### **APPENDIX D4 – Additional forest plots and**

### analyses 2<sup>nd</sup> stage

A	PPENI	DIX D4 – Additional forest plots and analyses 2 <sup>nd</sup> stage	1
1	Am	bulatory ECG review– further analyses	2
	1.1	Subgroup analysis: studies for which patients were included or	
	exclud	ded following secondary tests	2
	1.2	Ambulatory ECG – results for each type of test, by population	6
	1.3	Implantable Event Recorder only: subgroup analyses by patient or	-
	patien	t + automatic activation	.21
	1.4	Implantable Event Recorder results only: subgroup analyses by	
	durati	on, frequency and their product	.25
2	Tilt	test additional analyses	.33
	2.1	HUT-passive	.33
	2.2	HUT-GTN	.39
	2.3	HUT-IPN	.40
A	ppendi	ix D5: Other	.45
1	Pat	ient history for interactive diagnostic simulation	.45

### **1** Ambulatory ECG review– further analyses

## 1.1 Subgroup analysis: studies for which patients were included or excluded following secondary tests

The following set of forest plots explores further the population group, unexplained following secondary tests and divides the population into two subgroups, depending on whether:

(i) patients were excluded if they had a positive result on a prior test

(ii) they were not excluded even if they had a positive test on a prior test

## 1.1.1 No TLoC during monitoring; unexplained TLoC following secondary tests

Study or Subgroup	proportion	SE	Weight	proportion IV, Fixed, 95% CI	proportion IV, Fixed, 95% Cl
22.59.1 Holter i					_
Rockx 2005: Holter rec Subtotal (95% CI)	0.76	0.059	100.0% 1 <b>00.0%</b>	0.76 [0.64, 0.88] <b>0.76 [0.64, 0.88]</b>	
Heterogeneity: Not applica	ble				
Test for overall effect: Z = 7	12.88 (P < 0.00	0001)			
22.59.2 Holter ii					
Subtotal (95% CI)				Not estimable	
Heterogeneity: Not applica Test for overall effect: Not a					
22.59.3 ELR i					
Fogel 1997: ELR NS	0.68	0.059	31.8%	0.68 [0.56, 0.80]	│ _ <b>_</b>
Linzer 1990: ELR rec		0.055	25.4%	0.44 [0.31, 0.57]	│ _ <b>_</b>
Rockx 2005: ELR rec	0.44	0.000	20.4 % 30.8%	0.22 [0.10, 0.34]	│_ <b>_</b>
Schuchert 2003: ELR rec		0.096	12.0%	0.67 [0.48, 0.86]	
Subtotal (95% CI)	0.07	0.000	100.0%	<b>0.48 [0.41, 0.54]</b>	•
Heterogeneity: Chi <sup>2</sup> = 34.54	4, df = 3 (P < 0	.00001)	; l² = 91%		
Test for overall effect: Z =	14.31 (P < 0.00	0001)			
22.59.4 ELR ii					
Subtotal (95% CI)				Not estimable	
Heterogeneity: Not applica Test for overall effect: Not a					
22.59.8 ILR i					
Brignole 2005: ILR rec		0.049	12.2%	0.46 [0.36, 0.56]	
Farwell 2006: ILR rec	0.52	0.05	11.7%	0.52 [0.42, 0.62]	
Krahn 1998: ILR rec		0.068	6.3%	0.13 [-0.00, 0.26]	
Krahn 2001: ILR rec		0.089	3.7%	0.40 [0.23, 0.57]	
Krahn 2004: ILR rec	0.5	0.065	6.9%	0.50 [0.37, 0.63]	
Lombardi 2005: ILR rec	0.41	0.084	4.1%	0.41 [0.25, 0.57]	
Moya 2001: ILR rec		0.052	10.8%	0.66 [0.56, 0.76]	
Pezawas 2007: ILR rec	0.14	0.042	16.5%	0.14 [0.06, 0.22]	
Pierre 2008: ILR rec	0.55	0.051	11.2%	0.55 [0.45, 0.65]	
Seidl 2000: ILR rec Subtotal (95% CI)	0.38	0.042	16.5% <b>100.0%</b>	0.38 [0.30, 0.46] <b>0.41 [0.38, 0.44]</b>	
Heterogeneity: Chi <sup>2</sup> = 97.2					· · ·
Test for overall effect: Z = 2	24.01 (P < 0.00	0001)			
22.59.9 ILR ii					
Boersma 2004: ILR rec		0.076	11.9%	0.47 [0.32, 0.62]	— <b>—</b>
Donateo 2003: ILR rec		0.083	9.9%	0.50 [0.34, 0.66]	
Krahn 2002: ILR rec		0.032	66.9%	0.31 [0.25, 0.37]	
Nierop 2000: ILR rec Subtotal (95% CI)	0.31	0.078	11.3% <b>100.0%</b>	0.31 [0.16, 0.46] <b>0.35 [0.30, 0.40]</b>	
Heterogeneity: Chi <sup>2</sup> = 7.58	•			_ / 4	
	13.29 (P < 0.00	JUU'I )			
Test for overall effect: Z = <sup>-</sup>	,	,			

Test for subgroup differences:  $Chi^2 = 43.98$ , df = 3 (P < 0.00001), l<sup>2</sup> = 93.2%

## 1.1.2 Normal Rhythm during TLoC; unexplained TLoC following secondary tests

Study or Subgroup	proportion	SE	Weight	proportion IV, Fixed, 95% Cl	proportion IV, Fixed, 95% CI
22.69.1 Holter i					
Rockx 2005: Holter rec Subtotal (95% CI)	0.24	0.059	100.0% 1 <b>00.0%</b>	0.24 [0.12, 0.36] <b>0.24 [0.12, 0.36]</b>	
Heterogeneity: Not applic					
Test for overall effect: Z =	= 4.07 (P < 0.00	001)			
22.69.2 Holter ii					
Subtotal (95% CI)				Not estimable	
Heterogeneity: Not applic					
Test for overall effect: No	t applicable				
22.69.3 ELR i					
Fogel 1997: ELR NS	0.19	0.05	30.0%	0.19 [0.09, 0.29]	
Linzer 1990: ELR rec		0.037	54.7%	0.09 [0.02, 0.16]	<b>□</b>
Rockx 2005: ELR rec	0.61	0.07	15.3% 100.0%	0.61 [0.47, 0.75]	
Subtotal (95% CI)		0.0000		0.20 [0.14, 0.25]	
Heterogeneity: Chi <sup>2</sup> = 43. Test for overall effect: Z =			1); 1² = 95	//o	
22.69.4 ELR ii					
Subtotal (95% CI)				Not estimable	
Heterogeneity: Not applic	able				
Test for overall effect: No	t applicable				
22.69.5 ILR i					
Brignole 2005: ILR rec	0.13	0.033	15.7%	0.13 [0.07, 0.19]	-
Farwell 2006: ILR rec	0.23	0.042	9.7%	0.23 [0.15, 0.31]	
Krahn 1998: ILR rec	0.42	0.101	1.7%	0.42 [0.22, 0.62]	
Krahn 2001: ILR rec		0.055	5.6%	0.10 [-0.01, 0.21]	<b>—</b>
Krahn 2002: ILR rec		0.034	14.8%	0.41 [0.34, 0.48]	
Krahn 2004: ILR rec		0.056	5.4%	0.25 [0.14, 0.36]	
Lombardi 2005: ILR rec		0.055	5.6%	0.12 [0.01, 0.23]	
Moya 2001: ILR rec		0.035	13.9%	0.11 [0.04, 0.18]	
Pezawas 2007: ILR rec		0.058	5.1%	0.39 [0.28, 0.50]	
Pierre 2008: ILR rec		0.038	11.8%	0.17 [0.10, 0.24]	
Seidl 2000: ILR rec Subtotal (95% CI)	0.3	0.04	10.7% <b>100.0%</b>	0.30 [0.22, 0.38] 0.22 [0.20, 0.25]	▲
Heterogeneity: Chi <sup>2</sup> = 75.	13 df - 10 (P				· ·
Test for overall effect: Z =			ur, i− – 0	1 /0	
22.69.6 ILR ii					
Boersma 2004: ILR rec	0.28	0.068	20.0%	0.28 [0.15, 0.41]	<b></b>
Donateo 2003: ILR rec		0.038	64.0%	0.06 [-0.01, 0.13]	<b>—</b>
Nierop 2000: ILR rec Subtotal (95% CI)		0.076	16.0% <b>100.0%</b>	0.29 [0.14, 0.44] <b>0.14 [0.08, 0.20]</b>	
. ,	E7 df - 0 (D	0.000		0.14 [0.00, 0.20]	•
Heterogeneity: Chi <sup>2</sup> = 12. Test for overall effect: Z =			ı~ = ð4%		
		,			
					-1 -0.5 0 0.5

Test for subgroup differences:  $Chi^2 = 6.67$ , df = 3 (P = 0.08), I<sup>2</sup> = 55.0%

## 1.1.3 Arrhythmia during TLoC; unexplained TLoC following secondary tests

Phudu an Pulamana	man anti-	05	n Tetel	Tatal	Mainta	proportion	proportion
Study or Subgroup 22.57.1 Holter i	proportion	SE	rotal	ı otal	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
	-	-		-		N	
Rockx 2005: Holter rec Subtotal (95% CI)	0	0	51 51	0		Not estimable Not estimable	
( )			51	0		NULESUINADIE	
Heterogeneity: Not applicat							
Test for overall effect: Not a	applicable						
22.57.2 Holter ii							
Subtotal (95% CI)			0	0		Not estimable	
Heterogeneity: Not applicat	ble						
Test for overall effect: Not a	applicable						
22.57.3 ELR i							
Fogel 1997: ELR NS	0.13	0.043	62	0	13.3%	0.13 [0.05, 0.21]	
Linzer 1990: ELR rec		0.048	57	0	10.7%	0.16 [0.07, 0.25]	- <b>-</b> -
Rockx 2005: ELR rec	0.02	0.040	49	0	61.4%	0.02 [-0.02, 0.06]	<u> </u>
Schuchert 2003: ELR rec	0.02		24	0	14.6%	0.02 [-0.02, 0.00]	
Subtotal (95% CI)	0.04	0.041	192	0	100.0%	0.04 [-0.04, 0.12] 0.05 [0.02, 0.08]	•
Heterogeneity: Chi <sup>2</sup> = 11.00	) $df = 3 (P = 0)$	01)· I2 -		-			
Test for overall effect: Z = 3			. 570				
		,					
22.57.4 ELR ii			-	_			
Subtotal (95% CI)			0	0		Not estimable	
Heterogeneity: Not applicat							
Test for overall effect: Not a	applicable						
22.57.8 ILR i							
Brignole 2005: ILR rec	0.38	0.048	103	0	8.7%	0.38 [0.29, 0.47]	<del></del>
Farwell 2006: ILR rec	0.2	0.04	103	0	12.6%	0.20 [0.12, 0.28]	
Krahn 1998: ILR rec		0.102	24	0	1.9%	0.46 [0.26, 0.66]	
Krahn 2001: ILR rec		0.088	30	0	2.6%	0.37 [0.20, 0.54]	
Krahn 2002: ILR rec		0.029	206	0	23.9%	0.23 [0.17, 0.29]	
Krahn 2004: ILR rec		0.055	60	0	6.7%	0.23 [0.12, 0.34]	<del></del>
Lombardi 2005: ILR rec		0.083	34	0	2.9%	0.38 [0.22, 0.54]	
Moya 2001: ILR rec		0.003	82	0	10.9%	0.18 [0.10, 0.26]	
Pezawas 2007: ILR rec	0.10	0.045	70	0	5.6%	0.47 [0.35, 0.59]	<u> </u>
Pierre 2008: ILR rec		0.046	95	0	9.5%	0.28 [0.19, 0.37]	
Seidl 2000: ILR rec	0.23		133	0	9.3 <i>%</i> 14.7%	0.24 [0.17, 0.31]	-
Subtotal (95% CI)	0.24	0.007	940	0	100.0%	0.27 [0.24, 0.29]	♦
Heterogeneity: Chi <sup>2</sup> = 33.38	8, df = 10 (P = 0	).0002)	; l <sup>2</sup> = 70	)%			
Test for overall effect: Z = 1		'					
22.57.9 ILR ii							
Boersma 2004: ILR rec	0.26	0.067	43	0	40.6%	0.26 [0.13, 0.39]	- <b></b>
Donateo 2003: ILR rec	0.39		36	0	27.8%	0.39 [0.23, 0.55]	_ <b>_</b>
Nierop 2000: ILR rec	0.39		35	0	31.6%	0.29 [0.14, 0.44]	<b>_∎</b> _
Subtotal (95% CI)	0.23	5.570	114	Ő	100.0%	0.31 [0.22, 0.39]	•
Heterogeneity: Chi <sup>2</sup> = 1.59,	df = 2 (P = 0.4	5); l² =	0%				
Test for overall effect: $Z = 7$	`	<i>, , , , , , , , , ,</i>					
						1	
						-1	-0.5 0 0.5

Test for subgroup differences: Chi<sup>2</sup> = 111.54, df = 2 (P < 0.00001), l<sup>2</sup> = 98.2%

## 1.2 Ambulatory ECG – results for each type of test, by population

The following set of forest plots show the results for each test and each outcome, by population group.

### 1.2.1 Holter 24-hour monitoring

1.2.1.1	No TLoC during monitoring
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Study or Subgroup	proportion	8E	Total	Total	Weight	proportion IV, Fixed, 95% CI	proportion IV, Fixed, 95% CI
10.5.1 suspected arrhythn				TOLAI	weight	IV, FIXEU, 35 /0 CI	
Sarasin 2005: Ho not rec Subtotal (95% CI)		0.031	140 140	0 0	100.0% 1 <b>00.0%</b>	0.84 [0.78, 0.90] <b>0.84 [0.78, 0.90]</b>	<b>•</b>
Heterogeneity: Not applicab	le						
Test for overall effect: $Z = 2$	7.10 (P < 0.00	0001)					
10.5.2 NMS							
Fitchet 2003: Holter rec Subtotal (95% CI)	0.8	0.037	118 118	0 0	100.0% 1 <b>00.0%</b>	0.80 [0.73, 0.87] <b>0.80 [0.73, 0.87]</b>	
Heterogeneity: Not applicab	le						
Test for overall effect: $Z = 2$		0001)					
10.5.3 syncope unexplain	ed bv initial t	ests (re	curren	t or no	t stated)		
Comolli 1993: Holter NS		0.006	287	0	97.3%	0.99 [0.98, 1.00]	
Kapoor 1991: Holter rec Subtotal (95% CI)	0.85	0.036	0 287	0	2.7% 100.0%	0.85 [0.78, 0.92] 0.99 [0.97, 1.00]	
Heterogeneity: Chi <sup>2</sup> = 14.71	, df = 1 (P = 0	).0001);	l² = 93	%			
Test for overall effect: Z = 1	66.64 (P < 0.0	00001)					
10.5.4 syncope unexplain	ed after seco	ndarv t	ests				
Subtotal (95% CI)			0	0		Not estimable	
Heterogeneity: Not applicab Test for overall effect: Not a							
							-1 -0.5 0 0.5 1

Test for subgroup differences:  $Chi^2 = 44.84$ , df = 2 (P < 0.00001), l<sup>2</sup> = 95.5%

### 1.2.1.2 Normal rhythm during TLoC

#### No NM syncope patients had Holter monitoring and reported this outcome

				Control		proportion			roportion	
Study or Subgroup	proportion	SE	Total	Total	Weight	IV, Fixed, 95%	CI	IV, F	ixed, 95% Cl	
10.4.2 suspected arrhyth	mia without re	ecurren	t sync	оре						
Sarasin 2005: Ho not rec	0.093	0.025	140	0	100.0%	0.09 [0.04, 0.1	4]			
Subtotal (95% CI)			140	0	100.0%	0.09 [0.04, 0.1	4]		•	
Heterogeneity: Not applica	able									
Test for overall effect: Z =	3.72 (P = 0.00	02)								
10.4.3 syncope unexplai Comolli 1993: Holter NS	ned by initial t 0.003	•	currer 287	it or not s 0	stated) 99.3%	0.00 [-0.00, 0.0	1]			
Kapoor 1991: Holter rec	0.137	0.035	0	0	0.7%	0.14 [0.07, 0.2	1		Τ	
Subtotal (95% CI)			287	0	100.0%	0.00 [-0.00, 0.0	1j			
Heterogeneity: Chi <sup>2</sup> = 14.5	5, df = 1 (P = 0	).0001);	$l^2 = 93$	%						
Test for overall effect: Z =	1.33 (P = 0.18)	)								
								-0.5	0 0.5	

Test for subgroup differences:  $Chi^2 = 12.50$ , df = 1 (P = 0.0004),  $I^2 = 92.0\%$ 

### 1.2.1.3 Arrhythmia during TLoC

			n	% brady		proportion	proportion
Study or Subgroup	proportion	SE	Total	Total	Weight	IV, Fixed, 95% C	I IV, Fixed, 95% CI
10.2.1 suspected arrhythm	nia without re	ecurren	t sync	ope			
Sarasin 2005: Ho not rec	0.06	0.021	140		100.0%	0.06 [0.02, 0.10]	
Subtotal (95% CI)			140	78	100.0%	0.06 [0.02, 0.10]	•
Heterogeneity: Not applicate	ole						
Test for overall effect: $Z = 2$	2.86 (P = 0.004	4)					
10.2.3 syncope unexplain	ed by initial t	ests (re	curre	nt or not si	tated)		
Comolli 1993: Holter NS	0.01	0.005	287	0	80.0%	0.01 [0.00, 0.02]	<b>.</b>
Kapoor 1991: Holter rec	0.01	0.01	0	0	20.0%	0.01 [-0.01, 0.03]	•
Subtotal (95% CI)			287	0	100.0%	0.01 [0.00, 0.02]	
Heterogeneity: Chi <sup>2</sup> = 0.00,	df = 1 (P = 1.	00); I <sup>2</sup> =	0%				
Test for overall effect: Z = 2	2.24 (P = 0.03)						
10.2.5 Unexplained after s	secondary tes	sts (rec	urrent	or not sta	ted)		
Subtotal (95% CI)	-	-	0	0	-	Not estimable	
Heterogeneity: Not applicat	ole						
Test for overall effect: Not a	applicable						
							· · · · · ·
							-1 -0.5 0 0.5 1

Test for subgroup differences:  $Chi^2 = 5.42$ , df = 1 (P = 0.02), l<sup>2</sup> = 81.6%

