British Gynaecological Cancer Society recommendations for women with gynaecological cancer who received non-standard care during the COVID-19 pandemic

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Abstract

During the COVID-19 pandemic, pressures on clinical services required adaptation to how care was prioritised and delivered for women with gynaecological cancer. This document discusses potential 'salvage' measures when treatment has deviated from the usual standard of care. The British Gynaecological Cancer Society convened a multi-disciplinary working group to develop recommendations for the onward management and follow-up of women with gynaecological cancer who have been impacted by a change in treatment during the pandemic. These recommendations are presented for each tumour type and for healthcare systems, and the impact on gynaecological services are discussed. It will be important that patient concerns about the impact of COVID-19 on their cancer pathway are acknowledged and addressed for their ongoing care.

Background

During the COVID-19 pandemic, there have been significant pressures on clinical services that required adaptation to how care was delivered for women with gynaecological cancer.[1] There have been occasions when it was necessary for treatment to deviate from what would be considered standard of care, due to clinical resource availability, increased risk from COVID-19 infection and prioritisation frameworks.[2-7] In the international COVIDSurg study, 17% of 4722 women undergoing surgery for gynaecological cancer had alteration in first line treatment, including treatment delay or adaptation of surgery.[8]

In the United Kingdom, the COVID-19 pandemic severely impacted on gynaecological cancer services resulting in the need for prioritisation of care[1]. There was a loss of anaesthetic and intensive care availability with many centres having extremely limited or even no surgical capacity, while many staff members were redeployed to acute services. There was also national prioritisation of radiotherapy and systemic therapy availability, with alteration of regimens to reduce the risks of COVID-19 infection when immunocompromised.

The British Gynaecological Cancer Society convened a multi-disciplinary working group to develop recommendations for the onward management of women with gynaecological cancer who have been impacted by a change in treatment. This document discusses 'salvage' measures based on expert opinion with recommendations presented by tumour type and for healthcare systems.

Recommendations on Diagnostic Pathways and the Duty of Candour

The COVID-19 pandemic has led to increased numbers of women presenting with advanced gynaecological cancer and often as an emergency. This may have been due to a lack of medical access because of resource pressures, or due to a delay in presentation because of patient concerns about accessing medical care during the pandemic, particularly impacting on frailer patients. Whilst acknowledging their presentation may have been delayed, these women should be managed according to established national and international guidelines.

When there has been a delay or variation in treatment, there is a duty of candour to discuss with patients how their care varied from the normal pathway, whether this has potential impact on the survival benefits of treatment and the implications for their ongoing care.[9]

Recommendations for Ovarian Cancer

The COVID-19 pandemic led to significant issues in operating capacity, with many centres altering their 'usual' clinical practice according to COVID-19 infection rates and availability of high dependency units for post-operative care.

Patients with newly diagnosed ovarian cancer

1. Due to reduced operating capacity, many centers deferred primary surgery and some women were not offered surgery either in the primary or interval setting. As a result, some women may have missed the opportunity to

undergo cytoreductive surgery and their prognosis may have been impacted as a result.[10]

- Although evidence is not available, it is recommended that women who did not have primary or planned interval surgery should be offered surgery after six cycles of treatment (or within three months of the last cycle of treatment). If currently receiving maintenance treatment, including PARP inhibitors or bevacizumab, treatment would have to be interrupted in the peri-operative period.
- Women who started maintenance treatment after six cycles of chemotherapy and remain in remission should continue maintenance treatment and be considered for surgery at progression if appropriate candidate.
- Women who are on maintenance treatment and have residual disease can continue on maintenance treatment beyond 2 years until progression.
- Women with asymptomatic disease should be considered for surgery or can continue maintenance treatment. If a patient has stable disease on treatment, careful consideration should be given before stopping the maintenance drugs.

- Women with a symptomatic pelvic-abdominal mass should be considered for surgery regardless of the time from chemotherapy.

- Additional post-operative chemotherapy following delayed surgery (after 6 cycles of neoadjuvant chemotherapy) is not routinely recommended, but may be considered depending on time from last platinum-based chemotherapy, tumour burden at surgery, residual disease, pathologic response scores and chemotherapy toxicity. An ongoing study looking at the timing of interval cytoreductive surgery (after 3 or 6 cycles) will provide more evidence and help with the decision-making process (NCT 03579394).

