Multiple frequency bioimpedance devices (BCM - Body Composition Monitor, BioScan 920-II, BioScan touch i8, InBody S10, and MultiScan 5000) for fluid management in people with chronic kidney disease having dialysis

Erratum to the EAG DAR Addendum

Produced by Aberdeen Health Technology Assessment Group

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This erratum was produced following stakeholder comments on the EAG diagnostic assessment report (DAR). It is intended to replace the results presented in pages 8-10, 13-15, 17-20, and 22-29 of the EAG DAR Addendum that was prepared on 21 December 2016. The main reason for its production relates to a minor structural error identified in the modelled state transitions, which resulted in a small proportion of the peritoneal dialysis cohort (i.e. those listed for transplant and experiencing an incident CV event prior to a transplant) transitioning to the wrong post-transplant state.

The appropriate corrections only change the base case ICERs in the addendum by £2 (scenario 3, Table 1-2) to £8 (Scenario 1, Table 1-2). The subgroup analysis most affected by this change relates to the subgroup of PD patients (Table 5 of the EAG addendum). Here, the ICER changes by only £23 when the transition state is revised, from £14,982 to £14,959. Impacts on further scenario analyses are also minimal.

When checking through the economic results Tables, we also picked up on minor errors in the implementation of two of the subgroup analyses in Table 24 of our report – these are updated here but also have minimal impact on the ICERs: for those on dialysis with no comorbidity the ICER changes from £15,852 to £15,675; for those chronically overhydrated, the ICER changes from £59,701 to £59,382 (including dialysis costs) and from £14,409 to £14,576 (excluding dialysis costs).

Table 1 Deterministic cost-effectiveness scenarios for bioimpedance guided fluid management versus standard practice (including dialysis costs) – updates Table 20 of the original EAG report

Strategy	Mean costs	Incremental costs	Mean QALYs	Incremental QALYs	ICER	NMB
1. Applying the point estimate for the pooled effect of BCM on mortality only (HR = 0.689)						
Standard care	£158,124		2.7014			-£104,097
BCM	£193,805	£35,680	3.2719	0.5706	£62,532	-£128,366
2. Applying the point estimate for the pooled effect of BCM on mortality (HR = 0.689), and a linked effect on non-fatal CV events through the pooled reduction in PWV (HR=0.9318)						
Standard care	£158,124		2.7014			-£104,097
BCM	£193,497	£35,373	3.2791	0.5777	£61,228	-£127,916
3. Applying linked effects on mortality and non-fatal CV events through the pooled reduction in PWV (HR = 0.9318)						
Standard care	£158,124		2.7014			-£104,097
BCM	£165,077	£6,952	2.817	0.1157	£60,095	-£108,736
4. Applying linked effects on mortality and non-fatal CV events through the pooled reduction in PWV (HR=0.9318), and a 10% reduction in BP medications use						
Standard care	£158,124		2.7014			-£104,097
BCM	£165,014	£6,889	2.817	0.1157	£59,551	-£108,673
5. Modelling effects of bioimpedance testing through associations between severe OH and mortality and all cause-hospitalisation (assumes a 28% reduction in severe OH)						
Standard care	£162,059		2.77			-£106,708
BCM	£166,578	£4,519	2.84	0.07	£66,013	-£109,858

6. Modelling effects of bioimpedance guided fluid management through associations between severe OH and mortality and all cause-hospitalisation (assumes a 38% reduction in severe OH)						
Standard care	£162,059		2.77			-£106,708
BCM	£168,019	£5,960	2.86	0.09	£64,157	-£110,810

NMB at willingness to pay of £20,000 per QALY

Table 2 Deterministic cost-effectiveness scenarios for bioimpedance guided fluid management versus standard practice (excluding dialysis costs) - updates Table 21 of the original EAG report

Strategy	Mean costs	Incremental costs	Mean QALYs	Incremental QALYs	ICER	NMB
1. Applying the point estimate for the pooled effect of BCM on mortality only (HR = 0.689)						
Standard care	£46,234		2.7014			£7,793
BCM	£55,579	£9,345	3.2719	0.5706	£16,378	£9,859
2. Applying the point estimate for the pooled effect of BCM on mortality (HR = 0.689), and a linked effect on non-fatal CV events through the pooled reduction in PWV (HR=0.9318)						
Standard care	£46,234		2.7014			£7,793
BCM	£55,272	£9,038	3.2791	0.5777	£15,644	£10,309
3. Applying linked effects on mortality and non-fatal CV events through the pooled reduction in PWV (HR = 0.9318)						
Standard care	£46,234		2.7014			£7,793
BCM	£48,153	£1,919	2.817	0.1157	£16,587	£8,188
4. Applying linked effects on mortality and non-fatal CV events through the pooled reduction in PWV (HR=0.9318), and a 10% reduction in BP medications use						