### 1.2.1.4 Arrhythmia not during TLoC

			n	% brady		proportion		pro	oportion		
Study or Subgroup	proportion	SE	Total	Total	Weight	IV, Fixed, 95% Cl		IV, Fiz	xed, 95%	CI	
10.3.3 patients with sync	ope unexplai	ined by	initial	tests (rec	urrent or	not stated)					
Comolli 1993: Holter NS	0.192	0.023	287	58	64.5%	0.19 [0.15, 0.24]					
Kapoor 1991: Holter rec Subtotal (95% CI)	0.105	0.031	95 382	-	35.5% 1 <b>00.0%</b>	0.10 [0.04, 0.17] <b>0.16 [0.12, 0.20]</b>			<b>₩</b>		
Heterogeneity: $Chi^2 = 5.08$ Test for overall effect: Z =	, ,	<i>, , , , , , , , , ,</i>	= 80%				⊢				
Test for subgroup differen							-1	-0.5	0	0.5	1

### 1.2.1.5 No ECG during TLoC

			Test	Control		proportion		pro	oportion		
Study or Subgroup	proportion	SE	Total	Total	Weight	IV, Fixed, 95% CI		IV, Fix	ked, 95%	CI	
10.6.3 syncope unexplair	ed by initial	tests	(recur	rrent or no	ot stated)						
Comolli 1993: Holter NS Subtotal (95% CI)	0	0	287 <b>287</b>	0 0		Not estimable Not estimable					
Heterogeneity: Not applica Test for overall effect: Not											
							⊢ -1	-0.5	0	0.5	

Test for subgroup differences: Not applicable

#### 1.2.1.6 Adverse events

### No studies reported this outcome

### 1.2.2 48-hour Holter monitoring or longer

#### *1.2.2.1* No TLoC during recording period

proportion mia with rec					IV, Fixed, 95% CI	IV, Fixed, 95% CI
inna with ice	urrent			Weight	IV, FIXEU, 35 /0 CI	
0.87	0.042	63 63	0	100.0% <b>100.0%</b>	0.87 [0.79, 0.95] <b>0.87 [0.79, 0.95]</b>	
	0001)					
y mediated s	syncop	e (recu	rrent)			
0.8	0.037	118 <b>118</b>			0.80 [0.73, 0.87] <b>0.80 [0.73, 0.87]</b>	
ble						
1.62 (P < 0.0	0001)					
initial tests						
0.79	0.042	95 <b>95</b>			0.79 [0.71, 0.87] <b>0.79 [0.71, 0.87]</b>	
	0001)					
secondary t	ests w	ith recu	urrent	syncope		
0.76	0.059	51 <b>51</b>			0.76 [0.64, 0.88] <b>0.76 [0.64, 0.88]</b>	
	0001)					
					H_	-0.5 0 0.5
	ly mediated s 0.8 0le 21.62 (P < 0.0 initial tests 0.79 0le 8.81 (P < 0.0 secondary t 0.76 0le 2.88 (P < 0.0	20.71 (P < 0.00001) ly mediated syncop 0.8 0.037 ble 21.62 (P < 0.00001) initial tests 0.79 0.042 ble 18.81 (P < 0.00001) r secondary tests w 0.76 0.059 ble 12.88 (P < 0.00001)	ble 20.71 (P < 0.00001) ly mediated syncope (recu 0.8 0.037 118 118 ble 21.62 (P < 0.00001) initial tests 0.79 0.042 95 95 ble 18.81 (P < 0.00001) r secondary tests with recu 0.76 0.059 51 51 ble 12.88 (P < 0.00001)	ble 20.71 (P < 0.00001) <b>ly mediated syncope (recurrent)</b> 0.8 0.037 118 0 118 0 ble 21.62 (P < 0.00001) <b>initial tests</b> 0.79 0.042 95 0 95 0 ble 18.81 (P < 0.00001) <b>secondary tests with recurrent</b> s 0.76 0.059 51 0 51 0 ble 12.88 (P < 0.00001)	ble 20.71 (P < 0.00001) <b>ly mediated syncope (recurrent)</b> 0.8 0.037 118 0 100.0% 118 0 100.0% ble 21.62 (P < 0.00001) initial tests 0.79 0.042 95 0 100.0% 95 0 100.0% ble 18.81 (P < 0.00001) <b>secondary tests with recurrent syncope</b> 0.76 0.059 51 0 100.0% 51 0 100.0% ble 12.88 (P < 0.00001)	ble 20.71 (P < 0.00001) ly mediated syncope (recurrent) 0.8 0.037 118 0 100.0% 0.80 [0.73, 0.87] 118 0 100.0% 0.80 [0.73, 0.87] ble 21.62 (P < 0.00001) initial tests 0.79 0.042 95 0 100.0% 0.79 [0.71, 0.87] 95 0 100.0% 0.79 [0.71, 0.87] ble 18.81 (P < 0.00001) r secondary tests with recurrent syncope 0.76 0.059 51 0 100.0% 0.76 [0.64, 0.88] 51 0 100.0% 0.76 [0.64, 0.88] ble

Test for subgroup differences:  $Chi^2 = 3.06$ , df = 3 (P = 0.38),  $l^2 = 1.9\%$ 

### 1.2.2.2 Normal rhythm during TLoC

			n			proportion	proportion
/ 0 /	proportion				Weight	IV, Fixed, 95% Cl	IV, Fixed, 95% CI
10.14.1 suspected arrhyth	mia with recu	rrent	syncop	ре			
Ringqvist 1989: Ho rec Subtotal (95% CI)	0.063 0	0.031	63 63	0 0	100.0% 1 <b>00.0%</b>	0.06 [0.00, 0.12] <b>0.06 [0.00, 0.12]</b>	•
Heterogeneity: Not applicab	le						
Test for overall effect: Z = 2.	03 (P = 0.04)						
10.14.2 NMS							
Fitchet 2003: Holter rec Subtotal (95% CI)	0.119	0.03	118 <b>118</b>	0 0	100.0% 1 <b>00.0%</b>	0.12 [0.06, 0.18] 0.12 [0.06, 0.18]	
Heterogeneity: Not applicab	le					• • •	
Test for overall effect: Z = 3.		1)					
10.14.3 unexplained after i	nitial tests						
Kapoor 1991: Holter rec	0.2 0	0/1	95	0	100.0%	0.20 [0.12, 0.28]	
Subtotal (95% CI)	0.2 0	.041	95		100.0%	0.20 [0.12, 0.20]	
Heterogeneity: Not applicab	le						
Test for overall effect: Z = 4.	.88 (P < 0.000	01)					
10.14.4 Unexplained after	secondary tes	sts wi	th recu	rrent s	syncope		
Rockx 2005: Holter rec	0.24 0	0.059	51	0	100.0%	0.24 [0.12, 0.36]	- <mark></mark> -
Subtotal (95% CI)			51	0	100.0%	0.24 [0.12, 0.36]	▲
Heterogeneity: Not applicab	le						
Test for overall effect: Z = 4.	07 (P < 0.000	1)					
							FFF
							-1 -0.5 0 0.5

1.2.2.3 Arrhythmia during TLoC

			n	% brady		proportion	proportion
	roportion	-	Total		Weight	IV, Fixed, 95% C	I IV, Fixed, 95% CI
10.12.1 suspected arrhythmia	with recur	rent sy	ncope				
Arya 2005: Ho 2nd day rec	0.08	0.039	0	0	38.7%	0.08 [0.00, 0.16]	
Ringqvist 1989: Ho rec Subtotal (95% CI)	0.06	0.031	63 63	75 75	61.3% <b>100.0%</b>		◆
Heterogeneity: Chi <sup>2</sup> = 0.16, df =	1 (P = 0.69	); I <sup>2</sup> = 0 <sup>4</sup>	%				
Test for overall effect: Z = 2.79 (	P = 0.005)						
10.12.2 suspected neurally me	diated syn	icope (i	recurr	ent)			
Fitchet 2003: Holter rec	0.08	0.026	118	0		0.08 [0.03, 0.13]	
Subtotal (95% CI)			118	0	100.0%	0.08 [0.03, 0.13]	◆
Heterogeneity: Not applicable							
Test for overall effect: Z = 3.08 (	P = 0.002)						
10.12.3 unexplained after initia	al tests						
Kapoor 1991: Holter rec	0.01	0.01	95	100	100.0%	0.01 [-0.01, 0.03]	
Subtotal (95% CI)			95	100	100.0%	0.01 [-0.01, 0.03]	•
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.00 (	P = 0.32)						
10.12.4 Unexplained after seco	ondary test	ts with	recurr	ent synco	ре		
Rockx 2005: Holter rec	0	0	51	0		Not estimable	
Subtotal (95% Cl)			51	0		Not estimable	
Heterogeneity: Not applicable							
Test for overall effect: Not applic	able						
							-1 -0.5 0 0.5
T / /				07) 10 70			

Test for subgroup differences: Chi<sup>2</sup> = 9.83, df = 2 (P = 0.007), l<sup>2</sup> = 79.6%

Transient loss of consciousness: full guideline DRAFT (January 2010) Page 10 of 46

### 1.2.2.4 Arrhythmia not during TLoC

			n	% brady		proportion	proportion
Study or Subgroup	proportion	SE	Total	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
10.13.1 suspected arrhythm	nia with recurr	ent sy	ncope				
Arya 2005: Ho 2nd day rec	0.347	0.068	0	0	27.6%	0.35 [0.21, 0.48]	<b>_</b> _
Ringqvist 1989: Ho rec Subtotal (95% CI)	0.13	0.042	63 63	100 <b>100</b>	72.4% 1 <b>00.0%</b>	0.13 [0.05, 0.21] 0.19 [0.12, 0.26]	
Heterogeneity: Chi <sup>2</sup> = 7.37, d	f = 1 (P = 0.007)	7):   <sup>2</sup> =	86%				
Test for overall effect: $Z = 5.3$							
10.13.2 suspected neurally	mediated syn	cope (	recurre	ent)			
Fitchet 2003: Holter rec Subtotal (95% CI)	0	0	118 <b>118</b>	14 14		Not estimable Not estimable	
Heterogeneity: Not applicable Test for overall effect: Not ap							
10.13.3 unexplained after in	nitial tests						
Kapoor 1991: Holter rec Subtotal (95% CI)	0.211	0.042	95 <b>95</b>		100.0% 1 <b>00.0%</b>	0.21 [0.13, 0.29] <b>0.21 [0.13, 0.29]</b>	
Heterogeneity: Not applicable Test for overall effect: Z = 5.0		I)					
10.13.4 Unexplained after s	econdary test	s with	recurre	ent synco	ре		
Rockx 2005: Holter rec Subtotal (95% CI)	0	0	51 51	0 <b>0</b>		Not estimable Not estimable	
Heterogeneity: Not applicable Test for overall effect: Not ap							

Test for subgroup differences:  $Chi^{2}$  = 0.15, df = 1 (P = 0.70),  $I^{2}$  = 0%

### 1.2.2.5 No ECG during TLoC

No studies reported this outcome.

#### 1.2.2.6 Adverse events

No studies reported this outcome.

### 1.2.3 External event recorder

#### 1.2.3.1 No TLoC during recording period

			n			proportion	proportion
Study or Subgroup	proportion	SE	Total	Total	Weight	IV, Fixed, 95% CI	I IV, Fixed, 95% CI
10.25.1 suspected arrhyth	nmia without r	ecurre	nt sync	ope (h	ospital de	epartments)	
Rothman 2007: ELR NS	0.31	0.065	0	0	100.0%	0.31 [0.18, 0.44]	
Subtotal (95% CI)			0	0	100.0%	0.31 [0.18, 0.44]	•
Heterogeneity: Not applicat	ble						
Test for overall effect: $Z = 4$	.77 (P < 0.000	01)					
10.25.5 Unexplained after	secondary te	sts (red	current	or not	stated)		
Fogel 1997: ELR NS	0.68	0.059	62	0	31.8%	0.68 [0.56, 0.80]	
Linzer 1990: ELR rec	0.44	0.066	57	0	25.4%	0.44 [0.31, 0.57]	
Rockx 2005: ELR rec	0.22	0.06	49	0	30.8%	0.22 [0.10, 0.34]	<b> </b> − <b>∎</b> −
Schuchert 2003: ELR rec	0.67	0.096	24	0	12.0%	0.67 [0.48, 0.86]	
Subtotal (95% CI)			192	0	100.0%	0.48 [0.41, 0.54]	◆
Heterogeneity: Chi <sup>2</sup> = 34.54	l, df = 3 (P < 0	.00001)	; I <sup>2</sup> = 91	1%			
Test for overall effect: Z = 1	4.31 (P < 0.00	001)					
							-1 -0.5 0 0.5
							-1 -0.5 0 0.5

Test for subgroup differences:  $Chi^2 = 5.19$ , df = 1 (P = 0.02), I<sup>2</sup> = 80.7%

### 1.2.3.2 Normal rhythm during TLoC

			n			proportion		proportion	
Study or Subgroup	proportion	SE	Total	Total	Weight	IV, Fixed, 95% CI		IV, Fixed, 95% CI	
10.24.1 suspected arrhyt	hmia without	recurre	ent syn	cope (	hospital c	lepartments)			
Rothman 2007: ELR NS Subtotal (95% CI)	0.275	0.062	0 0	0 0	100.0% 1 <b>00.0%</b>	0.28 [0.15, 0.40] <b>0.28 [0.15, 0.40]</b>			
Heterogeneity: Not application	ble								
Test for overall effect: $Z = 4$	4.44 (P < 0.00	001)							
10.24.5 Unexplained after	secondary to	ests (re	currer	nt or no	t stated)				
Fogel 1997: ELR NS	0.19	0.05	62	0	30.0%	0.19 [0.09, 0.29]			
Linzer 1990: ELR rec	0.088	0.037	57	0	54.7%	0.09 [0.02, 0.16]		-	
Rockx 2005: ELR rec Subtotal (95% CI)	0.61	0.07	49 1 <b>68</b>	0 0	15.3% 1 <b>00.0%</b>	0.61 [0.47, 0.75] <b>0.20 [0.14, 0.25]</b>		•	-
Heterogeneity: Chi <sup>2</sup> = 43.5	1, df = 2 (P < 0	0.00001	); l <sup>2</sup> = 9	95%					
Test for overall effect: Z = 2	7.25 (P < 0.00	001)							
							-1 -(	+ + + + + + + + + + + + + + + + + + +	. 1

Test for subgroup differences:  $Chi^2 = 1.28$ , df = 1 (P = 0.26), l<sup>2</sup> = 21.7%

### 1.2.3.3 Arrhythmia during TLoC

			n	% brady		proportion		pro	portion	
Study or Subgroup	proportion	SE	Total	Total	Weight	IV, Fixed, 95% C	I	IV, Fix	ed, 95% Cl	
10.22.1 suspected arrhyt	hmia without i	recurre	nt syn	cope (hos	pital depa	rtments)				
Rothman 2007: ELR NS Subtotal (95% CI)	0.41	0.069	0	0 0	100.0% 100.0%	0.41 [0.27, 0.55] 0.41 [0.27, 0.55]				-
Heterogeneity: Not application	ble									
Test for overall effect: $Z = $	5.94 (P < 0.000	001)								
10.22.5 Unexplained after	secondary te	ests (ree	curren	t or not sta	ated)					
Rockx 2005: ELR rec	0.02	0.02	49	100	61.4%	0.02 [-0.02, 0.06]				
Linzer 1990: ELR rec	0.16	0.048	57	71	10.7%	0.16 [0.07, 0.25]				
Schuchert 2003: ELR rec	0.04	0.041	24	69	14.6%	0.04 [-0.04, 0.12]			- <b> </b>	
Fogel 1997: ELR NS	0.13	0.043	62	0	13.3%	0.13 [0.05, 0.21]				
Subtotal (95% CI)			192	240	100.0%	0.05 [0.02, 0.08]			•	
Heterogeneity: Chi <sup>2</sup> = 11.00	0, df = 3 (P = 0	.01); l <sup>2</sup> :	= 73%							
Test for overall effect: Z = 3	3.35 (P = 0.000	)8)								
		,								
							H			
							-1	-0.5	0 0.	5 I

Test for subgroup differences:  $Chi^2 = 25.53$ , df = 1 (P < 0.00001), I<sup>2</sup> = 96.1%

### 1.2.3.4 Arrhythmia not during TLoC

		n	% brady		proportion		р	roportion	1	
Study or Subgroup	proportion SE	Total	Total	Weight	IV, Fixed, 95% C	1	IV, F	ixed, 95%	6 CI	
10.23.1 suspected arrhythm	ia without recu	irrent s	yncope (he	ospital de	partments)					
Rothman 2007: ELR NS Subtotal (95% CI)	0 0	52 52	-		Not estimable Not estimable					
Heterogeneity: Not applicable										
Test for overall effect: Not app	licable									
10.23.3 Unexplained after se	condary tests	with re	current sy	ncope						
Rockx 2005: ELR rec	0 0	49	0		Not estimable					
Schuchert 2003: ELR rec	0 0	24	0		Not estimable					
Subtotal (95% CI)		73	0		Not estimable					
Heterogeneity: Not applicable										
Test for overall effect: Not app	licable									
						H				
						-1	-0.5	ò	0.5	1

Test for subgroup differences: Not applicable

### 1.2.3.5 No ECG during TLoC

			n			proportion		pro	oportion	
Study or Subgroup	proportion	SE	Total	Total	Weight	IV, Fixed, 95% CI		IV, Fiz	xed, 95% CI	
10.26.3 Unexplained after	secondary te	ests wit	h recur	rrent sy	/ncope					
Linzer 1990: ELR rec	0.32	0.062	57	0	33.5%	0.32 [0.20, 0.44]				
Rockx 2005: ELR rec	0.14	0.05	49	0	51.6%	0.14 [0.04, 0.24]				
Schuchert 2003: ELR rec	0.29	0.093	24	0	14.9%	0.29 [0.11, 0.47]				
Subtotal (95% CI)			130	0	100.0%	0.22 [0.15, 0.29]			•	
Heterogeneity: Chi <sup>2</sup> = 5.72,	df = 2 (P = 0.0)	06); l² =	65%							
Test for overall effect: Z = 6	6.20 (P < 0.000	001)								
							1	-0.5	0 0.5	1
							- 1	-0.5	0 0.5	

Test for subgroup differences: Not applicable

#### 1.2.3.6 Adverse events

No studies reported this outcome.

