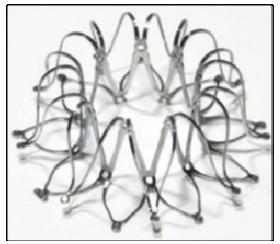
Corvia Medical IASD Clinical Results

Daniel Burkhoff

Cardiovascular Research Foundation

Standing in for: Mark Petrie, University of Glasgow

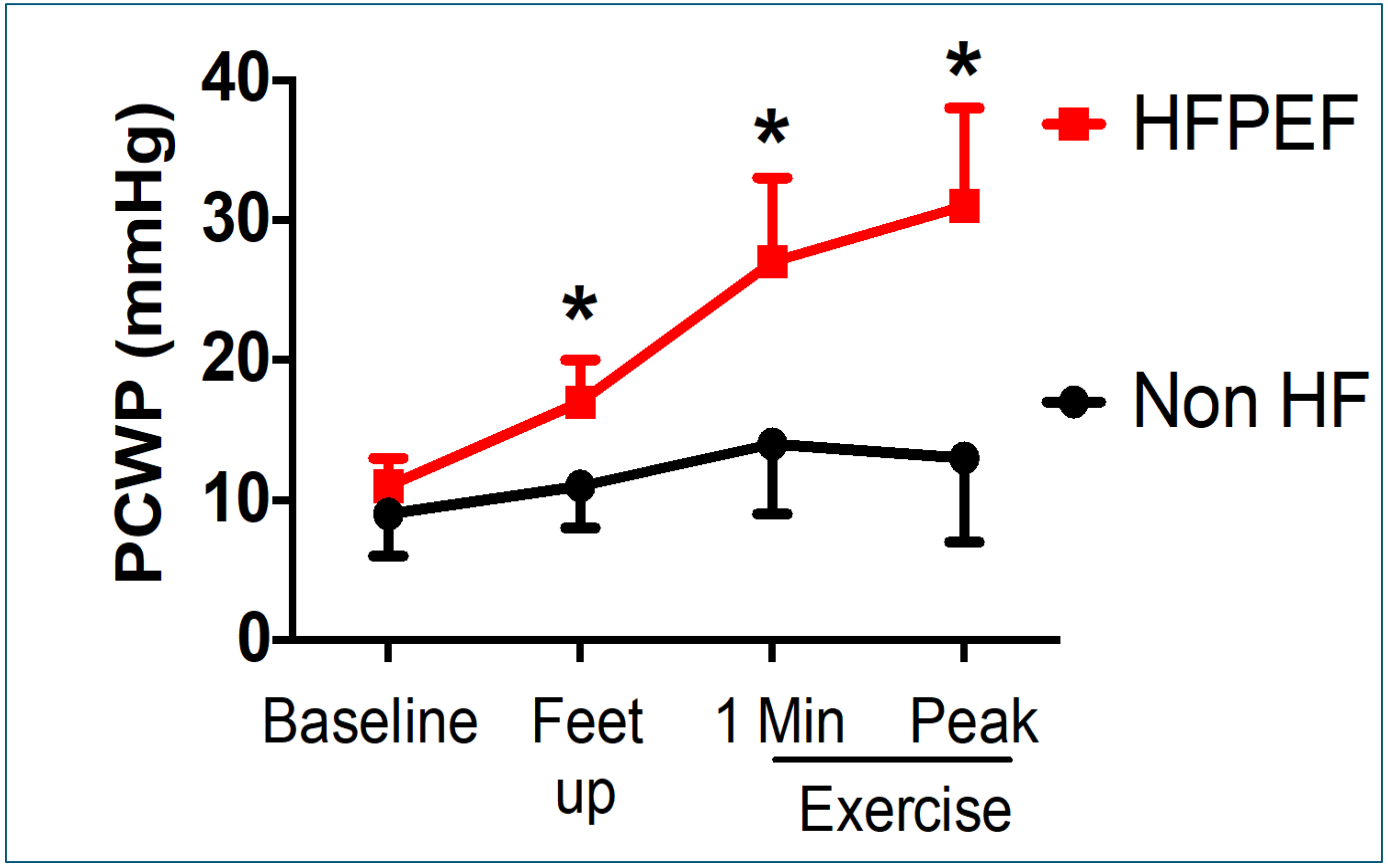


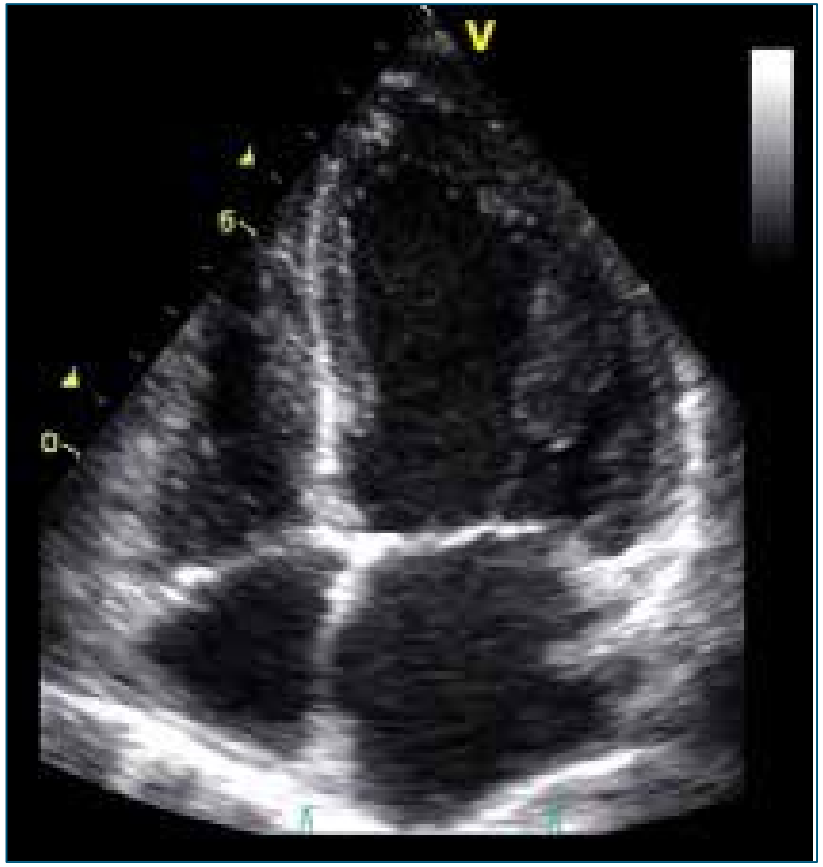
Conflict of interest

M Petrie:
Unpaid member of the Corvia Medical Inc. Scientific Advisory Group

D Burkhoff:
Hemodynamic Core Lab for/Consultant for Corvia

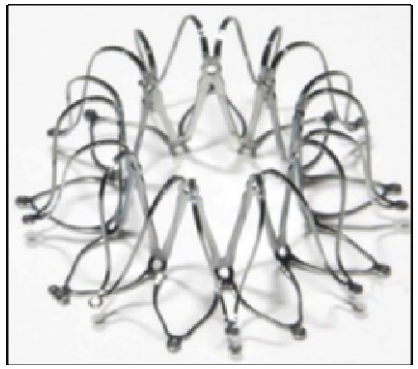
The Premise:
PCWP Increases Rapidly during Exericise





Circ Heart Failure 2010 Sep;3(5):588-95

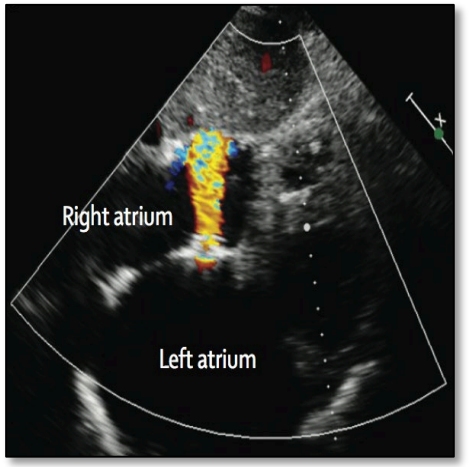
Interatrial Septal Device (IASD)

