PROTOCOL

Title:	**United Kingdom COVID and Gynaecological Cancer Study**
Acronym:	**UKCOGS**
Review & Approval:	**Clinical Effectiveness Unit, Joint Research Management Office Barts Health-Queen Mary University of London**
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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was discovered in Wuhan, China, in December 2019. It has resulted in a pandemic spreading to most countries in the world, leading to a major global health and economic crisis disrupting most health systems and economies worldwide. In the UK on 13.4.20 there were 88,621 cases and 11,329 deaths documented from COVID19.[1] Correspondingly it has affected over 1.8 million individuals and caused over 113,000 deaths worldwide.[2] Chinese data suggests the case rate reported in health professionals is much higher than the general population.[3] Cancer patients are potentially twice as likely to have COVID19 compared to the rest of the population.[4] However, corresponding UK relevant data are lacking. Additionally 43-50% carriers are likely to be asymptomatic,[5, 6] but can transmit the virus to others.[7] Much higher morbidity, need for ITU care and mortality have been reported in cancer patients with COVID19.[8] The risk of critical disease and poorer outcomes increase with age and multiple comorbidities. 20% mortality has been reported with post-operative COVID19 infections.[9]

The UK and other nations have taken multiple steps across the health and social care system to contain the rate of spread of COVID19 and impact of this disease. This has included public lockdown and self isolation strategies, as well as a massive increase in infrastructural hospital bed and ITU capacity for COVID19 patient management. As a result, it has led to cessation of large proportion of routine non-urgent patient care activity in the health system, and a reduction in urgent care activity with a major impact being felt on cancer care. A number of societies and international bodies have suggested guidelines and principles for modifying gynaecological oncology practice during this crisis.[10-12]

The 01559 Communique from NHS England on 30th March 2020 provides 'Guidance for trusts on the management of non-coronavirus patients requiring acute treatment: cancer'. It indicates that cancer diagnosis, essential treatment and urgent care needs to continue during the COVID-19 emergency.[13] The guidance provided regarding provision of cancer care indicates that cancer specialists should discuss with their patients whether it is riskier for them to undergo or to delay treatment at this time. Where referrals or treatment plans depart from normal practice, safety netting must be in place so that patients can be followed up. Urgent consideration should be given to consolidating cancer surgery in a COVID-free hub, with centralised triage to prioritise patients based on clinical need. All cancer patients need to continue to be considered by their multidisciplinary team (MDT). The increased mortality and morbidity risks from a potential COVID-19 infection caused by cancer surgery or anticancer treatment during the pandemic, and the options of deferring surgery or non-surgical treatments, need to be included in the informed consent process and clearly documented.[13]

The British Gynaecological Cancer Society (BGCS) has proposed a framework for Gynaecological Cancer Centres and Gynaecological Cancer Units in the UK to aid management decisions.[11] This guidance adheres to principles laid out in the NHS document, 01559, 'Clinical guide for the management of cancer patients during the coronavirus pandemic', March 2020. It also provides a Harms review template.[11] Additionally the National Institute for Health and care Excellence (NICE) has provided rapid guidance and principles for delivery of radiotherapy[14] and systemic anti-cancer treatment or chemotherapy during the COVID crisis.[15] The health system is having to cope with a combination of additional factors/stresses, including staff sickness/isolation, staff redeployment, reduced theatre availability, supply chain shortages, reduced hospital visits and remote/video/telephone consultations, etc.