2. Due to lack of intensive care availability, patients assessed as frail or high risk for peri-operative morbidity (as per local guidelines and practice) may not have been offered surgery during the surges of the pandemic. It is recommended that these patients be re-evaluated for fitness to undergo radical surgery when the COVID-19 prevalence changes. Once vaccination is established and infection rates drop, the concomitant risk of COVID-19 related morbidity from surgery should also reduce.[11] Age alone should not be a deciding factor for surgery regardless of COVID-19.

3. Many centres altered their systemic therapy schedules due to the potential risks for patients in the post-operative and neo-adjuvant settings. For example, some women stopped chemotherapy after 4 cycles and others were not offered maintenance treatment with bevacizumab. These changes might impact overall survival, particularly for women with stage IV or bulky residual disease. It is advised that women who discontinued chemotherapy after 4 cycles should continue on routine follow-up. Eligible women who

have not been offered maintenance bevacizumab or PARP inhibitors should continue with routine surveillance and be considered for PARP inhibitors, where appropriate at relapse.

Patients with recurrent ovarian cancer

1. During the COVID-19 pandemic some women with recurrent disease missed the opportunity to undergo secondary surgery which may have an impact on their survival.[12 13] Women with operable disease who did not have secondary debulking surgery should be considered for surgery at a further relapse if deemed appropriate candidate. Secondary surgery after 3 cycles of chemotherapy should not be routinely offered as there is no prospective randomised data supporting this approach. Such surgery should be considered on an individual basis where the treating team considers there is a clear benefit. For patients who did not have surgery at diagnosis, the Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) and iMODEL scores, used to predict operability at first recurrence of ovarian cancer, do not apply and will not be the accurate tools to identify surgical candidates at relapse.[14 15]

2. Systemic therapy for relapsed ovarian cancer remains platinum-based chemotherapy (at least 4 cycles) followed by a PARP inhibitor for responders.[16] In the UK, funding criteria during the COVID-19 pandemic did allow the use of PARP inhibitors without prior chemotherapy in exceptional circumstances. If patients were using PARP inhibitors as a treatment as opposed to a maintenance therapy, this should be continued for as long as

deemed clinically appropriate. Similarly, if patients were on bevacizumab maintenance they should continue for as long as they benefit or the treatment is funded. Chemotherapy can then be considered in the event of future progression.

3. Women with low grade ovarian cancer who had surgery deferred should be offered debulking surgery if deemed appropriate surgical candidates. Where possible these women should be managed as per established guidelines.

4. Some women have been treated on the basis of "positive" peritoneal cytology instead of a biopsy. In some cases, this approach might have led to a mis-diagnosis and/or a delay in determination of BRCA status. A biopsy remains the gold standard, but in certain cases it is acceptable to use a cell block to obtain a diagnosis including immunophenotyping where there is no easily accessible tissue to biopsy. Somatic testing for BRCA variants or homologous recombination deficiency (HRD) testing should be considered either on a biopsy or surgical specimen, but in selected cases may be possible where there is adequate DNA in the cell block.

Recommendations for Uterine Cancer

1. Low-grade, early-stage endometrial cancer was categorised as a lower priority for surgery during the pandemic, since a delay of more than 4 weeks in treatment initiation was unlikely to impact on survival.[17] When operating theatre capacity was limited, women were commenced on progestogen therapy until surgery was possible. However, in some

patients there might have been inadequate tumour response or progression, or there may have been non-concordant histological findings between a low-grade endometrial sample and a high-grade tumour on the definitive surgical specimen.

