Impact of Alcohol Abstinence in Moderate Drinkers with Atrial Fibrillation: Results from the Alcohol-AF Randomized Controlled Trial

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Disclosures

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- No commercial sponsor
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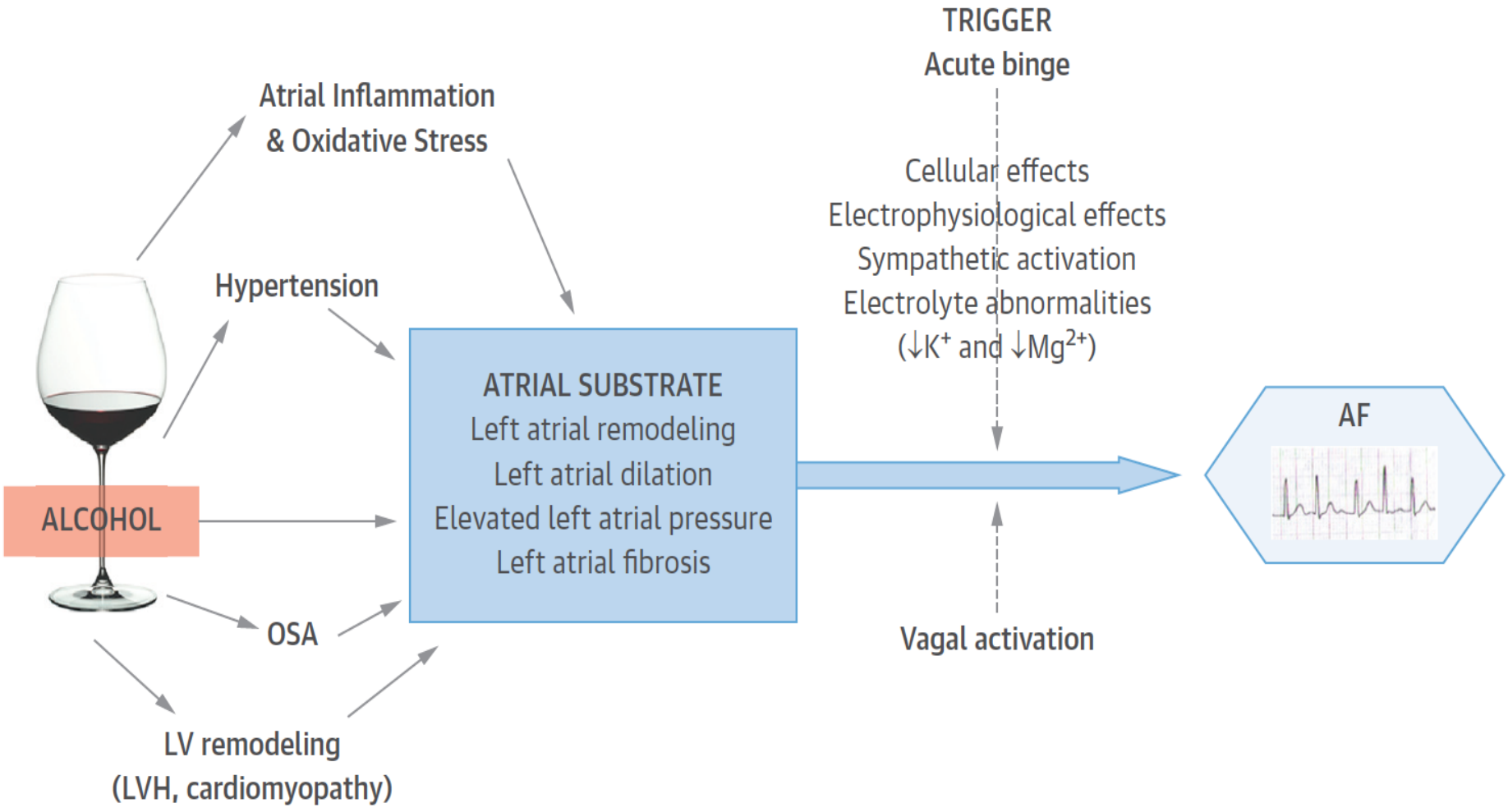
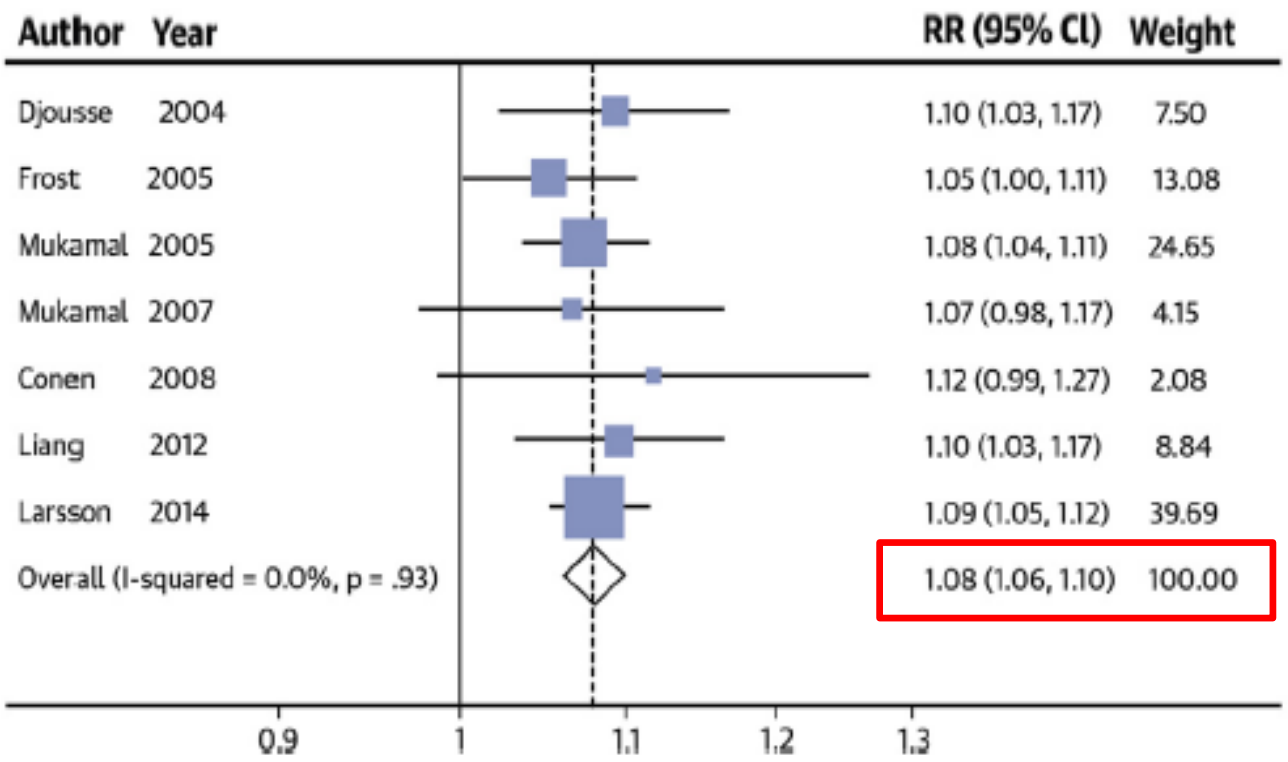
Multiple mechanisms linking alcohol to AF



