

 Table 1. Summary of Concept Subgroups

Note: Identified predictors and interventions are outlined per subgroup.

Abbreviations: ACO, accountable care organization; HADS, hospital anxiety and depression score; HD, hemodialysis; LTBI, latent tuberculosis infection; NT-proBNP, N-terminal pro b-type natriuretic peptide; PHQ-9, patient health questionnaire; SF-MPQ, short form McGill pain questionnaire.

Table 2. Abbreviated Data Extraction Table With Main Characteristics of Studies in the Dialysis Concept Subgroup

	Study D	Design	Study Populati	on		Results	
Study	Study Design	Study Measures	Country	Population Included	Dialysis Modalities Included	Key ED Utilization Findings	Downs and Black Quality Score
Assimon et al ¹⁸ (2018)	RCS	7-, 14-, and 30-d ED visits; 7-, 14-, and 30-d; hospitalizations (all-cause, cardiovascular, volume- related); short-term all- cause mortality; short-term cardiovascular mortality	United States	Medicare primary payer; at least 1 eKt/V measurement during the study interval	Maintenance HD	Frequent postdialysis weight >1 kg above the target was associated with increased risk of ED visit across the 7-30-d follow- up (ARR, 1.13-1.14); ARR for 30- d all-cause ED visits is higher at higher "kilogram thresholds."	Good
Bartolacci et al ¹⁹ (2018)	RCS	EMS event rate by day of the week; EMS response type; EMS transport event on the dialysis day vs off- day	Canada	Age 18 y or older; >2 years of dialysis treatment for analysis; 3× weekly HD	Maintenance HD	EMS transports to the ED occurred most frequently on Monday/Tuesday, the days after the long interdialytic interval $(P < 0.001)$	Fair
Chan et al ²⁰ (2014)	RCS	Admission rate after treatment; ED visit rate after treatment; ICU-CCU admission rate after treatment; total visit rate after treatment	United States	Diagnosis of ESRD; primary payer: Medicare	Maintenance HD	Risk of ED visit increased significantly after missed treatment (OR, 2.00); various barriers to attending dialysis associated with increased ED visit rate (+1.1 visits per patient- year) and missed dialysis (+5.6 missed sessions per patient-year)	Good
Chen et al ²¹ (2019)	RCS	No. of ED visits; Infection- related ED visits; Potentially avoidable ED visits (prevention quality indicators)	Taiwan	Diagnosis of ESRD; Dialysis treatment >90 d; interval between dialysis treatments <60 d	Long-term dialysis	Patients with early referral to nephrologist with frequent care had a lower risk of all-cause ED visit (HR, 0.92), lower risk of infection-related ED visit (HR, 0.76), and lower risk of avoidable ED visit (HR, 0.76)	Fair
Coentrão et al ²² (2012)	RCS	1-year mortality; 1-year dialysis access-related complication rate; No. of admissions; No. of ED visits	Portugal	Diagnosis of end-stage CKD; received outpatient long-term dialysis	Long-term dialysis (initiating)	Initiating HD-TCC was associated with higher ED visits and admissions than HD-AVF and PD	Good
Cohen et al ²³ (2020)	RCS	No. of hospitalizations; No. of ED visits; Mortality	United States	All dialysis sessions scheduled on 12 index days (MWF schedule); age 18 y or older; Medicare primary payer	Maintenance HD	Missed dialysis associated with an IRR of 2 for 5-d ED visit rate vs attended dialysis; rescheduled dialysis associated with an IRR of 1.33 for 5-d ED visit vs attended dialysis	Fair
Harel et al ³ (2015)	RCS	30-d all-cause rehospitalization; 30-d ED visit; 30-d death	Canada	Discharged alive from an index medical hospitalization; age 18-105 y	Maintenance HD	Positive history of hospitalizations 6 mo before index hospitalization associated with increased ED visit (3.0 vs 1.6)	Fair

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	Study D	Design	Study Populati	ion		Results	
Study	Study Design	Study Measures	Country	Population Included	Dialysis Modalities Included	Key ED Utilization Findings	Downs and Black Quality Score
Komenda et al ⁷ (2018)	RCS	ED visit rate	Canada	All ED visits in Winnipeg Regional Health Authority database	Long-term dialysis	Dialysis patients presented to the ED 8.5× as often as the general population ($P < 0.001$); ED utilization significantly higher after long interdialytic interval (on Monday/Tuesday; P < 0.001); in the 7 days before dialysis initiation, ED presentation rate 9× higher ($P < 0.001$) than general prevalent kidney disease patients; in the 7 days after dialysis initiation, ED presentation rate 4× higher than general prevalent kidney disease patients ($P < 0.001$)	Poor
Siracuse et al ²⁴ (2017)	RCS	30-d readmission; 90- d readmission; Cause for readmission (access- related, catheter related, other); 90-d ED visits w/o hospitalization	United States	Initiated new AVF for maintenance HD	Maintenance HD	Dialysis access creation associated with increased 30- and 90-d readmissions (25.5% and 47.7%, respectively, vs general Medicare rates of 17% and 27%, respectively); prosthetic grafts associated with procedure-related readmissions	Fair
Zhang et al ²⁵ (2019)	RCS	No. of ED visits; no. of hospitalizations; no. of ED visits w/o hospitalization; no. of hospitalizations w/o preceding ED visit	United States	Medicare primary payer; 3× weekly dialysis	Maintenance HD	A "sawtooth" pattern for ED visits observed, in which ED visits were higher on dialysis days vs off-dialysis days (F1); IRR for ED visits rose most from Sunday to Monday, illustrating a weekend effect; For MWF patients, IRR for ED visits were highest on Monday, whereas for TThS patients it was highest on T, demonstrating an interdialytic gap effect	Fair