Standard care	£46,234		2.7014			£7,793
BCM	£48,090	£1,856	2.817	0.1157	£16,044	£8,250
5. Modelling effects of bioimpedance testing through associations between severe OH and mortality and all cause-hospitalisation (assumes a 28% reduction in severe OH)						
Standard care	£47,066		2.77			£8,285
BCM	£48,517	£1,452	2.84	0.07	£21,206	£8,203
6. Modelling effects of bioimpedance guided fluid management through associations between severe OH and mortality and all cause-hospitalisation (assumes a 38% reduction in severe OH)						
Standard care	£47,066		2.77			£8,285
BCM	£48,863	£1,798	2.86	0.09	£19,350	£8,346

NMB at willingness to pay of £20,000 per QALY

Table 3 Breakdown of cumulative costs by categories under clinical effectiveness scenario 3 -updates Table 22 of the original EAG report

	Standard Care	Body Composition Monitor-BCM	Difference BCM versus standard care
Cumulative in-patient hospital costs	£21,795	£22,281	£486
Cumulative dialysis costs	£111,890	£116,923	£5,033
Cumulative medication costs	£10,792	£11,277	£485
Cumulative outpatient costs	£6,076	£6,349	£273
Cumulative acute transplant cost	£1,066	£1,093	£27
Cumulative post-transplant follow-up costs	£6,505	£6,663	£158
Bioimpedance testing costs	NA	£491	£491
Cumulative cost	£158,124	£165,077	£6,952

Deterministic sensitivity analysis

Figures 10 and 11 illustrate the effects of one way sensitivity analysis on key model input parameters, with dialysis costs included (Figure 16) and excluded (Figure 17). These reference ICERs for both these tornado diagrams reflect the revised clinical effectiveness scenario 3 (i.e. a hazard ratio of 0.9318, inferred through the pooled reduction in pulse wave velocity, applied to both all-cause mortality and CV hospitalisation).

When dialysis costs are included, the ICER for bioimpedance guided fluid management is most sensitive to changes in the hazard ratio for the effect on all-cause mortality. The most favourable ICER occurs when the hazard ratio on all-cause mortality is equal to one, as this equalises survival and eliminates the excess dialysis costs incurred in added years. However, under the revised clinical effectiveness scenario 3, the ICER only drops to £40,283 when no effect on mortality is applied (previously it dropped to £21,327). This is due to the smaller effect on CV hospitalisation now being applied.

When dialysis costs are excluded, the ICER remains most sensitive to the hazard ratio on all-cause mortality, but the in this case the least favourable ICER occurs when the hazard ratio is equal to 1.

Results are also moderately sensitive to the hazard ratio for CV hospitalisation, the utility multiplier for haemodialysis, and the cost of haemodialysis. However, when dialysis costs are included, the ICER for bioimpedance guided management now remains well above £30,000 when all parameters are varied within their ranges.

