DAP39 ADDENDUM

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]

Addendum

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1 INTRODUCTION

This document provides the results of additional scenarios and analyses requested by NICE, as well as the results of the incremental base case and probabilistic sensitivity analyses without the inclusion of the generic lead-I ECG device. Additional analyses relate to the effect of sensitivity and specificity on the model results.

The scenarios were:

- Scenario F: Cost of a supplementary smartphone or tablet added to the cost of the Kardia Mobile device. A threshold analysis was performed to determine the minimum unit cost of a smartphone or tablet that would result in Kardia Mobile no longer dominating the other lead-I ECG devices.
- Scenario G: Extending the lifespan of the RhythmPad GP device from 1 year to 3 years.
- Scenario H: Including a QALY decrement for bleeds.
- Scenario I: Using alternative sensitivity and specificity estimates for Kardia Mobile from the pooled analysis with interpretation of the trace from EP2.
- Scenario J: Assuming that rates of haemorrhagic stroke (HS) are the same for people treated with NOACs who do not have AF as rates of HS for people treated with NOACs who have AF.

2 BASE CASE ANALYSES WITHOUT GENERIC LEAD-I ECG DEVICE

Incremental cost effectiveness results for each of the four base case scenarios, excluding the results of the generic lead-I ECG device, are shown in Table 1 to Table 4. The four base case scenarios are:

- Base Case 1: 12-lead ECG in primary care, 2 days to 12-lead ECG
- Base Case 2: 12-lead ECG in primary care, 14 days to 12-lead ECG
- Base Case 3: 12-lead ECG in secondary care, 2 days to 12-lead ECG
- Base Case 4: 12-lead ECG in secondary care, 14 days to 12-lead ECG

Table 1 Base Case 1: Incremental cost effectiveness analysis (without generic lead-I ECG device)

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
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

Table 2 Base Case 2: Incremental cost effectiveness analysis (without generic lead-I ECG device)

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
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

Table 3 Base Case 3: Incremental cost effectiveness analysis (without generic lead-I ECG device)

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

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

Table 4 Base Case 4: Incremental cost effectiveness analysis (without generic lead-I ECG device)

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
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

3 PROBABILISTIC SENSITIVITY ANALYSES WITHOUT GENERIC LEAD-I ECG DEVICE

Pairwise and incremental cost effectiveness results for the Base Case 1 scenario, excluding the results of the generic lead-I device, are shown in Table 5 and Table 6. The cost effectiveness acceptability curve (CEAC) in Base Case 1 for all devices except the generic lead-I ECG device is shown in Figure 1.

Table 5 Base Case 1: PSA results, pairwise cost effectiveness analysis

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£523,563	455.105			
ImPulse	£540,595	456.108	£17,031	1.003	£16,975
Kardia Mobile	£525,003	456.370	£1,440	1.265	£1,139
MyDiagnostick	£530,831	456.144	£7,268	1.039	£6,994
RhythmPad*	£527,977	455.699	£4,414	0.594	£7,427
Zenicor-ECG	£527,963	456.320	£4,399	1.215	£3,621

ICER=incremental cost effectiveness ratio; PSA=probability sensitivity analysis; QALY=quality adjusted life year
*Algorithm interpretation

Table 6 Base Case 1: PSA results, incremental cost effectiveness analysis

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£523,563	455.105			
Kardia Mobile	£525,003	456.370	£1,440	1.265	£1,139
Zenicor-ECG	£527,963	456.320	£2,959	-0.050	Dominated
RhythmPad*	£527,977	455.699	£2,974	-0.670	Dominated
MyDiagnostick	£530,831	456.144	£5,828	-0.226	Dominated
ImPulse	£540,595	456.108	£15,591	-0.261	Dominated

ICER=incremental cost effectiveness ratio; PSA=probability sensitivity analysis; QALY=quality adjusted life year
*Algorithm interpretation