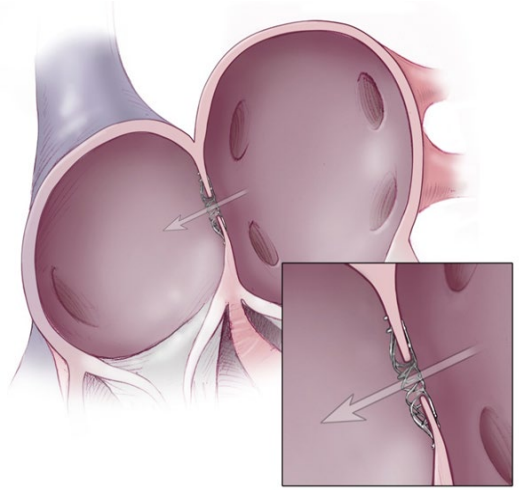


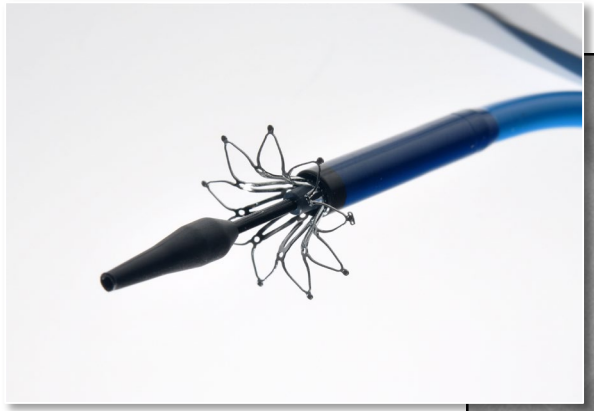
Elevated left atrial pressure - pulmonary congestion and symptoms

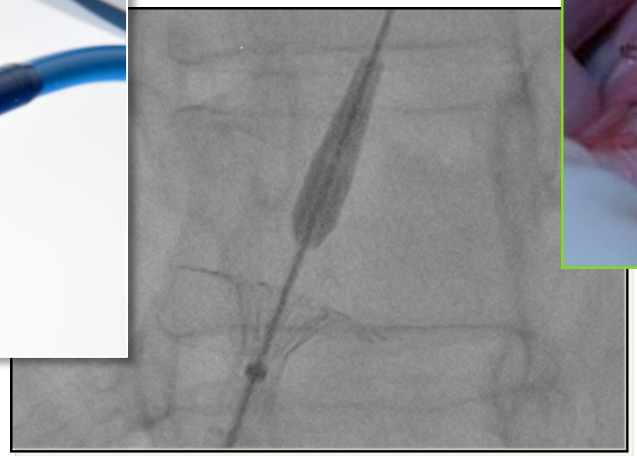
Transcatheter implant to create a small permanent interatrial shunt

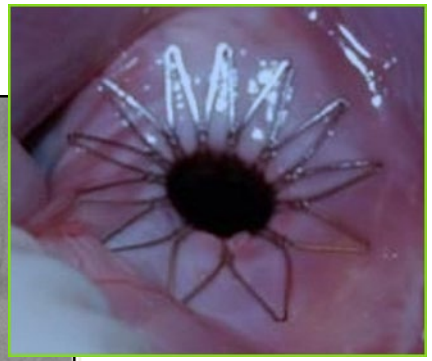
Reduce left atrial pressure







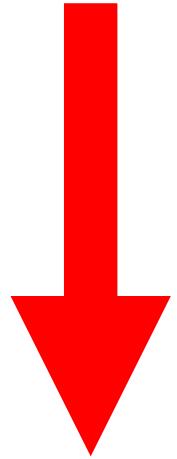




Studies and trials with Corvia IASD device

- Pilot study (n=11)
- **Observational study REDUCE-LAP HF (n=64)**
- Pilot RCT (REDUCE LAP RCT I) in HEF-PEF (n=44)
- Pivotal RCT (REDUCE LAP RCT II) now recruiting (n=608)
- Pilot study in HF-REF

2014



2019

REDUCE LAP-HF observational data (n=64)

1. **Chronic HF documented by one or more of the following**:
   - NYHA III/IV
   - One hospital admission for HF within the last 12 months

2. **LVEF ≥ 40% as determined by echocardiography**.

