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ORIGINAL RESEARCH

# Optimal Initial Intravenous Loop Diuretic Dosing in Acute Decompensated Heart Failure

Joshua A. Jacobs, PharmD,[a,b] Spencer J. Carter, MD,[c] Griffin Bullock, MD,[c] Jessica R. Carey, PharmD,[b,d] Irene Z. Pan, PharmD,[b] M. Shea Kinsey, PharmD, MBA, MHSA, MS,[b] Alexander R. Zheutlin, MD, MS,[e] Chris J. Kapelios, MD,[c] Shilpa Raju, MD,[f] James C. Fang, MD,[c] Kevin S. Shah, MD,[c] Adam P. Bress, PharmD, MS[a]

## ABSTRACT

**BACKGROUND** Nearly one-half of patients admitted with acute decompensated heart failure (ADHF) are discharged with unresolved congestion, elevating rehospitalization risk. This may be due to suboptimal intravenous (IV) loop diuretic dosing, which may be influenced by home oral diuretic dose.

**OBJECTIVES** The objective of this study was to determine the association between: 1) home oral loop diuretic dose and optimal initial IV loop diuretic dosing in ADHF; and 2)receiving optimal initial IV loop diuretic dosing and length of stay and 30-day readmission.

**METHODS** Retrospective analysis of adults admitted to a large U.S. hospital for ADHF on home oral loop diuretics from 1 January 2014 to 21 December 2021. Patients were categorized by home dose: low (≤40 mg furosemide equivalents), medium (>40-80 mg furosemide equivalents), and high (>80 mg furosemide equivalents). Optimal initial IV dosing was considered ≥2 times home oral dosing. Poisson regression models estimated prevalence ratios (CIs) for optimal initial IV loop diuretic dosing.

**RESULTS** Among 3,269 adults admitted for ADHF (mean age 63 years, 62% male), optimal initial IV dosing occurred in 2,218 (67.9%). The prevalence of optimal initial IV dosing among low, medium, and high home dosing was 95.5%, 59.9%, and 4.0%, respectively. Adjusted prevalence ratios for optimal IV dosing with high and medium home dosing, compared to low, were 0.05 (95% CI: 0.03-0.07) and 0.66 (95% CI: 0.62-0.70), respectively. There was no difference in length of stay or 30-day readmission between optimal and suboptimal initial IV diuretic dosing.

**CONCLUSIONS** Among patients with ADHF, higher home loop diuretic dose was strongly associated with a substantially lower likelihood of optimal initial IV diuretic dosing. (JACC Adv. 2024;3:101250) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

From the [a]Intermountain Healthcare Department of Population Health Sciences, Spencer Fox Eccles School of Medicine, University of Utah, Salt Lake City, Utah, USA; [b]Department of Pharmacy, University of Utah Health, University of Utah, Salt Lake City, Utah, USA; [c]Division of Cardiovascular Medicine, Department of Internal Medicine, Spencer Fox Eccles School of Medicine, University of Utah, Salt Lake City, Utah, USA; [d]Department of Pharmacotherapy, University of Utah College of Pharmacy, Salt Lake City, Utah, USA. [e]Division of Cardiology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, USA; and the [f]Department of Emergency Medicine, Spencer Fox Eccles School of Medicine, University of Utah, Salt Lake City, Utah, USA

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**ABBREVIATIONS AND ACRONYMS**

**ADHF** = acute decompensated heart failure

**EHR** = electronic health record

**FE** = furosemide equivalents

**GDMT** = guideline-directed medical therapy

**HFpEF** = heart failure with preserved ejection fraction

**HFrEF** = heart failure with reduced ejection fraction

**HR** = heart failure

**IQR** = interquartile range

**IV** = intravenous

**LOS** = length of stay

**PR** = prevalence ratio

Hospitalization rates for acute decompensated heart failure (ADHF) are increasing in the United States. Between 2012 and 2017, there was a 26% increase in ADHF hospitalizations.[1] Among adults hospitalized for ADHF, approximately 1 in 4 will be rehospitalized or die within 30 days after discharge.[2] An inadequate diuretic response is an independent predictor of readmission in patients with ADHF. Therefore, current guidelines emphasize prompt initiation of intravenous (IV) loop diuretics in patients with ADHF and volume overload.[3,4] However, effectively reducing volume overload in ADHF is challenging as up to 50% of patients are discharged with unrelieved congestion.[5-7] Identification of more effective diuretic optimization strategies during ADHF hospitalizations are crucial to reducing readmission and heart failure (HF)-related morbidity.

