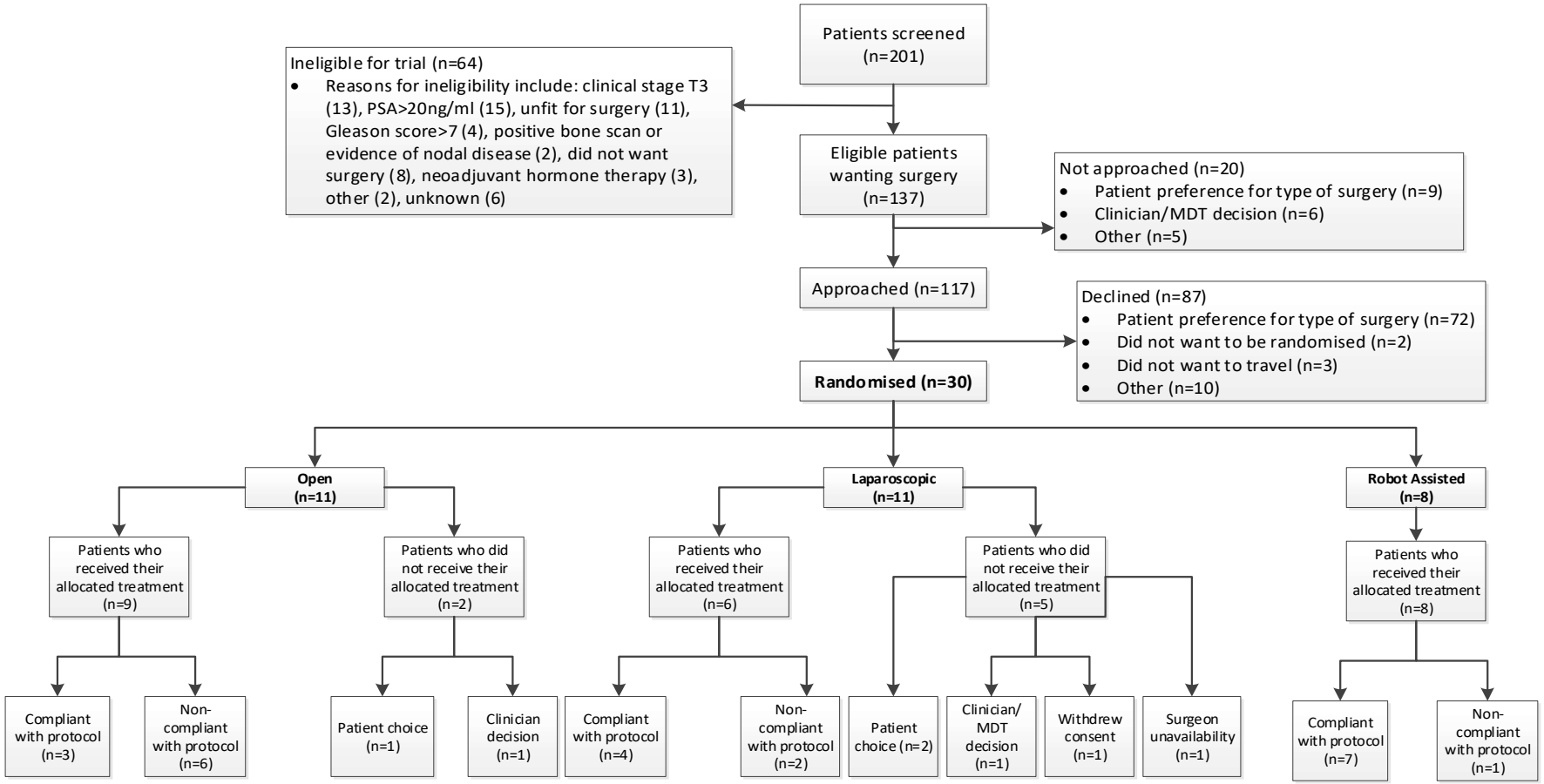
1. LopeRA Trial Participant Flow



NB. Compliance with the protocol is defined as: (1) receiving randomly allocated intervention, (2) group and save procedure performed, (3) no blood transfusion if haemoglobin >8g/dL, (4) deep vein thrombosis prophylaxis, (5) prophylactic antibiotics used, (6) indwelling urethral catheter removed 7-14 days post surgery, (7) length of hospital stay ≤5 days.

