The UK Mini Mitral Trial

Minimally invasive thoracoscopically-guided right minithoracotomy versus conventional sternotomy for mitral valve repair: a multicentre randomised controlled trial

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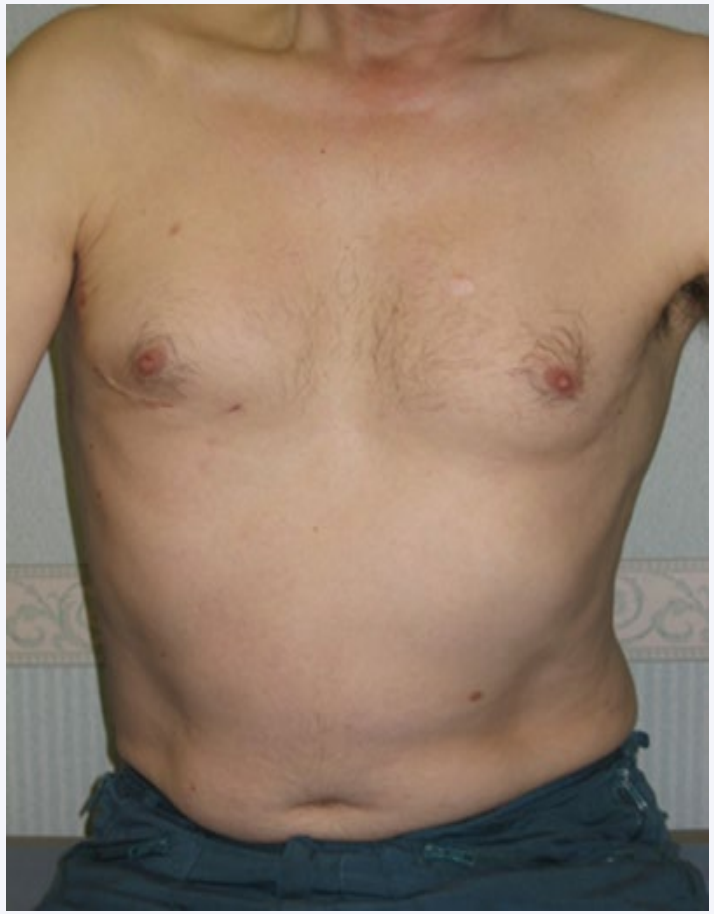
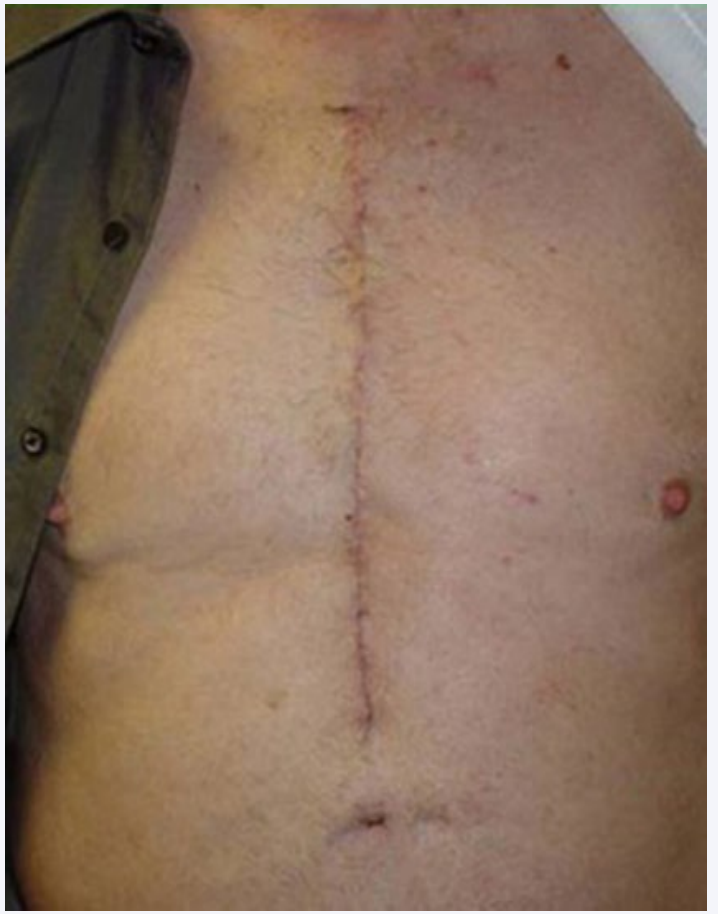
Disclosure Statement of Financial Interests

No relevant financial relationships with any commercial entity

Minimally invasive versus conventional sternotomy at 12 weeks post surgery





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Background

- The best surgical approach for mitral valve repair is widely debated
- Minimally Invasive MVrep via mini thoracotomy is preferred by patients
- However there are significant question marks which centre on:
  - *'can you repair as many' ?*
  - *'can you repair them as well' ?*
  - *'is it as safe' ?*
- The emergence of percutaneous strategies to treat DMR and the need for trials to determine which procedures benefit specific patients groups make defining the optimum surgical approach an **urgent priority**

