

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Health Technology Evaluation

Review Decision

Outcome of review of [MTG3: CardioQ-ODM oesophageal doppler monitor](#)

1. Background

The guidance was published in March 2011. At the GE meeting of 26 April 2016, it was agreed that we would consult on the recommendations made in the [review proposal](#). A 4-week consultation has been conducted with consultees and commentators and the responses are presented below (see Appendix 1).

2. Review proposal put to consultees

MTG3 should be updated within a NICE programme other than MTEP, in this case a suitable clinical guideline. It was also proposed that MTG3 should remain active until the guidance is updated and new guidance published. The current version of the technology (CardioQ-ODM+) would not be referred to on the guidance page, as this has an additional operating function to CardioQ-ODM, which is outside of the scope of MTG3.

3. Rationale for the review proposal

The guidance review¹ found that significant changes in the care pathway involving CardioQ-ODM meant there was a case for updating the guidance from both clinical and economic perspectives. Since MTG3 was published, system-wide initiatives to improve perioperative care, such as the Enhanced Recovery Programmes, may have resulted in interventions, including intraoperative fluid management (IOFM) using technologies such as CardioQ-ODM, becoming widely adopted for major surgery.

These changes meant that the cost-saving recommendations based on the original cost modelling may no longer be valid in the current care pathway, in which the average length of stay is shorter. In addition, CardioQ-ODM is now marketed as a newer version (CardioQ-ODM+), and a number of new randomised controlled trials (RCTs) and systematic reviews have been published involving CardioQ-ODM and its comparators and alternatives.

4. Recommendation post-consultation

MTG3 should be updated in a suitable clinical guideline, and the current guidance transferred to the static list and a statement added to overview page on the website to explain the review of the guidance and that a new version of the technology is available.

5. Rationale for the post-consultation recommendation

¹ The review proposal was informed by additional work undertaken by an External Assessment Centre which is published on the NICE website alongside this review decision.

The company did not agree that care pathways had changed sufficiently to warrant an update of MTG3. However, other consultees agreed with the review proposal to update the guidance within a suitable guideline on the basis that the care pathway had changed. One consultee specifically commented that the cost savings proposed in MTG3 were no longer realisable in clinical practice.

Consultees other than the company either made no comment on a review proposal recommendation or supported an update within a suitable guideline, because the additional functionality of the current version of the device, CardioQ-ODM+, meant that it would be used in different ways to the original device evaluated in MTG3.

6. Summary of consultee and commentator responses

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how review decisions are taken. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees (see Appendix 1).

Paper signed off by: Mark Campbell, Associate Director Date 12 May 2017

Appendix 1. MTG3 review proposal - consultation comments (Incorporates minor amendments after consultees were offered opportunity to fact check their comments. NICE responses are unchanged.)

Respondent: Deltex Medical Group plc (1)	NICE response
<p>Response to proposal: Disagrees with proposal to update MTG3</p> <p>Deltex Medical believes that the recommendations in MTG3 remain an important opportunity for the NHS to improve outcomes and reduce costs. Deltex Medical does not believe that the criteria to update MTG3 apply as there has been no material change to either the clinical evidence supporting CardioQ-ODM or the clinical environment of NHS surgical care. Deltex Medical notes below certain areas where NHS patients might benefit from clarification of MTG3.</p> <p>Clinical evidence re CardioQ-ODM</p> <p>Deltex Medical's assessment is that the evidence base supporting the use of CardioQ-ODM to guide fluid management via stroke volume optimisation during surgery has strengthened further since MTG3 was published and that MTG3 should not be updated with respect to the CardioQ-ODM evidence base other than to extend the scope of the recommendation to paediatric surgery. In particular, the results of the first multi-centre RCT of ODM guided stroke volume optimisation during surgery, which is also the largest ever ODM RCT, have been presented at a major international clinical meeting during this consultation process. These results show highly significant reductions in both complications and the numbers of individual patients suffering complications and in length of hospital stay. Substantial and significant reductions in specific complications were also reported including Acute Kidney Injury, pneumonia, superficial and deep surgical site infections and cardiopulmonary oedema. These results confirm both the validity of MTG3 and that its implementation should be a high priority across the NHS.</p> <p>Clinical evidence re comparator technologies to CardioQ-ODM</p> <p>Deltex Medical notes that, since the publication of MTG3, a body of clinical evidence has been established in respect of the use of comparator technologies during surgery to guide stroke volume optimisation fluid management strategies. The results of these trials have demonstrated that such technologies, which measure different physiological markers to ODM in different parts of the body, specifically Pulse Pressure Waveform Analysis ('PPWA') and Impedance Cardiography ('IC'), are</p>	<p>Thank you for your comments, which have been noted. Please see our responses below:</p> <p>The External Assessment Centre (EAC) report for the guidance review for MTG3 CardioQ and Cedar's systematic review for intraoperative fluid management technologies published in 2013 identified several changes to the care pathway which may affect the cost savings case for MTG3. These include:</p> <ul style="list-style-type: none">- introduction of enhanced recovery programmes (ERPs)- introduction and subsequent withdrawal of CQUIN incentivisation for IOFM- use of CardioQ and other comparator IOFM technologies alongside ERPs <p>The reports above and other consultees indicate that the changes to the technology (the new version, CardioQ-ODM+) and the care pathway are such that the original guidance cannot be updated. As described in the interim addendum for guidance review, MTG3 will now be transferred to the static list until it is updated as part of a new clinical guideline</p> <p>The EAC report also identified that further assessment of the clinical evidence was required by meta-analysis. Updating MTG3 as part of a clinical guideline will allow the</p>