The Diuretic Optimization Strategies Evaluation (DOSE) trial and the Randomized Evaluation of Heart Failure with Preserved Ejection Fraction Patients with Acute Heart Failure and Dopamine trial provided valuable insights into aiding to define optimal initial IV diuretic dosing in ADHF. Collectively, these trials suggest the optimal initial loop diuretic dosing strategy should be 2 to 2.5 times the home oral loop diuretic dose as an IV bolus.[8,9] However, there is wide practice variation and multiple factors contribute to receiving optimal initial IV diuretic dosing in ADHF as defined by DOSE and Randomized Evaluation of Heart Failure with Preserved Ejection Fraction Patients with Acute Heart Failure and Dopamine. For example, clinicians may be hesitant to use higher IV doses among patients on higher doses of home oral loop diuretic doses due to concern about side effects or intolerance, despite guideline support of improved decongestion.[3,10,11] The degree to which patients with ADHF receive optimal IV loop diuretic dosing and whether home loop diuretic dose is associated with initial IV diuretic dosing remains unclear. Additionally, whether receiving optimal initial IV loop diuretic dosing is associated with improved hospital length of stay (LOS) or 30-day readmissions is also unclear. Therefore, among patients on chronic home oral loop diuretic therapy hospitalized for ADHF at a large quaternary healthcare system, we evaluated: 1) the frequency of receiving optimal initial IV loop diuretic dosing; 2) the association between baseline home oral loop diuretic dose and receiving optimal initial IV loop diuretic dose; 3) the association between receiving optimal initial IV diuretic dose and hospital LOS; and 4) the association between receiving optimal initial IV diuretic dosing and 30-day all-cause and HF-related readmission.

## METHODS

**STUDY DESIGN.** We performed a retrospective analysis of adults ≥18 years old hospitalized for ADHF between January 1, 2014, and December 21, 2021, at a large, quaternary healthcare system. Patients were identified from an internal HF registry collected for national use, which identifies adults hospitalized for ADHF via International Classification of Diseases-9th/10th Revision codes.[12] The local institution started participating in the national registry beginning in January 1, 2014. The registry includes patients with both heart failure with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF). Trained registry personnel abstract and record data including patient demographics, past medical history, medications, examination and laboratory results, in-hospital treatment, provider and hospital characteristics, and hospital LOS. Additional information on clinicians, home medications, inpatient medication dosing, and 30-day readmission were abstracted from the local electronic health record (EHR) and linked to the patients identified from the local HF registry data. Exclusion criteria included end-stage renal disease, no home oral loop diuretic therapy prior to hospitalization, use of ethacrynic acid, and initial dosing of IV loop diuretic ordered as a continuous infusion as these likely reflected transfers from outside facilities already on a continuous infusion. A local institutional review board deemed the study exempt status.

**MAIN EXPOSURES AND OUTCOMES.** In the first analysis, the main exposure was home oral loop diuretic dosing and the outcome was optimal initial IV diuretic dosing. In the second analysis, the main exposure was receiving optimal initial IV diuretic dosing and the outcome was LOS and 30-day readmission.

Home oral loop diuretic dosing was abstracted from the prior-to-admission medication lists recorded in the EHR. The prior-to-admission medication list is collected by trained medication reconciliation technicians, interns, or pharmacists and is ultimately verified by a clinical pharmacist upon admission. Home oral loop diuretics were identified on the prior-to-admission medication list and was calculated as a single scheduled dose, which was used to determine optimal initial IV dosing. For example, a patient who uses 3 20-mg tablets of furosemide twice daily, the

single scheduled home oral diuretic dose would be 60 mg of furosemide. All loop diuretics were calculated as oral furosemide equivalents (FEs) based on the following conversions used in the DOSE trial: bumetanide 1 mg oral = furosemide 40 mg oral = torsemide 20 mg oral; furosemide 40 mg oral = furosemide 20 mg IV.[8,13,14] The main exposure was home oral loop diuretic dose defined as FEs ≤40 mg (low home dose) vs >40 to 80 mg FEs (medium home dose) and >80 mg FEs (high home dose).

Receiving optimal initial IV diuretic dosing, which was defined per DOSE and Randomized Evaluation of Heart Failure with Preserved Ejection Fraction Patients with Acute Heart Failure and Dopamine as at least 2 times the home oral loop diuretic dose in IV formulation. For example, if a patient was on 40 mg twice daily of torsemide at home, then the optimal initial IV dosing would be ≥80 mg IV FEs. Hospital LOS was defined as the number of nights a patient stayed in the hospital. In this analysis, 30-day readmission rates were defined based on all-cause admissions and HF-related readmissions. HF readmissions were collected based on International Classification of Diseases-9th/10th Revision codes for I50.x. In these analyses, receiving optimal initial IV diuretic dosing was used as the exposure variable.

