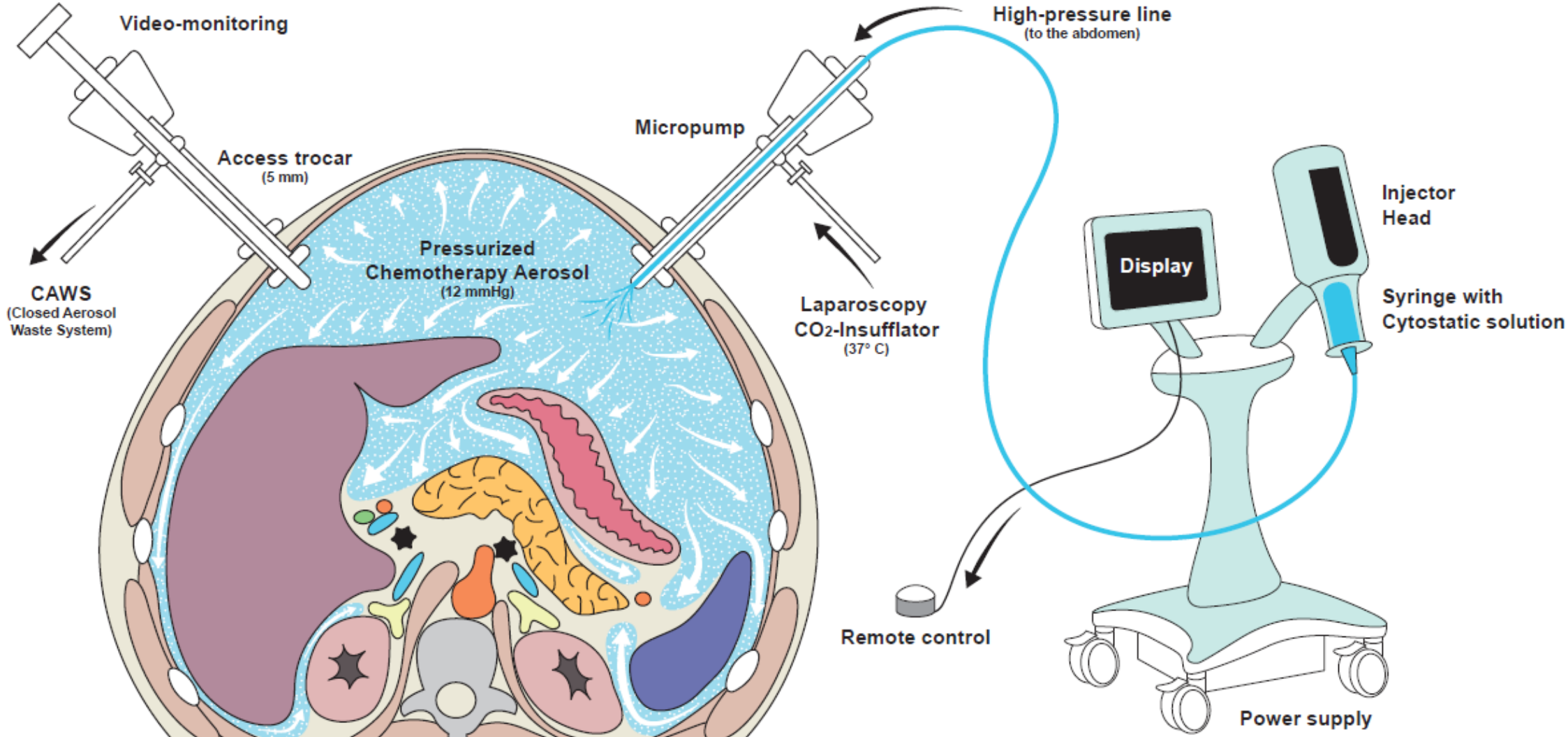
Role of PIPAC and the PICCOS Trial

Christopher Peters- Imperial College London

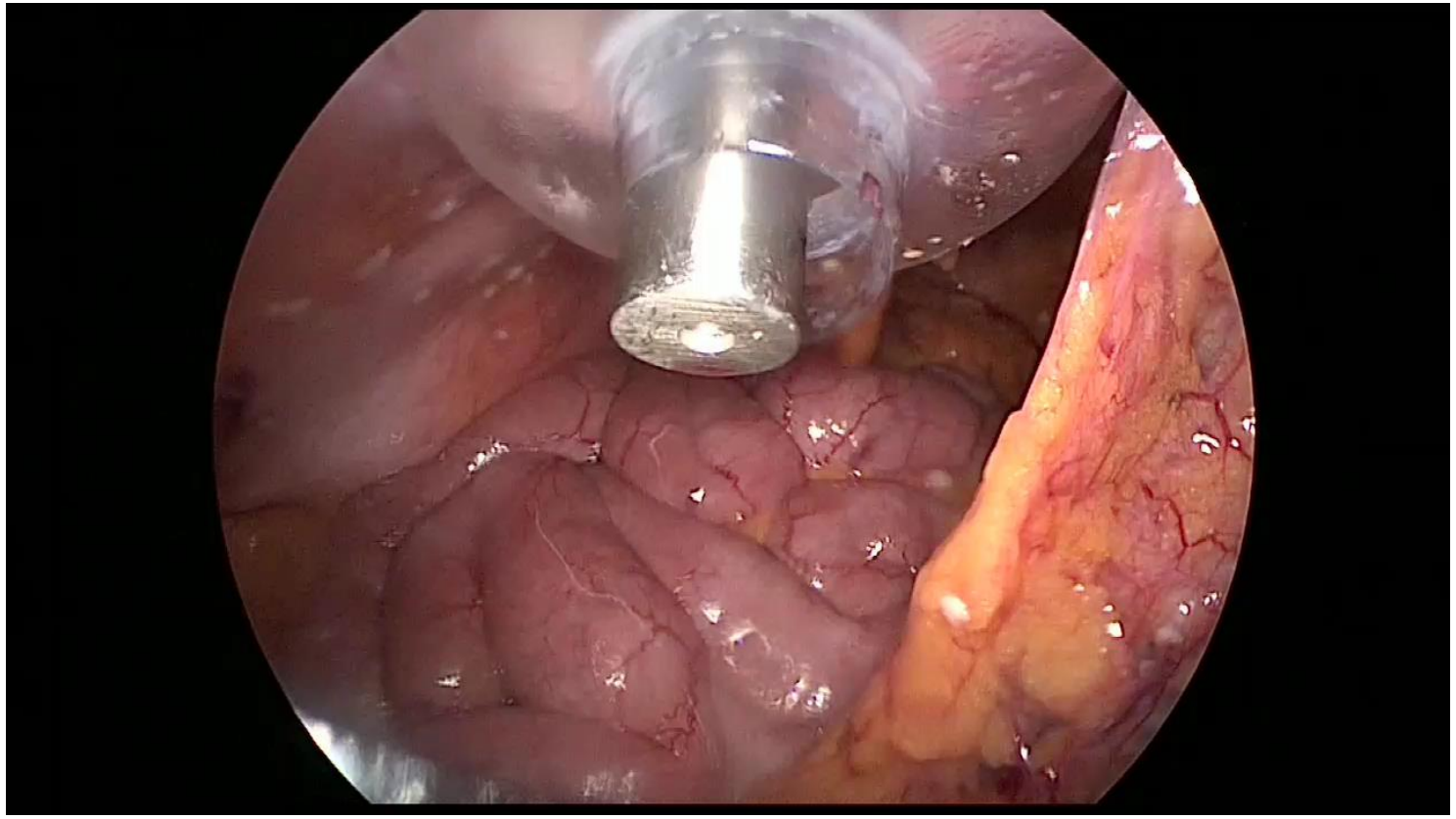
Sarah Gwynne- Swansea Bay UHB

What is PIPAC?- Treatment for Peritoneal Disease

- Pressurized Intra Peritoneal Aerosolized Chemotherapy (PIPAC)
- Aims to treat an unmet clinical need
- Peritoneal Metastasis seen in up to17% Gastric Cancer patients
- Goal of PIPAC is to maintain Quality of Life