- Women who commenced endocrine therapy due to lack of surgical availability should have definitive surgery ideally within three months of starting hormonal therapy or as soon as surgical capacity allows. There should be clinical review and repeat imaging after a maximum of three months with non-responders prioritized for surgery.
- There should be a robust failsafe system for ensuring all patients who had surgery deferred are tracked.
- Once surgical treatment is complete, there should be no change to standard ongoing management with adjuvant therapy based on the final histopathological findings. Molecular classification, if available, may help to identify patients with low risk tumours who may avoid adjuvant treatment.[18]

2. Many women with endometrial cancer have co-morbidities that put them at a higher risk of mortality from COVID-19 including obesity, diabetes and cardio-vascular disease.[19 20] Surgery may have been contraindicated or deferred during the pandemic, particularly when high dependency availability was very limited and there was less support for optimising patients including bariatric and pre-treatment optimisation services.
    - Re-evaluation of disease status should be undertaken including imaging to assess whether there has been disease progression.

- Women who commenced progestogen therapy due to co-morbidities that contra-indicated surgery should be reviewed to assess whether optimisation for surgery is possible or whether definitive radiotherapy is an option.

3. Due to the need to prioritise surgical time, there may have been a reduction in the number of patients who underwent surgical staging of lymph nodes. While this may have been a change in practice for some centres which would have resulted in an increase in the use pf pelvic radiotherapy, established adjuvant treatment algorithms are based on whether nodal status is known or unknown.[18] Therefore, no change from standard ongoing management is recommended.

4. Adjuvant treatment may have been omitted when it was unlikely to impact on overall survival, and, in particular, vaginal brachytherapy was not available in some centres. Patients may also have decided not to have adjuvant therapy due to concerns about having additional treatment during the pandemic. Therefore there will be a cohort of women who are at higher risk of relapse, particularly of loco-regional recurrence if vaginal vault brachytherapy or external beam radiotherapy was omitted.[21 22] Whereas low-grade, low risk endometrial cancer most frequently recurs in the vaginal vault within the first 2 years, loco-regional recurrence including lymph node metastases may occur later in intermediate and high-intermediate risk tumours.[23 24]

- Patients at increased risk of local recurrence should have regular clinical review with the aim of detecting a salvageable asymptomatic recurrence. They should not be recommended for patient-initiated follow-up.
- Surveillance imaging at 6 months and 18 months post-surgery should be considered for women with high-intermediate and high-risk disease who have not had external beam radiotherapy or nodal staging.

Recommendations for Cervical Cancer

Patients with early-stage cervical cancer

In the United Kingdom, there was suspension of the cervical screening programme during the initial phase of the COVID-19 pandemic. Delayed assessment may have resulted in women presenting with symptomatic or more advanced stage of disease. Surgery for early cervical cancer remained a high priority throughout the pandemic.[1] However, some women who had local excision of early-stage disease had completion surgery delayed or modified due to the increased risk of peri-operative mortality from major procedures when COVID-19 infection rates were high.[25]

- When surgical management including lymph node assessment varied from usual care pathways, closer surveillance should be considered with MRI imaging for 2 years.

Patients treated with radiotherapy

Definitive radiotherapy for cervical cancer involves a course of external beam radiotherapy followed by intrauterine brachytherapy. Lack of resources, including anaesthetic support or theatre capacity, may have necessitated changes to the intrauterine brachytherapy treatment pathway, using altered fractionation or referring to another hospital. Delays may have occurred due to lack of brachytherapy availability or due to patients having COVID-19 infection. It may even have been necessary to use additional external beam radiotherapy in place of brachytherapy.[1] There would be no significant impact to patient outcome if the change in brachytherapy fractionation still delivered treatment doses that met the GEC-ESTRO dose tolerances for tumour and organs at risk[26 27] A prolonged total treatment time with significant delay between external beam radiotherapy and brachytherapy will have a higher risk of persistent or recurrent disease, while omitting brachytherapy further reduces cure rates.[28-30] For patients with this higher risk of local recurrence, surveillance including MRI imaging may detect salvageable persistent or recurrent disease[31].

- No change to standard ongoing surveillance is required if the total tumour dose was consistent with GEC-ESTRO guidelines.
- Where there was a long gap with a total treatment time greater than 56 days, when lower tumour doses were delivered or when adjuvant radiotherapy was omitted, increased surveillance with MRI imaging six-monthly over the following 2 years is recommended.
- It is recommended that patients in whom intra-uterine brachytherapy was omitted or who had incomplete treatment should be evaluated by an examination under anaesthetic and biopsy for consideration of

completion surgery if there is persistent disease at 12-14 weeks after completing radiotherapy (subject to surgical capacity), provided there are no distant metastases on imaging.