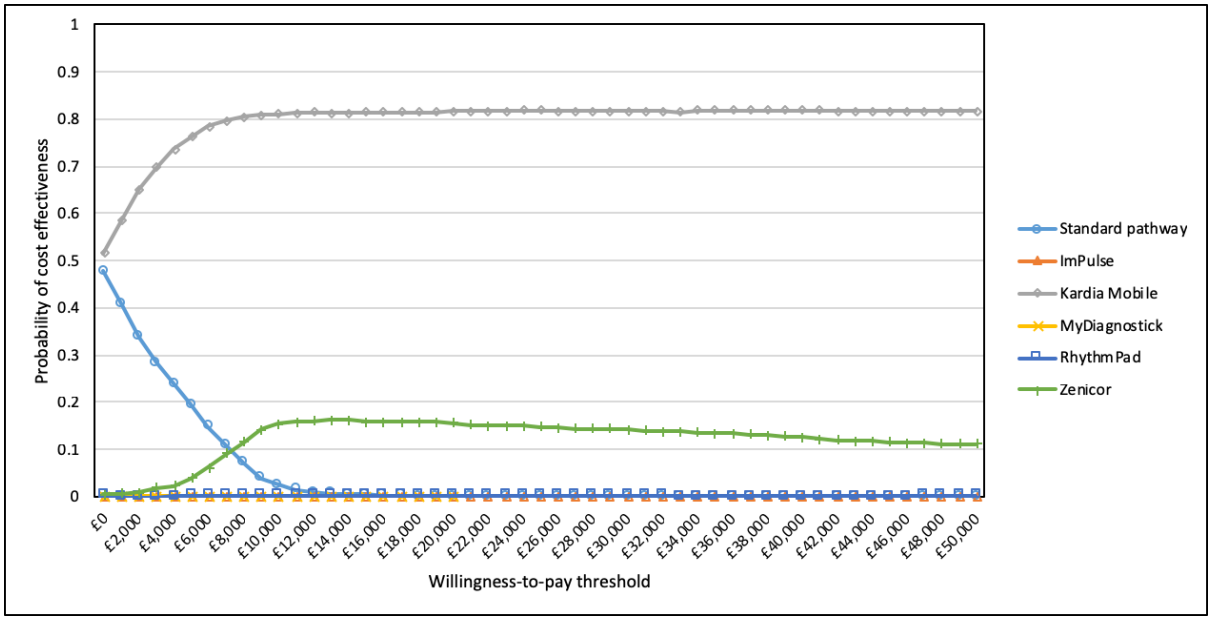

Figure 1 CEAC Base Case 1: all lead-I ECG devices except generic lead-I device

4 SCENARIOS

4.1 Scenario F: Cost of a smartphone or tablet added to the cost of the Kardia Mobile device

In order to perform a lead-I ECG with the Kardia Mobile device, it is necessary to connect the device to a smartphone or tablet. The EAG assumed in the base case that a GP would already have access to a smartphone or tablet that could be used alongside the Kardia Mobile device and would incur no extra cost. The cost of a supplementary smartphone or tablet for use alongside the Kardia Mobile device was investigated in a scenario analysis.

The cost of purchasing a smartphone or tablet varies substantially depending on the type of device, so any estimate of the cost of such a device may not reflect reality for some or any GP practices. The EAG considered it would be justified to perform a threshold analysis to estimate the level at which the extra cost of a supplementary smartphone or tablet would result in Kardia Mobile no longer dominating the other lead-I ECG devices or generating an ICER of £20,000 per QALY gained compared to the standard pathway. The estimated minimum cost of a supplementary smartphone or tablet for Kardia Mobile to no longer dominate ranged from £2,885 versus RhythmPad to £15,194 versus the ImPulse device. Provided a supplementary smartphone or tablet costs less than £24,362, then the ICER per QALY gained for Kardia Mobile compared to the standard pathway would be below £20,000.