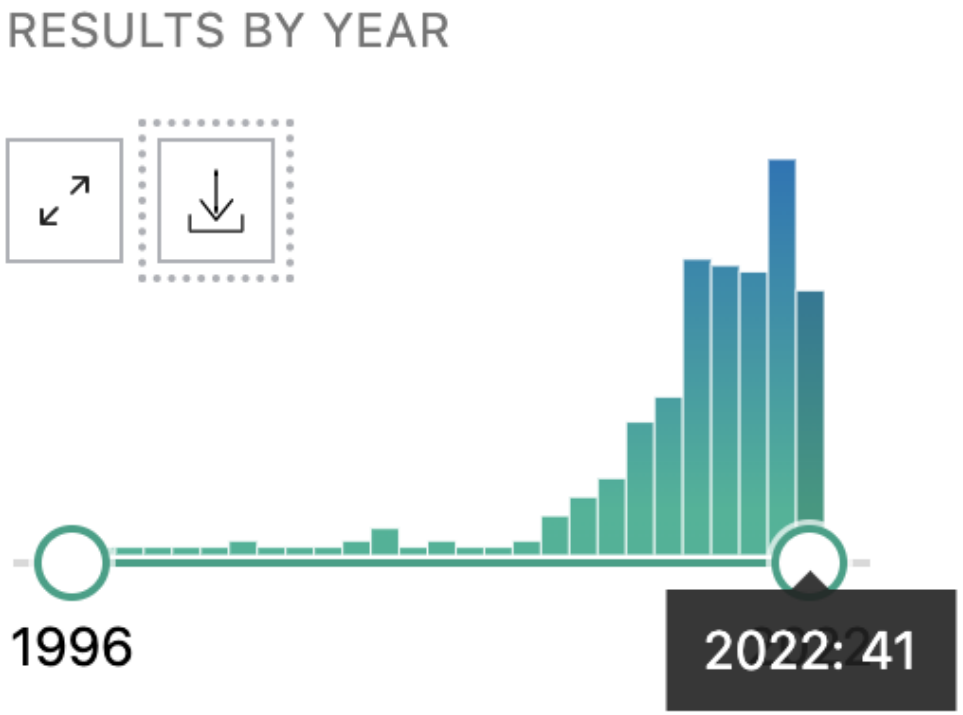

Video-monitoring
Access trocar
(5 mm)
CAWS
(Closed Aerosol
Waste System)
Pressurized
Chemotherapy Aerosol
(12 mmHg)
Micropump
High-pressure line
(to the abdomen)
Laparoscopy
CO2-Insufflator
(37° C)
Remote control
Display
Injector
Head
Syringe with
Cytostatic solution
Power supply

PIPAC Delivery..



Courtesy of M Hubner

Evidence….