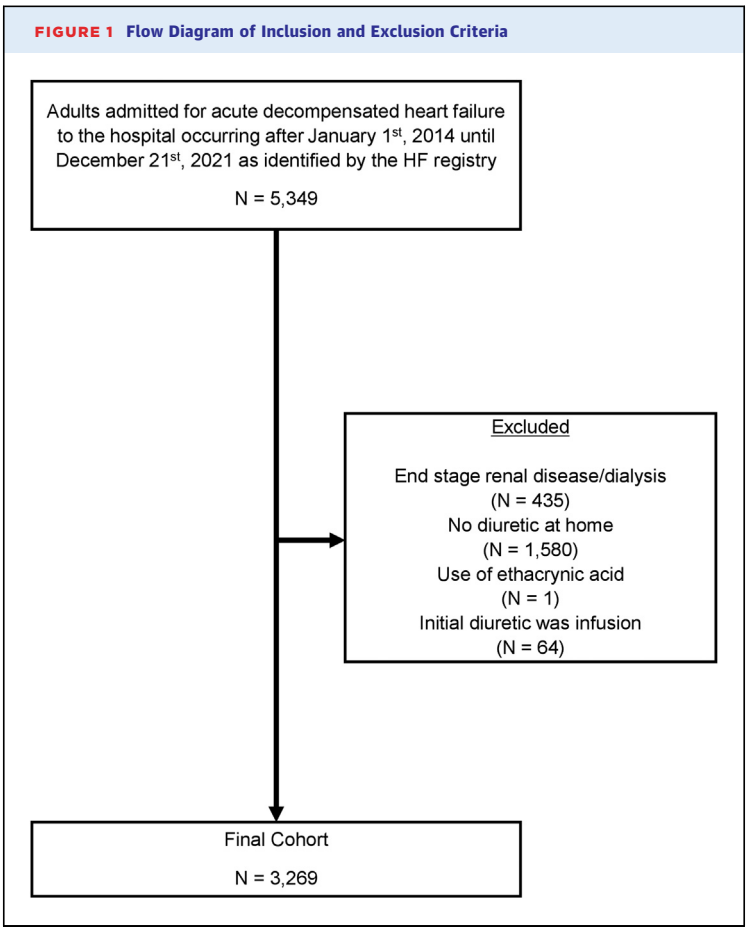
**COVARIATES.** Patient characteristics were collected for use in a national registry including baseline demographics, vital signs, laboratory values, past medical history, concomitant guideline-directed medical therapy (GDMT), HF etiology (ischemic vs nonischemic), left ventricular ejection fraction, and patient origin of hospitalization. Provider characteristics and home and initial hospital diuretic doses were collected from the EHR. Loop diuretics were categorized into available products of furosemide, bumetanide, or torsemide. Origin of admission was categorized as emergency department, transfer from outside facility, or direct admission from clinic. Admitting service was defined by attending physician, which was categorized as cardiology or noncardiology services. Estimated glomerular filtration rate was calculated based on laboratory values using the nonrace-based 2021 estimated glomerular filtration rate equations.[15]

**STATISTICAL ANALYSIS.** Characteristics of patients in the current analysis were calculated stratified by those receiving low, medium, and high home oral loop diuretic dosing and by those who received optimal vs suboptimal initial dosing. We conducted a series of nested modified Poisson regression models using generalized estimating equations with robust error variance to calculate prevalence ratios (PRs) for receiving optimal initial IV loop diuretic dosing associated with home oral diuretic dose.[16] Given the relative frequency of the outcome (>10%), use of prevalence ratios as opposed to odds ratios are recommended.[16] Model 1 was unadjusted. Model 2 included adjustment for age, sex, race, and ethnicity. Model 3 included variables in model 2 and body mass index, left ventricular ejection fraction category (≤40% vs >40%), HF etiology (ischemic vs nonischemic), previous HF admission(s), systolic blood pressure, estimated glomerular filtration rate, serum potassium, brain-natriuretic peptide, prior to admission GDMT use, diabetes, hypertension, atrial fibrillation/flutter, admitting service, origin of admission, and specific oral home and initial IV loop diuretic. Variables selected for adjustment were chosen based on clinical expertise and extensive literature review to minimize confounding.[10,17,18] We repeated the main analysis within subgroups of patients with HFrEF (EF ≤40%) and HFpEF (EF >40%). Additionally, the optimal initial IV loop diuretic dosing associated with home oral loop diuretic dosing, modeled by discrete categorical 20-mg increments, were calculated and displayed graphically using the predicted probability from the fully adjusted model. Next, zero-inflated Poisson regression models, adjusting for the same variables, were used to estimate the association between optimal vs suboptimal initial IV dosing and hospital LOS. Due to the heavily skewed nature of LOS data and the presence of a large proportion of very short hospital stays, we employed zero-inflated Poisson regression models, as supported by Fernandez et al.[19] Modified Poisson regression models with generalized estimating equations and robust error variance were again used to estimate the association between receiving optimal initial IV diuretic dosing and 30-day all-cause and HF-readmission and included all variables in the fully adjusted model from the primary analysis including home oral loop diuretic dose.

