AI Trials: Landscape

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Disclosures

- Received research grants from Novartis, Pfizer, Sanofi Pasteur, GSK, Novo Nordisk, AstraZeneca, Boston Scientific and GE Healthcare, consulting fees from Novo Nordisk, IQVIA, Parexel, Amgen, CSL Seqirus, GSK and Sanofi Pasteur, and lecture fees from AstraZeneca, Bayer, Novartis, Sanofi Pasteur, GE healthcare and GSK.

Agenda of this talk

- RCT's testing usability of AI methods in clinical practice
- How AI can be used to improve the execution of RCT's

Why is it important to test AI solutions in RCT's

- Strong political interest in implementing AI as a potential solution for several of the problems we see in the health care system

Sundhedsminister om positiv AI-udvikling: »Vi skal blive bedre til at udbrede det, vi ved virker«

Debat: Kunstig intelligens i sundhedsvæsenet er højt på regionernes liste

15.12.2023

"Sundhedsvæsenet har brug for kunstig intelligens - også i almen praksis og andre steder tættere på borgerne end udelukkende på de store højtspecialiserede hospitaler," skriver Lars Gaardhøj, formand for Danske Regioners politiske arbejdsgruppe om digitalisering og datadeling, i Børsen.

INDLAND

Minister vil bruge kunstig intelligens og rollebytte til at løse mangel på radiologer og radiografer

Manglen på radiologer og radiografer skaber flaskehalser på hospitaler.

LÆS OP ORDBOG TEKST

Ny AI-taskforce skal hjælpe med at frigøre 10.000 job i det offentlige. Minister har kun én afgørende rød linje

Det er afgørende, at der i sidste ende altid er et menneske, der træffer beslutningen. Men ellers har Taskforce for AI i det offentlige ingen begrænsninger i arbejdet med, hvor vi kan bruge teknologien, siger digitaliseringsminister Marie Bjerre.

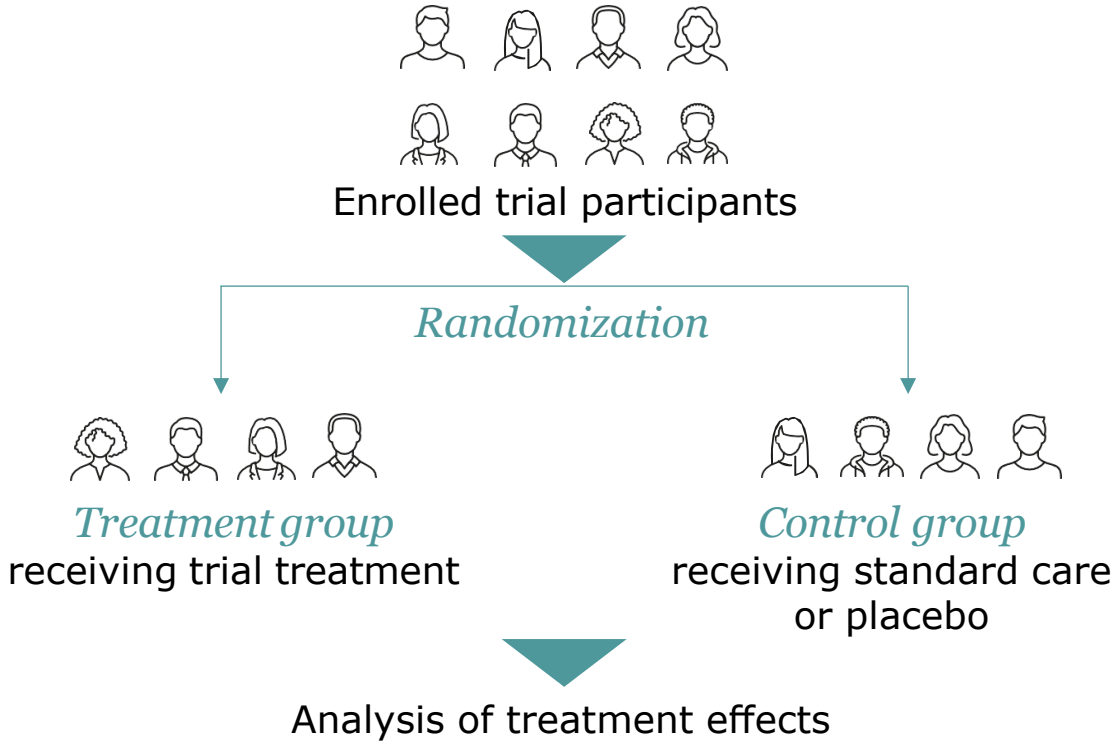
Marie Bjerre vil trække én rød linje for brug af kunstig intelligens i det offentlige - træffes der beslutninger, er det altid et menneske, der skal gøre det, mener hun. Foto: Thomas Traasdahl/Ritzau Scanpix

- If not properly evaluated, AI algorithms could be a waste of time, waste of money, and potentially lead to worse clinical outcomes

• Randomization ensures similar distribution of confounders

Randomized studies[2-4]

- Randomization ensures *a similar distribution of confounders* across groups
- Groups are *comparable* except for the treatment
- A *treatment-outcome relationship* can be determined



- **References: 1.** Steinke DT (2019). In Clinical Pharmacy Education, Practice and Research, pp203-14. **2.** Kendall JM. *Emerg Med J.* 2003;20:164-8. **3.** Ziemssen T. *BMC Med.* 2016;14:81. **4.** Collins R et al. *N. Engl J Med*. 2020;382(7):674-678.