There has been significant service reconfiguration, and changes to cancer care as a result of the COVID pandemic. Mitigation strategies have included changes to surgical and systemic chemotherapy plans, treatment delays, introduction of regimens requiring less-frequent administration and hypofractionated radiotherapy. MDT throughput and decision making has changed. It is critical that these changes are documented, analysed and audited. Only limited data are available on cancer outcomes, with very few reports which have small sample sizes, results not properly adjusted for confounders and populations not representative of a UK population or Gynae-oncology patients.[8, 16] Prospective data collection on the outcomes of all gynaecological cancer patients both with and without COVID-19 across all histologies and treatment modalities will enable a better understanding of the impact of COVID19 and more robust conclusions to be drawn.[16] These data need to be rapidly collated and shared. We have engaged with the BGCS leadership, charities, stakeholders across the Gynae-oncology community, the RCOG and the NCRI Gynaecological Cancer Clinical Studies Group. There is broad consensus and agreement for the need for a national audit. UKCOGS is a national audit of ongoing MDT decision making following the COVID19 crisis. This project is supported by the BGCS, RCOG and the NCRI Gynaecological Cancer Clinical Studies Group. We have also engaged with stakeholder charities- The Eve Appeal, Target Ovarian Cancer, Ovarian Cancer Action and Ovacome.

AIM

- To evaluate the MDT decision making for gynaecological cancer, patients outcomes across the UK in response to the COVID-19 pandemic.
- To document the structural and logistic changes implemented across Gynae-oncology cancer centres in response to the COVID-19 pandemic.

METHODOLOGY

Gynaecological Cancer Centres and Units across the UK will be invited to participate in this audit. Invitations will be sent through the BGCS and informal networks. Participating sites will register with the central audit team and be provided with unique access credentials for the database.

Each participating site (trust/hospital) will have a lead clinician (PI) who is responsible for data entry and participation in UKCOGS. The PI can have a bigger local reporting group/team with as many individuals as felt to be necessary to sustain the project throughout the pandemic. This can include trainees, nurses, and/or data managers in addition to clinicians. Each participating site will be provided a unique site code, individual username and password for database access. Inputting sites will only be able to access/see their own data and will not be able to see another site's data. The central coordinating centre team will be able to see individual data from all sites. An expression of interest form is given in Appendix-1 and site activation flow-chart in Appendix-2.

Inclusion criteria: All patients discussed at the Gynaecological Cancer MDT with a diagnosis or differential diagnosis or suspected diagnosis of gynaecological cancer

Patient data will be collected through gynaecological MDT and clinics from both Cancer centres and Cancer Units across the UK. Data will be captured from patients discussed in MDT or those requiring MDT decision making between the dates 1/3/2020 to 30/08/2020 or till a later date (as needed) depending on the duration of the COVID19 Pandemic. A customised data sheet will be filled. Pseudo-anonymised non-identifiable data will be collected. For each patient, data will be captured on

demographic variables, hospital site, diagnosis, cancer type, histology, stage, grade, MDT decision making, COVID19 status, potential impact, along-with compliance with BGCS and NICE guidance related to surgical oncology, medical oncology and clinical oncology care. The planned data sheet is given in Appendix-3 and may be subject to revision during the study in order to improve data quality. Study IDs are unique to each patient and will be automatically assigned when a patient is entered into the database. Study IDs will be assigned centrally by the REDCap bespoke database. The local site will add this Study ID to the patient record and the centre patient log. Only one study ID should be created for each patient discussed at the MDT. If the patient is re-discussed an updated CRF linked to the new date and earlier study ID should be used.

Individual centres will retain access to their patient data but not provide identifiable information on the national database. Local sites will retain information on NHS number, patient name, date of birth and patient postcode in a separate file but not share this with the central audit team. This information/file that links the study ID to the patient identifiers will be kept on the local NHS Trust server, in case further clarification of data is required.

Additionally, a short survey will be sent out to all gynaecological cancer centres/units to document the changes to logistics/ structure/ pathways implemented for gynaecological cancer care. This will be facilitated via an email through the BGCS (British Gynaecological Cancer Society) and associated networks. A standard survey platform like survey monkey will be used. No patient data is being collected in this survey. The survey form is attached (Appendix-4).