We performed a sensitivity analysis in the primary outcome where we utilized an alternative diuretic dosing conversion that is commonly used in practice (bumetanide 1 mg oral = furosemide 80 mg oral = torsemide 20 mg oral; furosemide 40 mg oral = furosemide 20 mg IV).[20] Additional sensitivity analyses were performed in those who did not receive oral metolazone or IV chlorothiazide ("thiazide") within the first 24 hours of admission as well as those who did not transfer from an outside facility.

Two-sided hypothesis tests were used with a significance level of 0.05. All statistical analyses were performed using a standard software package (Stata, version 17.0, StataCorp).

**FIGURE 1** Flow Diagram of Inclusion and Exclusion Criteria




## RESULTS

**DEMOGRAPHICS.** Among the 5,349 adults hospitalized for ADHF between January 1, 2014, and December 21, 2021, 3,269 were included in the final analysis (Figure 1). Of the 2,080 patients excluded, 1,580 (76.0%) were excluded for no baseline oral loop diuretic at home and 435 (20.9%) were excluded due to end-stage renal disease. Among included patients, 1,750 (53.5%), 868 (26.6%), and 651 (19.9%) had a low (≤40 mg FEs), medium (>40-80 mg FEs), and high (>80 mg FEs) home oral loop diuretic dose, respectively. The mean age of the population was 63.1 ± 15.4 years, with 37.9% female, and 82.3% non-Hispanic White (Table 1). The median home oral diuretic dose was 40 mg (IQR: 40-80). Baseline characteristics between home oral dosing groups were similar, with the exception of patients with higher home oral dosing had higher use of bumetanide or torsemide (vs furosemide) as a home oral diuretic ($P < 0.001$) and higher use of bumetanide (vs furosemide) as the initial IV diuretic ($P < 0.001$). Patients receiving optimal initial IV diuretic dosing had higher home oral loop diuretic dosing and had higher use of furosemide as the home oral loop diuretic and initial IV loop diuretic (Supplemental Table 1).

**PRIMARY OUTCOME.** Optimal initial IV diuretic dosing occurred in 2,218 (67.9%) of patients overall. Among patients with low, medium, and high home oral diuretic dosing, optimal initial IV diuretic occurred in 1,672 of 1,750 (95.5%), 520 of 868 (59.9%), and 26 of 651 (4.0%), respectively. The multivariable adjusted PRs for optimal initial IV diuretic dosing associated with home dosing of high and medium, vs low, were 0.05 (95% CI: 0.03-0.07) and 0.66 (95% CI: 0.62-0.70), respectively. The magnitude of association did not substantially differ between nested models (Table 2, Supplemental Table 2). The predicted probability of receiving optimal initial IV diuretic dosing decreased significantly as the prescribed home oral dose increased (Central Illustration). Results of the primary outcome were similar in the subgroups of patients with HFrEF (medium vs low PR 0.66; 95% CI: 0.61-0.72 and high vs low PR 0.03; 95% CI: 0.02-0.07) and HFpEF (medium vs low PR 0.65; 95% CI: 0.59-0.72 and high vs low PR 0.06; 95% CI: 0.03-0.11).

After full adjustment, being prescribed bumetanide as the home oral diuretic (PR: 0.79; 95% CI: 0.70-0.89; $P < 0.001$) and as the initial IV diuretic (PR: 0.83; 95% CI: 0.75-0.94; $P = 0.002$) were independently associated with a lower likelihood of receiving optimal initial IV diuretic dosing. No additional patient- or provider-level factors were associated with the primary outcome.

**LENGTH OF STAY AND 30 READMISSION.** After exclusion of 2 outliers with a LOS >300 days, there was no difference in overall hospital LOS between patients receiving optimal vs suboptimal initial IV diuretic dosing (median LOS 5 vs 5 days, respectively; estimate 1.01; 95% CI: 0.98-1.05; $P = 0.49$).

Eight-eight patients (2.7%) were excluded from the readmission analysis due to in-hospital mortality. In total, 899 (28.3%) of patients were readmitted within 30 days overall, 812 (25.3%) were for HF. Those who received optimal vs suboptimal initial IV diuretic dosing did not significantly differ in 30-day all-cause readmission (25.3% vs 34.5%; PR 0.97; 95% CI 0.80-1.17) or 30-day HF readmission (22.6% vs 31.6%; PR 0.97; 95% CI 0.79-1.19). There was no significant difference in the association between receiving optimal initial IV diuretic dosing and 30-day all-cause or HF readmission for patients with HFrEF vs HFpEF (p-interaction = 0.39 and 0.31, respectively).