<p>unable to deliver the same benefits as CardioQ-ODM. The results of these studies re PPWA reinforce the position set out in Appendix E of the manufacturer's submission re MTG3.</p> <p>Deltex Medical notes that NICE commissioned a separate report from its External Assessment Centre ('EAC') on this Appendix at the time of the original MTG3 and recommends that this supplemental report be updated and published as part of the Review process. Deltex Medical notes that this additional EAC report was published at the time of MTG3 without the manufacturer having the opportunity to comment on its factual accuracy. As a result, Deltex Medical is unable to comment on the completeness or factual accuracy of the EAC report. Deltex Medical notes that MTEP considers all sources of evidence and not just RCT evidence, however the EAC report appears only to have identified RCT evidence. Deltex Medical further recommends that NICE re-emphasises that MTG3 applies only to CardioQ-ODM either by clarifying the generic wording at the start of all MTGs or by updating MTG3 to identify specific technologies over which the clinical evidence supports the dominance of CardioQ-ODM. Deltex Medical has requested access to the EAC report from NICE but this has been denied.</p> <p>Clinical environment</p> <p>Deltex Medical believes that there has been no material change to the clinical environment of major surgery since MTG3: patients continue to suffer avoidable complications which lead to additional suffering and cost in both the short and long term.</p> <p>Implementation</p> <p>As noted in Deltex Medical's MTG3 Review Submission, use of CardioQ-ODM has fallen at over 20% per annum in calendar years 2014 and 2015 since NHS England decided to abandon CQUIN pre-qualification in respect of high impact innovations which specifically included ODM. In more than a decade up to the end of 2013 adoption of ODM in surgery had grown at an average of over 20% per annum, including prior to MTG3. As a result c17,000 fewer UK patients benefited from CardioQ-ODM in 2015 than in 2013 at a cost to the NHS of c£19m annually based on MTG3 identified average savings of £1,100 per patient. In the NHS in England, failure to adopt ODM means, compared to the NICE MTG3 costing template, that over 800,000 patients a year are being denied ODM through non-compliance with MTG3. Cumulatively this equates to missed savings of over £4 billion since MTG3 was published as well as several hundred thousand patients suffering avoidable complications with consequent reductions in likely post-operative survival.</p> <p>Deltex Medical notes that, in its view, the National Technology Adoption Pack on IOFM hampered</p>	<p>benefits and costs of fluid optimisation as an intervention to be considered.</p> <p>The EAC report has been published alongside the review decision. The wording at the start of MTG3 applies to all guidance produced by MTEP, according to our process and methods guides.</p> <p>NICE is a non-departmental arms-length public body, accountable but independent of the Department of Health and the government. CQUIN and the Innovation Scorecard are not within NICE's remit. At the time of publication</p>
---	--

<p>the implementation of MTG3 in two key ways. Firstly it only identified a fraction of major surgery as priority cases for IOFM and did not define factors making a patient high risk regardless of procedure. Secondly it bundled together all IOFM technologies without objective evaluation and, in its second iteration, removed the references to studies altogether.</p> <p>Deltex Medical notes that the NHS Innovation Scorecard incorrectly describes MTG3 as being about “cardiac output monitoring” rather than specific to CardioQ-ODM. Furthermore it bundles data from manufacturers who do not sell ODM products and whose products have repeatedly been shown to not be interchangeable with ODM, to be unable able to guide safely stroke volume optimisation during surgery or to not reduce either post-operative complications or length of stay. Deltex Medical is not aware of any other piece of NICE guidance where compliance (use of CardioQ-ODM) has been confused by NHS.</p>	<p>of the Adoption Pack, NTAC was not part of NICE.</p>
<p>Respondent: Royal College of Anaesthetists</p> <p>Response to proposal: Proposes that new guidance is produced</p> <p>General</p> <p>While it is entirely reasonable for NICE to re-examine the evidence for oesophageal Doppler monitoring we encourage the production of new guidance as soon as possible.</p> <p>NICE MTG3 divided our specialty. The existing guidance was strongly criticised from within the specialty with a number of cogent points being raised (see Anaesthesia, 2011 Dec; 66(12):1081-3); whilst other guidelines have promoted it.</p> <p>There may have been considerable confusion in the interpretation of NICE MTG3 when CQUIN payments, around the time of the Enhanced Recovery Partnership Programme, were linked to mandatory cardiac output monitoring. This was not helpful as the guidance was no stronger than “consider the use in...”</p> <p>There is also a strong feeling that in fully implemented enhanced recovery programmes, cardiac output monitoring may be unnecessary in many cases. Enhanced Recovery is a package of clinical measures with a certain goal; Cardio Q ODM (or is it Q+?) is a specific technology designed simply to estimate cardiac output. The two things are completely different. It is entirely possible – with success – to implement enhanced recovery without ever using the ODM. Doppler monitoring is not integral to enhanced recovery, and although earlier guidance from the DoH implied this, the Doppler was merely used as an example. Rather, an estimate of cardiac output is integral and</p>	<p>NICE response</p> <p>Thank you for your comments and insights into the changes in the care pathway and the technology with the introduction of the newer version, CardioQ-ODM+. Your comment supports the view changes in the care pathway and the technology are such that the original guidance cannot be updated. It is now proposed that MTG3 is transferred to the static list until it is updated as part of a clinical guideline. Updating the guidance within a new clinical guideline will allow evaluation of cardiac output monitoring as part of intraoperative fluid optimisation.</p> <p>A statement has been added to the overview page on the website to explain the review of</p>

there are many ways to estimate cardiac output. More focus in the original guidance should have been placed on the comparison of the accuracy of the devices in estimating the quantity being measured (i.e., cardiac output). In other words, simply because trials have shown enhanced recovery programmes improve outcomes, it does not mean that ODM is beneficial. At most, it means that the information provided by ODM is potentially beneficial when combined with an enhanced recovery approach. It is essential to separate the accuracy of a technology in measuring what it purports to measure from the way in which this accurate information is used.