Table 2 (Cont'd). Abbreviated Data Extraction Table With Main Characteristics of Studies in the Dialysis Concept Subgroup

Note: The full data extraction table is available in Supplemental Table 2.

Abbreviations: ARR, adjusted risk ratio; AVF, arteriovenous fistula; CKD, chronic kidney disease; ED, emergency department; EMS, emergency medical services; ESRD, end-stage renal disease; F1, Figure 1 of Zhang et al. (2019)²⁵; HD, hemodialysis; HR, hazard ratio; ICU-CCU, intensive care unit–critical care unit; IRR, incidence rate ratio; MWF, Monday, Wednesday, Friday; TThS, Tuesday, Thursday, Saturday; OR, odds ratio; PD, peritoneal dialysis; RCS, retrospective cohort study; TCC, transcutaneous catheter.

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Table 3. Abbreviated Data Extraction Table With Main Characteristics of Studies in the Social Determinants of Health Concept Subgroup

	Study Des	ign	Study Populat	tion		Results	
Study	Study Design	Study Measures	Country	Population Included	Dialysis Modalities Included	Key ED Utilization Findings	Downs and Black Quality Score
Balhara et al ²⁶ (2020)	Pilot study	Comorbid conditions (CCI); degree of disability (KD- QOL); depression (PHQ-9); economic stability (DCI); neighborhood and built environment (DCI and distance to HD center); education (highest level of formal education); health care access (REALM-SF); social and community context (Choices for Healthy Outcomes survey)	United States	Cases: presenting to ED after missed HD; age 18 y or older; English-speaking	Maintenance HD	Cases were more dependent on public transportation to reach dialysis ($P = 0.024$) and less likely to drive themselves ($P = 0.002$)	Poor
Golestaneh et al ²⁷ (2019)	RCS	ED visits without hospitalization	United States	Diagnosis of ESKD; 1+ index ED visit	Maintenance HD	Top 2 quintiles of Black resident proportion associated with an increased risk for ED revisit (IRRs, 1.15 and 1.15); when stratified by sex and adjusted for covariates, males in Q3-5 had significantly increased risks for ED visit (IRRs, 1.19, 1.28, and 1.21, respectively)	Good
Golestaneh et al ²⁸ (2018)	RCS	No. of avoidable ED visits before the index visit; no. of avoidable ED visits after the index visit	United States	Patients with at least 1 avoidable ED visit	Maintenance HD	Female sex associated with more avoidable ED visits in non-Hispanic Whites (IRR, 1.30); female sex associated with more avoidable ED visits in patients <44 y (IRR, 1.17)	Good
Green et al ²⁹ (2013)	PCS	Dialysis adherence; no. of ED visits; no. of hospitalizations related to ESRD	United States	Aged ≥18 y	Maintenance HD	Limited literacy associated with increased ED visits and hospitalizations related to ESRD	Fair
Thomas- Hawkins et al ³⁰ (2019)	RCS	No. of ED revisits	United States	Treat and release HD visits (to/from home without hospitalization); White/Black race (95% of the sample)	Maintenance HD	Living in communities with lower median income associated with a higher risk for ED revisit (ARR, 5.83); living in communities with higher racial segregation associated with higher risk for ED revisit (ARR, 3.13); Black race potentiated the above effects	Fair

Note: The full data extraction table is available in Supplemental Table 2.

Abbreviations: ARR, adjusted risk ratio; CCI, charleston comorbidity index; DCI, distressed communities index; ED, emergency department; ESKD, end-stage kidney disease; ESRD, end-stage renal disease; HD, hemodialysis; IRR, incidence rate ratio; KD-QOL, Kidney Disease Quality of Life Instrument; PCS, prospective cohort study; PHQ-9, patient health questionnaire; RCS, retrospective cohort study; REALM-SF, Rapid Estimate of Adult Literacy in Medicine-Short Form.