### 1.2.4 Implantable Event Recorder

### 1.2.4.1 No TLoC during recording period

Study or Subgroup	proportion	SE	n Total	Total	Weight	proportion IV, Fixed, 95% CI	proportion IV, Fixed, 95% CI
10.35.1 suspected arrhythmi	ia with recu	rrent s	yncope			, ,	
Brignole 2001: ILR rec	0.54	0.069	52	0	19.2%	0.54 [0.40, 0.68]	
Garcia-Civera 05: ILR rec	0.6	0.054	81	0	31.3%	0.60 [0.49, 0.71]	
Krahn 1999: ILR rec	0.32	0.05	85	0	36.5%	0.32 [0.22, 0.42]	
Menozzi 2002: ILR rec	0.46	0.084	35	0	12.9%	0.46 [0.30, 0.62]	
Subtotal (95% CI)			253	0	100.0%	0.47 [0.41, 0.53]	◆
Heterogeneity: Chi <sup>2</sup> = 15.83, d	lf = 3 (P = 0.	001); l²	= 81%				
Test for overall effect: Z = 15.4	49 (P < 0.00	001)					
10.35.3 suspected neurally n	nediated sv	ncope	(recurre	ent)			
Brianole 2006: ILR rec		0.024	392	0	88.3%	0.64 [0.59, 0.69]	
Deharo 2006: ILR rec	0.52	0.021	25	0	5.1%	0.52 [0.32, 0.72]	
Moya 2001: ILR rec		0.088	29	0	6.6%	0.66 [0.49, 0.83]	—
Subtotal (95% CI)			446	-	100.0%	0.64 [0.59, 0.68]	•
Heterogeneity: Chi <sup>2</sup> = 1.45, df	= 2 (P = 0.4	9); l² =	0%				
Test for overall effect: $Z = 28.1$	``		-				
10.35.4 unexplained after int	ial tosts (ro	CUITOR	t or not	stator	0		
Ermis 2003: ILR NS	•	0.046	50		<b>יי</b> 100.0%	0.88 [0.79, 0.97]	
Subtotal (95% CI)	0.08	0.040	50 50		100.0%	0.88 [0.79, 0.97]	
Heterogeneity: Not applicable						6/ d	
Test for overall effect: Z = 19.1	13 (P < 0.00	001)					
Test for overall effect: Z = 19.1		,					
Test for overall effect: Z = 19.1	condary te	sts with		-	•		
Test for overall effect: Z = 19.1 10.35.5 Unexplained after se Boersma 2004: ILR rec	condary te 0.47	sts witł 0.076	43	0	3.5%	0.47 [0.32, 0.62]	
Test for overall effect: Z = 19.1 10.35.5 Unexplained after se Boersma 2004: ILR rec Brignole 2005: ILR rec	condary te 0.47 0.46	sts with 0.076 0.049	43 103	0 0	3.5% 8.5%	0.46 [0.36, 0.56]	
Test for overall effect: Z = 19.1 10.35.5 Unexplained after se Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec	condary te 0.47 0.46 0.5	sts with 0.076 0.049 0.083	43 103 36	0 0 0	3.5% 8.5% 3.0%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66]	
Test for overall effect: Z = 19.1 10.35.5 Unexplained after se Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec	econdary te 0.47 0.46 0.5 0.52	sts with 0.076 0.049 0.083 0.05	43 103 36 103	0 0 0 0	3.5% 8.5% 3.0% 8.2%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62]	
Test for overall effect: Z = 19.1 10.35.5 Unexplained after se Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec	condary te 0.47 0.46 0.5 0.52 0.13	sts with 0.076 0.049 0.083 0.05 0.068	43 103 36 103 24	0 0 0 0 0	3.5% 8.5% 3.0% 8.2% 4.4%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62] 0.13 [-0.00, 0.26]	
Test for overall effect: Z = 19.1 10.35.5 Unexplained after se Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2001: ILR rec	econdary te 0.47 0.46 0.5 0.52 0.13 0.4	sts with 0.076 0.049 0.083 0.05 0.068 0.089	43 103 36 103 24 30	0 0 0 0 0 0	3.5% 8.5% 3.0% 8.2% 4.4% 2.6%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62] 0.13 [-0.00, 0.26] 0.40 [0.23, 0.57]	
Test for overall effect: Z = 19.1 10.35.5 Unexplained after se Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2001: ILR rec Krahn 2001: ILR rec	condary te 0.47 0.46 0.5 0.52 0.13 0.4 0.31	sts with 0.076 0.049 0.083 0.05 0.068 0.089 0.032	43 103 36 103 24 30 206	0 0 0 0 0 0 0	3.5% 8.5% 3.0% 8.2% 4.4% 2.6% 20.0%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62] 0.13 [-0.00, 0.26] 0.40 [0.23, 0.57] 0.31 [0.25, 0.37]	
Test for overall effect: Z = 19.1 <b>10.35.5 Unexplained after se</b> Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2001: ILR rec Krahn 2002: ILR rec Krahn 2002: ILR rec	condary te 0.47 0.46 0.5 0.52 0.13 0.4 0.4 0.31 0.5	sts with 0.076 0.049 0.083 0.05 0.068 0.089 0.032 0.065	43 103 36 103 24 30 206 60	0 0 0 0 0 0 0 0	3.5% 8.5% 3.0% 8.2% 4.4% 2.6% 20.0% 4.8%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62] 0.13 [-0.00, 0.26] 0.40 [0.23, 0.57] 0.31 [0.25, 0.37] 0.50 [0.37, 0.63]	
Test for overall effect: Z = 19.1 10.35.5 Unexplained after se Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2001: ILR rec Krahn 2002: ILR rec Krahn 2002: ILR rec Krahn 2002: ILR rec Krahn 2002: ILR rec	condary te 0.47 0.46 0.5 0.52 0.13 0.4 0.31 0.5 0.5 0.41	sts with 0.076 0.049 0.083 0.05 0.068 0.089 0.032 0.065 0.084	43 103 36 103 24 30 206 60 34	0 0 0 0 0 0 0 0 0	3.5% 8.5% 3.0% 8.2% 4.4% 2.6% 20.0% 4.8% 2.9%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62] 0.13 [-0.00, 0.26] 0.40 [0.23, 0.57] 0.31 [0.25, 0.37] 0.50 [0.37, 0.63] 0.41 [0.25, 0.57]	
Test for overall effect: Z = 19.1 10.35.5 Unexplained after se Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2001: ILR rec Krahn 2002: ILR rec Krahn 2002: ILR rec Moya 2001: ILR rec	condary te 0.47 0.46 0.5 0.52 0.13 0.4 0.31 0.5 0.41 0.66	sts with 0.076 0.049 0.083 0.05 0.068 0.089 0.032 0.065 0.084 0.052	43 103 36 103 24 30 206 60 34 82	0 0 0 0 0 0 0 0 0 0 0	3.5% 8.5% 3.0% 8.2% 4.4% 2.6% 20.0% 4.8% 2.9% 7.6%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62] 0.13 [-0.00, 0.26] 0.40 [0.23, 0.57] 0.31 [0.25, 0.37] 0.50 [0.37, 0.63] 0.41 [0.25, 0.57] 0.66 [0.56, 0.76]	
Test for overall effect: Z = 19.1 10.35.5 Unexplained after se Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 2001: ILR rec Krahn 2002: ILR rec Krahn 2004: ILR rec Krahn 2004: ILR rec Lombardi 2005: ILR rec Moya 2001: ILR rec Nierop 2000: ILR rec	condary te 0.47 0.46 0.5 0.52 0.13 0.4 0.31 0.5 0.41 0.66 0.31	sts with 0.076 0.049 0.083 0.05 0.068 0.089 0.032 0.065 0.084 0.052 0.078	43 103 36 103 24 30 206 60 34 82 35	0 0 0 0 0 0 0 0 0 0 0 0	3.5% 8.5% 3.0% 8.2% 4.4% 2.6% 20.0% 4.8% 2.9% 7.6% 3.4%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62] 0.13 [-0.00, 0.26] 0.40 [0.23, 0.57] 0.31 [0.25, 0.37] 0.50 [0.37, 0.63] 0.41 [0.25, 0.57] 0.66 [0.56, 0.76] 0.31 [0.16, 0.46]	
Test for overall effect: Z = 19.1 <b>10.35.5 Unexplained after se</b> Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2002: ILR rec Krahn 2004: ILR rec Lombardi 2005: ILR rec Moya 2001: ILR rec Nierop 2000: ILR rec Pezawas 2007: ILR rec	condary te 0.47 0.46 0.5 0.52 0.13 0.4 0.31 0.5 0.41 0.66 0.31 0.14	sts with 0.076 0.049 0.083 0.05 0.068 0.089 0.032 0.065 0.084 0.052 0.078 0.078 0.042	43 103 36 103 24 30 206 60 34 82 35 70	0 0 0 0 0 0 0 0 0 0 0 0 0 0	3.5% 8.5% 3.0% 8.2% 4.4% 2.6% 20.0% 4.8% 2.9% 7.6% 3.4% 11.6%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62] 0.13 [-0.00, 0.26] 0.40 [0.23, 0.57] 0.31 [0.25, 0.37] 0.50 [0.37, 0.63] 0.41 [0.25, 0.57] 0.66 [0.56, 0.76] 0.31 [0.16, 0.46] 0.14 [0.06, 0.22]	
Test for overall effect: Z = 19.1 <b>10.35.5 Unexplained after se</b> Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2001: ILR rec Krahn 2002: ILR rec Krahn 2004: ILR rec Lombardi 2005: ILR rec Moya 2001: ILR rec Nierop 2000: ILR rec Pezawas 2007: ILR rec Pierre 2008: ILR rec	condary te 0.47 0.46 0.5 0.52 0.13 0.4 0.31 0.5 0.41 0.66 0.31 0.14 0.55	sts with 0.076 0.049 0.083 0.05 0.068 0.089 0.032 0.065 0.084 0.052 0.078 0.078 0.042 0.051	43 103 36 103 24 30 206 60 34 82 35 70 95	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	3.5% 8.5% 3.0% 8.2% 4.4% 2.6% 20.0% 4.8% 2.9% 7.6% 3.4% 11.6% 7.9%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62] 0.13 [-0.00, 0.26] 0.40 [0.23, 0.57] 0.31 [0.25, 0.37] 0.50 [0.37, 0.63] 0.41 [0.25, 0.57] 0.66 [0.56, 0.76] 0.31 [0.16, 0.46] 0.14 [0.06, 0.22] 0.55 [0.45, 0.65]	
Test for overall effect: Z = 19.1 <b>10.35.5 Unexplained after se</b> Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2002: ILR rec Krahn 2004: ILR rec Lombardi 2005: ILR rec Moya 2001: ILR rec Nierop 2000: ILR rec Pezawas 2007: ILR rec	condary te 0.47 0.46 0.5 0.52 0.13 0.4 0.31 0.5 0.41 0.66 0.31 0.14 0.55	sts with 0.076 0.049 0.083 0.05 0.068 0.089 0.032 0.065 0.084 0.052 0.078 0.078 0.042	43 103 36 103 24 30 206 60 34 82 35 70	0 0 0 0 0 0 0 0 0 0 0 0 0 0	3.5% 8.5% 3.0% 8.2% 4.4% 2.6% 20.0% 4.8% 2.9% 7.6% 3.4% 11.6%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62] 0.13 [-0.00, 0.26] 0.40 [0.23, 0.57] 0.31 [0.25, 0.37] 0.50 [0.37, 0.63] 0.41 [0.25, 0.57] 0.66 [0.56, 0.76] 0.31 [0.16, 0.46] 0.14 [0.06, 0.22]	
Test for overall effect: Z = 19.1 <b>10.35.5 Unexplained after se</b> Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2001: ILR rec Krahn 2002: ILR rec Krahn 2004: ILR rec Lombardi 2005: ILR rec Moya 2001: ILR rec Nierop 2000: ILR rec Pezawas 2007: ILR rec Pierre 2008: ILR rec Seidl 2000: ILR rec	econdary te 0.47 0.46 0.52 0.13 0.4 0.31 0.41 0.66 0.31 0.14 0.55 0.38	sts with 0.076 0.049 0.083 0.05 0.068 0.089 0.032 0.065 0.084 0.052 0.078 0.042 0.071 0.042	43 103 36 103 24 30 206 60 34 82 35 70 95 133 1054	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	3.5% 8.5% 3.0% 8.2% 4.4% 2.6% 2.6% 2.9% 7.6% 3.4% 11.6% 7.9% 11.6%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62] 0.13 [-0.00, 0.26] 0.40 [0.23, 0.57] 0.31 [0.25, 0.37] 0.50 [0.37, 0.63] 0.41 [0.25, 0.57] 0.66 [0.56, 0.76] 0.31 [0.16, 0.46] 0.14 [0.06, 0.22] 0.55 [0.45, 0.65] 0.38 [0.30, 0.46]	
Test for overall effect: Z = 19.1 <b>10.35.5 Unexplained after se</b> Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2001: ILR rec Krahn 2002: ILR rec Krahn 2004: ILR rec Lombardi 2005: ILR rec Moya 2001: ILR rec Nierop 2000: ILR rec Pezawas 2007: ILR rec Pierre 2008: ILR rec Seidl 2000: ILR rec Subtotal (95% CI)	econdary te 0.47 0.46 0.52 0.13 0.4 0.31 0.4 0.66 0.31 0.14 0.55 0.38 df = 13 (P <	sts with 0.076 0.049 0.083 0.05 0.068 0.089 0.032 0.065 0.084 0.052 0.078 0.042 0.051 0.042 0.051 0.042	43 103 36 103 24 30 206 60 34 82 35 70 95 133 1054	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	3.5% 8.5% 3.0% 8.2% 4.4% 2.6% 2.6% 2.9% 7.6% 3.4% 11.6% 7.9% 11.6%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62] 0.13 [-0.00, 0.26] 0.40 [0.23, 0.57] 0.31 [0.25, 0.37] 0.50 [0.37, 0.63] 0.41 [0.25, 0.57] 0.66 [0.56, 0.76] 0.31 [0.16, 0.46] 0.14 [0.06, 0.22] 0.55 [0.45, 0.65] 0.38 [0.30, 0.46]	
Test for overall effect: Z = 19.1 <b>10.35.5 Unexplained after se</b> Boersma 2004: ILR rec Brignole 2005: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2001: ILR rec Krahn 2002: ILR rec Krahn 2002: ILR rec Lombardi 2005: ILR rec Moya 2001: ILR rec Nierop 2000: ILR rec Pezawas 2007: ILR rec Pierre 2008: ILR rec Seidl 2000: ILR rec Seidl 2000: ILR rec Subtotal (95% CI) Heterogeneity: Chi <sup>2</sup> = 108.80,	econdary te 0.47 0.46 0.52 0.13 0.4 0.31 0.4 0.66 0.31 0.14 0.55 0.38 df = 13 (P <	sts with 0.076 0.049 0.083 0.05 0.068 0.089 0.032 0.065 0.084 0.052 0.078 0.042 0.051 0.042 0.051 0.042	43 103 36 103 24 30 206 60 34 82 35 70 95 133 1054	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	3.5% 8.5% 3.0% 8.2% 4.4% 2.6% 2.6% 2.9% 7.6% 3.4% 11.6% 7.9% 11.6%	0.46 [0.36, 0.56] 0.50 [0.34, 0.66] 0.52 [0.42, 0.62] 0.13 [-0.00, 0.26] 0.40 [0.23, 0.57] 0.31 [0.25, 0.37] 0.50 [0.37, 0.63] 0.41 [0.25, 0.57] 0.66 [0.56, 0.76] 0.31 [0.16, 0.46] 0.14 [0.06, 0.22] 0.55 [0.45, 0.65] 0.38 [0.30, 0.46]	

Test for subgroup differences: Chi<sup>2</sup> = 161.04, df = 3 (P < 0.00001), l<sup>2</sup> = 98.1%

### 1.2.4.2 Normal rhythm during TLoC

		05	n	-		proportion	proportion
	proportion			lotal	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
10.34.1 suspected arrhythmi				_			
Brignole 2001: ILR rec		0.019	52	0	56.9%	0.02 [-0.02, 0.06]	<b>7</b>
Garcia-Civera 05: ILR rec		0.027	81	0	28.2%	0.06 [0.01, 0.11]	
Krahn 1999: ILR rec		0.051	85	0	7.9%	0.34 [0.24, 0.44]	
Menozzi 2002: ILR rec Subtotal (95% CI)	0.11	0.054	35 <b>253</b>	0	7.0% 100.0%	0.11 [0.00, 0.22] 0.06 [0.03, 0.09]	•
Heterogeneity: Chi <sup>2</sup> = 35.39, d	f = 3 (P < 0)	00001).		6			ľ
Test for overall effect: $Z = 4.39$			1 - 02				
40.24.2 evenested neurolly n			(				
10.34.3 suspected neurally n			•				
Brignole 2006: ILR rec	0.074		392	0	90.7%	0.07 [0.05, 0.10]	
Deharo 2006: ILR rec	0.2	0.08	25	0	2.4%	0.20 [0.04, 0.36]	
Moya 2001: ILR rec Subtotal (95% CI)	0.07	0.047	29 <b>446</b>	0	6.9% 1 <b>00.0%</b>	0.07 [-0.02, 0.16] 0.08 [0.05, 0.10]	T.
Heterogeneity: Chi <sup>2</sup> = 2.44, df	= 2 (P – 0 3)	0)· I2 −		Ŭ			ľ
Test for overall effect: Z = 6.20		<i>, , , , , , , , , ,</i>	10 /0				
L = 0.20	, < 0.000	51)					
10.34.4 unexplained after int	ial tests (re	curren	t or not	stated	d)		$\perp$
Ermis 2003: ILR NS	0.04	0.028	50	0	100.0%	0.04 [-0.01, 0.09]	
Subtotal (95% CI)			50	0	100.0%	0.04 [-0.01, 0.09]	•
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.43	(P = 0.15)						
10.34.5 Unexplained after se	condary tee	ste with		ont su	ncone		
Boersma 2004: ILR rec		0.068	43	0 0	3.1%	0.28 [0.15, 0.41]	
		0.068	43 103	-	3.1% 13.2%		
Brignole 2005: ILR rec Donateo 2003: ILR rec		0.033	36	0 0	13.2%	0.13 [0.07, 0.19] 0.06 [-0.01, 0.13]	
Farwell 2006: ILR rec		0.038	30 103	0	8.2%	0.06 [-0.01, 0.13]	
			24	0			
Krahn 1998: ILR rec		0.101			1.4%	0.42 [0.22, 0.62]	L
Krahn 2001: ILR rec Krahn 2002: ILR rec		0.055 0.034	30 206	0	4.8% 12.5%	0.10 [-0.01, 0.21]	
Krahn 2002: ILR rec Krahn 2004: ILR rec		0.034	206 60	0 0	4.6%	0.41 [0.34, 0.48]	
Lombardi 2005: ILR rec		0.056	60 34	0	4.6% 4.8%	0.25 [0.14, 0.36] 0.12 [0.01, 0.23]	
		0.055	34 82	0	4.8%		
Moya 2001: ILR rec Nierop 2000: ILR rec		0.035	82 35	0	2.5%	0.11 [0.04, 0.18]	
Pezawas 2007: ILR rec			35 70	0		0.29 [0.14, 0.44]	
Pezawas 2007: ILR rec Pierre 2008: ILR rec		0.058 0.038	70 95	0	4.3% 10.0%	0.39 [0.28, 0.50] 0.17 [0.10, 0.24]	
		0.038	95 133		9.0%		
Seidl 2000: ILR rec Subtotal (95% Cl)	0.3	0.04	133 1054	0 0	9.0% 100.0%	0.30 [0.22, 0.38] <b>0.21 [0.19, 0.23]</b>	♦
Heterogeneity: Chi² = 93.93, d	f = 13 (P < 0	.00001	); l <sup>2</sup> = 86	6%			
Test for overall effect: Z = 17.5	4 (P < 0.000	001)					
						F	<u> </u>