Voskoboinik A et al. JACC 2016;68:2567-76

Relative risk (RR) of incident AF per 1 drink/day increment in alcohol consumption



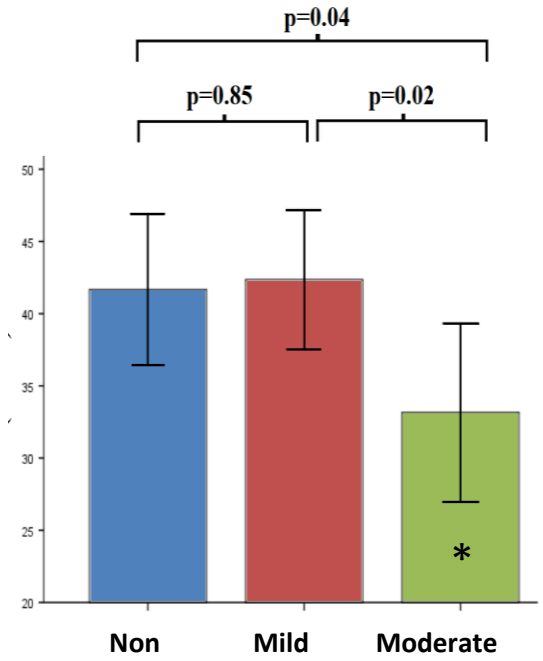
CENTRAL ILLUSTRATION Forest Plot of Relative Risks of Atrial Fibrillation Per 1 Drink/Day Increment in Alcohol Consumption

Larsson SC et al. JACC 2014;64(3):281-9

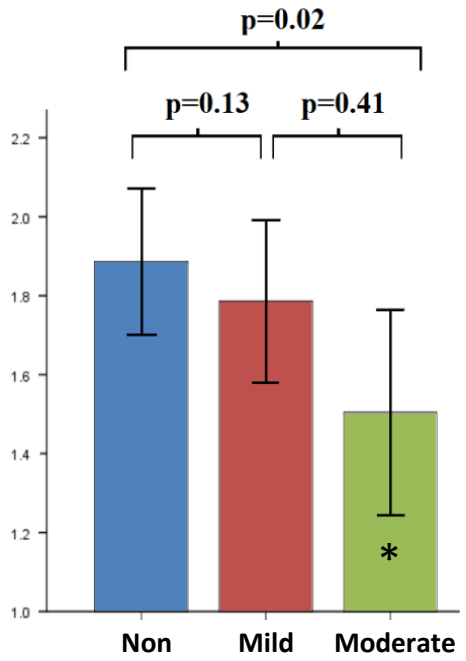
Adverse atrial remodelling and higher AF recurrence rates with increasing alcohol consumption

Atrial substrate

LA CONDUCTION VELOCITY

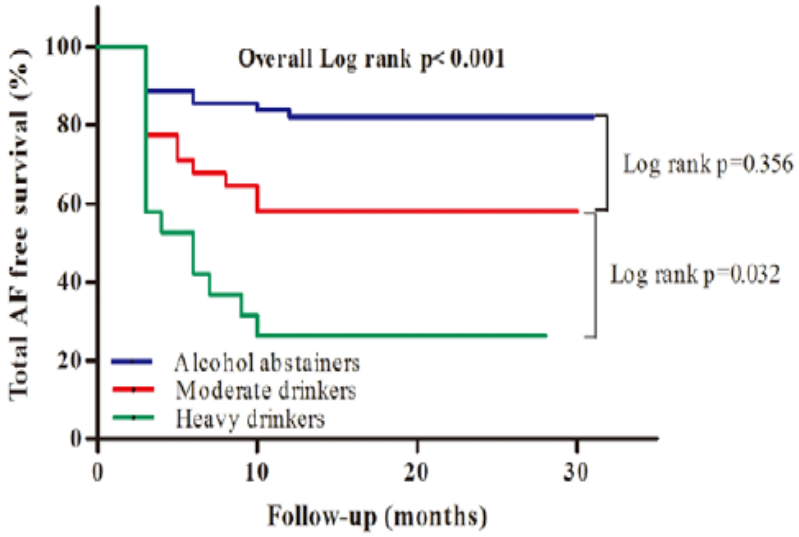


LA MEAN VOLTAGE



Voskoboinik A, et al. Heart Rhythm 2019;16(2):251-259.

AF Recurrence rates following ablation



Qiao Y, et al. J Am Heart Assoc 2015

* moderate: 7 - 28 standard drinks per week

Alcohol-AF trial

No randomized controlled trial to date looking at the impact of alcohol abstinence in moderate drinkers with atrial fibrillation.