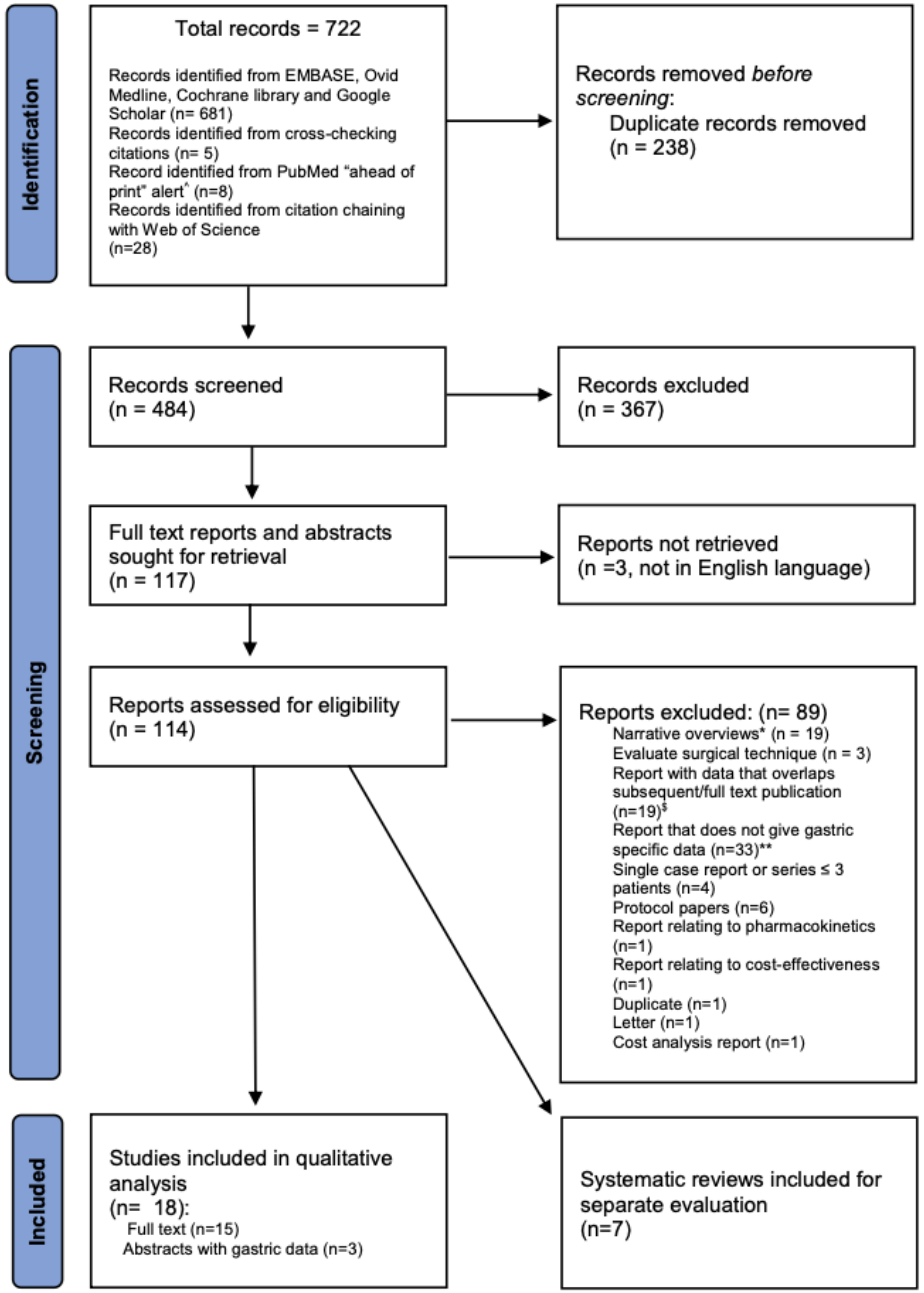


- Safety — Yes
- Phase 1 trials — Yes
- Phase 2 trials — Yes
- RCTs — None

271 papers on PUBMED

PIPAC for gastric cancer with peritoneal metastases: A systematic review by the PIPAC UK Collaborative

A. Case, S. Prosser , C.J. Peters, R. Adams, S. Gwynne, On behalf of the PIPAC UK Collaborative



Crit Rev Oncol Hematol 2022

- 751 patients with Gastric Cancer
  - 4 prospective
  - 11 retrospective
  - No phase III studies
- **Median overall survival was 8 – 19.1 months**
- **Complete response 0-35%**
- **Partial response 0-83.3%**
- Grade 3 and 4 toxicity was 0.7-25% and 0-4.1% respectively.

Conclusion

PIPAC may offer promising survival benefits, limited toxicity and maintain QOL for gastric cancer patients, but phase 3. randomised evidence is needed.