The results of the threshold analysis from Scenario F, which calculates the minimum cost of a supplementary smartphone or tablet device that would result in Kardia Mobile no longer being

dominant over each of the alternative strategies (using 12-lead ECG in primary care, 2 days to 12-lead ECG) are presented in Table 7.

Table 7 Scenario F: Minimum cost per supplementary smartphone or tablet device for a non-dominant ICER per QALY gained versus Kardia Mobile (the cost to make the ICER £20,000 per QALY for Kardia Mobile versus the standard pathway)

Strategy	Minimum cost per supplementary device
	Kardia Mobile ICER per QALY gained = £20,000
Standard pathway	£24,362
	Kardia Mobile non-dominant ICER per QALY gained
RhythmPad*	£2,885
Zenicor-ECG	£2,917
MyDiagnostick	£5,682
imPulse	£15,194

*Algorithm interpretation

4.2 Scenario G: Extending the lifespan of the RhythmPad GP device from 1 year to 3 years

The manufacturer of the RhythmPad GP device gave the minimum projected life of the device as 1 year, with the potential for it to last up to 3 years. Changing the lifespan of the RhythmPad GP from 1 year to 3 years reduces total costs; however, RhythmPad GP remains dominated by the Kardia Mobile device.

Incremental cost effectiveness results from Scenario G, which investigates the impact of extending the lifespan of the Rhythmpad GP device from 1 year to 3 years (using 12-lead ECG in primary care, 2 days to 12-lead ECG) are presented in Table 8.

Table 8 Scenario G: Impact of extending the lifespan of the Rhythmpad GP device from 1 year to 3 years, 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	1.2863	£1,060
RhythmPad*	£517,703	448.573	£2,152	-0.6759	Dominated
Zenicor-ECG	£518,468	449.199	£2,917	-0.0499	Dominated
MyDiagnostick	£521,233	449.024	£5,682	-0.2249	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 Scenario H: Including a QALY decrement for bleeds

In the base case analysis no disutility for bleeds was assumed as robust estimates on utlity of bleeds could not be identified in the literature. As these are rare events of short duration the

impact on QALYs was expected to be minor. To test the impact of the assumption of no QALY loss for bleeds, a value for utility loss and duration of bleed was taken from the apixaban technology appraisal where the company used a disutility for major bleeds of 0.1070 from a standard gamble exercise of patients with AF valuing different health outcomes and adverse events that could hypothetically occur whilst taking anticoagulation. The company in the apixaban submission assumed that major bleeds would last for 14 days although this was an assumption and no justification was provided. Applying the duration of bleed to the utility loss and assuming all bleeds are major means each bleed results in a 0.004 QALY loss. The impact of introducing a disutility for bleeds in the model (using 12-lead ECG in primary care, 2 days to 12-lead ECG) are presented in Table 9. As can be seen, whilst the standard pathway and lead-I devices all lose QALYs as expected, as the total lifetime number of bleeds for the cohort of patients in the model was only 0.017 higher with Kardia Mobile compared to the standard pathway and the QALY loss from bleeds was so small, the impact on incremental QALYs was almost zero and so the introduction of a disutility for bleeds did not affect the ICER per QALY gained.

Table 9 Scenario H: Impact of assuming a QALY loss from bleeds, incremental cost effectiveness analysis

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£514,187	447.901			
Kardia Mobile	£515,551	449.187	£1,364	1.286	£1,060
RhythmPad*	£518,436	448.511	£2,885	-0.676	Dominated
Zenicor-ECG	£518,468	449.137	£2,917	-0.050	Dominated
MyDiagnostick	£521,233	448.962	£5,682	-0.225	Dominated
imPulse	£530,745	448.925	£15,194	-0.262	Dominated

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

4.4 Scenario I: Using alternative sensitivity and specificity estimates for Kardia Mobile from the pooled analysis with interpretation of the trace by EP2

Incremental deterministic cost effectiveness results from Scenario I, which investigates the impact of using the sensitivity and specificity estimates based on interpretation of the Kardia Mobile lead-I ECG trace by EP2 (using 12-lead ECG in primary care, 2 days to 12-lead ECG) are presented in Table 10. Incremental probabilistic cost effectiveness results from Scenario I are presented in Table 11. The CEAC for Scenario I is presented in Figure 2.