2. **Baseline data for all randomised patients (n=30)**

	Laparoscopic N=11 n (%)	Open N=11 n (%)	Robot-assisted N=8 n (%)
Age			
Median (IQR)	63 (58, 72)	62 (60, 64)	59 (57, 64)
PSA (ng/mL)			
Median (IQR)	7.2 (5.3, 10.1)	7.2 (5.1, 10.8)	6.15 (3.75, 11.1)
ECOG performance status			
0	7 (64)	10 (100)	8 (100)
1	1 (9)	0	0
2	3 (27)	0	0
Unknown	0	1	0
ASA grade			
I	5 (50)	6 (60)	4 (50)
II	4 (40)	3 (30)	4 (50)
III	1 (10)	1 (10)	0
Unknown	1	1	0
Gleason score			
3+3	5 (45)	5 (45)	3 (38)
3+4	4 (36)	5 (45)	5 62)
4+3	2 (18)	0	0
Unknown	1	1	0
DRE clinical stage			
T1	3 (27)	7 (70)	2 (33)
T2a	3 (27)	3 (30)	2 (33)
T2b	4 (36)	0	2 (33)
T2c	1 (9)	0	0
Unknown	0	1	2

NB. This was a trial in prostate cancer, all participants were male

3. Outcome Measures

Primary outcome: Monthly recruitment

	2010							2011										Total
	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	
Number recruited each month	**1**	**4**	**3**	**7**	**4**	**3**	**1**	**1**	**1**	**2**	**1**	**1**	**0**	**0**	**0**	**0**	**1**	**30**

NB. Primary outcome measure was total number of patients recruited, with the aim to recruit at least 75 patients within a 12 month period

Secondary outcome measure: Patient acceptance of their randomised treatment allocation and fulfilling trial specific definition of protocol compliance – by randomised treatment (n=30)

			Laparoscopic N = 11	Open N = 11	Robot Assisted N = 8
Patient acceptance to receiving allocated treatment?	Yes		8	10	8
	No		3	1	0
Proportion who accepted to receive allocated treatment			0.73	0.91	1.0
Patient compliant with protocol?	Yes		4	3	7
	No		7	8	1
Proportion of patients who were compliant with protocol			0.36	0.27	0.88
95% CI			(0.11, 0.69)	(0.06, 0.61)	(0.47, 1.00)
Lower limit of one-sided 95% CI			0.14	0.08	0.53
Patient received allocated treatment?	Yes		6	9	8
	No, received	Laparoscopic		0	
		Open	0		
		Robot Assisted	3	1	
		No surgery	2	1	

NB. The proportion of patients compliant with treatment allocation is 0.47 (95% CI 0.28-0.66)

Secondary outcome measures: operation duration, blood loss, transfusion rates and intra-operative complications - by treatment received (n=27)

		Laparoscopic	Open	Robot-assisted
		N=6	**N=9**	**N=12**
Prostatectomy form completed		6	9	12
Overall time in theatre[1] (Hours)	Median	2.8	3.4	4.3
	Interquartile range	(2.8, 3.0)	(3.3, 3.7)	(4.1, 5.7)
	Range	2.6-4.5	3.3-4.3	3.4-6.7
	N	6	6	7
Operation duration[2] (Hours)	Median	2.3	2.8	3.1
	Interquartile range	(2.1, 2.5)	(2.4, 3.2)	(2.6, 3.8)
	Range	2.0-3.8	2.4-3.2	2.1-5.2
	N	6	6	7
Intra-operative blood loss (mls)	Median	175	600	100
	Interquartile range	(100, 300)	(10, 1500)	(75, 300)
	Range	100-350	2-1600	50-1000
	N	6	7	12
Intra-operative blood transfusion		N=6	N=9	N=12
Number of patients requiring a transfusion		0	1	0
Proportion of total		0 (0, 0.46)	0.11 (0.003, 0.48)	0 (0, 0.26)
Number of units required intra-operatively		0	2	0
Intra-operative complications		N=6	N=9	N=12
Intra-operative complication	Yes	1	2	1
	%	16.7	22.2	8.3
Type of complication	Anaesthetic	0	0	0
	%	0	0	0
	Equipment Failure	1	0	1
	%	100	0	100
	Rectal Injury	0	0	0
	%	0	0	0
	Blood loss > 1500 mls	0	1	0
	%	0	50	0

[1] Defined as time from entering anaesthetic room to the time drapes were off

[2] Defined as time from entering operating room to time drapes were off (for laparoscopic and open surgery patients) and time from robot docking to time console operating finished (for robot-assisted patients)

Secondary outcome measures: Post-operative outcomes and complications by treatment received (n=27)