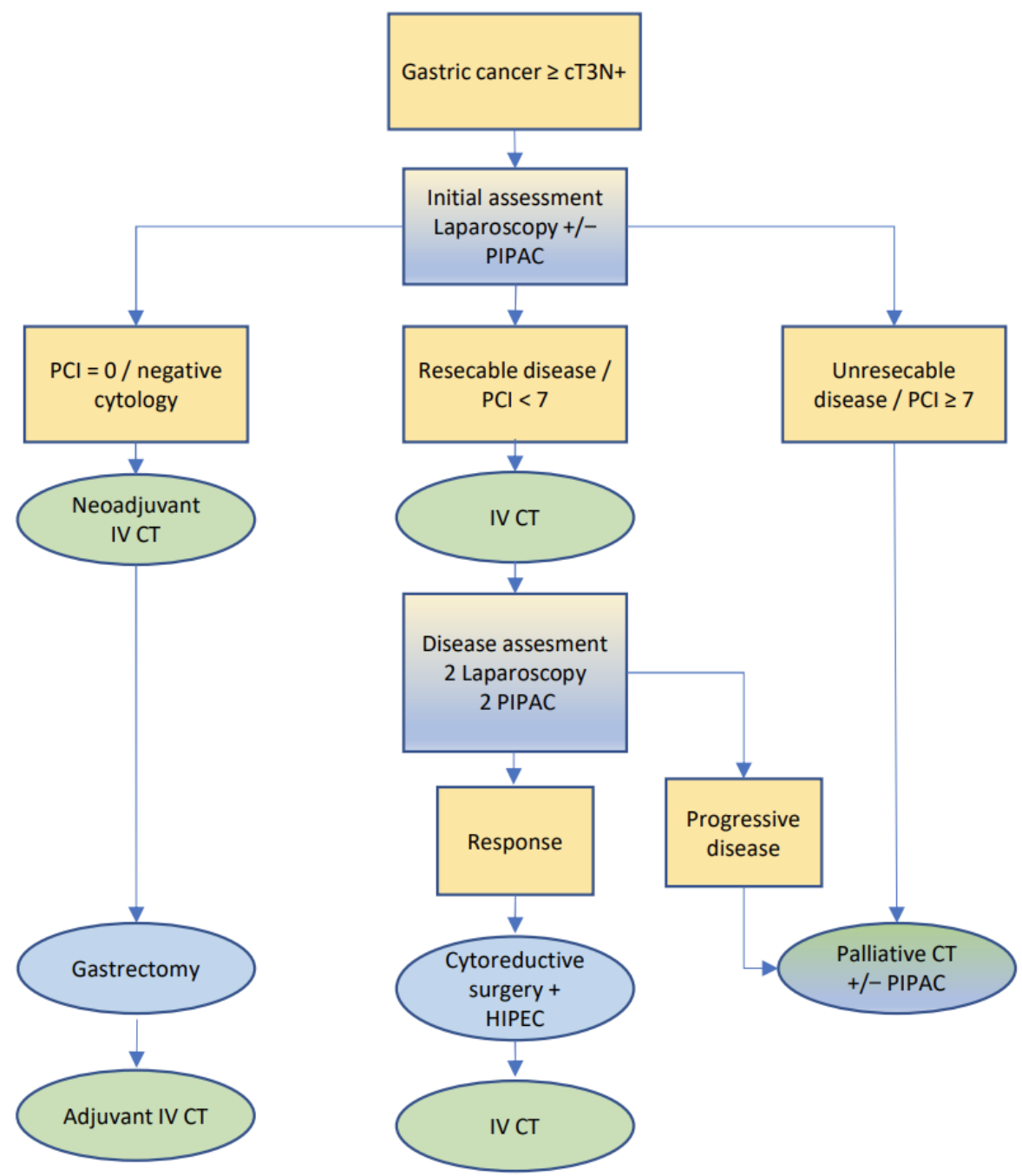


Figure 3. Treatment algorithm for gastric cancer.

1 2 3
8 0 4
7 6 5

SPCG

Swiss Peritoneal Cancer Group

Schweiz Suisse Svizzera Switzerland

Comprehensive Treatment Algorithms of the Swiss Peritoneal Cancer Group for Peritoneal Cancer of Gastrointestinal Origin

Cancers **2022**, *14*, 4275.
https://doi.org/10.3390/cancers14174275

Stage of innovation	Description	No. of patients	Proposed method of investigation	Studies included in this review
0 – Idea (pre-clinical)	Feasibility and definition of procedure	None	Simulated, cadaver, animal, modelling	Pre-clinical studies in animals (*in vivo* and post-mortem models) and *in vitro*
1 - Idea	Proof of concept. First in human	Very few	Case reports, small case series	Case reports, small case series, occupational health and safety studies. Data relates to safety and technical feasibility
2a - Development	Therapy evolving. Refining and modifying the technique.	Usually <30	Prospective development studies	Larger case series, non-randomised studies. Prospective and retrospective case series. Single-centre
2b – Exploration	Learning curves progressing, indication expanding	Many	Prospective series, multi-site, feasibility RCT.	Large multi-centre case series, studies looking at new indication
3 – Assessment	Procedure has clear definition and used by many surgeons, but needs to be tested against standard of care	Many	RCT	RCT and RCT protocols
4 – Long-term	Long-term follow up with registry data, to monitor late/rare complications	Many	Registry, late/rare case reports	N/A

The IDEAL Framework

The IDEAL Framework describes the stages surgical innovations pass though

- Idea
- Development
- Exploration
- Assessment
- Long-term follow-up

Fig. 2 Adoption of pressurized intraperitoneal aerosol chemotherapy according to the IDEAL criteria

Stage 0 Stage 1 Stage 2a Stage 2b Stage 3

	2000	2012	2013		2014		2015			2016				2017			2018				
Stage of innovation	I	I	I	D	I	D	I	D	E	I		D	E	I		D	I		D	E	A
	0	0	1	2a	1	2a	1	2a	2b	0	1	2a	2b	0	1	2a	0	1	2a	2b	3
Bochum, Germany	1	2	2	P*	2	1	1	2	1	5	1	3	1	2	1	2		1	3	1	
Zurich, Switzerland								P*													
Magdeburg, Germany										1											
Seoul, South Korea										1											
Odense, Denmark											1				1				2 + P	1 + P	
Turin, Italy											1	1							P*		
Moscow, Russia												1									
Rome, Italy												P*									
Dresden, Germany														2							
Ghent, Belgium														1	1					P†	
Paris, France														1						P	
Porto Algere, Brazil														1				1			
Tubingen, Germany														1			1		1	1	
Lausanne, Switzerland																3			1		
Lyon, France																1		1	2		P§
Eindhoven, the Netherlands																P‡					
Essen, Germany																	1				
Wroclaw, Poland																	3				
Manipal, India																		1			P
Mumbai, India																		1			
Munich, Germany																		1			
Singapore, Singapore																		P			
Saint-Herblain, France																		P¶			
Torun, Poland																		1	1		
Zurich, Switzerland																			1		
Leipzig, Germany																				1	
Frankfurt, Germany																					P#
Total publications by stage	1	2	2	1P	2	1	1	2 + 1P	1	7	3	5 + 1P	1	8	3	6 + 1P	5	7 + 2P	11 + 2P	4 + 3P	3P
Total publications by year	1	2	2 + 1P		3		4 + 1P			16 + 1P				17 + 1P			27 + 10P				
Cumulative total no. of active centres	1	1	1		1		2			9				17			28				

