The Digital Pill: Using a second-generation AI to improve the effectiveness of chronic drugs

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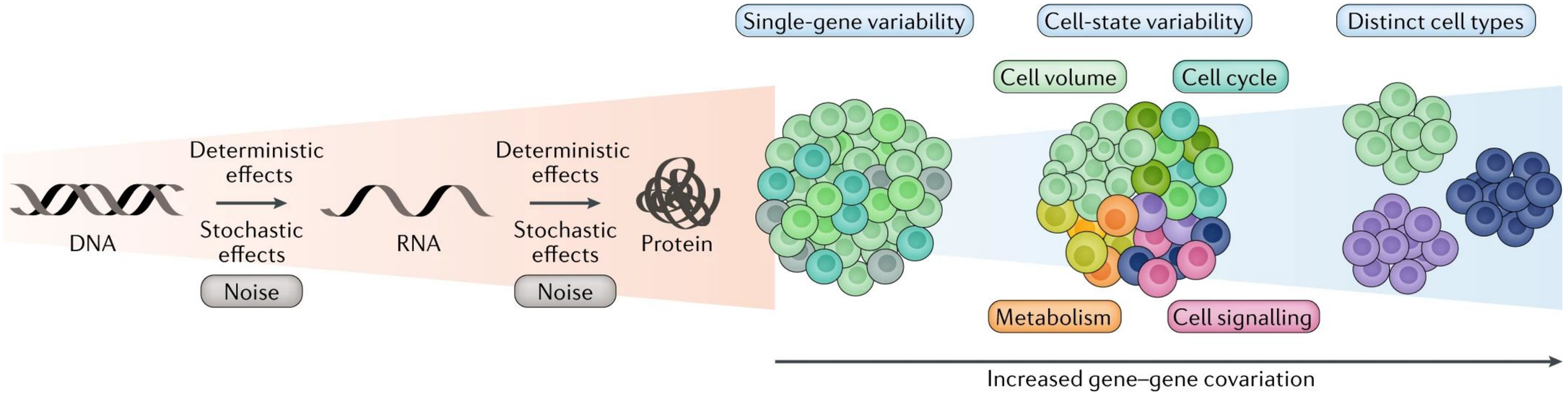
Disclosure

I have financial relationships with the companies below and the content of my presentation does include a discussion of the investigative use of products being developed by the companies below. The studies described were supported in part by several of these companies.

Consultant	Cytovia; Protalix; Sano NASH; Teva; SciM; ENZO; EHD; Plantylight; Abbott; Immuron; Therapix; Tiziana Pharma; Betalin Therapeutics; Immunepharma; JTI; Chiasma Pharma; Nasvax; Alcobra; One Day Pharma; Cure Tech; Lutea; Kamedis; MedWell; Accelmed; Medial; Exalenz Bioscience; Natural Shield; Oberon Sciences;
Ownership Interest	Oberon Sciences; Exalenz Biosciences; Immuron; Code Pharma; TerraGroup;

Noise is essential for the normal function of biological systems



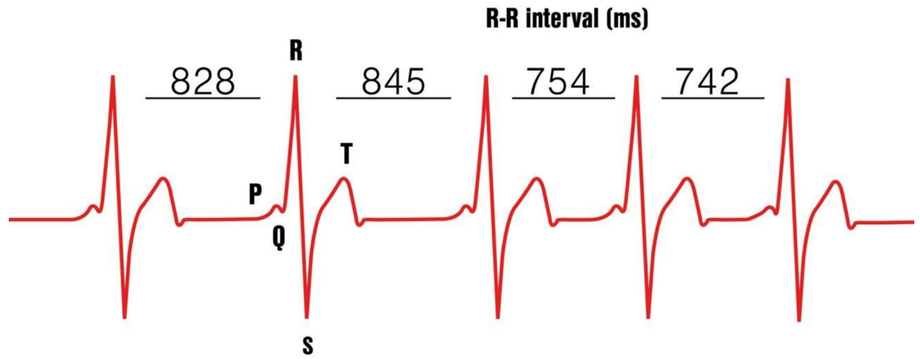
- Noise enriches phenotypic heterogeneity of genetically identical populations
- Enables flexibility and adaptability

Ian Y. J Biosci 2019;44.;Ilan Y. J Comput Biol 2020;27:20-29.;Ilan Y Cell Biol Int 2019;43:739-748.
Casanova MP, Nanoethics (2020) 14:113–122
https://pastel.archives-ouvertes.fr/file/index/docid/945214/filename/Thesis_Hahn.pdf
Physics of Life Reviews Volume 2, Issue 2, June 2005, Pages 157-175
Del Giudice et al., 1998; 2006; Buiatti M, Longo G. Theory Biosci. 2013 Sep;132(3):139-58

Variability in biological systems: Heart rate variability (HRV)

The autonomic nervous system regulates HRV:

- **Decreased** HRV during exercise and stress
- **Increased** HRV during sleep



Loss of variability is associated with a poor prognosis and increased mortality.

Kolben Y, Weksler-Zangen S, Ilan Y.. Obes Rev 2021;22:e13108.
Kenig A, Kolben Y, Asleh R, et al. Front Cardiovasc Med 2021;8:695547
https://www.firstbeat.com/en/blog/*
Goldberger, The Lancet 1996; 347:1312

Chronic medications lose their effect over time

US chronic disease market is valued at > 3 trillion USD/year

- > 40% of patients do not adhere to drugs
- 30-50% of patients lose the response
- “Regular” dosing leads to adaptation and resistance
  - significant burden on health systems: increased admissions, use of expensive drugs
  - significant loss to pharma companies

- Hypertension
- Diabetes
- Depression
- Heart failure
- Epilepsy
- Cancer
- Chronic pain
- Inflammatory bowel disease
- Arthritis
- Asthma
- Rare diseases

Ilan, Y 2020. Overcoming Compensatory Mechanisms. | Mol Ther Methods Clin Dev. 2020 Jun 10;18:335-344 | Nature Reviews 2017; 13:708

The Digital Pill

A drug regulated by patent-protected artificial intelligence

- Improves drug’s efficacy
- Simple for patients and physicians to use
- Data-driven variability in dosing & times of administration within the approved range
- Increases product loyalty and adherence: ensures a long-term sustainable effect

