DAP39 ERRATUM

LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP (LRiG)

The clinical and cost effectiveness of lead-I electrocardiogram (ECG) devices for detecting atrial fibrillation using single-time point testing in primary care [DAP39]

Erratum

This Diagnostics Assessment Report was commissioned by the NIHR HTA Programme as project number 16/30/05

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UNIVERSITY OF LIVERPOOL | LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP

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Corrections to the Assessment Report

- Figures 21 to 23 have been corrected (page 81 to page 83)
- Justification for utility values used for people without AF presenting at primary care with symptoms indicative of AF (page 99)
- The cost of the initial GP consultation is now assumed to be equal in both diagnostic pathways and is not included in the model (page 101)
- VAT has been excluded from device costs. The revised costs are presented in the corrected pages 100 to 101.
- Correction of cost effectiveness results with VAT excluded from device costs. The revised results are presented in the corrected pages 108 to 127.

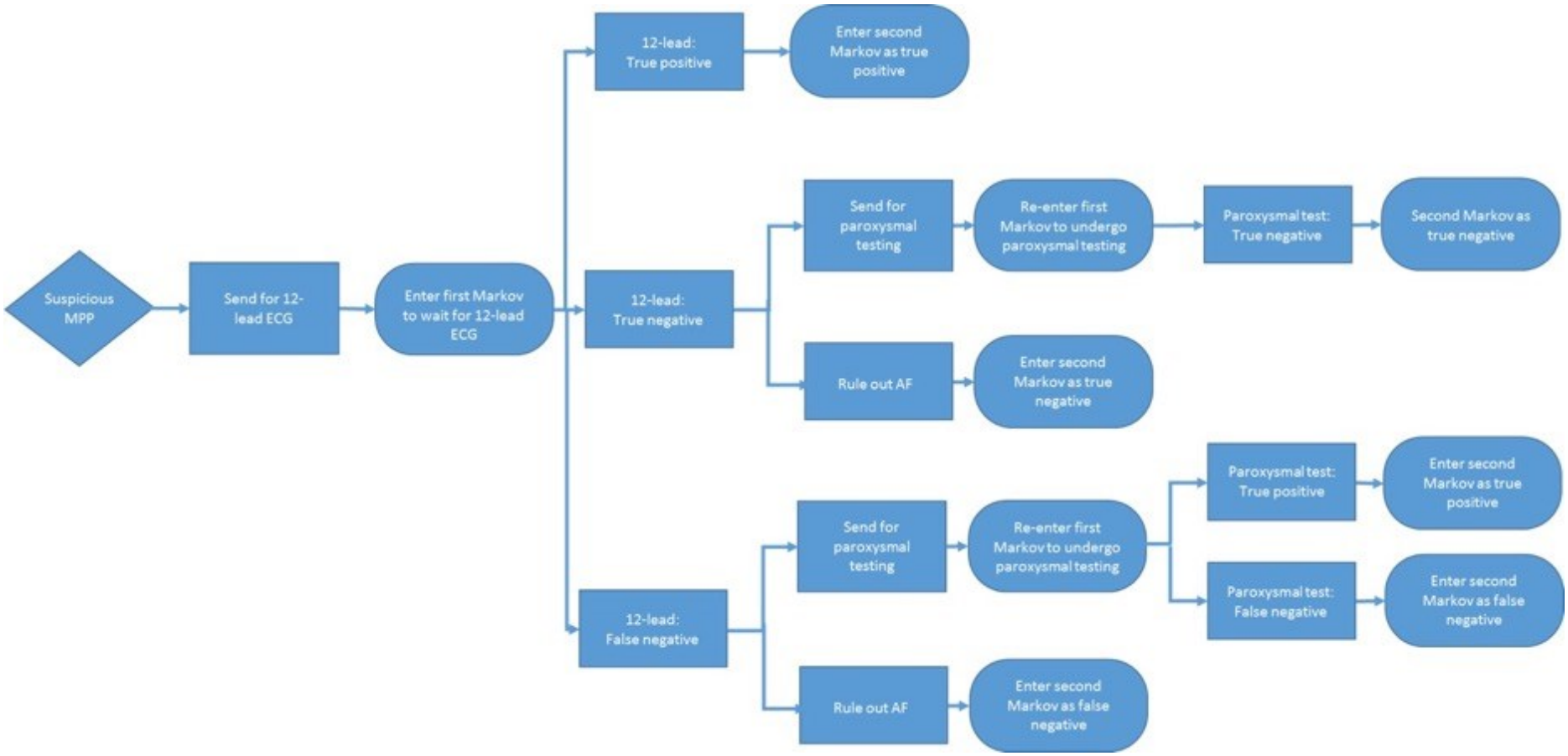

Figure 21 Diagnostic phase - decision tree: standard diagnostic pathway

AF=atrial fibrillation, ECG=electrocardiogram; MPP=manual pulse palpation

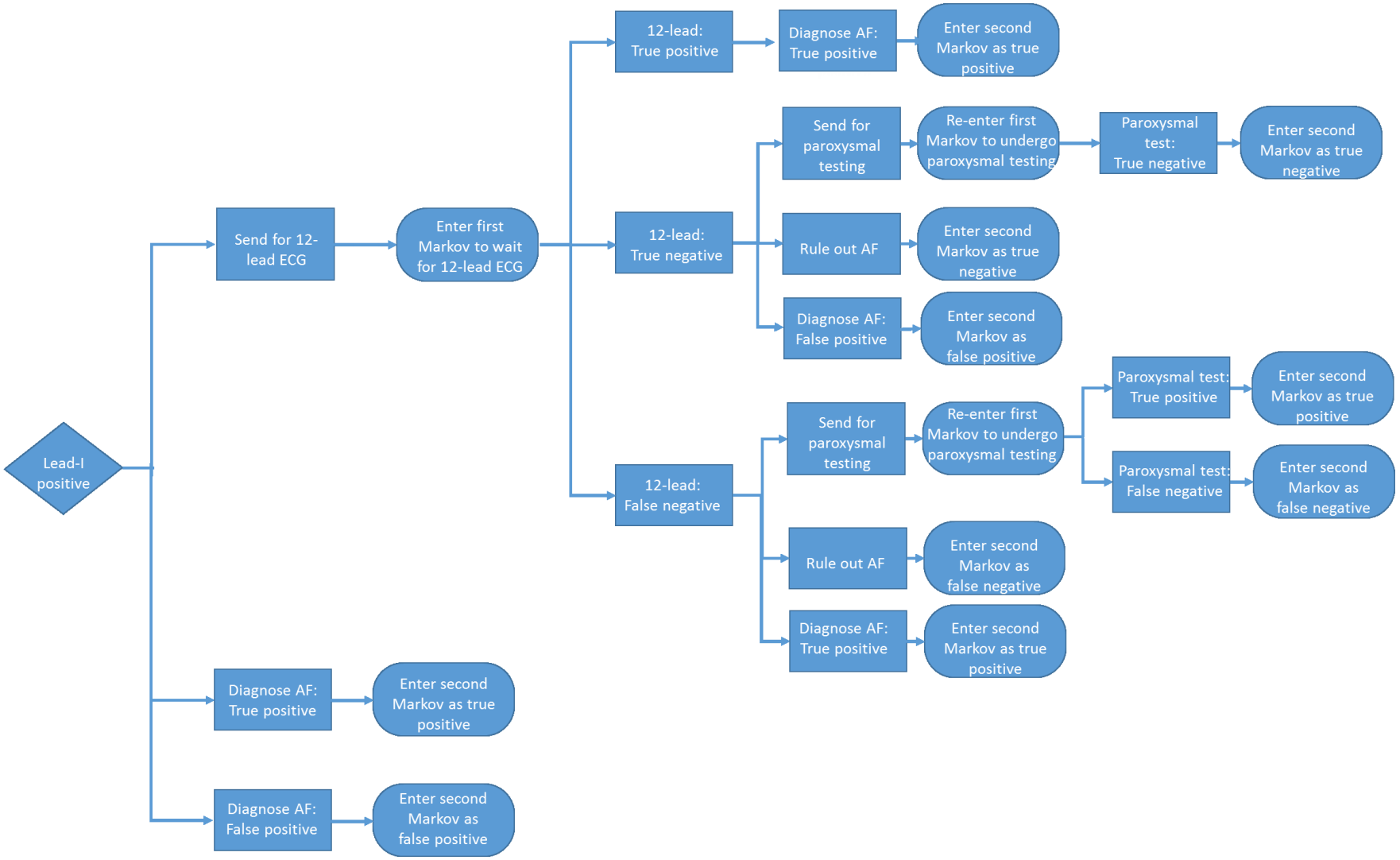

Figure 22 Diagnostic phase - decision tree: lead-I ECG diagnostic pathway (positive result)