UK Data	2021/2022	%
Sternotomy	1436	82.0%
Mini Thoracotomy	219	12.4%
Robot Assisted	5	0.3%
Other	17	1.0%
Missing	84	4.8%

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Objectives

Primary

- The primary objective was to determine if **physical function** and associated return to usual activities measured by change in **SF-36v2 physical functioning scale** from **baseline to 12 weeks** following index surgery was **superior in Mini** versus Sternotomy

'once I'm assured of surgical expertise, the key question influencing my choice of procedure is speed of recovery of physical function after surgery'

Secondary

- Physical function at 6 weeks
- Physical activity and sleep efficiency measured by accelerometery at 6 and 12 weeks
- Mitral valve repair rates
- Quality of mitral valve repair (rate of moderate or severe MR at 12 weeks and 1 year)
- Adverse events (death, stroke, heart failure hospitalisation, and repeat intervention on the mitral valve)

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Trial Methodology

- **Expertise based** superiority RCT
- Potentially eligible patients reviewed by Multi-Disciplinary Heart Team (MDT)
  - DMR
  - **Suitable for both approaches**
- Eligibility patients were **randomised 1:1** to a Mini or Conventional Sternotomy expert
- Patients had to move surgeons
- All had intra op TOE
- MVrep techniques were at the discretion of the surgeon

- **Follow-up for 1 year** post index surgery including
  - SF-36v2 physical function scores measured by a **blinded researcher**
  - **Echocardiogram** early (within 12 weeks) and at 1 year after surgery assessed by **blinded Core Laboratory**
  - **Physical activity and sleep efficiency** measured by accelerometers for 1 week at a time
  - Follow-up at 6, 12, 18, 24, 38, 52 weeks (post-intervention) with phone calls from the research team.

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Participating sites

1. Royal Infirmary of Edinburgh, Edinburgh
2. Blackpool Teaching Hospital, Blackpool
3. The James Cook Hospital, Middlesbrough
4. Liverpool Heart and Chest Hospital, Liverpool
5. Derriford Hospital, Plymouth
6. Bristol Royal Infirmary, Bristol
7. Harefield Hospital, Uxbridge
8. Hammersmith Hospital, London
9. King's College Hospital, London
10. Basildon University Hospital, Basildon

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Inclusion criteria

- Adult (≥18 years old at consent) patients with **degenerative mitral valve disease**, **requiring isolated MVr** (*patients requiring concomitant surgery for Atrial Fibrillation and/or Patent Foramen Ovale (PFO) closure were included*).
- Written informed consent.
- Fit for cardiac surgery and cardiopulmonary bypass.

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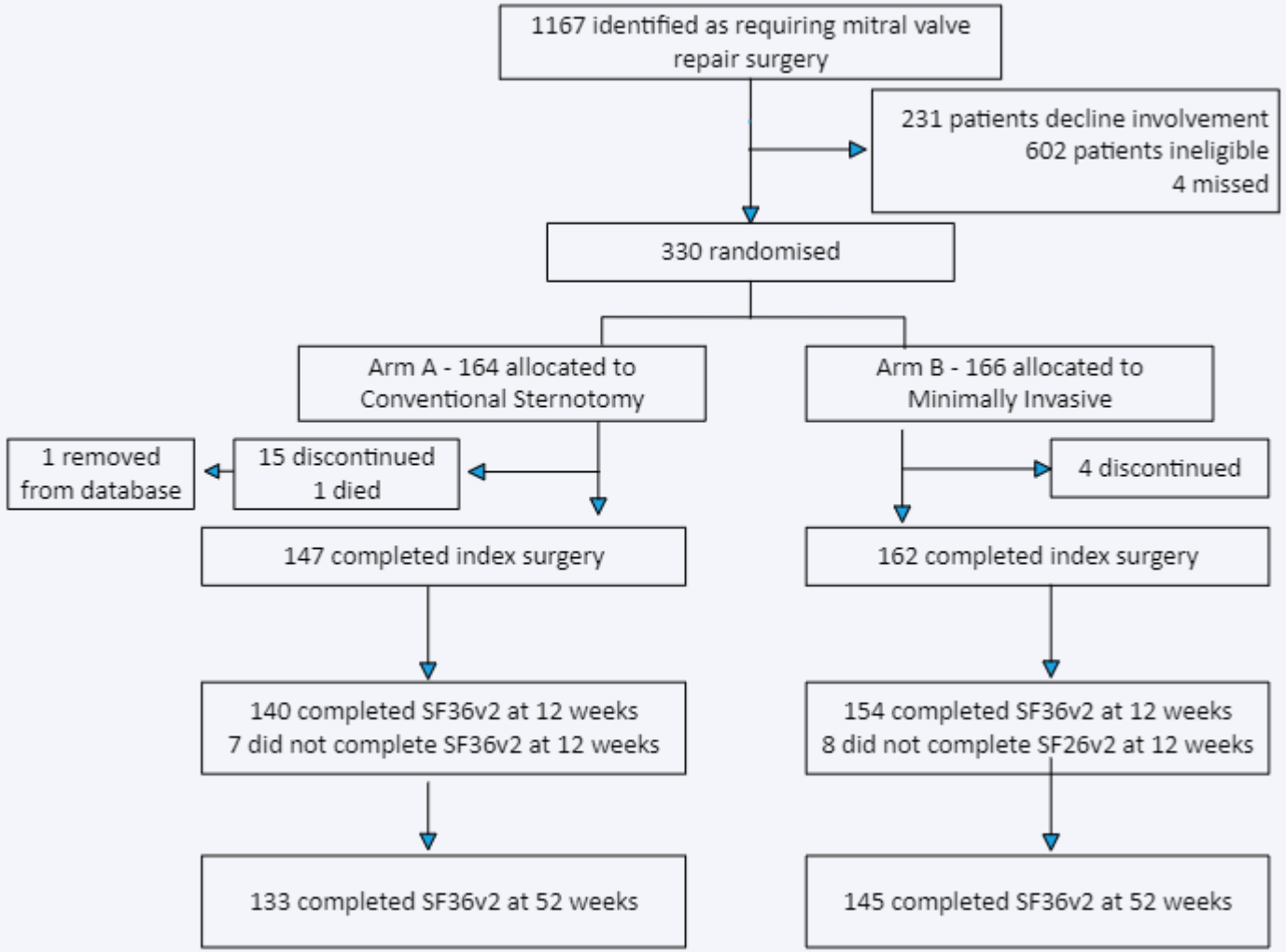
Participant flow



