CLINICAL PRACTICE GUIDELINES
MOH/P/PAK/294.15(GU)

MANAGEMENT OF CERVICAL CANCER
(SECOND EDITION)
STATEMENT OF INTENT

These clinical practice guidelines (CPG) are meant to be guides for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily guarantee the best outcome in every case. Every healthcare provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.

These guidelines were issued in 2015 and will be reviewed in 2019 or sooner if new evidence becomes available. When it is due for updating, the Chairman of the CPG or National Advisor of the related specialty will be informed about it. A discussion will be done on the need for a revision including the scope of the revised CPG. A multidisciplinary team will be formed and the latest systematic review methodology used by MaHTAS will be employed.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>No.</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Levels of Evidence &amp; Formulation of Recommendation</td>
<td>v</td>
</tr>
<tr>
<td></td>
<td>Guidelines Development and Objectives</td>
<td>vi</td>
</tr>
<tr>
<td></td>
<td>Guidelines Development Group</td>
<td>viii</td>
</tr>
<tr>
<td></td>
<td>Review Committee</td>
<td>ix</td>
</tr>
<tr>
<td></td>
<td>External Reviewers</td>
<td>x</td>
</tr>
<tr>
<td></td>
<td>Algorithm on Management of Cervical Cancer</td>
<td>xi</td>
</tr>
<tr>
<td>1.</td>
<td>INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>2.</td>
<td>EPIDEMIOLOGY</td>
<td>1</td>
</tr>
<tr>
<td>3.</td>
<td>RISK FACTORS</td>
<td>2</td>
</tr>
<tr>
<td>4.</td>
<td>CLINICAL PRESENTATION</td>
<td>2</td>
</tr>
<tr>
<td>5.</td>
<td>REFERRAL</td>
<td>3</td>
</tr>
<tr>
<td>6.</td>
<td>DIAGNOSIS</td>
<td>4</td>
</tr>
<tr>
<td>7.</td>
<td>STAGING</td>
<td>7</td>
</tr>
<tr>
<td>8.</td>
<td>TREATMENT</td>
<td>11</td>
</tr>
<tr>
<td>9.</td>
<td>SPECIAL CIRCUMSTANCES</td>
<td>21</td>
</tr>
<tr>
<td>10.</td>
<td>FOLLOW-UP</td>
<td>27</td>
</tr>
<tr>
<td>11.</td>
<td>RECURRENT DISEASE</td>
<td>29</td>
</tr>
<tr>
<td>12.</td>
<td>TREATMENT COMPLICATIONS</td>
<td>32</td>
</tr>
<tr>
<td>13.</td>
<td>PALLIATIVE CARE</td>
<td>34</td>
</tr>
<tr>
<td>14.</td>
<td>PSYCHOSEXUAL CARE AND SUPPORT</td>
<td>42</td>
</tr>
<tr>
<td>15.</td>
<td>IMPLEMENTING THE GUIDELINES</td>
<td>44</td>
</tr>
<tr>
<td>16.</td>
<td>REFERENCES</td>
<td>46</td>
</tr>
<tr>
<td>17.</td>
<td>Appendix 1 Examples of Search Strategy</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>Appendix 2 Clinical Questions</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>Appendix 3 WHO histological classification of tumours</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>of the uterine cervix</td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Title</td>
<td>Page</td>
</tr>
<tr>
<td>------</td>
<td>----------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td></td>
<td><strong>Appendix 4</strong> Reporting Proforma for Cervical Cancer</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>Excisional Cervical Biopsies/Hysterectomy Specimens</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Appendix 5</strong> Revised FIGO Cervical Cancer Staging 2009</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td><strong>Appendix 6</strong> Modified Delgado Score for Cervical Cancer</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td><strong>Appendix 7</strong> ECOG Performance Status</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td><strong>Appendix 8</strong> Systemic Therapy of Cancer Protocol</td>
<td>63</td>
</tr>
<tr>
<td></td>
<td><strong>Appendix 9</strong> Malaysian Hospice Directory</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td><strong>Appendix 10</strong> International Society of Lymphology (ISL)</td>
<td>67</td>
</tr>
<tr>
<td></td>
<td><strong>Appendix 11</strong> Distress Thermometer Screening Tool</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td><strong>Appendix 12</strong> Medication List</td>
<td>69</td>
</tr>
<tr>
<td></td>
<td>List of Abbreviations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acknowledgement</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>Disclosure Statement</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td>Source of Funding</td>
<td>71</td>
</tr>
</tbody>
</table>
In line with the current development in CPG methodology, the CPG Unit of MaHTAS is in the process of adapting Grading Recommendations, Assessment, Development and Evaluation (GRADE) in its work process. The quality of each retrieved evidence and its effect size are carefully assessed/reviewed by the CPG Development Group. In formulating the recommendations, overall balances of the following aspects are considered in determining the strength of the recommendations:-

