# Longitudinal Echocardiographic Changes in REDUCE-LAP II


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***on behalf of the REDUCE-LAP II Investigators***

# Disclosure of Relevant Financial Relationships

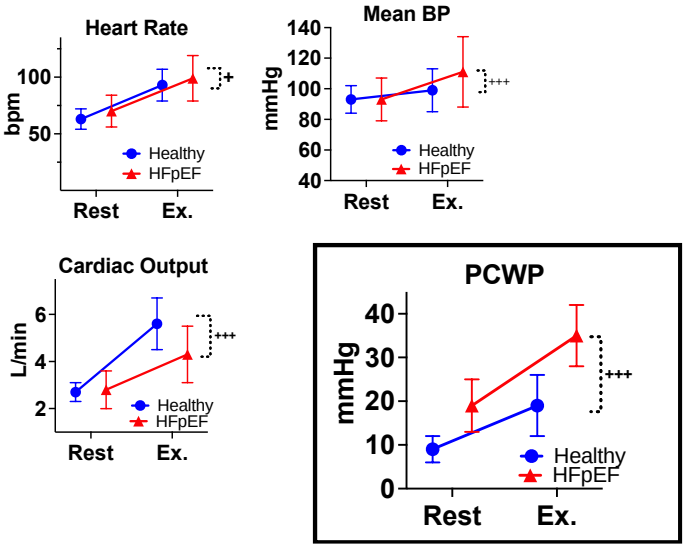
Within the prior 24 months, I have had a financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

| Nature of Financial Relationship | Ineligible Company |
| --- | --- |
| Grant/Research Support | Corvia Medical, XVIVO |
| Consultant Fees/Honoraria | Abbott, Bayer, Boehringer Ingelheim, Novartis |
| Individual Stock(s)/Stock Options | Cardiac Dimensions |

**All relevant financial relationships have been mitigated.**
Faculty disclosure information can be found on the app

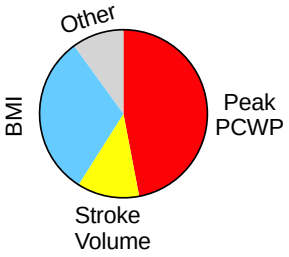
# Background: Rationale for Inter-Atrial Shunting in HFpEF

## HFpEF Physiology

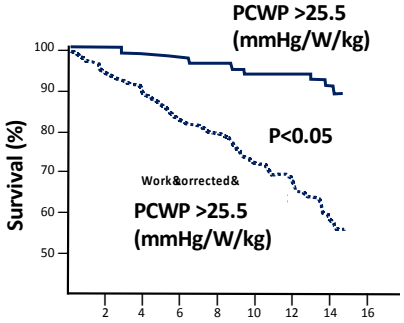



*Kaye JACC 2010,*
*Wolsk, Kaye EurJHF 2018*
*Wolsk, Kaye JACCHF 2019*

## HFpEF Symptoms

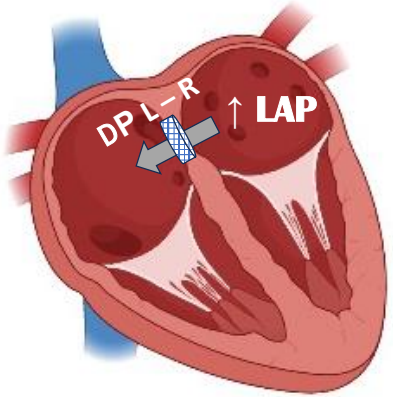



## CV Outcomes (?)




*Dorfs EurHF 2014*
*Kaye ESCHF 2019*

## Device-Based HFpEF Therapy



# Background: REDUCE LAP-HF II Trial

- Pivotal, phase 3, international, multicenter, sham-controlled RCT of Corvia Atrial Shunt Device in patients with HF and LVEF ≥40%
  - NYHA II-IV, GDMT, age ≥40, LVEF ≥40%, preserved RV fn
  - Ex RHC with peak exercise PCWP ≥25mmHg, L-R gradient >5mmHg
- Primary outcome: hierarchical composite (win ratio)
  - CV death, non-fatal ischemic CVA, HF events, KCCQ summary score