Screening	
	Total
Total Patients Screened	**1167**
Total Patients Ineligible	602
Total Patients Declined	231
Total Patients Missed	4
Total Patients Randomised	**330**

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Surgical expertise

- **28 surgeons** were approved by the Trial Steering Committee as experts able to perform surgery in the trial
- Experts had to have **completed 50 procedures**

Surgeon Expertise	Sternotomy (n=16)	Mini (n=12)	Total (n=28)
Number of **operations performed** prior to performing surgery in the trial *median (IQR;min-max)*	162 (100-400; 59-1000)	86 (55-200; 50-500)	110 (78.75-245.25; 50-1000)
Number of **years** performing the operation prior to performing surgery in the trial *median (IQR;min-max)*	14.5 (8-19.25; 4-26)	7.5 (4-10.5; 2.5-13)	9 (6.75-15.25; 2.5-26)

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Baseline Characteristics

KEY MESSAGES

Patients in both groups were similar

Average age	67
AF	40%
Women	30%
NYHA III/IV	50%
EuroScore II	1.7

	Sternotomy (N=163)	Mini (N=166)
Demographic		
Age at randomisation— yr	66.99±11.51	67.29±10.13
Male Sex — no. (%)	111 (68.1)	118 (71.1)
Race — no. (%)		
White	158 (96.9)	166 (100)
Non white	5 (3.1)	0 (0)
BMI—mean±SD; no.	26.2±4.21; 160	26.5±4.20; 165
Clinical — no./total no. (%)		
History of Atrial Fibrillation	69/160 (43.1)	69/165 (41.8)
History of Heart Failure	45/160 (28.1)	42/165 (25.5)
History of Stroke	13/160 (8.1)	7/165 (4.2)
History of previous MI	5/160 (3.1)	6/165 (3.6)
History of Chronic Obstructive Pulmonary Disease	11/160 (6.9)	14/165 (8.5)
Asthma	13/160 (8.1)	17/165 (10.3)
History of Peripheral Vascular Disease	1/160 (0.6)	4/165 (2.4)
History of Pulmonary Hypertension	24/150 (16)	30/162 (18.5)
Moderate (vs No)	16/150 (10.7)	17/162 (10.5)
Severe (vs No)	8/150 (5.3)	13/162 (8)
NYHA functional class III/IV	77/150 (51.3)	87/162 (53.7)
In-house urgent patient	18/150 (12)	14/162 (8.6)
Euroscore II — mean±SD; no.	1.7±1.43; 150	1.72±1.67; 162
Baseline physical function (SF-36 PF score)		
Low	36 (22.1)	36 (21.7)
Medium (vs Low)	58 (35.6)	60 (36.1)
High (vs Low)	69 (42.3)	70 (42.2)