Randomised controlled trials evaluating artificial intelligence in clinical practice: a scoping review

Ryan Han, Julián N Acosta, Zahra Shakeri, John P A Ioannidis, Eric J Topol, Pranav Rajpurkar**

2024

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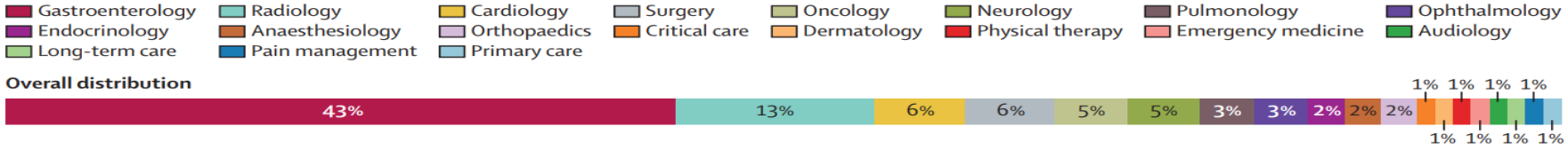

The RCT's identified:

- Were mainly in Gastroenterology

- Were mainly conducted in USA and China

- Were mainly single country and single center trials

- Were small (median size of 359 patients)

Randomised controlled trials evaluating artificial intelligence in clinical practice: a scoping review

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	Statistically significant improvement	No statistically significant effect	Showed non-inferiority	Statistically significant deterioration	Total
Care management	15	1	2	..	18
Clinical decision making	6	1	..	..	7
Diagnostic yield or performance	34	10	1	1	46
Patient behaviour and symptoms	10	3	2	..	15
Total	65	15	5	1	86

Data are n.

Table 1: **Primary endpoints and types for randomised controlled trials of artificial intelligence in clinical practice**

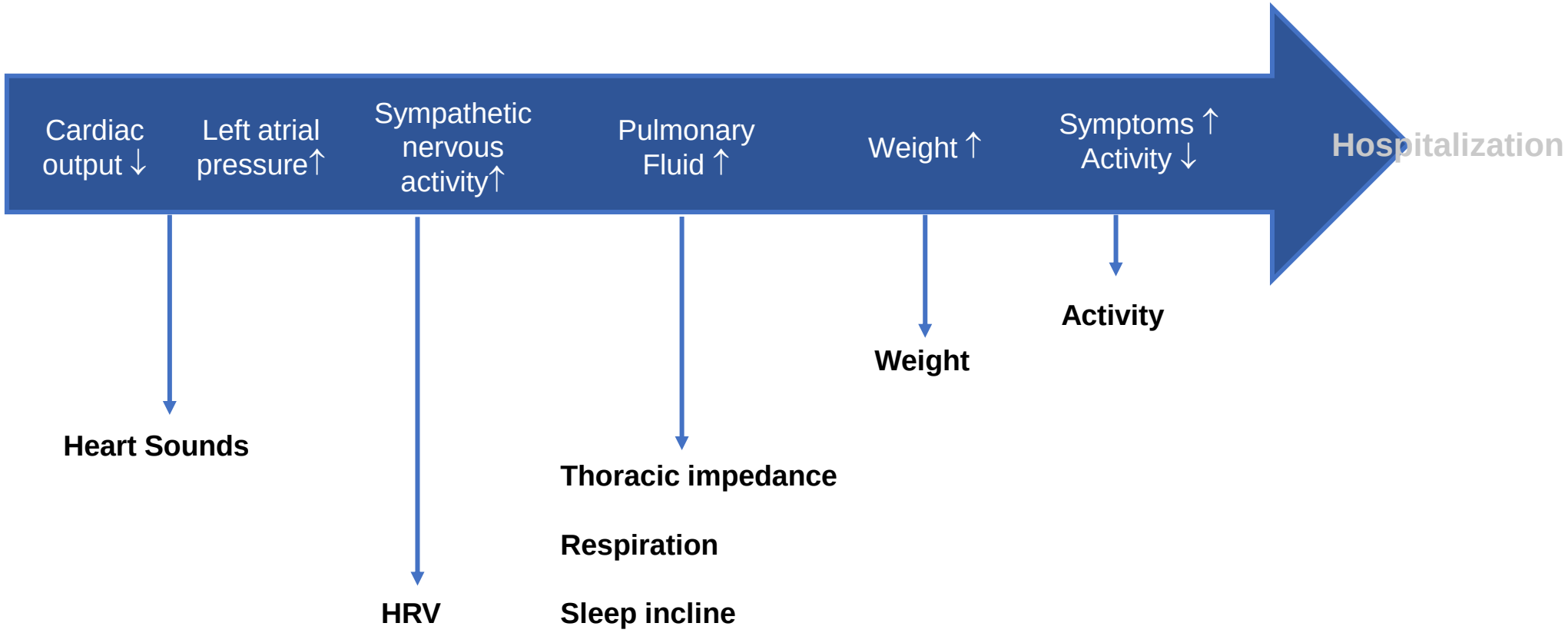
	Statistically significant improvement	No statistically significant effect	Showed non-inferiority	Statistically significant deterioration	Total
AI *vs* clinician	3	1	3	1	8
AI *vs* routine care	16	4	..	..	20
AI-assisted clinician *vs* unassisted clinician	46	10	2	..	58
Total	65	15	5	1	86

Data are n. AI=artificial intelligence.

