

Atrial Shunt for Heart Failure with Preserved and Mildly Reduced Ejection Fraction: **Five-Year Outcomes from the REDUCE LAP-HF II Trial**

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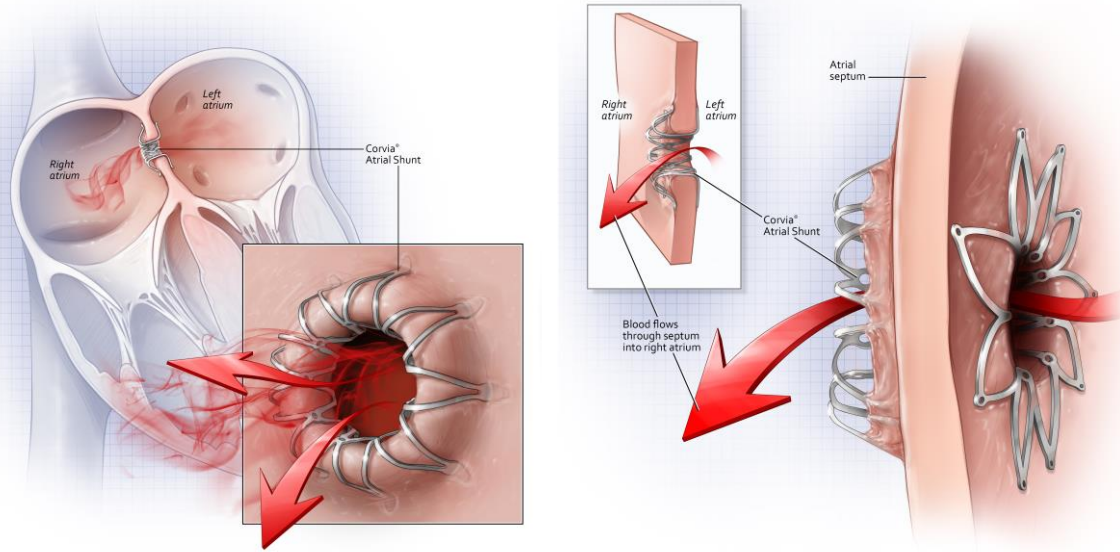
- AHA # 24SFRNPCN1291224

- AstraZeneca, Boston Scientific, Corvia, Pfizer, Tempus

- **Consulting / advisory board / steering committee:**

- 35Pharma, Abbott, Alleviant, AstraZeneca, Amgen, Axon Therapies, BaroPace, Bayer, Boehringer-Ingelheim, Boston Scientific, BMS, Corvia, Cytokinetics, Diastol Therapeutics, Edgewise, Edwards, Ensho Health, Eidos, Gordian, Imara, Impulse Dynamics, Intellia, Ionis, Lilly, Merck, Metabolic Flux, Novartis, Novo Nordisk, OrbiMed, Pfizer, Prothena, Regeneron, Rivus, SalubrisBio, Sardocor, Secretome, Shifamed, Tectonic, Tenax, Tenaya, Ultromics

Background: Corvia Atrial Shunt Device



Corvia Atrial Shunt device:

- Self-expanding nitinol cage
- Double-disc, flush with LA septum
- Single, 8-mm shunt diameter
- Qp:Qs 1.2-1.3

REDUCE LAP-HF II RCT (n=621):

- Randomized, double-blind, sham-controlled
- 93% HFpEF, 7% HFmrEF
- Exercise RHC in all; peak PCWP ≥ 25 mmHg

Primary result: Neutral (Win ratio=1.0, P=0.85)

Responder group (50%; n=313)

- Peak exercise PVR < 1.74 WU + no PPM/ICD/CRT
- Benefit at 1, 2, and 3 years

Key questions:

- Does benefit persist to 5 years?
- Are there long-term safety concerns?

REDUCE LAP-HF II 5-year analysis: Methods

Study Design:

- Final 5-year follow-up analysis
- Overall cohort (n=621 MITT) and pre-specified subgroups
- Unblinded after 2-year visit; crossovers (n=43) excluded

