TRUVETA

Reprieve®

Case study

De-risking clinical development and driving therapeutic innovation for heart failure

Arming early-stage companies with critical real-world data (RWD)

Background

In medtech, the margin for error is slim. Upwards of 90% of funding for an early-stage company may be allocated to engineering and clinical costs, making it essential to de-risk clinical programs. Access to a real-world, contemporary dataset can determine the success or failure of an innovation. However, studying representative, real-world standards of care is often challenging due to the lack of data sources with required clinical context and depth, especially for complex interventions.

Truveta provides complete, timely, and clean regulatory-grade electronic health record (EHR) data from a growing collective of 30 health systems. Data are linked across health systems and integrated with social drivers of health (SDOH), mortality, and claims data for a complete view of patient journeys. Truveta Data is normalized, de-identified, and updated daily.

This case study highlights how Reprieve Cardiovascular, a clinical-stage startup focused on decongestion for heart failure (HF), partnered with Truveta to understand the current standard of care for HF to de-risk their pivotal clinical study and optimize trial protocols

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Challenge

Despite advances in guideline-directed medical therapy, heart failure (HF) readmission rates have worsened over the past decade. Optimizing acute inpatient decongestion is critical in mitigating HF morbidity and mortality, but few new treatment strategies have emerged in recent years. Loop diuretics remain the cornerstone of treatment, requiring careful and frequent dosing adjustments to remove fluid without overtaxing the kidneys – a challenging balance to strike.

The lack of treatment evolution for HF is partly due to the difficulty and cost of studying complex inpatient interventions in depth. The best source of real-world data (RWD) on patients with HF, the Acute Decompensated Heart Failure National Registry (ADHERE), is nearly 20 years old. ADHERE described inpatient HF treatment patterns and decongestion outcomes in a prospective national database of HF hospitalizations across 275 community and academic medical centers. Creating ADHERE took four years and tens of millions of dollars, making regular updates or replication challenging.

Since ADHERE, researchers have used clinical trials, registries, and EHR data to study decongestion outcomes, but these sources have limitations. Clinical trials often involve patients with different characteristics and treatment conditions than those seen in routine practice. The Get With The Guidelines Heart Failure (GWTG-HF) registry lacks detailed data on inpatient medications. A study using Optum EHR data described in-hospital diuretic treatment patterns but did not report changes in weight – a common surrogate marker for clinical decongestion.

Reprieve Cardiovascular needed immediate access to a contemporary, nationally representative real-world dataset with complete, patient-level data and rich clinical detail. This was necessary to validate the need for a new HF decongestion device, optimize clinical trial design, and guide strategic decision-making.

Solution

Reprieve enlisted researchers from organizations including Stanford University, Kaiser Permanente San Francisco Medical Center, and Vanderbilt University Medical Center to study contemporary HF decongestion strategies and identify clinical predictors of weight loss in HF hospitalizations in the US.

Using Truveta Data, they developed the TREAT-AHF (Trajectory and Response to Emergently Administered Therapy for Acute Heart Failure) registry, describing baseline variables associated and benchmarking against ADHERE and GWTG-HF. The analysis required:

Deep clinical context at the patient level:

- **Lab values**: sodium, potassium, creatinine, blood urea nitrogen, and B-type natriuretic peptide
- **Inpatient medication administrations**: oral therapies, adjunctive diuretics, and intravenous therapies (loop diuretics, vasoactives, vasodilators)
- **Biometric data**: body weight and blood pressure over time
- **Procedural data**: implantation of a left ventricular assist device or orthotopic heart transplantation
- **Comorbidity and length of stay data**

Nationally representative data, encompassing diverse regions and health systems, including traditionally underrepresented communities, such as those in rural and low-income areas, and health systems with varying organizational resources