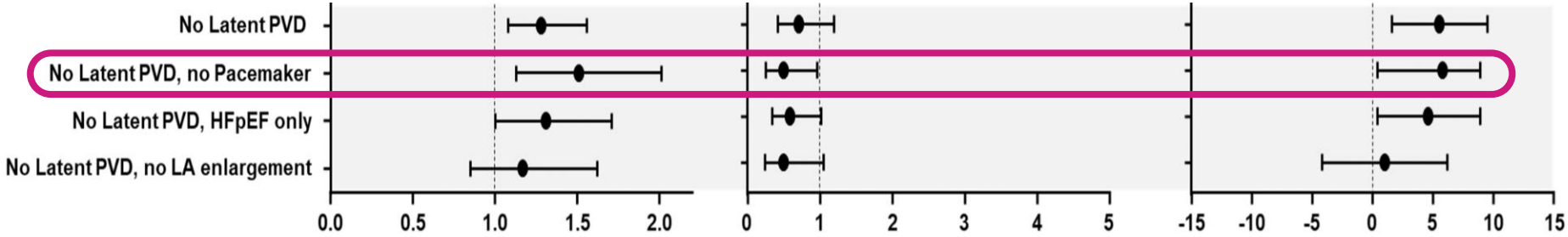
- N=626 randomized 1:1 to shunt (n=314) vs. sham (n=312)
- Overall trial was **neutral** (win ratio = 1.0 [95% CI 0.8-1.2])



*Shah SJ, et al. Lancet 2022*

# REDUCE LAP-HF II Responder Subgroup

- Post hoc, pre-specified analysis:
  - Large subgroup: 50% of randomized patients (n=313)
  - Peak exercise PVR <1.74 WU + no pacemaker/ICD
  - After 12 months of follow-up: Beneficial treatment response




**Responder Group**
**(shunt vs. sham)**

***↑Win ratio = 1.43 (p=0.009)***

***↓HF events (IRR 0.49, P=0.035)***

***↑KCCQ (+5.9 points; =0.01)***

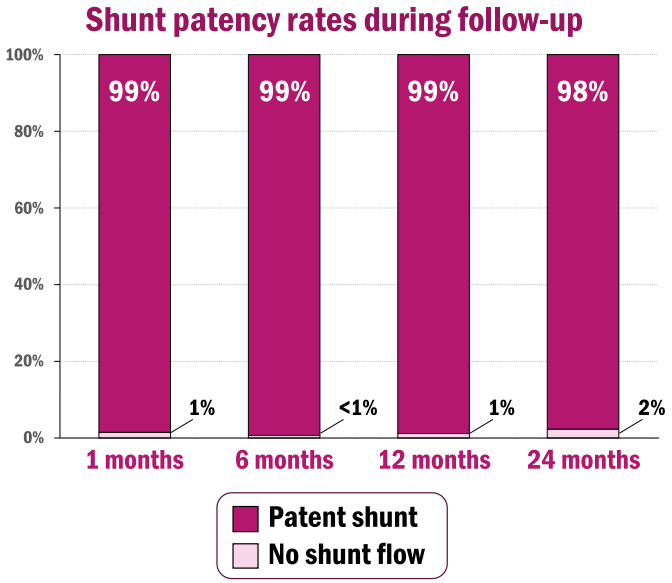
CRF THT

*Borlaug BA...Shah SJ. Circulation 2022*

# Effect of IAS on Cardiac Structure & Function?

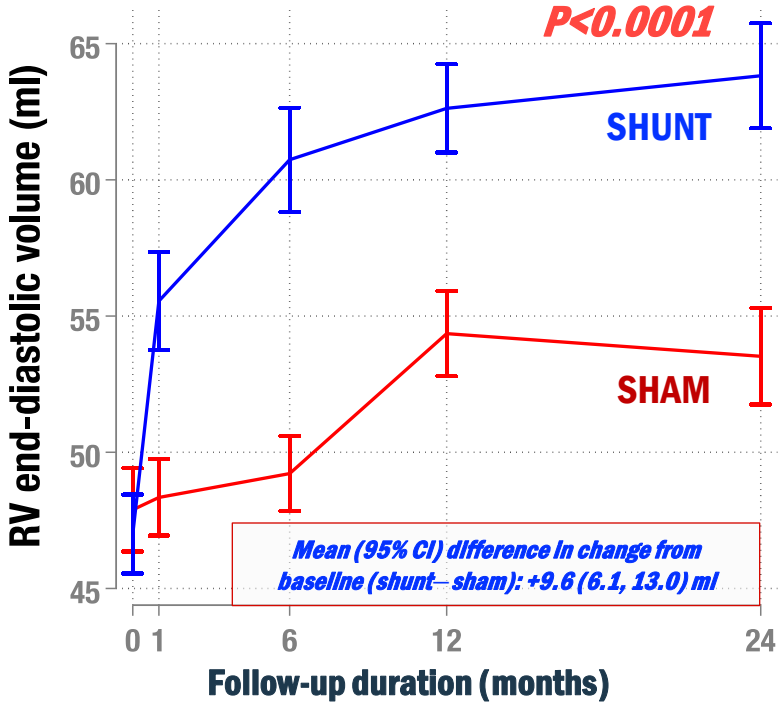
- Echo required at baseline and 1-, 6-, 12-, 24-month visits (UPenn Core Lab)