Test for subgroup differences: Chi<sup>2</sup> = 93.09, df = 3 (P < 0.00001), l<sup>2</sup> = 96.8%

### 1.2.4.3 Arrhythmia during TLoC

		05		brady		proportion	proportion
Study or Subgroup p 0.32.1 suspected arrhythmia	roportion		Total	lotal	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
, ,			· ·		47.00/	0.00.00.05.0.541	
Brignole 2001: ILR rec	0.38		52	95	17.8%	0.38 [0.25, 0.51]	
Barcia-Civera 05: ILR rec	0.33	0.05	81	78	32.0%	0.33 [0.23, 0.43]	
(rahn 1999: ILR rec	0.25		85	86	36.3%	0.25 [0.16, 0.34]	
lenozzi 2002: ILR rec Subtotal (95% CI)	0.29	0.076	35 <b>253</b>	40 200	13.9% 1 <b>00.0%</b>	0.29 [0.14, 0.44] 0.30 [0.25, 0.36]	
leterogeneity: Chi <sup>2</sup> = 2.91, df =	-2(P - 0.4)	1). 12 _ 1		235	100.070	0.50 [0.25, 0.50]	•
est for overall effect: Z = 10.76			U%				
	J (I < 0.000	501)					
0.32.3 suspected neurally m	ediated sy	ncope	(recurren	it)			
Brignole 2006: ILR rec	0.2	0.02	392	79	89.2%	0.20 [0.16, 0.24]	
Deharo 2006: ILR rec	0.28	0.09	25	86	4.4%	0.28 [0.10, 0.46]	—
loya 2001: ILR rec	0.21	0.075	29	100	6.3%	0.21 [0.06, 0.36]	
Subtotal (95% CI)			446	265	100.0%	0.20 [0.17, 0.24]	♦
leterogeneity: Chi <sup>2</sup> = 0.76, df =	2 (P = 0.68	B); I <sup>2</sup> = (	0%				
est for overall effect: Z = 10.8	1 (P < 0.000	001)					
		•					
0.32.4 unexplained after init				,			
Ermis 2003: ILR NS	0.08	0.038	50		100.0%	0.08 [0.01, 0.15]	
Subtotal (95% CI)			50	25	100.0%	0.08 [0.01, 0.15]	•
leterogeneity: Not applicable							
est for overall effect: Z = 2.11	(P = 0.04)						
0.32.5 Unexplained after sec	ondary tes	sts with	n recurrer	nt synco	ope		
Boersma 2004: ILR rec	0.26	0.067	43	82	4.0%	0.26 [0.13, 0.39]	<del></del>
Brignole 2005: ILR rec	0.38	0.048	103	87	7.9%	0.38 [0.29, 0.47]	
Donateo 2003: ILR rec	0.39		36	79	2.8%	0.39 [0.23, 0.55]	<del></del>
arwell 2006: ILR rec	0.2	0.04	103	75	11.3%	0.20 [0.12, 0.28]	
(rahn 1998: ILR rec	0.46	0.102	24	80	1.7%	0.46 [0.26, 0.66]	
(rahn 2001: ILR rec	0.37	0.088	30	91	2.3%	0.37 [0.20, 0.54]	
Krahn 2002: ILR rec		0.029	206	74	21.5%	0.23 [0.17, 0.29]	
Krahn 2004: ILR rec	0.23		60	71	6.0%	0.23 [0.12, 0.34]	
ombardi 2005: ILR rec		0.083	34	69	2.6%	0.38 [0.22, 0.54]	<del></del>
loya 2001: ILR rec	0.18		82	87	9.8%	0.18 [0.10, 0.26]	<del>-</del>
lierop 2000: ILR rec		0.076	35	40	3.1%	0.29 [0.14, 0.44]	
Pezawas 2007: ILR rec	0.23	0.06	70	54	5.0%	0.47 [0.35, 0.59]	
Pierre 2008: ILR rec	0.28		95	78	8.6%	0.28 [0.19, 0.37]	
Seidl 2000: ILR rec	0.20		133	69	13.2%	0.24 [0.17, 0.31]	
Subtotal (95% CI)	0.24	0.007	1054		100.0%	0.27 [0.24, 0.30]	♦
leterogeneity: Chi <sup>2</sup> = 35.75, df	= 13 (P = 0	.0006):	$l^2 = 64\%$				
est for overall effect: Z = 20.0		· · ·	2.70				
		• /					1

Test for subgroup differences: Chi<sup>2</sup> = 31.33, df = 3 (P < 0.00001), I<sup>2</sup> = 90.4%

### 1.2.4.4 Arrhythmia not during TLoC

		~ -	n	% brady		proportion	proportion
Study or Subgroup	proportion		Total		Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
10.33.1 suspected arrhy			-	•			
Brignole 2001: ILR rec	0.077	0.037	52	100	100.0%	0.08 [0.00, 0.15]	· · · · · · · · · · · · · · · · · · ·
Menozzi 2002: ILR rec Subtotal (95% CI)	0	0	35 <b>87</b>		100.0%	Not estimable 0.08 [0.00, 0.15]	•
Heterogeneity: Not applic	able						
Test for overall effect: Z =	= 2.08 (P = 0.0	4)					
10.33.2 suspected neur	ally mediated	synco	oe (rec	urrent)			
Brignole 2006: ILR rec Subtotal (95% CI)	0.028	0.008	392 <b>392</b>		100.0% 1 <b>00.0%</b>	0.03 [0.01, 0.04] <b>0.03 [0.01, 0.04]</b>	-
Heterogeneity: Not applic Test for overall effect: Z =		005)					
10.33.3 unexplained after	er intial tests	(recurre	ent or	not stated	)		
Ermis 2003: ILR NS	0.26	0.062	50		100.0%	0.26 [0.14, 0.38]	· <b>₩</b>
Subtotal (95% CI)			50	0	100.0%	0.26 [0.14, 0.38]	•
Heterogeneity: Not applic	able						
Test for overall effect: Z =	= 4.19 (P < 0.0	001)					
10.33.4 Unexplained aft	er secondary	tests w	ith re	current syr	соре		$\perp$
Boersma 2004: ILR rec	0.02	0.023	43	100	78.5%	0.02 [-0.03, 0.07]	<b>—</b>
Krahn 2004: ILR rec Subtotal (95% CI)	0.133	0.044	60 1 <b>03</b>		21.5% <b>100.0%</b>	0.13 [0.05, 0.22] 0.04 [0.00, 0.08]	<b>→</b>
Heterogeneity: Chi <sup>2</sup> = 5.1	8 df = 1 (P = 1	n ∩2\+ I2					•
Test for overall effect: Z =		· · ·	- 01%	)			
	= 2.17 (P = 0.0)	3)					
							-1 -0.5 0 0.5

Test for subgroup differences:  $Chi^2 = 15.43$ , df = 3 (P = 0.001), I<sup>2</sup> = 80.6%

### 1.2.4.5 No ECG during TLoC

		05	n	<b>T</b> . ( . )		proportion	proportion
Study or Subgroup p 10.36.1 suspected arrhythr	proportion				Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
Brignole 2001: ILR rec		0.032	52	0	50.0%	0.06 [-0.00, 0.12]	
Krahn 1999: ILR rec		0.032	85	0	50.0%	0.09 [0.03, 0.15]	-
Subtotal (95% CI)	0.00	0.002	137	Ő		0.07 [0.03, 0.12]	◆
Heterogeneity: Chi <sup>2</sup> = 0.44, c	df = 1 (P = 0	0.51); l²	= 0%				
Test for overall effect: $Z = 3.3$	31 (P = 0.0	009)					
0.36.2 suspected neurally	mediated	syncop	oe (recu	urrent)			
Brignole 2006: ILR rec	0.09	0.015	392	0	90.8%	0.09 [0.06, 0.12]	
Noya 2001: ILR rec	0.069	0.047	29	0	9.2%	0.07 [-0.02, 0.16]	<u>+-</u> -
Subtotal (95% CI)			421	0	100.0%	0.09 [0.06, 0.12]	♦
0.36.3 unexplained after in Subtotal (95% CI)	ntial tests	(recurre	entorn 0	not stat 0	ed)	Not estimable	
Heterogeneity: Not applicabl	е						
Fest for overall effect: Not ap	oplicable						
0.36.4 Unexplained after s	secondary	tests w	ith rec	urrent	syncope		
Brignole 2005: ILR rec	0.04	0.019	103	0	22.8%	0.04 [0.00, 0.08]	-
Donateo 2003: ILR rec	0.06	0.038	36	0	5.7%	0.06 [-0.01, 0.13]	+
Krahn 2002: ILR rec	0.05	0.015	206	0	36.6%	0.05 [0.02, 0.08]	-
ombardi 2005: ILR rec	0.09	0.049	34	0	3.4%	0.09 [-0.01, 0.19]	
Noya 2001: ILR rec	0.05	0.024	82	0	14.3%	0.05 [0.00, 0.10]	=
Nierop 2000: ILR rec	0.11	0.054	35	0	2.8%	0.11 [0.00, 0.22]	
Seidl 2000: ILR rec	0.08	0.024	133	0	14.3%	0.08 [0.03, 0.13]	
			629	0	100.0%	0.06 [0.04, 0.07]	
Seldi 2000: ILR rec Subtotal (95% CI)			029	0			1
	⅓ = 6 (P = 0	).75); l²		0		0.00 [0.04, 0.07]	ľ
Subtotal (95% CI)				U			ľ
Subtotal (95% CI) Heterogeneity: Chi <sup>2</sup> = 3.42, c				Ū			

Test for subgroup differences:  $Chi^2 = 3.84$ , df = 2 (P = 0.15),  $l^2 = 47.9\%$ 

Transient loss of consciousness: full guideline DRAFT (January 2010) Page 18 of 46

### 1.2.4.6 Number of patients started on therapy

			n			proportion	proportion
Study or Subgroup	proportion				Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
10.37.1 suspected arrhyth			yncope	•			
Brignole 2001: ILR rec		0.069	52	0	24.3%	0.44 [0.30, 0.58]	
Garcia-Civera 05: ILR rec	0.22	0.046	81	0	54.6%	0.22 [0.13, 0.31]	
Menozzi 2002: ILR rec Subtotal (95% CI)	0.26	0.074	35 168	0 0	21.1% 1 <b>00.0%</b>	0.26 [0.11, 0.41] <b>0.28 [0.22, 0.35]</b>	•
Heterogeneity: Chi <sup>2</sup> = 7.15,	df = 2 (P = 0.0)	)3); l² =	72%				
Test for overall effect: Z = 8	.29 (P < 0.000	01)					
10.37.3 suspected neurally	y mediated sy	/ncope	(recurr	ent)			
Brignole 2006: ILR rec	0.14	0.018	392	0	89.4%	0.14 [0.10, 0.18]	
Deharo 2006: ILR rec	0.28	0.09	25	0	3.6%	0.28 [0.10, 0.46]	— <b>-</b>
Moya 2001: ILR rec	0.14	0.064	29	0	7.1%	0.14 [0.01, 0.27]	
Subtotal (95% CI)			446	0	100.0%	0.15 [0.11, 0.18]	•
Heterogeneity: $Chi^2 = 2.33$ , Test for overall effect: $Z = 8$			14%				
10.37.4 unexplained after					,		
Ermis 2003: ILR NS Subtotal (95% CI)	0.32	0.066	50 <b>50</b>		100.0% 1 <b>00.0%</b>	0.32 [0.19, 0.45] <b>0.32 [0.19, 0.45]</b>	
	1-		50	0	100.076	0.52 [0.19, 0.45]	
Heterogeneity: Not applicab Test for overall effect: Z = 4		01)					
Test for overall effect. $Z = 4$	.05 (F < 0.000	01)					
10.37.5 Unexplained after	secondary te	sts with	n recur	rent sy	ncope		
10.37.5 Unexplained after Boersma 2004: ILR rec	-	sts with 0.068	n <mark>recur</mark> 43	rentsy 0	ncope 3.6%	0.28 [0.15. 0.41]	
•	0.28			-	•	0.28 [0.15, 0.41] 0.37 [0.28, 0.46]	
Boersma 2004: ILR rec	0.28 0.37	0.068	43	0	3.6%	. , .	
Boersma 2004: ILR rec Brignole 2005: ILR rec	0.28 0.37 0.25	0.068 0.048	43 103	0 0	3.6% 7.2%	0.37 [0.28, 0.46]	
Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec	0.28 0.37 0.25 0.16	0.068 0.048 0.072	43 103 36	0 0 0	3.6% 7.2% 3.2%	0.37 [0.28, 0.46] 0.25 [0.11, 0.39]	
Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec	0.28 0.37 0.25 0.16 0.46	0.068 0.048 0.072 0.036	43 103 36 103	0 0 0 0	3.6% 7.2% 3.2% 12.7%	0.37 [0.28, 0.46] 0.25 [0.11, 0.39] 0.16 [0.09, 0.23]	
Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec	0.28 0.37 0.25 0.16 0.46 0.17	0.068 0.048 0.072 0.036 0.102	43 103 36 103 24	0 0 0 0 0	3.6% 7.2% 3.2% 12.7% 1.6%	0.37 [0.28, 0.46] 0.25 [0.11, 0.39] 0.16 [0.09, 0.23] 0.46 [0.26, 0.66]	
Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2002: ILR rec	0.28 0.37 0.25 0.16 0.46 0.17 0.3	0.068 0.048 0.072 0.036 0.102 0.026	43 103 36 103 24 206	0 0 0 0 0	3.6% 7.2% 3.2% 12.7% 1.6% 24.4%	0.37 [0.28, 0.46] 0.25 [0.11, 0.39] 0.16 [0.09, 0.23] 0.46 [0.26, 0.66] 0.17 [0.12, 0.22]	+ + + +
Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2002: ILR rec Krahn 2004: ILR rec	0.28 0.37 0.25 0.16 0.46 0.17 0.3 0.35	0.068 0.048 0.072 0.036 0.102 0.026 0.059	43 103 36 103 24 206 60	0 0 0 0 0 0 0	3.6% 7.2% 3.2% 12.7% 1.6% 24.4% 4.7%	0.37 [0.28, 0.46] 0.25 [0.11, 0.39] 0.16 [0.09, 0.23] 0.46 [0.26, 0.66] 0.17 [0.12, 0.22] 0.30 [0.18, 0.42]	+ + + + +
Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2002: ILR rec Krahn 2004: ILR rec Lombardi 2005: ILR rec	0.28 0.37 0.25 0.16 0.46 0.17 0.3 0.35 0.12	0.068 0.048 0.072 0.036 0.102 0.026 0.059 0.082	43 103 36 103 24 206 60 34	0 0 0 0 0 0 0	3.6% 7.2% 3.2% 12.7% 1.6% 24.4% 4.7% 2.5%	0.37 [0.28, 0.46] 0.25 [0.11, 0.39] 0.16 [0.09, 0.23] 0.46 [0.26, 0.66] 0.17 [0.12, 0.22] 0.30 [0.18, 0.42] 0.35 [0.19, 0.51]	+ + + + +
Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2002: ILR rec Krahn 2004: ILR rec Lombardi 2005: ILR rec Moya 2001: ILR rec	0.28 0.37 0.25 0.16 0.46 0.17 0.3 0.35 0.12	0.068 0.048 0.072 0.036 0.102 0.026 0.059 0.082 0.036	43 103 36 103 24 206 60 34 82	0 0 0 0 0 0 0 0 0	3.6% 7.2% 3.2% 12.7% 1.6% 24.4% 4.7% 2.5% 12.7%	0.37 [0.28, 0.46] 0.25 [0.11, 0.39] 0.16 [0.09, 0.23] 0.46 [0.26, 0.66] 0.17 [0.12, 0.22] 0.30 [0.18, 0.42] 0.35 [0.19, 0.51] 0.12 [0.05, 0.19]	+ + + + +
Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2002: ILR rec Krahn 2004: ILR rec Lombardi 2005: ILR rec Moya 2001: ILR rec Nierop 2000: ILR rec	0.28 0.37 0.25 0.16 0.46 0.17 0.3 0.35 0.12 0.23 0.49	0.068 0.048 0.072 0.036 0.102 0.026 0.059 0.082 0.036 0.071	43 103 36 103 24 206 60 34 82 35	0 0 0 0 0 0 0 0 0 0 0	3.6% 7.2% 3.2% 12.7% 1.6% 24.4% 4.7% 2.5% 12.7% 3.3%	0.37 [0.28, 0.46] 0.25 [0.11, 0.39] 0.16 [0.09, 0.23] 0.46 [0.26, 0.66] 0.17 [0.12, 0.22] 0.30 [0.18, 0.42] 0.35 [0.19, 0.51] 0.12 [0.05, 0.19] 0.23 [0.09, 0.37]	+ + + + + + + + + + + + + + + + + + +
Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2002: ILR rec Lombardi 2005: ILR rec Moya 2001: ILR rec Nierop 2000: ILR rec Pezawas 2007: ILR rec	0.28 0.37 0.25 0.16 0.46 0.17 0.3 0.35 0.12 0.23 0.49 0.31	0.068 0.048 0.072 0.036 0.102 0.026 0.059 0.082 0.036 0.071 0.06	43 103 36 103 24 206 60 34 82 35 70	0 0 0 0 0 0 0 0 0 0 0 0 0	3.6% 7.2% 3.2% 12.7% 1.6% 24.4% 4.7% 2.5% 12.7% 3.3% 4.6%	0.37 [0.28, 0.46] 0.25 [0.11, 0.39] 0.16 [0.09, 0.23] 0.46 [0.26, 0.66] 0.17 [0.12, 0.22] 0.30 [0.18, 0.42] 0.35 [0.19, 0.51] 0.12 [0.05, 0.19] 0.23 [0.09, 0.37] 0.49 [0.37, 0.61]	+++ ++ ++ ++ +++
Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2002: ILR rec Lombardi 2005: ILR rec Moya 2001: ILR rec Nierop 2000: ILR rec Pezawas 2007: ILR rec Pierre 2008: ILR rec	0.28 0.37 0.25 0.16 0.46 0.17 0.3 0.35 0.12 0.23 0.49 0.31	0.068 0.048 0.072 0.036 0.102 0.026 0.059 0.082 0.036 0.071 0.06 0.047	43 103 36 103 24 206 60 34 82 35 70 95	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	3.6% 7.2% 3.2% 12.7% 1.6% 24.4% 4.7% 2.5% 12.7% 3.3% 4.6% 7.5%	0.37 [0.28, 0.46] 0.25 [0.11, 0.39] 0.16 [0.09, 0.23] 0.46 [0.26, 0.66] 0.17 [0.12, 0.22] 0.30 [0.18, 0.42] 0.35 [0.19, 0.51] 0.12 [0.05, 0.19] 0.23 [0.09, 0.37] 0.49 [0.37, 0.61] 0.31 [0.22, 0.40]	+ + + + + + + + +
Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2002: ILR rec Lombardi 2005: ILR rec Moya 2001: ILR rec Nierop 2000: ILR rec Pezawas 2007: ILR rec Pierre 2008: ILR rec Seidl 2000: ILR rec	0.28 0.37 0.25 0.16 0.46 0.17 0.3 0.35 0.12 0.23 0.49 0.31 0.24	0.068 0.048 0.072 0.036 0.026 0.059 0.082 0.036 0.071 0.06 0.047 0.037	43 103 36 103 24 206 60 34 82 35 70 95 133 1024	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	3.6% 7.2% 3.2% 12.7% 1.6% 24.4% 4.7% 2.5% 12.7% 3.3% 4.6% 7.5% 12.1%	0.37 [0.28, 0.46] 0.25 [0.11, 0.39] 0.16 [0.09, 0.23] 0.46 [0.26, 0.66] 0.17 [0.12, 0.22] 0.30 [0.18, 0.42] 0.35 [0.19, 0.51] 0.12 [0.05, 0.19] 0.23 [0.09, 0.37] 0.49 [0.37, 0.61] 0.31 [0.22, 0.40] 0.24 [0.17, 0.31]	+ + + + + + + +
Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2002: ILR rec Krahn 2004: ILR rec Lombardi 2005: ILR rec Moya 2001: ILR rec Nierop 2000: ILR rec Pezawas 2007: ILR rec Pierre 2008: ILR rec Seidl 2000: ILR rec Subtotal (95% CI)	0.28 0.37 0.25 0.16 0.46 0.17 0.3 0.35 0.12 0.23 0.49 0.31 0.24 , df = 12 (P <	0.068 0.048 0.072 0.036 0.102 0.026 0.059 0.082 0.036 0.071 0.06 0.047 0.037	43 103 36 103 24 206 60 34 82 35 70 95 133 1024	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	3.6% 7.2% 3.2% 12.7% 1.6% 24.4% 4.7% 2.5% 12.7% 3.3% 4.6% 7.5% 12.1%	0.37 [0.28, 0.46] 0.25 [0.11, 0.39] 0.16 [0.09, 0.23] 0.46 [0.26, 0.66] 0.17 [0.12, 0.22] 0.30 [0.18, 0.42] 0.35 [0.19, 0.51] 0.12 [0.05, 0.19] 0.23 [0.09, 0.37] 0.49 [0.37, 0.61] 0.31 [0.22, 0.40] 0.24 [0.17, 0.31]	+ + + + + + + + + +
Boersma 2004: ILR rec Brignole 2005: ILR rec Donateo 2003: ILR rec Farwell 2006: ILR rec Krahn 1998: ILR rec Krahn 2002: ILR rec Krahn 2004: ILR rec Moya 2001: ILR rec Nierop 2000: ILR rec Pezawas 2007: ILR rec Pierre 2008: ILR rec Seidl 2000: ILR rec <b>Subtotal (95% CI)</b> Heterogeneity: Chi <sup>2</sup> = 57.86	0.28 0.37 0.25 0.16 0.46 0.17 0.3 0.35 0.12 0.23 0.49 0.31 0.24 , df = 12 (P <	0.068 0.048 0.072 0.036 0.102 0.026 0.059 0.082 0.036 0.071 0.06 0.047 0.037	43 103 36 103 24 206 60 34 82 35 70 95 133 1024	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	3.6% 7.2% 3.2% 12.7% 1.6% 24.4% 4.7% 2.5% 12.7% 3.3% 4.6% 7.5% 12.1%	0.37 [0.28, 0.46] 0.25 [0.11, 0.39] 0.16 [0.09, 0.23] 0.46 [0.26, 0.66] 0.17 [0.12, 0.22] 0.30 [0.18, 0.42] 0.35 [0.19, 0.51] 0.12 [0.05, 0.19] 0.23 [0.09, 0.37] 0.49 [0.37, 0.61] 0.31 [0.22, 0.40] 0.24 [0.17, 0.31]	

