NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Professional Expert questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name: **Cytoreduction surgery followed by hyperthermic intraoperative peritoneal chemotherapy for peritoneal carcinomatosis**

Name of Professional Expert: Faheez Mohamed

Job title:

Professional Regulatory Body: GMC ☐x

Other (specify) ☐

Registration number: 4328029

Specialist Society: Association of Coloproctology of Great Britain and Ireland

Nominated by (if applicable):

1 About you and your speciality's involvement with the procedure

1.1 Do you have adequate knowledge of this procedure to provide advice?

☐x Yes.

☐ No – please answer no more questions and return the form

Comments:

I have been involved in the field of peritoneal malignancy for the last 17 years from my time as Dr Paul Sugarbaker's Research Fellow in the United States in 2001 to my appointment as Consultant Colorectal Surgeon at the Peritoneal Malignancy Institute in Basingstoke in 2009 where I currently work. I am one of four Consultant

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Surgeons involved in the treatment of peritoneal malignancy in Basingstoke which is one of 2 centres funded by National Highly Specialised Commissioning to treat appendix cancers as well as colorectal peritoneal metastases through Specialised Commissioning. We are also currently the only centre in the UK to offer cytoreductive surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) to patients with peritoneal mesothelioma selected through a National MDT.
I have contributed to the latest NICE Colorectal Cancer Guidelines update as Peritoneal Malignancy Specialist on the Committee chaired by Peter Hoskins due to publish in January 2020. We have reviewed current evidence to support this procedure.
In partnership with European colleagues from 7 countries we have recently been awarded a European Co-operation in Science and Technology grant(http://www.cost.eu/COST_Actions) from the European Union to establish a European wide research network for appendix tumours as part of the Cure4PMP consortium. I am also clinical lead for The UK and Ireland Colorectal Peritoneal Metastases database which has data on over 400 patients who have been treated over the last 18 months in 5 centres across the UK and Ireland. This provides valuable information on outcomes and will add to evidence to guide future commissioning.
I am a Clinical advisor to “Pseudomyxoma Survivors” which is one of the largest patient support groups for patients with appendix cancer and have taken part in a webinar for them as well as speaking at patient days for other groups such as Mesothelioma UK.
I am serving my second elected term on the Research and Audit Committee of the Association of Coloproctology of Great Britain and Ireland which involves peer review of grant applications for the Bowel Disease Research Foundation to shape research priorities.

1.2 Is this procedure relevant to your specialty?

☐**x** Yes.

☐ No - please answer no more questions. Please give any information you can about who is likely to be doing the procedure and return the form.

Comments:

Approximately 10 – 30% of patients with colorectal cancer will develop metastases to the peritoneum (peritoneal carcinomatosis). Those with limited disease may benefit from cytoreductive surgery with Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

1.3 Is this procedure performed by clinicians in specialities other than your own?

☐**x** Yes – please comment

☐ No

Comments:

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Gynaecological Oncologists also use cytoreductive surgery with HIPEC for ovarian cancer (outside of the UK) as well as Upper GI surgeons for Gastric cancer(outside the UK).

1.4 If you are in a specialty that does this procedure, please indicate your experience with it:

☐ I have never done this procedure.

☐ I have done this procedure at least once.

☐**x** I do this procedure regularly.

Comments:

I work in Basingstoke, one of the 3 Nationally commissioned centres for the treatment of peritoneal carcinomatosis from colorectal cancer with cytoreductive surgery and Hyperthermic intraperitoneal chemotherapy

1.5 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☐**x** I take part in patient selection or refer patients for this procedure regularly.

Comments:

Basingstoke runs a Specialist MDT weekly to select patients referred for this procedure. On average we receive 20 referrals a week including patients with appendix and colorectal cancer as well as peritoneal mesothelioma

1.6 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☐**x** I have done bibliographic research on this procedure.

☐x I have done research on this procedure in laboratory settings (e.g. device-related research).

☐x I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

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Comments: I have co-authored 69 peer reviewed publications in cytoreductive surgery including systematic reviews and have an international network of colleagues with whom experience and expertise is regularly shared.

1.7 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☐**x** Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

3 Nationally commissioned centres ; Basingstoke, the Christie Manchester and Good Hope Birmingham

2 About the procedure

2.1 Does the title used above describe the procedure adequately?

☐ Yes

☐**x** No - If no, please suggest alternative titles.

Comments:

Cytoreductive Surgery (CRS) with Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for colorectal peritoneal metastases.

2.2 Which of the following best describes the procedure (choose one):

☐**x** Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure’s safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

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This procedure was commissioned by NHS England in 2013 (NICE IPG331)
Clinical Commissioning Policy: Cytoreduction surgery for patients with peritoneal carcinomatosis April 2013
Reference : NHSCB/A08/P/a

2.3 What is/are the best comparator(s) (standard practice) for this procedure?

Systemic ant-cancer treatment or cytoreductive surgery alone (without hyperthermic intraperitoneal chemotherapy)

2.4 Are there any major trials or registries of this procedure currently in progress? If so, please list.

PRODIGE 7 (ASCO abstract – full publication awaited).

Study	Population	Intervention/Comparison	Outcome
RCTs and follow up studies			
PRODIGE 7 [Quenet 2016] Multi-centre RCT	N=264 patients aged 18-70 with histopathologically confirmed colorectal cancer; peritoneal carcinoma extension ≤ 25 (Sugarbaker Index, determined interoperatively) France	CRS + HIPEC + oxaliplatin versus CRS alone	• Progression free survival • Overall survival • Treatment-related mortality

UK and Ireland Colorectal Peritoneal metastases Registry with patients from Basingstoke, Manchester Birmingham , Dublin and Dundee treated by cytoreductive surgery with HIPEC.

2.5 Please list any abstracts or conference proceedings that you are aware of that have been *recently* presented / published on this procedure (this can include your own work). Please note that NICE will do a comprehensive literature search on this procedure and we are only asking you for any very recent or abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.

PRODIGE 7 [Quenet 2018]
Quenet, F., Dominique, E., Lise, R., Diane, G., Laurent, P., Marc, O., Facy, A., Catherine, A UNICANCER phase III trial of hyperthermic intra-peritoneal chemotherapy (HIPEC) for colorectal peritoneal carcinomatosis (PC): PRODIGE 7, Journal of Clinical Oncology, 36, LBA3503, 2018

3 Safety and efficacy of the procedure

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3.1 What are the potential harms of the procedure?

Please list any adverse events and major risks (even if uncommon) and, if possible, estimate their incidence:

Adverse events reported in the literature (if possible please cite literature)

1-2% risk of death, 8% risk of Grade 3 and 4 Claviend Dindo complications : return to theatre to deal with bleeding,DVT/Pulmonary embolus, wound and chest infections, heart attack and stroke.