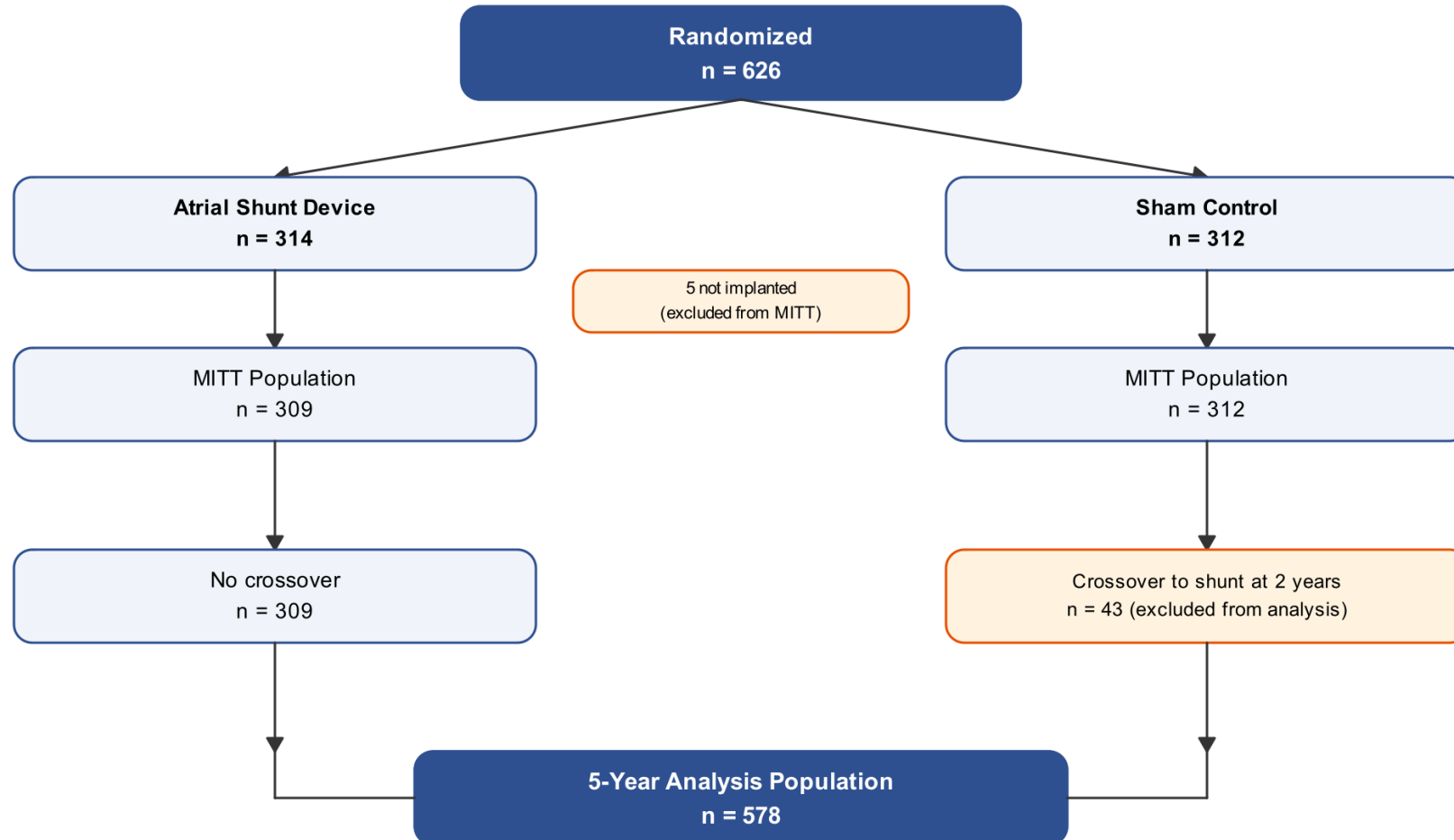
Primary Composite Endpoint (Win Ratio):

- CV death or non-fatal ischemic stroke
- Total (first + recurrent) HF events
- Change in KCCQ Overall Summary Score

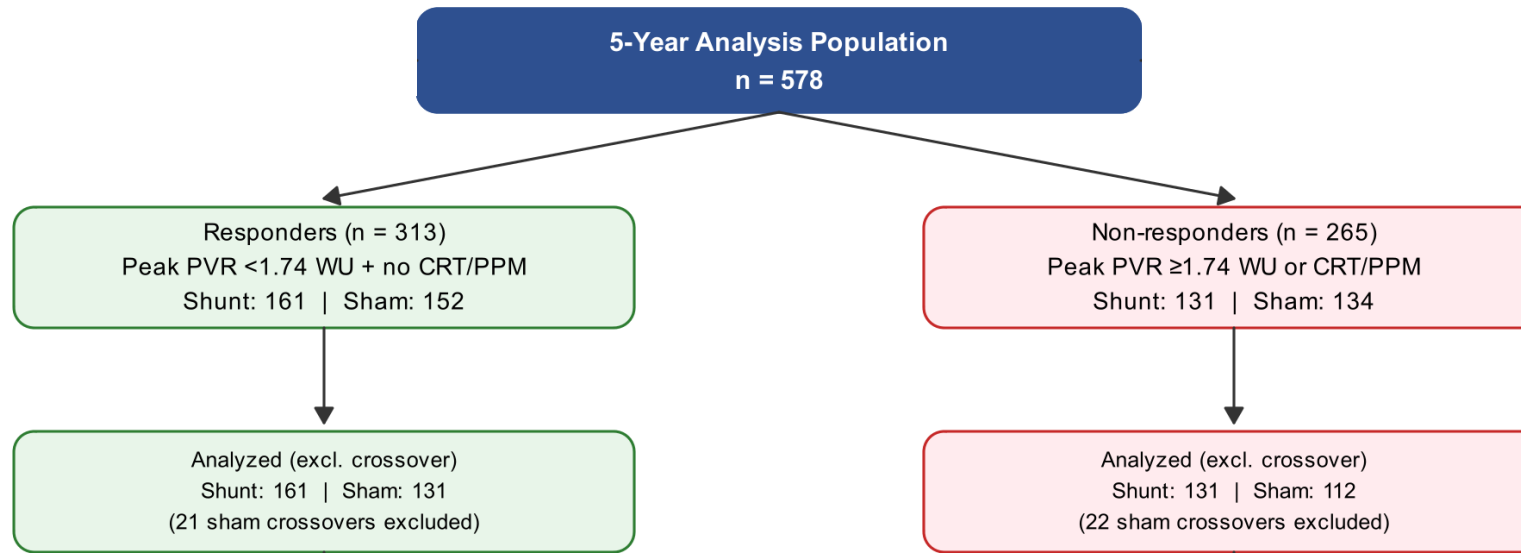
Statistical Methods:

- Composite: Finkelstein-Schoenfeld / win ratio
- CV death/stroke: logistic regression
- HF events: Cox and Poisson regression; KCCQ: ANCOVA (adjusted for baseline KCCQ value)

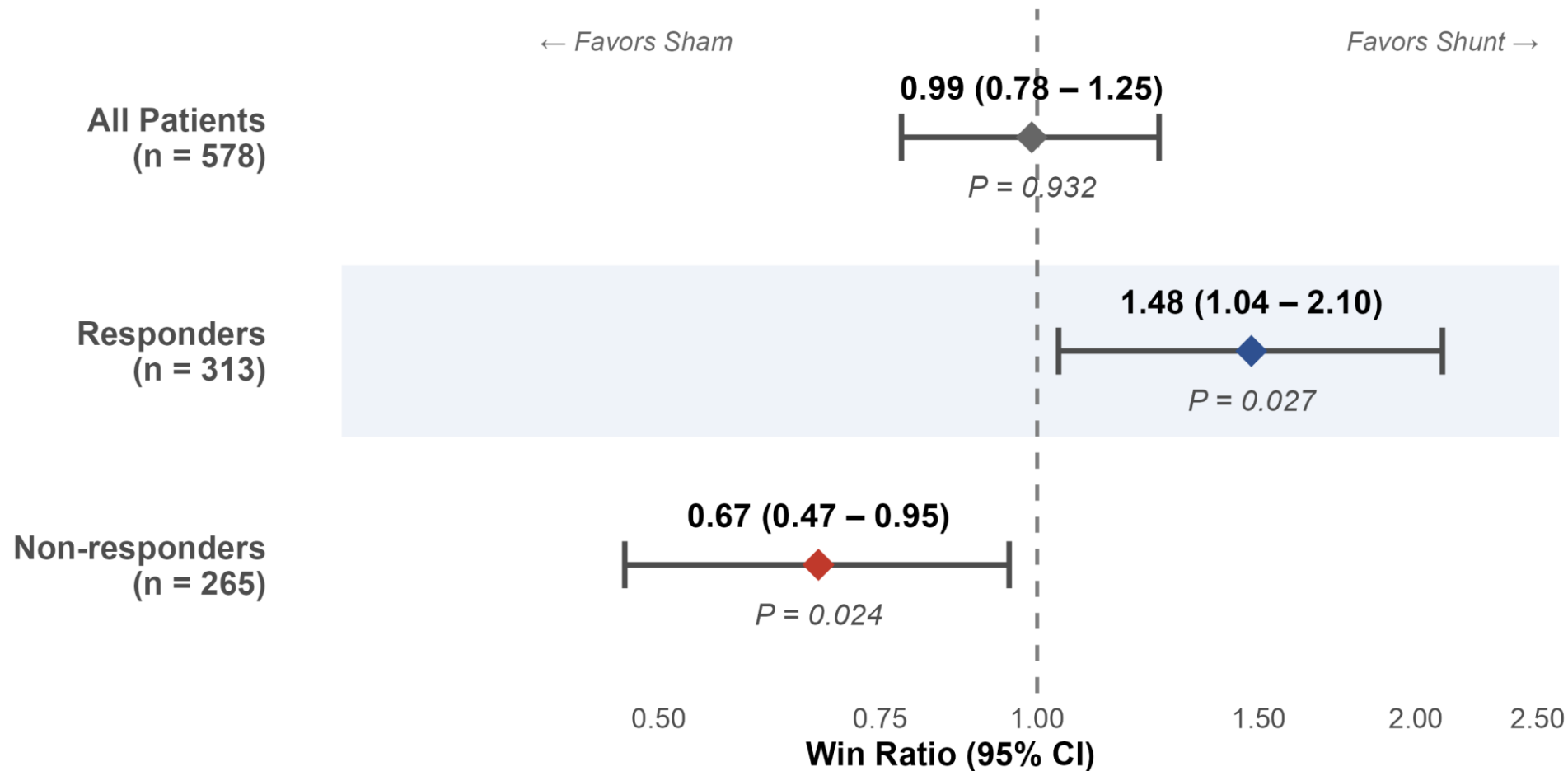
REDUCE LAP-HF II: Participant disposition