Table 10 Scenario I: Impact of using the sensitivity and specificity estimates based on interpretation of the Kardia Mobile lead-I ECG trace by EP2, incremental deterministic cost effectiveness analysis

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYs	ICER/ QALY gained
Kardia Mobile	£514,177	449.181			
Standard pathway	£514,187	447.963	£10	-1.219	Dominated
RhythmPad*	£518,436	448.573	£4,259	-0.608	Dominated
Zenicor-ECG	£518,468	449.199	£4,290	0.018	£242,994
MyDiagnostick	£521,233	449.024	£2,765	-0.175	Dominated
imPulse	£530,745	448.987	£12,277	-0.212	Dominated

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

Table 11 Scenario I: Impact of using the sensitivity and specificity estimates based on interpretation of the Kardia Mobile lead-I ECG trace by EP2, incremental probabilistic cost effectiveness analysis

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYs	ICER/ QALY gained
Kardia Mobile	£521,903	455.16065			
Standard pathway	£522,204	453.96612	£301	-1.1945	Dominated
RhythmPad*	£526,453	454.56963	£1,798	-0.5910	Dominated
Zenicor	£526,518	455.17774	£1,864	0.0171	£109,012
MyDiagnostick	£529,316	455.00675	£4,661	-0.1710	Dominated
ImPulse	£538,857	454.97117	£14,203	-0.2066	Dominated