AF=atrial fibrillation, ECG=electrocardiogram; MPP=manual pulse palpation

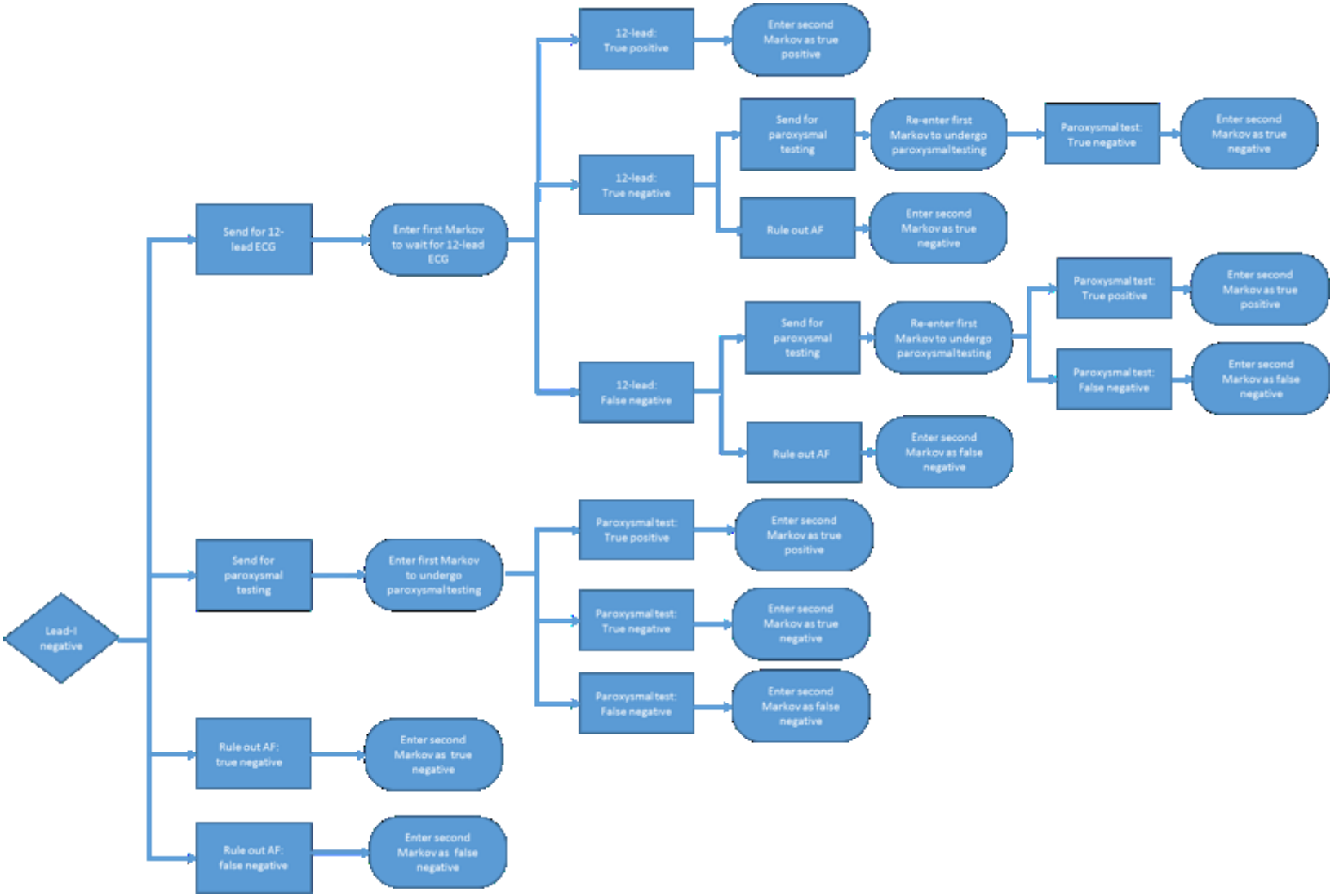

Figure 23 Diagnostic phase - decision tree: lead-I ECG diagnostic pathway (negative result)
AF=atrial fibrillation, ECG=electrocardiogram; MPP=manual pulse palpation

Utilities

State-specific utilities

Utility values have been estimated for symptomatic and asymptomatic populations with and without AF. Utility values are assumed to be the same for all populaions except those people with symptomatic (i.e. untreated) AF (Table 25).

Utility values for the symptomatic and asymptomatic AF-positive population are based on a study by Berg.[77] Berg provides the coefficients of two regression models fitted to the results of the EQ-5D-3L[90] questionnaire completed at baseline and follow-up as part of a large European survey of patients with AF. Mean age-specific utility values for symptomatic patients with AF were calculated using the baseline coefficients from the study by Berg[77] and adjusted for model age, sex ratio and symptom proportions. Mean age-specific utility values for asymptomatic patients with AF were calculated similarly using the coefficients at follow-up.

It was assumed that HRQoL for people without AF presenting at primary care with symptoms indicative of AF would be lower than for the general population, as these patients are still ill with symptoms assumed to be caused by atrial or ventricular ectopy. However, it was assumed that HRQoL would not be as low as for patients with symptomatic AF, since the recommended action for patients with atrial or ventricular ectopy (who are not showing immediate signs of a serious underlying cardiac cause or complication) is to reassure.[69] It was assumed that treatment for AF would not impact on HRQoL for patients without AF, as treatment is associated in the model with a reduction in symptoms of AF. Utility values for the AF-negative population (both treated and untreated) were assumed to be equal to the utility values for the treated AF population, whose AF is under control.

Table 25 Age- and sex-adjusted utility values (age 70) used in the base case model

	AF (95% CI)	No AF (95% CI)
Untreated (symptomatic)	0.665 (0.537 to 0.881)	0.744 (0.480 to 0.942)
Treated (asymptomatic)	0.744 (0.480 to 0.942)	0.744 (0.480 to 0.942)

AF=atrial fibrillation
Source: Adapted from Berg[77]

Cardiovascular and adverse event utility decrements

Lifetime utility decrements were assumed to apply to all ischaemic and haemorrhagic stroke events (Table 26). Utility decrements for stroke were taken from the study by Berg.[77] Utility decrements were applied at the time of the first IS or HS and no further decrements were applied for any subsequent IS or HS. Bleed and TIA events were assumed in the base case to be acute events that fully resolve and have no long-term impact on HRQoL.

Table 26 Utility decrements for acute adverse events

AE	Base case		Sensitivity analysis	
	Decrement	Source	Decrement or value	Source
Ischaemic stroke	-0.272 (95% CI: -0.345 to -0.198)	Berg 2010[77]	-0.59	Robinson 2001[92]
Haemorrhagic stroke	Assumed equal to ischaemic stroke		Value for ICH: -0.108 (95% CI: -0.135 to -0.082)	Berg 2010[77]

AE=adverse event; ICH=intracerebral haemorrhage; MI=myocardial infarction; SE=standard error; TIA=transient ischemic attack

Test costs

Annual lead-I ECG device unit costs

The annual cost of each lead-I ECG device was calculated as the unit cost per device (excluding VAT) divided across the expected life of the device in years plus any annual licence fee. No companies reported any maintenance costs associated with their devices, so these have not been included in the model. The cost of an accompanying smartphone or tablet for the Kardia Mobile device has not been included in the base case, as it was assumed that GPs would already have access to a smartphone or tablet. An average cost for a generic lead-I ECG device was calculated using the simple mean of the annual cost of individual devices. The annual cost of each index test included in the model is given in Table 27. Lead-I ECG devices are also likely to be used in populations other than the population with signs and symptoms of AF, which would decrease the unit cost per use of each device. The impact on cost effectiveness of not including the cost of the lead-I ECG device has been investigated in a sensitivity analysis.

Table 27 Annual costs of lead-I ECG devices and user licences

Device	Item	Lifetime cost (exc VAT)	Life	Annual cost
imPulse	Device	£175.00	2 years	£87.50
Kardia Mobile	Device	£82.50	5 years	£16.50
MyDiagnostick	Device	£450.00	5 years	£90.00
RhythmPadGP	Device	£1100.00	1 year	£1100.00
Zenicor ECG	Device and 36 month licence	£1980.00	10 years (device)	£613.27
	Extra 36 month licence	£1780.00		
Generic lead-I device				£381.45

Cost per lead-I ECG test

The cost per lead-I ECG test in the standard diagnostic pathway was zero, as it was assumed the only resource use in this context was the cost of the GP consultation. The cost of the initial GP consultation is assumed to be equal in both diagnostic pathways and is not included in the model. No extra time is included in the base case model to administer the lead-I ECG or to interpret the results during the initial consultation. It is assumed that review of the results of a

lead-I ECG test by a cardiologist would take 1 minute, in accordance with results from the study by Hobbs.[93] Assumptions about the time taken to administer and review a lead-I ECG test are varied in the sensitivity analysis.

The cost per lead-I ECG test was calculated as the annual cost per device divided by the number of patients in the eligible population per year plus any extra costs associated with each use of the device; the Zenicor-ECG device was the only index test included in the model to incur extra costs with each use, as the manufacturer recommends that the electrodes are replaced after 500 uses.

The costs per index test and cost of interpreting the lead-I ECG test included in the model are given in Table 28 and Table 29.

Table 28 Cost per lead-I ECG test

Device	Annual device cost (exc. VAT)	Number of patients tested per year	Peripherals cost per test	Unit cost per test*
imPulse	£87.50	54	0.00	£1.62
Kardia Mobile	£16.50	54	0.00	£0.31
MyDiagnostick	£90.00	54	0.00	£1.67
RhythmPadGP	£1,100.00	54	0.00	£20.42
Zenicor ECG	£613.27	54	0.02	£11.40
Generic lead-I device	£381.45	54	0.02	£7.10

*some costs may not calculate precisely due to rounding

Table 29 Cost per administration and interpretation of lead-I ECG test (base case)

	Unit cost	Source	Time taken	Cost per test
Algorithm	£0		0	£0
GP	£0		0	£0
Cardiologist	£107 per hour	PSSRU[94]	1 minute*	£1.78

*Based on data from Hobbs[93]

Cost per 12-lead ECG test

The cost per 12-lead ECG test varies depending on whether the test is carried out in primary or secondary care.

For 12-lead ECG tests carried out in primary care, the unit cost of a 12-lead ECG device is estimated to be £2,251 in line with the estimate used in NICE Guideline 45 (NG45)[95] inflated to 2017 prices using the Office for National Statistics Consumer Price Index (ONS CPI) for Medical Services [DKC3].[96] It is assumed in the model that a 12-lead ECG device may be used 1000 times before being replaced, in line with the assumption in NICE NG45,[95] which equates to £2.25 per use. The cost of disposables such as electrodes and gels is estimated to be £1.13 per use, uplifted to 2017 prices from the estimate used in NICE NG45.[95]

- Base Case 4: 12-lead ECG in secondary care, 14 days to 12-lead ECG

4.3.1 Base Case 1: 12-lead ECG in primary care, 2 days to 12-lead ECG

Costs and QALYs generated in Base Case 1 are shown in Table 37 and Table 38 respectively.

Table 37 Base Case 1: Total costs of annual number of symptomatic patients with positive MPP seen by a single GP'

Strategy	Lead-I ECG test	Treatment (NOACs & rate control)	CVEs and AEs	12-lead ECG	Paroxysmal testing (holter monitor)	Total costs
Standard pathway	£0	£90,630	£420,279	£536	£2,743	£514,187
Kardia Mobile	£26	£102,952	£409,881	£452	£2,240	£515,551
imPulse	£97	£116,317	£411,612	£454	£2,265	£530,745
MyDiagnostick	£100	£107,077	£411,358	£451	£2,247	£521,233
Generic lead-I device	£392	£103,746	£409,898	£452	£2,242	£516,730
Zenicor-ECG	£624	£104,938	£410,210	£452	£2,244	£518,468
RhythmPad*	£1,110	£100,358	£414,292	£446	£2,231	£518,436

AE=adverse events; CVE=cardiovascular events
*Algorithm interpretation

Table 38 Base Case 1: QALYs and patient outcomes

Strategy	IS	HS	TIA	False negatives	False positives	Bleeds	Total QALYs
Standard pathway	11.621	2.124	8.406	1.606	0.000	23.581	447.963
Kardia Mobile	11.452	1.996	8.359	0.144	1.379	23.751	449.249
imPulse	11.482	2.019	8.366	0.397	3.663	23.730	448.987
MyDiagnostick	11.478	2.015	8.365	0.361	2.155	23.720	449.024
Generic lead-I device	11.452	1.996	8.359	0.147	1.508	23.752	449.246
Zenicor-ECG	11.457	2.000	8.360	0.193	1.724	23.746	449.199
RhythmPad*	11.530	2.054	8.377	0.794	1.293	23.630	448.573

AE=adverse events; CVE=cardiovascular events; QALY=quality adjusted life year; IS=ischaemic stroke; HS=haemhorragic stroke; TIA=transient ischaemic accident
*Algorithm interpretation

Pairwise cost effectiveness results from the Base Case 1 analysis for each index test versus the standard diagnostic pathway are presented in Table 39 and incremental analysis are shown in Table 40.