REDUCE LAP-HF II: Participant disposition



REDUCE LAP-HF II: 5-year primary endpoint



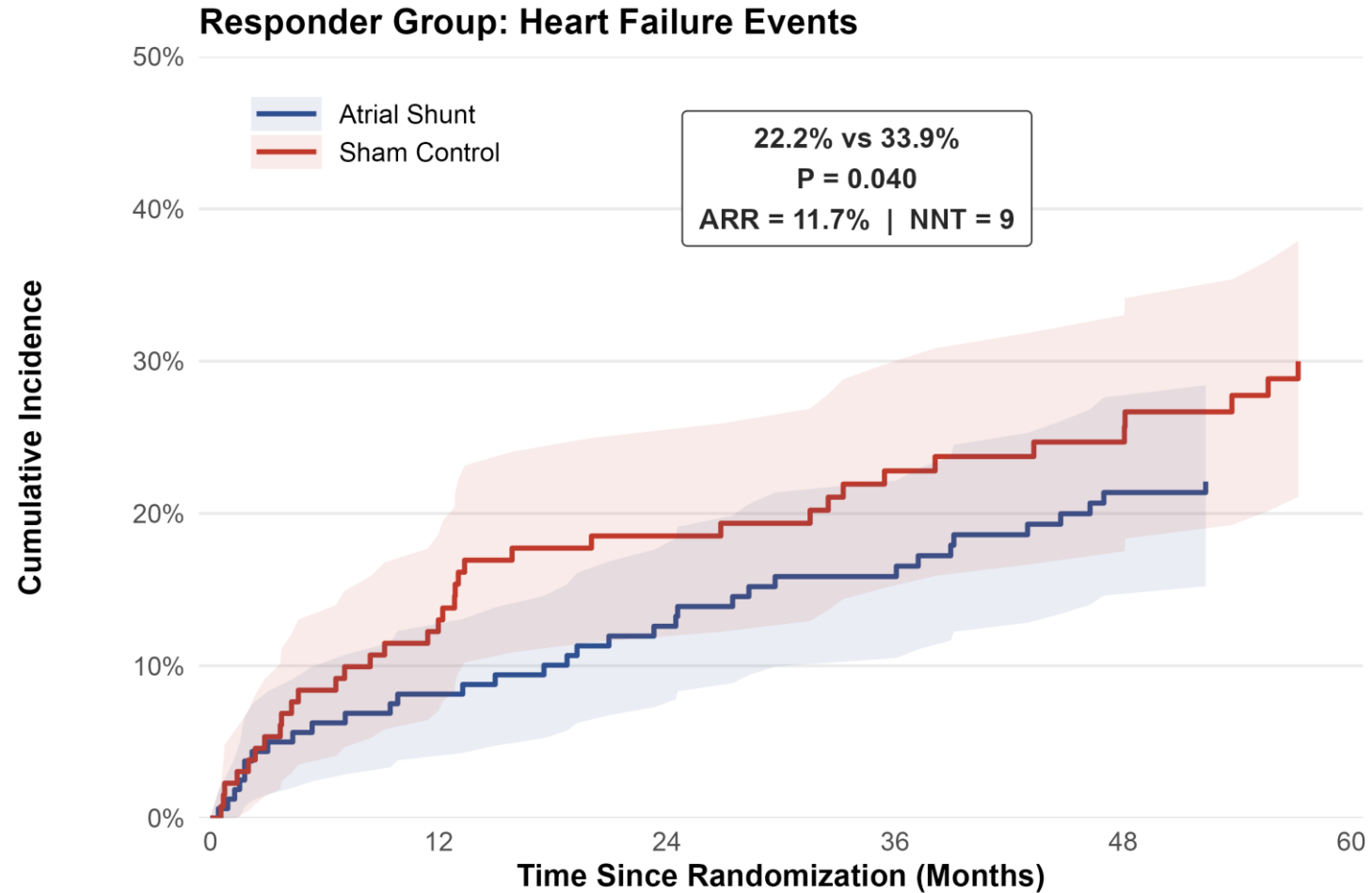
Components of the primary endpoint

Outcome (5-yr)	All Patients		Responders		Non-responders	
	Shunt (n=309)	Sham (n=312)	Shunt (n=161)	Sham (n=152)	Shunt (n=131)	Sham (n=134)
CV death or non-fatal stroke	15.0%	12.0%	9.8%	9.4%	21.4%	16.2%
CV death	11.2%	9.7%	7.9%	7.4%	14.6%	13.2%
Non-fatal stroke	4.0%	2.4%	1.9%	2.1%	7.4%	3.3%
HF event rate (per pt. year)	0.17	0.18	0.10	0.15	0.23	0.19
Δ KCCQ-OSS	14.2±20.9	10.5±25.1	19.1±20.4	9.3±25.2	6.7±24.6	11.2±24.5