Table 2: **Primary endpoint results and group comparisons for randomised controlled trials of AI in clinical practice**

Case study: Typical Time Course of HF Decompensation

Early detection using device-based sensors and remote monitoring may prevent or reduce HF hospitalizations



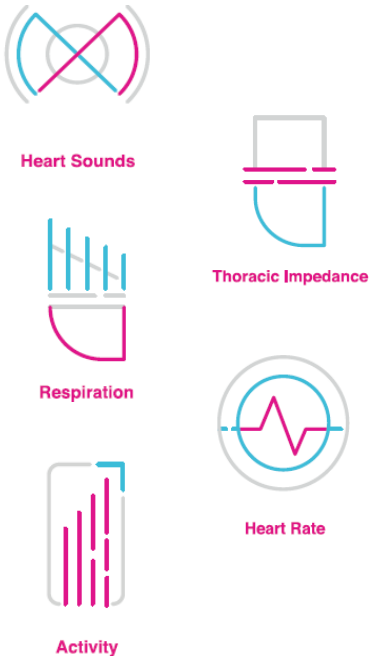
Patterns and time course vary widely, so it's important to monitor all parameters across time

Testing whether AI can assist in combing multiple sensors

MultiSENSE study

Development Group: 500 patient data sets used to develop the algorithm
Test Group: 400 patient data sets used to prospectively validate the algorithm

Feature Selection & Algorithm Optimization



Raw Sensor Data

Feature extraction

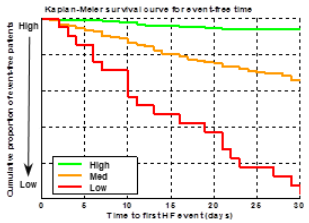
Evaluate individual feature correlation with HF events & identify key parameters

Develop multi-sensor fusion algorithms

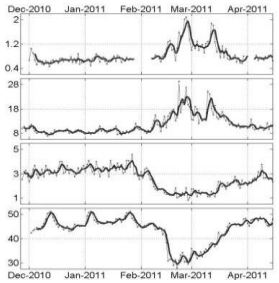
Assess algorithm robustness

Algorithm Concept

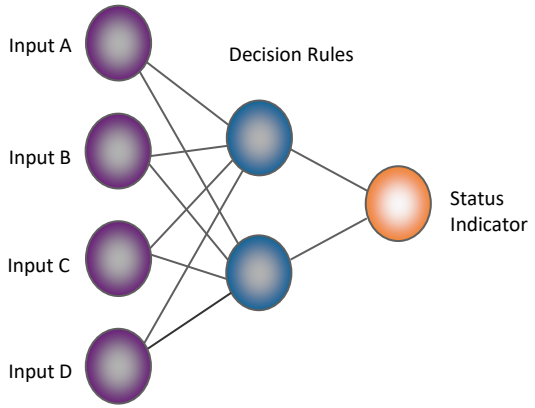
Assess patient risk for worsening HF



Evaluate patients' changes in physiology from their own baseline



Aggregate sensor changes based on patients' risk



Combine into a single, simple, index (0-100)

Issue alerts for worsening HF when crossing thresholds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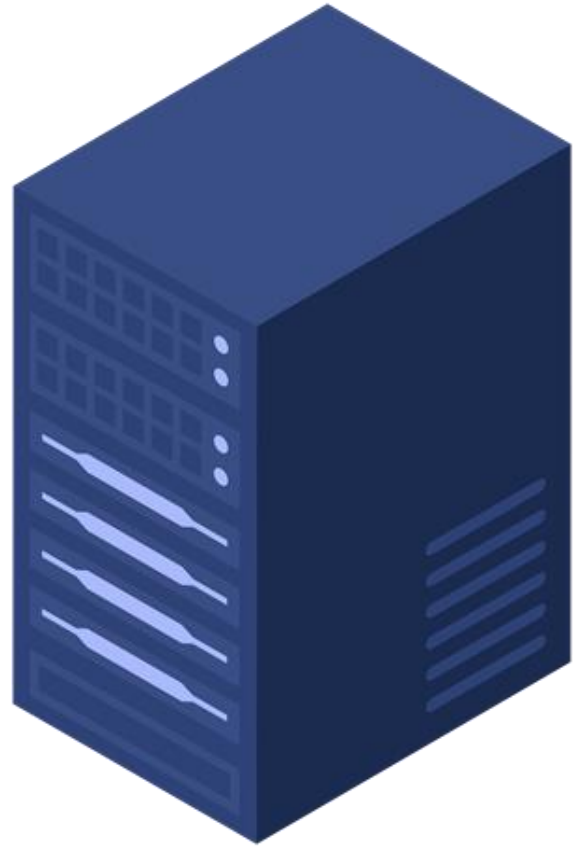