The Digital Pill
A drug regulated by artificial intelligence

Version 0.0:
a reminder to take medications

20 mg BID:
7 AM; 7 PM

Improves adherence by reminding

Low engagement with apps

Version 1.0
Alterations in times & dosages within an approved range

15 or 20 mg BID
7 AM ± 2 hours;
7 PM ± 2 hours

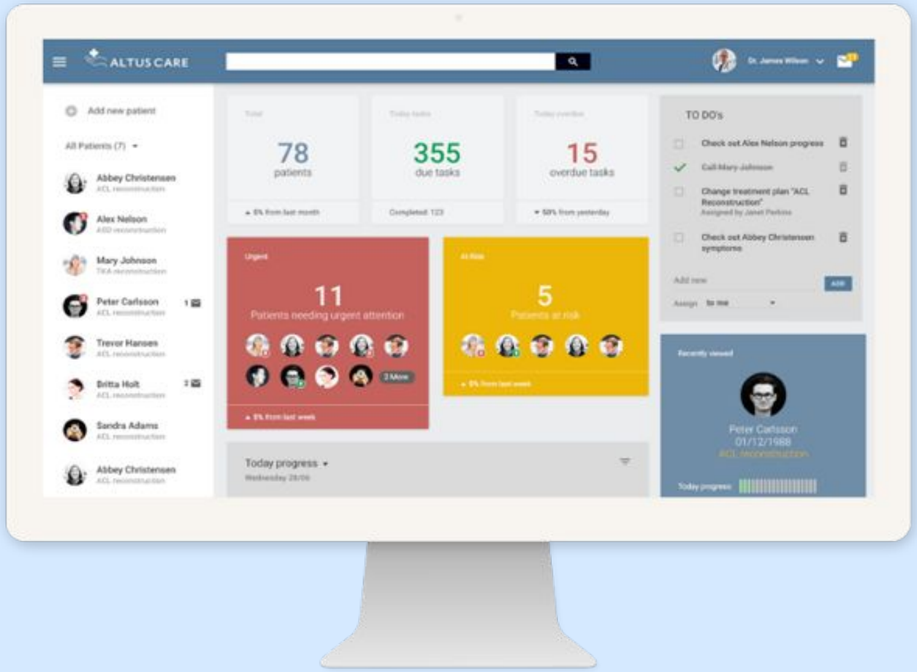
Increases adherence by improving outcomes

FDA exempt “no claim”-based app: A reminder within common practice & a short time to market

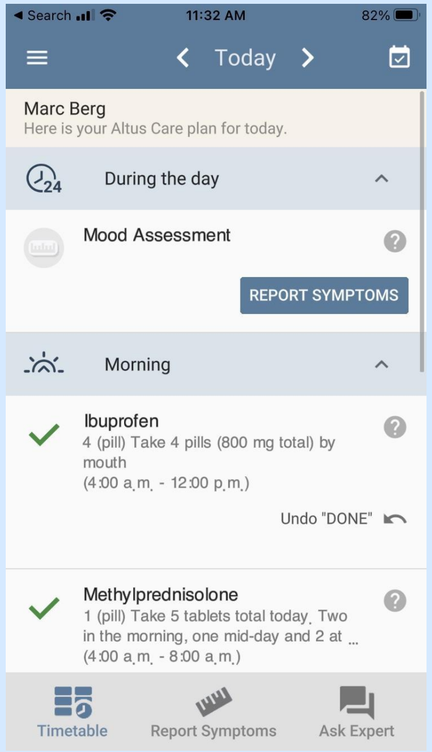
The Next Generation Digital Health Platform

Regulatory approved
In the market

Provider view



Patient view



- Applies to any disease
- Infinitely customizable
- Supports the provider
- Empowers the patient
- Gathers data on response to therapy
- Guiding future treatment
- Remote patient and therapy monitoring

The Digital Pill provides solutions to significant barriers

- Lack of patient engagement in digital health adoption
- Uncertainty about opportunities and risks of digital systems

→
- The Digital Pill ensures adoption by improving outcomes
- Patients view the app as part of their treatment

- New drugs add a burden on health systems

→
- An “Uber model”: using existing drugs
- Reducing costs to health systems
- Increasing pharma revenue

- “Big Data” is insufficient

→
- An insightful dataset-driven improved therapy
- Individualized parameters associated with drug effectiveness, adherence, side effects

www.healthcareitnews.com/news/emea/germany-studies-show-lack-patient-engagement-digital-health-adoption | www.oecd.org/health/health-spending-set-to-outpace-gdp-growth-to-2030.htm | www.nytimes.com/2018/11/12/upshot/why-prescription-drug-spending-higher-in-the-us.html

The Digital Pill increases effectiveness by introducing data-driven personalized regimens