Haemorrhage from hyperthermic intraperitoneal chemotherapy with Oxaliplatin

Neutropenia with Mitomycin C intraperitoneal chemotherapy

Complications of cytoreductive surgery and HIPEC in the treatment of peritoneal metastases, Mehta, S.S., Gelli, M., Agarwal, D., Indian Journal of Surgical Oncology, 7, 225-229, 2016

Randomized trial of cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy and palliative surgery in patients with peritoneal carcinomatosis of colorectal cancer. Verwaal, V.J., Van Ruth, S., De Bree, E. Journal of Clinical Oncology, 21, 3737-3743, 2003

The results of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in 1200 patients with peritoneal malignancy.

Moran B, Cecil T, Chandrakumaran K, Arnold S, Mohamed F, Venkatasubramaniam A.Colorectal Dis. 2015 Sep;17(9):772-8. doi: 10.1111/codi.12975

Anecdotal adverse events (known from experience)

N/A

Theoretical adverse events

N/A

3.2 Please list the key efficacy outcomes for this procedure?

Critical:

- Progression-free survival
- Overall survival
- Overall quality of life

Important:

- Treatment-related mortality
- Any grade 3 or 4 complications (Clavien-Dindo)
- Length of hospital stay

3.3 Please list any uncertainties or concerns about the *efficacy* of this procedure?

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PRODIGE7: the role of adding hyperthermic intraperitoneal chemotherapy – no added survival benefit compared with cytoreductive surgery alone. However RCT in ovarian cancer did show survival benefit with HIPEC (Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer.
van Driel WJ, Koole SN, Sikorska K, Schagen van Leeuwen JH, Schreuder HWR, Hermans RHM, de Hingh IHJT, van der Velden J, Arts HJ, Massuger LFAG, Aalbers AGJ, Verwaal VJ, Kieffer JM, Van de Vijver KK, van Tinteren H, Aaronson NK, Sonke GS.N Engl J Med. 2018 Jan 18;378(3):230-240

3.4 What clinician training is required to do this procedure safely?

Training in peritonectomy procedures and use of hyperthermic intraperitoneal chemotherapy. Data on learning curve suggests 40 cases mentored by experienced surgeon to optimise outcomes

3.5 What clinical facilities are needed to do this procedure safely?

OperatingTheatres, ITU and HIPEC machine

3.6 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

The role of Hyperthermic Intraperitoneal Chemotherapy (HIPEC) is currently uncertain and can increase morbidity of the surgical procedure.

4 Audit Criteria

Please suggest potential audit criteria for this procedure.

4.1 Beneficial outcome measures. This should include short and long term clinical outcomes, quality-of-life measures and patient related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured:

- 5 year Progression-free survival
- 5 year Overall survival
- Overall quality of life at 1 year post surgery

4.2 Adverse outcome measures. This should include early and late complications. Please state the post procedure timescales over which these should be measured.

90 day Treatment-related mortality
Any Clavien Dindo grade 3 or 4 complications

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5 Uptake of the procedure in the NHS

5.1 If it is safe and efficacious, in your opinion, how quickly do you think use of this procedure will be adopted by the NHS (choose one)?

☐x Rapidly (within a year or two).

☐ Slowly (over decades)

☐ I do not think the NHS will adopt this procedure

Comments:

Already being performed in 3 cnatinally commissioned centres in England.

5.2 If it is safe and efficacious, in your opinion, will this procedure be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

☐x Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

5.3 If it is safe and efficacious, in your opinion, the potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources:

☐ Major.

☐x Moderate.

☐ Minor.

Comments:

Approximately 300 – 400 patients may benefit from this procedure per year in the UK

6 Other information

6.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

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Comments: Soon To be published NICE Colorectal Cancer Guideline update focusing on Optimal combination and sequence of local and systemic treatments in patients presenting with metastatic colorectal cancer isolated in the peritoneum

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7 Data protection and conflicts of interest

7.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The professional expert questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

☑ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above. For more information about how we process your personal data please see our privacy notice

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7.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures. Conflicts of Interest for Specialist Advisers

Declarations of interest form			
Faheez Mohamed: Professional expert			
Type of interest	**Description of interest**	**Relevant dates**	
		Interest arose	**Interest ceased**
I undertake private practice at BMI Hampshire Clinic and North	*Direct , Financial*	*October 2009*	Ongoing

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Hampshire Hospital Basingstoke treating patients with all colorectal conditions, including those with colorectal cancer. *My private practice entirely mirrors my NHS practice, and I diagnose and treat patients with colorectal cancer in NHS and private practice as part of a MDT. As is the norm, I receive payment for my private practice, as I do for my NHS practice.* *Paid on a 'fee per service' basis.* *I spend approximately 30% of my time managing Private patients of which 5% have colorectal cancer. Private patients and NHS patients are treated identically.*			

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* Guidance notes for completion of the Declarations of interest form

Name and role	Insert your name and your position in relation to your role within NICE
Description of interest	Provide a description of the interest that is being declared. This should contain enough information to be meaningful to enable a reasonable person with no prior knowledge to be able to read this and understand the nature of the interest. Types of interest: **Direct interests** **Financial interests** - Where an individual gets direct financial benefits from the consequences of a decision they are involved in making. *For examples of financial interests please refer to the policy on declaring and managing interests.* **Non-financial professional and personal interests -** Where an individual obtains a non-financial professional or personal benefit, such as increasing or maintaining their professional reputation, from the consequences of a decision they are involved in making. *For examples of non-financial interests please refer to the policy on declaring and managing interests.* **Indirect interests -** Where there is, or could be perceived to be, an opportunity for a third party associated with the individual in question to benefit. A benefit may arise from both a gain or avoidance of a loss.
Relevant dates	Detail here when the interest arose and, if applicable, when it ceased.
Comments	This field should be populated by the guidance developer and outline the action taken in response to the declared interest. It should include the rationale for this action, and the name and role of the person who reviewed the declaration.

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mirella Marlow Programme Director

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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Professional Expert questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**Cytoreduction surgery followed by hyperthermic intraoperative peritoneal chemotherapy for peritoneal carcinomatosis**
Name of Professional Expert:	Haney Youssef
Job title:	Consultant Colorectal Surgeon
Professional Regulatory Body:	GMC ☒
	Other (specify) ☐
Registration number:	4401368
Specialist Society:	Association of Coloproctology of Great Britain and Ireland
Nominated by (if applicable):	

1 About you and your speciality's involvement with the procedure

1.1 Do you have adequate knowledge of this procedure to provide advice?

☒ Yes.