- overall quality of evidence
- balance of benefits versus harms
- values and preferences
- resource implications
- equity, feasibility and acceptability
GUIDELINES DEVELOPMENT AND OBJECTIVES

GUIDELINES DEVELOPMENT

The members of the Development Group (DG) for these CPG were from the Ministry of Health (MoH) and Ministry of Education (MoE). There was active involvement of a multidisciplinary Review Committee (RC) during the process of the CPG development.

The previous CPG entitled Management of Cervical Cancer 2003 was used as the basis for the development of the present guidelines. A literature search was carried out using the following electronic databases: Guidelines International Network (G-I-N); Medline via Ovid, Pubmed and Cochrane Database of Systemic Reviews (CDSR). Refer to Appendix 1 for Example of Search Strategy. The inclusion criteria are all literature on women with cervical cancer, regardless of study design. The search was limited to literature published in the last ten years and on humans and in English. In addition, the reference lists of all retrieved literature and guidelines were searched to further identify relevant studies. Experts in the field were also contacted to identify relevant studies. All searches were conducted from 11 Jan 2013 to 20 Feb 2013. Literature searches were repeated for all clinical questions at the end of the CPG development process allowing any relevant papers published before 28 February 2015 to be included. Future CPG updates will consider evidence published after this cut-off date. The details of the search strategy can be obtained upon request from the CPG Secretariat.

Reference was also made to other CPG on cervical cancer developed by Scottish Intercollegiate Guidelines Network (SIGN) 2008. The CPG was evaluated using the Appraisal of Guidelines for Research and Evaluation (AGREE) II prior to them being used as references.

A total of 13 clinical questions were developed under different sections. Members of the DG were assigned individual questions within these sections. Refer to Appendix 2 for Clinical Questions. The DG members met 26 times throughout the development of these guidelines. All literatures retrieved were appraised by at least two DG members using Critical Appraisal Skill Programme checklist, presented in evidence tables and further discussed in each DG meetings. All statements and recommendations formulated after that were agreed upon by both the DG and RC. Where evidence was insufficient, the recommendations were made by consensus of the DG and RC. Any differences in opinion are resolved consensually. These CPG are based largely on the findings of systematic reviews, meta-analyses and clinical trials, with local practices taken into consideration.
The literatures used in these guidelines were graded using the US/Canadian Preventive Services Task Force Level of Evidence (2001), while the grading of recommendation was done using the principles of GRADE (refer to the preceding page).

On completion, the draft guideline was reviewed by external reviewers. It was also posted on the MoH Malaysia official website for feedback from any interested parties. The draft was finally presented to the Technical Advisory Committee for CPG, and the HTA and CPG Council MoH Malaysia for review and approval.
OBJECTIVES

The objectives of the CPG are to provide evidence-based recommendations management of cervical cancer based on the following aspects:

i. Diagnosis and staging of cervical cancer
ii. Treatment
iii. Referrals and Follow-up

CLINICAL QUESTIONS

Refer to Appendix 2

TARGET POPULATION

Inclusion Criteria
• All women with cervical cancer

Exclusion Criteria
• Pre-invasive cervical disease
• Screening of cervical cancer

TARGET GROUP/USER

This CPG is intended to guide those involved in the management of cervical cancer either in primary or secondary/tertiary care namely:

i. Medical officers and general practitioners
ii. Allied health professionals
iii. Trainees and medical students
iv. Patients and their advocates
v. Professional societies

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ALGORITHM 1. ASSESSMENT OF CERVICAL CANCER

Histologically-confirmed cervical cancer

Staging by a gynaecologist/gynae-oncologist

Visible lesion

No

Pelvic examination
Cervical conisation
Laboratory tests as indicated

Stage 1A

Yes

Pelvic examination ± anaesthesia
Cystoscopy and sigmoidoscopy if indicated
Imaging assessment:
CT/MRI
If above not feasible:
CXR
U/S KUB
IVU
Skeletal survey if indicated
Laboratory test as indicated