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Tate et al

BJS Open 2020

Stage 3

Stage of innovation	2000	2012	2013	2014		2015		2016				2017				2018					2019					2020				2021				2022		
	I	I	I	I	D	I	E	I		D	E	I		D	E	I		D	E	A	I		D	E	A	I		D	E	I		D	E	I	D	E
	0	0	1	1	2a	1	2b	0	1	2a	2b	0	1	2a	2b	0	1	2a	2b	3	0	1	2a	2b	3	0	1	2a	2b	0	1	2a	2b	1	2a	2b
Geneva, Switzerland*	1																						P*										P*			
Magdeburg, Germany*		2						1																												
Bochum, Germany*			2	2	1	1	3	5	1	3	1	2	1	2		1		4	1		1							1				1			1
Seoul, South Korea								1																		1				4		P*				
Odense, Denmark									1				1					2+P	1+P				1+P*					3				1				
Turin, Italy										2													1					1				1+P				
Moscow, Russia										1																										
Rome, Italy										P*																	1	2								
Dresden, Germany												2																		1						
Ghent, Belgium												1	1					1			1		P			2				1						
Paris, France												1								P										1				1		
Porto Algere, Brazil												1									1															
Zurich, Switzerland														p*				1																		
Lausanne, Switzerland														3				1																1		
Lyon, France															1		1	1		P			1			2						P*	3		1	
Tubingen, Germany																1		1	1			1	1+P*							1						
Essen, Germany																1																				
Wroclaw, Poland																2					1															
Mumbai, India																	1						1													
Munich, Germany																	1																			
Torun, Poland																	1	1	1				1													
Bangalore, India																		1		P			1		P											
Leipzig, Germany																		1										1								
Singapore, Singapore																		P												1		1+P*				
Saint-Herblain, France																		P										1								
Frankfurt, Germany																				P																
Strasburg, Germany																						1														
London, U.K.																							P*													
Eindhoven, the Netherlands																								P								2	1+P			
Montpeiller, France																								1	P						1					
Orleans, France																										1										
Berlin, Germany																												1								
Nice, France																												1								
Tel Aviv, Israel																												P*								
Shanghai, China																												P*								
Padova, Italy																												P*								
St. Petersburg, Russia																													P*							
Limoges, France																															1					
Los Angeles, USA																																P				
Vilnius, Lithuania																																1				
Grenoble, France																																1+P*				
Valencia, Spain																																P*				
Milan, Italy																																P*				
Nancy, France																																P*				
Sao Paulo, Brazil																															1					
Adelaide, Australia																																P				
Total publications by stage	1	2	2	2	1	1	3	7	2	6+1P	1	7	3	5+1P	1	5	4	14+3P	4+1P	4P	4	2	7+5P	1+1P	2P	6	1	11+3P	1P	9	3	7+10P	6+2P	1	1	1
Total publications by year	1	2	2	3		4		16 + 1P				16 + 1P				27 + 8P					14 + 8P					18 + 4P				25 + 12P				3		
Cumulative total number of active centres	1	2	3	3		3		8				15				26					30					37				46				46		

Legend: Stage 0 | Stage 1 | Stage 2a | Stage 2b | Stage 3

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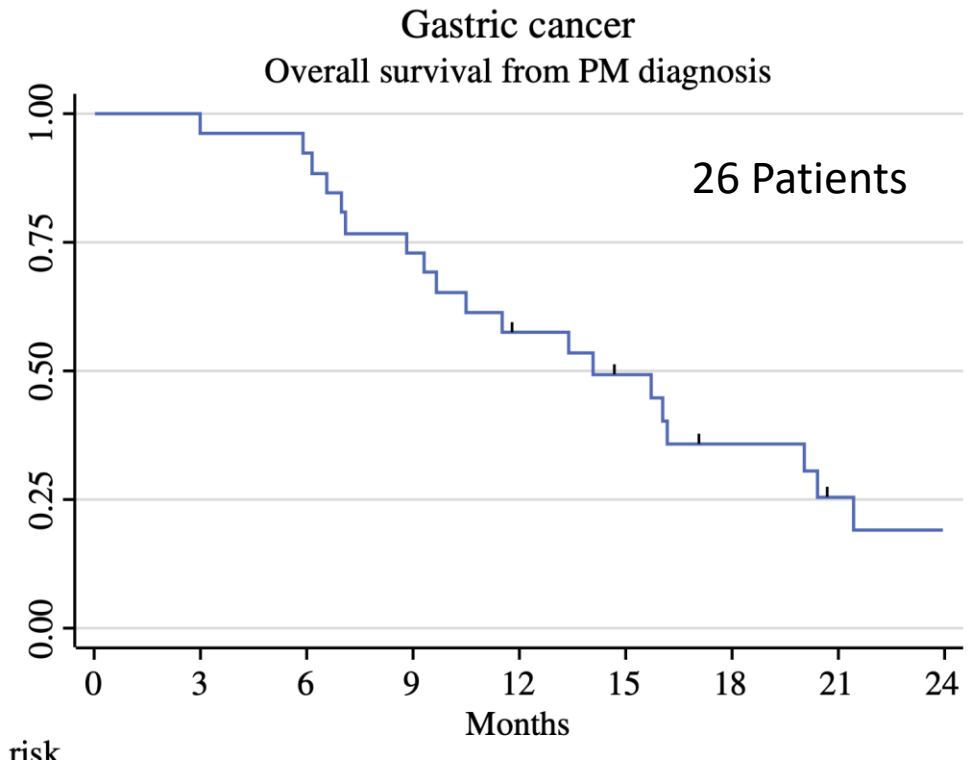
Baggaley et al