Baseline TTE

Variable	Sternotomy n/N(%)	Mini n/N(%)	Total n/N(%)
MR Severity			
Mild	0/103(0%)	0/106(0%)	0/209(0%)
Moderate	8/105(7.62%)	7/107(6.54%)	15/212(7.08%)
Severe	97/105(92.38%)	100/107(93.46%)	197/212(92.92%)
Missing	2/107(1.87%)	2/109(1.83%)	4/216(1.85%)
Location of Mitral Valve Pathology			
Type I	5/106(4.72%)	2/109(1.83%)	7/215(3.26%)
Type II	101/106(95.28%)	106/109(97.25%)	207/215(96.28%)
Type IIIa (leaflet restriction rheumatic)	0/106(0%)	1/109(0.92%)	1/215(0.47%)
Type IIIb (leaflet restriction ischemic)	1/106(0.94%)	0/109(0%)	1/215(0.47%)
Other	2/106(1.89%)	1/109(0.92%)	3/215(1.4%)
Missing	1/107(0.93%)	0/109(0%)	1/216(0.46%)
Location of Mitral Pathology			
Bileaflet involvement	24/105(22.86%)	28/108(25.93%)	52/213(24.41%)
Isolated anterior leaflet	8/105(7.62%)	8/108(7.41%)	16/213(7.51%)
Isolated posterior leaflet	68/105(64.76%)	71/108(65.74%)	139/213(65.26%)
Leaflets normal	5/105(4.76%)	1/108(0.93%)	6/213(2.82%)
Missing	2/107(1.87%)	1/109(0.92%)	3/216(1.39%)

KEY MESSAGES

92% had severe MR

96% had Type II MV pathology

65% had isolated P2 prolapse

23% had bileaflet prolapse

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Operative data

KEY MESSAGES

Mini procedure took more time

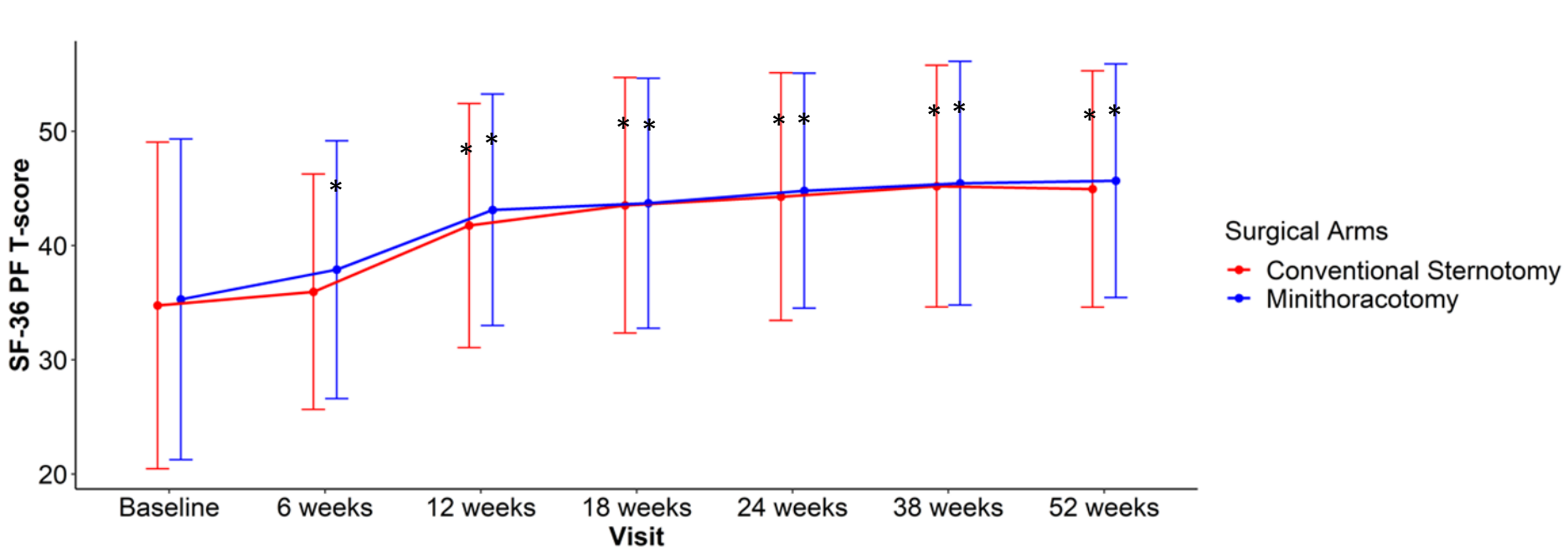
X clamp time 11 minutes

CPB time 30 minutes

Procedure time 44 minutes

Operative Data – no/total no%	Sternotomy (n=163)	Mini (n=166)
Mitral valve repair	**142/146 (97.3)**	**153/160 (95.6)**
AF surgery	20/69 (30%)	21/69 (30%)
TV surgery	10/111 (9)	2/120 (1.7)
Repair technique		
Resection	28/146 (19.2)	10/157 (6.4)
Chords	39/146 (26.7)	22/157 (14)
Premeasured loops	48/146 (32.9)	89/157 (56.6)
Edge to Edge	4/146 (2.7)	8/157 (5.1)
Mitral valve ring size— mm., mean±SD; no.	32.73±2.56; 142	31.5±2.9; 153
CPB time — m., mean±SD; no.	102.01±74.59; 146	134.77±41.04; 159
Aortic cross clamp time — m., mean±SD; no.	74.53±24.52; 146	85.6±30.82; 158
Duration of procedure — m., mean±SD; no.	184.34±42.65; 145	228.73±56.38; 159
Repeat bypass run for valve re repair or replacement	7/146 (4.8)	5/160 (3.1)