Inclusion criteria:

- **Paroxysmal AF** (atrial fibrillation and/or flutter), with minimum 2 episodes in the last 6 months **or persistent AF** requiring cardioversion (all patients in sinus rhythm and on stable medical therapy at randomization)
- Average alcohol intake **≥ 10 standard drinks per week** (1 SD ~ 12g ETOH)

Key exclusion criteria:

- Permanent AF
- Severe left ventricular systolic dysfunction (LVEF < 35%)
- Alcohol dependence or significant psychiatric comorbidity
- Liver cirrhosis

Study design

- Multicenter, prospective, open-label, randomized controlled trial at six Australian hospitals.
- Randomization 1:1 to undertake abstinence or continue usual consumption.
- Four week run-in phase
- Comprehensive rhythm monitoring
  - Implantable loop recorder or existing pacemaker
  - Twice daily AliveCor ® mobile phone app in conjunction with Holter monitoring
- Follow-up 6 months

Group allocation

Abstinence arm:

- All patients counselled to abstain completely.
- Provided verbal and written advice to assist with compliance
- Urine testing for ETG (alcohol metabolite)
- Positive reinforcement through monthly contact with study investigators

Control arm:

- Allowed to continue usual alcohol consumption.
- Not required to increase their usual drinking as part of the trial.

Co-primary endpoints – at 6 months

(1) Freedom from AF recurrence, defined as any atrial tachyarrhythmia lasting ≥ 30 seconds (after a 2-week blanking period)

(2) AF burden, defined as percentage of time in AF during the 6-month follow-up period.

- calculated based on the time-weighted average of the proportion of EKGs during the six months which indicated the presence of AF.

- Blinded adjudication by two cardiologists
- Primary endpoints shortened from 12 months to 6 months in June 2017 by the steering committee due to challenges with recruitment, in particular unwillingness to be randomized to abstinence for 12 months.

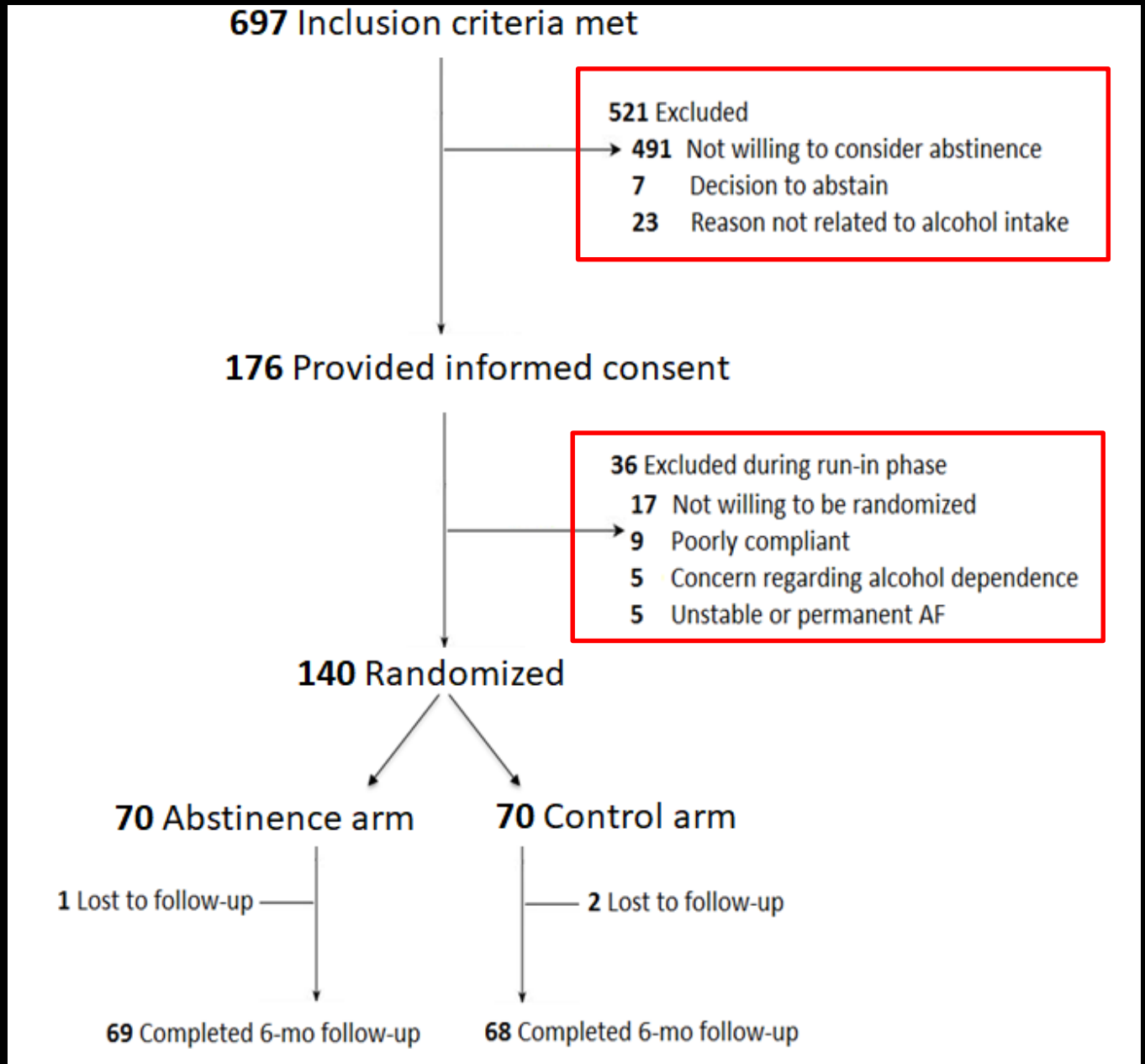
Secondary endpoints – at 6 months

- Change in weight
- Change in systolic and diastolic blood pressure
- Change in AF symptom severity
- AF-related hospitalizations
- Structural remodelling (cardiac MRI)

Pre-specified statistical analysis

- **Power calculation: 70 patients in each group** to provide a power of 0.8 at an alpha value of 0.05 to detect a minimum absolute difference in recurrence of 20% between groups (assuming a 30% recurrence rate).
- **Intention-to-treat analysis.**
- Performed by independent statisticians masked to group allocation.
- Time-to-event analyses for AF recurrence performed with Kaplan-Meier plots and the log-rank test. Univariate and multivariate analyses were performed using Cox's proportional hazards accounting for co-variates.
- AF burden: Shapiro-Wilk test performed to determine if the data was normally distributed. A student t-test was performed if data were normally distributed; otherwise a Mann-Whitney test was utilized.

