The ARCHITECT and Alinity urine NGAL assays, urine NephroCheck test, and urine and plasma BioPorto NGAL tests to help assess the risk of acute kidney injury for people who are being considered for admission to critical care

ADDENDUM to the EAG assessment report

Produced by Aberdeen HTA Group

Authors Miriam Brazzelli[1]
Lorna Aucott[1]
Magaly Aceves-Martins[1]
Clare Robertson[1]
Elisabet Jacobsen[2]
Mari Imamura[1]
Amudha Poobalan[3]
Paul Manson[1]
Graham Scotland[1,2]
Callum Kaye[4]
Simon Sawhney[5]
Dwayne Boyers[2]

1 Health Services Research Unit, University of Aberdeen, UK
2 Health Economics Research Unit, University of Aberdeen, UK
3 Institute of Applied Health Sciences, University of Aberdeen, UK
4 Consultant in Anaesthetics and Intensive Care Medicine, NHS Grampian, Aberdeen Royal Infirmary, Aberdeen, UK
5 Clinical Lecturer in Nephrology, University of Aberdeen, UK

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REASON FOR ADDENDUM SUBMISSION

This addendum was prepared by the EAG in response to the consultation comments for the assessment, where several comments were made in relation to the test costs applied for NephroCheck and NGAL (BioPorto), the cost applied for fluids in the KDIGO preventive care bundle, and the relative risk parameters applied in the model for averting and reducing the severity of AKI. With respect to the latter issue, the economic model used relative risk estimates derived from Meersch et al.[1] when another study by Gocze et al.[2] was also available. Therefore, in this addendum we present three further scenario analyses that explore: a) alternative test costs for NephroCheck and NGAL (BioPorto); b) alternative costs of fluids in those with a positive test who receive the care bundle; and c) alternative relative risks for the aversion and redistribution ok AKI in the cohort who receive the care bundle.

ADDITIONAL COST-EFFECTIVENESS RESULTS

The three additional scenario analyses are conducted on base case 1 (Table 1) and base case 2 (Table 2). The scenarios are labelled as 1R to 1S, and 2R to 2S.

In the first scenario analysis (1R and 2R) the alternative testing costs for NephroCheck and NGAL (BioPorto) were explored to address the company's (bioMérieux) concerns about the costing assumptions. The following assumptions were made in this alternative scenario as suggested by bioMérieux:

- Excluding all capital cost (on the basis that the company provide the capital equipment without charge)
- Assuming the liquid quality control for NephroCheck is conducted monthly. The monthly test throughput is assumed to be ~104 (=1253/12) where the test throughput of 1253 is based on throughput at an ICU department in a hospital in Leeds (St James teaching hospital) (Hall et al.). The liquid quality control cost is therefore slightly cheaper at £1.91 (= (£100+(2*£49.8))/(1253/12)).
- Assuming wastage may occur for NGAL (BioPorto) due to the four-week shelf-life of the calibrator and test control kit once opened. This results in a slightly more expensive test maintenance cost of £5.46 (= ((385+185)/(104/12))) for NGAL (BioPorto).

The impact on the cost-effectiveness results is very limited and does not change the cost-effectiveness conclusions.

In the second scenario (1S and 2S), we apply a more expensive buffered solution for fluids given as part of the KDIGO care bundle. The more expensive solution was assumed to be Hartmann's solution, at a list price of £3.25 per litre (personal communication with the manufacturer, Baxter). This resulted in a slightly higher care bundle cost (£7.11 higher care bundle cost overall) applied to those with a positive biomarker test result. However, the slightly higher care bundle cost had very little impact on the cost-effectiveness results.

In the third scenario (1T and 2T), the relative risk applied to the averted and redistributed cohort was equal to that reported in Gocze. The relative risk of having AKI versus no AKI, and AKI 1 given AKI and AKI 2/3 given AKI was 0.666, 1.347 and 0.509 respectively. Therefore, the effect sizes are larger than reported in the Meersch et al. study which was used in the base case. Consequently, all the tests accrued higher QALYs and greater ICU cost

savings in these scenarios, with all tests being dominant compared to standard care in base case 1. In base case 2, NephroCheck was the only dominant strategy.

Table 1 Additional scenario analyses on base case 1 (assuming that the NGAL tests can avert AKI)

Scenario	Cost	Inc. Cost	QALY	Inc. QALY	ICER (inc)	ICER vs. SC	p (C/E) @ 20k	p (C/E) @ 20k vs. SC
Base case 1								
Test 3 (NGAL urine - BioPorto)	£22,887	--	6.07332	--	--	Dominant	43.5%	54.6%
Test 2 (NGAL plasma - BioPorto)	£22,900	£14	6.07332	0.00001	£2,694,918	Dominant	11.1%	47.6%
Standard care (Scr)	£22,901	Dominated	6.07296	Dominated	Dominated	--	45.1%	--
Test 4 (NGAL urine - ARCHITECT)	£22,912	Dominated	6.07328	Dominated	Dominated	£32,131	0.1%	41.4%
Test 1 (NephroCheck)	£22,938	Dominated	6.07332	Dominated	Dominated	£101,456	0.2%	31.9%
1R. Alternative test costs for NephroCheck and NGAL (BioPorto)								
Test 3 (NGAL urine - BioPorto)	£22,746	--	6.074431	--	--	Dominant	39.6%	52.5%
Test 2 (NGAL plasma - BioPorto)	£22,758	£12	6.074439	0.000008	£1,621,578	Dominant	12.2%	45.7%
Standard care (Scr)	£22,760	Dominated	6.074090	Dominated	Dominated	--	46.8%	--
Test 4 (NGAL urine - ARCHITECT)	£22,766	Dominated	6.074404	Dominated	Dominated	£16,592	0.9%	42.6%
Test 1 (NephroCheck)	£22,789	Dominated	6.074438	Dominated	Dominated	£80,747	0.4%	34.3%
1S. Alternative solution for fluid assistance (Hartmann's solution)								
Test 3 (NGAL urine - BioPorto)	£23,121	--	6.071715	--	--	Dominant	39.3%	51.5%
Standard care (Scr)	£23,132	Dominated	6.071353	Dominated	Dominated	--	47.8%	--
Test 2 (NGAL plasma - BioPorto)	£23,135	£14	6.071729	0.00001	£1,015,368	£9,202	12.3%	46.7%
Test 4 (NGAL urine - ARCHITECT)	£23,146	Dominated	6.071686	Dominated	Dominated	£41,624	0.3%	40.7%