Version 1.0

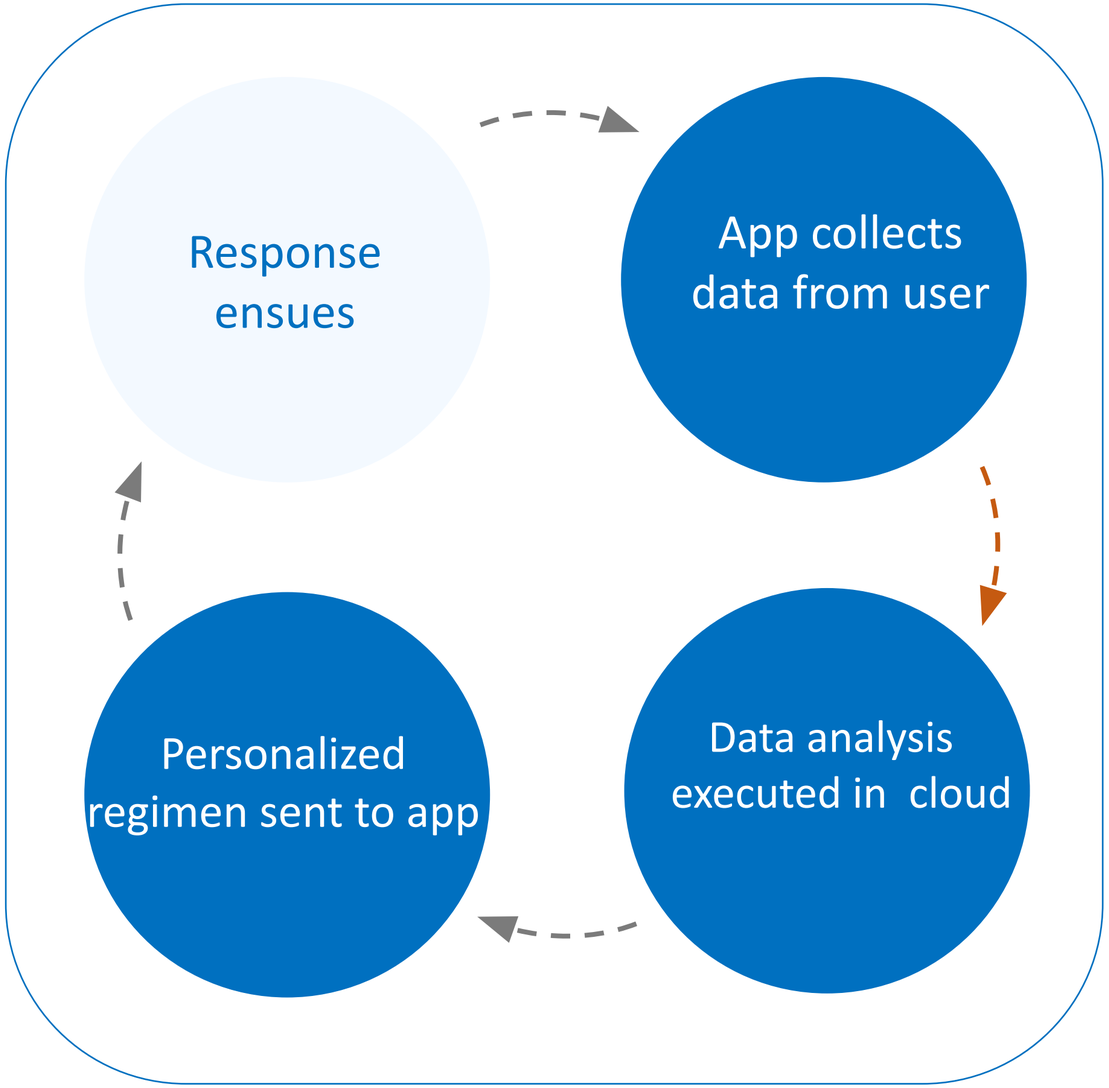
Introduces variability in dosing and times of administration within the approved range

Version 2.0

A closed-loop system that alters variability based on outcome

Version 3.0

Quantifying variability signatures and incorporating them into the algorithm



Reducing complexity
The Digital Pill adds value to all players of the health care system

Patients:
Improve response and reduce side effects

Physicians:
Improve outcomes and adherence

Payors:
Reduce costs

Pharma:
Market disruptor

World-class partnerships

Mass General Brigham

Hadassah University Hospital
Founded by Hadassah, the Women's Zionist Organization of America

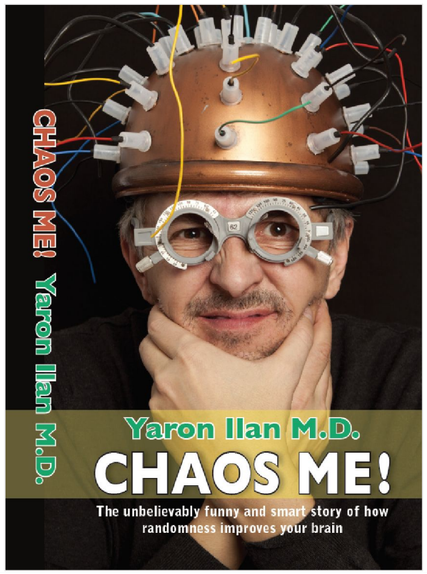
Beth Israel Lahey Health
Beth Israel Deaconess Medical Center

HARVARD UNIVERSITY

Apollo HOSPITALS
TOUCHING LIVES

The Digital Pill: Using a second-generation AI to improve the effectiveness of chronic drugs

- Humanizing AI: getting closer to human biology
- Augmenting physicians, not replacing: assisting in decision-making for improving patients' outcome
- Reducing complexity



YARON ILAN, MD

Chaos me!

THE UNBELIEVABLE FUNNY & SMART STORY OF HOW RANDOMNESS IMPROVES YOUR BRAIN

The scientist who swapped the routine for a random road to success

The Digital Pill: Using a second-generation AI to improve the effectiveness of diuretics in heart failure

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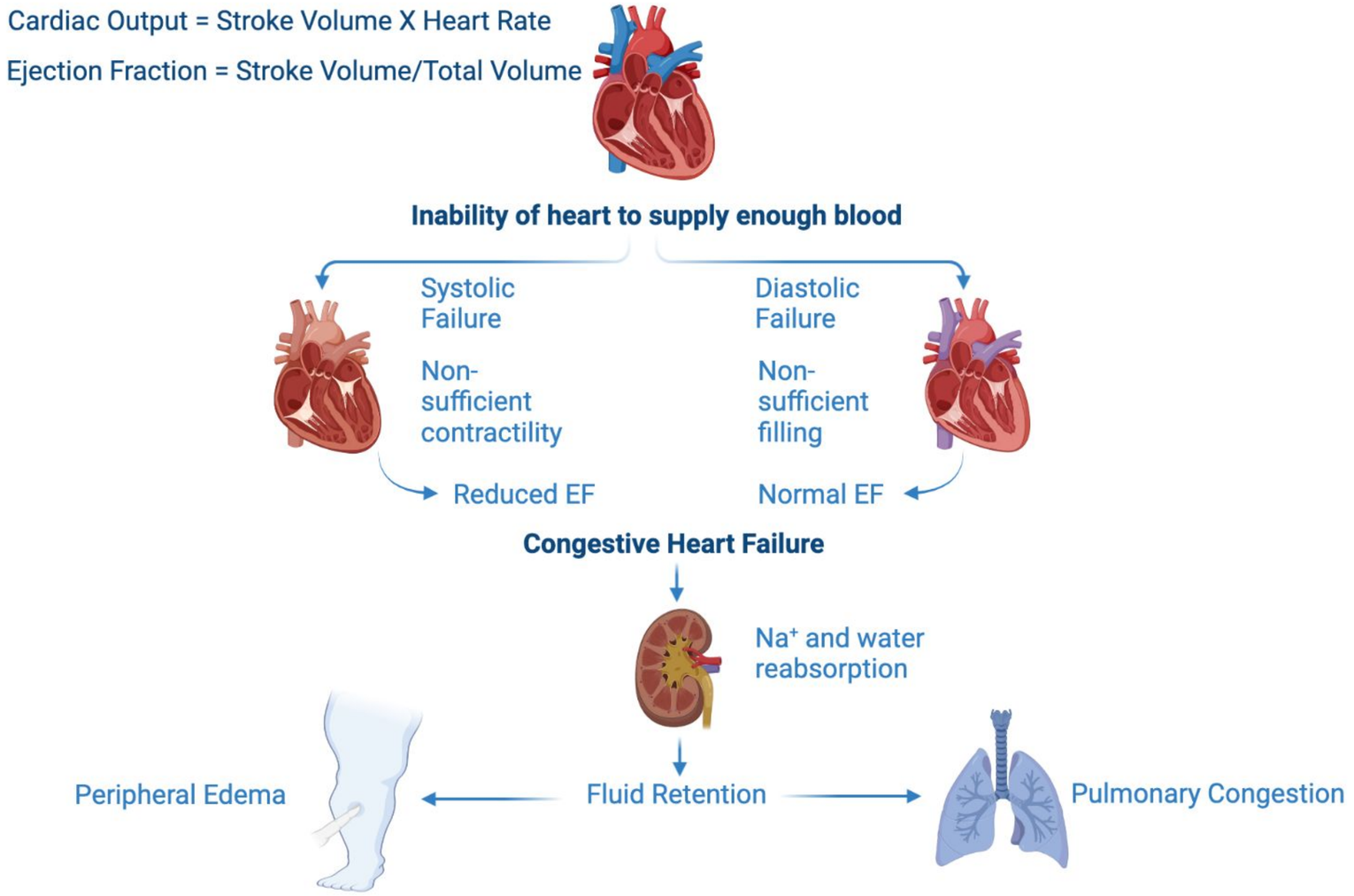
Department of Medicine[1] and Cardiology[2], Faculty of Medicine, Hebrew University and Hadassah Medical Center, Jerusalem, Israel; Stanford University, CA, USA[3]