☐ No – please answer no more questions and return the form

Comments:

I have 10 years of clinical experience in this specialist field and have carried out research and published peer review papers in this field.

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1.2 Is this procedure relevant to your specialty?

☒ Yes.

☐ No - please answer no more questions. Please give any information you can about who is likely to be doing the procedure and return the form.

Comments:

1.3 Is this procedure performed by clinicians in specialities other than your own?

☐ Yes – please comment

☒ No

Comments:

In the UK it is only performed by colorectal surgeons. Abroad, other specialties perform such as Gynae oncologists.

1.4 If you are in a specialty that does this procedure, please indicate your experience with it:

☐ I have never done this procedure.

☐ I have done this procedure at least once.

☒ I do this procedure regularly.

Comments:

I lead the Peritoneal Malignancy Unit at University Hospitals Birmingham, Good Hope Hospital, which is 1 of 3 units in England specialist commissioned by NHS England to provide cytoreductive surgery for colorectal peritoneal metastases. I have performed or supervised over 300 Cytoreductive surgery cases and currently perform 1 or 2 per week.

1.5 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☒ I take part in patient selection or refer patients for this procedure regularly.

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Comments:

I lead the Peritoneal specialist MDT at Good Hope Hospital, which is held weekly. The MDT makes decisions on patient selection for the procedure on approximately 10 patients per week with peritoneal metastases.

1.6 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☒ I have done bibliographic research on this procedure.

☒ I have done research on this procedure in laboratory settings (e.g. device-related research).

☒ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

I have collaborations with 2 laboratories at university of Birmingham investigating different aspects of peritoneal tumours in patients having cytoreductive surgery and HIPEC. I have also published patient outcome data on patients with peritoneal metastases, as well as metanalysis and systematic reviews.

1.7 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☒ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

There are only 3 units in England who receive specialist commissioning to provide the service – UHB NHS FT Good Hope Hospital, Hampshire Hospitals, Christie. This constitutes <5% of colorectal surgeons in England.

2 About the procedure

2.1 Does the title used above describe the procedure adequately?

☐ Yes

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☒ No - If no, please suggest alternative titles.

Comments:

I would change the term “peritoneal carcinomatosis” to “Resectable Peritoneal Metastases,” as this better describes the population we deal with. We generally don’t operate on patients with widespread peritoneal carcinomatosis, but on patients with limited resectable disease. Also, add the word “intraperitoneal.”
So I would change to “Cytoreduction surgery followed by hyperthermic intraoperative intraperitoneal chemotherapy for resectable peritoneal metastases”

2.2 Which of the following best describes the procedure (choose one):

☒ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure’s safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

This has become an established procedure worldwide and in the UK and is NHS commissioned for the treatment of colorectal and appendix peritoneal metastases. It’s role in other tumour types is currently under evaluation.

2.3 What is/are the best comparator(s) (standard practice) for this procedure?

The historical comparator for colorectal peritoneal metastases was systemic chemotherapy alone. However standard practice for colorectal peritoneal metastases is now a combination of systemic chemotherapy and cytoreductive surgery/HIPEC.
For gastric cancer, the comparator remains palliative chemotherapy alone.
For ovarian cancer, the best comparator is systemic chemotherapy + cytoreductive surgery (without HIPEC) versus systemic chemotherapy + CRS/HIPEC.

2.4 Are there any major trials or registries of this procedure currently in progress? If so, please list.

OVHIPEC 2 trial – for ovarian cancer
GASTRICHIP trial – for ovarian cancer

2.5 Please list any abstracts or conference proceedings that you are aware of that have been *recently* presented / published on this procedure (this can include your own work). Please note that NICE will do a comprehensive literature search on this procedure and we are only asking you for any very recent or abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a

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comprehensive reference list but it will help us if you list any that you think are particularly important.

PRODIGE 7 – ASCO, awaiting full publication

3 Safety and efficacy of the procedure

3.1 What are the potential harms of the procedure?

Please list any adverse events and major risks (even if uncommon) and, if possible, estimate their incidence:

Adverse events reported in the literature (if possible please cite literature)

In experienced centres, post-op mortality 1-2%, but much higher in other centres. Grade 3/4 (CTCAE or Clavien Dindo) complications 9-10 % in experienced centres but again much higher in less experienced centres.

Reported complications include bleeding, anastomotic leak, enterocutaneous fistula, infected fluid collections, chest infections, DVT, PE, neutropenia, renal impairment, wound infection

Anecdotal adverse events (known from experience)

As published

Theoretical adverse events

As published

3.2 Please list the key efficacy outcomes for this procedure?

For colorectal peritoneal mets – improved overall survival and DFS with CRS and HIPEC - Verwaal 2003 and 2008
For ovarian cancer – improved OS and DFS – OVHIPEC 1 trial
Improved QOL / return to baseinle by 6 months post op

3.3 Please list any uncertainties or concerns about the *efficacy* of this procedure?

Its role on gastric cancer is uncertain, but promising.
Since last NICE guidance, there has been significant new evidence in its role for ovarian cancer.
.

3.4 What clinician training is required to do this procedure safely?

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Clinicians should undergo formal training in an established peritoneal malignancy unt. 120-140 procedures has been shown to overcome the learning curve.

3.5 What clinical facilities are needed to do this procedure safely?

Well equipped and staffed hospitals. Service specification is well documented in NHS Commissioning Policy service specification.

3.6 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

PRODIGE 7 (abstract) trial has thrown in to question the role of oxaliplatin HIPEC in colorectal peritoneal mets but paper not yet published and several limitations to study.
No evaluation of other HIPEC regimens eg Mitomycin C. We don't know which drugs are best to use for HIPEC, for how long and at what temperature.

In UK, cytoreductive surgery is used for ovarian cancer without HIPEC. However important new trials have been published since last NICE guidance showing efficacy of HIPEC.

4 Audit Criteria

Please suggest potential audit criteria for this procedure.

4.1 Beneficial outcome measures. This should include short and long term clinical outcomes, quality-of-life measures and patient related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured:

Overall survival, disease-free survival, PCI score, Completeness of Cytoreduction (CC) score

4.2 Adverse outcome measures. This should include early and late complications. Please state the post procedure timescales over which these should be measured.

Grade 3-4 morbidity, postoperative mortality (in hospital and 90-day)

5 Uptake of the procedure in the NHS

5.1 If it is safe and efficacious, in your opinion, how quickly do you think use of this procedure will be adopted by the NHS (choose one)?

☒ Rapidly (within a year or two).

☐ Slowly (over decades)

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☐ I do not think the NHS will adopt this procedure

Comments:

The procedure has already been adopted in the NHS following commissioning policy by NHS England April 2013.