Stage 1B
Stage II
Stage III
Stage IV

Treatment
ALGORITHM 2. MANAGEMENT OF FIGO STAGE IA1

FIGO Stage IA1

- Fertility preservation required
  - Yes
    - Cervical conisation
      - Margin positive
        - Yes: Repeat Conisation*
          - No: Follow-up
    - No: Simple/extrafascial hysterectomy
      - Margin positive
        - Yes: Treat as FIGO stage IB
          - No: Follow-up
      - No: Follow-up
  - No: Follow-up

*If repeat conisation is not feasible, proceed with trachelectomy.
ALGORITHM 3. MANAGEMENT OF FIGO STAGE IA2

FIGO Stage 1A2

Fertility preservation required

Cervical conisation + pelvic lymphadenectomy

Simple/ extrafascial hysterectomy + pelvic lymphadenectomy

Node positive

Yes

Treat as FIGO stage IB

No

Margin positive

Yes

Repeat conisation*

No

Follow-up

Margin positive

Yes

Treat as FIGO stage IB

No

Follow-up

*If repeat conisation is not feasible, proceed with trachelectomy
**ALGORITHM 4: MANAGEMENT OF FIGO STAGE IB1 / IIA**

**FIGO Stage IB1 / IIA1**

- **Nodal involvement on imaging**
  - Yes
  - **Concurrent Chemoradiotherapy (CCRT)**
  - Microscopic FIGO Stage IB1
  - Cervical conisation + pelvic lymph nodes dissection
  - **Yes**
    - Node positive
      - Concurrent Chemoradiotherapy (CCRT)
  - Macroscopic FIGO Stage IB1 (up to 2 cm)
  - Radical trachelectomy + pelvic lymph nodes dissection
  - **No**
    - Margin positive
      - Repeat conisation. If margin still positive, then treat as macroscopic IB1
  - **No**
    - Fertility preservation
      - Radical hysterectomy + pelvic lymph nodes dissection
      - Consider adjuvant in high risk for recurrence

- **No**

Repeat conisation. If margin still positive, then treat as macroscopic IB1
1. INTRODUCTION

Cervical cancer remains an important health issue among women in Malaysia. Despite numerous screening programmes for early detection of pre-invasive disease of the cervix, many women have been diagnosed at invasive stage of cervical cancer. This has tremendous implications to the patients, carers and healthcare system.

The first edition of CPG on Management of Cervical Cancer was published in 2003. Many new development especially in the treatment of the condition has emerged which lead to variation in clinical practice. Based on these, the CPG have been updated using a systematic review methodology. It aims to guide healthcare providers on the evidence-based management of invasive cervical cancer in the Malaysian healthcare setting.

2. EPIDEMIOLOGY

There is an increasing trend of cancer worldwide. A total of 14.1 million new cancer cases and 8.2 million cancer deaths occurred in 2012, compared to 12.7 million and 7.6 million respectively in 2008. Cervical cancer is the fifth (3.7%) common cause of cancer following prostate (7.9%), colorectal (9.7%), breast (11.9%) and lung cancer (13.0%) globally. It is the fourth (7.9%) common cause of cancer among women after breast (25.2%), colorectal (9.2%) and lung cancer (8.8%). Seventy percent of cervical cancer cases occur in low resourced countries.\(^1\) level III

In Malaysia, cervical cancer is the second most common cancer among women following breast cancer.\(^1\) - \(^2\) level III The age-standardised rate is highest among Indians (10.3/100,000) followed by Chinese (9.5/100,000) and Malays (5.3/100,000). The rate increases after 30 years of age and peaks at 65 - 69 years. Among all cancer deaths, cervical cancer ranked fifth.\(^3\) level III

In the United States, a declining overall incidence of cervical cancer has been reported; largely attributed to the decrease in the incidence of squamous cell carcinoma. However, there is an unexplained rise of adenocarcinoma (AC).\(^4\) level II-2 There is no published local data on the trend of cervical cancer.
3. RISK FACTORS

The primary cause of cervical cancer is infection with certain types of Human Papilloma Virus (HPV) which is transmitted sexually. Multiple risk factors are associated with the development of the cancer:

- >3 sexual partners\(^5\), level II-2
- early sexual intercourse (<17 years old)\(^5\), level II-2
- >10 years’ use of oral contraceptive\(^5\), level II-2
- first delivery before age of 17\(^6\), level II-2
- high parity (≥7 full term pregnancies)\(^6\), level II-2
- smoking\(^6\) - 7, level II-2
- lower socioeconomic status\(^8\), level II-2

4. CLINICAL PRESENTATION

The symptoms associated with cervical cancer are commonly encountered at primary care. However, most data on clinical presentations are based on research at secondary care.