		Laparoscopic	Open	Robot-assisted
		N=6	N=9	N=12
Post-operative outcomes form completed (N)		6	9	12
Change in 12 hour post-operation haemoglobin level, from baseline (g/dL)	Median	-2.3	-4.2	-2.6
	Interquartile range	(-2.3, -2.2)	(-5.3, -2.9)	(-2.8, -1.4)
	Range	(-2.3, -2.1)	(-5.5, -1.6)	(-3.5, -1.3)
	N	4	8	9
Duration of hospital stay in days, from date of prostatectomy (day 1)	Median	2	6	3
	Interquartile range	(2, 2)	(5, 7)	(2, 4)
	Range	(2, 8)	(4, 11)	(2, 34)
	N	6	9	12
Frequency of patients reporting a post-operative complication	Yes	0	6	6
	%	0	66.7	50
Worst post-operative complication grade, amongst those experiencing a complication	Median		1	1.5
	Interquartile range		(1, 2)	(1, 2)
	Range		(1, 2)	(1 ,2)
Post-operative blood transfusion (N)				
Number of patients requiring a transfusion		0	0	0

Secondary outcome measure: Post-operative complications with Clavien grade – by treatment received

Patient ID	Treatment received	Complication 1	Clavien grade	Complication 2	Clavien grade
1	Robot Assisted	Constipation	2		
2	Robot Assisted	Pain	2		
3	Open	Constipation	2		
4	Open	Wound infection	2		
5	Robot Assisted	Pain	1	Constipation	2
6	Open	Anastomatic leak	1		
7	Open	Haematuria	1		
8	Robot Assisted	Pain (abdominal)	1		
9	Robot Assisted	Pain	1		
10	Robot Assisted	Pain in legs	1		
11	Open	Constipation	1		
12	Open	Pain	1		

Secondary outcome measure: Pathological specimen positive margin rates – by treatment received

		Treatment received		
Location	**Margins clear**	**Laparoscopic N=6**	**Open N=9**	**Robot Assisted N=12**
Apical	Yes	5 (83.3)	8 (88.9)	7 (58.3)
	No	1 (16.7)	1 (11.1)	5 (41.7)
Urethral	Yes	4 (100)	8 (100)	12 (100)
	No	0 (0)	0 (0)	0 (0)
Basal	Yes	5 (83.3)	8 (100)	12 (100)
	No	1 (16.7)	0 (0)	0 (0)
Bladder neck	Yes	4 (100)	8 (100)	12 (100)
	No	0 (0)	0 (0)	0 (0)
Circumferential	Yes	2 (33.3)	7 (77.8)	12 (100)
	No	4 (66.7)	2 (22.2)	0 (0)
All clear	Yes	2 (33.3)	6 (66.7)	7 (58.3)
	No	4 (66.7)	3 (33.3)	5 (41.7)
Proportion with all clear margins	Proportion	0.33	0.67	0.58
	95% CI	(0.04, 0.78)	(0.30, 0.93)	(0.28, 0.85)

Secondary outcome measure: Biochemical progression and clinical recurrence reported - by treatment received

		Laparoscopic (N=6)	Open (N=9)	Robot-Assisted (N=12)
Patient ever experienced disease progression?	Yes	0 (0)	1 (11.1)	3 (25)
	No	6 (100)	8 (88.9)	9 (75)
Type of progression	Biochemical progression	-	1 (100)	2 (66.7)
	Clinical recurrence and biochemical progression	-	0	1 (33.3)
Timepoint of first reporting of progression	6 weeks	-	0	0
	6 months	-	0	2 (66.7)
	12 months	-	1 (100)	0
	18 months	-	0	1 (33.3)

Secondary outcome measures: Patient reported outcomes assessed using the SF-12 (overall quality of life); University of California Prostate Cancer Index (UCLA-PCI) questionnaire (urinary function and urinary bother domain scores); International Continence Society (ICS-male-SF) questionnaire (voiding and incontinence) by treatment received