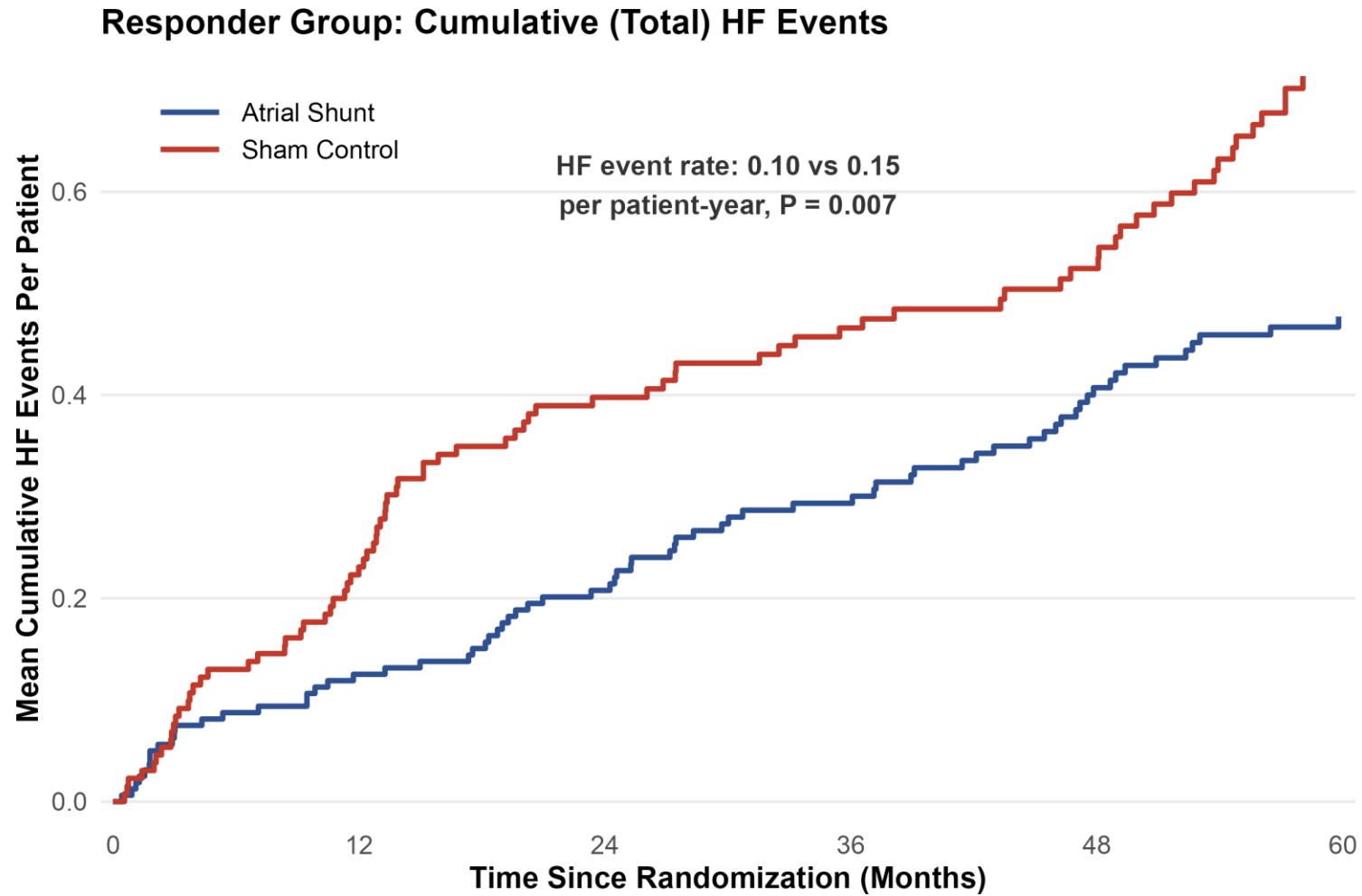
Components of the primary endpoint: Responders

Outcome at 5 Years	Atrial Shunt (n=161)	Sham Control (n=152)	P-value
CV death or non-fatal ischemic stroke	9.8% (3.9–15.7)	9.4% (2.0–16.8)	0.658
CV death	7.9% (2.5–13.2)	7.4% (0.7–14.1)	0.727
Non-fatal ischemic stroke	1.9% (0.0–4.8)	2.1% (0.0–5.8)	0.810
HF event rate (per pt-yr)	0.10	0.15	0.007
HF events (% of patients)	22.2%	33.9%	0.040
Δ KCCQ-OSS (mean ± SD)	+19.1 ± 20.4	+9.3 ± 25.2	0.030
Δ KCCQ-OSS (median [IQR])	18.4 (7.4, 30.6)	8.1 (–7.0, 27.6)	0.030
Win Ratio (95% CI)	1.48 (1.04 – 2.10)		0.027