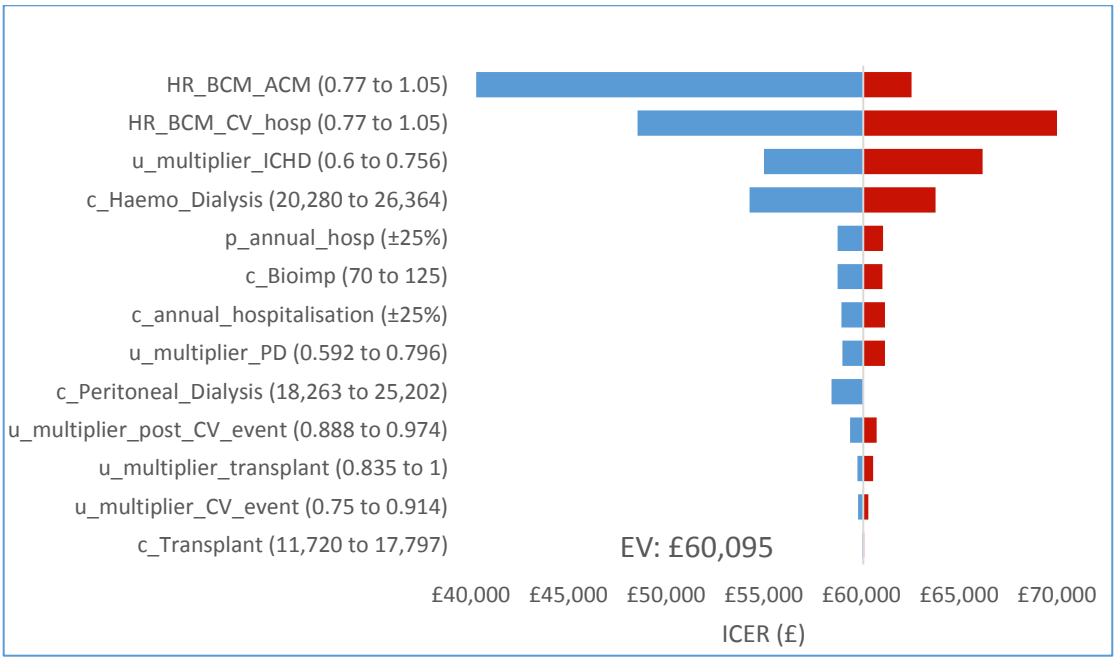

Figure 10 One-way sensitivity analysis: BCM – Body Composition Monitor versus standard care (Clinical effectiveness scenario 3 – including dialysis costs) – updates Figure 16 of original EAG report

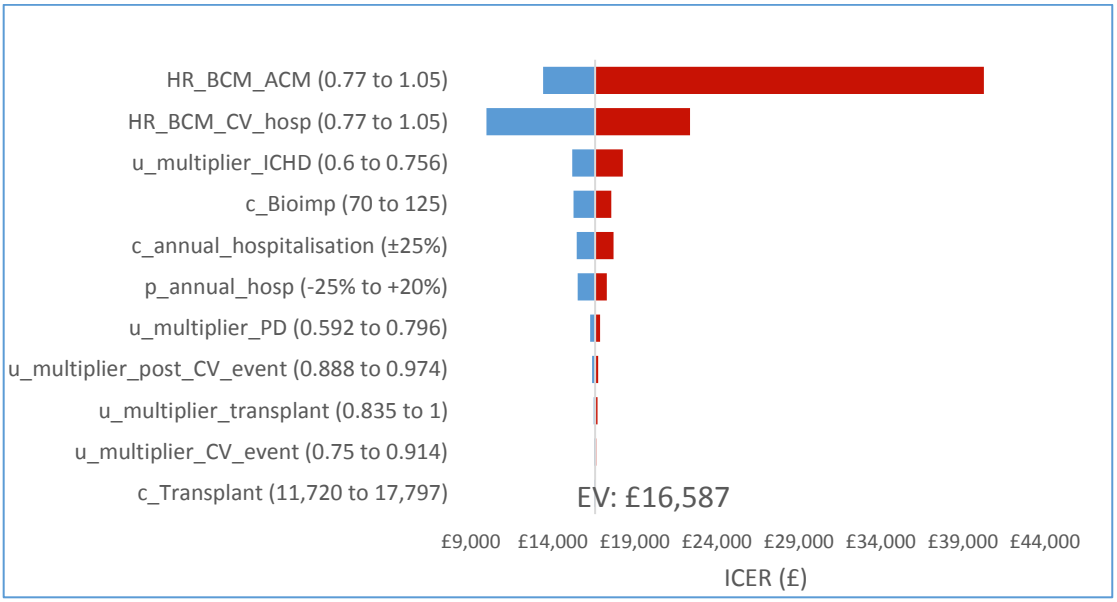

Figure 11 One-way sensitivity analysis: BCM – Body Composition Monitor versus standard care (Clinical effectiveness scenario 3 – excluding dialysis costs) - updates Figure 17 of original EAG report

Table 4 Scenario analyses referent to base clinical effectiveness scenario 3 (all analyses exclude dialysis costs unless stated otherwise) – updates Table 23 of the original EAG report