5.2 If it is safe and efficacious, in your opinion, will this procedure be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

☒ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

There are currently 3 commissioned centres. NHS England are planning to commission a 4th centre in England.

5.3 If it is safe and efficacious, in your opinion, the potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources:

☒ Major.

☐ Moderate.

☐ Minor.

Comments:

The treatment has already been demonstrated as safe and efficacious in colorectal peritoneal disease. If also safe and efficacious for ovarian cancer and even gastric cancer, a lot of patients will benefit from the treatment. Approximately 600 patients with colorectal cancer, 2000 with ovarian cancer and a few hundred patients with gastric cancer,

6 Other information

6.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

Comments:

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Although PRODIGE 7 trial questioned the benefits of intraperitoneal oxaliplatin's efficacy as a HIPEC drug, it did confirm the excellent survival results of cytoreductive surgery when carried out in a specialist centre.
The evidence for cytoreductive surgery and HIPEC in ovarian cancer has significantly increased since last NICE guidance and support of the procedure for ovarian cancer needs to seriously evaluated.

7 Data protection and conflicts of interest

7.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The professional expert questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

☑ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above. For more information about how we process your personal data please see our privacy notice

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7.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

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Declarations of interest form		
Type of	Description of	Relevant dates

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interest	interest	Interest arose	Interest ceased

* Guidance notes for completion of the Declarations of interest form

Name and role	Insert your name and your position in relation to your role within NICE
Description of interest	Provide a description of the interest that is being declared. This should contain enough information to be meaningful to enable a reasonable person with no prior knowledge to be able to read this and understand the nature of the interest. Types of interest: **Direct interests** **Financial interests** - Where an individual gets direct financial benefits from the consequences of a decision they are involved in making. *For examples of financial interests please refer to the policy on declaring and managing interests.* **Non-financial professional and personal interests -** Where an individual obtains a non-financial professional or personal benefit, such as increasing or maintaining their professional reputation, from the consequences of a decision they are involved in making. *For examples of non-financial interests please refer to the policy on declaring and managing interests.* **Indirect interests -** Where there is, or could be perceived to be, an opportunity for a third party associated with the individual in question to benefit. A benefit may arise from both a gain or avoidance of a loss.
Relevant dates	Detail here when the interest arose and, if applicable, when it ceased.
Comments	This field should be populated by the guidance developer and outline the action taken in response to the declared interest. It should include the rationale for this action, and the name and role of the person who reviewed the declaration.

Thank you very much for your help.

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Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mirella Marlow Programme Director

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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Professional Expert questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**Cytoreduction surgery followed by hyperthermic intraoperative peritoneal chemotherapy for peritoneal carcinomatosis**
Name of Professional Expert:	Jurgen Mulsow MD FRCSI
Job title:	Consultant Surgeon National Centre for Peritoneal Malignancy, Mater University Hospital Dublin, Ireland.
Professional Regulatory Body:	GMC ☐
	Other (specify) ☐
Registration number:	023848
Specialist Society:	Irish Medical Council
Nominated by (if applicable):	

1 About you and your speciality's involvement with the procedure

1.1 Do you have adequate knowledge of this procedure to provide advice?

Yes.

Comments:

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I am the lead surgeon at the National Centre for Peritoneal Malignancy in Ireland. Since 2013 we have performed in excess of 250 procedures of cytoreduction with HIPEC for peritoneal malignancy, including in excess of 100 cases for colorectal cancer peritoneal metastases.
I am a member of the Peritoneal Malignancy sub-committee of the Association of Coloproctology Great Britain and Ireland; a member of the Management Committee for COST Action CA17101: European Network on Pseudomyxoma Peritonei; the National Representative for Ireland of the European Society of Coloproctology; and a member of the National Colorectal Cancer Leads Group of the National Cancer Control Programme in Ireland.

1.2 Is this procedure relevant to your specialty?

Yes. The single National Centre for the treatment of patients with peritoneal malignancy is located at the Mater Hospital in Dublin.

Comments:

1.3 Is this procedure performed by clinicians in specialities other than your own?

Yes. Cytoreductive surgery with HIPEC is also performed by Gynaecology Oncology surgeons and Upper Gastrointestinal Surgeons working within our National Centre.

Comments:

1.4 If you are in a specialty that does this procedure, please indicate your experience with it:

I perform this procedure regularly. Approximately 60 cases per annum.

Comments:

1.5 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

I take part in patient selection or refer patients for this procedure regularly.
We host a weekly multi-disciplinary peritoneal malignancy MDT for patients from throughout the island of Ireland. We also participate in a monthly teleconferenced UK & Ireland Peritoneal Mesothelioma MDT.

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Comments:

1.6 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

I have done bibliographic research on this procedure.

I have done research on this procedure in laboratory settings (e.g. device-related research).

I have done clinical research on this procedure involving patients or healthy volunteers.

Sample of recent publications:

A model for peritoneal mesothelioma management: clinical and surgical outcomes of 155 patients treated on the basis of a monthly video-conferencing national multi-disciplinary team decision meeting
Brandl A, Westbrook S, Nunn S, Arbuthnot E, Carr N, Tzivanakis A, Dayal S, Mulsow J, Youssef H, Mohamed F, Moran B, Cecil T
Br J Surg Open 2019. In Press

Zap it track it: the application of Lean Six Sigma methods to improve the screening system of low-grade mucinous neoplasms of the appendix in an acute hospital setting.
McGrath K, Casserly M, O'Mara F, Mulsow J, Shields C, Staunton O, Teeling SP, Ward M.
Int J Qual Health Care 2019. In Press

Morbidity and mortality in women with advanced ovarian cancer who underwent primary cytoreductive surgery compared to cytoreductive surgery for recurrent disease: A meta-analysis.
Bartels H, Rogers A, Shields C, Conneely J, Mulsow J, Brennan D.
Pleura and Peritoneum 2019. In Press.