Change in PF from baseline up to 52 weeks



KEY MESSAGES

For **Mini, PF T-scores increased significantly from baseline to 6 weeks** and increased throughout the year.

For **Sternotomy, PF T-scores at 6 weeks are not significantly different** from baseline, however they become significantly different from 12 weeks and increase further throughout the year.

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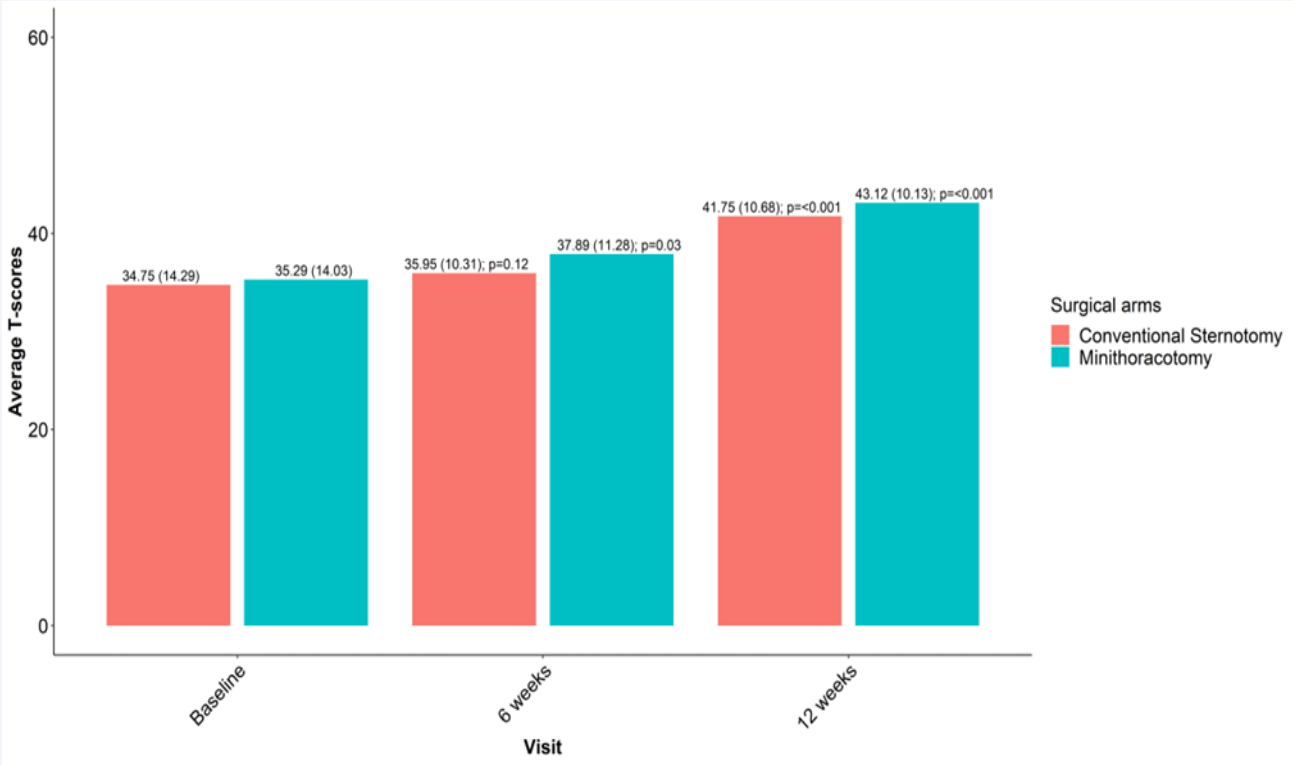
Primary Outcome: the difference in the change in PF from baseline to 12 weeks between groups was not significant



The mean difference in physical function (T-score) from baseline between groups: 0.675 (-1.89,3.26); 0.61