Recommendations for Vulval Cancer

Initial treatment

Apart from seeing more delayed diagnoses and more advanced presentation of vulval carcinoma during the COVID-19 pandemic, most gynaecological cancer centres in the United Kingdom maintained standard management of this disease. However, some hospitals may have encountered difficulty in accessing nuclear medicine resources for Technetium-99m sentinel lymph node procedures for small (<4 cm) tumours without clinical lymphadenopathy. Centres may also have proceeded with radical vulval surgery, but omitted systematic inguinofemoral lymphadenectomy for larger tumours in order to reduce surgical morbidity and COVID-related perioperative risks. As a consequence, there may be some women with vulval cancer who did not undergo standard surgical lymph node staging.

Groin node recurrence risk is greatest in the first two years after diagnosis, particularly during the first 12 months. Therefore, the morbidity associated with delayed surgical inguinal lymph node staging, performed some months after primary vulval surgery, may outweigh the benefit of the diminishing probability of early diagnosis of nodal involvement. One study suggested that three-monthly ultrasound of the groins for two years following negative sentinel node

dissection was cost-effective in the detection of lymph node metastasis following sentinel lymph node assessment.[32]

- Patients whose surgery excluded surgical lymph node staging may therefore be monitored with at least three-monthly clinical and ultrasound review until 12-24 months following surgery, aimed at early detection of nodal metastases.

Surveillance

The lack of clinical capacity and the risk to patients of in-person appointments during peak periods of the pandemic resulted in some patients missing follow up appointments or having virtual consultations.

- Due to the field change effect of pre-disposing conditions, in-person follow up with vulvoscopy/visual inspection should be re-instated as soon as possible [33 34].
- Patients should be encouraged to self-manage and report new lesions or, in those with lichen sclerosus, new symptoms or lesions that do not start to respond to daily clobetasol propionate 0.05% ointment within 2 weeks. Patients should be reviewed urgently in these situations.

Recommendations for Gynaecological Cancer Follow Up

Due to the need to reduce in-person hospital attendances, alternative follow up models were introduced with increased use of remote consultations and patient-initiated follow-up.[34] This was a necessary change during the pandemic and a

positive consequence has been more widespread experience of these models of care. However, the need for rapid change in practice may have meant there was a loss of risk stratification and some women were not included in the decision to have ongoing patient-initiated follow-up. Patients have reported feeling abandoned by the sudden change and many have had a long period without face-to-face review.

There is a particular risk that there has been reduced detection of additional needs for vulnerable patients or safeguarding issues, and there have been increased numbers of patients who have been lost to follow-up.

- Ongoing development of patient-initiated and remote consultation models should be supported.
- Centres should ensure women are appropriately selected and counselled for their ongoing follow up plan.

Recommendations on COVID-19 Vaccination

Vaccination significantly reduces the risks of infection and should be encouraged for all women planned for and undergoing cancer treatment.[35-37] When national vaccination programmes have a longer interval between vaccinations, clinicians may expedite the second dose of vaccine for patients undergoing treatment for cancer.[38] A third vaccination may be indicated for patients who were previously immunocompromised depending on national policy..

Supportive Care and Patient Perspectives

The challenges delivering care during the COVID-19 pandemic have profoundly impacted on holistic and psychological support for patients and their families. At a time of high uncertainty and anxiety for women with gynaecological cancer, the necessary reduction in direct patient contact will have affected their relationship with the clinical team. Many women had their care managed by a different team, or even in a different centre, and there may have been challenging palliative care decisions. This will impact on our ongoing rapport and communication with patients and it is essential to prioritise reinstatement of supportive care services.