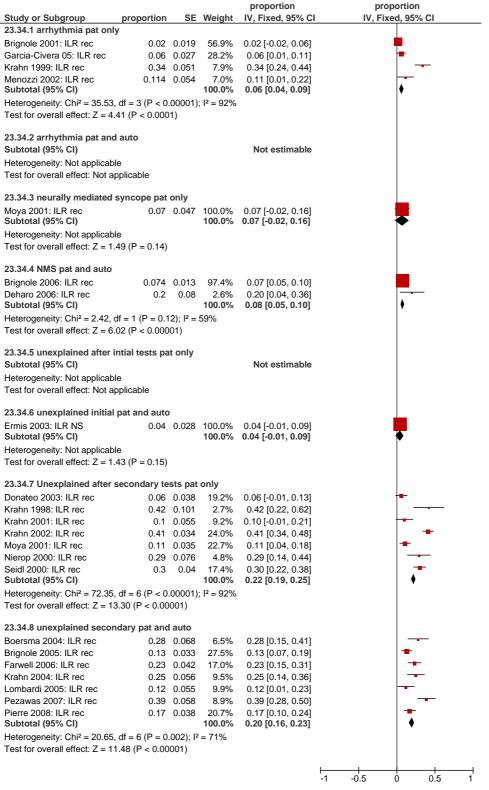
Test for subgroup differences:  $Chi^2 = 25.29$ , df = 3 (P < 0.0001), I<sup>2</sup> = 88.1%

#### 1.2.4.7 Adverse events

No studies reported this outcome.

### 1.3 Implantable Event Recorder only: subgroup analyses by patient or patient + automatic activation

### 1.3.1 Normal rhythm during TLoC



Test for subgroup differences:  $Chi^2 = 93.88$ , df = 5 (P < 0.00001), l<sup>2</sup> = 94.7%

Transient loss of consciousness: full guideline DRAFT (January 2010) Page 21 of 46

### 1.3.2 Arrhythmia during TLoC

Study or Subgroup pro	portion	SE	n Total	% brady Total	Weight	proportion IV, Fixed, 95% CI	proportion IV, Fixed, 95% CI
23.32.1 arrhythmia pat only		01		10101			
Brignole 2001: ILR rec	0.35	0.066	52	95	18.3%	0.35 [0.22, 0.48]	<b>—</b>
Krahn 1999: ILR rec		0.047	85	86	36.1%	0.25 [0.16, 0.34]	
Garcia-Civera 05: ILR rec	0.33		81	78	31.9%	0.33 [0.23, 0.43]	
Menozzi 2002: ILR rec		0.076	35	40	13.8%	0.29 [0.14, 0.44]	
Subtotal (95% CI)			253	299	100.0%	0.30 [0.24, 0.35]	•
Heterogeneity: Chi <sup>2</sup> = 2.08, df = 3 Fest for overall effect: Z = 10.60 (			0%				
23.32.2 arrhythmia pat and auto	)					Not optionally	
Subtotal (95% CI)			0	0		Not estimable	
Heterogeneity: Not applicable Fest for overall effect: Not applica	ble						
23.32.3 neurally mediated sync	ope pat	only					
Moya 2001: ILR rec		0.075	29	100	100.0%	0.21 [0.06, 0.36]	
Subtotal (95% Cl)	0.21	0.075	29 29		100.0%	0.21 [0.06, 0.36] 0.21 [0.06, 0.36]	
Heterogeneity: Not applicable Fest for overall effect: Z = 2.80 (P	= 0.005	i)					
23 32 4 NMS nat and auto							
23.32.4 NMS pat and auto	0.28	0.09	25	86	4.7%	0.28 [0.10, 0.46]	<b>_</b>
Deharo 2006: ILR rec Brignole 2006: ILR rec	0.28	0.09	25 392	86 79	4.7% 95.3%	0.28 [0.10, 0.46] 0.20 [0.16, 0.24]	
Subtotal (95% CI)	0.2	0.02	392 417	165	95.3% 100.0%	0.20 [0.16, 0.24] 0.20 [0.17, 0.24]	🔻
Heterogeneity: $Chi^2 = 0.75$ , df = 1 Fest for overall effect: Z = 10.44 (			0%				
23.32.5 unexplained initial tests Subtotal (95% CI)	pat on	у	0	0		Not estimable	
Heterogeneity: Not applicable Fest for overall effect: Not applica	ble						
23.32.6 unexplained initial pat a	nd auto	)					
Ermis 2003: ILR NS Subtotal (95% CI)	0.08	0.038	50 <b>50</b>		100.0% 1 <b>00.0%</b>	0.08 [0.01, 0.15] <b>0.08 [0.01, 0.15]</b>	•
Heterogeneity: Not applicable Fest for overall effect: Z = 2.11 (P	= 0.04)						
2 22 7 Uneveloined offer eccer			anhi				
23.32.7 Unexplained after secon			-	01	4 20/	0.07 [0.00, 0.54]	
Krahn 2001: ILR rec		0.088	30	91	4.3%	0.37 [0.20, 0.54]	
Moya 2001: ILR rec Krahn 1998: ILR rec		0.043 0.101	82 24	87 80	17.9%	0.18 [0.10, 0.26] 0.42 [0.22, 0.62]	<u> </u>
Donateo 2003: ILR rec		0.081	24 36	80 79	3.3% 5.1%	0.42 [0.22, 0.62]	<b>_</b>
Krahn 2002: ILR rec		0.081	206	75	39.5%	0.23 [0.17, 0.29]	<b>_</b>
Seidl 2000: ILR rec		0.029	133	69	39.5% 24.2%	0.23 [0.17, 0.29]	
Nierop 2000: ILR rec		0.037	35	40	24.2 <i>%</i> 5.7%	0.29 [0.14, 0.44]	
Subtotal (95% CI)	0.20	0.070	546		100.0%	0.25 [0.21, 0.28]	♦
Heterogeneity: Chi² = 11.13, df = Fest for overall effect: Z = 13.57 (			= 46%				
23.32.8 unexplained secondary	pat and	auto					
Brignole 2005: ILR rec	0.38	0.048	103	87	17.1%	0.38 [0.29, 0.47]	
Boersma 2004: ILR rec	0.26	0.067	43	82	8.8%	0.26 [0.13, 0.39]	<del></del>
Pierre 2008: ILR rec	0.28	0.046	95	78	18.6%	0.28 [0.19, 0.37]	
Farwell 2006: ILR rec	0.19	0.039	103	75	25.9%	0.19 [0.11, 0.27]	
Krahn 2004: ILR rec	0.23	0.055	60	71	13.0%	0.23 [0.12, 0.34]	<b></b> -
ombardi 2005: ILR rec	0.38	0.083	34	69	5.7%	0.38 [0.22, 0.54]	— <b>-</b>
Pezawas 2007: ILR rec Subtotal (95% CI)	0.49	0.06	70 <b>508</b>	54 516	10.9% 1 <b>00.0%</b>	0.49 [0.37, 0.61] <b>0.29 [0.26, 0.33]</b>	
Heterogeneity: Chi <sup>2</sup> = 23.77, df =	6 (P = 0	.0006):			100.070	0.20 [0.20, 0.00]	
Test for overall effect: Z = 14.83 (				-			
						1	

Test for subgroup differences: Chi<sup>2</sup> = 33.32, df = 5 (P < 0.00001), l<sup>2</sup> = 85.0%

Transient loss of consciousness: full guideline DRAFT (January 2010) Page 22 of 46

### 1.3.3 Arrhythmia not during TLoC

Study or Subgroup pr	roportion	SE	n ' Total	% brady Total	Weight	proportion IV, Fixed, 95% CI	proportion IV, Fixed, 95% Cl
23.33.1 arrhythmia pat only						,	
Brignole 2001: ILR rec	0.077	0.037	52	100	100.0%	0.08 [0.00, 0.15]	
Menozzi 2002: ILR rec	0	0	35	0		Not estimable	
Subtotal (95% CI)			87	100	100.0%	0.08 [0.00, 0.15]	•
Heterogeneity: Not applicable	e						
Test for overall effect: Z = 2.0	08 (P = 0.0	4)					
23.33.2 arrhythmia pat and	auto						
Subtotal (95% CI)			0	0		Not estimable	
Heterogeneity: Not applicable	Э						
Test for overall effect: Not ap	plicable						
23.33.3 neurally mediated s	syncope p	at only					
Subtotal (95% CI)		,	0	0		Not estimable	
Heterogeneity: Not applicable	Э						
Test for overall effect: Not ap	plicable						
23.33.4 NMS pat and auto							
Brignole 2006: ILR rec	0.028	0.008	392	100	100.0%	0.03 [0.01, 0.04]	
Subtotal (95% CI)			392	100	100.0%	0.03 [0.01, 0.04]	The second secon
Heterogeneity: Not applicable	e						
Test for overall effect: Z = 3.5	50 (P = 0.0	005)					
23.33.5 unexplained intial p	at only						
Subtotal (95% CI)			0	0		Not estimable	
Heterogeneity: Not applicable							
Test for overall effect: Not ap	plicable						
23.33.6 unexplained initial p	pat and au	ito					
Ermis 2003: ILR NS	0.26	0.062	50		100.0%	0.26 [0.14, 0.38]	
Subtotal (95% CI)			50	0	100.0%	0.26 [0.14, 0.38]	
Heterogeneity: Not applicable							
Test for overall effect: Z = 4.1	9 (P < 0.0	001)					
23.33.7 Unexplained second	dary pat o	only					
Subtotal (95% CI)			0	0		Not estimable	
Heterogeneity: Not applicable							
Test for overall effect: Not ap	plicable						
23.33.8 unexplained second	•••						$\perp$
Boersma 2004: ILR rec		0.023	43	100	78.5%	0.02 [-0.03, 0.07]	<b>—</b>
Krahn 2004: ILR rec	0.133	0.044	60	88	21.5%	0.13 [0.05, 0.22]	
Subtotal (95% CI)			103	188	100.0%	0.04 [0.00, 0.08]	•
Heterogeneity: Chi <sup>2</sup> = 5.18, d			= 81%				
Test for overall effect: Z = 2.1	17 (P = 0.0	3)					
						F	
							1 -0.5 0 0.5

Test for subgroup differences:  $Chi^2 = 15.43$ , df = 3 (P = 0.001), l<sup>2</sup> = 80.6%

### 1.3.4 No ECG during TLoC

Study or Subgroup		E Weight	proportion IV, Fixed, 95% Cl	proportion I IV, Fixed, 95% CI
23.36.1 arrhythmia pat or	-			
Brignole 2001: ILR rec	0.06 0.03		0.06 [-0.00, 0.12]	
Krahn 1999: ILR rec <b>Subtotal (95% Cl)</b>	0.09 0.03	2 50.0% 100.0%	0.09 [0.03, 0.15] <b>0.07 [0.03, 0.12]</b>	•
Heterogeneity: Chi <sup>2</sup> = 0.44 Test for overall effect: Z = 3		l <sup>2</sup> = 0%		
23.36.2 arrhythmia pat an	d auto			
Subtotal (95% CI)			Not estimable	
Heterogeneity: Not applica Test for overall effect: Not a				
23.36.3 neurally mediated	l syncope pat onl	у		
Brignole 2006: ILR rec	0.09 0.01	5 90.8%	0.09 [0.06, 0.12]	<b></b>
Moya 2001: ILR rec	0.069 0.04		0.07 [-0.02, 0.16]	1
Subtotal (95% CI)		100.0%	0.09 [0.06, 0.12]	▼
Heterogeneity: $Chi^2 = 0.18$ , Test for overall effect: $Z = 6$	( ),	l <sup>2</sup> = 0%		
23.36.4 NMS pat and auto	)			
Subtotal (95% CI)			Not estimable	
Heterogeneity: Not applica				
Test for overall effect: Not a	applicable			
23.36.5 unexpliained initi Subtotal (95% Cl)	al pat only		Not estimable	
Heterogeneity: Not applica	hle			
Test for overall effect: Not a				
23.36.6 unexplained initia	I pat and auto			
Subtotal (95% CI)			Not estimable	
Heterogeneity: Not applica				
Test for overall effect: Not a	applicable			
23.36.7 unexplained seco		o <b>-</b> 0/		
Donateo 2003: ILR rec	0.06 0.03		• • •	
Krahn 2002: ILR rec	0.05 0.01		0.05 [0.02, 0.08]	
Moya 2001: ILR rec Nierop 2000: ILR rec	0.05 0.02		0.05 [0.00, 0.10]	<b></b>
Seidl 2000: ILR rec	0.08 0.02		0.11 [0.00, 0.22] 0.08 [0.03, 0.13]	-
Subtotal (95% CI)	0.00 0.02	100.0%		♦
Heterogeneity: Chi <sup>2</sup> = 2.16,		l² = 0%	,	
Test for overall effect: Z = 5	5.57 (P < 0.00001)			
23.36.8 unexplained seco				
Brignole 2005: ILR rec	0.04 0.01		0.04 [0.00, 0.08]	<b>—</b>
Lombardi 2005: ILR rec Subtotal (95% CI)	0.09 0.04	9 13.1% 100.0%	0.09 [-0.01, 0.19] <b>0.05 [0.01, 0.08]</b>	•
Heterogeneity: Chi <sup>2</sup> = 0.91,	df = 1 (P = 0.34):		- / -	ľ
Test for overall effect: $Z = 2$	, ,			
				-1 -0.5 0 0.5
				-1 -0.5 0 0.5

Test for subgroup differences:  $Chi^2 = 4.20$ , df = 3 (P = 0.24), l<sup>2</sup> = 28.6%

### 1.4 Implantable Event Recorder results only: subgroup analyses by duration, frequency and their product

For these subgroup analyses, the populations, suspected arrhythmic syncope and unexplained after secondary tests, were combined. This is reported for the outcome, no TLoC during monitoring.