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

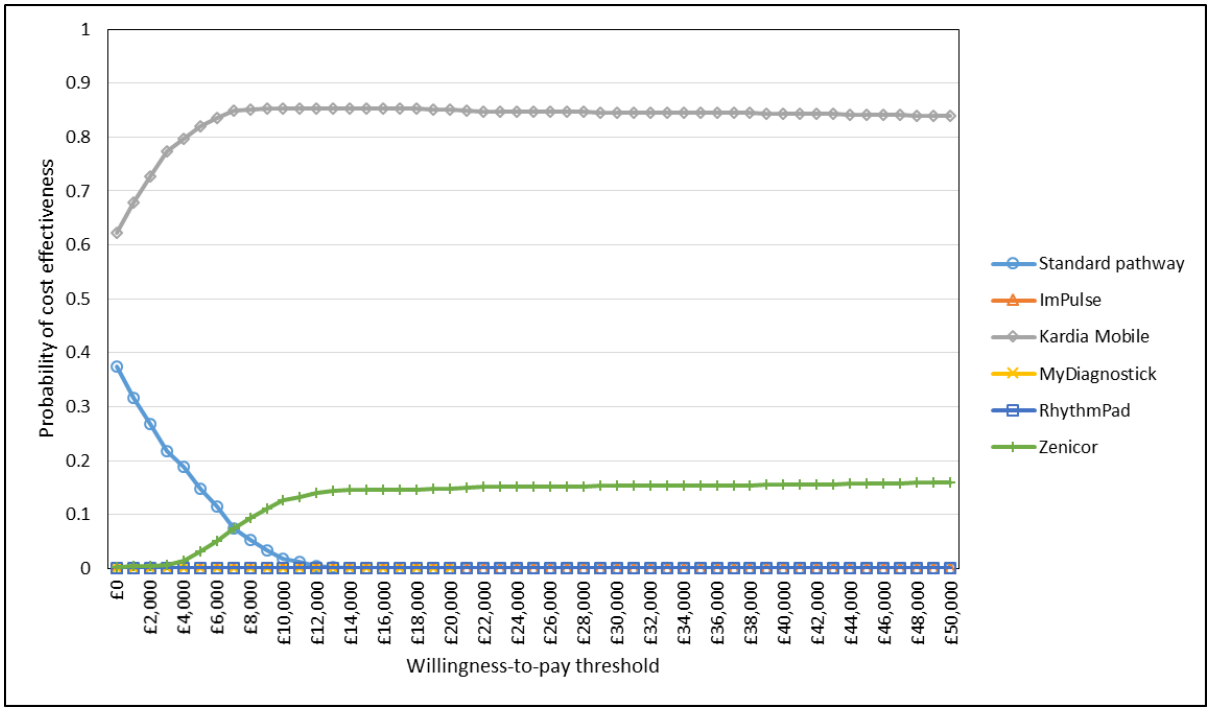

Figure 2 CEAC Scenario I: all lead-I devices

4.5 Scenario J: Assuming that rates of HS are the same for people treated with NOACs who do not have AF as rates of HS for people treated with NOACs who have AF

Incremental cost effectiveness results from Scenario J, which investigates the impact of assuming that rates of HS are the same for people treated with NOACs who do not have AF as the rates of HS for people treated with NOACs who have AF (using 12-lead ECG in primary care, 2 days to 12-lead ECG) are presented in Table 11.

Table 12 Scenario J: Impact of assuming that rates of HS are the same for people treated with NOACs who do not have AF as the rates of HS for people treated with NOACs who have AF, incremental cost effectiveness analysis

Strategy	Costs	QALYs	Incremental Costs	Incremental QALYs	ICER/ QALY gained
Standard pathway	£514,187	447.963			
Kardia Mobile	£516,109	448.697	£1,922	0.734	£2,618
RhythmPad*	£518,957	448.055	£2,848	-0.642	Dominated
Zenicor-ECG	£519,177	448.511	£3,068	-0.186	Dominated
MyDiagnostick	£522,133	448.166	£6,023	-0.530	Dominated
imPulse	£532,320	447.537	£16,211	-1.159	Dominated

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

5 EFFECT OF SENSITIVITY AND SPECIFICITY

High specificity (i.e. high true negative rate which results in a low false positive rate) has a greater impact on the model results than high sensitivity (i.e. high true positive rate), although the impact of high specificity is eroded the lower the sensitivity estimate becomes. For instance, the estimate of specificity for the RhythmPad GP device in the base case analysis is higher than for any other device (97.0%, 95% CI: 95.5% to 100.0%). However, the benefit of higher specificity for the RhythmPad GP device is eroded by an estimate of sensitivity (67.0%, 95% CI: 50.5% to 100.0%) that is substantially lower than the estimate of sensitivity for any of the other devices. In contrast, the Kardia Mobile device has an estimate of specificity (96.8%, 95% CI: 88.0% to 99.2%) similar to the RhythmPad GP device but a much higher estimate of sensitivity (94.0%, 95% CI: 81.5% to 97.7%).

High specificity is important, as it reduces the additional treatment costs associated with people incorrectly diagnosed with AF. It is assumed in the model that people incorrectly diagnosed with AF will remain misdiagnosed for the rest of their lives, so those who begin treatment with NOACs and rate control will remain on treatment for their lifetime. No benefit is assumed from treating people without AF with NOACs and rate control, and a higher risk of bleeding is assumed as a result of treatment with NOACs. Therefore, the higher the false positive rate (i.e. the lower the specificity), the greater are the costs that are accrued from the treatment itself and from treating bleeds associated with NOACs without any associated benefit from treatment.

Sensitivity is important, as the earlier people with AF are diagnosed, the sooner they can begin treatment and reduce their risk of having a cardiovascular event. Low sensitivity (low true positive rate) means that many people with AF may only be identified later and so do not benefit from early treatment with NOACs and rate control. However, the impact of the sensitivity estimate is mitigated in the model by the assumption that people with undiagnosed AF will have their AF diagnosed (and begin treatment) if they experience a cardiovascular event. This means that people with AF that is initially undiagnosed do not accrue the costs of treatment with NOACs and rate control for some months or years, which offsets some of the costs associated with their higher risk of experiencing a cardiovascular event.