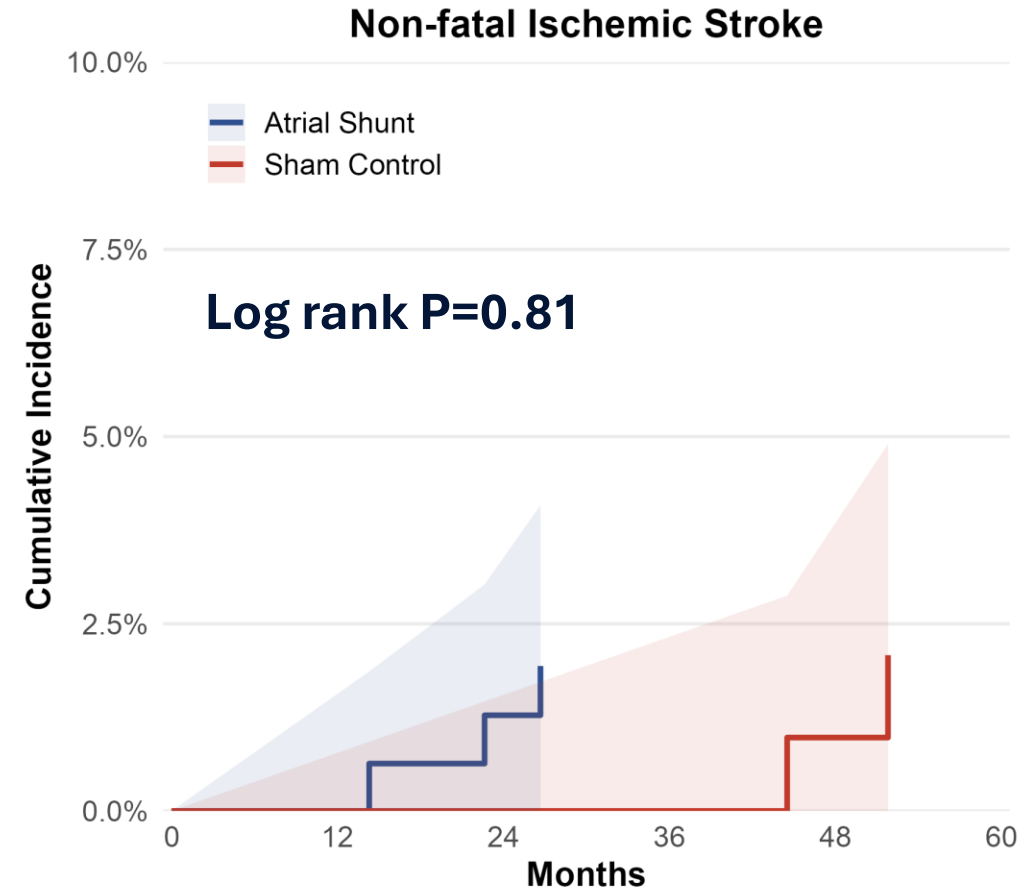
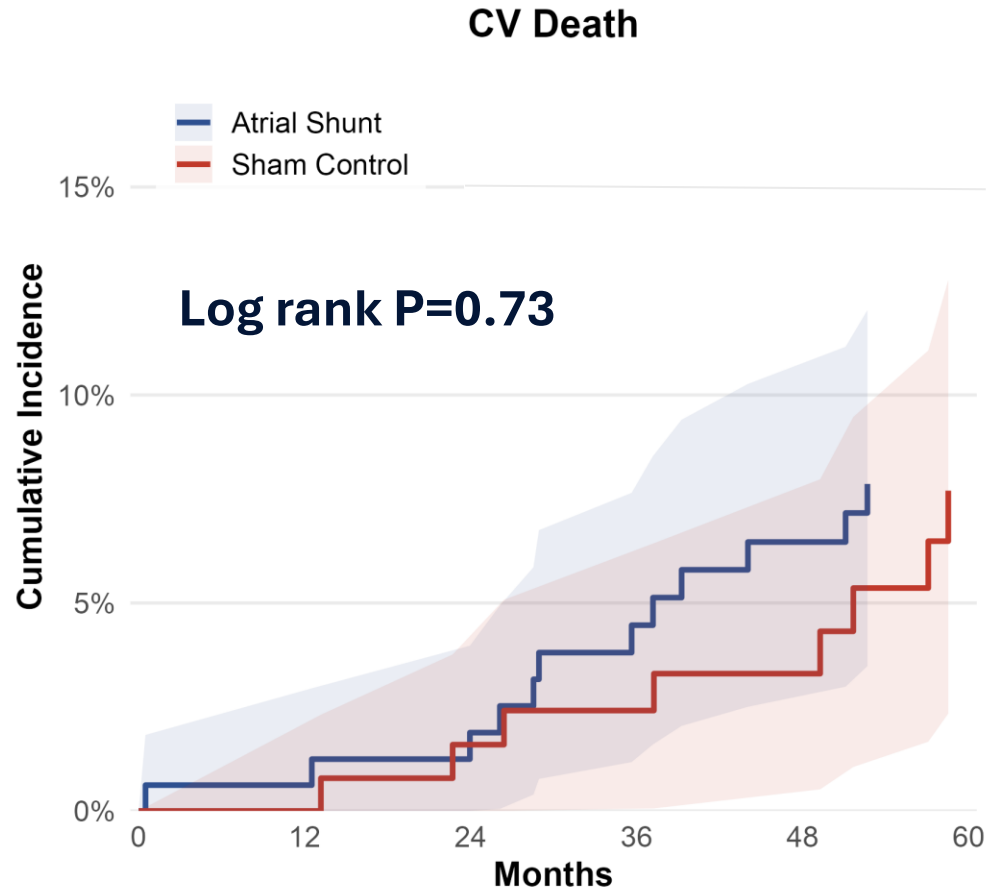
Responders: Time to first HF event