Increased Incidence of Central Venous Catheter-Related Infection in Patients Undergoing Cytoreductive Surgery and Hyperthermic Intra-Peritoneal Chemotherapy.
Waters PS, Smith AW, Fitzgerald E, Khan F, Moran BJ, Shields CJ, Lynch BL, O'Loughlin C, Lynch M, Mulsow J.
Surgical Infection 2019 (Epub ahead of print)

Peritoneal metastases from extra-abdominal cancer – a population-based study.
Flanagan M, Solon J, Chang KH, Deady S, Moran B, Cahill R, Shields C, Mulsow J
Eur J Surg Oncol. 2018 Nov;44(11):1811-1817

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An 18 year population-based study on site of origin and outcome of patients with peritoneal malignancy in Ireland.
Solon JG, O'Neill M, Chang KH, Deady S, Cahill R, Moran B, Shields C, Mulsow J. Eur J Surg Oncol. 2017 Oct;43(10):1924-1931

Registries on peritoneal surface malignancies throughout the world, their use and their options.
Verwaal VJ, Rau B, Jamali F, Gilly FN, de Hingh I, Takala H, Syk I, Pelz J, Mulsow J, van der Speeten K, Shigeki K, Iversen LH, Mohamed F, Glehen O, Younan R, Yarema R, Gonzalez-Moreno S, O'Dwyer S, Yonemura Y, Sugarbaker P.
Int J Hyperthermia. 2017 Aug;33(5):528-533

Mentored experience of establishing a national peritoneal malignancy programme - Experience of first 50 operative cases.
Chang KH, Kazanowski M, Staunton O, Cahill RA, Moran BJ, Shields C, Mulsow J. Eur J Surg Oncol. 2017 Feb;43(2):395-400

Comments:

1.7 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

Fewer than 10% of colorectal surgeons engaged in this area of work.

Comments:

2 About the procedure

2.1 Does the title used above describe the procedure adequately?

Yes

Comments:

2.2 Which of the following best describes the procedure (choose one):

Established practice and no longer new.

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Cytoreductive surgery and intra-peritoneal chemotherapy as a treatment for peritoneal malignancy was first described in the 1980s. Professor Paul Sugarbaker in Washington pioneered this approach.
The approach is now accepted as standard of care in the management of patients pseudomyxoma peritonei; selected patients with colorectal cancer peritoneal metastases; selected patients with gastric cancer peritoneal metastases; selected patients with advanced ovarian cancer; selected patients with peritoneal mesothelioma.

A Pubmed search using the terms ‘cytoreductive surgery’ AND ‘HIPEC’ yields 1929 results indicating the widespread interest in and expanding evaluation of this surgical approach to peritoneal malignancy.

Comments:

2.3 What is/are the best comparator(s) (standard practice) for this procedure?

For pseudomyxoma peritonei no alternative treatment option is currently available.

For patients with peritoneal metastases from colorectal cancer, gastric cancer, and advanced ovarian cancer systemic chemotherapy may be offered.

For peritoneal mesothelioma, systemic chemotherapy may be considered.

2.4 Are there any major trials or registries of this procedure currently in progress? If so, please list.

A search on Clinicaltrials.gov using the term ‘cytoreductive surgery, hipec’ identifies 115 studies

https://clinicaltrials.gov/ct2/results?cond=&term=cytoreductive+surgery%2C+hipec&cntry=&state=&city=&dist=

Of those, 62 studies are recruiting or have yet to begin recruiting while 28 have completed recruiting patients.

2.5 Please list any abstracts or conference proceedings that you are aware of that have been *recently* presented / published on this procedure (this can include your own work). Please note that NICE will do a comprehensive literature search on this procedure and we are only asking you for any very recent or abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.

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A UNICANCER phase III trial of hyperthermic intra-peritoneal chemotherapy (HIPEC) for colorectal peritoneal carcinomatosis (PC): PRODIGE 7.
François Quenet, Dominique Elias, Lise Roca, Diane Goere, Laurent Ghouti, Marc Pocard, Olivier Facy, Catherine Arvieux, Gerard Lorimier, Denis Pezet, Frederic Marchal, Valeria Loi, Pierre Meeus, Hélène De Forges, Trevor Stanbury, Jacques Paineau, Olivier Glehen, and UNICANCER-GI Group and the French BIG-Renape Group
Journal of Clinical Oncology 2018 36:18_suppl, LBA3503-LBA3503

3 Safety and efficacy of the procedure

3.1 What are the potential harms of the procedure?

Please list any adverse events and major risks (even if uncommon) and, if possible, estimate their incidence:

Adverse events reported in the literature (if possible please cite literature)

The risk of major morbidity (Clavien Dindo grade III-V) following cytoreductive surgery and HIPEC is typically in the order of 10-20%. Mortality rates are typically 1-2% in experienced centres. Common adverse events include:

Intra-abdominal sepsis

Haemorrhage

Thromboembolism

Respiratory tract infection

Pleural effusion

Wound related problems

Morbidity rates vary according to the extent of disease and the primary pathology. Post-operative morbidity following CRS HIPEC for gastric cancer is significantly higher than that following surgery for colorectal cancer peritoneal metastases for example.

Perioperative Systemic Chemotherapy, Cytoreductive Surgery, and Hyperthermic Intraperitoneal Chemotherapy in Patients With Colorectal Peritoneal Metastasis: Results of the Prospective Multicenter Phase 2 COMBATAC Trial. Glockzin G, Zeman F, Croner RS, Königsrainer A, Pelz J, Ströhlein MA, Rau B, Arnold D, Koller M, Schlitt HJ, Piso P. Clin Colorectal Cancer. 2018 Dec;17(4):285-296. doi: 10.1016/j.clcc.2018.07.011. Epub 2018 Jul 31. PMID: 30131226

Cytoreductive Surgery With or Without Hyperthermic Intraperitoneal Chemotherapy for Gastric Cancer With Peritoneal Metastases (CYTO-CHIP study): A Propensity Score Analysis. Bonnot PE, Piessen G, Kepenekian V, Decullier E, Pocard M, Meunier B, Bereder JM, Abboud K, Marchal F, Quenet F, Goere D, Msika S, Arvieux C, Pirro N, Wernert R, Rat P, Gagnière J, Lefevre JH, Courvoisier T, Kianmanesh R, Vaudoyer D, Rivoire M, Meeus P, Passot G, Glehen O; FREGAT and BIG-RENAPE

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Networks. J Clin Oncol. 2019 Aug 10;37(23):2028-2040. doi: 10.1200/JCO.18.01688. Epub 2019 May 14. PMID: 31084544

Anecdotal adverse events (known from experience)

Chemotoxicity is a rare event but rate varies depending on the type of chemotherapy used during the HIPEC phase.

Theoretical adverse events

3.2 Please list the key efficacy outcomes for this procedure?

Overall survival
Disease free survival
Time to relapse of peritoneal tumour
Rate of relapse of peritoneal tumour
Peri-operative morbidity rates
Avoidance of complication attributable to peritoneal malignancy
Impact on quality of life

3.3 Please list any uncertainties or concerns about the *efficacy* of this procedure?

Patient selection remains challenging, particularly for patients with colorectal cancer peritoneal metastases. This is a very heterogenous group – some will have synchronous disease, other metachronous; some will have received chemotherapy with varying response, others will not; there is variability in the primary tumour subtype, presence or absence of lymph node disease and/or the presence of non-peritoneal distant metastases. Furthermore the biology of peritoneal disease remains poorly understood.