CONSORT diagram



Baseline demographics

Parameter	Abstinence group (n=70)	Control group (n=70)
Age (years)	61.6±9.4	62.8±8.6
Gender (% male)	61 (87.1%)	58 (82.9%)
Weight (kg)	89.9±16.0	89.3±13.3
Body mass index (BMI)	28.4±4.4	28.5±4.5
Hypertension (%)	31 (44.3%)	26 (37.1%)
Diabetes mellitus (%)	5 (7.1%)	6 (8.6%)
TIA / stroke	7 (10.0%)	5 (7.1%)
Previous / current smoker	13 (18.6%)	11 (15.7%)
Obstructive sleep apnea	12 (17.1%)	16 (22.9%)
Coronary artery disease	10 (14.3%)	5 (7.1%)
Prior heart failure	6 (8.6%)	6 (8.6%)

Baseline AF & clinical characteristics

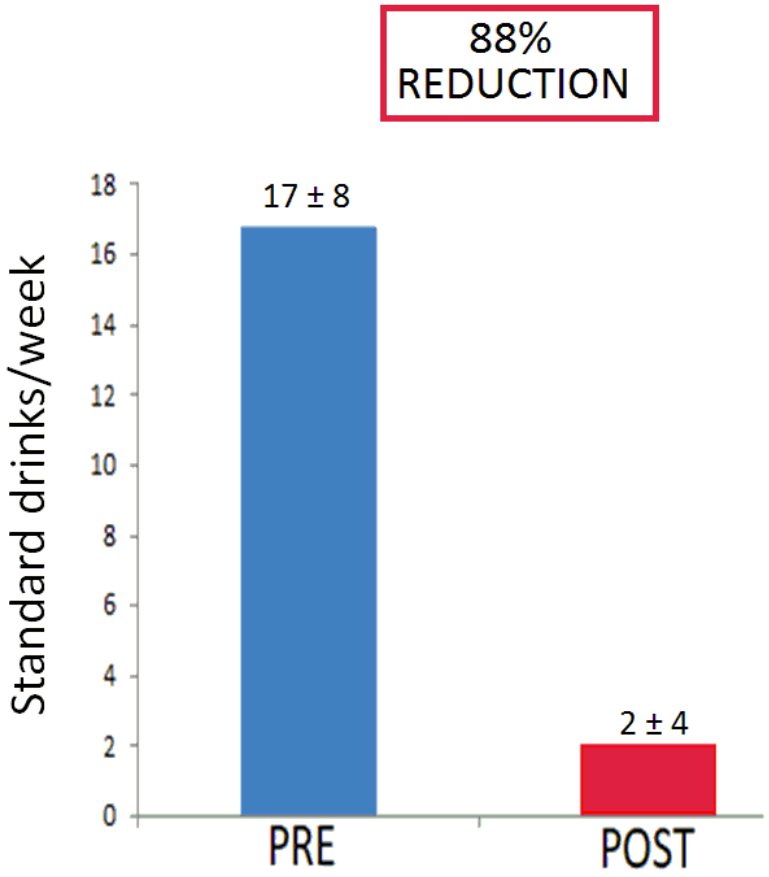
Parameter	Abstinence group (n=70)	Control group (n=70)
CHA_2DS_2-VASc score	1.5±1.2	1.3±1.1
Time from first AF diagnosis (yrs)	6.9±7.2	5.0±5.3
AF type (paroxysmal / persistent)	45/25 (64.3% / 35.7%)	43 / 27 (61.4% / 38.6%)
Previous AF ablation	20 (28.6%)	25 (35.7%)
Pacemaker or loop recorder	23 (32.9%)	27 (38.6%)
Antiarrhythmic therapy	44 (62.9%)	49 (70.0%)
Amiodarone	6 (8.6%)	4 (5.7%)
Sotalol	20 (28.6%)	23 (32.9%)
Flecainide	18 (25.7%)	22 (31.4%)
Echocardiographic variables		
LA area (cm^2)	27.3±8.3	26.8±6.8
LVEF (%)	57±8	57±11
LV mass index (g/m^2)	100.0±23.2	94.9±23.4

Baseline drinking status

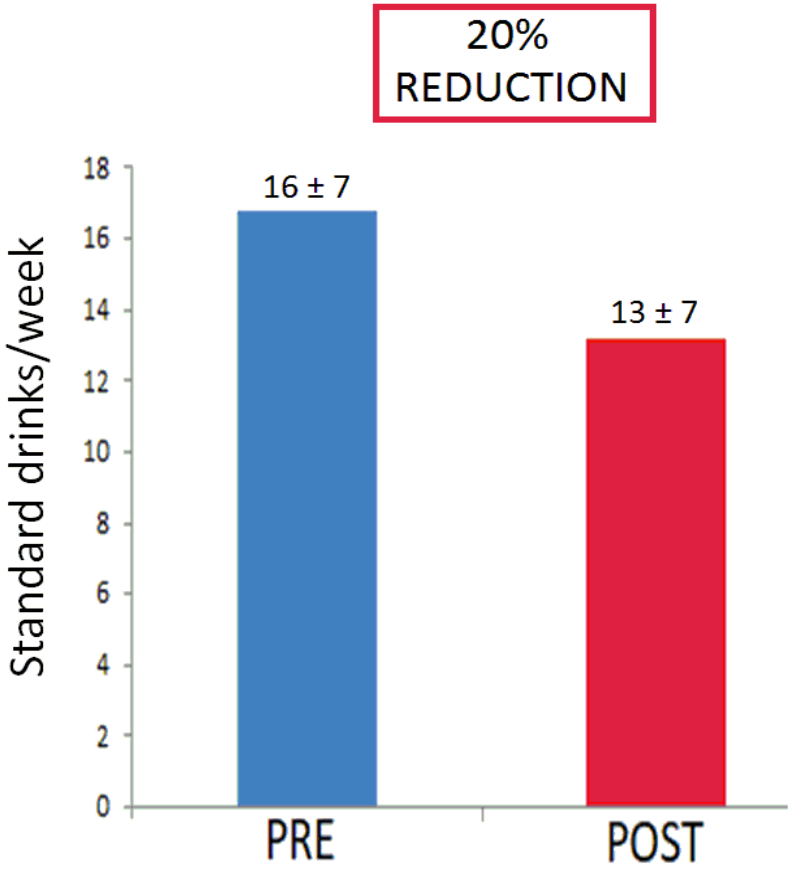
Parameter	Abstinence group (n=70)	Control group (n=70)
Alcohol intake (drinks/week)	16.8±7.7	16.4±6.9
Beverages consumed		
Wine	48 (68.6%)	47 (67.1%)
Beer	34 (48.6%)	34 (48.6%)
Spirits	13 (18.6%)	9 (12.9%)
Binge drinking	20 (28.6%)	16 (22.9%)
MCV (fL)	91±3	93±5
GGT (U/L)	41±29	47±26