Data Collection & Storage

We will ensure an Information-governance tool-kit, GDPR and Data-protection act compliant, robust data management policy and infrastructure. All data will be collected on a customised, secure, password protected central database at Barts CRUK Cancer Centre, Queen Mary Cancer Research Network (a secure subsection of the main Queen Mary University of London network). A central REDCap database hosted by Barts CRUK Cancer Centre will be used for this (specific location for this is https://ukcogs.bcc.qmul.ac.uk/). Data are stored on secure QMUL/BCI servers and backed up daily as per QMUL policy. Data access will be restricted through a secure user-credentialing process. An information-governance compliant BCI/QMUL IG tool-kit will be followed. There is a separate dedicated IT team to help manage data access, storage and security. This is supported by the BCC IT team led by Mr Jonathan Croft. The sponsor will be the custodian of the data.

CLINICAL EFFECTIVENESS UNIT/ETHICS APPROVAL

This project is a clinical audit, hence, formal ethics approval is not necessary. This has been reviewed by the Barts Health Clinical Effectiveness Unit and reviewed by the Join Research Management Office and R&D Team at Barts Health & QMUL (Project ID 11123).

STATISTICAL ANALYSIS

Baseline characteristics are analysed with descriptive statistics. Appropriate statistical tests will be used for analyses. Analysis will focus on describing MDT decision making and changes to patient care processes. We will assess compliance with national guidance on BGCS Surgical Priority level, Chemotherapy priority level, and Radiotherapy priority level. We are assuming a gold standard of 90% compliance. MDT decision making for changes needed to patient care will be evaluated. Potential factors affecting decision making and outcomes will be evaluated. Analysis will also consider changes/trends across centres/types of centres/ geographical areas as well as for changes over time and economic impact. Progress on data collection and summary statistics will be reported

to the Steering Committee at their regular meetings Analysis of the full data set will be undertaken at the end of the study.

No formal sample size calculation has been undertaken or is required as the aim is to capture all decision making during the pandemic crisis as it evolves across the country over time.

Data dissemination/sharing

Results will be shared with all participating site PIs, collaborators, stakeholders, supporting societies and patient support groups and charities. Data will be presented at scientific meetings/conferences and submitted for peer review publication.

Study Management

The study (audit) will be run through the Central Coordinating Centre team based at the Wolfson Institute of Preventive Medicine, Barts Cancer Centre, QMUL. The team will be responsible for logistics and study management activities. A customised database will be developed for data collection and running the study. The core central management team will include the study Chief Investigators (Prof Ranjit Manchanda, Prof Sadaf Ghaem-Maghami, Prof Sean Kehoe), a research fellow, study coordinator, Prof Gabe (Director, Clinical Trials Unit, WIPM, QMUL), Dr Brentnall (study statistician). The team will be supported by a broader Steering Committee, comprising co-investigators and key stakeholders. The core Coordinating Centre Team will have regular contact to ensure day to day running of the study, and the Steering Committee will meet 1-2 monthly as needed.

Stakeholder Endorsement

This study/audit is fully supported by the BGCS (British Gynaecological Cancer Society), RCOG (Royal College of Obstetricians & Gynaecologists) and the NCRI (National Cancer Research Institute) Gynaecological Cancer Clinical Studies Group. We have also engaged with and received endorsement and support from charities and patient support groups: Ovacome, The Eve Appeal, Target Ovarian Cancer, Ovarian Cancer Action, Jo's Cervical CancerTrust and GO Girls.

Appendix 1: Expression of Interest Form

UKCOGS – UK COVID and Gynaecological Cancer Study

Expression of Interest:

Name:

Centre/Unit:

Address:

Email Contact:

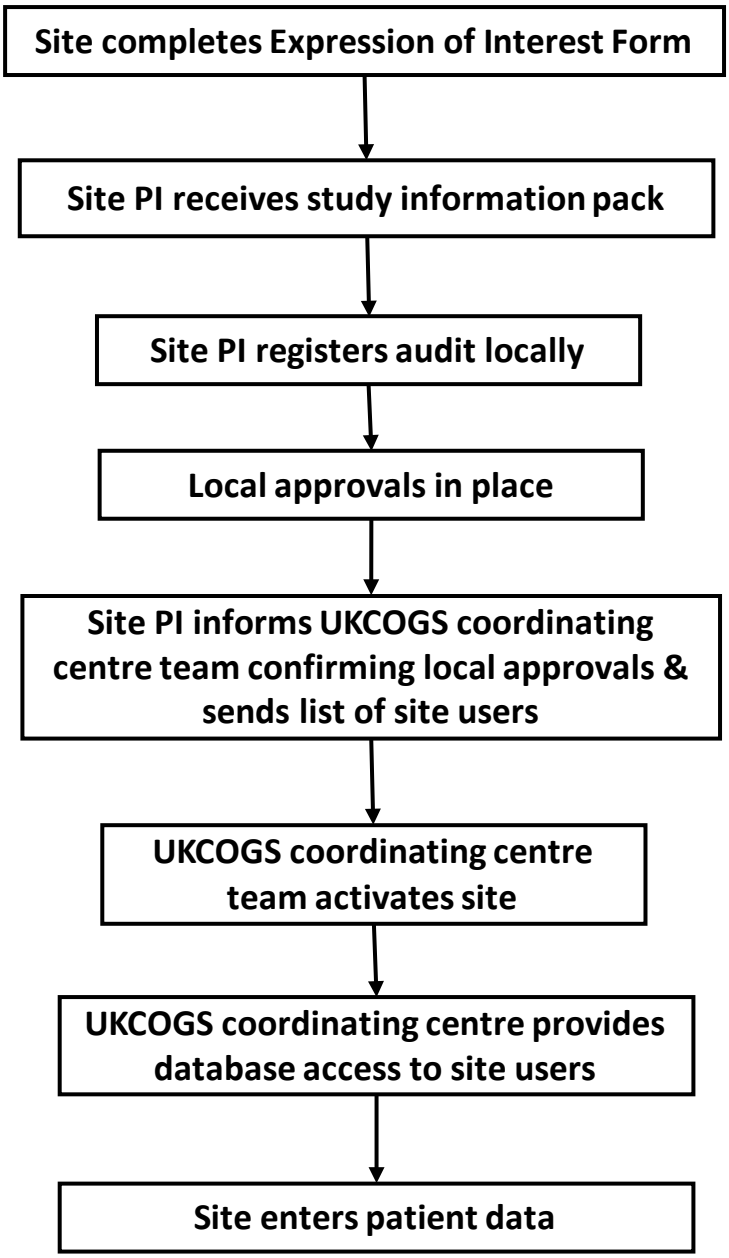
Telephone number:

I wish to be a collaborator in the above study and will act as the point of reference for the Centre/Unit as shown above.

Signature_____

Please email the filled form to bcc-ukcogs@qmul.ac.uk

Appendix-2: Site activation flow-chart



Appendix-3: United Kingdom COVID Gynaecological Cancer Study (UKCOGS)

Study ID		**Hospital**	
Age		**Cancer Centre /Unit**	
MDT date		**Consultant name**	
Performance Status		**Centre/Unit Contact Email**	
Ethnicity	White/Caucasian ☐ Black ☐ Asian ☐ Other Ethnic minority ☐		
2 week wait referral	Yes ☐	No ☐ **Date of referral**	
BMI		**Date of Diagnosis**	
Diagnosis			
Patient Comorbidities			
Cancer Type			
Vulval	Vaginal	Endometrial	Uterine (Sarcoma)
☐	☐	☐	☐
Tubo-Ovarian/ PPC	Cervical	Other	Unknown
☐	☐	☐	☐
FIGO Stage	Stage based on	Clinical ☐ Imaging ☐ Surgery ☐ Histology ☐	
Histological type			
Grade 1 ☐ 2☐ 3☐		Other	
Recurrence	Yes ☐	If Yes, which no. (1/2/3/4/etc)	
COVID Testing	Date of test		
Covid19 Status	Pos swab ☐	Neg swab ☐	Unknown (not tested) ☐
Other COVID19 tests	Serology ☐	IgG ☐ IgM ☐ Neg ☐	
	Chest CT/CXR suggests COVID		Yes ☐ No ☐ NA ☐
Patient Pathway	Altered ☐	Normal ☐	
Treatment Deferred	Yes ☐ No ☐	If yes for how many weeks _____	
Standard MDT decision (Pre-COVID situation)			
MDT decision changed due to COVID	Yes ☐ No ☐		
Revised MDT decision (If any change)			
BGCS Surgical Priority level	1a ☐ 1b☐ 2☐ 3 ☐		
Chemotherapy priority level	1 ☐ 2☐ 3☐ 4 ☐ 5 ☐ 6 ☐		
Radiotherapy priority level	1 ☐ 2☐ 3☐ 4 ☐ 5 ☐		
Change in treatment Plan			
Potential Impact	minimal ☐	moderate ☐	High ☐ Unknown ☐
Free Text / Notes			
Date Form Filled		Filled by	