The suggestion that the Doppler element of the Q+ can be regarded in isolation is not supported by any cogent argument. There is a suggestion that the PPV function is 'not recommended' and MTG3 has made the arbitrary decision not to focus on this. However, the reality is that the function exists and the real question (amenable to further study) is how and to what extent this influences the overall interpretation of the data and hence, patient outcomes. If PPV was not intended to be integral to the device function, then why incorporate it at all? These statements come across as both confused and confusing and do not seem a persuasive justification for assessing the Doppler function in isolation.

We have concerns that some phraseology is highly inappropriate, such as, the implication that central line CVC catheters are rarely used. Can this be substantiated by any evidence? There is a concern that practitioners may as a result be led to abandoning a technique that is well established and often necessary (e.g., for giving drugs).

We recommend that, if the current guidance should stand then the actual wording of the guidance be highlighted (i.e. **Consider for use in...**etc.). In other words, that the general principles of the guidance (i.e. consider cardiac output monitoring in certain patients) be emphasised rather than that a single technology be used. This is of course, notwithstanding that the words 'consider for use in' also mean *pari passu* 'consider should **not be used** in...'.

Furthermore, we advise that new guidance be produced as soon as possible. There are a number of large multicentre RCTs in elective and emergency surgery patients that will help craft these guidelines that are underway and supported by the College. The nature of these trials suggests equipoise and their design is consistent with a "consider in..." approach for selected patients in the context of local results and guidance.

Recommendation

Given that the review has noted that the likes of ERAS programmes have possibly affected the positive case for OD, shouldn't centres be encouraged to review their progress with regards to the

the guidance and that a new version of the technology is available.

Any new RCT evidence can be considered as part of the development of a suitable clinical guideline.

successful implementation of Enhanced Recovery and consider if NICE MTG 3 guidance is pertinent to their current practice. There are reports that progress in the adoption of ERAS stalled in 2012 and the National Audits of Colorectal Surgery Outcomes supports this view.

Technology availability & changes

The original guidance is for ODM not ODM+. So surely the guidance has no remit for ODM+. ODM is no longer available for purchase.

Despite the manufacturers stating that the additional PPV should not to be used to guide IOFM, users will do what they will.

Changes to clinical practice

Advice from 2 clinical experts – we question how reasonable it is to have only 2 opinions on an aspect of care which splits the specialty. Where is the evidence on the comments regarding CVC usage?

Summary of new evidence and implications for review

Commentary on Randomised Control Trials (RCTs) does not match the table.

We received information that this was clinical practice in some hospitals; use of central venous catheters may be considered in the development of a suitable clinical guideline.

Thank you for highlighting an inconsistency in the review proposal. The follow 2 corrections should be made:

In the table of new studies, Phan 2014 should be “No difference for any complications or for minor complications. For major complications: favoured GDT.” under complications.

In section 7 - Summary of new evidence and implications for review, this should state “Of the 12 studies, two report a shorter hospital stay in patients treated with CardioQ-ODM (Ibrahim 2015 [difference 1.4 days] and El Sharkawy [difference 1.3 days]).”

<p>Respondent: Department of Health</p> <p>Response to proposal: No comment</p> <p>I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.</p>	<p>NICE response</p> <p>Comment noted. No action required.</p>
<p>Respondent: Northern, Eastern and Western Devon Clinical Commissioning Group</p> <p>Response to proposal: No comment</p> <p>Local acute trusts in Devon have expressed some concerns and difficulties in the uptake of this technology locally. Anaesthetists at the local hospitals have reported that use of the ODM was trialled but it was found difficult to use and as such different systems for non-invasive cardiac output measurement are preferred and in use. It was reported that ODM devices are not ideal as they are expensive, the signal is affected by diathermy and the probes can be awkward to site. It was also reported that using these monitors during contemporary elective surgery is not beneficial and that other methods are available; the most user friendly are the ones that analyse the pulse variability of an arterial line trace or pulse oximeter.</p> <p>Uptake of this technology was the most significant area of estimated saving identified on the cost saving list published by NICE in April 2015, developed in recognition of the challenging financial situation that the NHS is facing. We contacted local acute trusts in Devon in order to establish the current local position and uptake of this technology. The responses on their experience of the use of this technology indicate that this guidance has not represented the cost savings originally anticipated. As this represents the experience of the use of this technology in four acute trust providers within Devon it is likely to be similar to that experienced in other areas of the country.</p> <p>Two published studies have also been brought to our attention [Challand et al, British Journal of Anaesthesia (2012) 108(1):53-62 and Lai et al, British Journal of Anaesthesia (2015) 115(4):578-589] where use of monitors was not associated with benefit, and in fact had a quite strong signal for harm (promotes fluid overload).</p>	<p>NICE response</p> <p>Thank you for your comment and insights into the clinical use of Cardio-ODM in your Trust and your experience of the cost consequences of its implementation. This comment supports the view of other consultees, which indicates that the changes to the technology (the new version, CardioQ-ODM+) and the care pathway are such that the original guidance cannot be updated. As described in the interim addendum for guidance review, it is now proposed that MTG3 is transferred to the static list until it is updated as part of a clinical guideline.</p> <p>A statement has been added to the overview page on the website to explain the review of the guidance and that a new version of the technology is available.</p>

Respondent: Deltex Medical Limited (continued)

Response to proposal: Agrees with the proposal that MTG3 remains active

Deltex Medical agrees that MTG3 should remain active. Further it should remain active until such time as CardioQ-ODM is fully adopted throughout the NHS in accordance with the recommendations in MTG3.