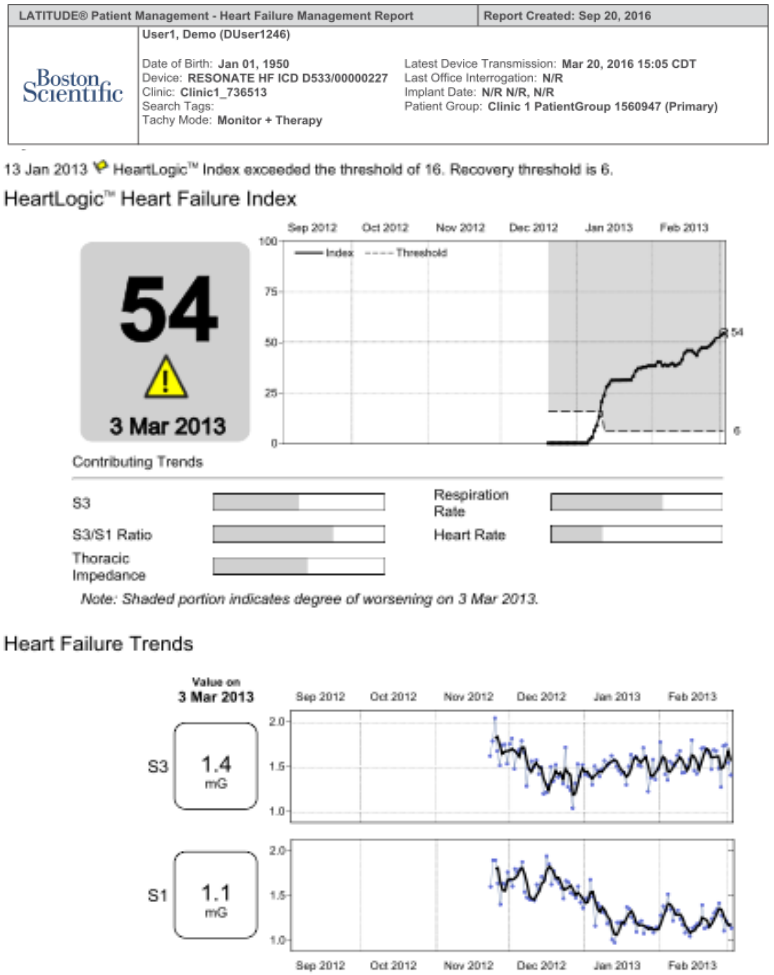
DANLOGIC-HF Trial Design

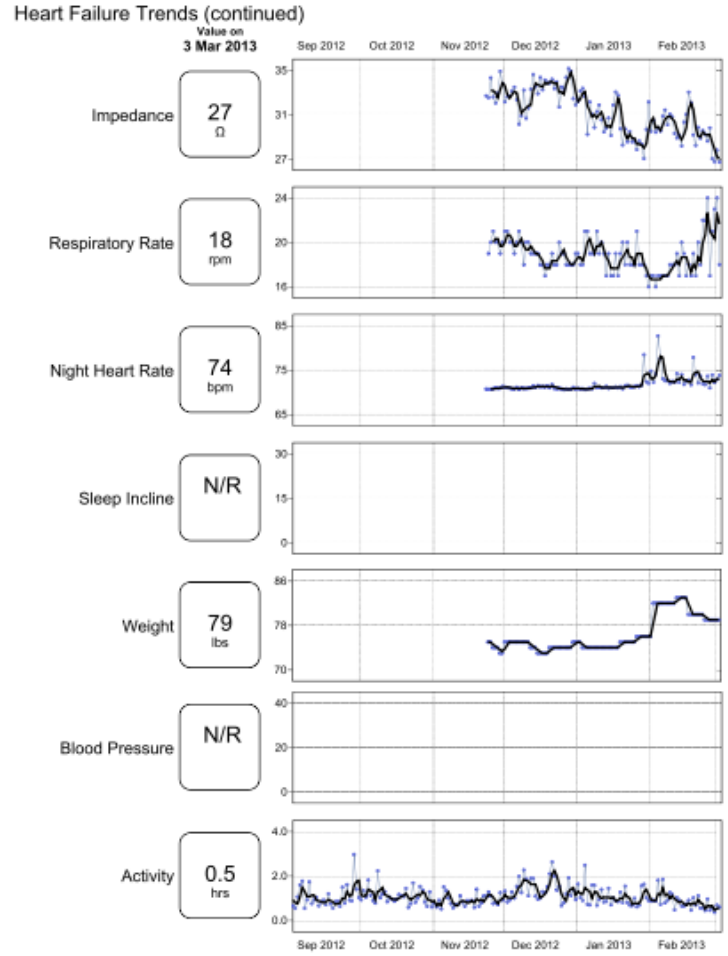
HeartLogic Heart Failure Diagnostic

Implemented in Resonate family ICD and CRT-D devices

Monitored remotely with LATITUDE(TM) NXT Remote Patient Management system

Heart Failure Management Reporting



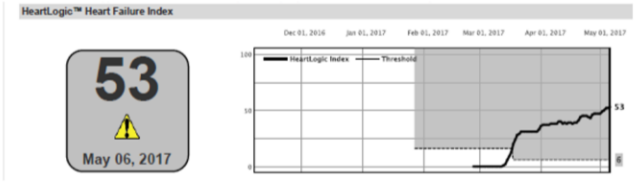


DANLOGIC-HF Trial Design

All Danish patients with eligible CRT-D and ICD devices

N ~ 1500

1:1



Invitation to HeartLogic-guided management

Coordinated by central trial site