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Table 4. Abbreviated Data Extraction	Table With Main Characteristics of Studies in the Undocument	ted Immigrant Populations Concept Subgroup

	Study Design		Study Popula	tion		Results	
Study	Study Design	Study Measures	Country	Population Included	Dialysis Modalities Included	Key ED Utilization Findings	Downs and Black Quality Score
Ahmed et al ³¹ (2016)	RCS	No. of ED visits; no. of emergency HD sessions; potassium levels	United States	Undocumented persons	Emergency-only HD	On average, patients on furosemide had 3.1 fewer ED visits than those not on furosemide, although the effect was not significant; when adjusted for dialysis vintage and serum potassium levels, patients on furosemide had 1.1 fewer ED visits than those not on furosemide	Fair
Cervantes et al ³² (2018)	RCS	Death; acute care days; ambulatory care visits; bacteremia rate	United States	Undocumented persons; diagnosis of ESRD	Chronic HD (>3 mo)	The number of acute care days was nearly 10× greater for the emergency- only group (rate ratio, 9.81)	Fair
Nguyen et al ³³ (2019)	RCS	Death; ED visits; hospitalizations; no. of hospital days; total cost of care per person per month	United States	Undocumented immigrants (self-report); age 18 y or older; diagnosis of ESRD; receiving emergency-only HD at recruitment	Chronic HD	Beginning scheduled dialysis associated with reduced ED visit rate (-5.2 visits/month vs +1.1)	Fair
Sheikh-Hamad et al ³⁴ (2007)	RCS	ED visits; no. of admissions; length of stay; no. of dialysis treatments; total cost of care	United States	Undocumented immigrants; ≥4 mo of consecutive care; ESRD diagnosis	Chronic HD	The emergent group had significantly more ED visits than the chronic care group (26.3 vs 1.4, respectively; P < 0.0001); Cost per patient per year significantly higher in the emergent care group than the chronic care group (\$13,100 vs \$514, respectively; $P < 0.0001$)	Poor
Sher et al ³⁵ (2017)	Case series	No. of ED visits; hospital nights; ICU days	United States	Age 18 y or older; undocumented persons; all dialysis sessions had at study facility during at least 1 study phase	Emergent dialysis	ED visits decreased after transition to criterion-based emergent dialysis (early transition vs baseline, late transition baseline both $P < 0.001$)	Fair

Note: The full data extraction table is available in Supplemental Table 2. Abbreviations: ED, emergency department; ESRD, end-stage renal disease; HD, hemodialysis; ICU, intensive care unit; RCS, retrospective cohort study.

Table 5. Abbreviated Data Extraction Table With Main Characteristics of Studies in the Medications and Adverse Drug Events Concept Subgroup

	Study Design		Study Populati	on		Results	
Study	Study Design	Study Measures	Country	Population Included	Dialysis Modalities Included	Key ED Utilization Findings	Downs and Black Quality Score
Chan et al ³⁶ (2018)	RCS	ED visit rate; ED visit for adverse drug event rate	United States	ED visits in 33 states (NEDS 2008-2013)	Long-term dialysis	ED visits for adverse drug event rate per year were >10× higher in the dialysis group (65.8-88.5 per 1,000 patients vs 4.6-5.4 per 1,000 patients, respectively; $P < 0.001$); In the dialysis group, hematologically active medications (94% anticoagulants) associated with adverse drug events resulting in ED visits	Good
Hamadah et al ³⁷ (2016)	Case series	ED visit without hospitalization rate; hospitalization rate; symptoms of tuberculosis therapy	United States	Diagnosis for tuberculosis or other mycobacterial infection	Maintenance HD	In the LTBI group, increased hospitalizations and ED visits without admission were associated with the initiation of treatment $(0 \rightarrow 6, 0 \rightarrow 4)$	Fair
Ishida et al ³⁸ (2019)	RCS	First episode of AMS, fall, fracture resulting in ED visit ± hospitalization	United States	Age 65 y or older; Medicare D coverage	Maintenance HD	Anticholinergic antidepressants associated with higher hazard of AMS, fall, and fracture ED visit/ hospitalization (HRs, 1.25, 1.27, and 1.39, respectively)	Good
Ishida et al ³⁹ (2018)	RCS	First episode of AMS, fall, fracture resulting in ED visit ± hospitalization	United States	Medicare D coverage	Maintenance HD	Gabapentin associated with increased ED visits in study categories across all dosage ranges; Pregabalin associated with increased ED visits	Good
Mina et al ⁴⁰ (2019)	RCS	First episode of AMS, fall, fracture resulting in ED visit ± hospitalization	United States	Age 18-100 y; Medicare coverage	Maintenance HD	Muscle relaxant use was associated with a higher risk for ED visit/ hospitalization for AMS (HR, 1.39) and fall (HR, 1.18)	Good

Note: The full data extraction table is available in Supplemental Table 2.