Patient perspectives

COVID-19 has significantly affected cancer patients and family members. In a study including 1251 patients from 16 countries, the European Society of Gynecological Oncology -European Network of Gynecological Cancer Advocacy Groups (ENGAGe) found women were more fearful of cancer progression (71%) than developing COVID-19. Many patients, however, had high level anxiety that the disruption and uncertainty resulting from the pandemic would lead to changes to their cancer treatment with 33% reporting modification to their treatment or follow-up.[39]

Studies have reported high levels of patient anxiety and a perception of medical abandonment during the pandemic.[40-43] A qualitative analysis of 800 online forum posts with UK gynaecology cancer charities shows that patients are extremely anxious about the impact of these changes to their current and future cancer care and contacted cancer charities to avoid burdening health care staff

[personal communication S. Sundar, June 2021]. It will be important for health care professionals to acknowledge and address these concerns as services recover so they may provide reassurance and appropriate care to their patients.

Clinical Nurse Specialists

Significant changes in care occurred when many nurse specialists were redeployed to support the general nursing demands of the pandemic, leaving women without appropriate essential support. The clinical nurse specialist will be pivotal to drive and support an effective "restart and recovery" agenda, delivering effective remote assessment, helping patients navigate new technology, and advocating for patients.[44 45] The nurse specialist workforce is highly skilled, often with a deep understanding of the needs for individual patients. Educating patients about the benefits of therapeutic well-being events and support groups as well as referral to specialist psychological support should help to address aspects of psychological distress[46].

- Centres should recognise the need for additional clinical nurse specialist and holistic support resources for patients and carers in the recovery period.

Implications for Gynaecology Oncology Services

Once hospitals start to recover from the acute pressures of the pandemic, there will be a significant backlog of patients awaiting investigations and surgery.[47] There is likely to be a surge of referrals for patients who have deferred presentation, and a higher proportion with advanced disease. Due to clinical pressures, there may have been delay or even cessation of screening and surveillance programmes, while prophylactic surgery was deferred. Centres should aim to reinstate these preventative services as soon as possible.

The alteration in clinical pathways and working practices may have impacted on team dynamics, with a risk of increased stress, anxiety and sickness. Workforce planning and holistic support to staff should be prioritised during the recovery period. It is likely that training will have been impacted with many trainees redeployed to alternative roles, and it will be important to optimise ongoing training opportunities.

Gynaecological Cancer Research

At the beginning of the pandemic, most UK sites paused active trial recruitment with research staff redeployed to COVID-19 wards. There were amendments to many trials to allow for remote monitoring and consent. After the pandemic, there will be residual clinical pressures with significant pressure on the availability of imaging and research biopsies. Currently COVID-19 studies remain prioritised with resources diverted away from cancer research. The immediate priorities should include resource-sparing trials including chemotherapy-sparing regimens, de-escalation radiotherapy schedules, and registration, data-collection and bio-bank studies.

Conclusions

COVID -19 has resulted in unprecedented disruption to cancer care requiring rapid and flexible adaptation to our delivery of care for women with gynaecological cancer. Almost no evidence exists on how best we can restore outcomes for women adversely impacted when care deviated from standard practice. With new coronavirus variants rapidly evolving, there may need to be future adaptation to these recommendations. We hope that our consensus document will help guide women and clinicians on best options for 'salvage' and follow-up. Careful data collection into outcomes will provide insight into how these measures work in practice and provide valuable learning for future surges.