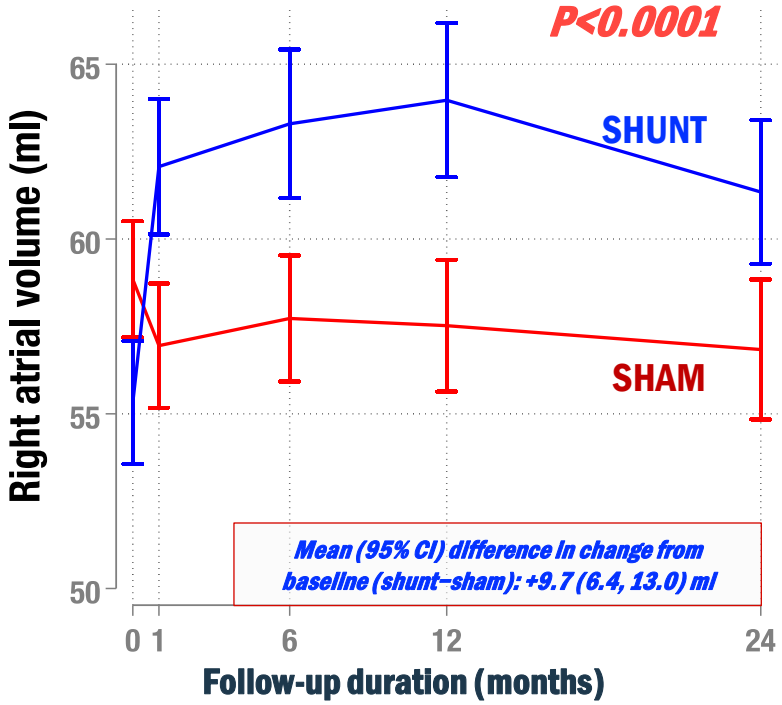
| Echo status | Follow-up time point | | | |
|---|---|---|---|---|
| | 1-mo. | 6 mo. | 12 mo. | 24 mo. |
| Interpretable | 88% | 84% | 82% | 71% |
| Not evaluable | 4% | 6% | 9% | 13%* |
| Not completed | 7% | 10% | 8% | 9%* |
| Patient deceased | <1% | <1% | 1% | 7% |