Compliance

Abstinence arm (n=70)

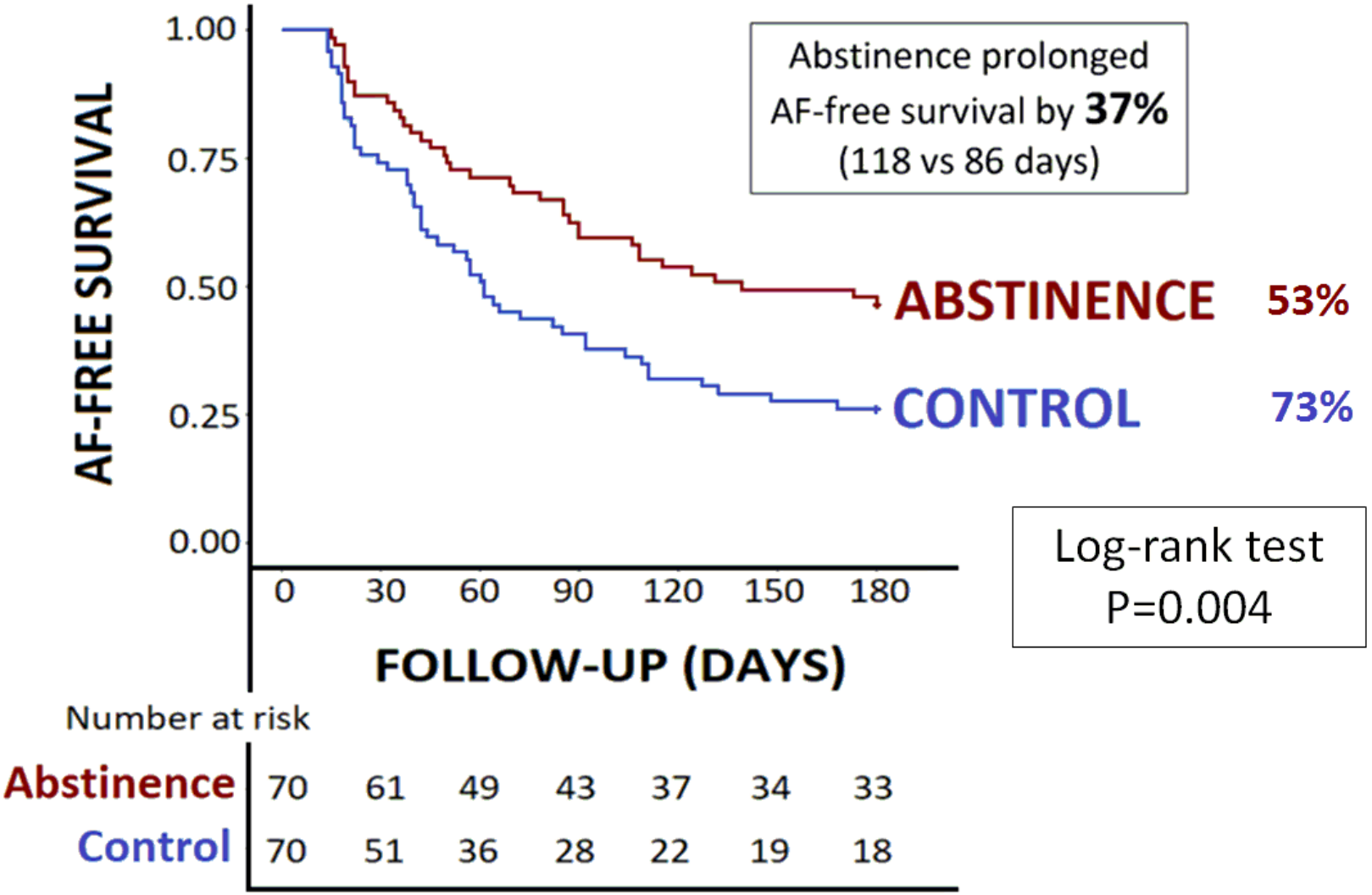


Control arm (n=70)



*Complete abstinence (n=43, 61.4%)