BJS 2022

Stage 3

PIPAC-OPC2 Study

Prospective, controlled phase II trial in patients with peritoneal metastasis from GI, gynaecological, HPB, primary peritoneal, or unknown primary cancer.



Complete or major histological response to treatment was observed in 38 patients (61%) who had three PIPACs.

Ann Surg Oncol https://doi.org/10.1245/s10434-022-13010-0

Interventional procedures recommendations

- 1. Standard arrangements
- 2. Special arrangements
- 3. Only in research
- 4. Do not use

NHS
National Institute for Health and Clinical Excellence

Published October 2020

1 Recommendations

1.1 Evidence on the safety of pressurised intraperitoneal aerosol chemotherapy for peritoneal carcinomatosis shows that this procedure can cause serious but well-recognised side effects. Evidence on its efficacy is inadequate in quality. Therefore, this procedure should only be used in the context of research. Find out what only in research means on the NICE website.

1.2 Further research should be in the form of randomised controlled trials comparing pressurised intraperitoneal aerosol chemotherapy with standard care. Studies should report details of patient selection including type of tumour, the chemotherapy drugs used, survival and quality-of-life outcomes.

PIPAC UK COLLABORATIVE

UKIOG Meeting January 2023

PICCOS

PIPAC in Cancers of the Colon, Ovaries and Stomach

Principle Investigators

Jared Torkington
Sadie Jones

Leads for Gastric Cancer

Sarah Gwynne
Christopher Peters

Current status of PIPAC in UK

Demonstrated efficacy (PFS and QOL) in the settings of peritoneal metastases from gynae, colorectal and gastric malignancy – but heterogeneous data

Had been being used for selected colorectal cases in Imperial and Cardiff

Currently no PIPAC available in UK

PICCOS trial

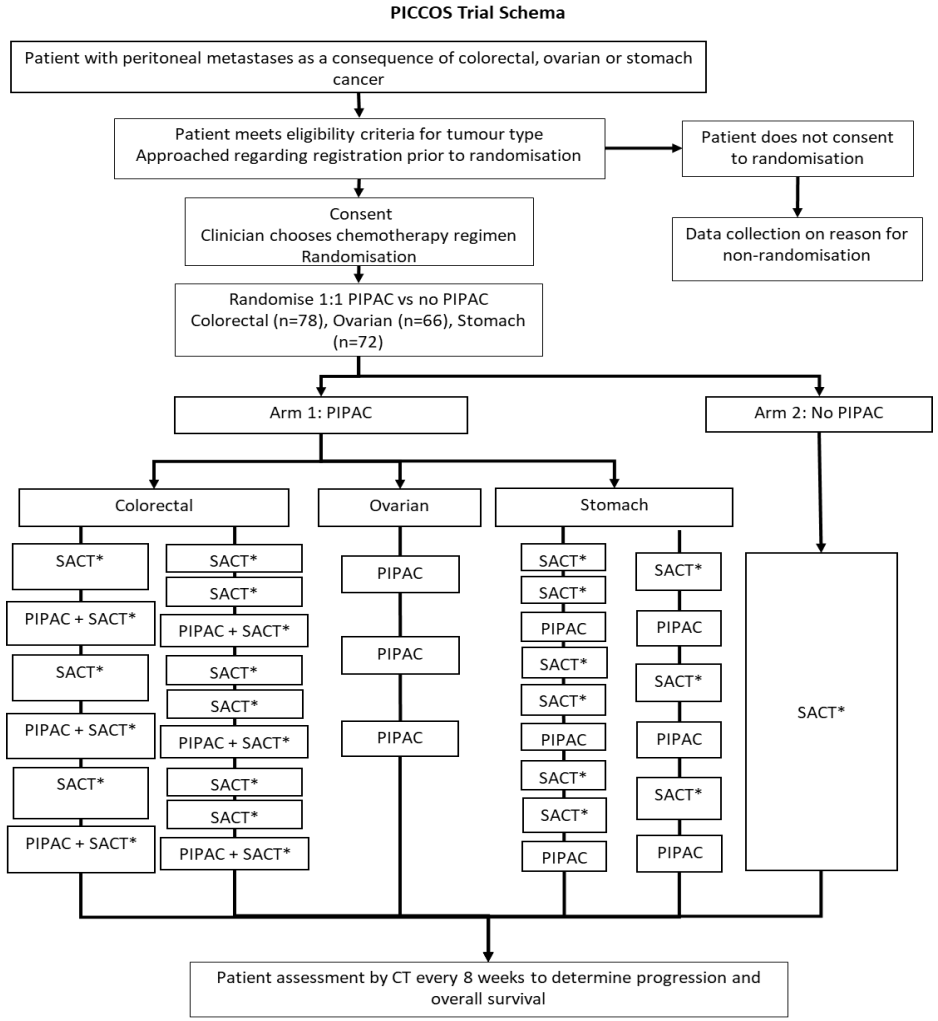
Pressurised IntraPeritoneal Aerosolised Chemotherapy (PIPAC) in the management of cancers of the ***colon, ovary and stomach***: a randomised controlled phase II trial of efficacy in peritoneal metastases