**TABLE 1** Patient Demographics by Home Oral Diuretic Dose in an Acute Decompensated Heart Failure Admission

| | Home Oral Loop Diuretic Dose | | | |
|---|---|---|---|---|
| | ≤40 mg Oral FEs (N = 1,750) | >40-80 mg Oral FEs (N = 868) | >80 mg Oral FEs (N = 651) | *P* Value |
| Age, y | 63.1 ± 15.4 | 63.1 ± 16.3 | 63.1 ± 16.5 | 0.99 |
| Female | 640 (36.6%) | 335 (38.6%) | 263 (40.4%) | 0.20 |
| Race/ethnicity | | | | |
| Non-Hispanic White | 1,436 (82.1%) | 703 (81.0%) | 551 (84.6%) | 0.61 |
| Non-Hispanic Black | 84 (4.8%) | 43 (5.0%) | 25 (3.8%) | |
| Non-Hispanic Other | 94 (5.4%) | 47 (5.4%) | 34 (5.2%) | |
| Hispanic | 136 (7.8%) | 75 (8.6%) | 41 (6.3%) | |
| Ejection fraction, % | 40.7 ± 19.1 | 40.6 ± 19.3 | 40.6 ± 18.9 | 0.99 |
| EF <40% | 905 (52.1%) | 444 (51.7%) | 342 (52.6%) | 0.94 |
| BMI, kg/m$^2$ | 33.3 ± 10.9 | 32.9 ± 10.6 | 33.8 ± 10.8 | 0.32 |
| Ischemic heart failure etiology | 589 (33.7%) | 302 (34.8%) | 200 (30.7%) | 0.23 |
| Previous heart failure hospitalization | 494 (28.2%) | 268 (30.9%) | 197 (30.3%) | 0.32 |
| Systolic blood pressure on admission, mmHg | 125.7 ± 24.9 | 126.0 ± 25.8 | 125.7 ± 26.4 | 0.72 |
| Diastolic blood pressure on admission, mmHg | 76.1 ± 17.9 | 76.1 ± 18.0 | 76.0 ± 18.5 | 0.99 |
| Heart rate on admission, bpm | 88.7 ± 20.6 | 89.2 ± 20.4 | 88.9 ± 20.7 | 0.87 |
| Serum creatinine on admission, mg/dL | 1.41 ± 0.80 | 1.44 ± 0.79 | 1.39 ± 0.65 | 0.48 |
| eGFR on admission, mL/min/1.73 m$^2$ | 63.3 ± 26.6 | 61.8 ± 26.5 | 61.9 ± 26.0 | 0.29 |
| Serum potassium on admission, mEq/L | 4.2 ± 0.6 | 4.2 ± 0.7 | 4.2 ± 0.6 | 0.52 |
| BNP, pg/mL | 1,240.3 ± 1,408.4 | 1,300.8 ± 1,390.2 | 1,288.3 ± 1,445.4 | 0.52 |
| GDMT use prior to admission | | | | |
| ACEI/ARB/ARNI | 835 (47.7%) | 384 (44.2%) | 290 (44.5%) | 0.16 |
| Beta blocker | 973 (55.6%) | 502 (57.8%) | 361 (55.5%) | 0.51 |
| MRA | 457 (26.1%) | 240 (27.6%) | 177 (27.2%) | 0.68 |
| SGLT2I | 48 (2.7%) | 26 (3.0%) | 22 (3.4%) | 0.71 |
| Digoxin | 117 (6.7%) | 65 (7.5%) | 42 (6.5%) | 0.67 |
| Hydralazine/Isosorbide | 4 (0.2%) | 3 (0.3%) | 2 (0.3%) | 0.85 |
| Ivabradine | 0 (0.0%) | 3 (0.3%) | 1 (0.2%) | 0.06 |
| Co-morbidities | | | | |
| Hypertension | 1,198 (68.5%) | 607 (69.9%) | 445 (68.4%) | 0.71 |
| Atrial fibrillation/flutter | 691 (39.5%) | 333 (38.4%) | 247 (37.9%) | 0.74 |
| COPD/asthma | 489 (27.9%) | 246 (28.3%) | 175 (26.9%) | 0.81 |
| Diabetes | 696 (39.8%) | 344 (39.6%) | 264 (40.6%) | 0.93 |
| Hyperlipidemia | 779 (44.5%) | 396 (45.6%) | 300 (46.1%) | 0.74 |
| Prior PCI | 326 (18.6%) | 170 (19.6%) | 116 (17.8%) | 0.68 |
| Prior CABG | 232 (13.3%) | 112 (12.9%) | 78 (12.0%) | 0.71 |
| Current smoker | 367 (21.0%) | 176 (20.3%) | 122 (18.8%) | 0.49 |
| ICD/CRT history | 386 (22.1%) | 201 (23.2%) | 166 (25.5%) | 0.20 |
| Cardiology admitting service | 1,153 (65.9%) | 559 (64.4%) | 424 (65.1%) | 0.75 |
| Origin of admission | | | | |
| Emergency department | 1,070 (61.4%) | 497 (57.6%) | 381 (58.9%) | 0.12 |
| Transfer from outside facility | 374 (21.4%) | 199 (23.1%) | 163 (25.2%) | |
| Direct admit from clinic | 300 (17.2%) | 167 (19.4%) | 103 (15.9%) | |
| Home oral loop diuretic | | | | |
| Furosemide | 1,436 (82.1%) | 448 (51.6%) | 41 (6.3%) | <0.001 |
| Bumetanide | 92 (5.3%) | 191 (22.0%) | 216 (33.2%) | |
| Torsemide | 222 (12.7%) | 229 (26.4%) | 394 (60.5%) | |
| Initial IV loop diuretic | | | | |
| Furosemide | 1,637 (93.5%) | 689 (79.4%) | 337 (51.8%) | <0.001 |
| Bumetanide | 113 (6.5%) | 179 (20.6%) | 314 (48.2%) | |

Values are mean ± SD or n (%). *P* values are calculated using chi-square or ANOVA for categorical and continuous variables, respectively.