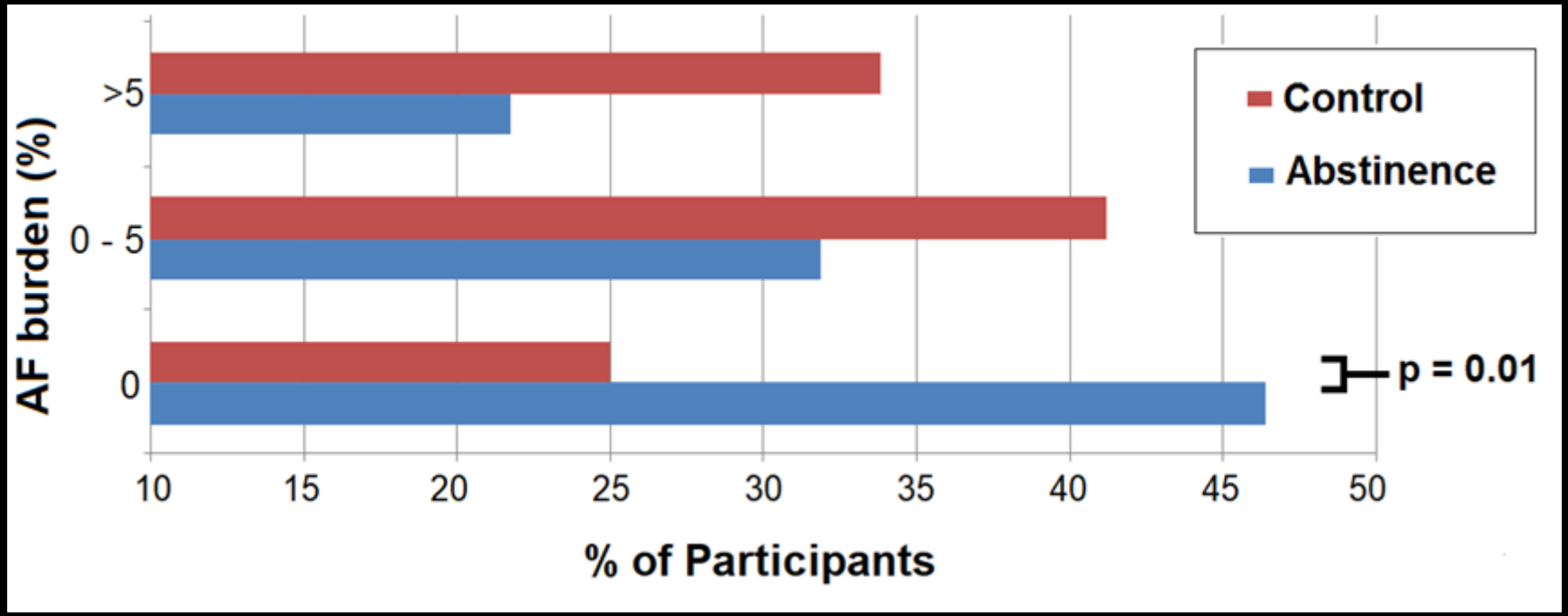
Time to AF recurrence



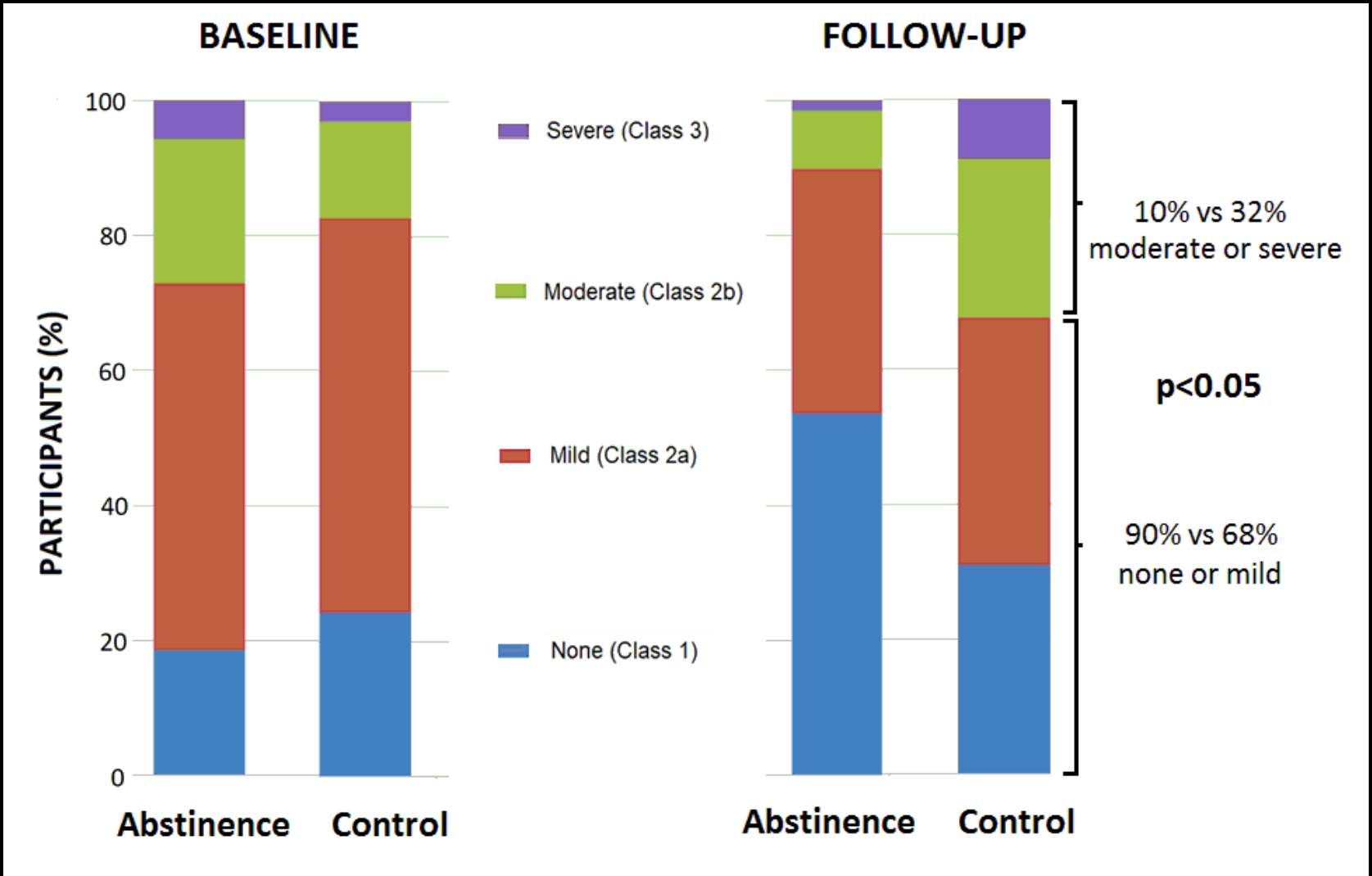
AF burden

AF burden significantly lower in the Abstinence group (p=0.016):

	Mean	Median
Abstinence group	5.6 ± 12.4%	0.5% (IQR 0–3.7%)
Control group	8.2 ± 14.5%	1.2% (IQR 0.0–10.5%)



AF symptom severity (EHRA score)



AF-related hospitalizations occurred in 6 (9%) of Abstinence patients and 14 (20%) Controls (p=0.053).