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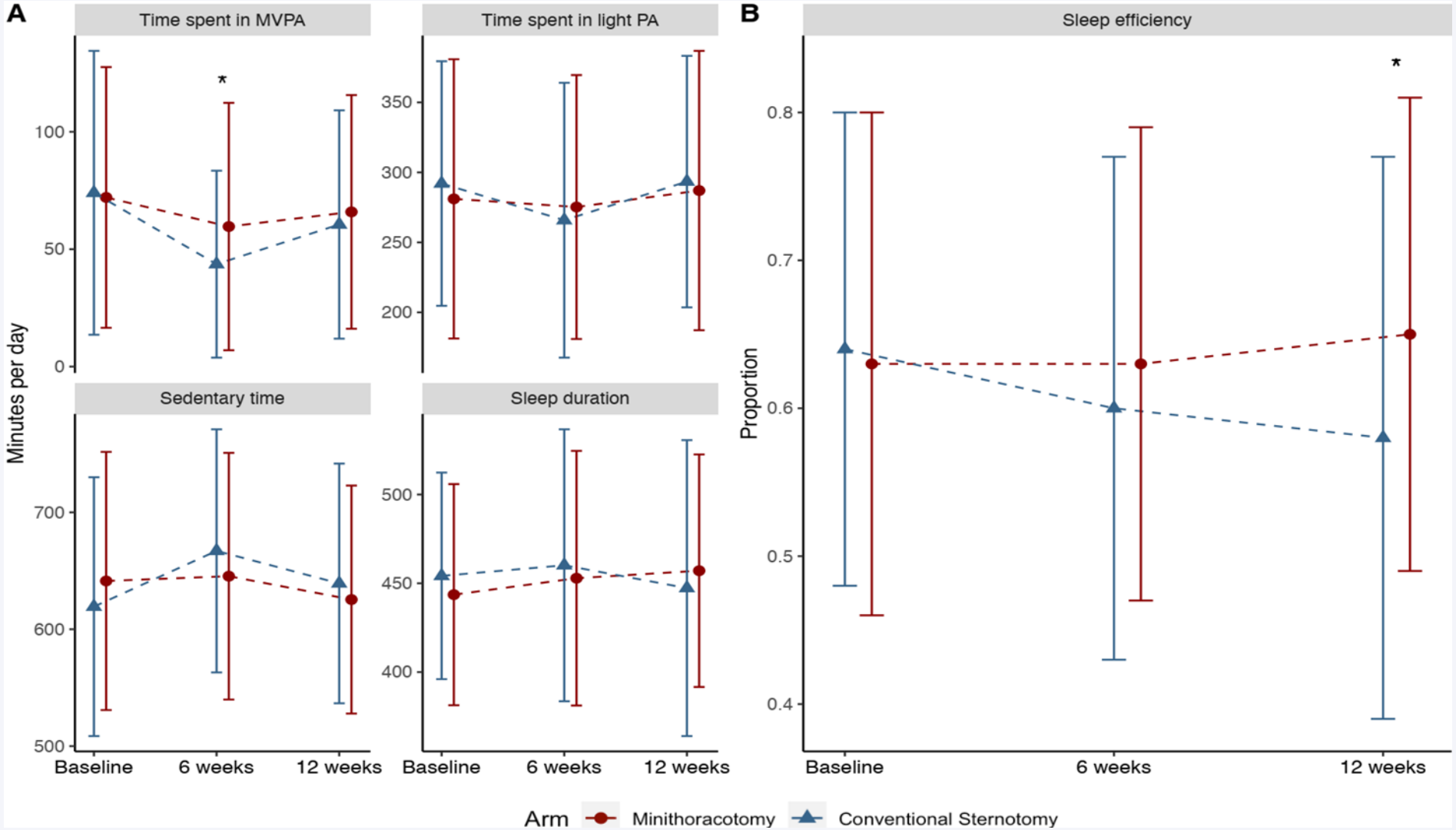
Physical Activity and Sleep (Accelerometer)