Strategy	Mean costs	Incremental costs	Mean QALYs	Incremental QALYs	ICER	NMB
Base case scenario 3: applying linked effects on mortality and non-fatal CV events, estimated through the pooled reduction in PWV (HR of 0.9318 applied to both all-cause mortality and CV hospitalisation)						
Standard care	£46,234		2.7014			£7,793
Bioimpedance guided	£48,153	£1,919	2.817	0.1157	£16,587	£8,188
1. Applying an increased cost of monitoring in adults by increasing the number of tests per patient to 12 annually (229.65)						
Standard care	£46,234		2.7014			£7,793
BCM	£48,774	£2,540	2.817	0.1157	£21,953	£7,567
2. Applying the estimated costs of bioimpedance monitoring in paediatric centres with lower throughput (assuming 4 tests annually)* (£245.32)						
Standard care	£46,234		2.7014			£7,793
BCM	£48,850	£2,616	2.817	0.1157	£22,609	£7,491
3. Applying the estimated costs of bioimpedance monitoring in paediatric centres with lower throughput (assuming 12 tests annually)* (£347.06)						
Standard care	£46,234		2.7014			£7,793
BCM	£49,342	£3,108	2.817	0.1157	£26,866	£6,998
4. Applying the cost of BioScan for bioimpedance monitoring (£84.51)						
Standard care	£46,234		2.7014			£7,793
BioScan	£48,071	£1,837	2.817	0.1157	£15,880	£8,269
5. Applying the cost of Inbody S10 for bioimpedance monitoring (£90.36)						

Standard care	£46,234		2.7014			£7,793
Inbody S10	£48,100	£1,865	2.817	0.1157	£16,125	£8,241
6. Applying the cost of MultiScan 5000 for bioimpedance monitoring (£91.22)						
Standard care	£46,234		2.7014			£7,793
MultiScan 5000	£48,104	£1,870	2.817	0.1157	£16,161	£8,237
7. Applying the lowest estimated annual bioimpedance monitoring from Table 15 (£70)						
Standard care	£46,234		2.7014			£7,793
BCM	£48,001	£1,767	2.817	0.1157	£15,273	£8,340
8. Applying the highest estimated annual bioimpedance monitoring cost from 15 (£125)						
Standard care	£46,234		2.7014			£7,793
BCM	£48,267	£2,033	2.817	0.1157	£17,575	£8,073
9. Applying an alternative lower cost per CV hospitalization event (£1386 per CV event)						
Standard care	£44,136		2.7014			£9,891
BCM	£46,110	£1,974	2.817	0.1157	£17,063	£10,231
10. Applying alternative age adjusted utility multipliers for dialysis and post-transplant[123]						
Standard care	£46,234		2.9813			£13,392
BCM	£48,153	£1,919	3.1108	0.1295	£14,822	£14,062
11. Assume bioimpedance guided management results in a 2% improvement in the health state utility over the lifetime of dialysis patients (including dialysis costs)						
Standard care	£158,124		2.7014			-£104,097
BCM	£165,077	£6,952	2.866	0.1646	£42,230	-£107,757
12. Assume bioimpedance guided management results in a 2% improvement in the health state utility over the lifetime of dialysis patients (excluding dialysis costs)						

Standard care	£46,234		2.7014			£7,793
BCM	£48,153	£1,919	2.866	0.1646	£11,656	£9,166
13. Assume bioimpedance guided management results in a 5% improvement in the health state utility over the lifetime of dialysis patients (including dialysis costs)						
Standard care	£158,124		2.7014			-£104,097
BCM	£165,077	£6,952	2.9394	0.238	£29,206	-£106,289
14. Assume bioimpedance guided management results in a 5% improvement in the health state utility over the lifetime of dialysis patients (excluding dialysis costs)						
Standard care	£46,234		2.7014			£7,793
BCM	£48,153	£1,919	2.9394	0.238	£8,062	£10,635
15. Assume bioimpedance guided management results in a 10% reduction in dialysis costs over the lifetime of patients						
BCM	£153,384		2.817			-£97,043
Standard care	£158,124	£4,740	2.7014	-0.1157	Dominated	-£104,097
16. Assume bioimpedance guided management results in a 5% reduction in dialysis costs over the lifetime of patients						
Standard care	£158,124		2.7014			-£104,097
BCM	£159,230	£1,106	2.817	0.1157	£9,560	-£102,890
17. Applying only an effect on non-fatal CV events (HR= 0.9318), excluding any effect on mortality (including dialysis costs)						
Standard care	£158,124		2.7014			-£104,097
BCM	£158,348	£224	2.7069	0.0056	£40,283	-£104,210
18. Applying a smaller effect on mortality and non-fatal CV events (HR = 0.95 for both)						
Standard care	£46,234		2.7014			£7,793
BCM	£47,757	£1,523	2.7853	0.084	£18,135	£7,949
19. Applying a larger effect of bioimpedance monitoring on both CV events and mortality (0.844); consistent with the cross sectional main effect of a unit change in PWV reported by Verbeke et al[106].						