Secondary endpoints

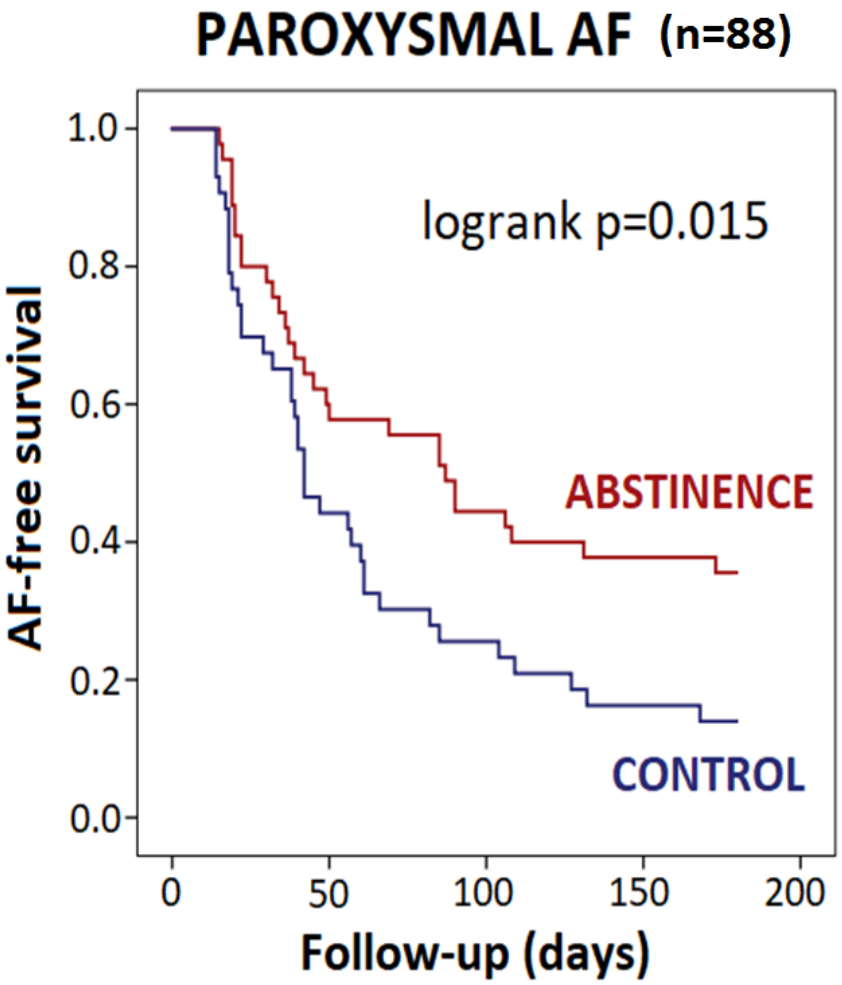
- Abstinence associated with significant reductions in:
  - **Blood pressure**
  - **Weight**
  - **Body mass index**

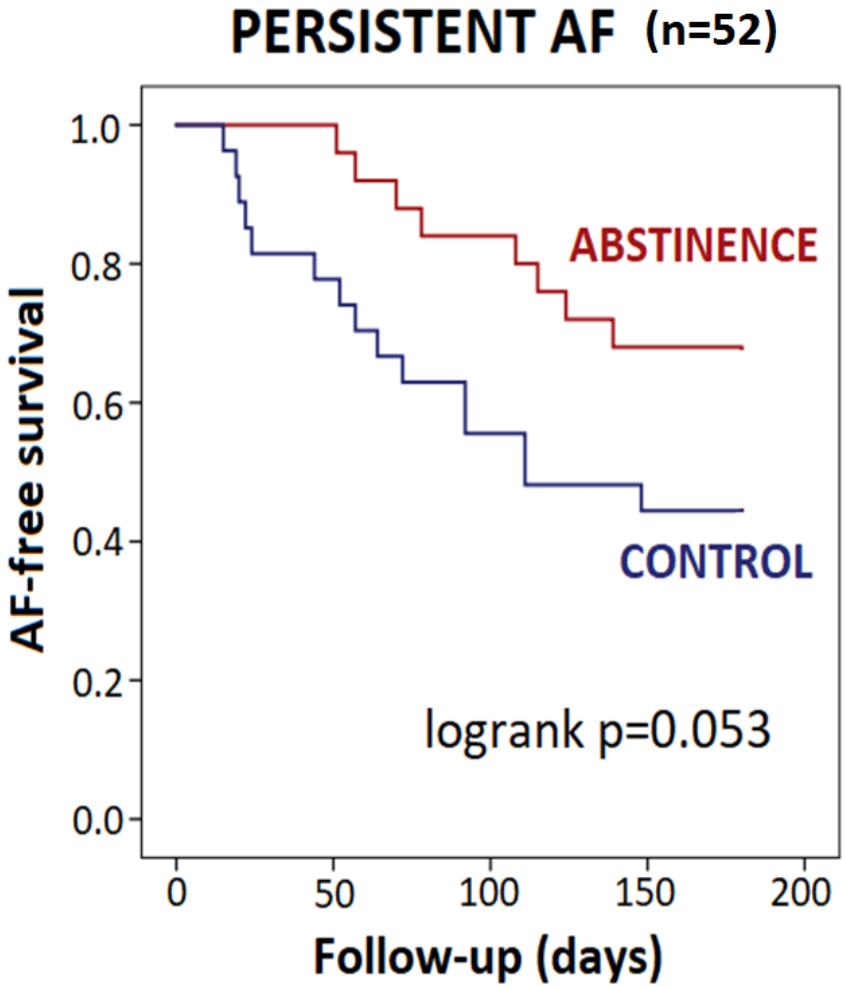
	Abstinence			Control		
	Baseline	Follow-up	P	Baseline	Follow-up	P
Blood pressure						
Systolic BP (mmHg)	138±16	126±17	<0.001	133±17	131±15	0.40
Diastolic BP (mmHg)	78±10	75±12	0.03	77±10	76±11	0.62
Mean BP (mmHg)	98±10	92±12	<0.001	96±11	95±10	0.48
Weight (kg)	90±16	87±14	<0.001	89±13	91±14	0.04
BMI	28.4±4.4	27.7±3.8	<0.001	28.5±4.5	28.9±4.9	0.03