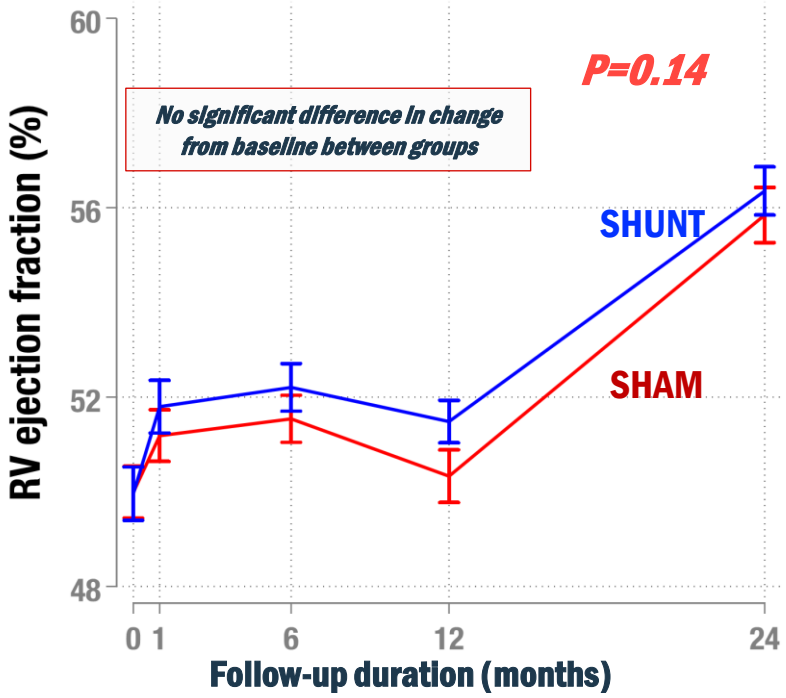

**Of patent shunts only 2 bidirectional; none R to L**

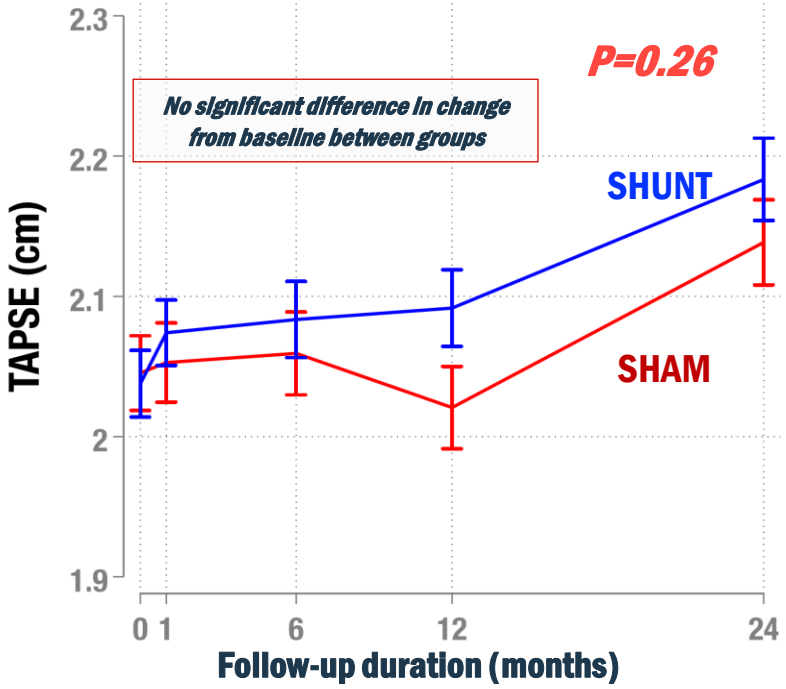
# L-R Shunt: RV and RA Volumes



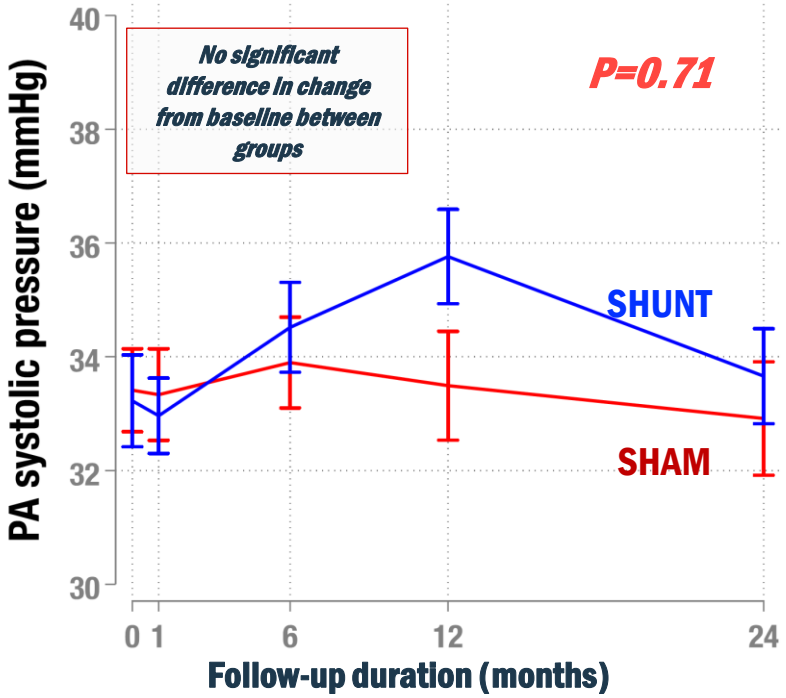