Responders: Cumulative total HF events

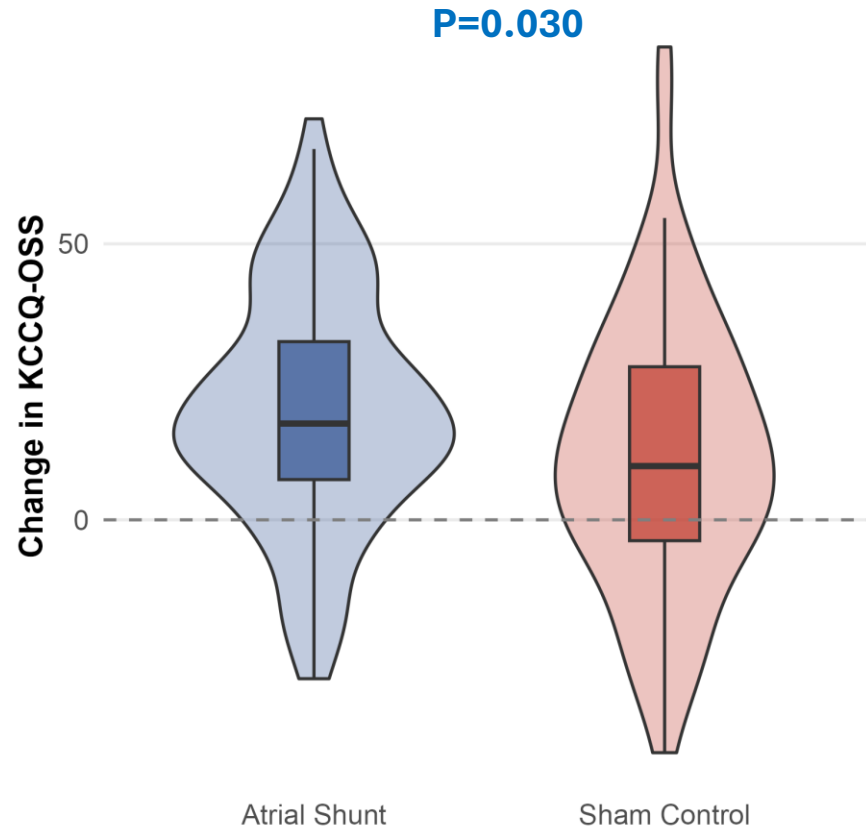


Responders: CV death and non-fatal ischemic stroke

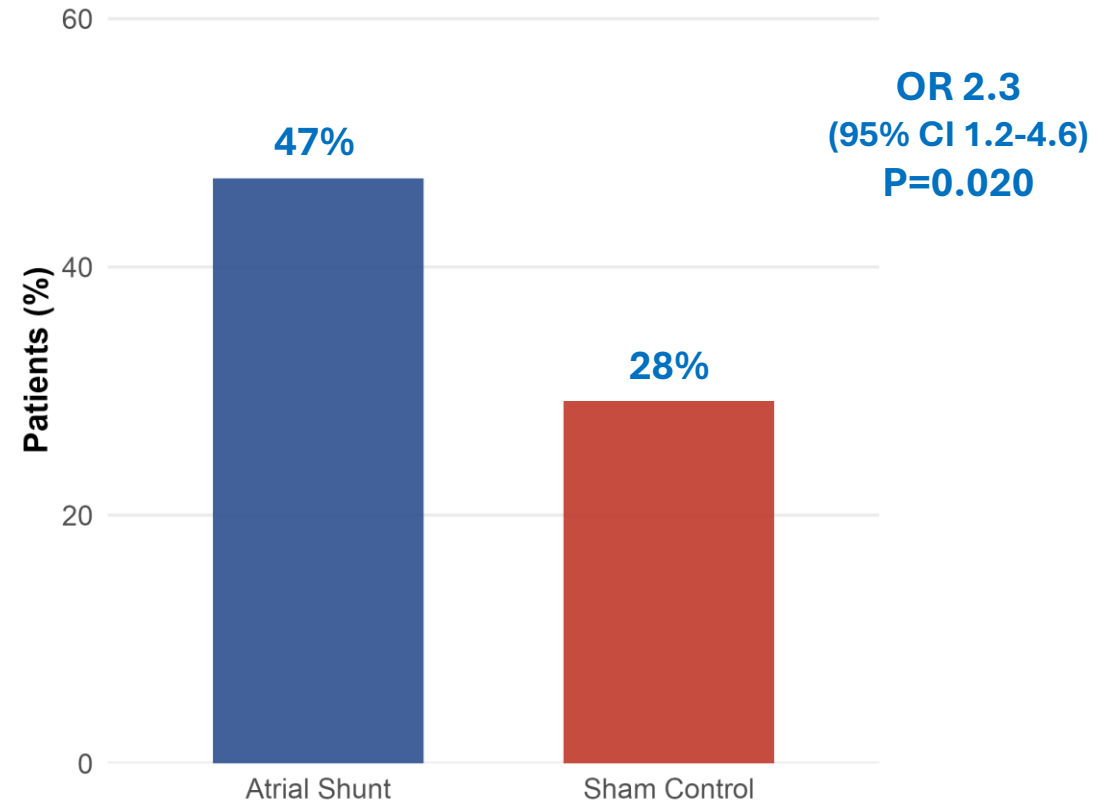


Responders: Health status (QOL, symptoms)

Change in KCCQ-OSS at 5 years



≥20-point improvement in KCCQ-OSS at 5 years



Safety results (all patients)

Safety Endpoint	Atrial Shunt (n=309)	Sham Control (n=312)	P-value
Composite safety endpoint	34.0% (99/291)	30.9% (77/249)	0.444
Cardiovascular death	11.0% (32/291)	8.8% (22/249)	0.405
Non-fatal ischemic stroke	3.8% (11/291)	2.0% (5/249)	0.234
New-onset/worsening kidney dysfunction	15.8% (46/291)	18.5% (46/249)	0.412
MACE	15.1% (44/291)	9.6% (24/249)	0.057
Cardiac death	10.3% (30/291)	8.0% (20/249)	0.364
Myocardial infarction	5.5% (16/291)	2.8% (7/249)	0.130
Cardiac tamponade	1.0% (3/291)	0.0% (0/249)	—
Emergency cardiac surgery	0.3% (1/291)	0.0% (0/249)	—
Thromboembolic complications	1.4% (4/291)	1.2% (3/249)	0.862
TIA	1.4% (4/291)	1.2% (3/249)	0.862
Systemic embolic events	0.0% (0/291)	0.0% (0/249)	—
New-onset persistent AF/flutter	6.5% (19/291)	6.0% (15/249)	0.810