Secondary endpoints

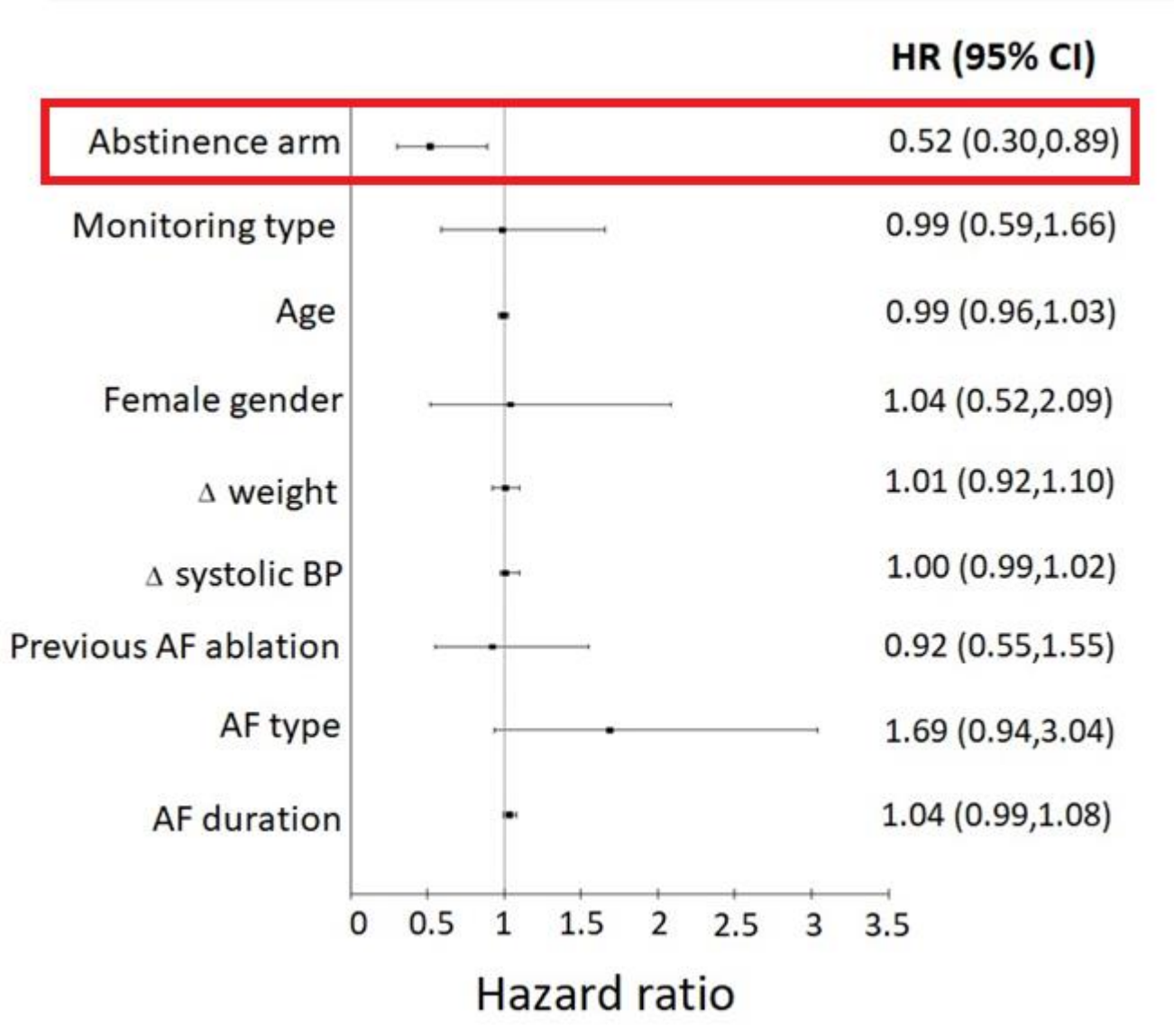
	Abstinence			Control		
Cardiac MRI	Baseline	Follow-up	p value	Baseline	Follow-up	p value
LA area (cm^2)	29.5±4.9	27.1±4.5	<0.01	31.7±6.0	31.9±7.2	0.84
LAVI (mL/m^2)	56.7±11.9	53.7±6.4	0.09	56.0±16.7	50.0±4.4	0.40
LA emptying fraction (%)	42±14	50±8	0.02	38±11	41±5	0.27
Epicardial fat area (cm^2)	4.3±2.4	3.9±1.8	0.19	4.3±3.7	5.5±3.0	0.07
LVEF (%)	58.3±10.5	58.8±9.8	0.30	60.0±6.0	56.6±9.8	0.39

Recurrence by AF type





Multivariate predictors of AF recurrence



ABSTINENCE ARM: Hazard ratio 0.52, 95% CI 0.30 – 0.89

Conclusion

- In AF patients with moderate alcohol consumption, alcohol abstinence was independently associated with:
  - Reduction in AF burden
  - Reduction in AF recurrence rates
  - Improvement in symptom severity.
  - Weight loss and improved blood pressure control

Significant reduction in alcohol intake should be part of the lifestyle intervention in moderate drinkers with AF.