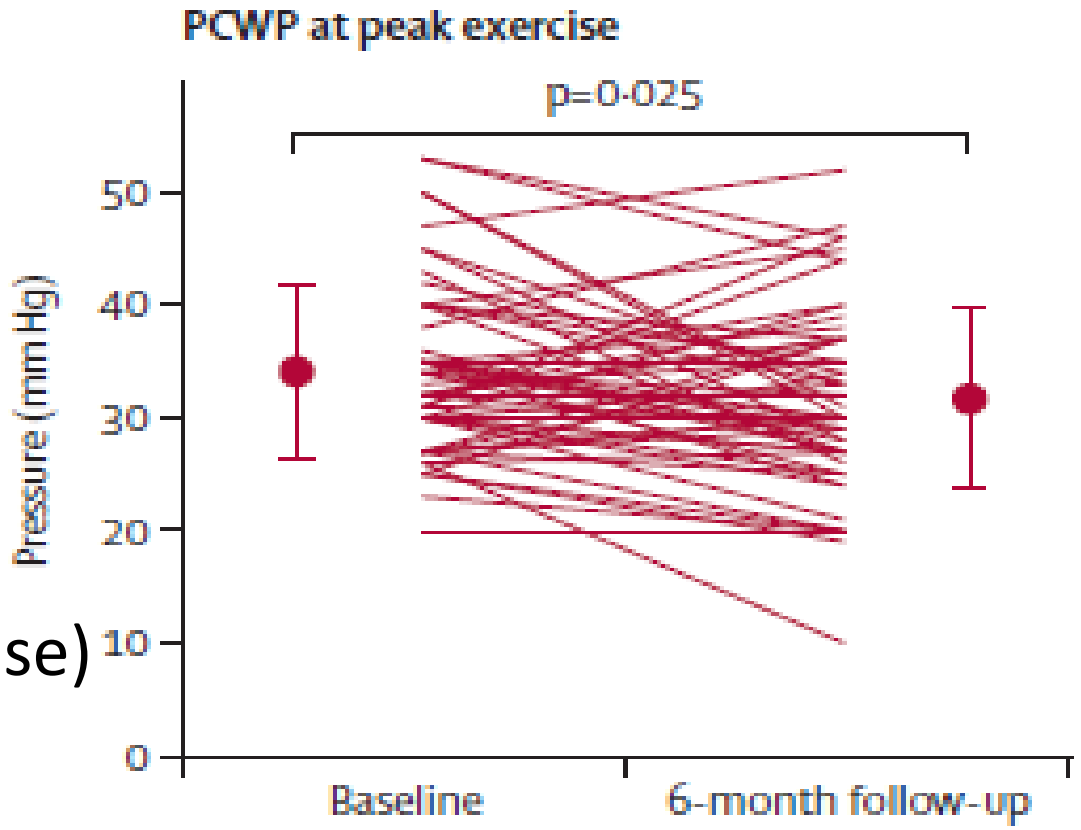
3. **Hemodynamic inclusion criteria**
   - PCWP at rest ≥15 mmHg and greater than CVP, **OR**
   - PCWP during supine bike exercise ≥25mm Hg

Lancet 2016;387:1298-304

REDUCE LAP-HF - data at 6 months

- Improved NYHA class
- Improved quality of life
- Improved 6 minute walk
- Improved exercise time

- Improved cardiac output (rest and exercise)
- Reduced PCWP (20W and peak exercise)



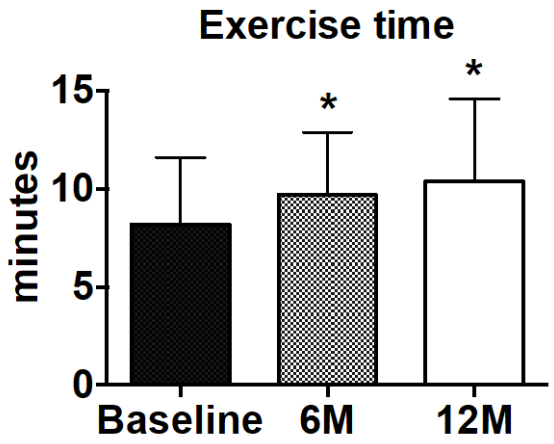
Lancet 2016;387:1298-304

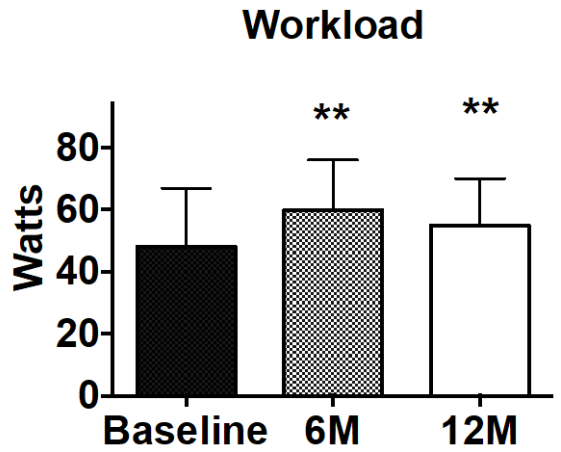
REDUCE LAP-HF - data at 12 months

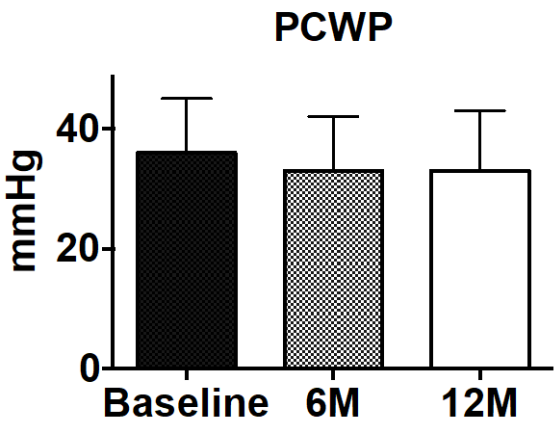
Inclusion criteria:

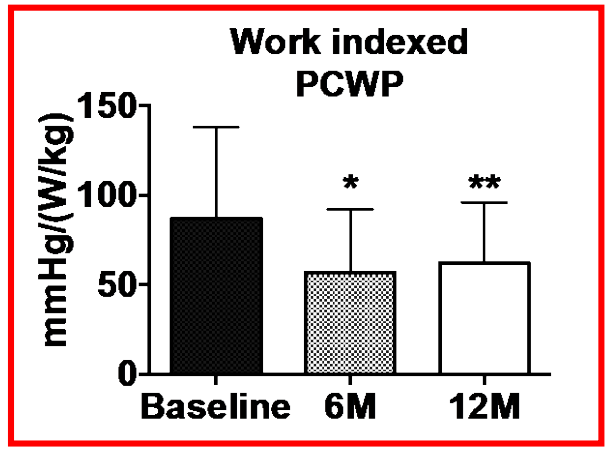
- Open label
- LVEF ≥ 40%,
- NYHA class II-IV
- Elevated PCWP
  - ≥ 15 mmHg (rest) or
  - ≥ 25 mmHg (supine bicycle exercise)

Acceptable safety profile at 12, 24 months

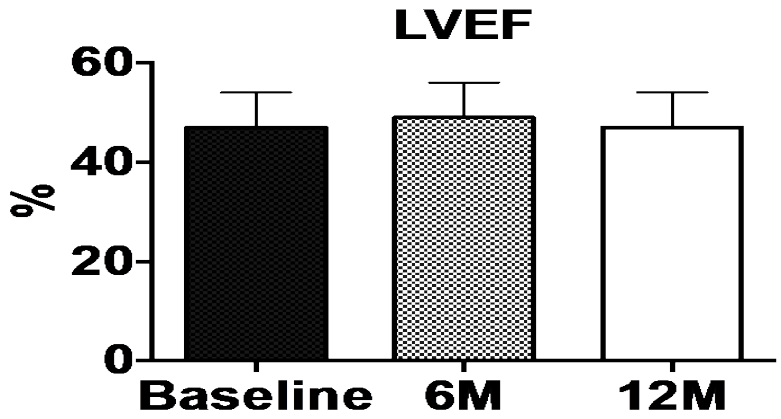


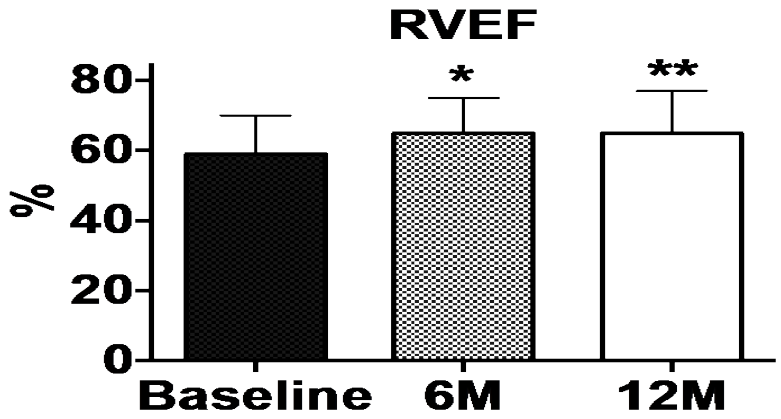


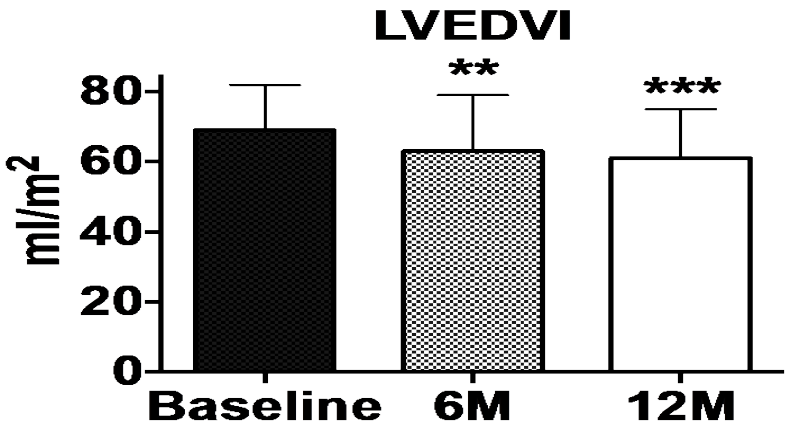


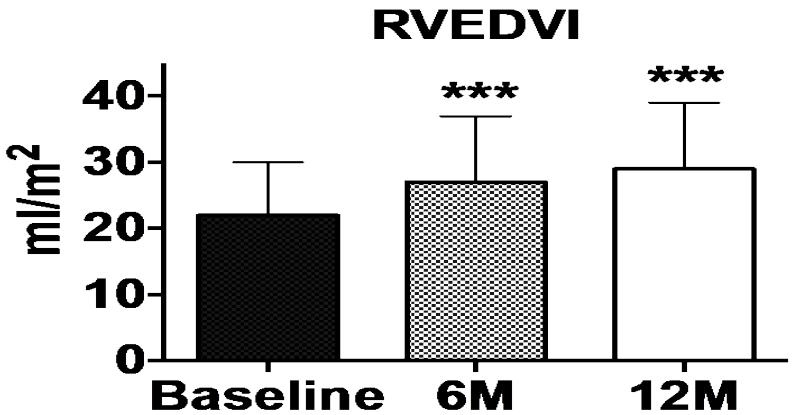


REDUCE LAP-HF – echocardiographic data at 1 year