Standard care	£46,234		2.7014			£7,793
BCM	£50,163	£3,929	2.9791	0.2777	£14,145	£9,419
20. Applying differential effects on mortality (HR = 0.95) and non-fatal CV events (HR = 0.844) – including dialysis costs						
Standard care	£158,124		2.7014			-£104,097
BCM	£162,903	£4,778	2.7946	0.0933	£51,222	-£107,010
21. Applying differential effects on mortality (HR = 0.95) and non-fatal CV events (HR = 0.844) – excluding dialysis costs						
Standard care	£46,234		2.7014			£7,793
BCM	£47,359	£1,125	2.7946	0.0933	£12,054	£8,534
22. Excluding all non-CV causes of hospitalisation form the analysis – including dialysis costs						
Standard care	£144,951		2.7138			-£90,676
BCM	£151,315	£6,364	2.83	0.1163	£54,726	-£94,714
23. Applying no effects of bioimpedance monitoring beyond 3 years; HR for all-cause mortality and CV hospitalisation = 0.9318 up to three years						
Standard care	£46,234		2.7014			£7,793
BCM	£47,531	£1,297	2.7663	0.065	£19,963	£7,795
24. Applying no effects of bioimpedance monitoring beyond 3 years; HR for all-cause mortality and CV hospitalisation = 0.95 up to three years						
Standard care	£46,234		2.7014			£7,793
BCM	£47,308	£1,074	2.7488	0.0474	£22,642	£7,667

*Note, these scenarios are not conducted for child cohorts, they just reflect higher estimated costs of bioimpdence testing based on the level of throughput observed in paediatric dialysis centres; NMB at willingness to pay of £20,000 per QALY

Table 5 Subgroup analysis (using clinical effectiveness scenario 3 unless otherwise stated) - updates Table 24 of the original EAG report

Strategy	Mean costs	Incremental costs	Mean QALYs	Incremental QALYs	ICER	NMB
1. People on dialysis who have comorbidities and higher hospitalisation rate*						
Standard care	£47,021		2.6974			£6,927
BCM	£48,961	£1,940	2.813	0.1156	£16,780	£7,299
2. People on dialysis with no comorbidities and lower hospitalisation rate*						
Standard care	£42,638		2.7166			£11,693
BCM	£44,456	£1,818	2.8325	0.116	£15,675	£12,195
3. People on haemodialysis (start age: 67; years on dialysis: 3)						
Standard care	£45,833		2.5803			£5,773
BCM	£47,763	£1,930	2.6933	0.113	£17,078	£6,103
4. People on peritoneal dialysis (start age: 64; years on dialysis: 2)						
Standard care	£53,237		3.3991			£14,745
BCM	£55,021	£1,783	3.5183	0.1192	£14,959	£15,346
5. Mixed haemodialysis/peritoneal dialysis cohort aged 55						
Standard care	£80,080		4.7224			£14,368
BCM	£82,251	£2,171	4.8502	0.1278	£16,986	£14,753
6. Patients listed for a transplant*						
Standard care	£87,370		4.1844			-£3,682
BCM	£89,563	£2,193	4.2891	0.1047	£20,950	-£3,781

7. Patients not listed for transplant*						
Standard care	£39,807		2.4696			£9,586
BCM	£41,683	£1,876	2.587	0.1174	£15,980	£10,058
8. Chronically overhydrated patients only, at increased risk of mortality and all-cause hospitalisation; using modelling structure and assumptions of clinical effectiveness scenario 6 (38% reduction of chronic overhydration with bioimpedance monitoring relative to standard practice) – dialysis costs included						
Standard care	£119,413		2.04			-£78,613
BCM	£168,019	£48,606	2.86	0.82	£59,382	-£110,819
9. Chronically overhydrated patients only, at increased risk of mortality and all-cause hospitalisation; using modelling structure and assumptions of clinical effectiveness scenario 6 (38% reduction of chronic overhydration with bioimpedance monitoring relative to standard practice) – dialysis costs excluded						
Standard care	£36,932		2.04			£3,868
BCM	£48,863	£11,931	2.86	0.82	£14,576	£8,337

*Note, the model is not designed to adjust for different mortality rates in these subgroups; NMB at willingness to pay of £20,000 per QALY

Probabilistic cost-effectiveness results

For comparison with the deterministic results in Table 1 and 2, Tables 6 and 7 presents the results for the revised clinical effectiveness scenarios 3 and 4 based on 1000 probabilistic iterations of the model, with dialysis costs included (Table 6) and excluded (Table 7). The effects in scenario 1 remain unchanged from the original EAG report, but are included for comparison.

The point estimates for the ICERs remain very similar to the deterministic ICERs. However, with the greater uncertainty surrounding the pooled effect of bioimpedance monitoring on PWV, there is greater uncertainty surrounding the cost-effectiveness results.