There is significant variability in the reported literature with respect to HIPEC protocols – type of chemotherapy, delivery method, dosage, temperature, duration etc. with the result that there are few universally agreed and accepted protocols.

3.4 What clinician training is required to do this procedure safely?

Fellowship training and/or mentorship by and experienced centre.

3.5 What clinical facilities are needed to do this procedure safely?

Multi-disciplinary team including gastrointestinal surgeons, liver surgeons, urologists, gynaecologists, medical oncologists, radiology and interventional radiology,

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anaesthesia and critical care medicine, dedicated pathology, specialist nursing, dietetics, physiotherapy, psychology, stoma care.

Theatre equipped with HIPEC perfusion system and trained staff.

Experienced critical care unit.
Experienced interventional radiology

3.6 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

There is a lack of consensus with the respect to the protocol for HIPEC.

4 Audit Criteria

Please suggest potential audit criteria for this procedure.

4.1 Beneficial outcome measures. This should include short and long term clinical outcomes, quality-of-life measures and patient related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured:

Overall survival – 1, 3, 5 year rates and median overall survival
Disease free and progression free survival
Time to peritoneal relapse
Quality of life at 3, 6, 12 months post surgery

4.2 Adverse outcome measures. This should include early and late complications. Please state the post procedure timescales over which these should be measured.

30 and 90 day morbidity and mortality rates to include a breakdown of morbidity (Clavien Dindo Grade I - V)

5 Uptake of the procedure in the NHS

5.1 If it is safe and efficacious, in your opinion, how quickly do you think use of this procedure will be adopted by the NHS (choose one)?

Slowly (over decades)

International comparison suggests that one Centre for Peritoneal Malignancy is needed for every 5 million of population. It is expected that each centre would have an operating volume of 50-60 cases per annum. The recent expansion of CRS HIPEC to advanced ovarian cancer (van Driel. N Eng J Med 2018 Jan 18;378(3):230-240) is likely to further increase the operating volume in each centre. Given this anticipated volume and requirement for trained surgeons it is likely to take a number of years before such a service could be delivered throughout the NHS.

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Comments:

5.2 If it is safe and efficacious, in your opinion, will this procedure be carried out in (choose one):

Fewer than 10 specialist centres in the UK.

Comments:

5.3 If it is safe and efficacious, in your opinion, the potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources:

Moderate.

For a population of 50 million approximately 10 centres may be required. A conservative estimate of annual case volume nationally for the NHS would be 600 CRS HIPEC per annum.
Typical in-patient hospital stay after CRS HIPEC is 14 days, with 2-3 days in critical care / high dependency.

Comments:

6 Other information

6.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

Comments:

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7 Data protection and conflicts of interest

7.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The professional expert questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

☐ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above. For more information about how we process your personal data please see our privacy notice

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7.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the “Conflicts of Interest for Specialist Advisers” policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures. Conflicts of Interest for Specialist Advisers

Declarations of interest form			
Type of interest	Description of interest	Relevant dates	
		Interest arose	Interest ceased

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* Guidance notes for completion of the Declarations of interest form

Name and role	Insert your name and your position in relation to your role within NICE
Description of interest	Provide a description of the interest that is being declared. This should contain enough information to be meaningful to enable a reasonable person with no prior knowledge to be able to read this and understand the nature of the interest. Types of interest: **Direct interests** **Financial interests** - Where an individual gets direct financial benefits from the consequences of a decision they are involved in making. *For examples of financial interests please refer to the policy on declaring and managing interests.* **Non-financial professional and personal interests -** Where an individual obtains a non-financial professional or personal benefit, such as increasing or maintaining their professional reputation, from the consequences of a decision they are involved in making. *For examples of non-financial interests please refer to the policy on declaring and managing interests.* **Indirect interests -** Where there is, or could be perceived to be, an opportunity for a third party associated with the individual in question to benefit. A benefit may arise from both a gain or avoidance of a loss.
Relevant dates	Detail here when the interest arose and, if applicable, when it ceased.
Comments	This field should be populated by the guidance developer and outline the action taken in response to the declared interest. It should include the rationale for this action, and the name and role of the person who reviewed the declaration.

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mirella Marlow
Programme Director

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Interventional Procedures Programme

Professional Expert questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**Cytoreduction surgery followed by hyperthermic intraoperative peritoneal chemotherapy for peritoneal carcinomatosis.**
Name of Professional Expert:	John [Ian] T Jenkins
Job title:	Consultant Colorectal Surgeon
Professional Regulatory Body:	GMC
	Other (specify)
Registration number:	4449137
Specialist Society:	ACPGBI
Nominated by (if applicable):	Mr Faheez Mohammad.

1. About you and your speciality's involvement with the procedure

1.1. Do you have adequate knowledge of this procedure to provide advice?

Yes

1.2. Is this procedure relevant to your specialty?

Yes.

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1.3 Is this procedure performed by clinicians in specialities other than your own?

<u>Yes – please comment</u>

Comments: Ovarian Cancer-Gynaecological Oncology Surgeons/ Gastric Cancer- UGI surgeons. Other- mesothelioma

1.4 If you are in a specialty that does this procedure, please indicate your experience with it:

<u>I do this procedure regularly.</u>

1.5 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

<u>I take part in patient selection or refer patients for this procedure regularly.</u>

1.6. Please indicate your research experience relating to this procedure (please choose one or more if relevant):

I have done bibliographic research on this procedure.

~~I have done research on this procedure in laboratory settings (e.g. device-related research).~~

I have done clinical research on this procedure involving patients or healthy volunteers.

~~I have had no involvement in research on this procedure.~~

Other (please comment)

Comments:

1.7. Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

~~More than 50% of specialists engaged in this area of work.~~

~~10% to 50% of specialists engaged in this area of work.~~

Fewer than 10% of specialists engaged in this area of work.

~~Cannot give an estimate.~~

Comments:

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2. About the procedure

2.1. Does the title used above describe the procedure adequately?

Yes

2.2. Which of the following best describes the procedure (choose one):

Established practice and no longer new.

~~A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.~~

~~Definitely novel and of uncertain safety and efficacy.~~

~~The first in a new class of procedure.~~

Comments: Controversy regarding optimal HIPEC regimen although role of cytoreductive surgery more clear.

2.3. What is/are the best comparator(s) (standard practice) for this procedure?

Systemic chemotherapy/ "inoperable" disease/ cytoreductive surgery alone

2.4. Are there any major trials or registries of this procedure currently in progress? If so, please list.

For CPM; Recently completed trials include PRODIGE7, COLOPEC
ICARuS, CAIRO6, ProphyloCHIP,
For Ovarian Cancer: OVHIPEC-I, CHIPPI Trial, UNICANCER,
For Gastric Cancer- GASTROCHIP, GASTRIPEC,
PIPAC Trials:

2.5. Please list any abstracts or conference proceedings that you are aware of that have been *recently* presented / published on this procedure (this can include your own work). Please note that NICE will do a comprehensive literature search on this procedure and we are only asking you for any very recent or abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.