### 1.4.1 Subgroup analysis by duration for IER: populations combined

Subgroup analysis was carried out for the pre-specified durations, but this did not explain the heterogeneity.

		0-	M	proportion	proportion
Study or Subgroup	proportion	SE	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
10.56.1 ILR < 6 months					
Brignole 2001: ILR rec		0.069	3.5%	0.54 [0.40, 0.68]	
Krahn 1998: ILR rec		0.068	3.6%	0.13 [-0.00, 0.26]	
Krahn 2002: ILR rec	0.31	0.032	16.3%	0.31 [0.25, 0.37]	
Subtotal (95% CI)			23.5%	0.32 [0.26, 0.37]	•
Heterogeneity: Chi <sup>2</sup> = 18.06		,.	l <sup>2</sup> = 89%		
Test for overall effect: Z = 1	1.86 (P < 0.00	001)			
10.56.2 ILR 6-12 months					
Garcia-Civera 05: ILR rec	0.6	0.054	5.7%	0.60 [0.49, 0.71]	
Krahn 1999: ILR rec	0.32	0.05	6.7%	0.32 [0.22, 0.42]	
Krahn 2001: ILR rec	0.4	0.089	2.1%	0.40 [0.23, 0.57]	
Krahn 2004: ILR rec	0.5	0.065	4.0%	0.50 [0.37, 0.63]	<del></del>
Lombardi 2005: ILR rec	0.41	0.084	2.4%	0.41 [0.25, 0.57]	
Moya 2001: ILR rec	0.66	0.052	6.2%	0.66 [0.56, 0.76]	
Nierop 2000: ILR rec	0.31	0.078	2.7%	0.31 [0.16, 0.46]	
Pierre 2008: ILR rec		0.051	6.4%	0.55 [0.45, 0.65]	
Seidl 2000: ILR rec	0.38	0.042	9.5%	0.38 [0.30, 0.46]	
Subtotal (95% CI)			45.7%	0.47 [0.43, 0.51]	•
Heterogeneity: Chi² = 40.75 Test for overall effect: Z = 2		,	; l² = 80%		
	4.55 (1 < 0.00	001)			
10.56.3 ILR >12 months					
Boersma 2004: ILR rec	0.47	0.076	2.9%	0.47 [0.32, 0.62]	
Brignole 2005: ILR rec	0.46	0.049	7.0%	0.46 [0.36, 0.56]	_ <b>_</b> _
Donateo 2003: ILR rec	0.5	0.083	2.4%	0.50 [0.34, 0.66]	
Farwell 2006: ILR rec	0.52	0.05	6.7%	0.52 [0.42, 0.62]	
Menozzi 2002: ILR rec	0.46	0.084	2.4%	0.46 [0.30, 0.62]	
Pezawas 2007: ILR rec	0.14	0.042	9.5%	0.14 [0.06, 0.22]	
Subtotal (95% CI)			30.8%	0.38 [0.33, 0.42]	◆
Heterogeneity: Chi <sup>2</sup> = 47.56	, ,	,	; l² = 89%		
Test for overall effect: Z = 1	6.26 (P < 0.00	001)			
Total (95% CI)			100.0%	0.41 [0.38, 0.43]	♦
	7 df 17 (D		1). 12 - 87	0/_	
Heterogeneity: Chi <sup>2</sup> = 129.8	7, ui = 17 (P <	0.0000	· 1), I <sup>_</sup> = 01	70	-1 -0.5 0 0.5

Transient loss of consciousness: full guideline DRAFT (January 2010) Page 25 of 46

### 1.4.2 Subgroup analysis by frequency for IER: populations combined

The GDG had pre-specified separating the studies into highly frequent, frequent and infrequent, but all the studies for IER fell into the infrequent category. Firstly, we carried out an analysis, ordering the studies by frequency of previous TLoC and then carried out a post-hoc subgroup analysis, splitting the studies into three categories, 1 to 5 events per year, 5 to 10 and more than 10 events per year. There is some indication that the frequency is important and reduces the heterogeneity.

				proportion		pro	portion
Study or Subgroup	proportion	SE	Weight	IV, Fixed, 95% CI		IV, Fix	ced, 95% Cl
Menozzi 2002: ILR rec	0.46	0.084		0.46 [0.30, 0.62]			- <b>-</b>
Donateo 2003: ILR rec	0.5	0.083		0.50 [0.34, 0.66]			
Farwell 2006: ILR rec	0.52	0.05		0.52 [0.42, 0.62]			+
Brignole 2001: ILR rec	0.54	0.069		0.54 [0.40, 0.68]			
Lombardi 2005: ILR rec	0.41	0.084		0.41 [0.25, 0.57]			- <b></b>
Krahn 2004: ILR rec	0.5	0.065		0.50 [0.37, 0.63]			
Moya 2001: ILR rec	0.66	0.052		0.66 [0.56, 0.76]			+
Krahn 2001: ILR rec	0.4	0.089		0.40 [0.23, 0.57]			
Boersma 2004: ILR rec	0.47	0.076		0.47 [0.32, 0.62]			
Garcia-Civera 05: ILR rec	0.6	0.054		0.60 [0.49, 0.71]			-
Krahn 1999: ILR rec	0.32	0.05		0.32 [0.22, 0.42]			-
Nierop 2000: ILR rec	0.31	0.078		0.31 [0.16, 0.46]			
Seidl 2000: ILR rec	0.38	0.042		0.38 [0.30, 0.46]			+
Krahn 1998: ILR rec	0.13	0.068		0.13 [-0.00, 0.26]			<b>⊢</b> ŧ−
					⊢ -1	-0.5	0 0.5 1

*1.4.2.1* No TLoC during monitoring, IER, studies ordered by frequency

				proportion	proportion
Study or Subgroup	proportion	SE	Weight	IV, Fixed, 95% CI	
10.60.1 freq =1-5/year				, ,	
Boersma 2004: ILR rec	0.47	0.076	4.8%	0.47 [0.32, 0.62]	
Brignole 2001: ILR rec	0.54	0.069	5.8%	0.54 [0.40, 0.68]	_ <del></del>
Donateo 2003: ILR rec	0.5	0.083	4.0%	0.50 [0.34, 0.66]	
Farwell 2006: ILR rec	0.52	0.05	11.0%	0.52 [0.42, 0.62]	
Garcia-Civera 05: ILR rec	0.6	0.054	9.4%	0.60 [0.49, 0.71]	
Krahn 2001: ILR rec	0.4	0.089	3.5%	0.40 [0.23, 0.57]	
Krahn 2004: ILR rec	0.5	0.065	6.5%	0.50 [0.37, 0.63]	
Lombardi 2005: ILR rec	0.41	0.084	3.9%	0.41 [0.25, 0.57]	
Menozzi 2002: ILR rec	0.46	0.084	3.9%	0.46 [0.30, 0.62]	
Moya 2001: ILR rec	0.66	0.052	10.2%	0.66 [0.56, 0.76]	
Subtotal (95% CI)			62.9%	0.53 [0.49, 0.57]	♦
Heterogeneity: Chi <sup>2</sup> = 13.82	, df = 9 (P = 0.	13); l² =	= 35%		
Test for overall effect: Z = 2	5.45 (P < 0.00	001)			
10.60.2 frequency >5 per y	/ear				
Krahn 1998: ILR rec	0.13	0.068	5.9%	0.13 [-0.00, 0.26]	
Krahn 1999: ILR rec	0.32	0.05	11.0%	0.32 [0.22, 0.42]	
Nierop 2000: ILR rec	0.31	0.078	4.5%	0.31 [0.16, 0.46]	
Seidl 2000: ILR rec	0.38	0.042	15.6%	0.38 [0.30, 0.46]	
Subtotal (95% CI)			37.1%	0.31 [0.26, 0.37]	•
Heterogeneity: Chi <sup>2</sup> = 9.81,	df = 3 (P = 0.0	2); l² =	69%		
Test for overall effect: Z = 1	1.51 (P < 0.00	001)			
Total (95% CI)			100.0%	0.45 [0.42, 0.48]	•
Heterogeneity: Chi <sup>2</sup> = 64.17	. df = 13 (P < (	0.00001	):   <sup>2</sup> = 80%		
Test for overall effect: $Z = 2$			,,. 20,	-	-1 -0.5 0 0.5 1
Test for subgroup difference	•		1 (P < 0.00	0001). l² = 97.5%	
		,		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	

### 1.4.2.2 Post hoc subgroup analysis by frequency of TLoC

### 1.4.3 Sensitivity analysis taking into consideration frequency of previous TLoC – IER and EER

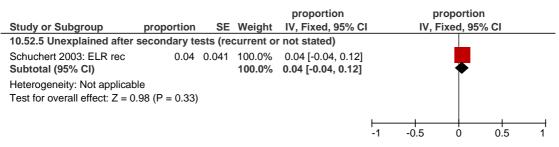
All the studies that reported the frequency of previous TLoC fall into the 'infrequent' category (i.e. less than 24 events per year). We carried out a sensitivity analysis, including only the studies that reported more than 5 events per year, this restricts the analyses to the following studies: Boersma (2004), Deharo (2006), Krahn (1999), Nierop (2000), Schuchert (2003) and Seidl (2000).

### *1.4.3.1* External event recorder: no TLoC during monitoring

Study or Subgroup	proportion	SE	Weight	proportion IV, Fixed, 95% C	I		oportio ixed, 95		
10.51.5 Unexplained after	secondary tests	(red	current o	r not stated)					_
Schuchert 2003: ELR rec Subtotal (95% CI)	0.67 0.0	96	100.0% 1 <b>00.0%</b>	0.67 [0.48, 0.86] <b>0.67 [0.48, 0.86]</b>					<b>→</b>
Heterogeneity: Not applical Test for overall effect: $Z = 6$									
					⊢ -1	-0.5	0	0.5	

Test for subgroup differences: Not applicable

#### 1.4.3.2 External event recorder: arrhythmia during TLoC



Test for subgroup differences: Not applicable

Study or Subgroup	proportion	SE	Weight	proportion IV, Fixed, 95% Cl	proportion IV, Fixed, 95% CI
10.53.1 suspected arrhyt					
Krahn 1999: ILR rec Subtotal (95% CI)	0.32		100.0% 1 <b>00.0</b> %	0.32 [0.22, 0.42] <b>0.32 [0.22, 0.42]</b>	
Heterogeneity: Not applica	able				
Test for overall effect: Z =	6.40 (P < 0.0	0001)			
10.53.3 suspected neura	lly mediated	synco	pe (recurr	ent)	
Deharo 2006: ILR rec Subtotal (95% CI)	0.52	0.1	100.0% 1 <b>00.0%</b>	0.52 [0.32, 0.72] 0.52 [0.32, 0.72]	
Heterogeneity: Not applica	able				
Test for overall effect: Z =	5.20 (P < 0.00	0001)			
40 F0 4				- ( - ( - 1)	
10.53.4 unexplained afte	r Intial tests (	recurre	ent or not	,	
Subtotal (95% CI)				Not estimable	
Heterogeneity: Not applica					
Test for overall effect: Not	applicable				
10.53.5 Unexplained afte	r secondary	tests w	ith recur	rent syncope	
Boersma 2004: ILR rec	0.44	0.076	18.0%	0.44 [0.29, 0.59]	<b></b>
Nierop 2000: ILR rec	0.31	0.078	17.1%	0.31 [0.16, 0.46]	│ <b></b>
	0.31	0.04	64.9%	0.31 [0.23, 0.39]	📕
Seidl 2000: ILR rec			100.0%	0.33 [0.27, 0.40]	
Seidi 2000: ILR rec Subtotal (95% CI) Heterogeneity: Chi <sup>2</sup> = 2.40	), df = 2 (P = 0	).30); l²		. / .	, i i i i i i i i i i i i i i i i i i i
Subtotal (95% CI)		<i>,</i> .			
Subtotal (95% CI) Heterogeneity: Chi <sup>2</sup> = 2.40		<i>,</i> .		. / .	
Subtotal (95% CI) Heterogeneity: Chi <sup>2</sup> = 2.40		<i>,</i> .			-1 -0.5 0 0.5 1

### 1.4.3.3 Implantable event recorder: no TLoC during monitoring

Test for subgroup differences:  $Chi^2 = 3.43$ , df = 2 (P = 0.18), I<sup>2</sup> = 41.7%

mia with re 0.25 le .32 (P < 0.0 y mediated 0.28	0.047	100.0% 100.0%	0.25 [0.16, 0.34] 0.25 [0.16, 0.34]		
le .32 (P < 0.0 <b>y mediated</b>	0001)	100.0%			
.32 (P < 0.0 <b>y mediated</b>	,				
y mediated	,				
	synco				
0.28		pe (recurr	ent)		
	0.09	100.0% 1 <b>00.0%</b>	0.28 [0.10, 0.46] <b>0.28 [0.10, 0.46]</b>		
le					
.11 (P = 0.0	02)				
nitial tests	(recuri	rent or no	,		
			Not estimable		
le					
pplicable					
secondary	tests w	ith recuri	rent syncope		
0.26	0.067	19.8%	0.26 [0.13, 0.39]		<b>−−</b>
0.29	0.076	15.4%	0.29 [0.14, 0.44]		
0.24	0.037	64.9%	0.24 [0.17, 0.31]		
		100.0%	0.25 [0.19, 0.31]		•
df = 2 (P = (	0.83); l²	= 0%			
.45 (P < 0.0	0001)				
	,				
					0 0.5
	11 ( $P = 0.0$ initial tests le pplicable secondary 0.26 0.29 0.24 df = 2 ( $P = 1$ 45 ( $P < 0.0$	.11 (P = 0.002) initial tests (recurr le pplicable secondary tests w 0.26 0.067 0.29 0.076 0.24 0.037	11 (P = 0.002) initial tests (recurrent or no le pplicable secondary tests with recurr $0.26 \ 0.067 \ 19.8\%$ $0.29 \ 0.076 \ 15.4\%$ $0.24 \ 0.037 \ 64.9\%$ 100.0% df = 2 (P = 0.83); I <sup>2</sup> = 0% .45 (P < 0.00001)	11 (P = 0.002) initial tests (recurrent or not stated) Not estimable le pplicable secondary tests with recurrent syncope 0.26 0.067 19.8% 0.26 [0.13, 0.39] 0.29 0.076 15.4% 0.29 [0.14, 0.44] 0.24 0.037 64.9% 0.24 [0.17, 0.31] 100.0% 0.25 [0.19, 0.31] df = 2 (P = 0.83); l <sup>2</sup> = 0% .45 (P < 0.00001)	11 (P = 0.002) initial tests (recurrent or not stated) Not estimable le pplicable secondary tests with recurrent syncope 0.26 0.067 19.8% 0.26 [0.13, 0.39] 0.29 0.076 15.4% 0.29 [0.14, 0.44] 0.24 0.037 64.9% 0.24 [0.17, 0.31] 100.0% 0.25 [0.19, 0.31] df = 2 (P = 0.83); l <sup>2</sup> = 0%

### 1.4.3.4 Implantable event recorder: Arrhythmia during TLoC

Test for subgroup differences:  $Chi^2 = 0.10$ , df = 2 (P = 0.95), l<sup>2</sup> = 0%

## 1.4.4 Subgroup analysis by the product of duration x frequency for the outcome, no TLoC during monitoring

Within the subgroup, studies are ordered by increasing duration x frequency product in the following pre-specified subgroups: below 0.1, 0.1 to 0.99, 1 to 10 and over 10 (not shown). However, all but one of the studies were in the 1 to 10 category. We then divided the 1-10 group studies post-hoc into three subgroups: 1 to 2.99; 3 to 5.99 and 6 and over. The product does not seem to be particularly important for explaining heterogeneity.