Alternative NICE programmes

Deltex Medical agrees that there may be additional benefit to patients and the NHS from further guidance relevant to CardioQ-ODM being developed within other NICE programmes, however this ought not to be relevant to any decision for MTG3 to remain active which is a separate recommendation specific to CardioQ-ODM based on the evidence specific to CardioQ-ODM.

Future NICE guidance

Deltex Medical understands that the cost savings identified in MTG3 are the largest cost savings attributable to any medical technology identified by any NICE programme: the cost savings arise because of CardioQ-ODM's proven ability to improve materially the outcomes of large numbers of NHS patients. To date the NHS has not followed the recommendations meaning that the cost saving opportunity identified by NICE of over £0.75 billion annually has not been realised, that tens of thousands of patients each year are suffering harm from avoidable complications after surgery and that scarce NHS resources are routinely being absorbed to treat complications that should have been avoided. If the ODM evidence base is to be evaluated under an alternative NICE programme, it is important that this be done under the programme most likely to drive meaningful and rapid adoption of ODM.

NICE HTA programme

Deltex Medical strongly recommends that ODM intra-operative and peri-operative fluid management be assessed under NICE's Health Technology Appraisal programme. This would bring the additional force of a funding mandate to the NHS. A QALY economic model based on the ODM evidence base would be highly compelling: complications after surgery on average reduce patient's lives by over 7 years (Khuri et al. Determinants of Long-Term Survival After Major Surgery and the Adverse Effect of Postoperative Complications. Annals of Surgery; 242; 3 Sept 2005); at £25,000 per QALY, the NHS would pay £175,000 or more for each patient that enjoys this benefit; Deltex Medical's internal meta-analysis shows ODM to allow one patient in seven to avoid a

NICE response

Thank you for your comments which have been noted. Please see our response to your previous comment above.

The cost savings modelled in MTG3 used central venous catheter monitoring as the comparator and an average length of stay in the comparator group of 7.5 days. Both of these assumptions are now subject to considerable uncertainty due to changes in clinical practice and the implementation of enhanced recovery pathways (see previous comment above).

Updating MTG3 within a suitable guideline would allow the benefits and costs of intraoperative fluid optimisation as an intervention to be assessed.

Although adoption levels of ERPs may not have reached 100% in the NHS, their

complication suggesting a QALY benefit of over £25,000 per patient. At a cost of c£80 per patient, ODM is over 300 times more cost-effective than needed to meet the QALY threshold.

NICE clinical guideline

Insufficient information is given in the Review Proposal to determine whether a clinical guideline would be beneficial to patients. However, there are a number of common areas of confusion around haemodynamic management which might be clarified by a robust NICE evidence-based assessment. This should cover where it is reasonable to administer intra-vascular fluids, inotropes and vaso-active agents 'blind', where monitoring is advisable and at what level of precision and sophistication, where haemodynamic management protocols are advisable and which ones are applicable with which monitoring technology: there are further areas of uncertainty over choices of fluids, inotropes and vaso-active drugs as well as broader aspects of peri-operative fluid management, some of which were addressed in a recent NICE clinical guideline on in-hospital fluid administration for adults excluding in critical care or under anaesthesia.

Care pathway changes

No evidence is presented in the Review Proposal to support the assertion that there have been "Significant changes in the care pathway" nor is any evidence presented that such changes, if any, are likely to have a material effect on the recommendations in the existing guideline from either clinical or economic perspectives. There is therefore no change in care pathway basis to update MTG3.

Deltex Medical notes that no evidence is presented to support the assertion that IOFM technologies have become standard care for major surgery as part of enhanced recovery programmes and believes that the assertion is incorrect:

1. Adoption of enhanced recovery programmes is far from complete and, where adopted, compliance with the protocols is often poor. Audit data from the Enhanced Recovery Partnership Programme (Source: presentation slides from National Clinical Lead) showed that compliance with IOFM in participating sites was 55%; in a multi-centre implementation or enhanced recovery, overall compliance was 65% and that re ODM 46% (Ramirez et al. Enhanced Recovery in Colorectal Surgery: a Multi-centre Study BMC Surgery 2011 11:9). As participating sites sharing data in these studies were motivated and early enhanced recovery adopters, it is probable that compliance in the rest of the NHS is considerably lower.

continued implementation affects the cost case of CardioQ in MTG3.