Table 39 Base Case 1: Pairwise cost effectiveness analysis

Strategy	Costs	QALYs	Incremental costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£514,187	447.963			
Kardia Mobile	£515,551	449.249	£1,364	1.286	£1,060
imPulse	£530,745	448.987	£16,557	1.024	£16,165
MyDiagnostick	£521,233	449.024	£7,046	1.061	£6,638
Generic lead-I device	£516,730	449.246	£2,543	1.284	£1,981
Zenicor-ECG	£518,468	449.199	£4,281	1.236	£3,462
RhythmPad*	£518,436	448.573	£4,249	0.610	£6,962

ICER=incremental cost effectiveness ratio; QALY=quality adjusted life year
*Algorithm interpretation

Table 40 Base Case 1: Incremental cost effectiveness analysis

Strategy	Costs	QALYs	Incremental costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£514,187	447.963			
Kardia Mobile	£515,551	449.249	£1,364	1.286	£1,060
Generic lead-I device	£516,730	449.246	£1,179	-0.002	Dominated
RhythmPad*	£518,436	448.573	£2,885	-0.676	Dominated
Zenicor-ECG	£518,468	449.199	£2,917	-0.050	Dominated
MyDiagnostick	£521,233	449.024	£5,682	-0.225	Dominated
imPulse	£530,745	448.987	£15,194	-0.262	Dominated

ICER=incremental cost effectiveness ratio; QALY=quality adjusted life year
*Algorithm interpretation

4.3.2 Base Case 2: 12-lead ECG in primary care, 14 days to 12-lead ECG

Costs and QALYs generated in Base Case 2 are shown in Table 41 and Table 42 respectively.

Table 41 Base Case 2: Total costs of annual number of symptomatic patients with positive MPP seen by a single GP

Strategy	Lead-I ECG test	Treatment (NOACs & rate control)	CVEs and AEs	12-lead ECG	Paroxysmal testing (holter monitor)	Total costs
Standard pathway	£0	£90,431	£420,710	£535	£2,741	£514,416
Kardia Mobile	£26	£102,842	£409,851	£451	£2,239	£515,408
imPulse	£97	£116,189	£411,588	£453	£2,263	£530,590
MyDiagnostick	£100	£106,951	£411,334	£451	£2,245	£521,080
Generic lead-I device	£392	£103,636	£409,868	£451	£2,240	£516,587
Zenicor-ECG	£624	£104,824	£410,181	£451	£2,242	£518,323
RhythmPad*	£1,110	£100,198	£414,279	£445	£2,229	£518,261

AE=adverse events; CVE=cardiovascular events
*Algorithm interpretation

Table 42 Base Case 2: QALYs and patient outcomes

Strategy	IS	HS	TIA	False negatives	False positives	Bleeds	Total QALYs
Standard pathway	11.620	2.123	8.407	1.606	0.000	23.572	447.895
Kardia Mobile	11.451	1.996	8.358	0.144	1.378	23.743	449.220
imPulse	11.482	2.018	8.365	0.396	3.660	23.721	448.956
MyDiagnostick	11.477	2.015	8.364	0.360	2.153	23.711	448.994
Generic lead-I device	11.451	1.996	8.358	0.147	1.507	23.744	449.217
Zenicor-ECG	11.457	2.000	8.360	0.192	1.722	23.738	449.170
RhythmPad*	11.529	2.054	8.376	0.793	1.292	23.620	448.540

AE=adverse events; CVE=cardiovascular events; QALY=quality adjusted life year; IS=ischaemic stroke; HS=haemhorragic stroke; TIA=transient ischaemic accident
*Algorithm interpretation

Pairwise cost effectiveness results from the Base Case 2 analysis for each index test versus the standard diagnostic pathway are presented in Table 43 and incremental analysis are shown in Table 44.

Table 43 Base Case 2: Pairwise cost effectiveness analysis

Strategy	Costs	QALYs	Incremental costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£514,416	447.895			
Kardia Mobile	£515,408	449.220	£992	1.324	£749
imPulse	£530,590	448.956	£16,174	1.061	£15,246
MyDiagnostick	£521,080	448.994	£6,664	1.098	£6,068
Generic lead-I device	£516,587	449.217	£2,171	1.322	£1,642
Zenicor-ECG	£518,323	449.170	£3,907	1.274	£3,066
RhythmPad*	£518,261	448.540	£3,845	0.644	£5,966

ICER=incremental cost effectiveness ratio; QALY=quality adjusted life year
*Algorithm interpretation

Table 44 Base Case 2: Incremental cost effectiveness analysis

Strategy	Costs	QALYs	Incremental costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£514,416	447.895			
Kardia Mobile	£515,408	449.220	£992	1.324	£749
Generic lead-I device	£516,587	449.217	£1,179	-0.002	Dominated
RhythmPad*	£518,261	448.540	£2,853	-0.680	Dominated
Zenicor-ECG	£518,323	449.170	£2,915	-0.050	Dominated
MyDiagnostick	£521,080	448.994	£5,672	-0.226	Dominated
imPulse	£530,590	448.956	£15,182	-0.264	Dominated

ICER=incremental cost effectiveness ratio; QALY=quality adjusted life year
*Algorithm interpretation

4.3.3 Base Case 3: 12-lead ECG in secondary care, 2 days to 12-lead ECG

Costs and QALYs generated in Base Case 3 are shown in Table 45 and Table 46 respectively.

Table 45 Base Case 3: Total costs of annual number of symptomatic patients with positive MPP seen by a single GP

Strategy	Lead-I ECG test	Treatment (NOACs & rate control)	CVEs and AEs	12-lead ECG	Paroxysmal testing (holter monitor)	Total costs
Standard pathway	£0	£90,630	£420,279	£2,801	£2,743	£516,453
Kardia Mobile	£26	£102,952	£409,881	£2,361	£2,240	£517,460
imPulse	£97	£116,317	£411,612	£2,373	£2,265	£532,663
MyDiagnostick	£100	£107,077	£411,358	£2,359	£2,247	£523,140
Generic lead-I device	£392	£103,746	£409,898	£2,362	£2,242	£518,640
Zenicor-ECG	£624	£104,938	£410,210	£2,362	£2,244	£520,378
RhythmPad*	£1,110	£100,358	£414,292	£2,330	£2,231	£520,320

AE=adverse events; CVE=cardiovascular events
*Algorithm interpretation

Table 46 Base Case 3: QALYs and patient outcomes

Strategy	IS	HS	TIA	False negatives	False positives	Bleeds	Total QALYs
Standard pathway	11.621	2.124	8.406	1.606	0.000	23.581	447.963
Kardia Mobile	11.452	1.996	8.359	0.144	1.379	23.751	449.249
imPulse	11.482	2.019	8.366	0.397	3.663	23.730	448.987
MyDiagnostick	11.478	2.015	8.365	0.361	2.155	23.720	449.024
Generic lead-I device	11.452	1.996	8.359	0.147	1.508	23.752	449.246
Zenicor-ECG	11.457	2.000	8.360	0.193	1.724	23.746	449.199
RhythmPad*	11.530	2.054	8.377	0.794	1.293	23.630	448.573

AE=adverse events; CVE=cardiovascular events; QALY=quality adjusted life year; IS=ischaemic stroke; HS=haemhorragic stroke; TIA=transient ischaemic accident
*Algorithm interpretation

Pairwise cost effectiveness results from the Base Case 3 analysis for each index test versus the standard diagnostic pathway are presented in Table 47 and incremental analysis are shown in Table 48.

Table 47 Base Case 3: Pairwise cost effectiveness analysis

Strategy	Costs	QALYs	Incremental costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£516,453	447.963			
Kardia Mobile	£517,460	449.249	£1,007	1.286	£783
imPulse	£532,663	448.987	£16,211	1.024	£15,826
MyDiagnostick	£523,140	449.024	£6,688	1.061	£6,301
Generic lead-I device	£518,640	449.246	£2,187	1.284	£1,704
Zenicor-ECG	£520,378	449.199	£3,925	1.236	£3,175
RhythmPad*	£520,320	448.573	£3,868	0.610	£6,337

ICER=incremental cost effectiveness ratio; QALY=quality adjusted life year
*Algorithm interpretation

Table 48 Base Case 3: Incremental cost effectiveness analysis

Strategy	Costs	QALYs	Incremental costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£516,453	447.963			
Kardia Mobile	£517,460	449.249	£1,007	1.286	£783
imPulse	£518,640	449.246	£1,180	-0.002	Dominated
MyDiagnostick	£520,320	448.573	£2,860	-0.676	Dominated
Generic lead-I device	£520,378	449.199	£2,918	-0.050	Dominated
Zenicor-ECG	£523,140	449.024	£5,680	-0.225	Dominated
RhythmPad*	£532,663	448.987	£15,203	-0.262	Dominated

ICER=incremental cost effectiveness ratio; QALY=quality adjusted life year
*Algorithm interpretation

4.3.4 Base Case 4: 12-lead ECG in secondary care, 14 days to 12-lead ECG

Costs and QALYs generated in Base Case 4 are shown in Table 49 and Table 50 respectively.