### 1.4.4.1 Pre-specificied subgroup analysis

		05		proportion	proportion
Study or Subgroup	proportion	SE	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
10.57.1 Duration x freq =0.		0.000	100.00/	0 5 4 50 40 0 001	
Brignole 2001: ILR rec Subtotal (95% CI)	0.54	0.069	100.0% 1 <b>00.0%</b>	0.54 [0.40, 0.68] 0.54 [0.40, 0.68]	
( <i>,</i>			100.076	0.54 [0.40, 0.00]	· · · · · · · · · · · · · · · · · · ·
Heterogeneity: Not applicable		04)			
Test for overall effect: $Z = 7$ .	83 (P < 0.000	01)			
10.57.2 Duration x freq =1-	10				
Lombardi 2005: ILR rec	0.41	0.084	4.1%	0.41 [0.25, 0.57]	
Menozzi 2002: ILR rec	0.46	0.084	4.1%	0.46 [0.30, 0.62]	
Moya 2001: ILR rec	0.66	0.052	10.8%	0.66 [0.56, 0.76]	
Krahn 2004: ILR rec	0.5	0.065	6.9%	0.50 [0.37, 0.63]	
Farwell 2006: ILR rec	0.52	0.05	11.7%	0.52 [0.42, 0.62]	
Donateo 2003: ILR rec	0.5	0.083	4.2%	0.50 [0.34, 0.66]	
Krahn 2001: ILR rec	0.4	0.089	3.7%	0.40 [0.23, 0.57]	
Garcia-Civera 05: ILR rec	0.6	0.054	10.0%	0.60 [0.49, 0.71]	
Krahn 1998: ILR rec	0.13	0.068	6.3%	0.13 [-0.00, 0.26]	
Boersma 2004: ILR rec	0.47	0.076	5.1%	0.47 [0.32, 0.62]	
Krahn 1999: ILR rec	0.32	0.05	11.7%	0.32 [0.22, 0.42]	
Nierop 2000: ILR rec	0.31	0.078	4.8%	0.31 [0.16, 0.46]	— <del>.</del>
Seidl 2000: ILR rec	0.38	0.042	16.6%	0.38 [0.30, 0.46]	
Subtotal (95% CI)			100.0%	0.45 [0.41, 0.48]	♦
Heterogeneity: Chi <sup>2</sup> = 62.41,	df = 12 (P <	0.00001	); l <sup>2</sup> = 81%	6	
Test for overall effect: Z = 26	6.08 (P < 0.00	001)			
10.57.3 Duration x freq not	stated				
Brignole 2005: ILR rec		0.049	0.0%	0.46 [0.36, 0.56]	
Pezawas 2007: ILR rec		0.040	0.0%	0.14 [0.06, 0.22]	
Pierre 2008: ILR rec		0.051	0.0%	0.55 [0.45, 0.65]	
Krahn 2002: ILR rec		0.032	0.0%	0.31 [0.25, 0.37]	
Subtotal (95% CI)	0.01	0.00L	0.070	Not estimable	
Heterogeneity: $Chi^2 = 0.00$ , o	df = 3 (P < 0.0	0001):	l² = 0%		
Test for overall effect: $Z = 16$	•	<i>,</i> · ·			
		,			
					-1 -0.5 0 0.5

### 1.4.4.2 Post-hoc subgroup analysis

				proportion	proportion
Study or Subgroup	proportion	SE	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
10.58.1 Duration x freq =0					
Brignole 2001: ILR rec	0.54	0.069	5.8%	0.54 [0.40, 0.68]	
Subtotal (95% CI)			5.8%	0.54 [0.40, 0.68]	
Heterogeneity: Not applicat					
Test for overall effect: Z = 7	.83 (P < 0.000	01)			
10.58.2 Duration x freq 1-2	2.99				
Krahn 2001: ILR rec	0.4	0.089	3.5%	0.40 [0.23, 0.57]	
Krahn 1998: ILR rec	0.13	0.068	5.9%	0.13 [-0.00, 0.26]	
Garcia-Civera 05: ILR rec	0.6	0.054	9.4%	0.60 [0.49, 0.71]	
Farwell 2006: ILR rec	0.52	0.05	11.0%	0.52 [0.42, 0.62]	
Donateo 2003: ILR rec	0.5	0.083	4.0%	0.50 [0.34, 0.66]	
Krahn 2004: ILR rec	0.5	0.065	6.5%	0.50 [0.37, 0.63]	
ombardi 2005: ILR rec	0.41	0.084	3.9%	0.41 [0.25, 0.57]	
/lenozzi 2002: ILR rec	0.46	0.084	3.9%	0.46 [0.30, 0.62]	
Moya 2001: ILR rec	0.66	0.052	10.2%	0.66 [0.56, 0.76]	
Subtotal (95% CI)			58.3%	0.50 [0.45, 0.54]	♦
Heterogeneity: Chi <sup>2</sup> = 45.26	6, df = 8 (P < 0	.00001)	; l² = 82%		
Fest for overall effect: Z = 2	2.82 (P < 0.00	001)			
0.58.3 Duration x freq =3	-6				
(rahn 1999: ILR rec	0.32	0.05	11.0%	0.32 [0.22, 0.42]	
Boersma 2004: ILR rec	0.47	0.076	4.8%	0.47 [0.32, 0.62]	
Seidl 2000: ILR rec	0.38	0.042	15.6%	0.38 [0.30, 0.46]	
Nierop 2000: ILR rec	0.31	0.078	4.5%	0.31 [0.16, 0.46]	
Subtotal (95% CI)			35.9%	0.36 [0.31, 0.42]	•
Heterogeneity: $Chi^2 = 3.34$ , Fest for overall effect: $Z = 1$	``		10%		
$\frac{1}{2} = 1$	5.17 (1 < 0.00	001)			
Fotal (95% CI)			100.0%	0.45 [0.42, 0.48]	
Heterogeneity: Chi <sup>2</sup> = 64.17			); l <sup>2</sup> = 80%	0	-1 -0.5 0 0.5
<pre>Fest for overall effect: Z = 2</pre>	``	,			
Fest for subgroup difference	es: Chi² = 15.5	7, df = 2	2 (P = 0.00	004), l² = 87.2%	

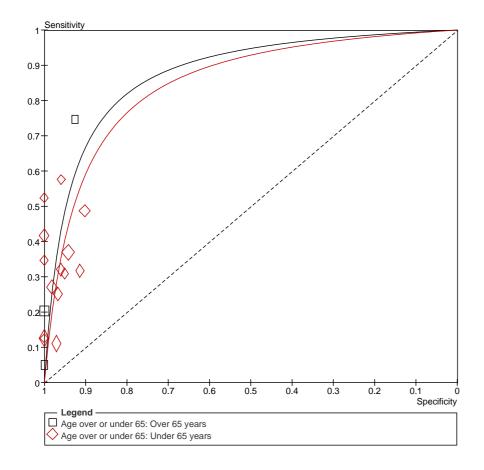
### 2 Tilt test additional analyses

### 2.1 HUT-passive

## 2.1.1 Age over or under 65 years (sorted by mean age in studies ('age continuous'); youngest to oldest)

2.1.1.1 Forest plot of sensitivity and specificity (ordered by ag
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Study	TP	FP	FN	TN	Age over or under 65	age continuous	Sensitivity	Specificity	Sensitivity	Specificity
Hermosillo 2000	50	0	70	50	Under 65 years	33.0	0.42 [0.33, 0.51]	1.00 [0.93, 1.00]		-
Oraii 1999	20	1	45	19	Under 65 years	34.0	0.31 [0.20, 0.43]	0.95 [0.75, 1.00]		
Lazzeri 2000	23	0	21	20	Under 65 years	35.0	0.52 [0.37, 0.68]	1.00 [0.83, 1.00]		
Gielerak 2002	23	1	17	23	Under 65 years	35.0	0.57 [0.41, 0.73]	0.96 [0.79, 1.00]		
Morillo 1995	30	1	90	29	Under 65 years	40.0	0.25 [0.18, 0.34]	0.97 [0.83, 1.00]	-	
Theodorakis 2000	19	0	36	22	Under 65 years	40.0	0.35 [0.22, 0.49]	1.00 [0.85, 1.00]		
Theodorakis 2003	34	1	92	53	Under 65 years	41.0	0.27 [0.19, 0.36]	0.98 [0.90, 1.00]	+	-
Del Rosso 2002 under 65s	28	0	196	35	Under 65 years	41.0	0.13 [0.08, 0.18]	1.00 [0.90, 1.00]	+	
Aerts 1997	4	0	28	20	Under 65 years	43.0	0.13 [0.04, 0.29]	1.00 [0.83, 1.00]	-	
Lagi 1992	35	7	37	64	Under 65 years	47.0	0.49 [0.37, 0.61]	0.90 [0.81, 0.96]		-
Del Rosso 1998	22	1	180	33	Under 65 years	49.0	0.11 [0.07, 0.16]	0.97 [0.85, 1.00]	+	
Oribe 1997	74	6	127	96	Under 65 years	51.0	0.37 [0.30, 0.44]	0.94 [0.88, 0.98]		-
Shen 1999	35	2	76	21	Under 65 years	55.0	0.32 [0.23, 0.41]	0.91 [0.72, 0.99]	-8-	
Brignole 1991	32	1	68	24	Under 65 years	60.0	0.32 [0.23, 0.42]	0.96 [0.80, 1.00]		
Fitzpatrick 1991	53	2	18	25	Over 65 years	69.0	0.75 [0.63, 0.84]	0.93 [0.76, 0.99]		
Mussi 2001	26	0	102	101	Over 65 years	72.0	0.20 [0.14, 0.28]	1.00 [0.96, 1.00]	-	-
Del Rosso 2002 over 65s	5	0	95	29	Over 65 years	73.0	0.05 [0.02, 0.11]	1.00 [0.88, 1.00]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1



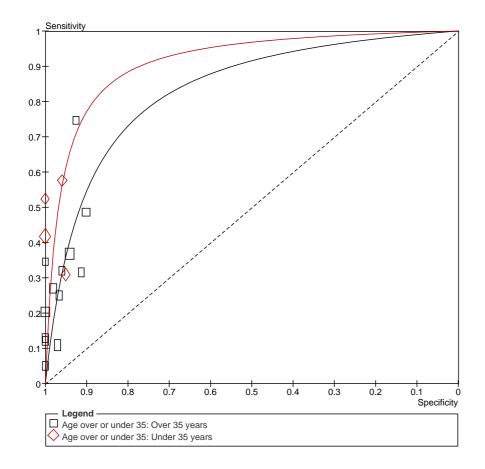
2.1.1.2 ROC curve (over versus under 65 years)

### 2.1.2 Age over or under 35 years

### 2.1.2.1 Forest plot (ordered by mean age)

Study	ΤР	FP	FN	ΤN	age continuous	Age over or under 35	Sensitivity	Specificity	Sensitivity	Specificity
Hermosillo 2000	50	0	70	50	33.0	Under 35 years	0.42 [0.33, 0.51]	1.00 [0.93, 1.00]		-
Oraii 1999	20	1	45	19	34.0	Under 35 years	0.31 [0.20, 0.43]	0.95 [0.75, 1.00]		
Lazzeri 2000	23	0	21	20	35.0	Under 35 years	0.52 [0.37, 0.68]	1.00 [0.83, 1.00]		
Gielerak 2002	23	1	17	23	35.0	Under 35 years	0.57 [0.41, 0.73]	0.96 [0.79, 1.00]		
Morillo 1995	30	1	90	29	40.0	Over 35 years	0.25 [0.18, 0.34]	0.97 [0.83, 1.00]		
Theodorakis 2000	19	0	36	22	40.0	Over 35 years	0.35 [0.22, 0.49]	1.00 [0.85, 1.00]		
Theodorakis 2003	34	1	92	53	41.0	Over 35 years	0.27 [0.19, 0.36]	0.98 [0.90, 1.00]		-
Del Rosso 2002 under 65s	28	0	196	35	41.0	Over 35 years	0.13 [0.08, 0.18]	1.00 [0.90, 1.00]	+	
Aerts 1997	4	0	28	20	43.0	Over 35 years	0.13 [0.04, 0.29]	1.00 [0.83, 1.00]		
Lagi 1992	35	7	37	64	47.0	Over 35 years	0.49 [0.37, 0.61]	0.90 [0.81, 0.96]		
Del Rosso 1998	22	1	180	33	49.0	Over 35 years	0.11 [0.07, 0.16]	0.97 [0.85, 1.00]	<b>*</b>	
Oribe 1997	74	6	127	96	51.0	Over 35 years	0.37 [0.30, 0.44]	0.94 [0.88, 0.98]	-	-
Shen 1999	35	2	76	21	55.0	Over 35 years	0.32 [0.23, 0.41]	0.91 [0.72, 0.99]		
Brignole 1991	32	1	68	24	60.0	Over 35 years	0.32 [0.23, 0.42]	0.96 [0.80, 1.00]		
Fitzpatrick 1991	53	2	18	25	69.0	Over 35 years	0.75 [0.63, 0.84]	0.93 [0.76, 0.99]		
Mussi 2001	26	0	102	101	72.0	Over 35 years	0.20 [0.14, 0.28]	1.00 [0.96, 1.00]		•
Del Rosso 2002 over 65s	5	0	95	29	73.0	Over 35 years	0.05 [0.02, 0.11]	1.00 [0.88, 1.00]	0 0.2 0.4 0.6 0.8 1 0	0.2 0.4 0.6 0.8 1

Transient loss of consciousness: full guideline DRAFT (January 2010) Page 34 of 46

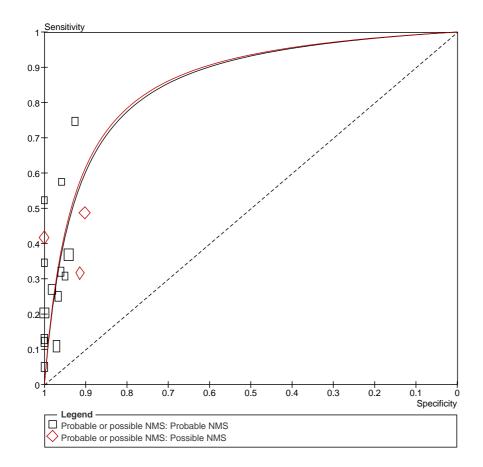


2.1.2.2 ROC curve (over versus under 35 years)

### 2.1.3 Subgroups for possible/probable NMS

2.1.3.1 Forest plot (probable versus possible NMS)

Study	ΤР	FP	FN	ΤN	Probable or possible NMS	Sensitivity	Specificity	Sensitivity	Specificity
Oribe 1997	74	6	127	96	•	0.37 [0.30, 0.44]	0 94 [0 88 0 98]	- · ·	· · · · · -
Del Rosso 1998	22	1	180	33		0.11 [0.07, 0.16]		+	
Lazzeri 2000	23	0	21	20		0.52 [0.37, 0.68]			
Morillo 1995	30	1	90	29		0.25 [0.18, 0.34]			
Theodorakis 2003	34	1	92	53		0.27 [0.19, 0.36]			-
Brignole 1991	32	1	68	24		0.32 [0.23, 0.42]			
Gielerak 2002	23	1	17	23		0.57 [0.41, 0.73]			
Fitzpatrick 1991	53	2	18	25	Probable NMS	0.75 [0.63, 0.84]	0.93 [0.76, 0.99]		
Theodorakis 2000	19	0	36	22		0.35 [0.22, 0.49]			
Aerts 1997	4	0	28	20	Probable NMS	0.13 [0.04, 0.29]	1.00 [0.83, 1.00]		
Mussi 2001	26	0	102	101	Probable NMS	0.20 [0.14, 0.28]	1.00 [0.96, 1.00]		•
Del Rosso 2002 under 65s	28	0	196	35	Probable NMS	0.13 [0.08, 0.18]	1.00 [0.90, 1.00]	•	
Oraii 1999	20	1	45	19	Probable NMS	0.31 [0.20, 0.43]	0.95 [0.75, 1.00]		
Del Rosso 2002 over 65s	5	0	95	29	Probable NMS	0.05 [0.02, 0.11]	1.00 [0.88, 1.00]	+	
Hermosillo 2000	50	0	70	50	Possible NMS	0.42 [0.33, 0.51]	1.00 [0.93, 1.00]	-	-
Shen 1999	35	2	76	21		0.32 [0.23, 0.41]			
Lagi 1992	35	7	37	64	Possible NMS	0.49 [0.37, 0.61]	0.90 [0.81, 0.96]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1



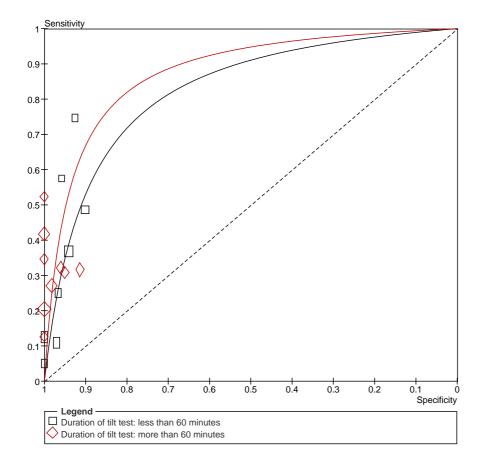
2.1.3.2 ROC curve (probable versus possible NMS)

## 2.1.4 Subgroup analysis by duration of tilt test (more or less than60 minutes – median value)

#### 2.1.4.1 Forest plot (ordered by duration of tilt)

Study	ΤР	FP	FN	ΤN	Duration of tilt test	Duration of test continuous	Sensitivity	Specificity	Sensitivity	Specificity
Lagi 1992	35	7	37	64	less than 60 minutes			0.90 [0.81, 0.96]	<b></b>	-
Morillo 1995	30	1	90	29	less than 60 minutes	45.0	0.25 [0.18, 0.34]			
Del Rosso 2002 under 65s	28	0	196	35	less than 60 minutes		0.13 [0.08, 0.18]		+	
Del Rosso 2002 over 65s	5	0	95	29	less than 60 minutes		0.05 [0.02, 0.11]		<b>.</b>	
Del Rosso 1998	22	1	180	33	less than 60 minutes		0.11 [0.07, 0.16]		+	
Oribe 1997	74	6	127	96	less than 60 minutes		0.37 [0.30, 0.44]		-	-
Gielerak 2002	23	1	17	23	less than 60 minutes		0.57 [0.41, 0.73]			
Fitzpatrick 1991	53	2	18	25	less than 60 minutes	60.0	0.75 [0.63, 0.84]	0.93 [0.76, 0.99]		
Theodorakis 2003	34	1	92	53	more than 60 minutes	65.0	0.27 [0.19, 0.36]	0.98 [0.90, 1.00]	+	
Theodorakis 2000	19	0	36	22	more than 60 minutes	65.0	0.35 [0.22, 0.49]	1.00 [0.85, 1.00]		
Brignole 1991	32	1	68	24	more than 60 minutes	70.0	0.32 [0.23, 0.42]	0.96 [0.80, 1.00]		
Aerts 1997	4	0	28	20	more than 60 minutes	70.0	0.13 [0.04, 0.29]	1.00 [0.83, 1.00]		
Lazzeri 2000	23	0	21	20	more than 60 minutes	75.0	0.52 [0.37, 0.68]	1.00 [0.83, 1.00]		
Mussi 2001	26	0	102	101	more than 60 minutes	75.0	0.20 [0.14, 0.28]	1.00 [0.96, 1.00]	+	-
Shen 1999	35	2	76	21	more than 60 minutes	90.0	0.32 [0.23, 0.41]	0.91 [0.72, 0.99]	-	
Oraii 1999	20	1	45	19	more than 60 minutes	100.0	0.31 [0.20, 0.43]	0.95 [0.75, 1.00]		
Hermosillo 2000	50	0	70	50	more than 60 minutes	122.0	0.42 [0.33, 0.51]	1.00 [0.93, 1.00]		0 0.2 0.4 0.6 0.8 1

Transient loss of consciousness: full guideline DRAFT (January 2010) Page 36 of 46



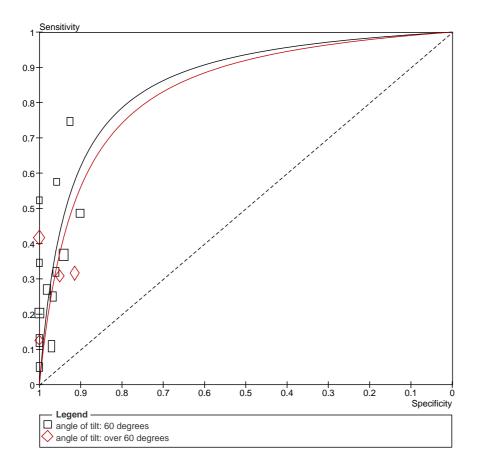
2.1.4.2 ROC curve (over versus under 60 minutes duration)