Control group

Will not be informed of trial – data collected through registries

Primary endpoint:

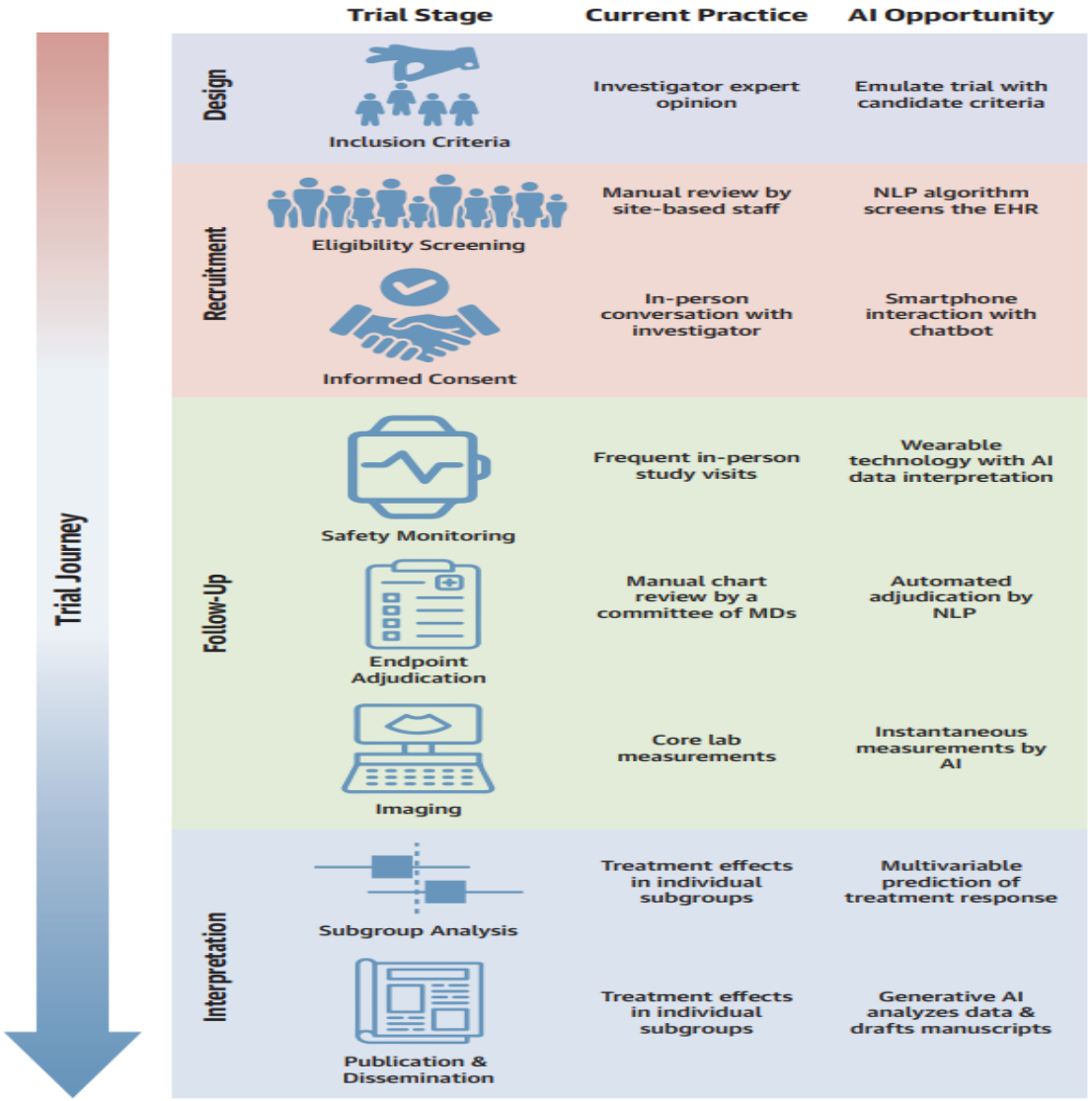
HF hospitalization or all-cause death

Event-driven: 380 events needed for 80% power to detect HR 0.75

Primary analysis: ITT, first-event

Pragmatic trial with registry-based data collection

AI can also be used to improve the execution of RCT's



JACC

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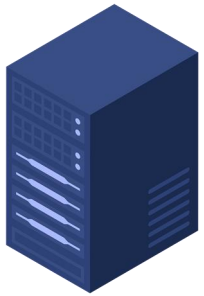
Cunningham et al.
AI in Cardiovascular Clinical Trials