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blockers; ARNI = angiotensin receptor/neprilysin inhibitor; BMI = body mass index; BNP = brain natriuretic peptide; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; CRT = cardiac resynchronization therapy; eGFR = estimated glomerular filtration rate; FE = furosemide equivalents; GDMT = guideline-directed medical therapy; HF = heart failure; ICD = implantable cardiac defibrillator; MRA = mineralocorticoid receptor antagonist; PCI = percutaneous intervention; SGLT2I = sodium-glucose cotransporter-2 inhibitor.

**TABLE 2 Prevalence Ratios of Receiving Optimal Initial Intravenous Diuretic Dosing in an Acute Decompensated Heart Failure Admission**

| | Model 1 | Model 2 | Model 3 |
|---|---|---|---|
| Baseline home oral diuretic dose | | | |
| FE >80 mg/dose | 0.04 (0.03-0.06) | 0.04 (0.03-0.06) | 0.05 (0.03-0.07) |
| FE >40-80 mg/dose | 0.63 (0.59-0.66) | 0.63 (0.59-0.66) | 0.66 (0.62-0.70) |
| FE ≤40 mg/dose | 1.00 (Ref) | 1.00 (Ref) | 1.00 (Ref) |

Values are PR (95% CI). Model 1 is unadjusted. Model 2 includes age, sex, and race/ethnicity. Model 3 includes variables in Model 2 and BMI, LVEF category, HF etiology, previous HF admission(s), SBP, eGFR, serum potassium, BNP, prior to admission GDMT use, diabetes, hypertension, atrial fibrillation/flutter, admitting service, origin of admission, and specific loop diuretic.

BMI = body mass index; BNP = brain natriuretic peptide; FE = furosemide equivalent; GDMT = guideline-directed medical therapy; HF = heart failure; LVEF = left ventricular ejection fraction; PR = prevalence ratio; SBP = systolic blood pressure.

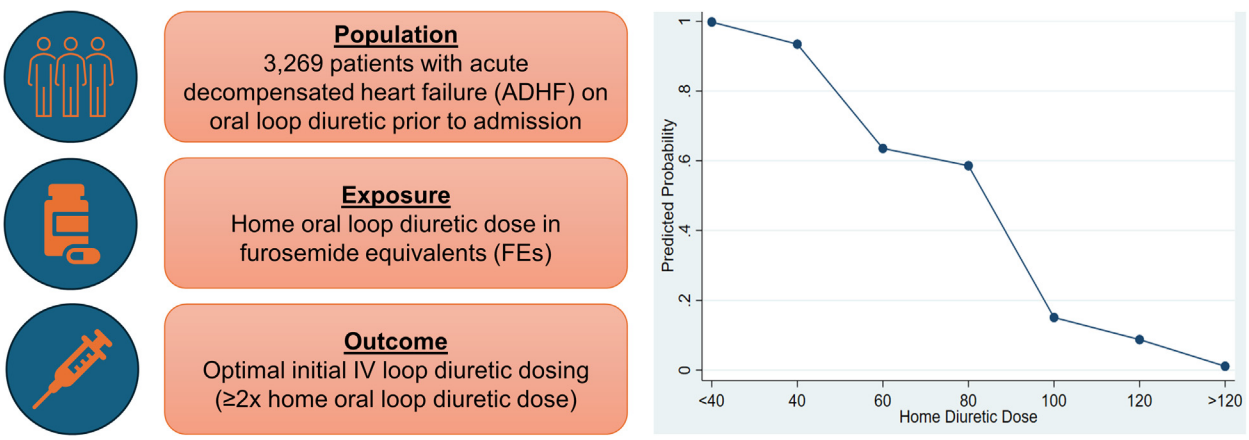
**SENSITIVITY ANALYSES.** Using the alternative loop diuretic conversion strategy, results were consistent with the main study findings. Optimal initial IV diuretic dosing occurred in 1,954 (59.8%) of all admissions with 1,429 of 1,483 (96.4%) of patients with low, 451 of 715 (63.1%) with medium, and 74 of 1,071 (6.9%) with high home dose (medium vs low PR 0.56; 95% CI: 0.51-0.61; $P < 0.001$ and high vs low PR 0.06; 95% CI: 0.03-0.10; $P < 0.001$) (Figure 2). In those who did not receive a thiazide diuretic in the first 24 hours and those who did not transfer from an outside facility, the results of the primary outcome did not qualitatively differ from the main result (Supplemental Table 4).