Table 49 Base Case 4: Total costs of annual number of symptomatic patients with positive MPP seen by a single GP

Strategy	Lead-I ECG test	Treatment (NOACs & rate control)	CVEs and AEs	12-lead ECG	Paroxysmal testing (holter monitor)	Total costs
Standard pathway	£0	£90,431	£420,710	£2,797	£2,741	£516,678
Kardia Mobile	£26	£102,842	£409,851	£2,358	£2,239	£517,315
imPulse	£97	£116,189	£411,588	£2,370	£2,263	£532,507
MyDiagnostick	£100	£106,951	£411,334	£2,356	£2,245	£522,985
Generic lead-I device	£392	£103,636	£409,868	£2,359	£2,240	£518,495
Zenicor-ECG	£624	£104,824	£410,181	£2,359	£2,242	£520,231
RhythmPad*	£1,110	£100,198	£414,279	£2,327	£2,229	£520,142

AE=adverse events; CVE=cardiovascular events
*Algorithm interpretation

Table 50 Base Case 4: QALYs and patient outcomes

Strategy	IS	HS	TIA	False negatives	False positives	Bleeds	Total QALYs
Standard pathway	11.620	2.123	8.407	1.606	0.000	23.572	447.895
Kardia Mobile	11.451	1.996	8.358	0.144	1.378	23.743	449.220
imPulse	11.482	2.018	8.365	0.396	3.660	23.721	448.956
MyDiagnostick	11.477	2.015	8.364	0.360	2.153	23.711	448.994
Generic lead-I device	11.451	1.996	8.358	0.147	1.507	23.744	449.217
Zenicor-ECG	11.457	2.000	8.360	0.192	1.722	23.738	449.170
RhythmPad*	11.529	2.054	8.376	0.793	1.292	23.620	448.540

AE=adverse events; CVE=cardiovascular events; QALY=quality adjusted life year; IS=ischaemic stroke; HS=haemhorragic stroke; TIA=transient ischaemic accident
*Algorithm interpretation

Pairwise cost effectiveness results from the Base Case 4 analysis for each index test versus the standard diagnostic pathway are presented in Table 51 and incremental analysis are shown in Table 52.

Table 51 Base Case 4: Pairwise cost effectiveness analysis

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£516,678	447.895			
Kardia Mobile	£517,315	449.220	£637	1.324	£481
imPulse	£532,507	448.956	£15,829	1.061	£14,921
MyDiagnostick	£522,985	448.994	£6,307	1.098	£5,743
Generic lead-I device	£518,495	449.217	£1,817	1.322	£1,374
Zenicor-ECG	£520,231	449.170	£3,553	1.274	£2,788
RhythmPad*	£520,142	448.540	£3,464	0.644	£5,376

ICER=incremental cost effectiveness ratio; QALY=quality adjusted life year
*Algorithm interpretation

Table 52 Base Case 4: Incremental cost effectiveness analysis

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£516,678	447.895			
Kardia Mobile	£517,315	449.220	£637	1.324	£481
Generic lead-I device	£518,495	449.217	£1,180	-0.002	Dominated
RhythmPad*	£520,142	448.540	£2,828	-0.680	Dominated
Zenicor-ECG	£520,231	449.170	£2,916	-0.050	Dominated
MyDiagnostick	£522,985	448.994	£5,670	-0.226	Dominated
imPulse	£532,507	448.956	£15,192	-0.264	Dominated

ICER=incremental cost effectiveness ratio; QALY=quality adjusted life year
*Algorithm interpretation

4.3.5 Summary of base case cost effectiveness results

The results of the pairwise analysis show that all lead-I ECG tests lie on the efficiency frontier in each of the four base case analyses with ICERs below the £20,000-£30,000 threshold usually considered to be cost effective by NICE. Kardia Mobile is the most cost effective option in a full incremental analysis with an ICER no higher than £1,060 per QALY gained compared to the standard pathway and dominates the other lead-I ECG devices (costing less and generating more QALYs).

Lead-I ECG devices are more cost effective when there is a longer wait to 12-Lead ECG (as treatment for AF with a lead-I ECG device is assumed in the model to start earlier than in the standard pathway) and if the 12-lead ECG is perfomed in hospital. The majority of the patient benefit, however, comes after diagnosis due to a greater proportion of patients who are correctly diagnosed with AF and treated for AF even if this benefit is slightly offset by an increase in patients incorrectly diagnosed with AF with a lead-I ECG device.

4.4 Scenario analyses

Scenario analyses were undertaken to investigate the impact on the ICER per QALY gained of varying some of the base case assumptions. Results for scenario analyses using the least cost effective base case (Base Case 1 [12-lead ECG in primary care, 2 days to 12-lead ECG]) are presented; if the conclusions drawn from results remain unchanged from the least cost effective scenario for lead-I ECG testing, they should also remain unchanged for the more cost effective scenarios.

The scenario analyses were:

- Scenario A: The unit cost associated with the lead-I ECG device changed from full cost of the device to no cost. This assumption was varied to take into account other populations that might use a lead-I ECG device in primary care that would share the cost of the device
- Scenario B: Sensitivity and specificity estimates from interpretation of the MyDiagnostick lead-I ECG trace by EP2
- Scenario C: Diagnosis and decisions made to refer for paroxysmal testing based only on the lead-I ECG results ie. no referral for 12-lead ECG or holter monitor.
- Scenario D: The time horizon is limited to 5 years to reflect clinical feedback to the EAG that it is plausible that all patients with paroxysmal AF not correctly diagnosed with AF after Lead-I, 12-lead ECG or holter monitoring will be picked up within 5 years if they do not have a CVE.

- Scenarios E1 to E40: The proportions of patients sent for further testing for paroxysmal AF depending on the outcomes of the combined lead-I ECG and 12-lead ECG tests are varied. Clinical advice provided to the EAG highlighted the significant difference in clinical practice around how patients with positive or negative lead-I ECG and 12-lead ECG results would continue on the diagnostic pathway so each scenario may represent the true 'base case' scenario for a specific GP or practice depending on the diagnostic pathway they follow.

4.4.1 Scenario A: Unit cost associated with the lead-I ECG device

Incremental cost effectiveness results from Scenario A, which investigates the impact of removing the unit cost of the lead-I ECG device from the analysis (using 12-lead ECG in primary care, 2 days to 12-lead ECG) are presented in Table 53.

Table 53 Scenario A: Impact of removing the unit cost of the lead-I ECG device from the analysis, incremental cost effectiveness analysis

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£514,187	447.963			
Kardia Mobile	£515,535	449.249	£1,347	1.286	£1,047
Generic lead-I device	£516,348	449.246	£813	-0.002	Dominated
RhythmPad*	£517,336	448.573	£1,802	-0.676	Dominated
Zenicor-ECG	£517,854	449.199	£2,319	-0.050	Dominated
MyDiagnostick	£521,143	449.024	£5,608	-0.225	Dominated
imPulse	£530,657	448.987	£15,123	-0.262	Dominated

ICER=incremental cost effectiveness ratio; QALY=quality adjusted life year
*Algorithm interpretation

4.4.2 Scenario B: Alternative sensitivity and specificity estimates for MyDiagnostick

Incremental cost effectiveness results from Scenario B, which investigates the impact of using the sensitivity and specificity estimates based on interpretation of the MyDiagnostick lead-I ECG trace by EP2 (using 12-lead ECG in primary care, 2 days to 12-lead ECG), are presented in Table 54.

Table 54 Scenario B: Impact of using the sensitivity and specificity estimates based on interpretation of the MyDiagnostick lead-I ECG trace by EP2, incremental cost effectiveness analysis

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYs	ICER/ QALY gained
MyDiagnostick	£513,623	448.898			
Standard pathway	£514,187	447.963	£565	-0.9359	Dominated
Kardia Mobile	£515,551	449.249	£1,928	0.3504	£5,503
Generic lead-I device	£516,730	449.246	£1,179	-0.0025	Dominated

RhythmPad*	£518,436	448.573	£2,885	-0.6759	Dominated
Zenicor-ECG	£518,468	449.199	£2,917	-0.0499	Dominated
imPulse	£530,745	448.987	£15,194	-0.2620	Dominated

ICER=incremental cost effectiveness ratio; QALY=quality adjusted life year

4.4.3 Scenario C: Diagnosis without 12-Lead ECG and holter monitor

Incremental cost effectiveness results from scenario C which investigates the impact of removing 12-lead ECG and holter monitoring from the lead-I ECG diagnostic pathway (compared to using 12-lead ECG in primary care, 2 days to 12-lead ECG) are presented in Table 55.

Table 55 Scenario C: Impact of removing 12-lead ECG and holter monitoring from the lead-I ECG diagnostic pathway, incremental analysis

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£514,187	447.963			
Kardia Mobile	£515,356	448.896	£1,169	0.9335	£1,252
Generic lead-I device	£516,575	448.888	£1,218	-0.0085	Dominated
Zenicor-ECG	£519,081	448.726	£3,725	-0.1697	Dominated
MyDiagnostick	£524,667	448.131	£9,311	-0.7647	Dominated
RhythmPad*	£529,083	446.597	£13,727	-2.2991	Dominated
imPulse	£534,767	448.004	£19,411	-0.8924	Dominated

ICER=incremental cost effectiveness ratio; QALY=quality adjusted life year
*Algorithm interpretation

4.4.4 Scenario D: 5-year time horizon

Incremental cost effectiveness results from scenario D investigating a 5-year time horizon as a proxy for all undiagnosed patients being identified within 5 years (12-lead ECG in primary care, 2 days to 12-lead ECG) are presented in Table 56.

Table 56 Scenario D: Impact of 5-year time horizon, incremental analysis

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£101,668	173.979			
Kardia Mobile	£102,543	174.550	£876	0.5706	£1,534
Generic lead-I device	£103,234	174.549	£691	-0.0011	Dominated
Zenicor-ECG	£104,051	174.527	£1,508	-0.0224	Dominated
RhythmPad*	£104,073	174.247	£1,530	-0.3028	Dominated
MyDiagnostick	£104,774	174.449	£2,231	-0.1008	Dominated
imPulse	£108,573	174.432	£6,030	-0.1175	Dominated

ICER=incremental cost effectiveness ratio; QALY=quality adjusted life year

4.4.5 Scenario E1 to E40: Varying proportion of patients sent for holter testing after lead-I ECG and 12-lead ECG results

Incremental cost effectiveness results from scenarios E1 to E40 exploring the uncertainty in the proportion of people sent for paroxysmal testing following lead-I ECG and 12-lead ECG results (12-lead ECG in primary care, 2 days to 12-lead ECG) are presented in Table 57. Given the complexity of the results, each scenario is only shown for the standard pathway compared to Kardia Mobile, the lead-I ECG test that was found to be the most cost effective option in the base case analyses.