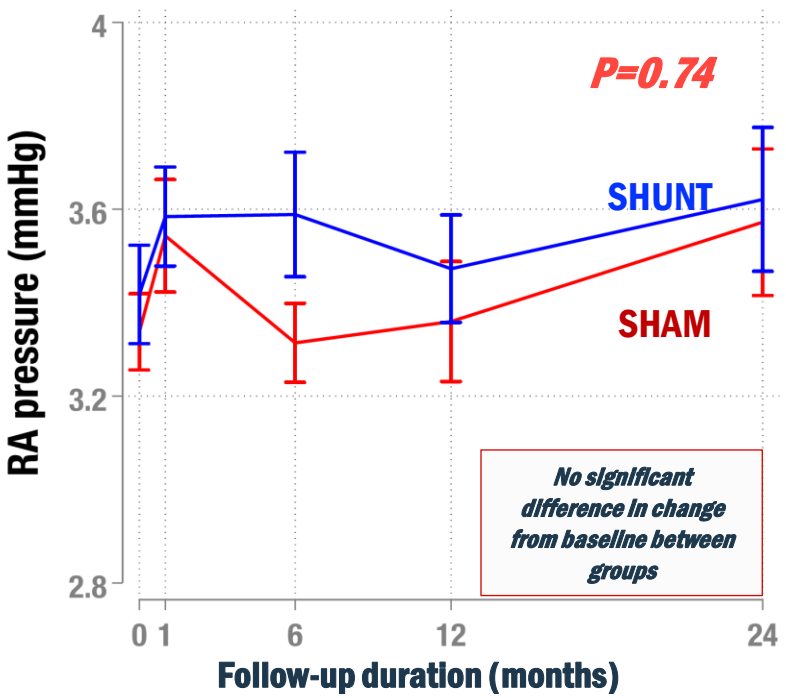
# L-R Shunt: RV Function



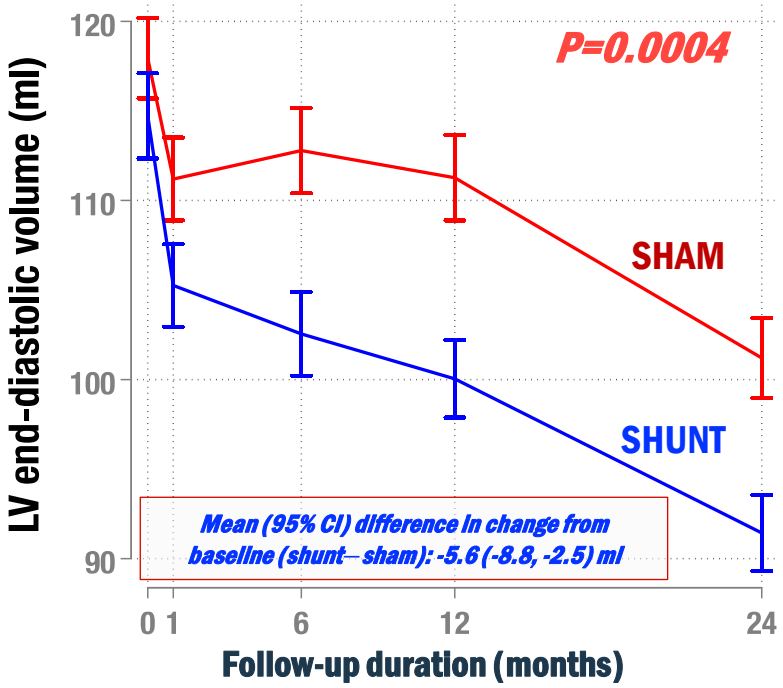



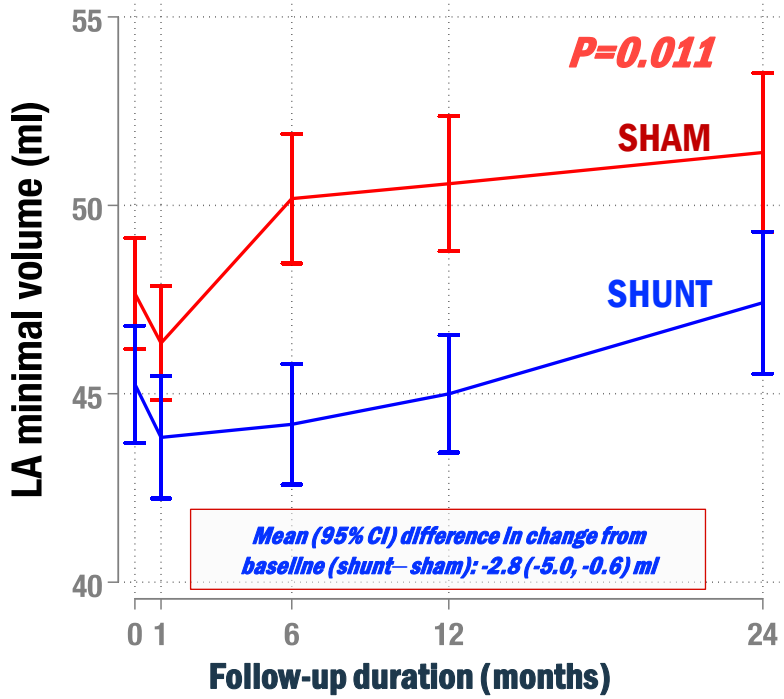
# L-R Shunt: Right Heart Pressures (by Echo)