## 2.1.5 Subgroup analysis by angle of tilt (above and below 60 degrees – median value)

#### 2.1.5.1 Forest plot

Study	TP	FP	FN	ΤN	angle of tilt	Angle of tilt continuous	Sensitivity	Specificity	Sensitivity	Specificity
Oribe 1997	74	6	127	96	60 degrees	60.0	0.37 [0.30, 0.44]	0.94 [0.88, 0.98]	-	-
Del Rosso 1998	22	1	180	33	60 degrees	60.0	0.11 [0.07, 0.16]	0.97 [0.85, 1.00]	•	
Lazzeri 2000	23	0	21	20	60 degrees	60.0	0.52 [0.37, 0.68]	1.00 [0.83, 1.00]		
Morillo 1995	30	1	90	29	60 degrees	60.0	0.25 [0.18, 0.34]	0.97 [0.83, 1.00]		
Theodorakis 2003	34	1	92	53	60 degrees	60.0	0.27 [0.19, 0.36]	0.98 [0.90, 1.00]		-
Brignole 1991	32	1	68	24	60 degrees	60.0	0.32 [0.23, 0.42]	0.96 [0.80, 1.00]		
Gielerak 2002	23	1	17	23	60 degrees	60.0	0.57 [0.41, 0.73]	0.96 [0.79, 1.00]		
Fitzpatrick 1991	53	2	18	25	60 degrees	60.0	0.75 [0.63, 0.84]	0.93 [0.76, 0.99]		
Theodorakis 2000	19	0	36	22	60 degrees	60.0	0.35 [0.22, 0.49]	1.00 [0.85, 1.00]		
Mussi 2001	26	0	102	101	60 degrees	60.0	0.20 [0.14, 0.28]	1.00 [0.96, 1.00]		-
Del Rosso 2002 under 65s	28	0	196	35	60 degrees	60.0	0.13 [0.08, 0.18]	1.00 [0.90, 1.00]	<ul> <li>*</li> </ul>	
Lagi 1992	35	7	37	64	60 degrees	60.0	0.49 [0.37, 0.61]	0.90 [0.81, 0.96]		
Del Rosso 2002 over 65s	5	0	95	29	60 degrees	60.0	0.05 [0.02, 0.11]	1.00 [0.88, 1.00]	<b>•</b>	
Aerts 1997	4	0	28	20	over 60 degrees	70.0	0.13 [0.04, 0.29]	1.00 [0.83, 1.00]		
Hermosillo 2000	50	0	70	50	over 60 degrees	70.0	0.42 [0.33, 0.51]	1.00 [0.93, 1.00]	-	-
Shen 1999	35	2	76	21	over 60 degrees	70.0	0.32 [0.23, 0.41]	0.91 [0.72, 0.99]		
Oraii 1999	20	1	45	19	over 60 degrees	70.0	0.31 [0.20, 0.43]	0.95 [0.75, 1.00]		
					0		- / -	- / -	0 0.2 0.4 0.6 0.8 1	0.2 0.4 0.6 0.8 1

2.1.5.2 ROC curve

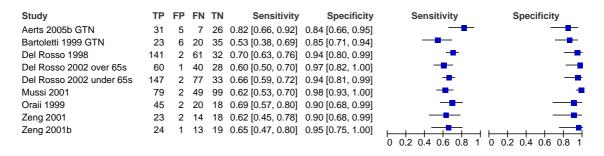


Transient loss of consciousness: full guideline DRAFT (January 2010) Page 38 of 46

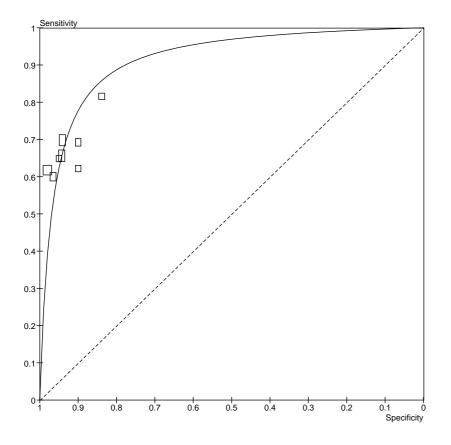
### 2.2 HUT-GTN

Nine studies used GTN stimulated HUT. There was high specificity for each study, and the studies were generally fairly homogeneous.

### 2.2.1.1 Forest plot of all HUT-GTN studies



2.2.1.2 ROC curve for all studies of HUT-GTN



### 2.3 HUT-IPN

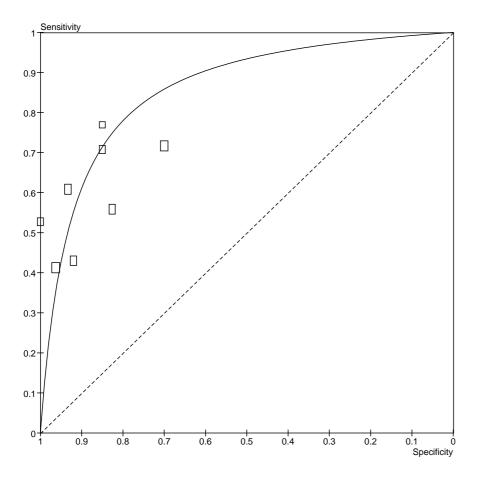
Eight studies used HUT-IPN; there was some heterogeneity. Subgroup analyses were conducted for age above and below 35 years (there were no studies with a mean age above 65 years); and probable or possible NMS.

### 2.3.1 All IPN studies

### 2.3.1.1 Forest plot of all IPN studies

Study	ΤР	FP	FN	ΤN	Sensitivity	Specificity	Sensitivity	Specificity
Brignole 1991	43	2	57	23	0.43 [0.33, 0.53]	0.92 [0.74, 0.99]		
Doi 2002exerciseunrelated	20	3	6	17	0.77 [0.56, 0.91]	0.85 [0.62, 0.97]		
Hermosillo 2000	86	15	34	35	0.72 [0.63, 0.80]	0.70 [0.55, 0.82]		
Morillo 1995	73	2	47	28	0.61 [0.52, 0.70]	0.93 [0.78, 0.99]		
Oraii IPN 1999	46	3	19	17	0.71 [0.58, 0.81]	0.85 [0.62, 0.97]		
Shen 1999	62	4	49	19	0.56 [0.46, 0.65]	0.83 [0.61, 0.95]		
Theodorakis 2000	29	0	26	22	0.53 [0.39, 0.66]	1.00 [0.85, 1.00]		
Theodorakis 2003	52	2	74	52	0.41 [0.33, 0.50]	0.96 [0.87, 1.00]		2 0.4 0.6 0.8 1

### 2.3.1.2 ROC curve for all HUT-IPN studies

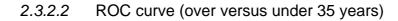


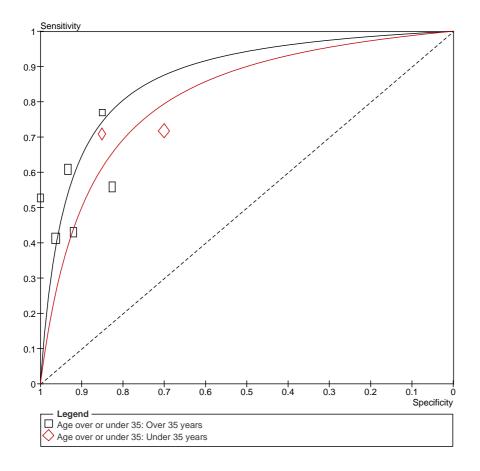
Transient loss of consciousness: full guideline DRAFT (January 2010) Page 40 of 46

### 2.3.2 Subgroup analysis by age over or under 35 years

### 2.3.2.1 Forest plot (ordered by mean age)

Study	ΤР	FP	FN	ΤN	age continuous	Age over or under 35	Sensitivity	Specificity	Sensitivity	Specificity
Hermosillo 2000	86	15	34	35	33.0	Under 35 years	0.72 [0.63, 0.80]	0.70 [0.55, 0.82]		
Oraii 1999	46	3	19	17	34.0	Under 35 years	0.71 [0.58, 0.81]	0.85 [0.62, 0.97]		
Morillo 1995	73	2	47	28	40.0	Over 35 years	0.61 [0.52, 0.70]	0.93 [0.78, 0.99]		
Theodorakis 2000	29	0	26	22	40.0	Over 35 years	0.53 [0.39, 0.66]	1.00 [0.85, 1.00]		
Theodorakis 2003	52	2	74	52	41.0	Over 35 years	0.41 [0.33, 0.50]	0.96 [0.87, 1.00]		
Doi 2002 ISO	20	3	6	17	46.0	Over 35 years	0.77 [0.56, 0.91]	0.85 [0.62, 0.97]		
Shen 1999	62	4	49	19	55.0	Over 35 years	0.56 [0.46, 0.65]	0.83 [0.61, 0.95]		
Brignole 1991	43	2	57	23	60.0	Over 35 years	0.43 [0.33, 0.53]	0.92 [0.74, 0.99]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

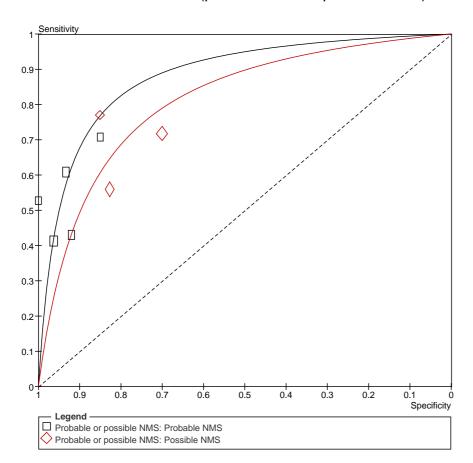




### 2.3.3 Subgroup analysis by probable or possible NM syncope

#### 2.3.3.1 Forest plot (probable versus possible NMS)

Study	TP	FP	FN	ΤN	Probable or possible NMS	Sensitivity	Specificity	Sensitivity	Specificity
Oraii 1999	46	3	19	17	Probable NMS	0.71 [0.58, 0.81]	0.85 [0.62, 0.97]		
Morillo 1995	73	2	47	28	Probable NMS	0.61 [0.52, 0.70]	0.93 [0.78, 0.99]		
Theodorakis 2000	29	0	26	22	Probable NMS	0.53 [0.39, 0.66]	1.00 [0.85, 1.00]		
Theodorakis 2003	52	2	74	52	Probable NMS	0.41 [0.33, 0.50]	0.96 [0.87, 1.00]		
Brignole 1991	43	2	57	23	Probable NMS	0.43 [0.33, 0.53]	0.92 [0.74, 0.99]		
Hermosillo 2000	86	15	34	35	Possible NMS	0.72 [0.63, 0.80]	0.70 [0.55, 0.82]		<b></b>
Doi 2002 ISO	20	3	6	17	Possible NMS	0.77 [0.56, 0.91]	0.85 [0.62, 0.97]		
Shen 1999	62	4	49	19	Possible NMS	0.56 [0.46, 0.65]	0.83 [0.61, 0.95]		0.2 0.4 0.6 0.8 1



2.3.3.2 ROC curve (probable versus possible NMS)

### 2.3.4 Subgroup analysis comparing duration of tilt over or under60 minutes

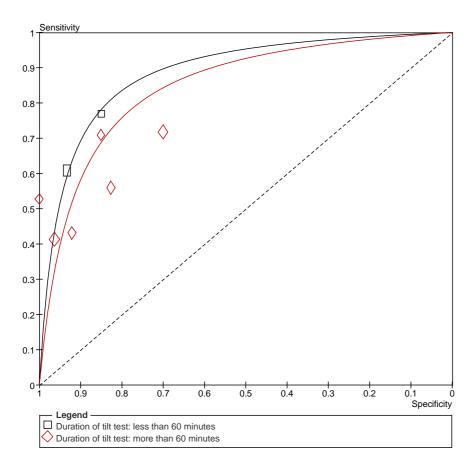
We note that there are only two studies with a duration of tilt below 60 minutes, so the subgroup analysis is not really meaningful.

Transient loss of consciousness: full guideline DRAFT (January 2010) Page 42 of 46

### 2.3.4.1 Forest plot (ordered by duration of tilt)

Study	ΤР	FP	FN	ΤN	Duration of tilt test	Duration of test continuous	Sensitivity	Specificity	Sensitivity	Specificity
Morillo 1995	73	2	47	28	less than 60 minutes	45.0	0.61 [0.52, 0.70]	0.93 [0.78, 0.99]		
Doi 2002 ISO	20	3	6	17	less than 60 minutes	45.0	0.77 [0.56, 0.91]	0.85 [0.62, 0.97]		
Theodorakis 2003	52	2	74	52	more than 60 minutes	65.0	0.41 [0.33, 0.50]	0.96 [0.87, 1.00]		
Theodorakis 2000	29	0	26	22	more than 60 minutes	65.0	0.53 [0.39, 0.66]	1.00 [0.85, 1.00]		
Brignole 1991	43	2	57	23	more than 60 minutes	70.0	0.43 [0.33, 0.53]	0.92 [0.74, 0.99]		
Shen 1999	62	4	49	19	more than 60 minutes	90.0	0.56 [0.46, 0.65]	0.83 [0.61, 0.95]		
Oraii 1999	46	3	19	17	more than 60 minutes	100.0	0.71 [0.58, 0.81]	0.85 [0.62, 0.97]		
Hermosillo 2000	86	15	34	35	more than 60 minutes	122.0	0.72 [0.63, 0.80]	0.70 [0.55, 0.82]		0.2 0.4 0.6 0.8 1

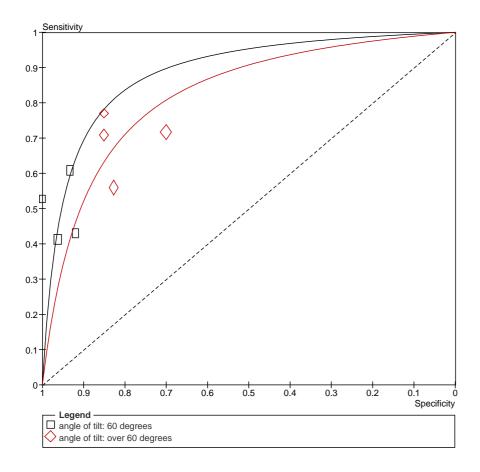
### 2.3.4.2 ROC curve (over versus under 60 min duration)



### 2.3.5 Subgroup analysis comparing angle of tilt over or under 60 degrees

#### 2.3.5.1 Forest plot (ordered by angle)

Study	TP	FP	FN	ΤN	angle of tilt	Angle of tilt continuous	Sensitivity	Specificity	Sensitivity	Specificity
Brignole 1991	43	2	57	23	60 degrees	60.0	0.43 [0.33, 0.53]	0.92 [0.74, 0.99]		
Theodorakis 2003	52	2	74	52	60 degrees	60.0	0.41 [0.33, 0.50]	0.96 [0.87, 1.00]	-8-	
Morillo 1995	73	2	47	28	60 degrees	60.0	0.61 [0.52, 0.70]	0.93 [0.78, 0.99]		
Theodorakis 2000	29	0	26	22	60 degrees	60.0	0.53 [0.39, 0.66]	1.00 [0.85, 1.00]		
Shen 1999	62	4	49	19	over 60 degrees	70.0	0.56 [0.46, 0.65]	0.83 [0.61, 0.95]		
Hermosillo 2000	86	15	34	35	over 60 degrees	70.0	0.72 [0.63, 0.80]	0.70 [0.55, 0.82]		
Oraii 1999	46	3	19	17	over 60 degrees	70.0	0.71 [0.58, 0.81]	0.85 [0.62, 0.97]		
Doi 2002 ISO	20	3	6	17	over 60 degrees	80.0	0.77 [0.56, 0.91]	0.85 [0.62, 0.97]		



2.3.5.2 ROC curve (over versus under 60 degrees tilt)

### **Appendix D5: Other**

# 1 Patient history for interactive diagnostic simulation

Name:	Sheila Jones
Date of Birth:	08.11.1951
Married:	37 years with two chidren, both left home
Employment:	PA to CEO of a non-governmental organisation

### Medical history:

**11 year history** of **chest pain/light headed feeling**, with this I can get a feeling of pressure actually in my chest. Sometimes this is associated with pain in my teeth/jaw. Lots of visits to the GP and A and E, nothing ever really established, **something that does worry my husband and I. Three previous blackouts**, never explained, just told not to worry about them.

**Previous cardiology** referral about three years ago; I was told I do not have a cardiac problem, and not to worry about the blackouts. **Having experienced them for over ten years, I am not going to die from them!** It might be gall stones, but nothing showed on an ultrasound.

Quite a few ECGs, never showed anything. BP has been high, on medication. Had a treadmill test which only showed something right at the end, which I understand is normal. I was told I might have too much acid, and was started on Lansoprazole for 3 months, but this was continued. Loads of blood tests, all inconclusive, and I guess over time I have become dissatisfied that no one can tell me what is wrong. I've lost count of how many doctors I have seen, it just keeps happening, and I suppose I have learnt to accept that this is just the way it is going to be.

### **Medication:**

Solifenacin	10mg morning (urinary condition)
Lansoprazole	15mg morning (heartburn)
Aspirin	75mg morning (high blood pressure)
Lisinopril	20mg morning and evening (high blood pressure)
Nicorandil	10mg morning and evening (smoking, 25 day for 34 years, gave up 5 years ago)
Simvastin	10mg morning (cholesterol)
Amitriptylene	1 – 3 before bed (help me sleep)

### What happened today:

Whilst reading/babysitting, had a very sharp pain in my chest which lasted 15 – 20 minutes. Pain straight across chest, just a flicker in my jaw. Started at 8.35pm and stopped at 9pm. Ambulance arrived at 9.05pm, my BP was 120/90. I felt slightly sick and about to faint. It was similar to last time. I wanted to drink but didn't feel I had energy to lift the cup, asked for a straw. Bill my husband called for an ambulance because I wasn't with it for about 10 minutes, he said I was unconscious for about 4 minutes. I had an ECG with the ambulance crew, he thought it might show 'ischaemia' and that I should go to hospital.