## DISCUSSION

In the current analysis of adults admitted for ADHF who were on a home oral loop diuretic between 2014 and 2021, optimal initial IV diuretic defined as at least 2 times the home oral dosing only occurred in 67.9% of patients. There was a notable strong association between higher home oral dose and a lower likelihood of receiving optimal initial IV diuretic dosing. For patients with high home oral doses (>80 mg FEs), merely 4% received an optimal initial IV dose. Among those with medium home doses (>40-80 mg FEs), half received an optimal initial IV dose. In contrast, patients receiving lower home doses (≤40 FEs) were more likely to receive an optimal initial IV loop diuretic dosing (96%). There was no significant difference between those receiving optimal and suboptimal initial IV diuretic doses observed in hospital LOS, 30-day all-cause readmission, or 30-day HF readmission. Despite compelling evidence from randomized trials informing optimal initial IV loop diuretic dosing in ADHF, the initial IV dosing for patients hospitalized with ADHF in the current analyses was often suboptimal, particularly among those on higher diuretic doses.

Optimizing HF medical therapy from admission to discharge is critical in reducing morbidity and mortality associated with ADHF hospitalizations. Performance and quality benchmarks such as initiating

**CENTRAL ILLUSTRATION Optimal Initial Intravenous Loop Diuretic Dosing in Acute Decompensated Heart Failure**

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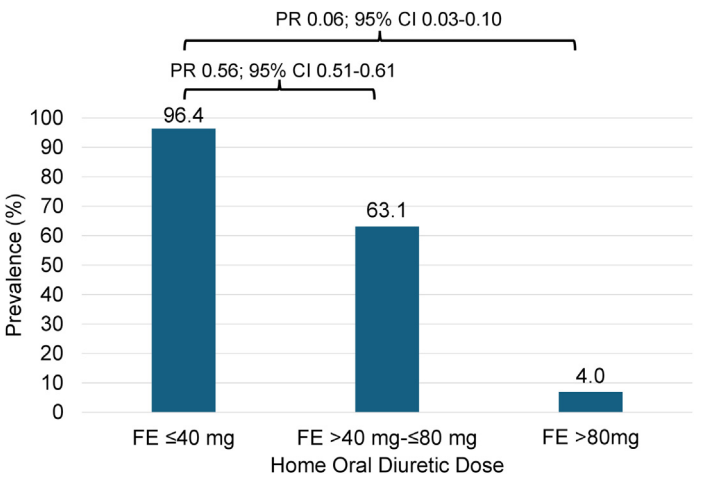
Predicted probability of receiving optimal initial intravenous diuretic dosing by home oral diuretic dose.

GDMT before discharge and implementing thorough monitoring and follow-up postdischarge have been shown to reduce HF readmissions.[21-23] While individual strategies for hospital diuretic management can reduce patient-reported congestion and improve urine output, they have not been shown to reduce hospital LOS, readmissions, or mortality.[8,9,24,25] To enhance the quality of care for diuretic management in ADHF patients, a comprehensive, multidisciplinary approach is required early in hospital management, akin to the early, goal-directed therapy bundles used in septic shock.[26] The concept of early "door-to-diuretic" has shown promising outcomes, associating with reduced 30-day readmission and mortality.[27,28] Therefore, a comprehensive approach should include the early administration of optimal initial IV diuretics, coupled with vigilant monitoring and diuretic adjustment based on patient response to both initial and subsequent dosing.[10,18] The inclusion of key collaborators involved in the first 24 hours of admission is crucial to these time-sensitive efforts and includes first responders, the emergency department team, and any admitting teams (both cardiology and non-cardiology services). The recently concluded Efficacy of a Standardized Diuretic Protocol in Acute Heart Failure and Pragmatic Urinary Sodium-based Treatment Algorithm in Acute Heart Failure trials provide valuable insights into such strategies with standardized natriuresis-guided diuretic strategies in patients admitted for ADHF.[29,30]