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3. Safety and efficacy of the procedure

3.1. What are the potential harms of the procedure?

Please list any adverse events and major risks (even if uncommon) and, if possible, estimate their incidence:

Adverse events reported in the literature (if possible please cite literature)

Extent of carcinomatosis (PCI), duration of surgery, number of GI anastomoses, more than four peritonectomy procedures and perioperative blood loss have been associated with severe morbidity after CRS and HIPEC

GI complications [5-15%]: anastomotic leak, enteric fistulas, intraperitoneal abscess,

Haematological complications: 4-40% rate, neutropenia and related sepsis complications [4-40%],

Pulmonary complications: major pulmonary complications in 10-15%, increased with diaphragmatic peritonectomies, pneumonia [5-10%], pleural effusions

Other complications: AKI, VTE, UTI, Bleeding

Anecdotal adverse events (known from experience)

CVA,

Theoretical adverse events

Device related injuries, thermal injuries

3.2. Please list the key efficacy outcomes for this procedure?

Disease-free survival and overall survival, morbidity and mortality

3.3. Please list any uncertainties or concerns about the *efficacy* of this procedure?

Extent of disease and success of salvage surgery, role of HIPEC with complete cytoreduction, role of HIPEC with incomplete cytoreduction; regimen and dosing of HIPEC; role of concurrent systemic chemotherapy,

3.4. What clinician training is required to do this procedure safely?

MDT decision making processes, experience in extended surgical resections, perfusion device management, chemotherapy safety, prescribing and disposal protocols, theatre staff training, anaesthesia and ITU staff training. Special arrangements for clinical governance, consent and audit or research.

3.5. What clinical facilities are needed to do this procedure safely?

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MDT, Intensive care facilities and critical care facilities, HIPEC perfusion devices, trained ward nursing, disposal bins.

3.6. Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

Cost and Cost-effectiveness

4 Audit Criteria

Please suggest potential audit criteria for this procedure.

4.1 Beneficial outcome measures. This should include short and long term clinical outcomes, quality-of-life measures and patient related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured:

Completeness of cytoreduction
Overall survival
QoL at baseline, predischarge, 3, 6 and 12 months e.g. SF-36 v 2

4.2 Adverse outcome measures. This should include early and late complications. Please state the post procedure timescales over which these should be measured.

Complications in 30 days e.g. Clavien-Dindo
Readmissions/ reoperations within 1 year
Mortality at 90 days
Mortality at 1 year
Time to disease recurrence [standardised follow-up protocols]

5 Uptake of the procedure in the NHS

5.1 If it is safe and efficacious, in your opinion, how quickly do you think use of this procedure will be adopted by the NHS (choose one)?

Rapidly (within a year or two).

Slowly (over decades)

I do not think the NHS will adopt this procedure

Comments:

5.2 If it is safe and efficacious, in your opinion, will this procedure be carried out in (choose one):

Most or all district general hospitals.

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A minority of hospitals, but at least 10 in the UK.

Fewer than 10 specialist centres in the UK.

Cannot predict at present.

Comments:

5.3 If it is safe and efficacious, in your opinion, the potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources:

Major.

Moderate.

Minor.

Comments:

6 Other information

6.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

Comments:

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7 Data protection and conflicts of interest

7.1 Data Protection

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X I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above. For more information about how we process your personal data please see our privacy notice

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Declarations of interest form

Type of interest	Description of interest	Relevant dates	
		Interest arose	Interest ceased
NONE			

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Relevant dates	Detail here when the interest arose and, if applicable, when it ceased.
Comments	This field should be populated by the guidance developer and outline the action taken in response to the declared interest. It should include the rationale for this action, and the name and role of the person who reviewed the declaration.

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mirella Marlow
Programme Director

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Professional Expert questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**Cytoreduction surgery followed by hyperthermic intraoperative peritoneal chemotherapy for peritoneal carcinomatosis**
Name of Professional Expert:	Sarah T O'Dwyer
Job title:	Professor of Surgery

✓ Professional Regulatory Body: GMC ☐

Other (specify) ☐

Registration number: 2503426

Specialist Society: Association of Coloproctology Great Britain and Ireland

Nominated by (if applicable):

Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS)

1 About you and your speciality's involvement with the procedure

1.1 Do you have adequate knowledge of this procedure to provide advice?

✓ ☐ Yes.

☐ No – please answer no more questions and return the form

Comments:

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1.2 Is this procedure relevant to your specialty?

✓ ☐ Yes.

☐ No - please answer no more questions. Please give any information you can about who is likely to be doing the procedure and return the form.

Comments:

1.3 Is this procedure performed by clinicians in specialities other than your own?

✓ ☐ Yes – please comment
In the UK the leads for this service are all from a colorectal specialty but internationally there are specialties including Upper GI, HPB involved

☐ No

Comments:
Most units work as part of a multispecialty team involving specialist hepatibiliary surgeons as required

Although you use the term peritoeneal carcinomatosis most specialists would now use peritoneal metastases (PM) and specify which primary disease is involved eg colorectal, gastric, ovarian, HPB
Current commissioning From NHS England only involves colorectal PM although in Europe the procedure is widely adopted for ovarian and gastric cancer
NIHR/HTA are currently supporting an evidence base assessment on this topic which is expected to report in 2021

1.4 If you are in a specialty that does this procedure, please indicate your experience with it:

☐ I have never done this procedure.

☐ I have done this procedure at least once.

✓ ☐ I do this procedure regularly.

Comments:

We Have undertaken over 1300 cases since 2002 and are currently commissioned to undertake 175 procedures/year for appendix and colorectal neoplasia

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1.5 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

✓ ☐ I take part in patient selection or refer patients for this procedure regularly.

Comments: We have processed >3200 referrals since 2002

1.6 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

✓ ☐ I have done bibliographic research on this procedure.

✓ ☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

✓ ☐ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

✓ ☐ Other (please comment)
We are currently undertaking the NIHR/HTA evidence review in conjunction with UCL
We have recently been awarded a CRUK Accelerator award to undertake detailed evaluation of genomics in patient samples of those suffering with Pseudomyxoma Peritonei who undergo this procedure

Comments:

1.7 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

✓ ☐ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:
There are only three commissioned units in England to date

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NHS England has recently asked for bids to offer this for colorectal PM to cover four Lots in England- the intention to increase provision to include a unit for London.