*p<0.05, **p<0.01, ***p<0.001

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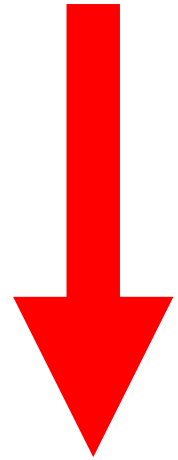


2019

REDUCE LAP-HF I RCT - hypothesis

Implantation of the IASD System II in patients with HF and EF ≥ 40% compared to sham control will result in:

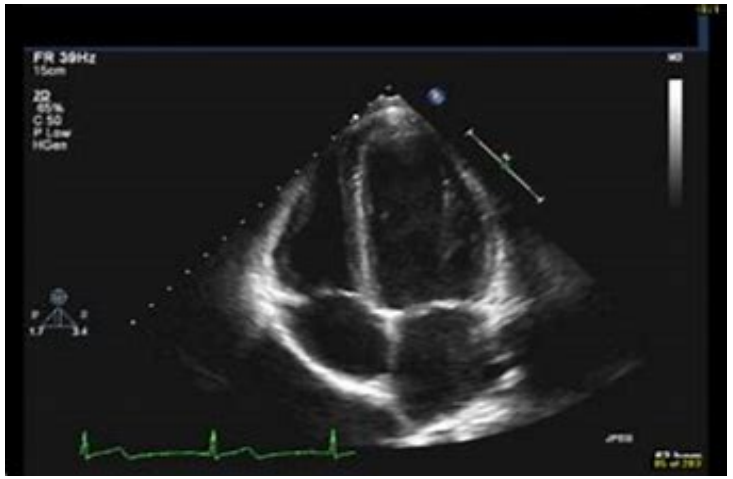
- Reduction in exercise PCWP

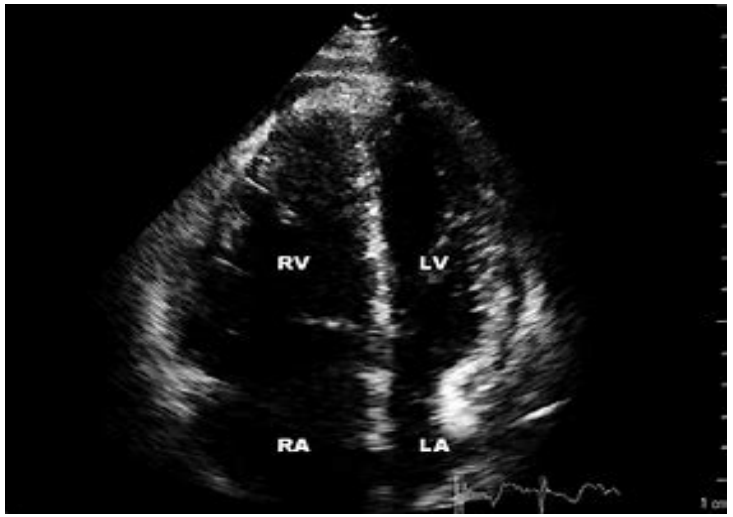
REDUCE LAP-HF I RCT – inclusion criteria