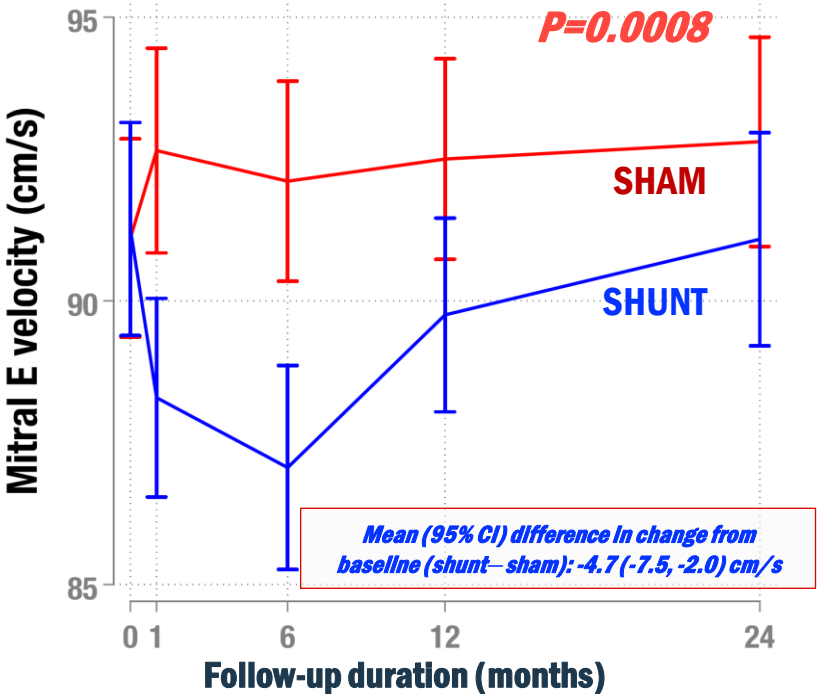



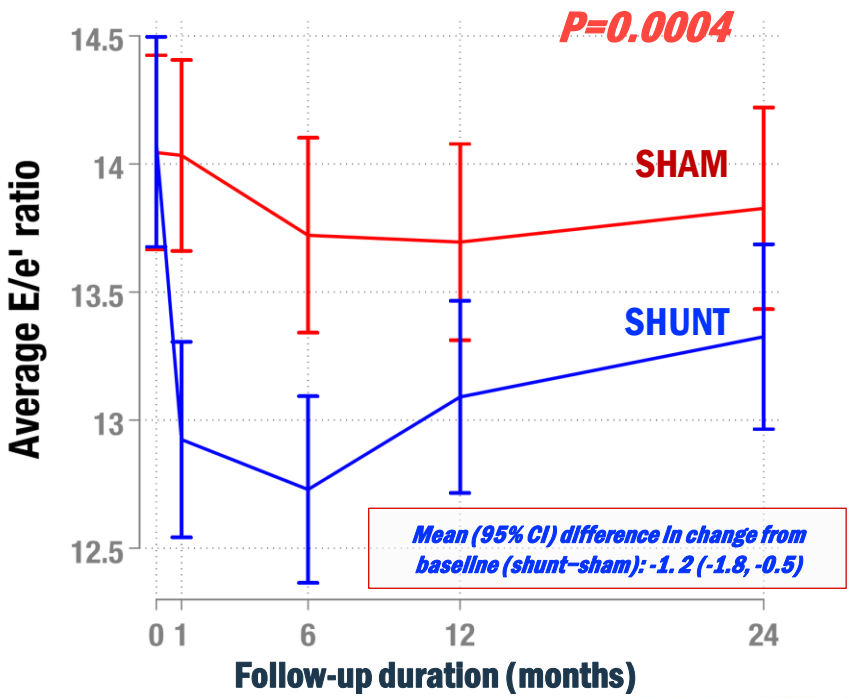
# L-R Shunt: LV and LA Volumes



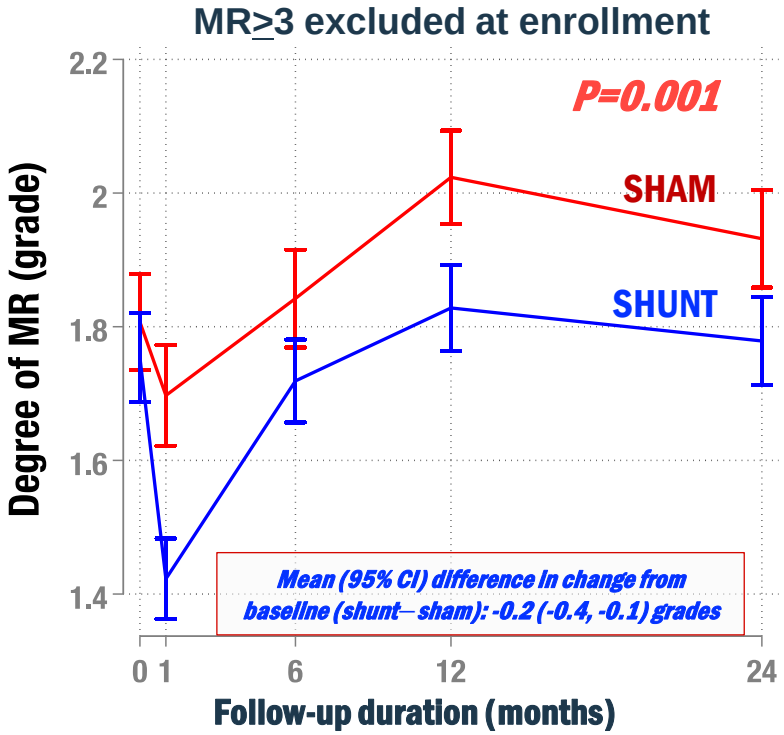



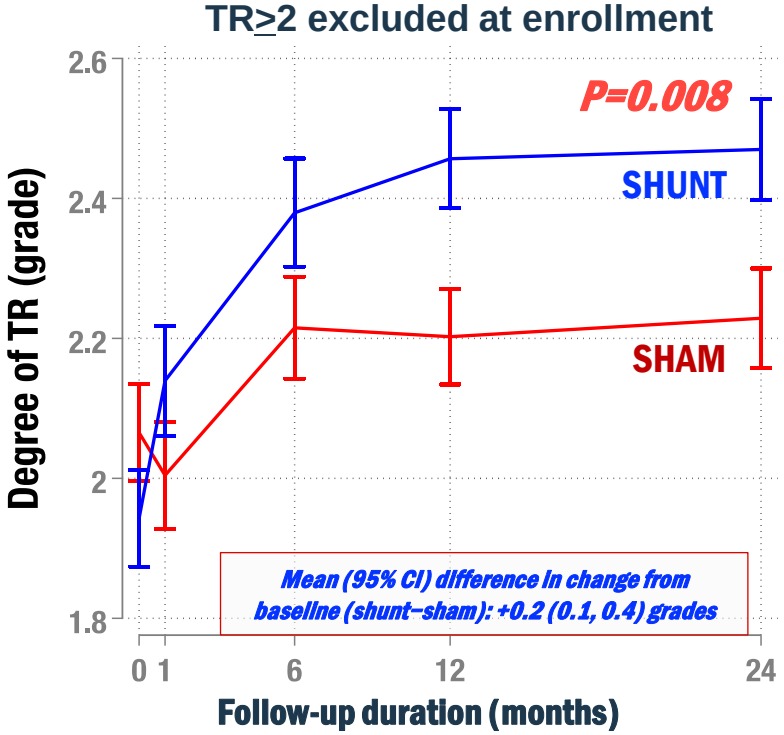
# L-R Shunt: LV Diastolic Indices



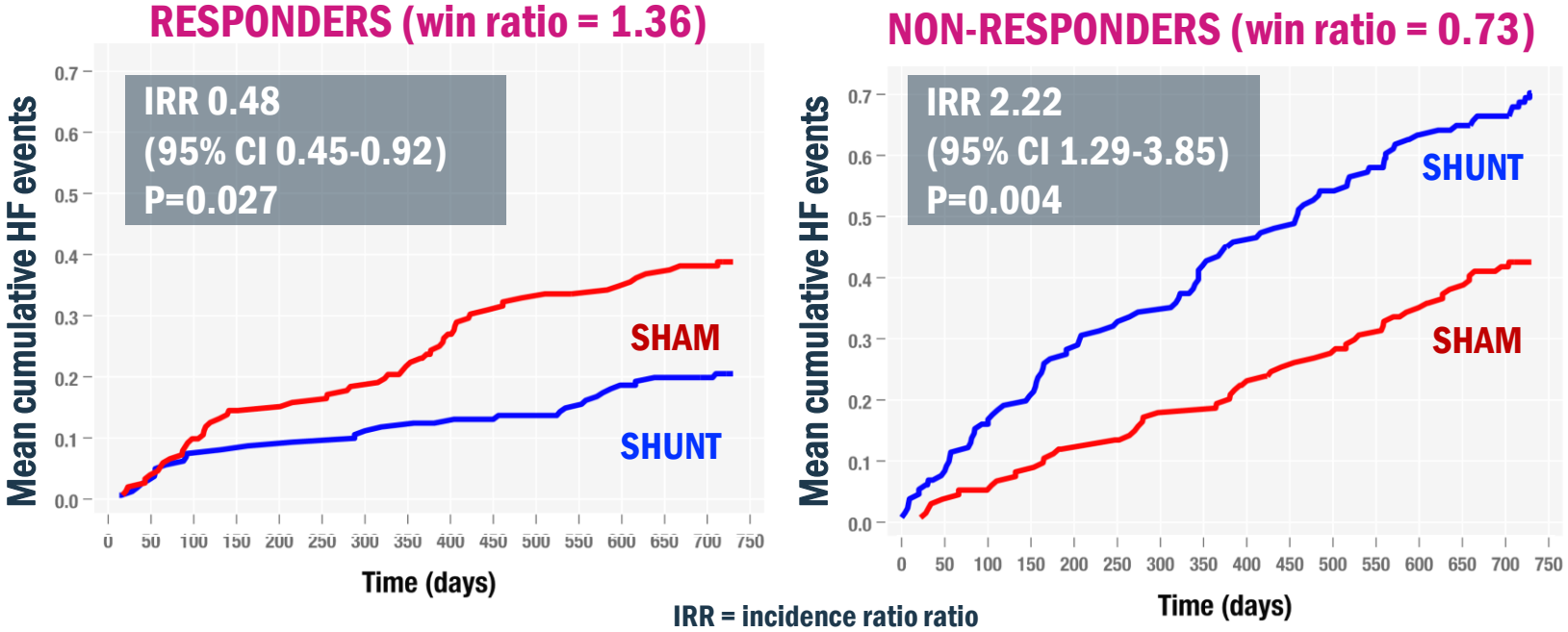
# L-R Shunt: Mitral and Tricuspid Regurgitation



# HF events by