Table 57 Scenario E Varying percentage of patients sent for holter monitoring for paroxysmal AF depending on the lead-I ECG and 12-lead ECG results, incremental analysis

Scenario	Lead-I pathway (% of patients being referred for holter monitoring)		Standard pathway (% of patients being referred for holter monitoring)	Standard pathway		Lead-I ECG pathway (Kardia Mobile)		Incremental		ICER
	Lead-I ECG negative, 12-lead negative	Lead-I ECG positive, 12-lead negative	MPP positive, 12-lead negative	Costs	QALYs	Costs	QALYs	Costs	QALYs	
E1	0%	0%	0%	£515,456	447.256	£513,532	449.215	-£1,924	1.959	Dominates
E2	0%	100%	0%	£515,456	447.256	£513,973	449.216	-£1,482	1.959	Dominates
E3	0%	75%	0%	£515,456	447.256	£513,863	449.215	-£1,593	1.959	Dominates
E4	0%	50%	0%	£515,456	447.256	£513,753	449.215	-£1,703	1.959	Dominates
E5	0%	25%	0%	£515,456	447.256	£513,642	449.215	-£1,813	1.959	Dominates
E6	25%	100%	0%	£515,456	447.256	£514,873	449.232	-£583	1.976	Dominates
E7	25%	75%	0%	£515,456	447.256	£514,762	449.232	-£693	1.976	Dominates
E8	25%	50%	0%	£515,456	447.256	£514,652	449.232	-£804	1.976	Dominates
E9	25%	25%	0%	£515,456	447.256	£514,541	449.232	-£914	1.976	Dominates
E10	50%	100%	0%	£515,456	447.256	£515,772	449.249	£316	1.993	£159
E11	50%	75%	0%	£515,456	447.256	£515,661	449.249	£206	1.993	£103
E12	50%	50%	0%	£515,456	447.256	£515,551	449.249	£96	1.992	£48
E13	75%	100%	0%	£515,456	447.256	£516,671	449.266	£1,215	2.010	£605
E14	75%	75%	0%	£515,456	447.256	£516,561	449.266	£1,105	2.009	£550
E15	100%	100%	0%	£515,456	447.256	£517,570	449.283	£2,114	2.026	£1,043
E16	0%	100%	25%	£514,824	447.610	£513,973	449.216	-£851	1.606	Dominates
E17	0%	75%	25%	£514,824	447.610	£513,863	449.215	-£961	1.606	Dominates
E18	0%	50%	25%	£514,824	447.610	£513,753	449.215	-£1,071	1.606	Dominates
E19	0%	25%	25%	£514,824	447.610	£513,642	449.215	-£1,182	1.606	Dominates
E20	0%	100%	50%	£514,187	447.963	£513,973	449.216	-£214	1.253	Dominates

E21	0%	75%	50%	£514,187	447.963	£513,863	449.215	-£324	1.253	Dominates
E22	0%	50%	50%	£514,187	447.963	£513,753	449.215	-£435	1.253	Dominates
E23	0%	100%	75%	£513,545	448.315	£513,973	449.216	£428	0.901	£476
E24	0%	75%	75%	£513,545	448.315	£513,863	449.215	£318	0.900	£353
E25	0%	100%	100%	£512,895	448.667	£513,973	449.216	£1,078	0.549	£1,966
E26	25%	25%	25%	£514,824	447.610	£514,541	449.232	-£282	1.622	Dominates
E27	50%	50%	50%	£514,187	447.963	£515,551	449.249	£1,364	1.286	£1,060
E28	50%	50%	25%	£514,824	447.610	£515,551	449.249	£727	1.639	£444
E29	75%	75%	25%	£514,824	447.610	£516,561	449.266	£1,737	1.656	£1,049
E30	75%	75%	50%	£514,187	447.963	£516,561	449.266	£2,373	1.303	£1,821
E31	75%	75%	75%	£513,545	448.315	£516,561	449.266	£3,016	0.951	£3,172
E32	100%	100%	25%	£514,824	447.610	£517,570	449.283	£2,746	1.673	£1,641
E33	100%	100%	50%	£514,187	447.963	£517,570	449.283	£3,383	1.320	£2,562
E34	100%	100%	75%	£513,545	448.315	£517,570	449.283	£4,025	0.968	£4,159
E35	25%	50%	50%	£514,187	447.963	£514,652	449.232	£464	1.270	£366
E36	50%	50%	75%	£513,545	448.315	£515,551	449.249	£2,006	0.934	£2,148
E37	25%	75%	75%	£513,545	448.315	£514,762	449.232	£1,217	0.917	£1,327
E38	25%	75%	75%	£513,545	448.315	£514,762	449.232	£1,217	0.917	£1,327
E39	50%	75%	75%	£513,545	448.315	£515,661	449.249	£2,116	0.934	£2,266
E40	100%	100%	100%	£512,895	448.667	£517,570	449.283	£4,675	0.616	£7,594

ICER=incremental cost effectiveness ratio; MPP=manual pulse palpation; QALY=quality adjusted life year

4.5 Deterministic sensitivity analysis

One-way sensitivity analyses were run to identify the individual parameters with the biggest impact on the model results. Tornado diagrams are presented in Figure 27 to Figure 32 for each index test using Base Case 1 (12-lead ECG in primary care, 2 days to 12-lead ECG).

