NICE National Institute for Health and Care Excellence

DIAGNOSTICS ASSESSMENT PROGRAMME

Tests to help assess risk of acute kidney injury for people being considered for critical care admission (ARCHITECT and Alinity i Urine NGAL assays, BioPorto NGAL test and NephroCheck test)

Diagnostics Consultation Document – Comments

Diagnostics Advisory Committee date: 29 January 2020

THEME: Economic model

Comment number	Name and organisation	Section number	Comment	NICE response
1	The Renal Association	3.25	We note that the staff costs for all biomarker tests were calculated as £37.62. The NephroCheck, Bioporto NGAL (urine), and Abbott NGAL test are very simple, ie they only require a urine sample which is put on a strip and read 20 minutes later. It can be performed by any member of the medical or nursing team. The costs of £37.62 appear high. This is different from the BioPorto NGAL (plasma) test which requires a blood sample.	Thank you for your comment which the committee considered. Discussions with clinical experts at scoping indicated that all the biomarkers included in this diagnostic assessment, including the urine biomarkers (NephroCheck; urine NGAL BioPorto; and urine NGAL ARCHITECT, Abbott), would be analysed in a laboratory and would not be implemented as point of care tests in the NHS. This was consistent with the diagnostic accuracy studies included in this assessment where the biomarkers were measured in clinical or hospital laboratories. The External Assessment Group (EAG) explained that reducing the time taken to collect a urine sample from 15 to 2 minutes and reducing a biochemist's time for analysis of all tests from 20 to 5 minutes does not materially change the base case

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				conclusions, with no clearly cost-effective strategy under either of the base case model specifications. The committee noted that increasing automation of clinical laboratories means that samples can potentially be handled with less staff time, and that costs related to this used in the EAG's model may have been overestimated. However, this was unlikely to have a large effect on cost effectiveness results to the extent that it would change the committee's decision and recommendations.
2	The Renal Association	3.28	It is not clear why "the outcomes 5 years post transplant and transplant failure" were included in the base-case assumptions and modelling.	Thank you for your comment which the committee considered. The EAG explained that the economic model is exploratory and consequently it is intended to capture the greatest possible scope of long-term consequences of detecting acute kidney injury while a patient is in hospital. In the model, after leaving hospital patients can develop chronic kidney disease and subsequent events including end stage renal disease, dialysis or

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				kidney transplant (which can either be a success or failure). Therefore, the EAG considered it important to include kidney transplant in the economic model. They used 5-year data for modelling kidney transplant because these were the only suitable data available when the model was developed and populated (obtained from the UK Renal Registry Annual Report).

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THEME: Current practice in the NHS

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3	The Renal Association	4.2	The committee made the assumption that patients in the NHS should already be having all available interventions to prevent AKI. Unfortunately, this is not the case in routine clinical practice. A recent paper by Kullmar M et al which includes patients from 2 large hospitals in the NHS shows that adherence with the KDIGO recommendations after cardiac surgery is poor. (Kullmar M et al. Anesth Analg 2020;Jan 8)	Thank you for your comment which the committee considered. The committee considered the results of Kullmar et al. and noted that it showed poor adherence to KDIGO recommendations after cardiac surgery in a study that included patients from 2 NHS hospitals. Clinical experts acknowledged that there was likely to be variation in implementation of care bundles in practice across the NHS. The committee considered that if preventative measures for acute kidney injury are not already routinely used in a hospital, they may not be used even in the event of a positive result from the NephroCheck or NGAL tests; reducing any benefit of the tests in guiding preventative care. The committee concluded that there was considerable uncertainty about who in

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				the NHS could benefit from the tests (this is described in section 4.2 of the diagnostics guidance document).

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THEME: Clinical significance of the different stages of acute kidney injury

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4	The Renal Association	4.3	The committee felt that there was uncertainty about the clinical significance of the different stages of AKI. This is surprising given the number of papers in the literature (including patients in the NHS) showing that the risk of mortality, short-term complications and long-term effects increases with increasing AKI stage.	Thank you for your comment which the committee considered. Clinical experts did agree that there is stronger evidence linking later stage acute kidney injury with adverse clinical outcomes. The committee acknowledged that section 4.3 in the diagnostics consultation document oversimplified this issue. This section has been amended to note that studies identified for this assessment varied in which stage of acute kidney injury the tests were detecting; from any stage of the condition to just higher stages. Clinical experts commented that the staging of the condition in classification systems (such as Kidney Disease Improving Global Outcomes [KDIGO]) was developed by clinical consensus and there was uncertainty about the clinical significance of sub-clinical or early stage (stage 0 or stage 1) acute kidney injury and its correlation with clinical outcomes. The

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THEME: Clinical significance of the different stages of acute kidney injury

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				committee concluded that there was uncertainty about how well the tests could detect emerging acute kidney injury, and the clinical significance of what they detect in studies of test accuracy.

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THEME: Further evidence (1): Trial in progress

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5	The Renal Association	General comment	The PrevAKI II study has been completed. It is a multi-center study in 12 hospitals including 2 hospitals in the UK using the same protocol as the PrevAKI as the study by Meersch et al. The results will be available this year.	Thank you for your comment which the committee considered. The committee noted that results from this study are not yet available. NICE reviews guidance 3 years after publication to ensure that any relevant new evidence is identified. However, NICE may review and update the guidance at any time if significant new evidence becomes available; please send any significant new evidence to diagnostics@nice.org.uk

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THEME: Further evidence (2): Unpublished study

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6	University of Liverpool		Please find attached a copy of our manuscript entitled 'Identifying Critically Ill Children at High Risk of Acute Kidney Injury and Renal Replacement Therapy'	Thank you for your comment and provided document which the committee considered. The results of this study were provided as academic in confidence.

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THEME: Factual accuracy / Further comments

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7	The Renal Association	3.8	The document states that “no studies were identified in people who had major non-cardiac surgery”. We would like to point out that the BigpAK study by Gocze et al was conducted in patients after major non-cardiac surgery. (Ann Surg 2018;267:1013)	Thank you for your comment which the committee considered. The Gocze et al. study was considered in the diagnostics assessment report and also the guidance (see section 3.24 of the diagnostics guidance document). Section 3.8 of the diagnostics consultation document discussed the availability of evidence on the sensitivity and specificity of the NephroCheck test to detect emerging acute kidney injury, which Gocze et al. does not provide data for.
8	Abbott Diagnostics		Abbott will not return comments, we are satisfied with the consultation document.	Thank you for your comment which the committee considered.
9	Royal College of Physicians		The RCP is grateful for the opportunity to respond to the above consultation.	Thank you for your comment which the committee considered.

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			We would like to endorse the response submitted by the Renal Association (RA).	
10	BioPorto Diagnostics		We have not any further comments to the document	Thank you for your comment which the committee considered.