Stanford University

Hadassah University Hospital

Heart Failure is a complex syndrome and a global pandemic
Diuretic resistance is a major challenge in the treatment of heart failure

- Diuretics are a mainstay therapy for heart failure
- Over a third of heart failure patients develop diuretic resistance
- Attempts to overcome resistance are insufficient



Aims of Clinical Trial

An open-label, proof-of-concept clinical trial sought to investigate how to improve diuretic resistance by implementing variability-based algorithm-controlled therapeutic regimens

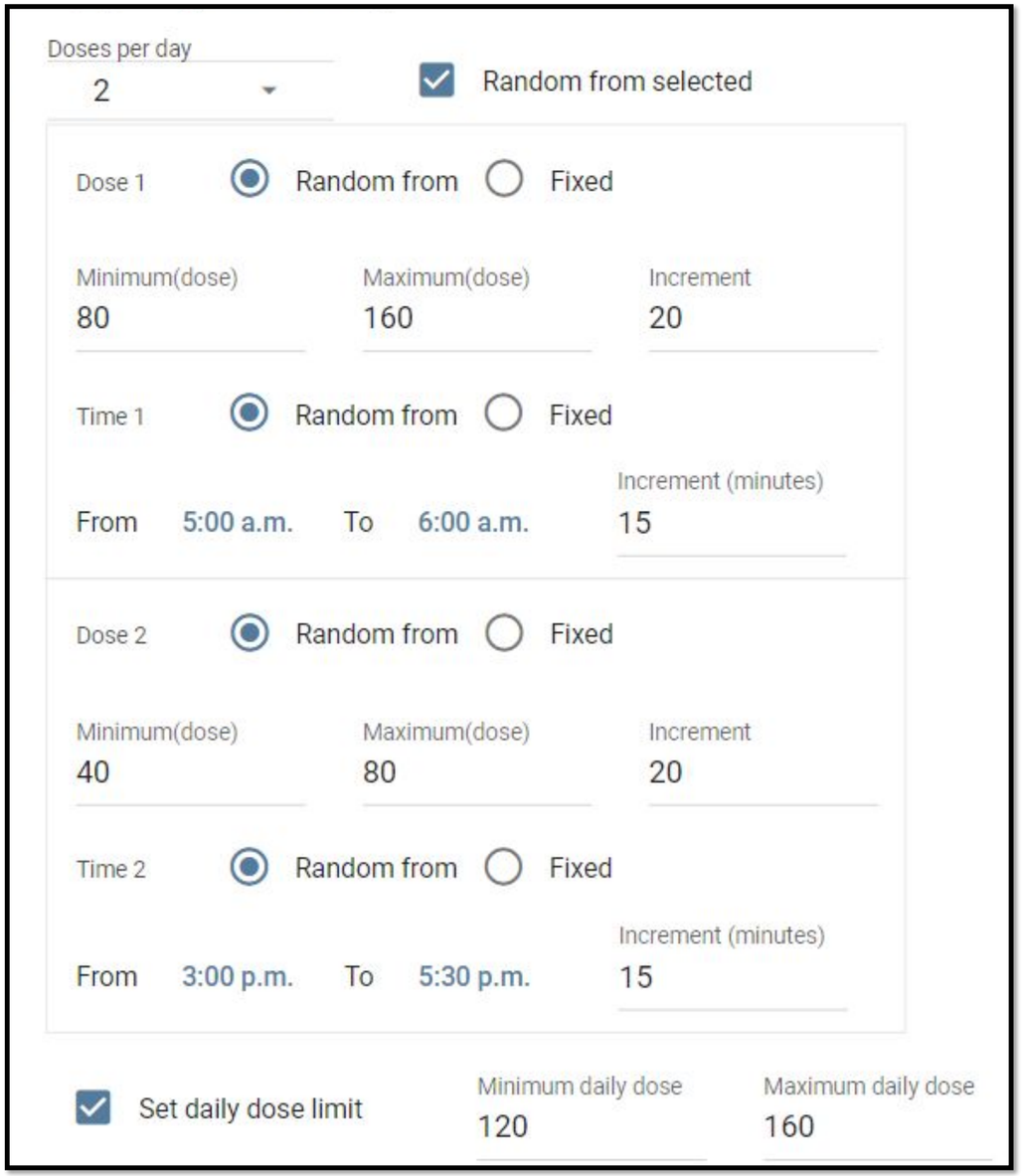
Methods

- Nine heart failure patients with diuretic resistance were enrolled in an open-labeled trial where the app managed dosage and administration times of diuretics
- A variability regimen in dosages and times of administration within pre-defined ranges