Abbreviations: AMS, altered mental status; ED, emergency department; HD, hemodialysis; HR, hazard ratio; LTBI, latent tuberculosis infection; NEDS, Nationwide Emergency Department Sample; RCS, retrospective cohort study.

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Table 6. Abbreviated Data Extraction Table With Main Characteristics of Studies in the Laboratory Value/Scoring Form Concept Subgroup

	Study Des	ign	Study Popula	tion		Results	Downs and
Study	Study Design	Study Measures	Country	Population Included	Dialysis Modalities Included	Key ED Utilization Findings	Black Quality Score
Berman et al ⁴¹ (2011)	Pilot Study	No. of admissions; no. of ED visits; no. of admission days; ED/admission cost; SF-36 quality of life measure	United States	Age 21 y or older; living at home; hospitalization risk score > 1.2	Maintenance HD	Home-based remote telemonitoring reduced ED visits (<i>P</i> = 0.035)	Fair
Brunelli et al ⁴² (2017)	RCS	4-day death; 4-day hospitalization; 4-day ED visit; 4-day hospital costs	United States	Age 18 y or older; 1+ routine serum potassium level measurement (no missed dialysis <7 d prior); Medicare A+B	Maintenance HD	Increased serum potassium level associated with increased ED visits; risk of ED visit >2×more in the >7+ potassium group compared with the 4-4.5 potassium group (OR, 2.62)	Fair
Brunelli et al ⁴³ (2018)	RCS	Same-/next-day deaths; same-/next- day hospitalizations; same-/next-day ED visits	United States	Age 18 y or older; routine laboratory checks on Monday, Wednesday, or Friday; Medicare A+B coverage	Maintenance HD	The 4-5 and 5+ potassium gradient groups had significantly higher same-day ED visits than the 2-3 referent group (16% and 41% increased adjusted risks, respectively); The 3-4, 4-5, and 5+ potassium gradient groups had significantly higher next-day ED visit rates (6%, 17%, and 54% increased adjusted risks, respectively)	Fair
Chen et al ⁴⁴ (2019)	PCS	No. of ED visits; no. of ICU admissions; no. of cardiovascular events	Taiwan	Aged ≥18 y; 3× weekly HD	Maintenance HD	Higher NT-proBNP quartile associated with increased ED visit ($P = 0.001$); NT-proBNP predictive power for ED visit peaked on the fifth day after value	Poor
Garcia-Canton et al ⁴⁵ (2019)	PCS	No. of admissions; no. of ED visits	Spain	>3 mo HD treatment; age 18 y or older; ability to understand/sign consent	Maintenance HD	Severely frail patients (EFS score, 12-17) had increased risk of ED visit vs the nonfrail population (IRR, 1.91)	Good
Minatodani & Berman ⁴⁶ (2013)	RCT	No. of admissions; no. of ED visits; no. of admission days; ED/admission cost	United States	Diagnosis of ESRD	Long-term dialysis (>3 mo)	Home-based remote telemonitoring reduced hospital/ED charges, but the effect was not significant ($P = 0.011$); Effects on no. of ED visits was also not significant ($P = 0.229$)	Fair

Note: The full data extraction table is available in Supplemental Table 2.

Abbreviations: ED, emergency department; EFS, edmonton fail scale; ESRD, end-stage renal disease; HD, hemodialysis; ICU, intensive care unit; IRR, incidence rate ratio; NT-proBNP, N-terminal pro b-type natriuretic peptide; OR, odds ratio; PCS, prospective cohort study; RCT, randomized controlled trial; RCS, retrospective cohort study; SF-36, 36-item short form survey.

Table 7. Abbre	viated Da	Table 7. Abbreviated Data Extraction Table With Main Characteristics of Studies in the Psychiatric Illness Concept Subgroup	in Characteristic:	s of Studies in the Psychia	tric Illness Concept St	rþgroup	
	Study Design	Jesign	Study Population	ų		Results	Downs and
Study	Study Design	Study Design Study Measures	Country	Population Included	Dialysis Modalities Included	Key ED Utilization Findings	Black Quality Score
Abbas Tavallaii et al ⁴⁷ (2009)	PCS	No. of Admissions; home Iran nurse visits; no. of outpatient physician visits; no. of ED visits	Iran	Undergoing HD for prior 6 mo; clinically stable	Chronic HD	Depressed patients were significantly more likely to use the ED (14/19 patients vs 20/49 non-depressed patients)	Fair
El-Majzoub et al ⁴⁸ (2019)	PCS	Time to first hospitalization; time to first ED visit	Canada	Age 18 y or older	Maintenance HD	Psychosocial distress associated with faster time to first hospitalization, but not to ED visit	Good
Vork et al ⁴⁹ (2018)	RCS	No. of Hospitalizations; no. of ED visits w/o subsequent hospitalization; time to first hospitalization	United States	Age 18-44 y at maintenance HD initiation	Maintenance HD	There was no significant difference in ED Fair visit rate between the treated and untreated groups	Fair
Weisbord et al ⁵⁰ (2014)	PCS	PHQ-9; SF-MPQ; missed HD sessions; ED visits; hospitalizations; mortality	United States	English-speaking	Maintenance HD	Increasing PHQ-9 scores correlated w/ increased ED visits (IRR, 1.24); increasing SF-MPQ score correlated with increased ED visits (IRR, 1.58)	Fair
<i>Note:</i> The full data Abbreviations: ED	a extraction emergency	<i>Note:</i> The full data extraction table is available in Supplemental Table 2. Abbreviations: ED, emergency department; HD, hemodialysis; IRR, incid	able 2. , incidence rate ratio;	PCS, prospective cohort study; P	'HQ-9, patient health questio	Note: The full data extraction table is available in Supplemental Table 2. Abbreviations: ED, emergency department; HD, hemodialysis; IRR, incidence rate ratio; PCS, prospective cohort study; SF-MPQ, short form McGill pain	ort form McGill pain