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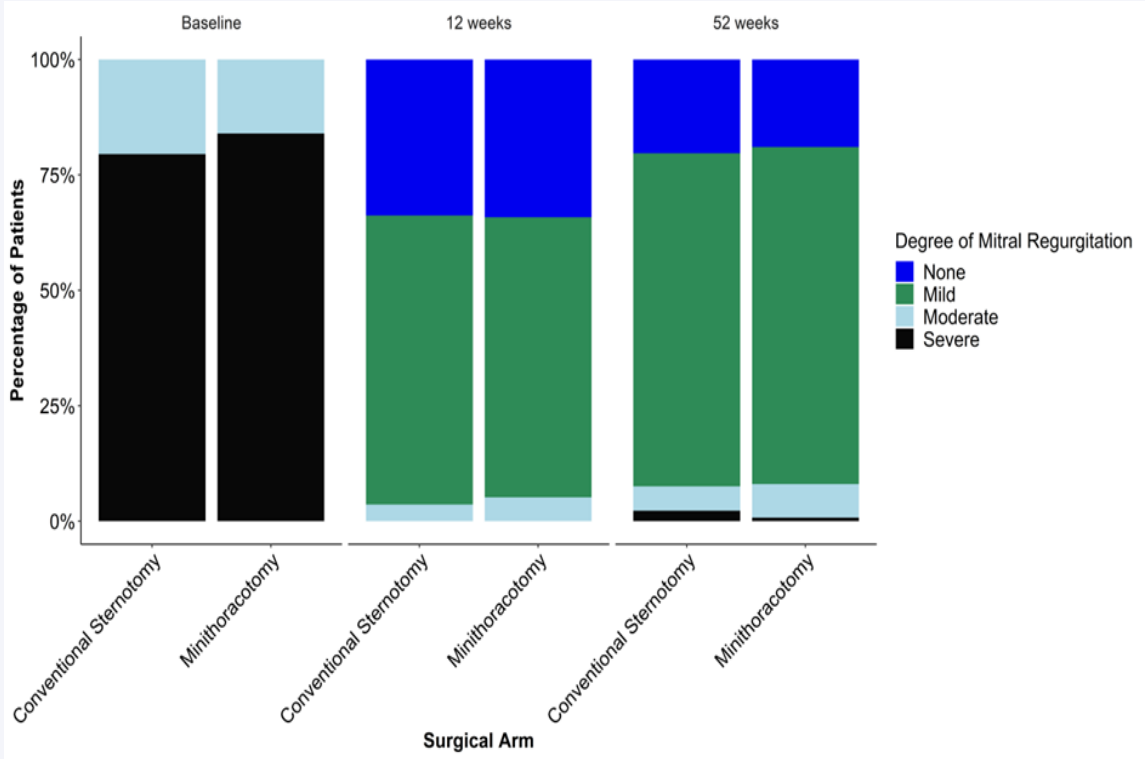
Echocardiographic outcomes



- MR reduced to grade none or mild for 95% of participants in both groups at 12 weeks and 92% at 52 weeks.
- At 52 weeks 3 Sternotomy participants and 1 Mini participant had severe MR
- At 52 weeks, in both groups, left ventricular dimensions and volumes reduced significantly compared to baseline with no significant differences between groups

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Early outcomes safety (up to 12 weeks)

	Sternotomy	Mini	Odds Ratio (95%CI); p-value
Death	4(2.5)	1 (0.6)	0.24 (0.03,2.2); 0.2
Stroke with permanent deficit	5 (3.1)	1 (0.6)	0.19 (0.02,1.67); 0.13
MI	1 (0.6)	0 (0)	-
Tracheostomy	0 (0)	3 (1.8)	-
Renal Impairment – AKIN criteria (150% increase over baseline /- replacement therapy)	4 (2.5)	3 (1.8)	0.63 (0.14,2.92); 0.55
Prolonged ventilation (>48 Hrs)	3 (1.8)	4 (2.41)	1.19 (0.26,5.47); 0.82
ICU LOS (hours) – median (IQR)	21.7 (9.2)	23.03 (21.6)	P=0.07
Proportion of prolonged CICU stay (>48 hours)	19 (11.7)	21 (12.7)	1.25 (0.62,2.52); 0.54

Length of stay (LOS)

	Sternotomy	Mini	Odds Ratio (95%CI); p-value
Hospital LOS - median (IQR)	6 (3)	5 (3)	p=0.003
Early discharge (<=4 days post-surgery)	25 (15.3)	55 (33.1)	2.81 (1.6,4.94); <0.001

KEY MESSAGES

Mini patients had a **reduced length of stay**

Mini patients were **twice as likely to be discharged early**

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Days alive and out of Hospital (DAOH)

	Sternotomy (N=163)	Mini (N=166)	Diff (95% CI); p-value
DAOH at 30 days after surgery mean±SD; n	22.38±5.13; 147	23.57±4.45; 161	1.05 (1.01,1.11); 0.03
DAOH at 90 days after surgery mean±SD; n	80.52±14.17; 147	82.7±9.96; 161	1.03 (1,1.05); 0.03

- DAOH is an important measure of quality. It accounts for:
  - The initial hospital stay if prolonged by peri-op complications
  - Readmissions due to inappropriate discharges or complications (e.g. wound infections)
  - Deaths
- Now recognised as an important outcome for trials and used as a primary outcome in key trials

KEY MESSAGE

DAOH was **higher for Mini** at 30 and 90 days

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Late safety outcomes (up to 1 year)

	Sternotomy (N=163)	Mini (N=166)	Odds Ratio (95% CI); p-value
Death n (%)	4 (2.5)	4 (2.4)	0.98 (0.24,4.05); 0.98
Hospitalisation for Heart Failure (HHF) at 1 year n (%)	5 (3.1)	5 (3)	0.98 (0.27,3.51); 0.97
Repeat mitral valve surgery at 1 year n (%)	1 (0.6)	0 (0)	-
Composite of death, HHF, and repeat mitral valve surgery at 1 year n (%)	10 (6.1)	9 (5.4)	0.88 (0.34,2.25); 0.78