Test 1 (NephroCheck)	£23,173	Dominated	6.071724	Dominated	Dominated	£112,505	0.3%	31.4%
1T. Alternative RR parameters (Gocze et al.)								
Test 3 (NGAL urine - BioPorto)	£23,079	--	6.082680	--	--	Dominant	49.3%	67.1%
Test 2 (NGAL plasma - BioPorto)	£23,091	£12	6.082690	0.000010	£1,158,117	Dominant	16.8%	62.2%
Test 4 (NGAL urine - ARCHITECT)	£23,107	Dominated	6.082632	Dominated	Dominated	Dominant	0.3%	57.5%
Test 1 (NephroCheck)	£23,129	Dominated	6.082688	Dominated	Dominated	Dominant	0.9%	47.9%
Standard care (Scr)	£23,135	Dominated	6.082137	Dominated	Dominated	--	32.7%	--

Table 2 Additional scenario analyses on base case 2 (assuming that the NGAL tests cannot avert AKI)

Scenario	Cost	Inc. Cost	QALY	Inc. QALY	ICER (inc)	ICER vs. SC	p (C/E) @ 20k	p (C/E) @ 20k vs. SC
Base case 2								
Standard care (Scr)	£22,978	--	6.07277	--	--	--	64.5%	--
Test 1 (NephroCheck)	£23,016	£38	6.07313	0.00036	£105,965	£105,965	29.7%	32.0%
Test 3 (NGAL urine - BioPorto)	£23,049	Dominated	6.07290	Dominated	Dominated	£539,041	5.3%	11.0%
Test 2 (NGAL plasma - BioPorto)	£23,064	Dominated	6.07290	Dominated	Dominated	£633,846	0.3%	7.3%
Test 4 (NGAL urine - ARCHITECT)	£23,065	Dominated	6.07289	Dominated	Dominated	£725,061	0.0%	6.3%
2R. Alternative test costs for NephroCheck and NGAL (BioPorto)								
Standard care (Scr)	£22,865	--	6.07020	--	--	--	65.0%	--
Test 1 (NephroCheck)	£22,899	£34	6.07055	0.00035	£97,745	£97,771	31.2%	33.0%
Test 3 (NGAL urine - BioPorto)	£22,937	Dominated	6.07033	Dominated	Dominated	£581,613	3.1%	9.6%
Test 4 (NGAL urine - ARCHITECT)	£22,951	Dominated	6.07032	Dominated	Dominated	£751,404	0.0%	6.1%
Test 2 (NGAL plasma - BioPorto)	£22,952	Dominated	6.07033	Dominated	Dominated	£686,614	0.7%	7.2%
2S. Alternative solution for fluid assistance (Hartmann's solution)								
Standard care (Scr)	£22,934	--	6.07636	--	--	--	65.5%	--
Test 1 (NephroCheck)	£22,977	£42	6.07671	0.00035	£119,969	£119,969	29.1%	31.1%
Test 3 (NGAL urine - BioPorto)	£23,002	Dominated	6.07648	Dominated	Dominated	£545,923	4.6%	11.3%
Test 2 (NGAL plasma - BioPorto)	£23,017	Dominated	6.07648	Dominated	Dominated	£650,943	0.8%	8.3%

Test 4 (NGAL urine - ARCHITECT)	£23,019	Dominated	6.07647	Dominated	Dominated	£751,697	0.0%	6.3%
2T. Alternative RR parameters (Gocze et al)								
Test 1 (NephroCheck)	£23,048	--	6.06367	--	--	Dominant	38.9%	46.9%
Standard care (Scr)	£23,051	Dominated	6.06314	Dominated	Dominated	--	45.6%	--
Test 3 (NGAL urine - BioPorto)	£23,099	Dominated	6.06341	Dominated	Dominated	£175,838	12.6%	29.5%
Test 2 (NGAL plasma - BioPorto)	£23,115	Dominated	6.06342	Dominated	Dominated	£227,728	2.9%	25.1%
Test 4 (NGAL urine - ARCHITECT)	£23,118	Dominated	6.06339	Dominated	Dominated	£268,527	0.0%	20.9%

REFERENCES

1. Meersch M, Schmidt C, Hoffmeier A, et al. Prevention of cardiac surgery-associated AKI by implementing the KDIGO guidelines in high risk patients identified by biomarkers: the PrevAKI randomized controlled trial. *Intensive Care Med* 2017; 43(11), 1551-61.
2. Gocze I, Jauch D, Gotz M, et al. Biomarker-guided Intervention to Prevent Acute Kidney Injury after Major Surgery. *Ann Surg* 2018; 267(6), 1013-20.