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patients has been associated with reduced ED visits, whereas another study demonstrated that implementing strict laboratory cutoffs to determine the need for emergency HD reduced subsequent ED utilization.^{31,35}

The comorbid condition burden core concept included 15 studies. Depression and pain predicted increased ED utilization, but no association was found with antidepressant use or measured psychosocial distress.^{47–50} Medications whose use predicts ED utilization include psychoactive anticholinergics, gabapentin and pregabalin, muscle relaxants, anticoagulants, and those used for the treatment of latent tuberculosis.^{36–40} Finally, several laboratory values predicted ED utilization: high serum potassium level, high serum-dialysate potassium gradients, and N-terminal pro b-type natriuretic peptide.^{42–44,55} Laboratory values were also integrated into a frailty score and a remote telemonitoring platform, which predicted and reduced ED utilization, respectively.^{41,45,46}

The new health care models core concept included 3 studies. Of note, several excluded studies were related to its constituent subgroups. Receiving care at a dialysis center organized by an ESRD Seamless Care Organization and the use of home palliative care both predicted lower ED utilization. ^{51,53} Another study found that establishing a payer-provider relationship at a dialysis center reduced ED utilization by its HD patients. ⁵²

The 4 studies that tested interventions are summarized in Table 10.^{35,41,46,52} The average population size for these intervention studies was ~90, which is much smaller than the overall average for our included studies (334,556). Furthermore, no studies tested an intervention in the ED.

DISCUSSION

questionnaire.

Our thematic framework highlights key areas that affect ED utilization by HD patients; we identified diverse predictors of ED utilization across our 3 core concepts.

Access to care is key to the management of chronic diseases and is our first core concept.⁵⁶ Because most patients treated with dialysis are unemployed, access to health insurance is of paramount importance for this population.^{57,58} Nephrology experts have recently highlighted the need for research on the effects of improving access to nephrology care through health insurance expansion.⁵⁹ As of 2021, certain HD patients in the United States remain excluded from Medicare, including undocumented persons.⁵⁴ Dialysis patients with Medicaid have higher ED utilization than those with Medicare.² Access to care is also modulated by other social determinants of health, such as race and residential segregation.^{30,60}

HD patients require regularly scheduled dialysis, which is among the greatest burdens of their disease experience.^{1,61} Missed dialysis is associated with ED visits, hospitalizations, and mortality.^{20,23,62} Furthermore, the United States had the highest proportion of

	Study Design	esign	Study Population	pulation		Results	
Study	Study Design	Study Design Study Measures	Country	Dialysis N Country Population Included	Dialysis Modalities Included	Key ED Utilization Findings	Downs and Black Quality Score
Nesrallah et al ⁵¹ RCS (2018)	RCS	ACG comorbid condition estimate; ED visits; ICU visits; time from dialysis initiation to death; place of death	Canada	Canada Deceased long-term Long-term dialysis dialysis patients	Long-term dialysis	Patients receiving home palliative care had less ED visits	Fair
<i>Note:</i> The full data Abbreviations: AC	extraction ta à, Johns Hop	<i>Note:</i> The full data extraction table is available in Supplemental Table 2. Abbreviations: ACG, Johns Hopkins Adjusted Clinical Group System; ED, emergency department; ICU, intensive care unit; RCS, retrospective cohort study.	smergency dep	partment; ICU, intensive care u	unit; RCS, retrospective cohort	study	

Table 8. Abbreviated Data Extraction Table With Main Characteristics of Studies in the Palliative Care Concept Subgroup

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patients with missed treatments (24%) among the 40 countries in the 3-year international Dialysis Outcomes and Practice Patterns Study (DOPPS). ⁶³ These findings suggest that reducing rates of missed dialysis may help reduce ED visits, although predictors of both missed dialysis and increased ED visits warrant further investigation. Although we did not identify any interventions in this subgroup, Chen et al²¹ found that more frequent predialysis care by a nephrologist was associated with lower ED visit rates following HD initiation, suggesting that optimized predialysis care may help HD patients avoid the ED. Furthermore, Harel et al³ observed that dialysis centers in Canada frequently share records systems with hospitals and have lower hospitalization rates for their patients than American dialysis centers. It is possible that improving access to dialysis center medical records may facilitate better care management, which could subsequently reduce hospitalizations and their antecedent ED visits.