shunt responder status

- 24-month recurrent HF events analysis

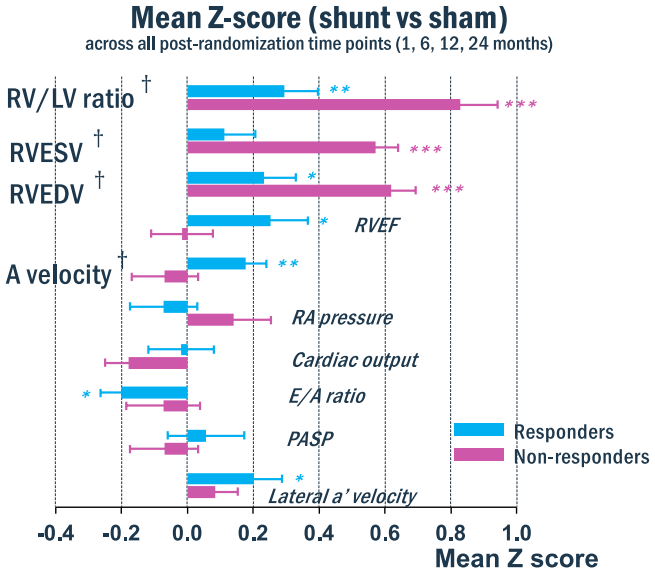



IRR = incidence ratio ratio



Gustafsson F...Shah SJ. ESC-HFA 2023

# Responder Status: Serial Echocardiographic Changes




- ***4 echo parameter treatment effects were significantly different between responders vs. non-responders*** ($P_{interaction}$ <0.05):
  - **Lower RV/LV volume ratio**
  - **Lower RVESV, RVEDV**
  - **Higher transmitral A velocity**

***RESPONDER-HF (NCT05425459): Ongoing RCT of Corvia Atrial Shunt in Responder Gp:***
***NYHA II-IV, LVEF≥40%, GDMT, ExPVR<1.75, No Pacemaker***

*P<0.05 vs. sham, **P<0.01 vs. sham, ***P<0.001 vs. sham. † Interaction P<0.05