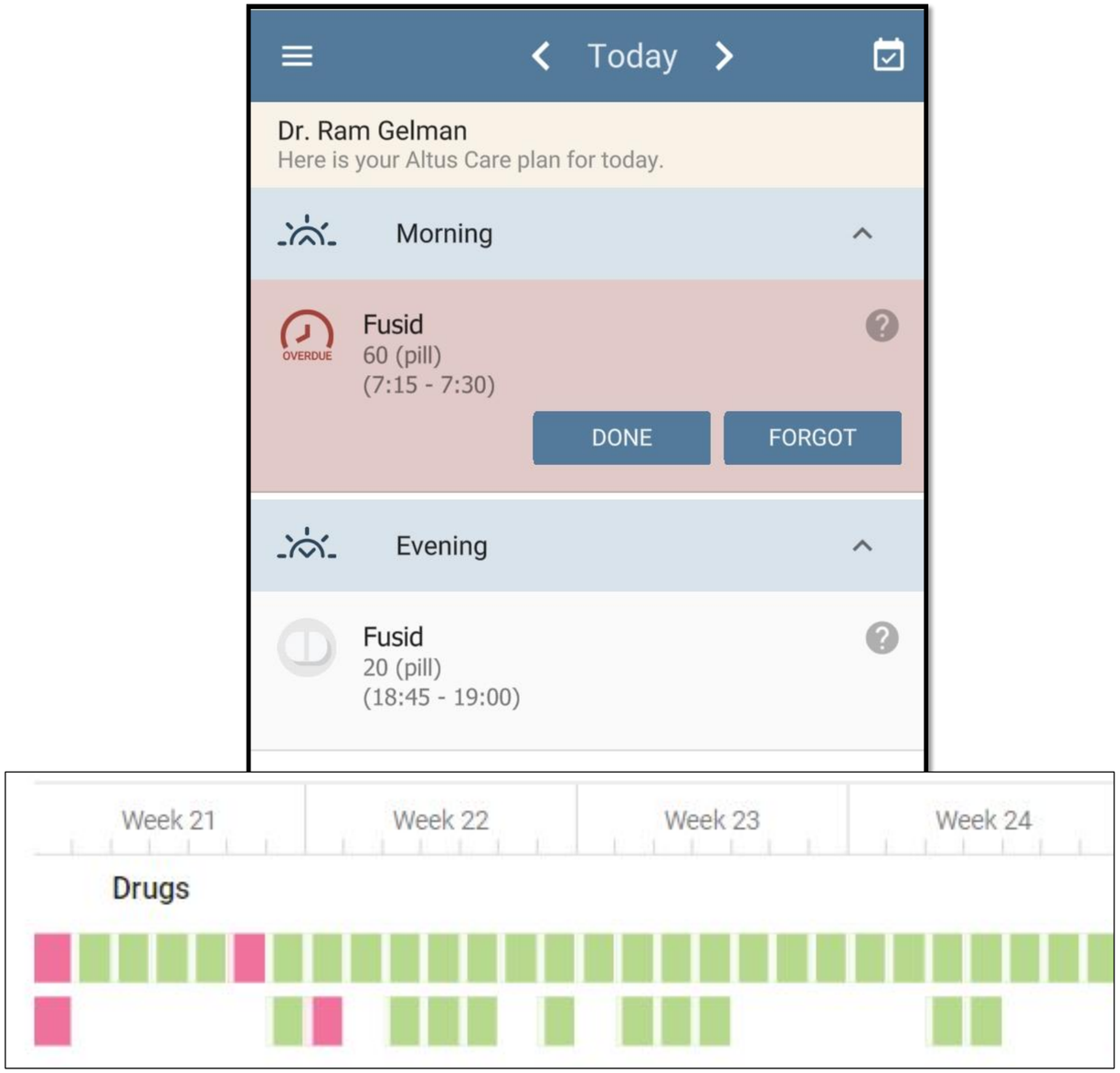
Follow up:

- Furosemide dose- intra venous and per os.
- Kansas City Cardiomyopathy Questionnaire (KCCQ) score
- 6-minute walk test (SMW)
- N-terminal pro-brain natriuretic peptide (NT-proBNP)
- Renal function