Undocumented persons receiving HD have higher rates of hospitalization, increased hospitalization days, and higher mortality.^{32,33,64} In a Texas cohort, individuals receiving emergency-only dialysis had a 5-fold higher mortality rate than those receiving scheduled dialysis.³³ Undocumented persons receiving HD do not qualify for Medicare insurance, so many rely on the ED for dialysis, which contributes to their higher rate of ED utilization.^{32–34,54,65} To address this gap in care, some states are using emergency Medicaid to pay for outpatient dialysis treatments.⁶⁶ In the absence of regularly scheduled dialysis, alternate approaches to care may help reduce these patients' ED visit rates.31,35

Finally, several other social determinants of health also predict increased ED utilization. Given the strong association between social determinants and poor health outcomes, it follows that HD patients experiencing barriers to longitudinal care, such as poor community income and a lack of health literacy, are more likely to require emergency care, or "safety net" care.⁶⁷

Health care access is critical for HD patients, and many studies have identified predictors of ED utilization that stemmed from suboptimal access to care. One intervention identified in this core concept used laboratory cutoffs and vital signs to decide whether emergency HD was required, which reduced subsequent ED utilization.³⁵ The success of this novel study could inform comparable protocols for patients who frequently miss dialysis, which are a cohort at increased risk for ED visits, hospitalizations, and mortality.^{20,23,62} However, health care nonadherence, like missed dialysis, is influenced by complex social factors that warrant further clarification to guide interventions.^{26,68,69} Furthermore, we did not identify published work describing an intervention that directly improved access to HD care.

The comorbid condition burden is an independent risk factor for ED utilization by HD patients and serves as our second core concept.² Understanding what comorbid

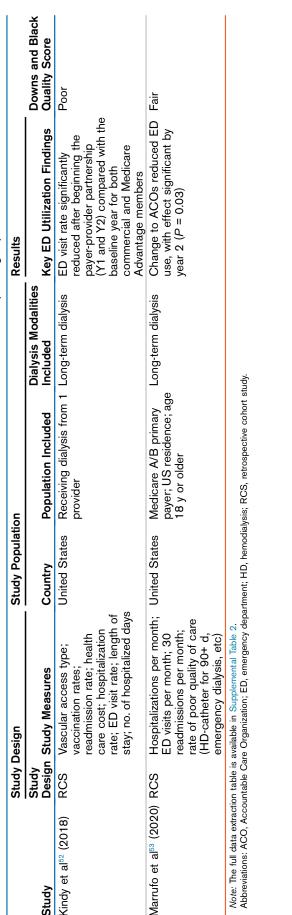




Figure 2. Conceptual framework for organizing emergency department utilization-associated factors in hemodialysis patients. Eight concept subgroups each correspond to 1 of 3 core concepts: access to care, comorbid condition burden, and new health care models.

conditions are most associated with increased ED utilization has the potential to inform future interventions.

Depression is the most common psychiatric comorbid condition in HD patients and was linked with ED utilization in Iranian and US cohorts.^{47,50,70} However, research on other psychiatric measures produced equivocal results.^{48,49} Although a psychiatric comorbid condition is a prevalent and morbid concern for the HD population, research to date has not elucidated what psychiatric measures best predict ED utilization in this population.

HD patients are at high risk for adverse drug events. Polypharmacy is common among HD patients, with daily pill intake often >20.⁷¹ Moreover, elevated creatinine levels have been associated with a higher risk of ED visits due to adverse drug events.⁷² Many medications require renal dosing adjustments because of nephrotoxicity and renal excretion, compounding risks for adverse drug events in HD patients. National data reflect this vulnerability, as there is a 10-fold higher incidence of ED encounters for adverse drug events in maintenance dialysis patients than in nondialysis patients.³⁶ Our included studies corroborate this; several medications are associated with higher ED use. Some studies specifically investigated the association between medications and ED visits by older HD patients owing to a fall, fracture, or altered mental status, limiting their generalizability to allcause ED utilization.³⁸⁻⁴⁰ Regardless, the use of medications with significant side effect profiles, especially those renally dosed for patients with decreased kidney function, are consistently associated with increased ED utilization. Interventions to reduce the risks of adverse events due to polypharmacy should be developed, such as robust medication reconciliation processes that could reduce accidental over- or underdosing of medications and subsequent ED utilization.