Safety results: Responder group

Safety Endpoint	Atrial Shunt (n=161)	Sham Control (n=152)	P-value
Composite safety endpoint	28.8% (44/153)	36.4% (44/121)	0.181
Cardiovascular death	7.8% (12/153)	6.6% (8/121)	0.697
Non-fatal ischemic stroke	2.0% (3/153)	1.7% (2/121)	0.850
New-onset/worsening kidney dysfunction	13.7% (21/153)	22.3% (27/121)	0.065
MACE	11.8% (18/153)	8.3% (10/121)	0.345
Cardiac death	7.2% (11/153)	5.8% (7/121)	0.642
Myocardial infarction	5.2% (8/153)	3.3% (4/121)	0.444
Cardiac tamponade	1.3% (2/153)	0.0% (0/121)	--
Emergency cardiac surgery	0.0% (0/153)	0.0% (0/121)	--
Thromboembolic complications	1.3% (2/153)	2.5% (3/121)	0.479
TIA	1.3% (2/153)	2.5% (3/121)	0.479
Systemic embolic events	0.0% (0/153)	0.0% (0/121)	--
New-onset persistent AF/flutter	7.8% (12/153)	10.7% (13/121)	0.409

Safety results: Responder group

Safety Endpoint	Atrial Shunt (n=161)	Sham Control (n=152)	P-value
Composite safety endpoint	28.8% (44/153)	36.4% (44/121)	0.181
Cardiovascular death	7.8% (12/153)	6.6% (8/121)	0.697
Non-fatal ischemic stroke	2.0% (3/153)	1.7% (2/121)	0.850
New-onset/worsening kidney dysfunction	13.7% (21/153)	22.3% (27/121)	0.065
MACE	<p>No long-term safety signal in responders; trend toward less renal dysfunction (13.7% vs 22.3%, P=0.065)</p>		0.345
Cardiac death			0.642
Myocardial infarction			0.444
Cardiac tamponade			--
Emergency cardiac surgery			--
Thromboembolic complications	1.3% (2/153)	2.5% (3/121)	0.479
TIA	1.3% (2/153)	2.5% (3/121)	0.479
Systemic embolic events	0.0% (0/153)	0.0% (0/121)	--
New-onset persistent AF/flutter	7.8% (12/153)	10.7% (13/121)	0.409

Safety results: Non-responder group

Safety Endpoint	Atrial Shunt (n=131)	Sham Control (n=134)	P-value
Composite safety endpoint	40.2% (49/122)	28.0% (30/107)	0.055
Cardiovascular death	13.9% (17/122)	12.1% (13/107)	0.690
Non-fatal ischemic stroke	6.6% (8/122)	2.8% (3/107)	0.198
New-onset/worsening kidney dysfunction	17.2% (21/122)	15.9% (17/107)	0.788
MACE	18.0% (22/122)	12.1% (13/107)	0.220
Cardiac death	13.1% (16/122)	11.2% (12/107)	0.662
Myocardial infarction	5.7% (7/122)	2.8% (3/107)	0.288
Cardiac tamponade	0.8% (1/122)	0.0% (0/107)	—
Emergency cardiac surgery	0.8% (1/122)	0.0% (0/107)	—
Thromboembolic complications	1.6% (2/122)	0.0% (0/107)	—
TIA	1.6% (2/122)	0.0% (0/107)	—
Systemic embolic events	0.0% (0/122)	0.0% (0/107)	—
New-onset persistent AF/flutter	5.7% (7/122)	1.9% (2/107)	0.153

Safety results: Non-responder group

Safety Endpoint	Atrial Shunt (n=131)	Sham Control (n=134)	P-value
Composite safety endpoint	40.2% (49/122)	28.0% (30/107)	0.055
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Non-fatal ischemic stroke	6.6% (8/122)	2.8% (3/107)	0.198
New-onset/worsening kidney dysfunction			0.788
MACE			0.220
Cardiac death			0.662
Myocardial infarction	5.7% (7/122)	2.8% (3/107)	0.288
Cardiac tamponade	0.8% (1/122)	0.0% (0/107)	—
Emergency cardiac surgery	0.8% (1/122)	0.0% (0/107)	—
Thromboembolic complications	1.6% (2/122)	0.0% (0/107)	—
TIA	1.6% (2/122)	0.0% (0/107)	—
Systemic embolic events	0.0% (0/122)	0.0% (0/107)	—
New-onset persistent AF/flutter	5.7% (7/122)	1.9% (2/107)	0.153

Non-responders: Trend toward worse composite safety (40.2% vs 28.0%, P=0.055); numerically higher stroke (6.6% vs 2.8%)

REDUCE LAP-HF II 5-year outcomes: Conclusions

- 1** In the overall trial cohort, the primary endpoint remained neutral at 5 years (Win ratio 0.99, P=0.93)
- 2** Responder group: (50% of pts): **Currently being validated in RESPONDER-HF**
 - Significant benefit on primary composite (WR 1.48, P=0.027)
 - 34% relative reduction in HF events (22% vs 34%; P=0.04)
 - 2-fold greater improvement in KCCQ-OSS (+19 vs +9; P=0.03)
 - No safety concerns through 5 years of follow-up
- 3** In non-responders, atrial shunting was associated with worse outcomes (WR 0.67, P=0.024) and trend toward worse safety
- 4** Patient selection based on exercise hemodynamics is essential for optimal outcomes with atrial shunting in HFpEF