With dialysis costs included, the probability of bioimpedance testing being cost-effective is ~13% in the revised effectiveness scenarios 3 and 4 (previously < 6%).

With the dialysis costs excluded, the probability of bioimpedance testing being cost-effective is now ~61%-63% in the revised effectiveness scenarios 3 and 4 (Table 7). This is substantially lower than the previous probabilities of 69%-75% respectively, reflecting the greater uncertainty surrounding the pooled effect in PWV, and consequently the linked effects on all-cause mortality and CV hospitalisation.

The revised incremental cost-effectiveness scatter-plots for bioimpedance testing versus standard practice, and the corresponding cost effectiveness acceptability curves, are presented in Figures 12 and 13 below, for the revised effectiveness scenario 3 (including dialysis costs). The corresponding revised figures with dialysis costs excluded are presented in Figures 14 and 15.

Table 6 Probabilistic cost-effectiveness scenarios for bioimpedance guided fluid management versus standard practice (including dialysis costs) – updates Table 25 of the original EAG report

Strategy	Mean costs	Incremental costs	Mean QALYs	Incremental QALYs	ICER	Probability cost-effective at £20,000 threshold
1. Clinical effectiveness scenario 1; applying the point estimate for the pooled effect of BCM on mortality only						
Standard care	£159,712		2.6868			0.737
BCM	£191,748	£32,036	3.1875	0.5007	£63,983	0.263
2. Clinical effectiveness scenario 3; applying linked effects on mortality and non-fatal CV events through the pooled reduction in PWV (HR = 0.9318 on both CV events and mortality)						
Standard care	£157,558		2.6952			0.875
BCM	£164,632	£7,074	2.8138	0.1186	£59,666	0.125
3. Clinical effectiveness scenario 4; applying linked effects on mortality and non-fatal CV events through the pooled reduction in PWV (HR = 0.9318 on both CV events and mortality), and a 10% reduction in BP medications use						
Standard care	£158,312		2.6887			0.87
BCM	£165,217	£6,906	2.8038	0.1151	£59,981	0.13

Table 7 Probabilistic cost-effectiveness scenarios for bioimpedance guided fluid management versus standard practice (excluding dialysis costs) - updates Table 26 of the original EAG report

Strategy	Mean costs	Incremental costs	Mean QALYs	Incremental QALYs	ICER	Probability cost-effective at £20,000 threshold
1. Clinical effectiveness scenario 1; applying the point estimate for the pooled effect of BCM on mortality only						
Standard care	£45,967		2.7003			0.328
BCM	£53,907	£7,940	3.1884	0.4881	£16,269	0.672
2. Clinical effectiveness scenario 3; applying linked effects on mortality and non-fatal CV events through the pooled reduction in PWV (HR = 0.9318 on both CV events and mortality)						
Standard care	£45,966		2.6905			0.387
BCM	£47,836	£1,871	2.8063	0.1158	£16,150	0.613
3. Clinical effectiveness scenario 4; applying linked effects on mortality and non-fatal CV events through the pooled reduction in PWV (HR = 0.9318 on both CV events and mortality), and a 10% reduction in BP medications use						
Standard care	£46,190		2.6873			0.369
BCM	£48,004	£1,814	2.8017	0.1144	£15,859	0.631