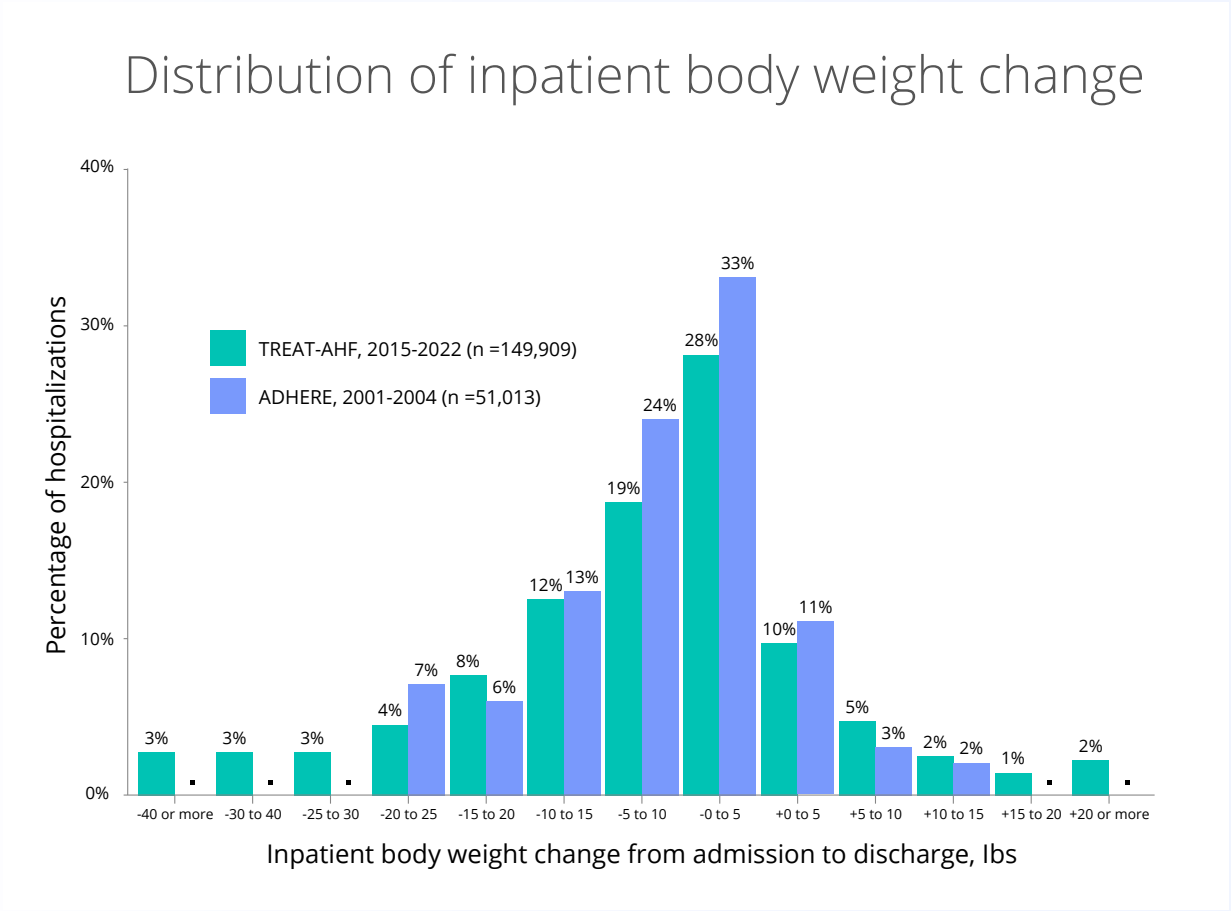
Sufficient scale to ensure large sample sizes after application of rigorous inclusion/exclusion (I/E) criteria

A dynamic analytics platform enabling rapid, iterative I/E testing

Results

Overall, the findings suggest that contemporary decongestion during acute HF hospitalization remains suboptimal, indicating a need for safer and more effective diuretic strategies. Specifically, the researchers found that:

- Changes in body weight, a common marker for clinical decongestion, have not significantly changed in the past 20 years. Median inpatient weight loss was 5.3 pounds, with 33% of encounters showing weight loss >10 pounds vs. 26% in ADHERE, and 20% of encounters showing weight gain, vs 16% in ADHERE.



- Discharge weights were minimally changed or higher than outpatient baseline weights in 60.6% of patients.
- More than 30% of the cohort experienced worsening renal function, which was associated with decreased weight loss.
- Utilization of adjunctive diuretic agents remained low during the study period, despite their importance in acute HF management.
- TREAT-AHF patients had higher frequencies of cardiovascular comorbidities, facility disposition, and inotrope use, suggesting a potentially higher-risk population than prior registry analyses. As a result, inpatient mortality and median length of stay observed in TREAT-AHF were higher than those seen in ADHERE and GWTG-HF.
- There was a significant uptake in use of novel therapies, including ARNi and SGLT2i, during the study period. These therapies were not reflected in older registry data, which could impact efforts to ensure patient safety during clinical trials.

Baseline characteristics of the TREAT-AHF registry compared with other HF registries

		TREAT-A HF (N - 262,673)	**GWTG-HF** (N - 423,333)	**ADHERE** (N - 97,794)
	Study period	2015-2022	2010-2016	2001-2004
Baseline medications	ACEI	24.1	33.7	41.2
	ARB	18.2	14.5	12.0
	ARNI	4.2	–	–
	BB	59.2	68.5	48.4
	MRA	16.2	12.7	10.5
	SGLT2i	1.9	–	–
	Loop diuretic	56.7	60.0	70.5
	Digoxin	6.7	10.8	28.2

Impact

Through their research with Truveta, Reprieve:

- Published two manuscripts in *JACC: Heart Failure* on contemporary HF care patterns (2015-2022) from a patient population 3x the size of ADHERE registry
- Gathered insight needed to optimize trial design by enabling prediction of expected trial enrollment and outcomes

165K

ADHF patient journeys studied to understand real-world outcomes and patient care trends

10K

ADHF patients analyzed as a concurrent real-world control in conjunction with Pilot RCT