References

1. BGCS RCOG framework for care of patients with gynaecological cancer during the COVID-19 Pandemic [Available from: www.bgcs.org.uk/professionals/covid19-resources accessed 12/6/21.
2. Akladios C, Azais H, Ballester M, et al. Recommendations for the surgical management of gynecological cancers during the COVID-19 pandemic - FRANCOGYN group for the CNGOF. *J Gynecol Obstet Hum Reprod* 2020;49(6):101729. doi: 10.1016/j.jogoh.2020.101729 [published Online First: 2020/04/05]
3. Colombo I, Zaccarelli E, Del Grande M, et al. ESMO management and treatment adapted recommendations in the COVID-19 era: gynaecological malignancies. *ESMO Open* 2020;5(Suppl 3) doi: 10.1136/esmoopen-2020-000827 [published Online First: 2020/07/29]
4. Ramirez PT, Chiva L, Eriksson AGZ, et al. COVID-19 Global Pandemic: Options for Management of Gynecologic Cancers. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society* 2020;30(5):561-63. doi: 10.1136/ijgc-2020-001419 [published Online First: 2020/03/30]
5. Srinivasa GY, Dey T, Suri V, et al. Rationalizing Treatment for Gynecological Cancers During the COVID-19 Pandemic: An Indian Experience. *Indian J Gynecol Oncol* 2020;18(3):101. doi: 10.1007/s40944-020-00448-x [published Online First: 2020/09/26]
6. Tse KY, Domingo EJ, Konar H, et al. COVID-19 and gynecological cancers: Asia and Oceania Federation of Obstetrics and Gynecology oncology committee opinion. *J Obstet Gynaecol Res* 2021;47(5):1643-50. doi: 10.1111/jog.14579 [published Online First: 2021/03/03]
7. Uwins C, Bhandoria GP, Shylasree TS, et al. COVID-19 and gynecological cancer: a review of the published guidelines. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society* 2020;30(9):1424-33. doi: 10.1136/ijgc-2020-001634 [published Online First: 2020/06/25]
8. Sundar SS, Leung E, Khan T, et al. Impact of the covid pandemic on gynaecological cancer surgery – results from the covidsurg gynaecological cancer international study. *International Journal of Gynecologic Cancer* 2020;30(Suppl 4):A123-A24. doi: 10.1136/ijgc-2020-ESGO.218
9. Francis R. The Mid Staffordshire NHS Foundation Trust Public Inquiry; 2015.
10. Du Bois A, Reuss A, Pujade-Lauraine E, et al. Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: A combined exploratory analysis of 3 prospectively randomized phase 3 multicenter trials. *Cancer* 2009;115(6):1234-44. doi: 10.1002/cncr.24149
11. CovidSurg Collaborative, GlobalSurg Collaborative. SARS-CoV-2 vaccination modelling for safe surgery to save lives: data from an international prospective cohort study. *British Journal of Surgery* 2021;108(9):1056-63. doi: 10.1093/bjs/znab101
12. Bois AD, Sehouli J, Vergote I, et al. Randomized phase III study to evaluate the impact of secondary cytoreductive surgery in recurrent ovarian cancer: Final analysis of AGO DESKTOP III/ENGOT-ov20. *Journal of Clinical Oncology* 2020;38(15_suppl):6000-00. doi: 10.1200/JCO.2020.38.15_suppl.6000
13. Coleman RL, Spirtos NM, Enserro D, et al. Secondary Surgical Cytoreduction for Recurrent Ovarian Cancer. *New England Journal of Medicine* 2019;381(20):1929-39. doi: 10.1056/nejmoa1902626
14. Harter P, Bois AD, Hahmann M, et al. Surgery in Recurrent Ovarian Cancer: The Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) DESKTOP OVAR Trial. *Annals of surgical oncology* 2006;13(12):1702-10. doi: 10.1245/s10434-006-9058-0