2. Emergency surgery is associated with the highest mortality rates in the NHS (Pearse et al. Identification and characterisation of the high-risk surgical population in the United Kingdom. *Critical Care* 2006, 10:R81) and there is no evidence that IOFM is practised as a standard of care in emergency surgery. The October 2015 report from the National Emergency Laparotomy audit found that 'goal directed fluid therapy', which was broadly defined, was only used in the care of half (52%) of the patients included in the audit: 37% of the total having a cardiac output monitor and the remaining 15% unspecified "alternative methods". Deltex Medical notes that only a portion of those 37% of patients are likely to have been treated with ODM guided stroke volume optimisation, and that stroke volume optimisation using non-Doppler technologies has been shown to be ineffective, suggesting very low (less than 20%) actual compliance with MTG3.
3. A recent audit of 6 NHS hospitals (Harris et al. Perioperative intravenous fluid prescribing: a multi-centre audit. *Perioperative Medicine* (2015) 4:15) identified wide variation in IOFM despite some signs of adoption of other enhanced recovery principles. The authors concluded: "The wide variation of intraoperative volume for three common elective procedures is of concern and needs to be investigated further".
4. Anecdotal evidence suggests that many NHS hospitals have chosen to apply a 'fluid restriction' strategy rather than use of IOFM technologies. Overly restrictive fluids are associated with additional complications, additional costs and longer lengths of hospital stay (Thacker et al. Perioperative Fluid Utilization Variability and Association With Outcomes. *Annals of Surgery* 2015).
5. Anecdotal evidence suggests that the incidence of post-operative Acute Kidney Injury ('AKI') has increased substantially in the NHS in recent years. It is probable that this is, at least in part, related to increased practice of fluid restriction. HES data (attached) shows the rates of hospital acquired AKI to have doubled in the three years from April 2011. Prior to this increase, the NHS estimated the cost of treating AKI in hospitals at c£0.5 billion a year suggesting increased costs of a further £0.5 billion a year by the end of the 2013/14 financial year (Reference: "It is estimated that the additional cost is £500 million (data from NHS Kidney Care 2012). <https://www.england.nhs.uk/patientsafety/akiprogramme/>). Deltex Medical notes that the recently presented Spanish multi-centre trial of ODM in surgery found a significant 81% reduction (5/224 v 21/226) reduction in post-operative AKI.
6. The Oxford AHSN report on IOFM reported that compliance with the limited selection of the CQUIN pre-qualification procedures list of less than 10% of major surgery was only 67%. With the NHS having abandoned CQUIN pre-qualification, it is highly probable that usage in these procedures has fallen since the audit. Furthermore, despite all participating hospitals

Updating MTG3 within a suitable guideline would allow the benefits and costs of intraoperative fluid optimisation as an intervention to be assessed.

The review proposal acknowledged that a significant amount of new evidence has been published since the original guidance.

stating that they usually practiced IOFM in emergency laparotomies, a 10 week audit found only 35% compliance. It is highly probable that usage outside a period of audit is lower.

7. Recently updated AAGBI minimum monitoring standards did not specify use of IOFM and stated that the use of cardiac output monitors was “not established as routine”.

On the above basis, the recommendation is still valid and still required to drive better outcomes at lower costs.

No evidence or data is provided in the Review Proposal to support the speculative comments that implementation of enhanced recovery protocols may have confounded the clinical effects and cost consequences and Deltex Medical has been denied any access to the EAC report. As set out above, Deltex Medical considers it extremely unlikely that there has been any material change in either the clinical effects or cost consequences of ODM since MTG3. Until the compliance to enhanced recovery implementation and the inter-related compliance to adoption of MTG3 is ascertained then this assumption can only be considered speculative. Deltex Medical notes that adoption of CardioQ-ODM has fallen sharply since the removal of national CQUIN pre-qualification requirements for High Impact Innovations as identified in the Government/NHS Innovation, Health & Wealth report and is now lower than before MTG3 was published and concludes that effective implementation of enhanced recovery may also have gone backwards in the last two or more years.

CardioQ-ODM is an effective addition to enhanced recovery programmes

Data from a major UK hospital due to be presented in early July is expected to show a two day length of stay reduction in an established enhanced recovery programme when comparing CardioQ-ODM guided fluid management and Lidco guided fluid management. As the latter has repeatedly been shown to be ineffective, these data demonstrate that the length of stay reductions shown previously with ODM are still achievable post enhanced recovery implementation.

In addition Deltex Medical notes that several positive trial results using ODM within an enhanced recovery programme have previously been published (examples: Noble et. Randomized clinical trial assessing the effect of Doppler-optimized fluid management on outcome after elective colorectal resection. British Journal of Surgery 2006; 93: 1069–1076. McKenney et al. .Introduction of Oesophageal Doppler-guided Fluid Management in a Laparoscopic Colorectal Surgery Enhanced Recovery Programme: An Audit of Effect on Patient Outcome Irish Medical Journal May 2014. 107:5) as well as studies showing the benefit of ODM within an enhanced recovery

We received information that this was clinical practice in some hospitals; use of central venous catheters may be considered in the development of a suitable clinical guideline.

programme implementation (Miller et al. Reduced Length of Hospital Stay in Colorectal Surgery after Implementation of an Enhanced Recovery Protocol. Anaesthesia-Analgesia May 2014; 118:5): within the Miller programme, sub-analysis of the data (Source: Premier Inc analysis – available on request) showed approximately half of the total benefit of the whole enhanced recovery programme came when primarily just the ODM element had been implemented: mean length of stay reduced from 8.4 to 6.3 days with the introduction of ODM and then to 5.7 days with a full enhanced recovery programme; total hospital costs, which exclude physician costs and costs of readmissions, reduced from a mean of \$22,984 to \$21,140 with the introduction of ODM and then to \$17,815 with a full enhanced recovery programme reflecting less routine use of ICU time in the full enhanced recovery cohort.