- NYHA III or IV AND recent HF hospitalisation or NT-BNP>425 SR, >1265 AF
- EF≥40%
- End-expiratory PCWP during supine ergometer exercise ≥ 25mm Hg and greater than RAP by ≥ 5 mm Hg.
- Site determined echocardiographic evidence of “diastolic dysfunction”

REDUCE LAP-HF I RCT – exclusion criteria

- Significant RV dysfunction
  - TAPSE < 1.4 cm, RV > LV size
- PVR > 4 Wood units





REDUCE LAP-HF I RCT (n=44)

Randomised: 1:1 randomization to IASD vs. sham control

i) IASD: Sedation, femoral venous access with ICE/TEE
+ trans-septal IASD implantation

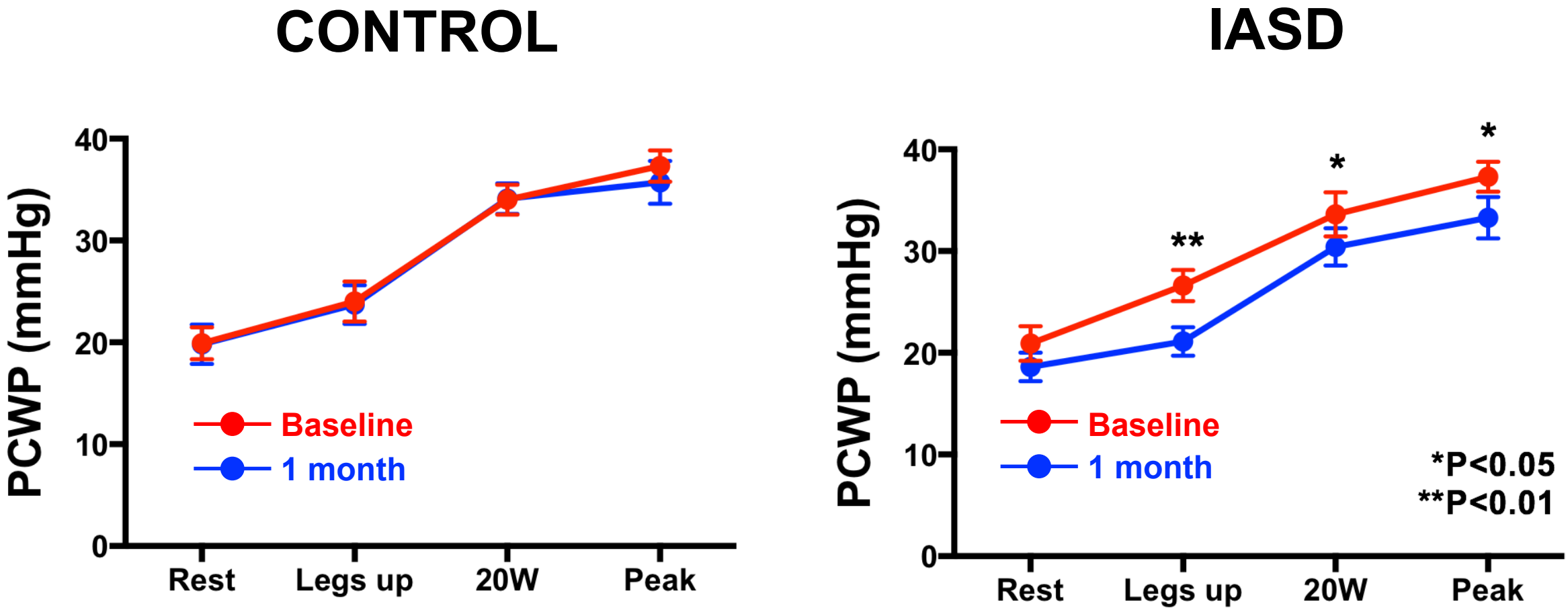
ii) Sham control: Sedation, femoral venous access with examination of interatrial septum and LA with ICE/TEE