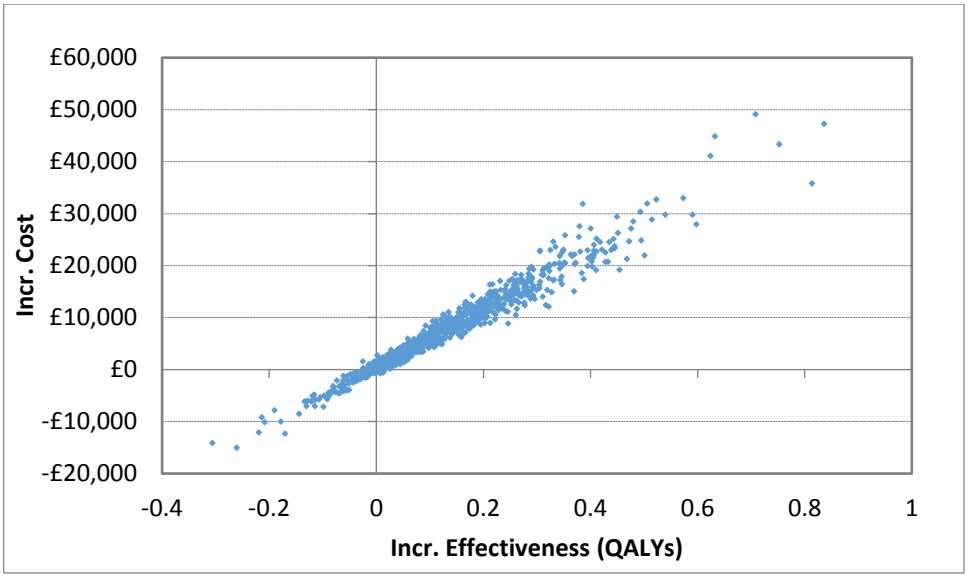

Figure 12 Incremental cost-effectiveness scatter plot: BCM – Body Composition Monitor versus standard care (Clinical effectiveness scenario 3 – including dialysis costs) - updates Figure 20 of the original EAG report

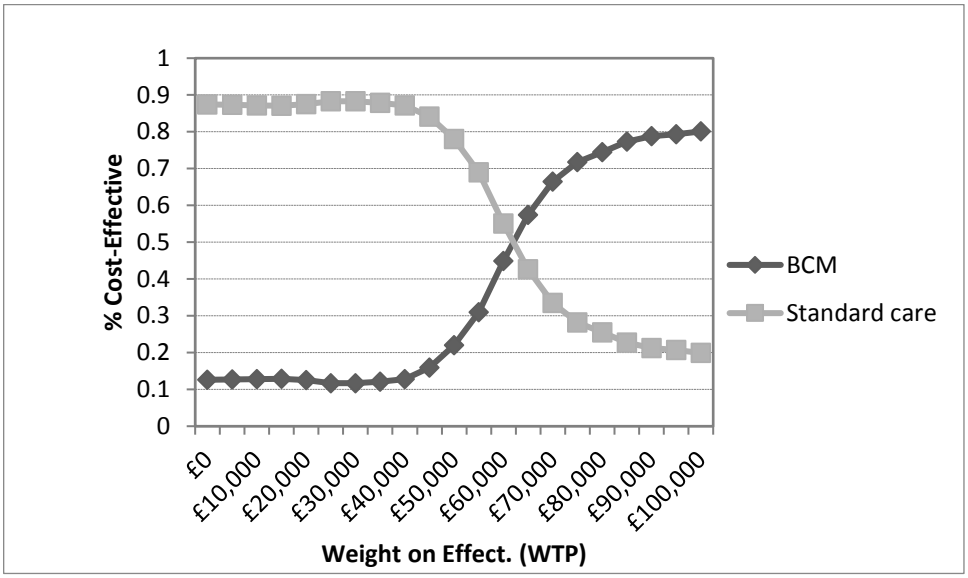

Figure 13 Cost-effectiveness acceptability curves: BCM – Body Composition Monitor versus standard care (Clinical effectiveness scenario 3 – including dialysis costs) - updates Figure 21 of the original EAG report

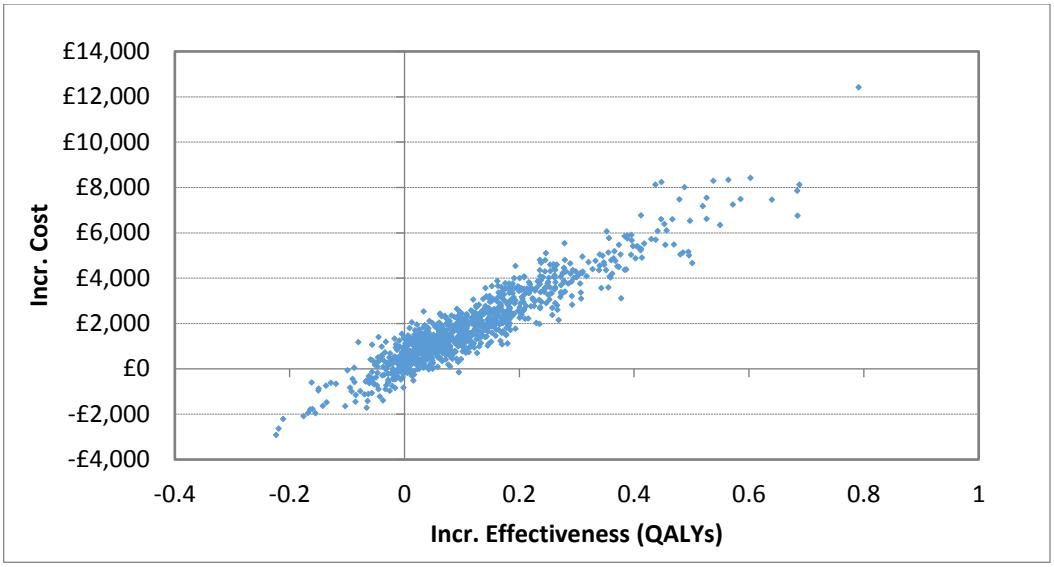

Figure 14 Incremental cost-effectiveness scatter plot: BCM – Body Composition Monitor versus standard care (Clinical effectiveness scenario 3 – excluding dialysis costs) - updates Figure 24 of the original EAG report