15. Tian W-J, Chi DS, Sehouli J, et al. A Risk Model for Secondary Cytoreductive Surgery in Recurrent Ovarian Cancer: An Evidence-Based Proposal for Patient Selection. *Annals of surgical oncology* 2012;19(2):597-604. doi: 10.1245/s10434-011-1873-2
16. Poveda A, Floquet A, Ledermann JA, et al. Final overall survival (OS) results from SOLO2/ENGOT-ov21: A phase III trial assessing maintenance olaparib in patients (pts) with platinum-sensitive, relapsed ovarian cancer and a BRCA mutation. *Journal of Clinical Oncology* 2020;38(15_suppl):6002-02. doi: 10.1200/JCO.2020.38.15_suppl.6002
17. Pergialiotis V, Haidopoulos D, Tzortzis AS, et al. The impact of waiting intervals on survival outcomes of patients with endometrial cancer: A systematic review of the literature. *European journal of obstetrics, gynecology, and reproductive biology* 2020;246:1-6. doi: 10.1016/j.ejogrb.2020.01.004 [published Online First: 2020/01/11]
18. Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society* 2021;31(1):12-39. doi: 10.1136/ijgc-2020-002230 [published Online First: 2021/01/06]
19. Sanyaolu A, Okorie C, Marinkovic A, et al. Comorbidity and its Impact on Patients with COVID-19. *SN Comprehensive Clinical Medicine* 2020;2(8):1069-76. doi: 10.1007/s42399-020-00363-4
20. Gasmi A, Peana M, Pivina L, et al. Interrelations between COVID-19 and other disorders. *Clin Immunol* 2021;224:108651. doi: 10.1016/j.clim.2020.108651 [published Online First: 2020/12/18]
21. Creutzberg CL, Nout RA, Lybeert ML, et al. Fifteen-year radiotherapy outcomes of the randomized PORTEC-1 trial for endometrial carcinoma. *International journal of radiation oncology, biology, physics* 2011;81(4):e631-8. doi: 10.1016/j.ijrobp.2011.04.013 [published Online First: 2011/06/07]
22. Keys HM, Roberts JA, Brunetto VL, et al. A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. *Gynecologic oncology* 2004;92(3):744-51. doi: 10.1016/j.ygyno.2003.11.048 [published Online First: 2004/02/27]
23. Bendifallah S, Ouldamer L, Lavoue V, et al. Patterns of recurrence and outcomes in surgically treated women with endometrial cancer according to ESMO-ESGO-ESTRO Consensus Conference risk groups: Results from the FRANCOGYN study Group. *Gynecologic oncology* 2017;144(1):107-12. doi: 10.1016/j.ygyno.2016.10.025 [published Online First: 2016/10/30]
24. Collins A, Taylor A, Guttery DS, et al. Innovative Follow-up Strategies for Endometrial Cancer. *Clinical oncology* 2021 doi: 10.1016/j.clon.2021.06.001 [published Online First: 2021/06/27]
25. Glasbey JC, Nepogodiev D, Simoes JFF, et al. Elective Cancer Surgery in COVID-19–Free Surgical Pathways During the SARS-CoV-2 Pandemic: An International, Multicenter, Comparative Cohort Study. *Journal of Clinical Oncology* 2021;39(1):66-78. doi: 10.1200/jco.20.01933
26. Prescribing, Recording, and Reporting Brachytherapy for Cancer of the Cervix. *J ICRU* 2013;13(1-2):NP. doi: 10.1093/jicru/ndw027 [published Online First: 2013/04/01]
27. Potter R, Haie-Meder C, Van Limbergen E, et al. Recommendations from gynaecological (GYN) GEC ESTRO working group (II): concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy-3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology. *Radiotherapy*