Blinded: patient, HF physician, and research staff

Primary end point: Change in supine exercise PCWP at 1 month

Independent DSMB, CEC, hemodynamic, and echocardiographic core lab

Change in PCWP: Baseline to 1 month



0/22 MACCRE events in IASD group

1/22 MACCRE events in control group

Feldman T Circulation. 2018;137:364–375

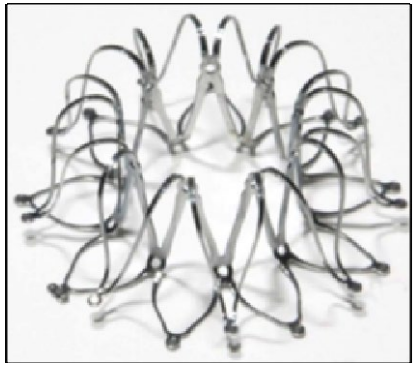
What next?
The pivotal trial – REDUCE-LAP RCT II

608 patients

IASD implantation

No IASD implantation

BLINDED, SHAM-CONTROLLED



REDUCE LAP RCT II – patient population

- Chronic symptomatic HF documented by the following:
  - Symptoms of HF on diuretics for ≥ 30 days
  - NYHA II (history of III)-IV **HF**
  - ≥ 1 HF hospital admission **OR** elevated NT-BNP
- Ongoing stable HF management according to the 2017 ACC/AHA Guidelines for the Management of Heart Failure
- Site determined echocardiographic evidence of diastolic dysfunction
- PCWP during supine ergometer exercise ≥ 25mm Hg and greater than RAP by ≥ 5 mm Hg

REDUCE LAP RCT II

Randomised: 1:1 randomization to IASD vs. sham control

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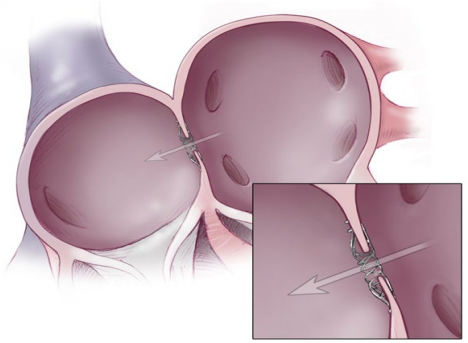
Blinded: patient, HF physician, and research staff

Independent DSMB, CEC, hemodynamic, and echocardiographic core lab

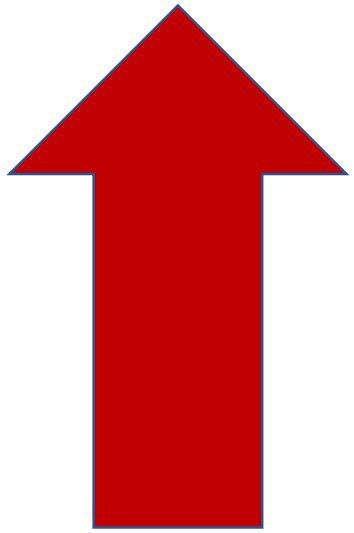
Primary end point

- Cardiovascular mortality or non-fatal, ischemic stroke through 12 months
- Rate of total HF admissions or healthcare facility visits for IV diuresis for HF through 12 months
- Change in KCCQ score between baseline and 12 months



Primary end point

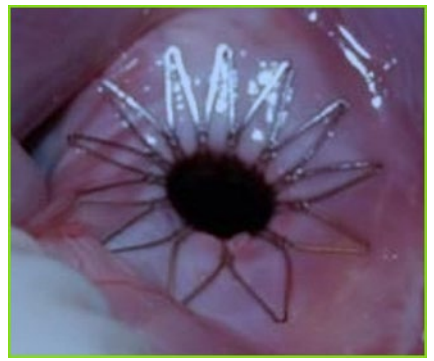
Hierarchy of end points



- CV death or CVA
- HF hospitalisation (recurrent)
- Change in KCCQ

Safety-related measures

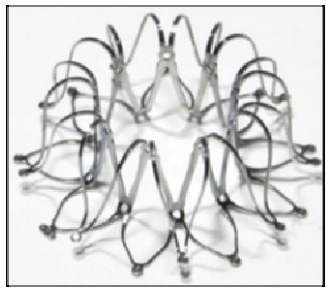
- Device and or procedure related SAEs through 12 months
- All serious adverse events (SAEs) through 12 months
- Systemic embolic events through 12 months
- Increase in RV size/decrease in RV function through 12 months



Conclusion

Corvia

- Observational 64 patient study promising
- Pilot, feasibility, randomised, sham-controlled trial proved proof of concept
- Large RCT with hard end points is well underway



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