Multi-variate analysis by the GERM enhanced group in Spain (see <https://www.fascrs.org/video/s45-enhanced-recovery-protocols-colorectal-scheduled-surgery-could-we-do-better-doing-less>) found that goal directed fluid therapy was an indicator of a shorter length of stay within an enhanced recovery programme. The datasets on which this analysis was based included only patients treated with ODM (ref various publications by Ramirez & fellow authors).

ODM included in enhanced recovery protocols because of evidence

Deltex Medical notes that ODM is included within enhanced recovery programmes because its use is evidence based. Health Technology Appraisal methodologies are suitable for evaluating single technologies or interventions rather than bundled care pathways. As a result, it is always a distinct possibility that the benefit of a whole pathway compared to standard care is less than the sum of the benefit of the individual pathway components. Deltex Medical believes the argument that the value of ODM is diminished in some way by enhanced recovery is weak: the same would apply to all the other steps included in enhanced recovery protocols including minimally invasive surgery, early mobilisation and advanced pain management and it would be absurd to dispense with all of them. If NICE is to develop further relevant clinical guidelines, it should consider doing so for enhanced recovery protocols.

Central venous catheters

Deltex Medical agrees that the usage of central venous catheters appears to be reducing during surgery but notes that the impact of this change is readily identifiable from the economic model submitted with MTG3 and is not material to the conclusions of that model or MTG3 recommendations.

Respondent: Deltex Medical Ltd (continued)

Evidence needs to be evaluated by meta-analysis

Deltex Medical strongly supports the reported EAC recommendation that any update to MTG3 should include a new meta-analysis. The presentation of a list of studies in the Review Proposal is unhelpful and potentially misleading. Deltex Medical does not consider it appropriate to comment on all the trials but notes:

- Brandstrup was testing an alternative, resource intensive, approach to try and achieve the same ends as ODM guided fluid management and should not be included in any evaluation comparing to standard care. The results of this trial were included in the original MTG3 process.
- Challand results were submitted to MTAC within the consultation for the original MTG3 and thus considered at that time. The trial did show a non-significant 25% reduction in serious complications which adds further weight to meta-analysis. Furthermore data subsets presented at a clinical meeting in Australia (Challand et al. Goal directed fluid therapy for elective rectal resections. *Colorectal Disease* 2011. 13 (Suppl 5 (1-40) 103) showed a 2 day length of stay reduction in unfit rectal resection patients which is not highlighted in the published paper.
- Feldheiser 2013 used ODM in both arms and was not studying ODM outcomes.
- McKenny 2013 showed a non-significant 1 day reduction in length of stay and a 48% reduction in complications: both results would add weight to a meta-analysis
- Pillai showed a mean 4 day reduction in length of stay which was not significant but adds weight to a meta-analysis.
- Phan showed a non-significant 75% reduction in major complications which would add weight to a meta-analysis.
- The table omits published case series studies, which are routinely evaluated within MTEP, including a case series from McKenny (McKenney et al. .Introduction of Oesophageal Doppler-guided Fluid Management in a Laparoscopic Colorectal Surgery Enhanced Recovery Programme: An Audit of Effect on Patient Outcome *Irish Medical Journal* May 2014. 107:5) in enhanced recovery laparoscopic surgery showing significantly reduced complications, admissions to ICU and return to diet.
- The table omits a third study by Feldheiser (Feldheiser et al. . Development and Feasibility Study of an Algorithm for Intraoperative Goal-directed Haemodynamic Management in Noncardiac Surgery. *The Journal of International Medical Research* 2012; 40: 1227 – 1241)

NICE response

Thank you for your comment. Please see the response to your previous comments. Any new evidence could be submitted as part of any new NICE notification for the newer version of your device, CardioQ-ODM+.

and colleagues comprising the Enhanced Recovery After Surgery Anaesthesia Working Group. The ODM implementation delivered statistically significant reductions in each of length of hospital stay, the need for post-operative ventilator therapy and the number of prolonged hospital stays.

- The table omits studies which have not yet been published but which are expected to further reinforce the value of ODM and would be considered in any update. These include the Ripolles study described below and two RCTs from a major UK hospital highlighted in Deltex Medical's Review submission and expected to show additional benefit from ODM guided stroke volume optimisation for six hours in awake patients post-operatively and superior outcomes from ODM compared to PPWA.

Results from major multi-centre RCT

Results from the largest ever RCT of ODM intra-operatively and the first multi-centre ODM RCT were presented at the Euroanaesthesia conference on 28 May 2016 (Poster & abstract. Ripolles et al Euroanaesthesia 2016. Copy abstract to be published post congress and attached). The trial was sponsored by the Spanish Government and included 450 patients undergoing one of urological, gastrointestinal, orthopaedic or gynaecological surgery in five Spanish hospitals.

Significant results: The key results were:

- 72% reduction in total number of complications from 198 to 56 ($p < 0.01$).
- 45% reduction in number of patients suffering one or more complications meaning Doppler use saved 1 additional patient in every 8 from suffering any complication at all (15% v 28%: $p < 0.01$)
- 2 day reduction in median length of stay ($p < 0.01$)

In addition the study found statistically significant reductions in five types of major complication:

- Acute Kidney Injury: 75% reduction (5 patients v 21)
- Cardiopulmonary oedema: 100% reduction (0 patients v 13)
- Pneumonia: 83% reduction (4 patients v 22)
- Superficial surgical site infection: 75% reduction (4 patients v 16)
- Deep surgical site infection: 74% reduction (6 patients v 23)

Modern surgical techniques involve many patients being positioned in prone positions to improve surgeon access and facilitate minimally invasive approaches. Being face down or both face down and head down presents additional risks of adverse haemodynamic events, including heart failure