Figure 27 Tornado diagram: Base Case 1: ImPulse

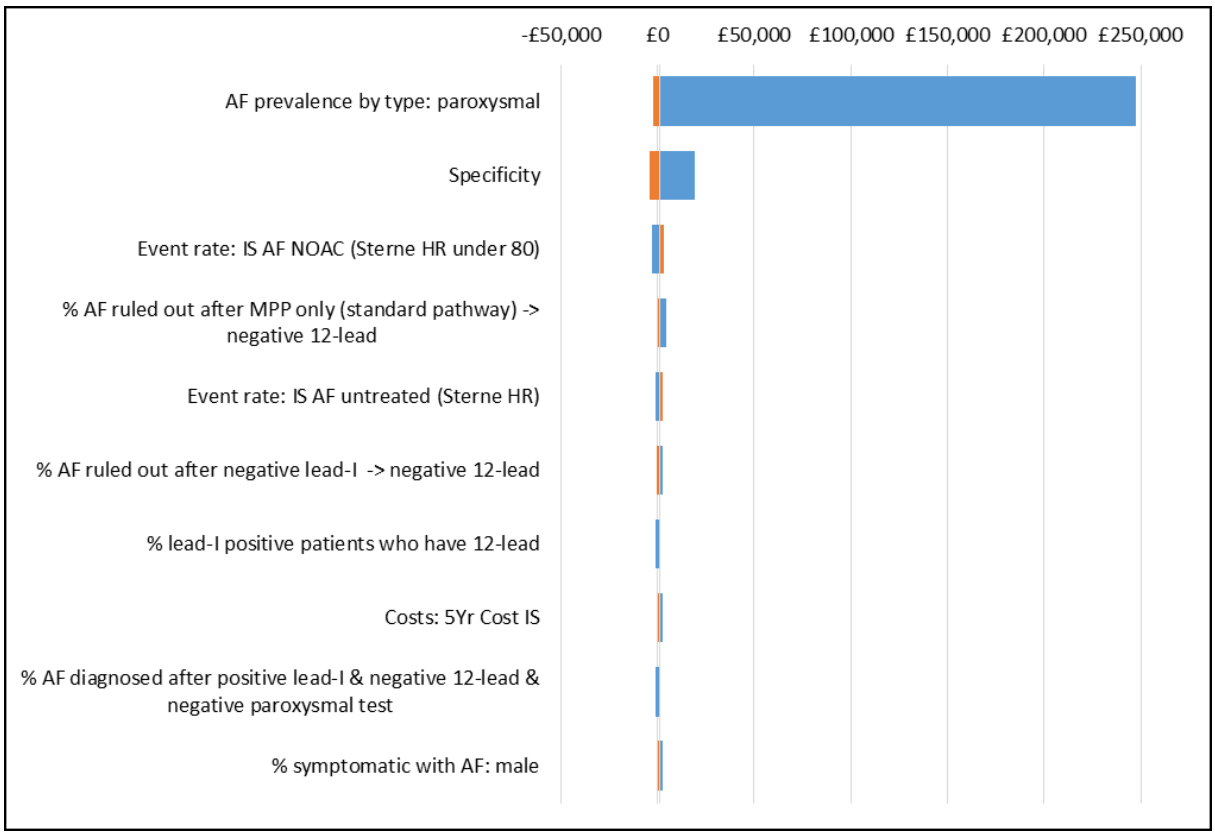

Figure 28 Tornado diagram: Base Case 1: Kardia Mobile

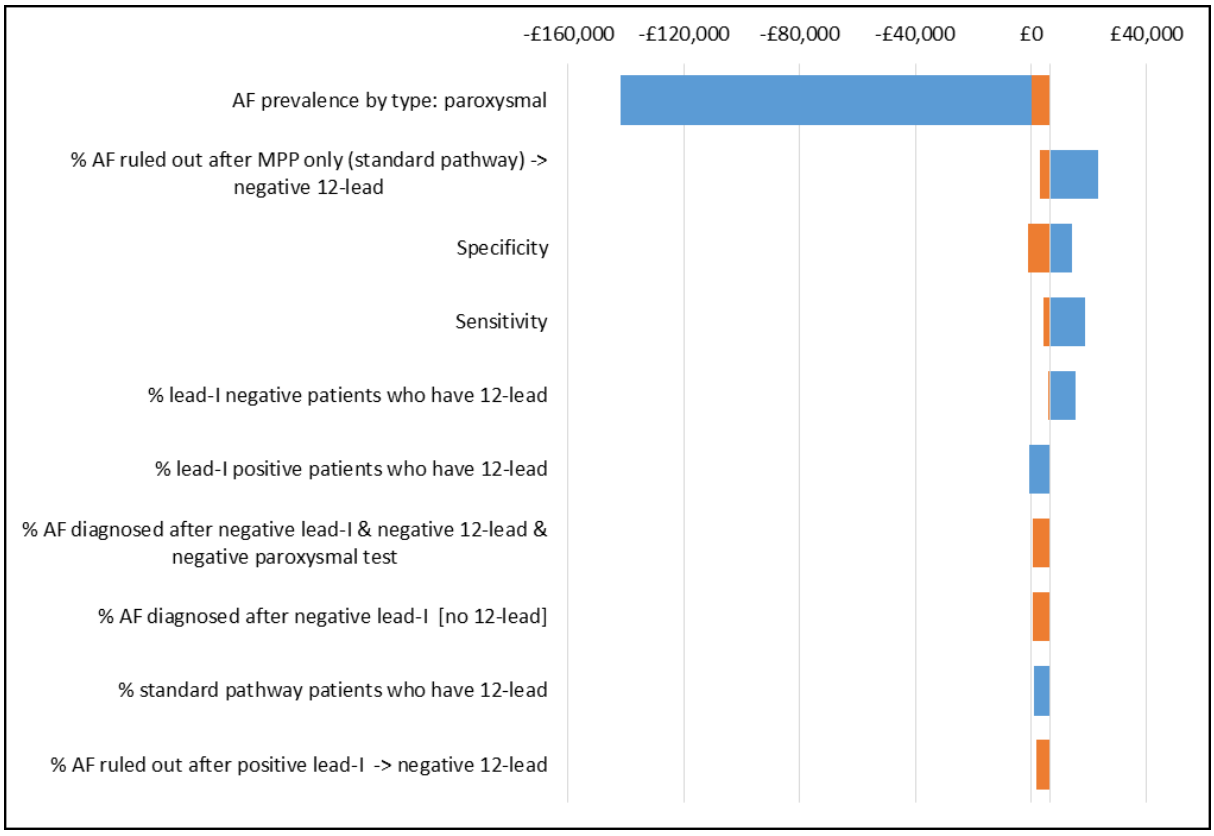

Figure 29 Tornado diagram: Base Case 1: MyDiagnostick

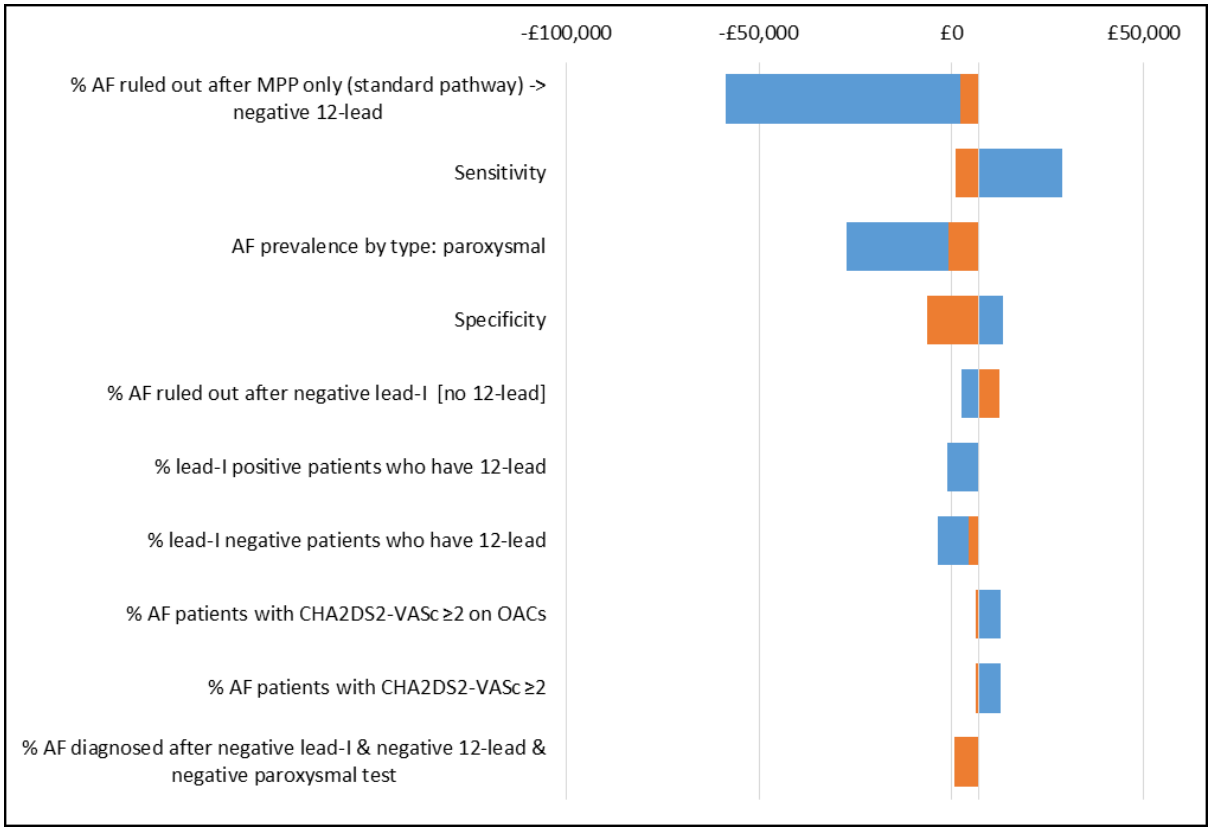

Figure 30 Tornado diagram: Base Case 1: RhythmPad GP

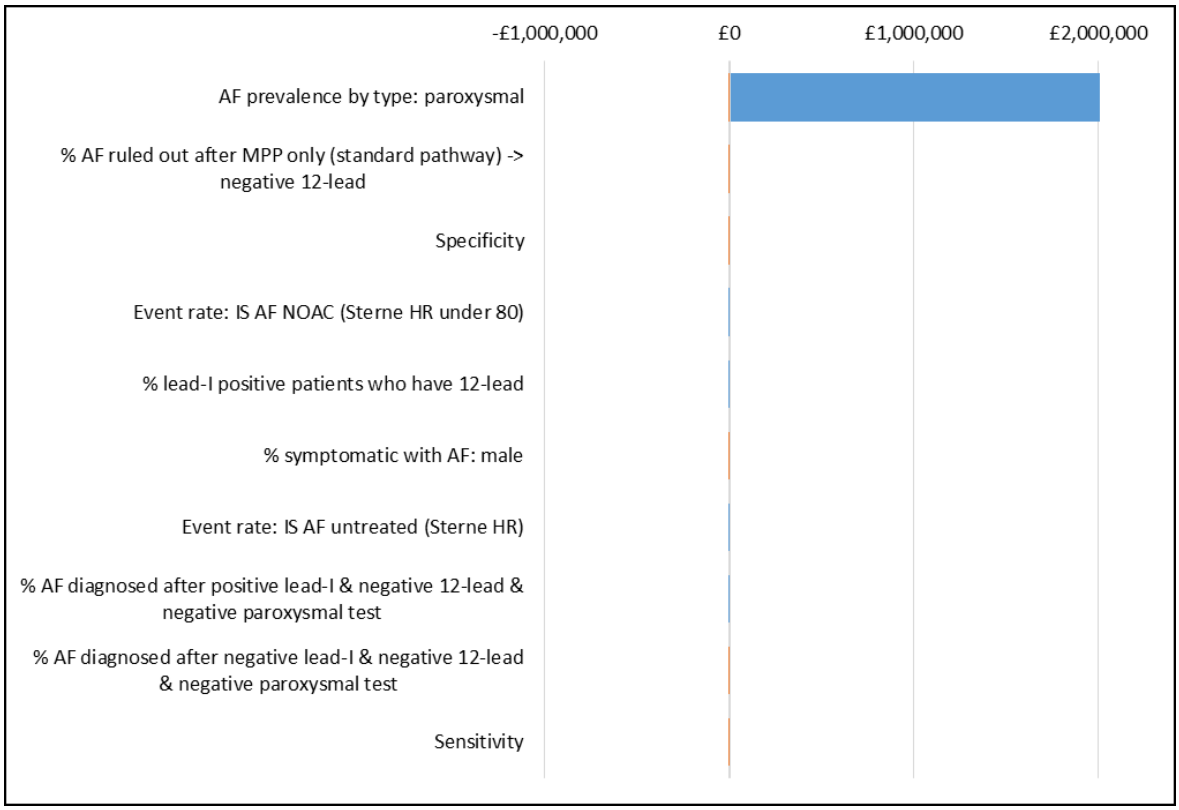

Figure 31 Tornado diagram: Base Case 1: Zenicor ECG

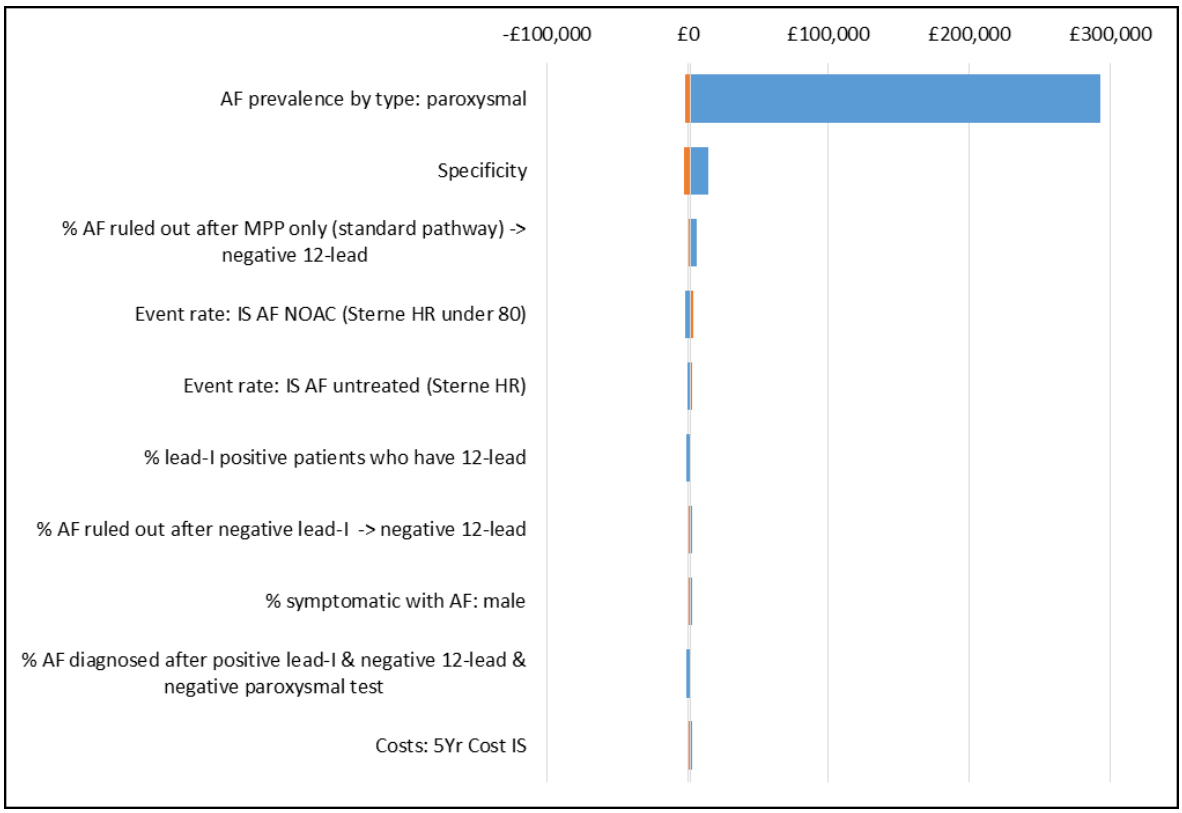

Figure 32 Tornado diagram: Base Case 1: Generic lead-I device

4.6 Probabilistic sensitivity analysis

Probability sensitivity analyses were undertaken for the lead-I ECG pathway with each index test compared with the standard diagnostic pathway. The cost effectiveness acceptability curves (CEACs) in Base Case 1 for each device are presented in Figure 33 to Figure 38. The CEAC for all devices is shown in Figure 39. The parameters for the probability sensitivity analysis are presented in Appendix 8.