Funded NIHR EME 2022

Trial opening Summer 2023

CIs Jared Torkington, Sadie Jones

SACT at local site, PIPAC at nearest PIPAC centre open to the trial (for all arms)



* SACT = Systemic Anti-Cancer Therapy. Should be as per standard of care options listed within the PICCOS protocol. There are 2 or 3 weekly options for colorectal/ stomach groups, regimen given is chosen by treating clinician, ovarian SACT is 4 weekly.

Stomach arm

Co- leads Sarah Gwynne and Chris Peters

Support of NCRI OG subgroup

Support from Guts UK

PPI involvement from inception

Protocol informed by international consensus,
other trial protocols and
engagement with potential PIs

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1st line

Adenocarcinoma of stomach or Siewert type 3 gastro-oesophageal junction tumour

Peritoneal only mets (abdominal LNs allowed)

No prev SACT/RT/surgery

SACT SOC – inc Herceptin and nivolumab

Visible measurable peritoneal lesions on

Stomach arm

Co- leads Sarah Gwynne and Chris Peters

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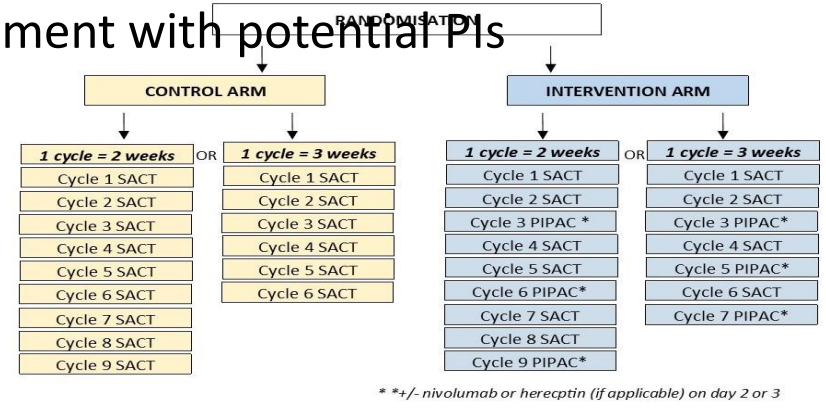

SACT - SOC
PIPAC - cis dox

1st line

Adenocarcinoma of stomach or Siewert type 3 gastro-oesophageal junction tumour

Peritoneal only mets (abdominal LNs allowed)

No prev SACT/RT/surgery

SACT SOC – inc Herceptin and nivolumab

Visible measurable peritoneal lesions on computerised tomography (CT)

Endpoints

Primary

- Peritoneal progression free survival*

Secondary

- QOL
- Safety
- Proportion of patients completing PIPAC
- Numbers of conversion to operable disease (stomach, colorectal)
- OS
- Peritoneal specific ORR
- Peritoneal specific DCR

* Radiology subgroup led by Professor Gina Brown tackling the complexities of this!

With thanks to the PICCOS trial team

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- sarah.gwynne@wales.nhs.uk
- christopher.peters@imperial.ac.uk