Study ID should be kept by the Consultant/PI separately in a file along-with patient identifiable details (name, dob, NHS number) as a pseudo-anonymised record which can be accessed later if needed. No identifiable data should be entered in this form.

Appendix 4: COVID19 Survey of Gynae-oncology Centres and Units

Do you represent a Centre or Unit	Centre ☐	Unit ☐	
Name of Centre or Unit			
Regarding staffing, have you experienced significant reduction in staff numbers	Yes ☐	No ☐	
If Yes, is this due to COVID related sickness or redeployment or both (please enter/tick accordingly). For example if Junior doctor staff numbers are reduced from 10 to 7 (i.e. by 30%) then enter 30 in the % reduced column.	**COVID**	**Redeployment**	**% reduced**
Junior doctor staff numbers	☐	☐	
GO Sub-specialty Trainee numbers (hospitals where applicable)	☐	☐	
Consultant staff numbers	☐	☐	
CNS staff numbers	☐	☐	
Regarding MDT functioning, have you implemented any changes	Yes ☐	No ☐	
If Yes, tick all that apply			
Moved to Virtual MDT	☐		
Mixed virtual and face to face MDT	☐		
Suspended MDT	☐		
Reduced MDT frequency	☐		
Reduced number of attendees	☐	% reduced _____	
Regarding Out-patient clinics			
What proportion of your out-patient clinic is remote consultation (telephone/ video)			_____
Please answer questions below in terms of Gynae Oncology related activity: (for example if number of theatre sessions are reduced from 10 to 7 (i.e. by 30%) then enter 30 in the % reduced column.			**% reduced**
Re theatre time, how much reduction in theatre time has occurred? (If not reduced enter '0')			_____
What is the proportion of surgical cases postponed (if no cases postponed, enter '0')			_____
Re Medical Oncology access/capacity, how much is this reduced by? (If not reduced enter '0', If unknown enter NK)			_____
Re Clinical Oncology access/capacity, how much is this reduced by? (If not reduced enter '0', If unknown enter NK)			_____
Re Radiology access/capacity, how much is this reduced by? (If not reduced enter '0', If unknown enter NK)			_____
Re Pathology access/capacity, how much is this reduced by? (If not reduced enter '0', If unknown enter NK)			_____
Re Palliative care access/capacity, how much is this reduced by? (If not reduced enter '0', If unknown enter NK)			_____
How much have your rapid access referrals dropped by? (If not reduced enter '0')			_____
How much has your weekly MDT list/workload reduced by? (If not reduced enter '0')			_____
Have you needed to move activity off site to another hospital (e.g. Independent sector)	Yes	No	
Moved operating lists	☐	☐	
Moved Clinics	☐	☐	
Moved other activity	☐	☐	
Not yet moved but are planning to move	☐	☐	
Do you need to go via a central hub or committee to access operating	☐	☐	
Are you undertaking Minimal access procedures	Yes ☐	No ☐	
Please use the box below to provide any free text comments.			

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