Following a randomised controlled trial published in February 2018 in ovarian cancer many gynaecological units are considering undertaking the procedure for ovarian cancer

2 About the procedure

2.1 Does the title used above describe the procedure adequately?

☐ Yes

✓ ☐ No - If no, please suggest alternative titles.
Cytoreductive surgery (CRS) and hyperthermic intraoperative peritoneal chemotherapy (HIPEC) for peritoneal metastases : include the primary cancers to be treated eg colorectal and ovarian cancer

Comments:

2.2 Which of the following best describes the procedure (choose one):

✓ ☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

Although established for specific tumour types there is current debate regarding the details of HIPEC in different tumours. Studies are required to evaluate the optimal intraperitoneal treatments for each primary tumour

2.3 What is/are the best comparator(s) (standard practice) for this procedure?

Palliative systemic chemotherapy

2.4 Are there any major trials or registries of this procedure currently in progress? If so, please list.

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ERERPET TRIAL list 1112.xlsx

2.5 Please list any abstracts or conference proceedings that you are aware of that have been *recently* presented / published on this procedure (this can include your own work). Please note that NICE will do a comprehensive literature search on this procedure and we are only asking you for any very recent or abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.

given the short time I have had to provide you with this I am not in a position to include info here as would require consent from other participants

3 Safety and efficacy of the procedure

3.1 What are the potential harms of the procedure?

Please list any adverse events and major risks (even if uncommon) and, if possible, estimate their incidence:

Adverse events reported in the literature (if possible please cite literature)

Anecdotal adverse events (known from experience)

included in our annual report is the table of M and M since 2010

HSS CPOC Service Annual Report 2019

Theoretical adverse events

3.2 Please list the key efficacy outcomes for this procedure?

Potential cure and long term cancer free survival in 40% of patients suitable for the procedure
Overall improved median survival from 16 months to 41months

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3.3 Please list any uncertainties or concerns about the *efficacy* of this procedure?

Questions raised regarding the type and length of chemotherapy exposure: see 3.6 below

3.4 What clinician training is required to do this procedure safely?

At least two experienced surgeons who have undergone training to the level of the ESSO ESPOI Fellowship with mentorship for two years

3.5 What clinical facilities are needed to do this procedure safely?

See NHS service specification 2013

3.6 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

Due to recent debate regarding an unpublished (abstract only) trial of CRS v CRS and HIPEC in colorectal PM some providers in Europe have questioned the need for adding HIPEC to the treatment in CRC.
This has the danger of individual surgeons undertaking CRS alone without the necessary training in this complex surgical procedure

4 Audit Criteria

Please suggest potential audit criteria for this procedure.

4.1 Beneficial outcome measures. This should include short and long term clinical outcomes, quality-of-life measures and patient related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured:

Peritoneal disease free survival (DFS), total DFS, overall survival 3, 5, 10 years
Cancer related QOL scores 0-2years
Return to employment at 2 years

4.2 Adverse outcome measures. This should include early and late complications. Please state the post procedure timescales over which these should be measured.

Postoperative morbidity using Clavidian Dindo grading using a prosepective recording method
90day mortality
Delayed discharge beyond 14 days
Delayed discharge from CCU beyond 48hrs
Reoperation rates 30d

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Readmission rates 60d
Permanent stoma rate beyond 18 months

5 Uptake of the procedure in the NHS

5.1 If it is safe and efficacious, in your opinion, how quickly do you think use of this procedure will be adopted by the NHS (choose one)?

✓ ☐ Rapidly (within a year or two).

☐ Slowly (over decades)

☐ I do not think the NHS will adopt this procedure

Comments:

Once the evidence has been reviewed there will be a need for a lead in time to train up additional centres with mentorship from established centres. It is well documented that the learning curve is in the order of 100-120 procedures to minimise morbidity and mortality.
If additional cancers are commissioned eg ovarian training in CRS will be over a two-three year period

5.2 If it is safe and efficacious, in your opinion, will this procedure be carried out in (choose one):

☐ Most or all district general hospitals.

✓ ☐ A minority of hospitals, but at least 10 in the UK.

✓ ☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

Whether 10 or fewer will depend on the evidence review for individual cancers eg for colorectal cancer this may be 10 but for less common cancers eg ovarian this maybe 4-6

5.3 If it is safe and efficacious, in your opinion, the potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources:

✓ ☐ Major.

☐ Moderate.

☐ Minor.

Comments:

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The UK lags behind Europe and the rest of the world in adopting these techniques and extending them to additional cancers.
Appropriate selection can have a major impact on individual patient survival and QOL
In addition the cost benefit when appropriately applied has potential significance in that patients are otherwise entering into palliative treatments that may in themselves be expensive and a significant drain on resources.

It must

6 Other information

6.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

Comments:
I am surprised you are undertaking this review at this time given that NIHR/HTA are currently funding a comprehensive evidence review to report in 2021.
It would have seemed a better use of resource to await that report.

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7 Data protection and conflicts of interest

7.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The professional expert questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

☑ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above. For more information about how we process your personal data please see our privacy notice

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7.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures. Conflicts of Interest for Specialist Advisers

Declarations of interest form			
Type of interest	**Description of interest**	**Relevant dates**	
		Interest arose	**Interest ceased**
NHS Job plan	*Part funded from commissioned work in this area*	*2002 - date*	**current**
Research	Current research grants in UK and	**2019-2025**	**current**

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	internationally		
Education	Supported by RAND Academy who sponsors two meetings/ year in UK	**2015**	**current**

* Guidance notes for completion of the Declarations of interest form

Name and role	Insert your name and your position in relation to your role within NICE
Description of interest	Provide a description of the interest that is being declared. This should contain enough information to be meaningful to enable a reasonable person with no prior knowledge to be able to read this and understand the nature of the interest. Types of interest: **Direct interests** **Financial interests** - Where an individual gets direct financial benefits from the consequences of a decision they are involved in making. *For examples of financial interests please refer to the policy on declaring and managing interests.* **Non-financial professional and personal interests -** Where an individual obtains a non-financial professional or personal benefit, such as increasing or maintaining their professional reputation, from the consequences of a decision they are involved in making. *For examples of non-financial interests please refer to the policy on declaring and managing interests.* **Indirect interests -** Where there is, or could be perceived to be, an opportunity for a third party associated with the individual in question to benefit. A benefit may arise from both a gain or avoidance of a loss.
Relevant dates	Detail here when the interest arose and, if applicable, when it ceased.
Comments	This field should be populated by the guidance developer and outline the action taken in response to the declared interest. It should include the rationale for this action, and the name and role of the person who reviewed the declaration.

Thank you very much for your help.

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Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair	**Mirella Marlow Programme Director**

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