	Baseline			1 week after catheter removal			6 weeks			12 months		
	LA	OP	R-A	LA	OP	R-A	LA	OP	R-A	LA	OP	R-A
SF-12 General Health score[1]												
N	9	6	12	7	5	9	8	5	9	9	6	12
Median	75	87.5	62.5	50	75	50	75	75	75	75	87.5	62.5
IQR	50-75	50-100	50-87.5	50-75	25-75	50-75	50-75	50-75	50-100	50-75	50-100	50-87.5
UCLA PCI urinary function[2]												
N	9	6	12	7	5	10	7	6	9	9	6	12
Median	100	85.1	95.0	45.0	20.0	55.9	55.0	36.68	48.4	95.0	85.1	85.1
IQR	86.8-100.0	51.6-100.0	93.4-100.0	31.6-58.4	20.0-41.8	48.0-63.4	28.4-63.4	20.0-58.4	47.3-60.0	75.0-100.0	75.0-91.8	75.0-95.9
UCLA PCI urinary bother[2]												
N	8	6	12	7	4	9	7	6	9	9	6	11
Median	87.5	75.0	100.0	50.0	0	50.0	75.0	37.5	75.0	100.0	100.0	100.0
IQR	62.5-100.0	50.0-75.0	75.0-100.0	25.0-75.0	0-25.0	25.0-75.0	25.0-100.0	0-75.0	25.0-100.0	75.0-100.0	75.0-100.0	75.0-100.0
ICS-male voiding score[3]												
N	9	6	11	7	5	9	7	6	9	9	6	12
Median	3	6.5	6	6	6	1	4	3	1	3	2.5	1.5
IQR	2-7	5-8	3-10	2-7	4-7	0-5	0-5	1-5	1-1	0-4	0-4	0-4
ICS-male incontinence score[4]												
N	9	6	11	7	5	10	7	6	9	9	6	12
Median	1	3.5	2	5	14	6	5	5.5	3	3	3	3.5
IQR	1-2	0-7	1-4	4-6	8-15	3-8	4-6	3-14	2-10	2-4	1-4	0-6.5

[1] SF-12 General Health score ranges from 0 to 100 (higher scores represent better quality of life)
[2] Urinary function and bother scores range from 0 to 100 (higher scores represent better quality of life)
[3] ICS-male voiding score ranges from 0 to 20 (most severe symptoms)
[4] ICS-male incontinence score ranges from 0 to 24 (most severe symptoms)

4. Adverse events

Adverse events reported using CTCAE scoring criteria within 30 days of surgery by treatment received (n=27)

CTCAE symptom	Laparoscopic N=6	Open N=9	Robot-Assisted N=12
Fatigue			
0	5	5	8
1	0	2	2
2	0	0	2
3/4	0	0	0
Unknown	1	2	0
Weight loss			
0	5	6	11
1	0	1	1
2	0	0	0
3/4	0	0	0
Unknown	1	2	1
Abdominal pain			
0	5	5	10
1	0	0	2
2	1	0	0
3/4	0	0	0
Unknown	0	4	0
Diarrhoea			
0	5	7	11
1	0	0	1
2	0	0	0
3/4	0	0	0
Unknown	1	2	0
Haemorrhage			
0	5	7	12
1	0	0	0
2	0	0	0
3/4	0	0	0
Unknown	1	2	0
Nausea			
0	5	6	12
1	0	1	0
2	0	0	0
3/4	0	0	0
Unknown	1	2	0
Proctitis			
0	5	7	12
1	0	0	0
2	0	0	0
3/4	0	0	0
Unknown	1	2	0
Dysuria			
0	5	7	12
1	0	0	0

2	0	0	0
3/4	0	0	0
Unknown	1	2	0
Haematuria			
0	5	7	10
1	0	0	2
2	0	0	0
3/4	0	0	0
Unknown	0	2	0
Micturition urgency			
0	5	7	10
1	0	0	2
2	0	0	0
3/4	0	0	0
Unknown	1	2	0
Nocturia			
0	5	7	8
1	0	0	2
2	0	0	2
3/4	0	0	0
Unknown	1	2	0
Urinary frequency			
0	4	7	11
1	0	0	0
2	0	0	1
3/4	0	0	0
Unknown	3	2	0
Urinary retention			
0	5	6	11
1	0	0	1
2	0	1	0
3/4	0	0	0
Unknown	1	2	0
Other toxicities			
1	0	1	3
2	1	2	2
3	2[1]	0	0

[1] Grade 3 adverse events were urinary tract infection and relapse of a multi-resistant urinary tract infection which the patient had prior to surgery

Line listing of all serious adverse events reported – by treatment received

SAE no.	Treatment received	Days from surgery to onset	Type of SAE	Symptoms/ diagnosis	CI relationship	Expectedness
001	Laparoscopic surgery	20	Hospitalisation	Testicular Pain – grade 3	Unlikely	Unexpected
002	Laparoscopic surgery	18	Hospitalisation	Klebsiella in urine	Possible	Expected
003	Open Surgery	1	Other	Haemorrhage/ Intraoperative bloodloss over 1500mls (1600mls)	Definite	Expected
004	Open surgery	1	Other	Blood loss over 1500mls - no blood transfusion given	Definite	Expected
005	Open surgery	3	Prolongation of hospitalisation	Wound infection – grade 2	Probable	Expected