A treatment plan

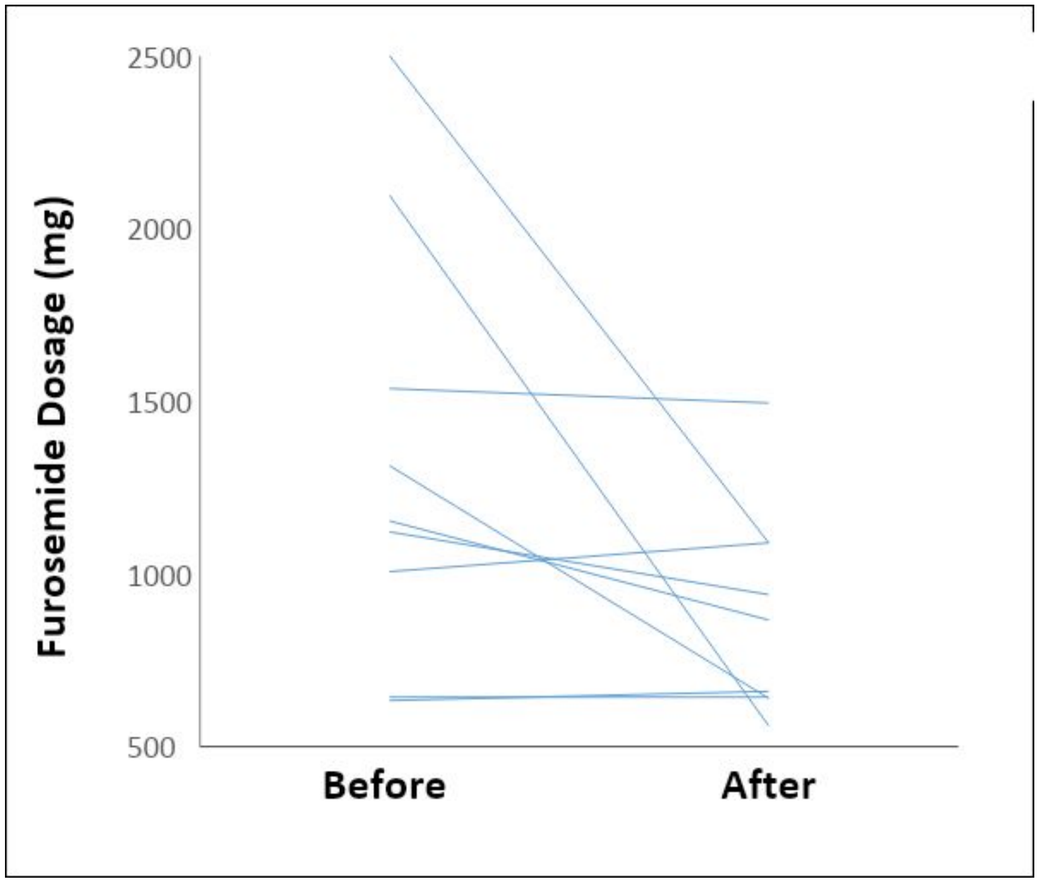


Patient's screen

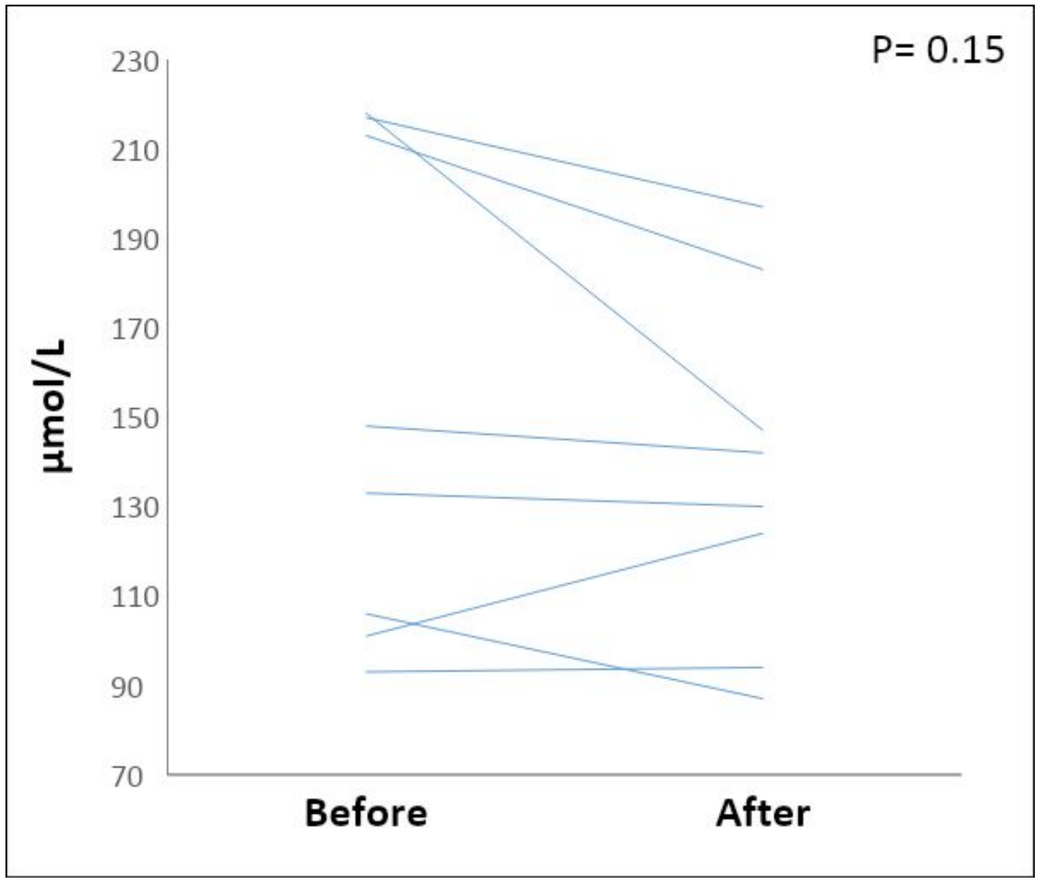


Results

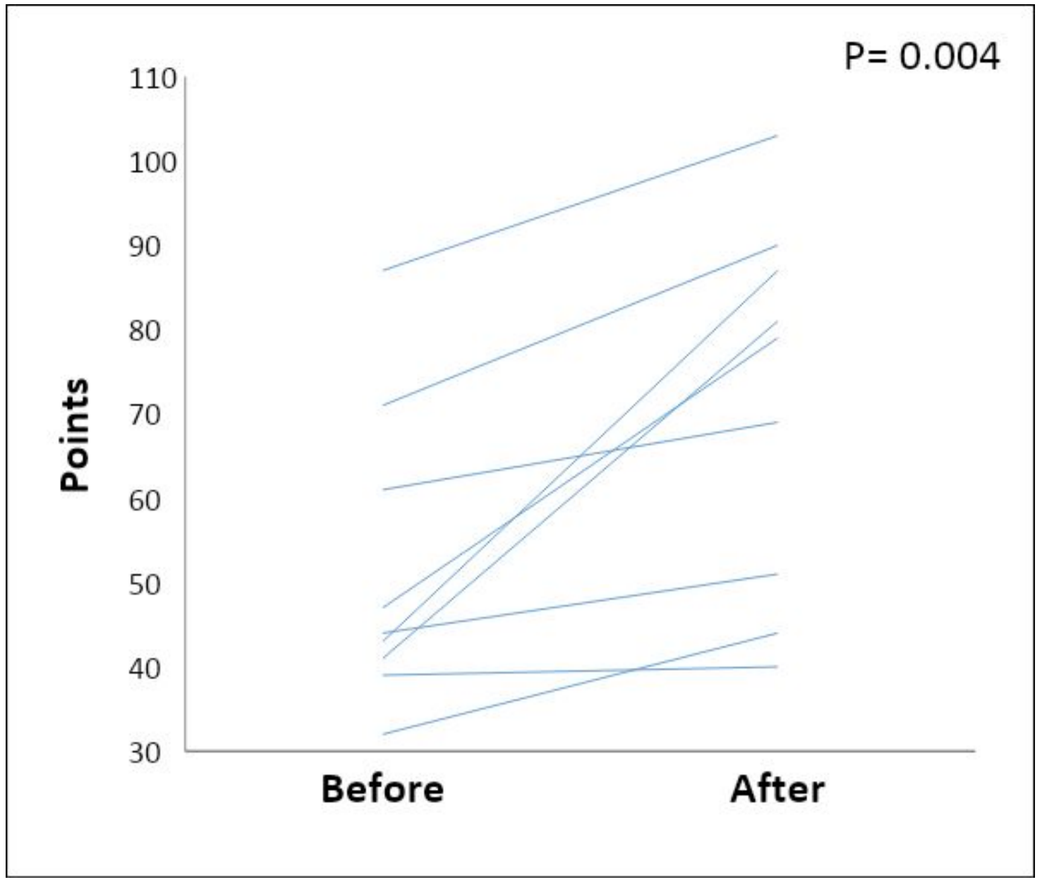
Reduces diuretic dosages