The relationship between elevated creatinine and ED visits underlies the potential utility in laboratory values of predicting and managing ED utilization by HD patients.⁷² Loss of kidney function results in electrolyte dysregulation, pathophysiologic changes, and poor clearance,

Table 9. Abbreviated Data Extraction Table With Main Characteristics of Studies in the New Health Care Models Concept Subgroup

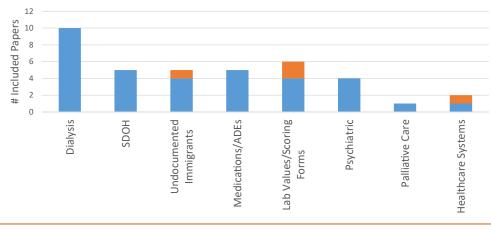


Figure 3. Distribution of included papers per concept subgroup. The majority of included articles described predictors of emergency department utilization (34/38 articles), with most subgroups lacking an associated intervention. Blue bars indicate predictor studies, and orange bars indicate intervention studies. Abbreviations: ADE, adverse drug event; SDOH, social determinants of health.

resulting in abnormal laboratory values. Even modest elevations in serum potassium levels are associated with death, hospitalization, and cardiovascular events in HD patients.^{73–75} Brain natriuretic peptide is also an independent marker of mortality.⁵⁵ Although several included studies have highlighted both potassium and brain natriuretic peptide as predictors of ED utilization, none have demonstrated that a reduction in potassium levels or volume status management reduced ED utilization.^{42,43} Further investigation of laboratory test markers like brain natriuretic peptide and their association with HD patients' clinical volume status would help translate these findings to clinical practice, such as risk stratification using brain natriuretic peptide and clinical volume status in parallel.

Understanding the comorbid condition burden is important for understanding ED utilization by HD patients. Various diagnoses, scoring measures, and medications are associated with increased ED use in this population, but we did not find investigations of comorbid chronic diseases such as congestive heart failure or chronic obstructive pulmonary disease. Similarly, no studies investigating the role of opioid use in ED utilization by HD patients were identified, despite the prevalence of pain and a high rate of opioid prescription in this population.^{76,77} These gaps in the literature underscore the lack of research on causal factors driving ED utilization by HD patients and any associated interventions.

Finally, the rising cost of HD patient care has generated momentum to reimagine health care delivery for these patients.⁷⁸ Our third core concept, health care models, seeks to capture the results of these efforts.

The high cost of HD care has driven federal initiatives to introduce new financial models, such as ESRD Seamless Care Organizations.^{11,12} Two included studies demonstrated that changing the financial structures for dialysis centers can affect ED utilization by HD patients.^{52,53} More

research is needed to further explore causality, as well as the effects of these changes on total health care costs. Although articles on home HD were excluded from our review, home HD is another way dialysis providers may reduce costs and improve quality of life for in-center HD patients.⁷⁹ The literature on the benefits of care at home is growing, and we expect further developments to emerge in the coming years.^{80,81} In a similar vein, the only clinical intervention described to reduce ED utilization by HD patients was remote patient monitoring. Telehealth has been rapidly expanding in the United States, accelerated most recently by the COVID-19 pandemic.⁸² It has potential in telemonitoring HD patients and reducing rates of missed dialysis, which may subsequently reduce ED encounters.41,46 However, given the social vulnerability of the population with ESRD, telehealth-based interventions will need to circumvent technical and social barriers to implementation, as has been seen in telehealth expansions for other patient populations.^{83,84}

As of 2015, >80% of all dialysis patients were admitted to the hospital in the last 90 days of life, considerably higher than the 62.5% reported for other Medicare beneficiaries.⁸⁵ Because the majority of unscheduled hospitalizations arise from ED encounters, this represents significant ED use by HD patients in the last 90 days of life.⁸⁶ Recent studies have explored this high rate of ED visits by patients with end-of-life conditions like kidney failure and highlighted the need to develop ways to better serve terminally ill patients and provide cost-effective and meaningful care.⁸⁷ Although only 1 study met the criteria for inclusion in this review, we reviewed many articles describing palliative care for kidney disease in the United States and abroad.^{51,88–90} Results are promising, with reduced ED utilization demonstrated following the initiation of palliative care plans for kidney failure patients who decline dialysis.⁸⁸ The high mortality of maintenance HD