Although there may not be differences in clinical outcomes associated with different loop diuretic medications, there are relevant and important pharmacokinetic differences in relative potencies and bioavailability.[13,14,31] These differences dictate relative conversions between loop diuretics and as shown in the current analysis, as the magnitude of dose increases, the likelihood of receiving optimal initial IV dosing decreases. This finding may reflect either a discomfort in practice when selecting an initial dose that surpasses a particular threshold or inadequate pharmacokinetic equipotent conversions between loop diuretics. Both potential mechanisms are further supported in our study by the 20 to 25% lower probability of optimal dosing with the use of bumetanide as a home oral diuretic or as an initial IV diuretic. This may indicate a misinterpretation of pharmacokinetic equivalences between bumetanide and furosemide. Furthermore, results remained consistent in our sensitivity analysis with an alternative diuretic dosing conversion. While these mechanisms may be driven by the goal of minimizing medication-related side effects, there are limited reports of adverse events from exceeding dosing thresholds for IV loop diuretics in patients with ADHF.[10] Hearing loss or tinnitus, rare side effects of loop diuretics, are only notable in rapid IV bolus doses exceeding 500 mg of FEs, which is rarely seen within current HF management.[32] Furthermore, acute kidney injury in the setting of volume overload and diuresis is not associated with long-term worsening renal function, which diverges from the pedagogical “nephrotoxicity” side effect of loop diuretics during initial ADHF volume management.[32,33] In fact, a retrospective analysis of the Renal Optimization Strategies Evaluation-Acute Heart Failure trail demonstrated that worsening acute kidney injury biomarkers among those with ADHF were associated with an improvement in survival vs those without acute kidney injury biomarker changes.[33]

Despite the substantial morbidity linked to suboptimal diuresis in ADHF, the symptomatic relief from congestion provided by optimal dosing, and the American College of Cardiology/American Heart Association Heart Failure Guidelines’ endorsement for rapid, appropriate IV diuretic administration during hospitalization, quality outcome benchmarks are yet to be established.[5-7,9,10,21] Data suggest that up to 50% of ADHF patients are discharged with persistent signs of unresolved congestion, and an inadequate diuretic response often predicts a poor prognosis for HF-related morbidity and mortality.[4-7] The current analysis supports the needs for including initial IV loop diuretic dosing in the management of ADHF. Additionally, GDMT initiation and optimization during hospitalizations should be a central focus in tandem

**FIGURE 2** Sensitivity Analysis with Alternative Loop Diuretic Dose Conversions




FE = furosemide equivalent; PR = prevalence ratio.

with decongestion strategies. Despite the mixed population of HFrEF and HFpEF in our study, the use of GDMT upon admission was suboptimal and should be a focus for future research.[34]

There are notable strengths and limitations to the present study. The rigorous nature of abstraction of data for the national HF registry, as well as the linkage of data with the local EHR, enhances the reliability of the study data. Additionally, this is the first study to assess a benchmark for initial diuretic dosing management in patients with ADHF Furthermore, the median hospital LOS of 5 days (IQR: 3-9) at our institution was comparable to the national median reported in the American Heart Association GWTG-HF registry, which was 4 days (IQR: 3-7). The 1-day longer LOS at our institution may be attributed to our unique service to a large rural and frontier patient population, which presents distinct challenges with discharge coordination related to transportation and placement, often extending hospital LOS. A more contemporary analysis, TREAT-AHF, which included 262,673 admissions from 2015 to 2022, showed a median stay of 5.8 days (IQR: 3.7-9.6).[35] While we adjusted for clinically appropriate confounders, the analysis is limited by its retrospective nature, which may result in unmeasured or residual confounding. For example, patients with high home oral dose were more likely be on bumetanide or torsemide, which may indicate more diuretic resistance or a higher severity of heart failure, ultimately necessitating higher diuretic dosing overall. Additionally, we did not account for total daily dose of diuretics as we tried to capture initial dosing, whereas optimization and escalation typically can occur within the first 24 hours of admission. Repeat encounters for patients who were readmitted were also not captured. Furthermore, this is a single-center study at a HF referral institution, which limits the generalizability of these results without replication on a larger scale. Finally, despite clinical evidence of improved decongestion from doubling the home oral diuretic dose, both the American Heart Association/American College of Cardiology and European Society of Cardiology guidelines have not formalized recommendations on optimal initial IV diuretic dosing, therefore the results should be interpreted with caution.

## CONCLUSIONS

Optimal initial IV diuretic dosing in adults admitted for ADHF only occurred in 67.9% of patients and higher home loop diuretic dose was associated with a substantially lower likelihood of optimal initial IV diuretic dosing. While loop diuretics remain the mainstay of therapy for ADHF, there is a great need to improve current diuretic management strategies.

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**ADDRESS FOR CORRESPONDENCE:** Dr Joshua A. Jacobs, Spencer Fox Eccles University of Utah School of Medicine, 295 Chipeta Way, Salt Lake City, Utah 84112-5820, USA. E-mail: joshua.jacobs@utah.edu.

## PERSPECTIVES

**COMPETENCY IN PATIENT CARE:** Current optimal initial diuretic management is low, especially in patients taking higher home oral loop diuretic doses. Initial optimal intravenous loop diuretic dosing was not associated with 30-day readmission or length of stay.

**TRANSLATIONAL OUTLOOK:** A novel diuretic quality management benchmark and a comprehensive diuretic management strategy are needed to improve quality of care for patients hospitalized for acute decompensated heart failure.

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**KEY WORDS** diuretics, heart failure, hospitalization, quality of care

**APPENDIX** For supplemental tables, please see the online version of this paper.