and oncology : journal of the European Society for Therapeutic Radiology and Oncology 2006;78(1):67-77. doi: 10.1016/j.radonc.2005.11.014 [published Online First: 2006/01/13]
28. Perez CA, Grigsby PW, Castro-Vita H, et al. Carcinoma of the uterine cervix. I. Impact of prolongation of overall treatment time and timing of brachytherapy on outcome of radiation therapy. *International journal of radiation oncology, biology, physics* 1995;32(5):1275-88. doi: 10.1016/0360-3016(95)00220-S [published Online First: 1995/07/30]
29. Lin S-M, Ku H-Y, Chang T-C, et al. The prognostic impact of overall treatment time on disease outcome in uterine cervical cancer patients treated primarily with concomitant chemoradiotherapy: a nationwide Taiwanese cohort study. *Oncotarget* 2017;8(49):85203-13. doi: 10.18632/oncotarget.19617
30. Han K, Milosevic M, Fyles A, et al. Trends in the utilization of brachytherapy in cervical cancer in the United States. *International journal of radiation oncology, biology, physics* 2013;87(1):111-9. doi: 10.1016/j.ijrobp.2013.05.033 [published Online First: 2013/07/16]
31. Angeles MA, Baissas P, Leblanc E, et al. Magnetic resonance imaging after external beam radiotherapy and concurrent chemotherapy for locally advanced cervical cancer helps to identify patients at risk of recurrence. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society* 2019;29(3):480-86. doi: 10.1136/ijgc-2018-000168 [published Online First: 2019/02/04]
32. Pouwer AW, Mus R, IntHout J, et al. The efficacy of ultrasound in the follow up after a negative sentinel lymph node in women with vulvar cancer: a prospective single-centre study. *Bjog* 2018 doi: 10.1111/1471-0528.15341 [published Online First: 2018/06/21]
33. Morrison J, Baldwin P, Buckley L, et al. British Gynaecological Cancer Society (BGCS) vulval cancer guidelines: Recommendations for practice. LID - S0301-2115(20)30338-9 [pii] LID - 10.1016/j.ejogrb.2020.05.054 [doi]. 2020(1872-7654 (Electronic))
34. Newton C, Nordin A, Rolland P, et al. British Gynaecological Cancer Society recommendations and guidance on patient-initiated follow-up (PIFU). *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society* 2020;30(5):695-700. doi: 10.1136/ijgc-2019-001176 [published Online First: 2020/04/22]
35. Garassino MC, Vyas M, De Vries EGE, et al. The ESMO Call to Action on COVID-19 vaccinations and patients with cancer: Vaccinate. Monitor. Educate. *Annals of Oncology* 2021;32(5):579-81. doi: 10.1016/j.annonc.2021.01.068
36. Desai A, Gainor JF, Hegde A, et al. COVID-19 vaccine guidance for patients with cancer participating in oncology clinical trials. *Nature Reviews Clinical Oncology* 2021;18(5):313-19. doi: 10.1038/s41571-021-00487-z
37. Trapani D, Curigliano G. COVID-19 vaccines in patients with cancer. *The Lancet Oncology* 2021;22(6):738-39. doi: 10.1016/s1470-2045(21)00250-3
38. Covid vaccination for cancer patients [Available from: https://www.acpgbi.org.uk/news/covid-vaccination-for-cancer-patients/.
39. Gultekin M, Ak S, Ayhan A, et al. Perspectives, fears and expectations of patients with gynaecological cancers during the COVID-19 pandemic: A Pan-European study of the European Network of Gynaecological Cancer Advocacy Groups (ENGAGe). *Cancer medicine* 2021;10(1):208-19. doi: 10.1002/cam4.3605 [published Online First: 2020/11/19]

40. Lou E, Teoh D, Brown K, et al. Perspectives of cancer patients and their health during the COVID-19 pandemic. *PloS one* 2020;15(10):e0241741. doi: 10.1371/journal.pone.0241741 [published Online First: 2020/10/31]
41. Hintermayer M, Sorin M, Romero J, et al. Cancer patient perspectives during the COVID-19 pandemic: A thematic analysis of cancer blog posts. *Patient Experience Journal* 2020;7(3) doi: 10.35680/2372-0247.1514
42. De Joode K, Dumoulin DW, Engelen V, et al. Impact of the coronavirus disease 2019 pandemic on cancer treatment: the patients' perspective. *European journal of cancer* 2020;136:132-39. doi: 10.1016/j.ejca.2020.06.019
43. Koinig KA, Arnold C, Lehmann J, et al. The cancer patient's perspective of COVID-19-induced distress—A cross-sectional study and a longitudinal comparison of HRQOL assessed before and during the pandemic. *Cancer medicine* 2021;10(12):3928-37. doi: 10.1002/cam4.3950
44. Booker R. COVID-19 and cancer nursing: Challenges and opportunities. *Can Oncol Nurs J* 2020;30(4):236-38. [published Online First: 2020/11/10]
45. NHS. Excellence in Cancer Care: The Contribution of the Clinical Nurse Specialist. 2010 [Available from: https://www.macmillan.org.uk/documents/aboutus/commissioners/excellenceincancercarethecontributionoftheclinicalnursespecialist.pdf accessed 05/06/2021.
46. Miaskowski C, Paul SM, Snowberg K, et al. Stress and Symptom Burden in Oncology Patients During the COVID-19 Pandemic. *J Pain Symptom Manage* 2020;60(5):e25-e34. doi: 10.1016/j.jpainsymman.2020.08.037 [published Online First: 2020/09/06]
47. Cancer Research UK (2021). Cancer services during COVID-19: 40,000 fewer people starting treatment. [Available from: https://scienceblog.cancerresearchuk.org/2021/02/02/cancer-services-during-covid-19-40000-fewer-people-starting-treatment/ accessed 05/04/2021.