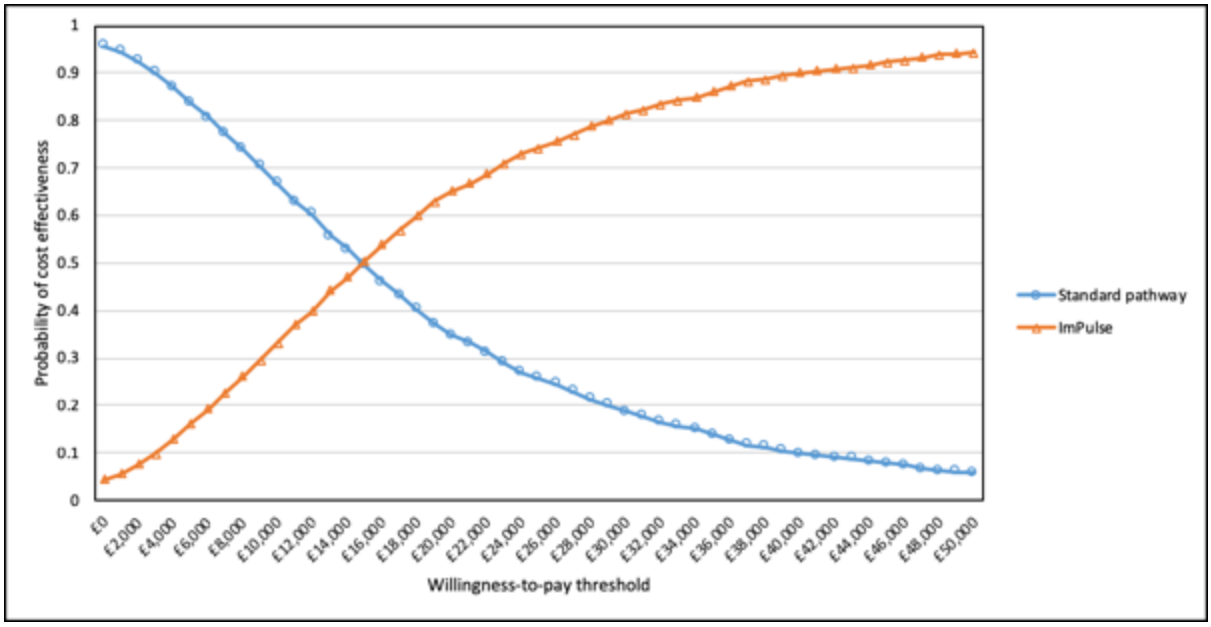

Figure 33 CEAC Base Case 1: imPulse

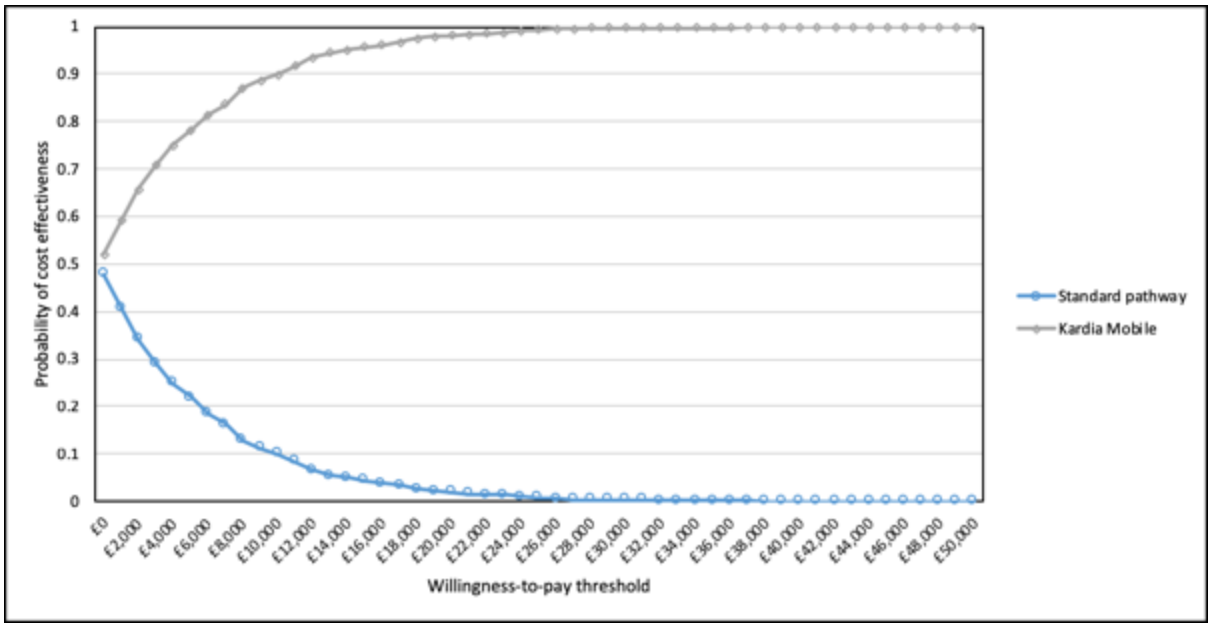

Figure 34 CEAC Base Case 1: Kardia Mobile

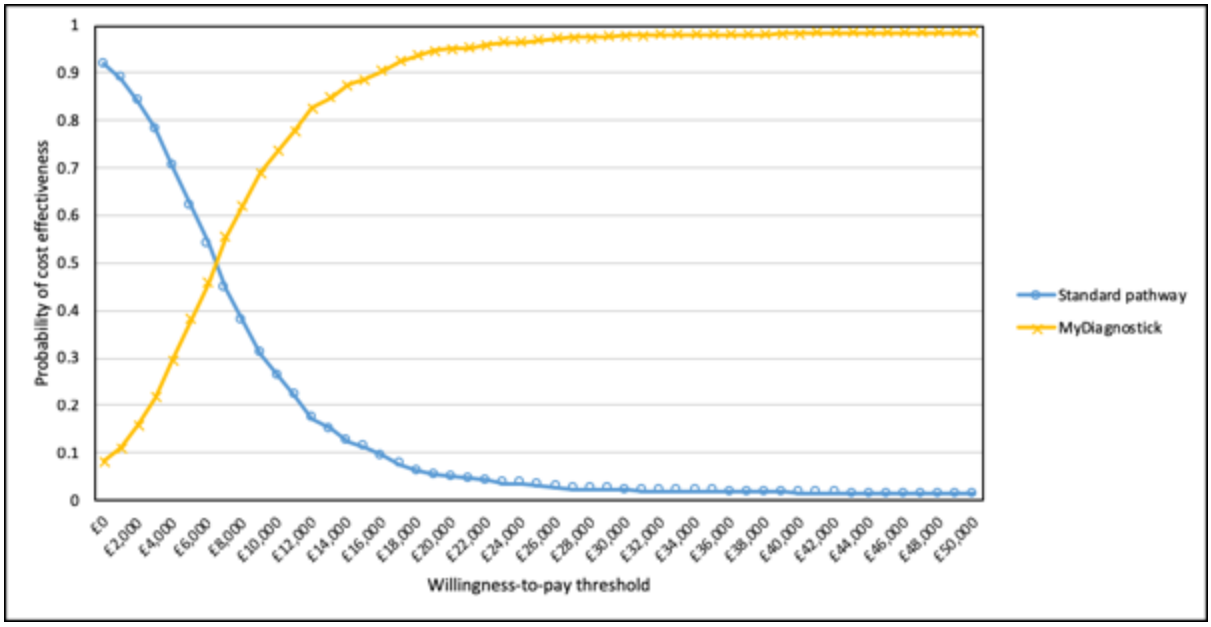

Figure 35 CEAC Base Case 1: MyDiagnostick

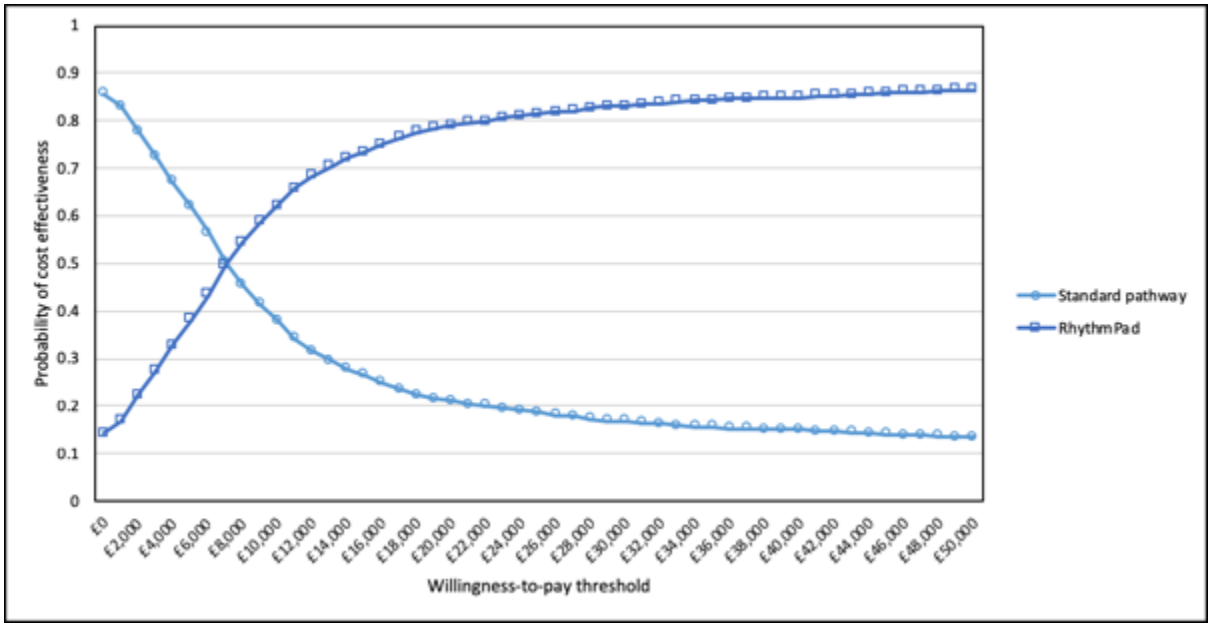

Figure 36 CEAC Base Case 1: RhythmPad GP

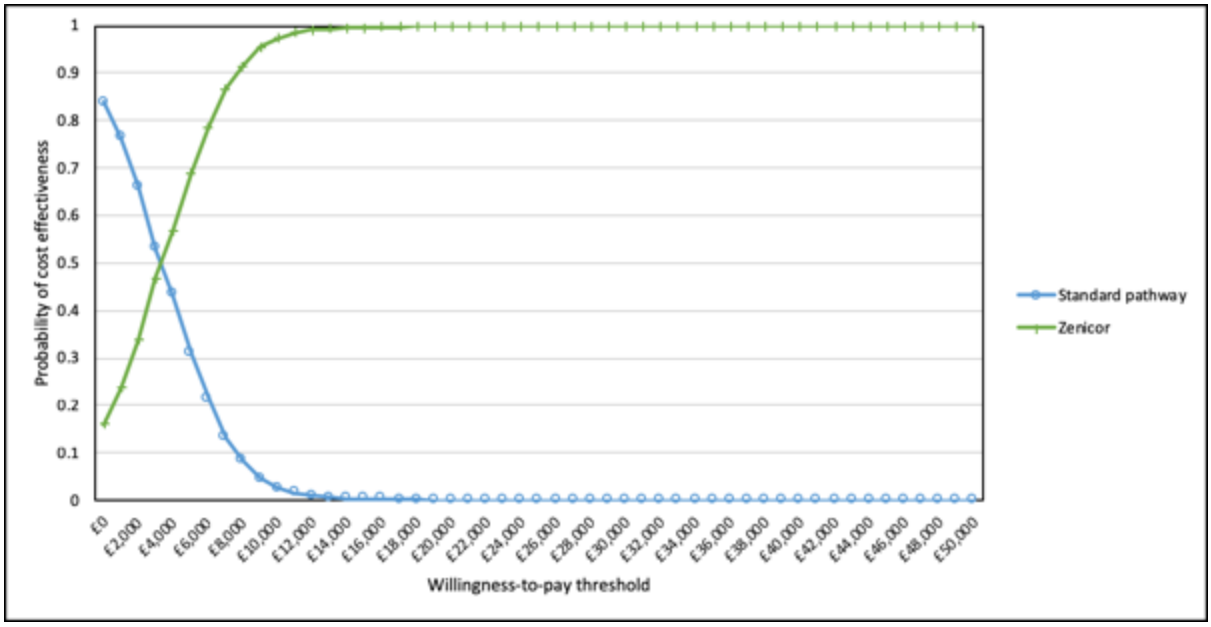

Figure 37 CEAC Base Case 1: Zenicor ECG

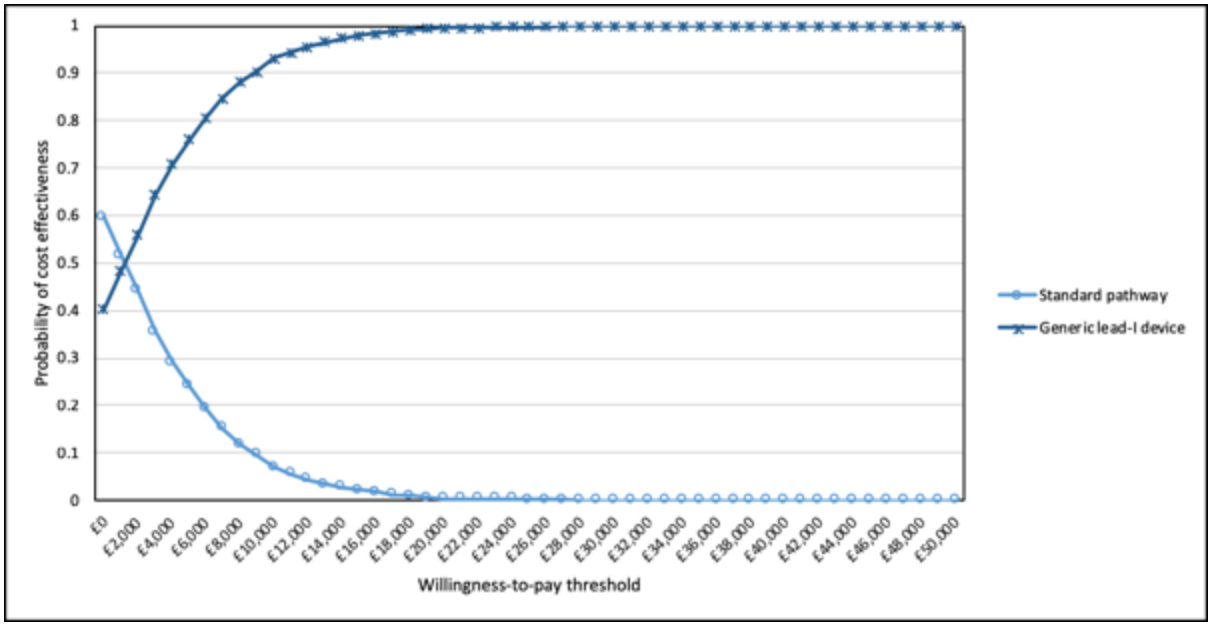

Figure 38 CEAC Base Case 1: Generic lead-I ECG device

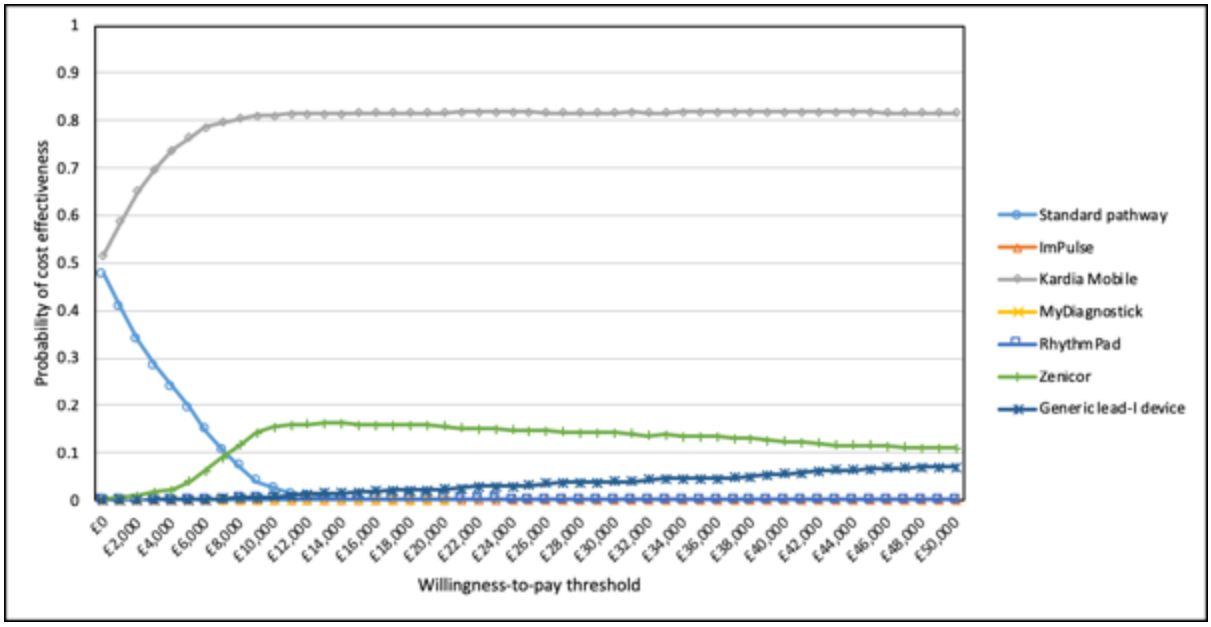

Figure 39 CEAC Base Case 1: all lead-I ECG devices

4.6.1 Summary of scenario and sensitivity analyses cost effectiveness results

The one-way sensitivity analysis showed that the results were sensitive to the assumed prevalence of paroxysmal AF versus persistent and permanent AF. Decreased prevalence of paroxysmal AF increased incremental costs and decreased incremental QALYs for lead-I ECG devices versus the standard pathway. At the extreme, where the prevalence of paroxysmal AF was assumed to be zero, incremental QALYs decreased sufficiently to become negative and resulted in some lead-I ECG devices (ImPulse, MyDiagnostick and RhythmPad) being dominated by the standard pathway. The ICERs per QALY gained yielded for other lead-I ECG devices when the prevalence of paroxysmal AF was zero were very large due to very small incremental QALYs. When the prevalence of paroxysmal AF was assumed to be 1, incremental costs decreased and incremental QALYs increased. Increasing the prevalence of paroxysmal AF to 1 resulted in all lead-I ECG devices except ImPulse and MyDiagnostik dominating the standard pathway.

The results of the probability sensitivity analysis indicate that in pairwise comparisons all lead-I ECG devices included in this assessment were cost effective in at least 50% of iterations with a willingness to pay (WTP) threshold of around £15,000 per QALY. When all devices were consider together, at a threshold of £20,000 per QALY just over 80% of iterations showed Kardia Mobile would be the most cost effective option with Zenicor-ECG being the most cost effective in around 15% of iterations. In no iterations at a WTP threshold of £20,000 per QALY was the standard pathway found to be the most cost effective option.