Inclusion of data from patients positioned in the prone position can be considered during

<p>and hypotension. A recent RCT using ODM to manage haemodynamics in prone patients undergoing surgery found that the time spent in a hypotensive state was halved and that patients managed with ODM had less than half the number of hypotensive events (Picard et al. Oesophageal Doppler to optimize intra-operative haemodynamics during prone position. A randomized controlled trial (2016), http://dx.doi.org/10.1016/j.accpm.2015.12.011). Focus on minimising hypotensive events is an increasing area of patient safety focus: in a recent review of over 100,000 patients, a strong association was found between intra-operative hypotensive episodes and post-operative myocardial injury. Circa one non-cardiac surgical patient in ten was found to have a myocardial injury within 30 days of surgery, 80% of which events were clinically silent, and 10% of those with such myocardial injury had died within 30 days of surgery meaning a 1% 30 day mortality rate associated with intra-operative hypotension (Mascha et al. Intraoperative Mean Arterial Pressure Variability and 30-day Mortality in Patients Having Noncardiac Surgery. Anesthesiology 2015; 123, 79-91). These two trials reinforce the case for widescale use of ODM to monitor and manage haemodynamics during surgery and indicate a potentially important direction for future research into peri-operative patient safety.</p>	<p>the scoping of the review questions for the clinical guideline.</p>
---	--

<p>Respondent: Deltex Medical (continued)</p> <p>Clarification re PPWA technologies</p> <p>Deltex Medical agrees that the additional operating function added to the CardioQ-ODM for the upgrade to CardioQ-ODM+ which includes a PPWA function calibrated directly from the ODM function, is outside the scope of MTG3 as are all PPWA technologies except as comparators. This clarification should be made in the introduction to MTG3 immediately.</p> <p>Deltex Medical agrees that it is relevant for NICE to address the question of which technologies should be used to guide which approach or approaches to fluid management. The question is not, however, about determining cardiac output but about ability to guide safely and appropriately fluid management protocols and this should have been made clear in the Review Proposal. Additionally, use of terms like “intraoperative fluid management (IOFM) technologies, such as CardioQ-ODM” have proved deleterious to the adoption of MTG3. No IOFM technology other than ODM measures blood flows directly and continuously in the central circulation and any implication that they should be grouped together should be avoided to reduce the risk of potential users extrapolating the ODM evidence base to apply to other, very different, technologies. The manufacturers of the most common such technologies marketed for IOFM have chosen not to submit their products for</p>	<p>NICE response</p> <p>Thank you for your comments which have been noted. Please see our responses to your comments above. The wording at the start of MTG3 applies to all guidance produced by MTEP, according to our process and methods guides.</p>
---	--

evaluation under MTAP and NICE has not evaluated them other than as comparators to CardioQ-ODM. The MTG3 review should make this lack of evaluation explicit.

Confusion with alternative cardiac output monitoring technologies

“a number of new randomised controlled trials (RCTs) and systematic reviews have been published involving CardioQ-ODM and its comparators and alternatives”

In its submission to the MTG3 review, Deltex Medical identified a number of new RCTs which have been published since MTG3 using comparator or alternative technologies and recommended that MTG3 be updated to make it clear that ODM is dominant over both the technologies involved. Such trials using a stroke volume optimisation strategy guided by non-ODM technologies show that the PPWA and Cardiac Impedance technologies, which are far less precise than ODM and frequently liable to report change in the wrong direction, are unable to reduce either complications or lengths of stay after surgery.

Risk of harm to patients

Deltex Medical believes that patients are being harmed through suffering avoidable complications from doctors using alternative technologies in the mistaken belief that they are equivalent to ODM. The generic wording in the introduction to MTG3 about alternative technologies has been widely misinterpreted to infer NICE guidance in MTG3 applies to all IOFM technologies regardless of the actual evidence for their use.

Clarification of ODM dominance over alternatives required

For example a recently published RCT (Lai et al. Randomized controlled trial of stroke volume optimization during elective major abdominal surgery in patients stratified by aerobic fitness. *Br J Anaes.* 2015; 115 (4): 578–89) showed no benefit from using a Lidco monitor during surgery and the paper concluded: “Our study suggests that in patients having elective bowel surgery, algorithm-driven SVO is of no benefit when superimposed on a liberal baseline fluid regimen. In the light of this, this study does not support current National Institute for Health and Care Excellence recommendations for intraoperative cardiac output monitoring during a wide array of elective major surgeries.” Such misunderstanding is commonplace, yet NICE has neither evaluated intraoperative cardiac output monitoring nor recommended it. It has evaluated and recommended CardioQ-ODM. In fact Lai’s findings were absolutely consistent with all other published RCTs using Lidco products intra-operatively and are not relevant to MTG3 other than in establishing ODM’s dominance over PPWA. Deltex Medical notes that its economic model submitted re MTG3 showed the addition of PPWA during surgery as an additional cost leading to the benefit of ODM over PPWA being greater