Case: DANUTRIO-HF Trial



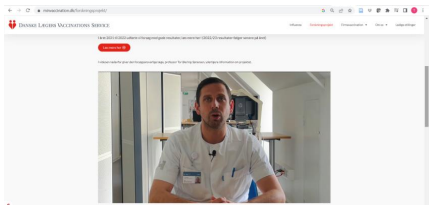
5,064 HFrEF patients randomized 1:1:1:1

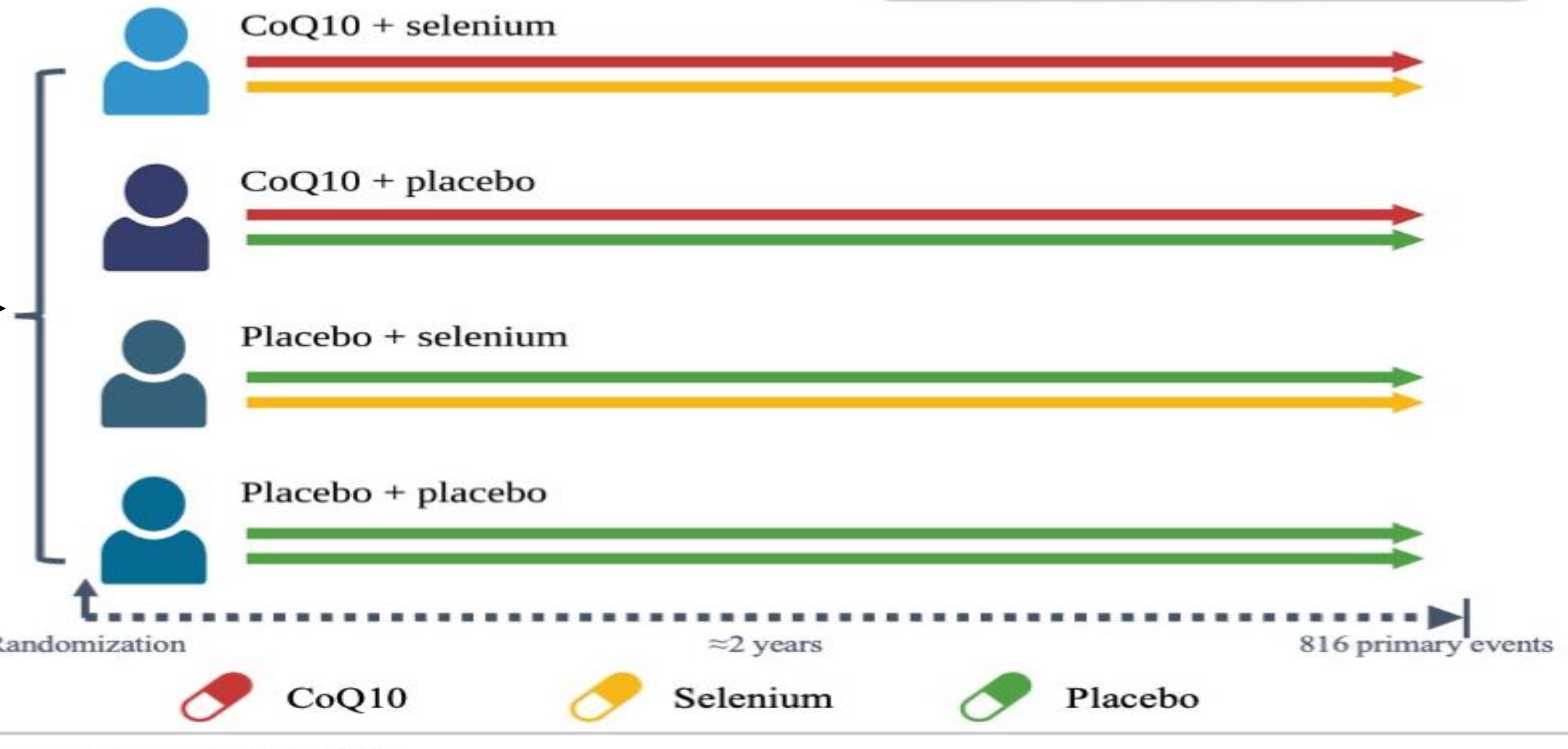
- Identified in the Danish National Registries
- Recruited via DigitalPost

Trial information

- Factorial 2 x 2 randomization
- Follow-up in the registers until 816 primary events occur (estimated follow-up ≈2 years)
- Event evaluation every 6 months

All participants will be randomized 1:1 to receive CoQ10 200 mg/daily or placebo. **All participants** will also be randomized 1:1 to receive selenium 200 µg/daily or placebo. Thus, **all participants** will take two treatments daily (≈25% will receive CoQ10 + placebo, ≈25% will receive selenium + placebo, ≈25% CoQ10 + selenium, and ≈25% will receive two placebo tablets).