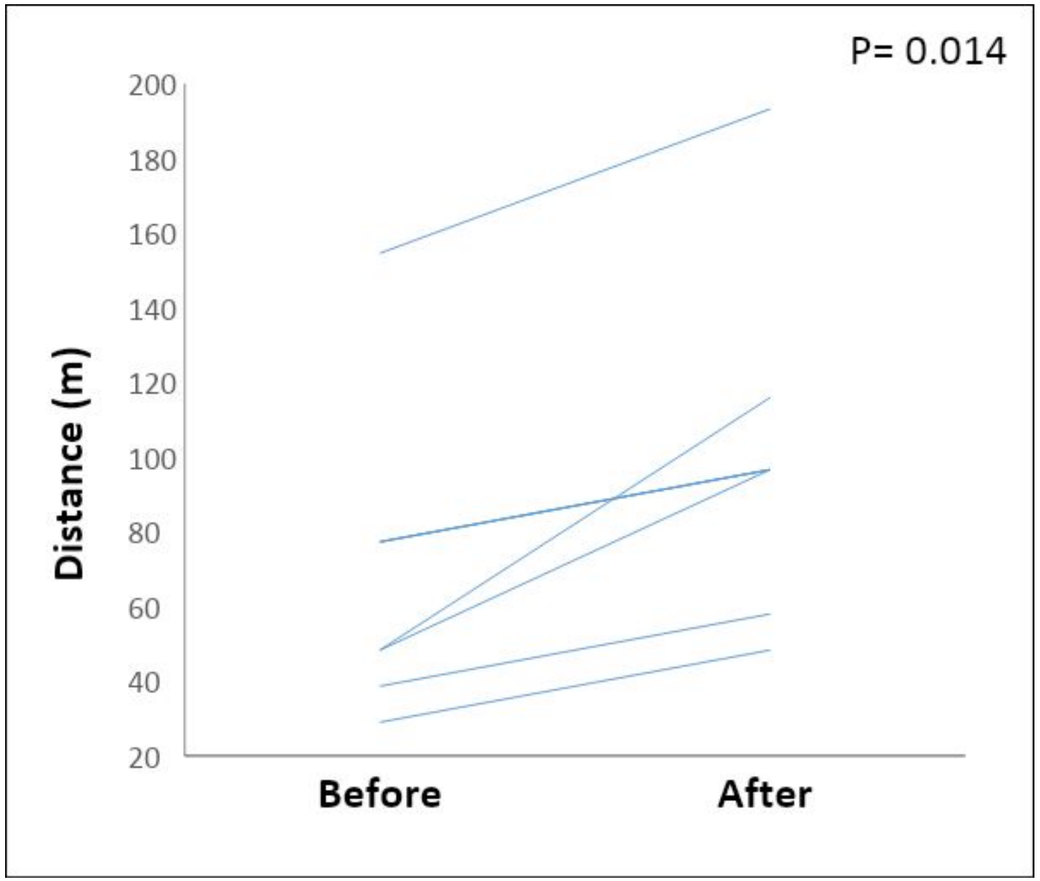
Reduces serum creatinine: improves kidney function



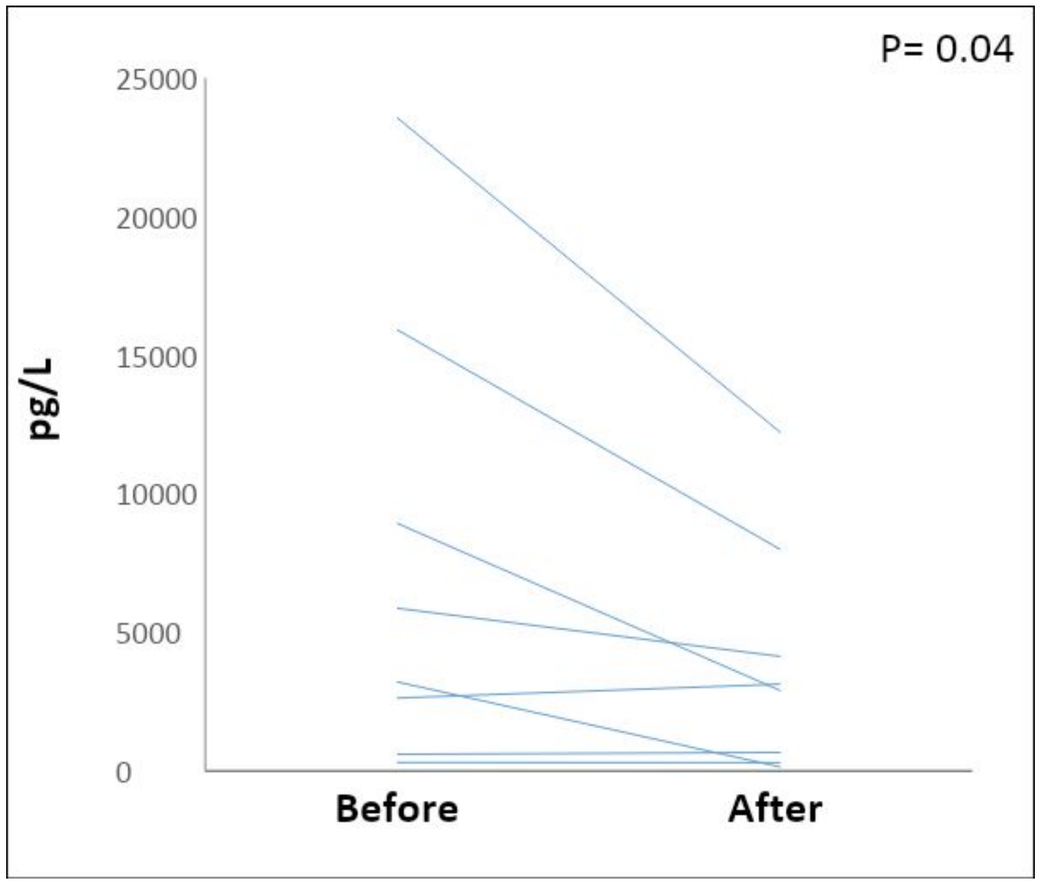
Improves Kansas City Cardiomyopathy Questionnaire: Functional capacity of patients