than that over standard care: this approach is further validated now that there are eight published studies using Lidco devices intra-operatively none of which has shown significant reductions in either complications or length of stay. (Harten, J., et al., Effect of intraoperative fluid optimisation on renal function in patients undergoing emergency abdominal surgery: a randomised controlled pilot study. *Int J Surg*, 2008. 6(3): p. 197-204. Bartha et al Randomized controlled trial of goal-directed haemodynamic treatment in patients with proximal femoral fracture. *Br J Anaesth* 2012; 110(4): 545-53. Bisgaard et al. Optimising stroke volume and oxygen delivery in abdominal aortic surgery: a randomised controlled trial. *Acta Anaesthesiol Scand*. 2012; 57(2):178-88. Bisgaard et al. Haemodynamic optimisation in lower limb arterial surgery: room for improvement? *Acta Anaesthesiol Scand*. 2012; 57(2):189-98. Pearse et al (for the OPTIMISE Study Group). Effect of a perioperative, cardiac output-guided hemodynamic therapy algorithm on outcomes following major gastrointestinal surgery: A randomized clinical trial and systematic review. [JAMA](#). 2014; Jun 4;311(21):2181-90. Moppett. LiDCO-based fluid management in patients undergoing hip fracture surgery under spinal anaesthesia: a randomized trial and systematic review. *Br J Anaesth* 114:3 444-459, Jammer IB et al. Stroke volume variation to guide fluid therapy: is it suitable for high-risk surgical patients? A terminated randomized controlled trial. *Perioperative Medicine* (2015) 4:6)

Deltex Medical notes that the only RCT using the Cheetah Medical impedance cardiography system also showed no difference in outcome and is also not relevant to an assessment of the ODM evidence base (Pestana et al. Perioperative goal-directed hemodynamic optimization using noninvasive cardiac output monitoring in major abdominal surgery: a prospective, randomized, multicenter, pragmatic trial: POEMAS Study (PeriOperative goal-directed therapy in Major Abdominal Surgery). *Anesth Analg*. 2014; Sep;119(3):579-87).

Alternative fluid management strategy based on respiratory swing

Deltex Medical notes that there is some evidence of reduced complications, but not length of stay, using one particular PPWA device (Edwards Vigileo monitor with FloTrac catheters) to guide a fluid management strategy involving the suppression of respiratory swing. For the avoidance of doubt, this approach has not generated positive results when tested with other PPWA devices (Pulsion and Lidco). Deltex Medical believes that this approach might be recommended with regard to Flotrac if reviewed by NICE and that such guidance would be helpful to the NHS as it would also provide clarity on the many contra-indications to the approach which include awake patients, laparoscopic procedures, low ventilator settings (now commonly regarded as unsafe), arrhythmia including atrial fibrillation, lung morbidity and open chests. Studies (Maguire et al. Respiratory Variation in Pulse Pressure and Plethysmographic Waveforms: Intraoperative Applicability in a

North American Academic Center. *Anaesthesia & Analgesia* Jan 2011; 112:1, Jammer IB et al. Stroke volume variation to guide fluid therapy: is it suitable for high-risk surgical patients? A terminated randomized controlled trial. *Perioperative Medicine* (2015) 4:6).

Current validity of cost saving recommendations

“These changes mean that the cost-saving recommendations based on the original cost modelling may no longer be valid in the current care pathway, in which the average length of stay is shorter” HES data is no longer publically available so Deltex Medical has been unable to challenge the assumption that length of stay has reduced across the NHS. If this were the case, it would be simple to update the economic model submitted as part of MTG3 for new data and to also account for the effect of increases in NHS costs since 2010. However, Deltex Medical notes that published Enhanced Recovery Partnership Programme audit data showing reduced lengths of stay (Simpson et al. *Enhanced recovery from surgery in the UK: an audit of the enhanced recovery partnership programme 2009–2012. British Journal of Anaesthesia*, 2015, 1–9) already include the benefit in large numbers of patients of having used ODM; however in orthopaedic surgery, where IOFM compliance was lower allowing visibility of its impact, the authors reported that IOFM was associated with shorter lengths of stay.

Alternative cost consequence measures than length of stay

Deltex Medical notes that length of stay is used as an economic measure re the NHS because that is often the only meaningful data available. The real value of CardioQ-ODM comes from the reduction in post-operative complications and the real saving to the NHS is in not having to deploy resources to treat these complications. Recent US data (Michard et al. *Potential return on investment for implementation of perioperative goal-directed fluid therapy in major surgery: a nationwide database study. Perioperative Medicine* 2015) identifies the additional hospital costs, including readmission costs, of a post-operative complication at \$11,824, representing a 75% increase on the \$15,783 costs of treating surgical patients who avoided complications. This cost difference (c£8,000) represents the cost of each patient suffering a complication. Deltex Medical notes that its internally produced meta-analysis (Murrell http://www.deltexmedical.com/wp-content/uploads/2014/11/Meta_analysis-11_14-cm.pdf) shows CardioQ-ODM reducing a complication in one patient in seven and that the newly presented results from a major Spanish multi-centre trial show one additional patient in eight avoiding any post-operative complication if treated with ODM. In both cases the average benefit per patient would be approximately equal to the cost saving estimated in MTG3. Alternatively, there is a compelling economic case for ODM on a cost consequence basis: at £80 per patient and a cost per complication of, say, £8,000, ODM

An update of MTG3 within a clinical guideline will allow the most appropriate outcomes for clinical and cost-effectiveness analyses to be identified during scoping, such as length of stay or reduction in complications.

A statement has been added to the overview page on the website to explain the review of the guidance and that a new version of the technology is available.

<p>would only need to avoid a complication in one patient in every 100 to be cost consequence neutral so is at least 12 times more effective than needed to be cost saving at point of care.</p> <p>Deltex Medical believes that it is extremely unlikely that new economic modelling would show any conclusion other than that there remain enormous potential cost-savings to the NHS from adopting CardioQ-ODM.</p>	
--	--