The scenario analysis showed that results were sensitive to using alternative sensitivity and specificity values for MyDiagnostick. MyDiagnostick yielded the lowest overall costs of all the strategies when sensitivity and specificity estimates from interpretation of the MyDiagnostick lead-I ECG trace by EP2 were used. Kardia Mobile remained as the index test with the highest overall QALYs in this scenario, which yielded an incremental ICER per QALY gained of £5,503 versus MyDiagnostick (using EP2).

The scenario analysis showed that results were invariant to the following assumptions:

- Whether the cost of the lead-I ECG device is included in the analysis
- Patients with AF incorrectly ruled out are not diagnosed with AF prior to a CVE
- Removal of 12-lead ECG and holter monitoring from the lead-I ECG pathway
- Shortening the time horizon to 5 years

The finding that removal of 12-lead ECG and holter monitoring from the lead-I ECG pathway did not affect cost effectiveness results is unsurprising given that if a patient had paroxysmal AF they were assumed to be in AF at the time of lead-I ECG monitoring and as such the majority of paroxysmal AF would be detected with lead-I ECG without the need for 12-lead ECG or holter monitoring. However, this result should be interpreted with caution as the potential further benefits of a specific diagnosis of paroxysmal AF or of the more detailed diagnosis from 12-lead ECG testing was not considered in the model. Similarly, the extensive scenario analyses on the use of holter monitoring following 12-lead ECG tests, with or without lead-I ECG testing, showed that, if holter monitoring is not routinely used for the majority of patients with a negative 12-lead ECG, Kardia Mobile will always have an ICER below £10,000 per QALY gained compared to the standard pathway and in some circumstances would be a dominant strategy.