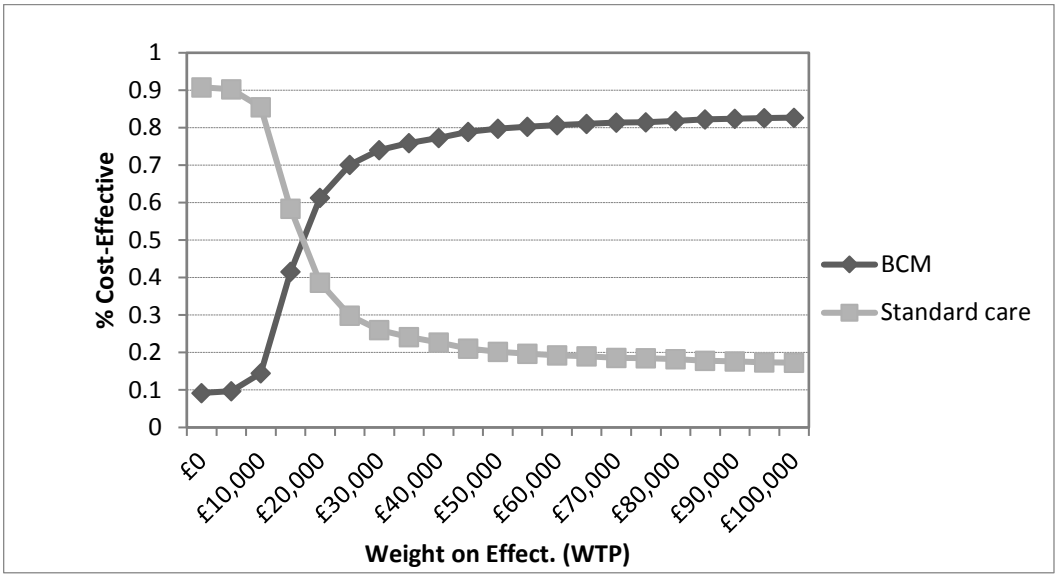

Figure 15 Cost-effectiveness acceptability curves: BCM – Body Composition Monitor versus standard care (Clinical effectiveness scenario 3 – excluding dialysis costs) - updates Figure 25 of the original EAG report

Interpretation of the revised cost-effectiveness results

The revised cost-effectiveness results in the tables above, reflect a slightly smaller and more uncertain effect of bioimpedance monitoring on arterial stiffness, and consequently a smaller linked effect on CV hospitalisation and/or all-cause mortality. This is the consequence of the exclusion of Onofriescu et al. 2012 from the meta-analysis on arterial stiffness (PWV).

The impact of this change on the point estimates of the ICERs for bioimpedance guided management is fairly limited. The ICER point estimates for all the main clinical effectiveness scenarios remain well above £30,000 when dialysis costs are included, and mostly below £20,000 when dialysis costs are excluded from the economic model.

They key impact of the revised effect of bioimpedance testing on PWV, is the increased uncertainty surrounding the cost-effectiveness estimates. With dialysis costs included, the probability of bioimpedance monitoring being cost-effective at standard thresholds remains low. With the dialysis costs excluded, the probability of bioimpedance testing being cost-effective drops to ~61%-63% with the revised effectiveness scenarios 3 and 4 (Table 7). This is substantially lower than the previous probabilities of 69%-75% respectively (Table 26 of the original EAG report).

The revised cost-effectiveness results remain dependent on very limited evidence for the effect of bioimpedance guided fluid management on PWV. With the exclusion of Onofriescu et al. 2012, only two trials, with inconsistent findings, were included in the PWV meta-analysis. This further increases the uncertainty surrounding the validity and robustness of the cost-effectiveness findings based on this surrogate endpoint. Added to this uncertainty is the lack of available evidence by which to link the intervention induced changes in this surrogate endpoint to changes in health outcomes. Therefore, the indirect/linked modelling scenarios rely on observational associations to estimate possible effects of bioimpedance guided fluid management on final health outcomes.