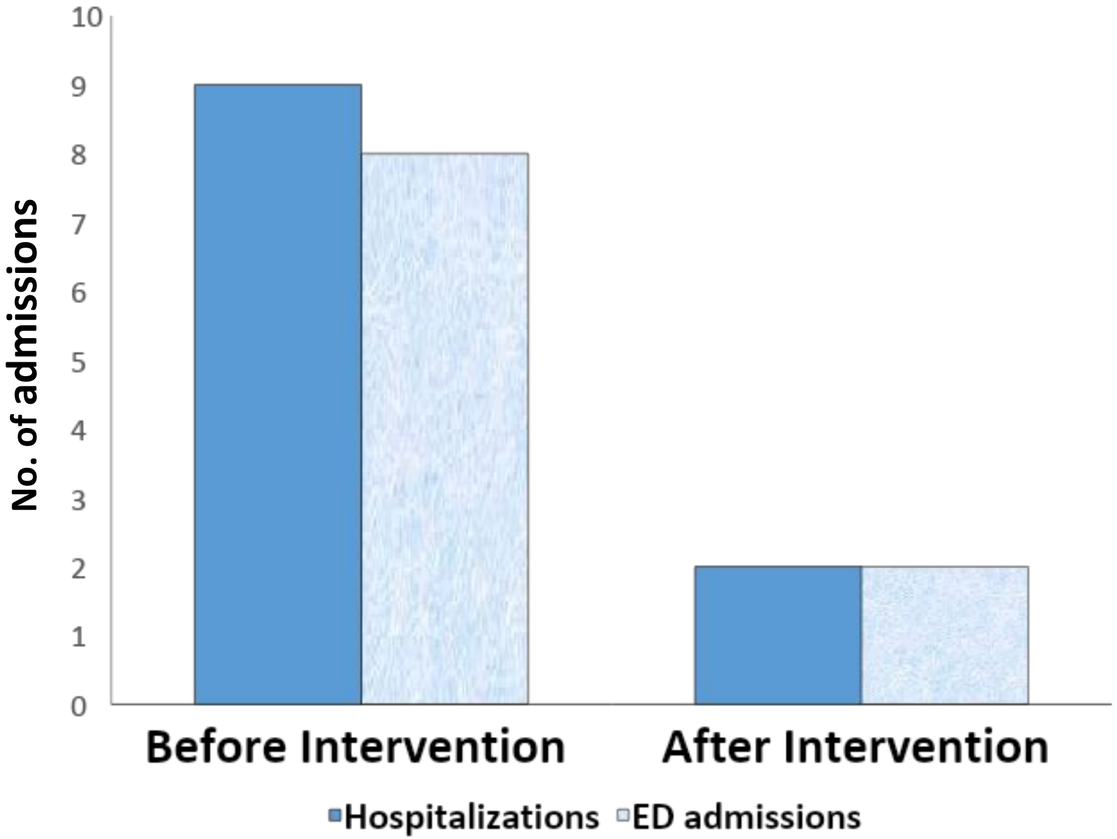
Improves 6-minute walk test



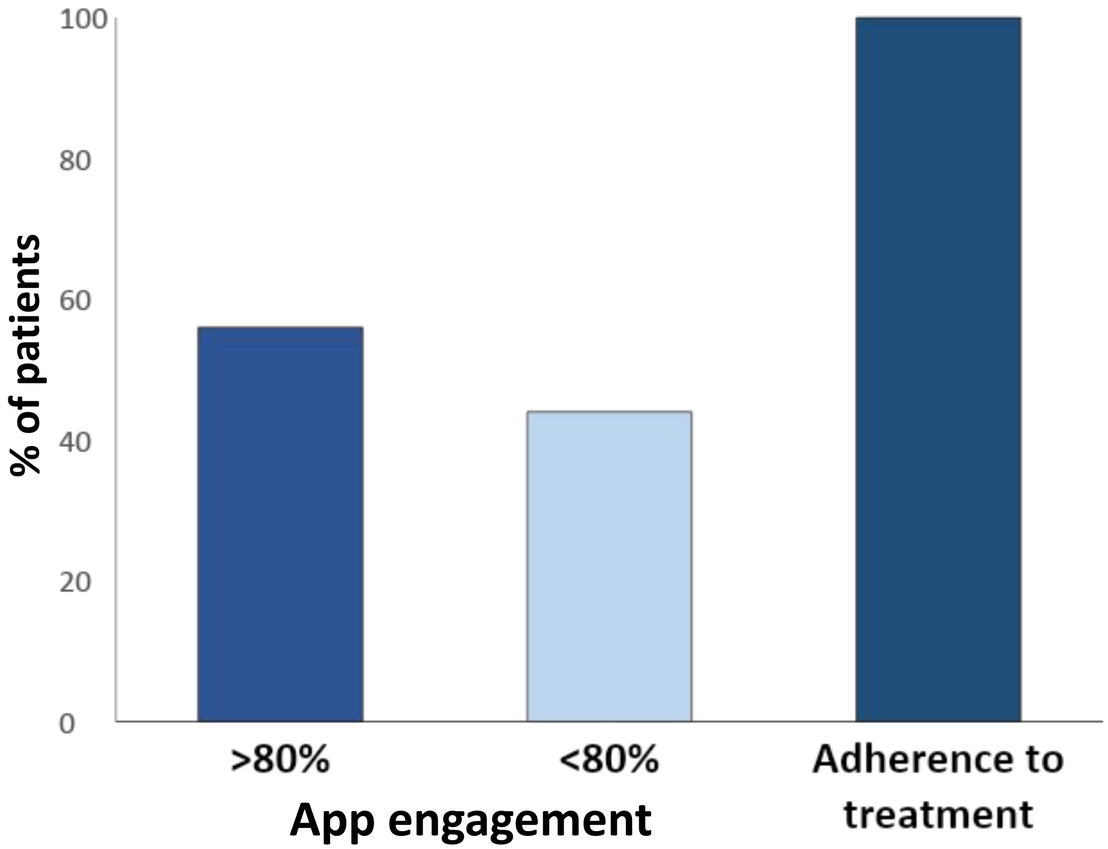
Reduces serum NT-ProBNP: a measure of the degree of severity of heart failure



Reduces hospitalizations and emergency room admissions



Improves engagement and adherence



Limitations

- A small number of patients enrolled
- A single-center, open-labeled
- Application as a reminder
- Relative short period

Summary

- Randomization of diuretic regimens guided by a second-generation personalized AI improves the response to diuretic therapy

- Large prospective studies are needed to confirm these findings

Thank You