Trial objective and primary endpoint

To evaluate the effect of the dietary supplements CoQ10 vs placebo (A) and selenium vs placebo (B) in reducing the primary endpoint of hospitalization for HF and/or CV death (first event) in Danish HFrEF patients

• Case: DANFLU-2

- A pragmatic, registry-based, open-label, active-controlled, individually randomized trial

  Inviting ~ 1,000,000 Danes in the aged 65 and above each season

DANFLU-2
Randomized RWE

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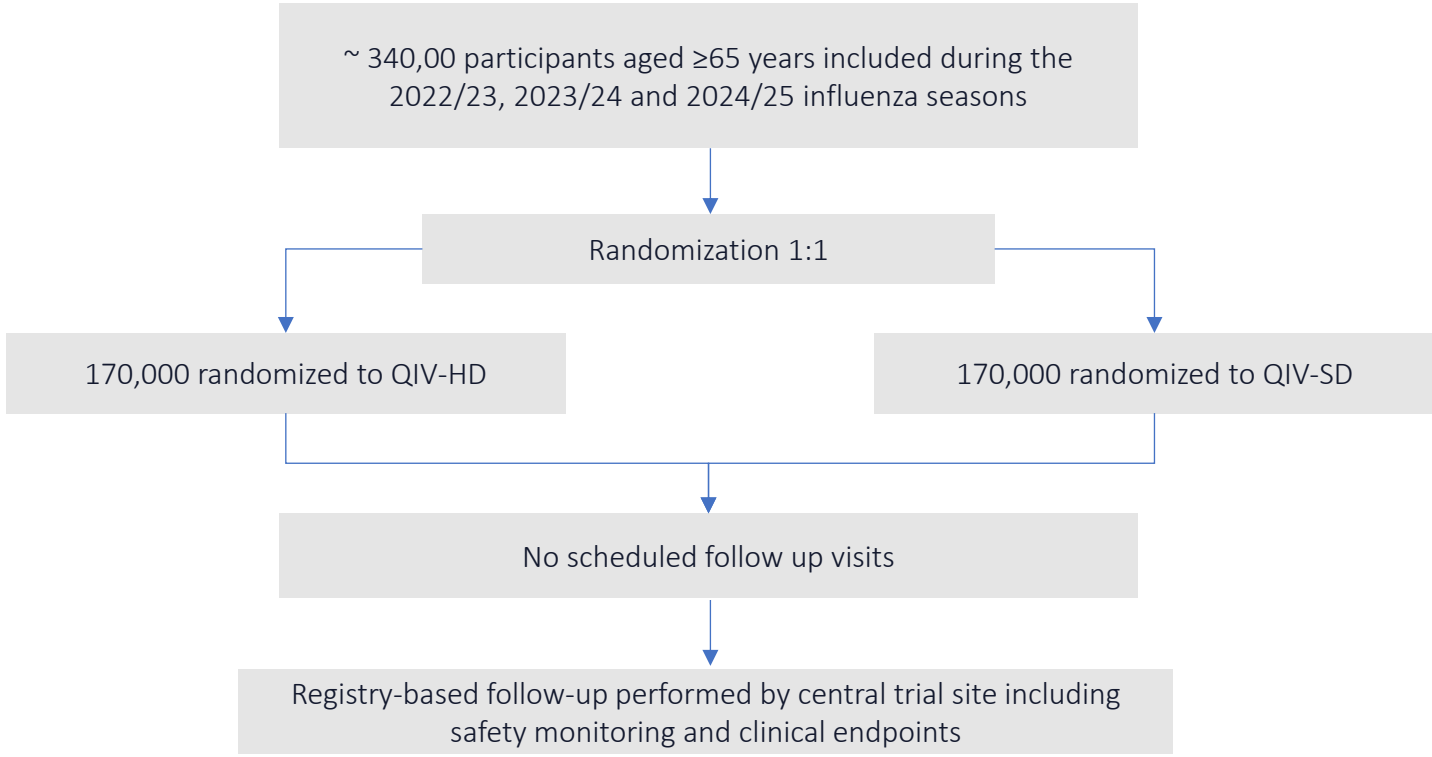
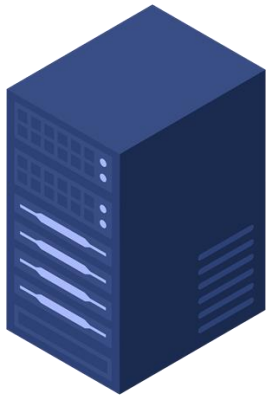
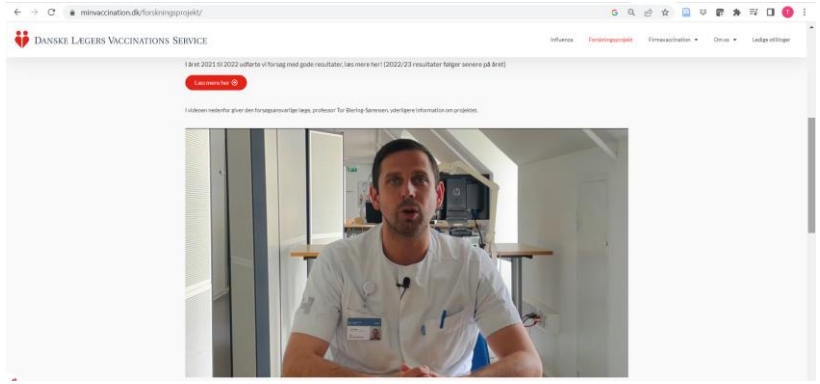


- QIV-HD, high-dose quadrivalent influenza vaccines; QIV-SD, standard-dose quadrivalent influenza vaccines; RWE, real-world evidence.