KEY MESSAGES

There was **no difference** in important safety outcomes at 1 year:

- Death
- A repeat operation
- HHF

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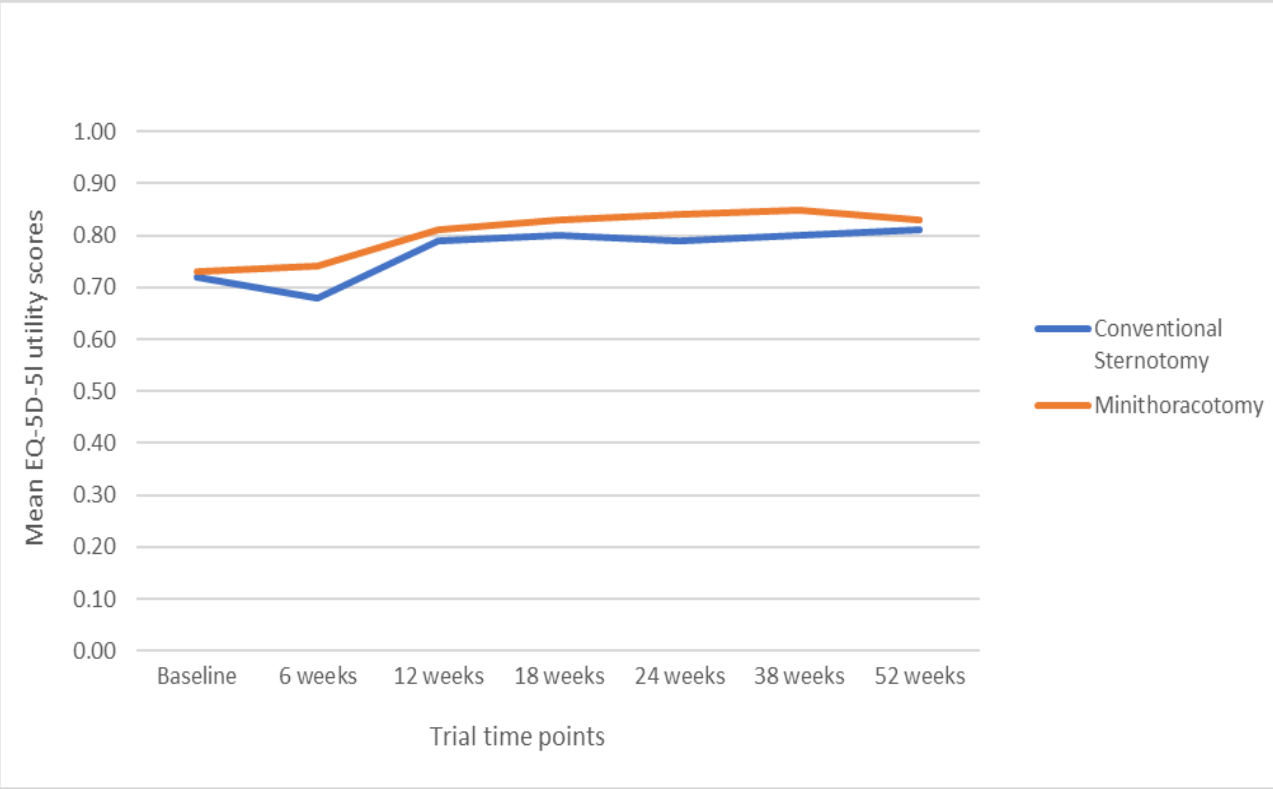
Quality of life outcomes at 6 and 12 weeks



KEY MESSAGES

Quality of life score fell after surgery in both groups but less in the Mini than Conventional

The differences were small and of uncertain clinical significance

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Summary of findings

- First and largest multicentre RCT.
- Expertise based randomisation to account for the learning curve was successfully performed.
- **The difference in the change in PF from baseline to 12 weeks between groups was not significant.**

- Physical function improves from baseline to 6 weeks in Mini but not Sternotomy patients.
- Moderate-Vigorous PA and sleep efficiency were significantly greater with Mini at 6 weeks.
- Reduced post-operative LOS for Mini.
- Early discharge more than **twice as likely with Mini.**
- DAOH was greater for Mini at 30 and 90 days.
- Small differences in QoL in favour of Mini at all time points (Full cost effectiveness analysis awaited).

- **High repair rate in both arms (96%)** and echo outcomes at 1 year were excellent (93% mild MR or less).
- Rates of Death, HHF, reintervention on the mitral valve at 1 year were similar and low.

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Conclusions

- Mini MVr is as safe and effective as Sternotomy MVr for DMR.
- Recovery from baseline to 6 weeks is better with Mini.
- At 12 weeks the mean change in physical function from baseline is the same
- The findings should give confidence to patients and clinicians and aid adoption of Mini MVRep .

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