Table 10. Sumi	Table 10. Summary of Intervention Studies	lies				
Study	Study Design	z	Demographics	Study Measures	Intervention	Key Findings
Berman et al ⁴¹ (2011)	Pilot study	44	Remote telemonitoring: 7 F, 12 M, mean age 57 y. Usual care: 11 F, 14 M, mean age 62 v.	No. of admissions; no. of ED Remote home visits; no. of admission days; telemonitoring ED/admission cost; SF-36 QOL measure	Remote home telemonitoring	Home-based remote telemonitoring reduced ED visits
Kindy et al ⁵² (2018)	Retrospective cohort study	197	197 Year 1: 99; year 2: 101; baseline: 197	Vascular access type; vaccination rates; readmission rate; health care cost; hospitalization rate; ED visit rate; length of stay; no. of hospitalized days	Initiation of a payer- provider relationship at the study dialysis center	ED visit rate was significantly reduced after beginning the payer-provider partnership (Y1 and Y2) compared with the baseline year for both commercial and Medicare Advantage members
Minatodani & Berman ⁴⁶ (2013)	Pilot study	66	Remote telemonitoring: 18 F, 25 M, mean age 58.6 y. Usual Care: 26 F, 30 M, mean age 63.1 y.	No. of admissions; no. of ED Remote home visits; no. of admission days; telemonitoring ED/admission cost	Remote home telemonitoring	Home-based remote telemonitoring reduced hospitalizations, but the reduction of ED utilization was not statistically significant ($P = 0.229$)
Sher et al ³⁵ (2017)	Case series	19	Overall: 6 F, 13 M, mean age 36.6 y.	No. of ED visits; hospital nights; ICU days	Criterion-based emergent dialysis	ED visits decreased after transition to criterion-based emergent dialysis (early transition vs baseline, late transition baseline both $P < 0.001$)
Note: The full data	Note: The full data extraction table is available in Supplemental Table 2.	Supplem	ental Table 2.			

Note: The full data extraction table is available in Supplemental Table 2. Abbreviations: ED, emergency department; ICU, intensive care unit; OOL, quality of life; SF-36, 36-item short form survey. and the paucity of transplants makes establishing end-oflife goals of care an important consideration for all HD

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patients.¹ This systematic review is subject to several limitations. Most included studies were retrospective chart reviews, and only 1 was a randomized controlled trial. Therefore, most of the reviewed findings were associations with ED utilization rather than proven causality. Although the quality of our included studies was high, we found significant heterogeneity (dialysis population, country of study, etc) among the data, which precluded the ability to perform a meta-analysis. During our fulltext review, we could not find associated full texts for 21 of the abstracts. If full texts for some of these articles do exist, it is possible that some would have met the criteria for inclusion.

As systemic reviews are limited by random and human error, we minimized chances for error by developing a protocol (submitted to PROSPERO), clearly articulating the inclusion and exclusion criteria, developing a peerreviewed comprehensive search strategy, and performing title and abstract screening and full-text screening. Quality assessment of the screening process was achieved by having at least 2 independent reviewers working in parallel, adjudicating disagreements first by consensus, and, if necessary, by a third reviewer.

We limited the scope of our systematic review to HD patients because of the higher rate of ED utilization in this population than in populations using other forms of dialysis.¹ However, this limits our ability to compare different dialysis populations in this study. We also excluded studies whose study populations included adolescents (aged <18 years), even if adults were also included. We decided to exclude pediatric populations because adolescents are a nonrepresentative minority of HD patients; in 2019, only 1% of all patients with ESKD were aged <21 years.¹ The characteristics of the pediatric ESKD population are significantly different from those of the overall ESKD population, as illustrated by the 20.8% transplant rate in this subgroup, versus 2.9% overall.¹

In summary, our systematic review uncovers a broad range of studies describing predictors of ED utilization by HD patients, as well as 4 studies that test interventions to reduce ED use (Table 10). Our concept subgroups spanned the core concepts of access to care, the comorbid condition burden, and new health care models, which underscore the complex causality behind HD patients' ED utilization. The predictors we have compiled in this review provide rich ground for the development of a risk stratification tool to predict future all-cause ED visits by HD patients. An ED screening tool could be used to direct limited ED case management resources to the highest-risk patients, providing interventions to potentially improve post-ED outcomes. The next step for developing such a tool would be to perform a multivariate analysis on the predictors identified in this study to further our understanding

of which predictors best predict increased ED utilization by HD patients.

We identified only 4 studies measuring the effect of interventions on ED utilization, with none performed in the ED. These include investigations on the efficacy of home telemonitoring, which had equivocal results.^{41,46} There is a great deal of room for further research, since care at home like telemedicine and home HD has the potential to improve access and overcome barriers to inperson care.^{41,46,80,81} Although the lower rates of ED utilization by patients on peritoneal dialysis and home HD were not covered in this review, they also merit further investigation.¹ Palliative and hospice care may also provide alternative modes of care at the end of life, and payment models incentivizing these various modes of care may reduce ED use for this vulnerable and often poorly understood population.^{51,88}

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Item S1: PRISMA 2020 Checklist for Systematic Reviews.

Item S2: PRISMA 2020 Abstract Checklist for Systematic Reviews. Item S3: Final database search strategy for The Cochrane Library.

Item S4: Final database search strategy for Ovid Medline.

Item S5: Final database search strategy for Ovid EMBASE.

 Table S1: Categories for the full data extraction form.

 Table S2: Additional extracted information from the 38 included articles not included in Tables 2-9.

ARTICLE INFORMATION

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