Vaccination clinic network:

- Open year-round – not just for flu vaccination
- Vaccinates >200,000 persons/year and rapidly upscaling
- Inclusion and randomization
- Administration of study drug

Initial participant data

University of Copenhagen

Region H

Gentofte Hospital

Center for Pragmatic Randomized Trials

- Central trial site
- Study oversight
- Database management
- Nationwide access to all medical records and lab results

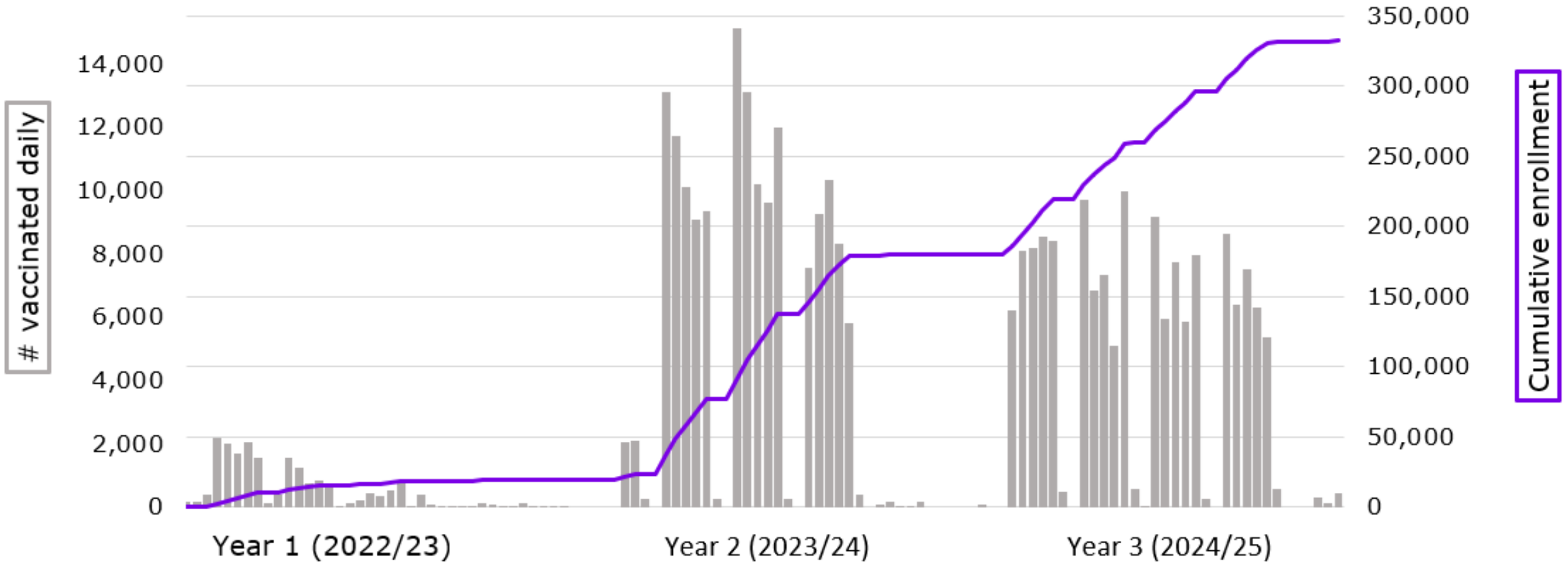
Participant SSN

Baseline characteristics and outcomes

Registry data:

- Nationwide tax-funded public health system
- Nationwide registries can be crosslinked using social security numbers (SSN)
- Every hospital contact, death, redeemed prescription is captured in the registries

DANFLU-2 Total Randomization



PRO & Swab substudy: ~2000 individuals ~10000 individuals

A total of **332,438 participants randomized** during 3 seasons

• Conclusion

How to improve RCT's testing AI methods in clinical practice:

- Future trials assessing the usability of AI methods for improved patient care should include more than one center and include more countries to increase generalizability
- They should be large and sufficiently powered
- Pre-registration, adherence to the CONSORT-AI guideline and publication of negative trials would minimize the current risk of publication bias
- Patient outcomes should be included when relevant
- Cost-effectiveness analysis should be implemented

How can AI be used to improve the execution of RCT's

- Identifying eligible patients for the study
- Patient screening
- Patient enrolment (direct contact to patients through the registries)
- Recording patient consent (electronic consent)
- Obtaining information about baseline characteristics
- Obtaining information about endpoints
- Reduced burden on
  - site staff
  - participants
- Enable novel trial designs (e.g. direct-to-participant, embedded registry trials)
- Lower cost → larger trials, more trials

Thank you for the attention

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