Common presenting symptoms in cervical cancer are postmenopausal bleeding (84.0%), vaginal discharge (72.0%), postcoital bleeding (PCB) (64.0%) and abdominal pain (56.0%).\(^9\), level III The prevalence of PCB in cervical cancer ranges between 0.7% to 39%.\(^10\), level III In patients with PCB, cervical cancer is found in 3.6% of women with no record of smear or with normal smear and 5% of women with abnormal smear.\(^11\), level III

- Most patients are asymptomatic. However, common presenting symptoms that may suggest cervical cancer are:
  - postmenopausal bleeding
  - vaginal discharge
  - post-coital bleeding
  - abdominal pain

Among those with PCB:\(^12\), level III

- cervical cytology (conventional pap smear) has sensitivity, specificity and positive predictive value (PPV) of 50%, 86.5% and 92.8% respectively for cervical cancer
- colposcopy has sensitivity and PPV of 78.6% and 23.4% respectively for cervical cancer

Based on the Malaysian National Cancer Statistics 2007, 21% of cervical cancer patients presented at stage I, 34.7% at stage II, 25.6% at stage III and 18.7% at stage IV.\(^3\), level III
5. REFERRAL

Appropriate referral mechanism can improve the quality of care given to patients. Referral to gynaecology/gynae-oncology clinic after abnormal cytology/pap smear is important to establish prompt diagnosis. The proposed criteria and time frame for referral is shown in Table 1.

**Table 1. Time frame for referral of abnormal cytology to gynaecology clinic**

<table>
<thead>
<tr>
<th>Time frame for referral</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Within 8 weeks</strong></td>
<td>• After three consecutive inadequate samples</td>
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<td>• After three tests reported as inflammatory smear in a series</td>
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<td></td>
<td>• One test reported as AGC-US or AGC-H</td>
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<tr>
<td></td>
<td>• After two tests reported as LSIL or ASCUS*</td>
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<td></td>
<td>• HPV DNA testing should be considered if available. If positive for high risk HPV, to refer for colposcopy.</td>
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<tr>
<td><strong>Within 4 weeks</strong></td>
<td>• One test reported as HSIL</td>
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<td><strong>Within 2 weeks</strong></td>
<td>• One test reported as possible invasion</td>
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<td></td>
<td>• One test reported as possible glandular neoplasia</td>
</tr>
<tr>
<td></td>
<td>• Women with symptoms of postcoital bleeding particularly &gt;40 years, intermenstrual bleeding and persistent vaginal discharge</td>
</tr>
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*Modified:

Once diagnosed with cervical cancer, patients should receive definitive treatment within 31 days of agreeing to their care plan or within 62 days on the referral pathway.\(^{13}\), level III
6. DIAGNOSIS

a. Histopathological Examination

A definitive diagnosis of cervical cancer is made by histopathological examination of cervical tissue. Type of cervical tumour is diagnosed based on the World Health Organization (WHO) histological classification of tumours of the uterine cervix (refer to Appendix 3). Histological reports of cervical cancers in small resection (loop/cone biopsies) and hysterectomy specimens should follow the minimum Dataset for Histological reporting of cervical neoplasia (3rd edition) of the Royal College of Pathologists. Meticulous and accurate reporting of gross pathological and histological parameters determine treatment and prognosis of the patients. Regular tumour board meetings are also advocated to optimise patient management decisions.

There are numerous independent histopathologic prognostic factors which are important in determining the patient’s management, which includes lymph node status (p=0.0004), parametrial invasion (p=0.016), lymph vascular space invasion (LVSI), p=0.046) and histology of pure AC (p=0.012). The presence of LVSI must be recorded for tumours of all types and stages. It is the only significant prognostic factor for cumulative 5-year survival rate in tumour confined to uterus (p=0.0078).

Based on survival analysis, patients can be stratified into three prognostic risk groups.

- Low risk: Tumour confined to uterus not associated with LVSI (estimated 5-year survival rate of 100 ± 0%).
- Intermediate risk: Tumour confined to uterus associated with positive LVSI or squamous/adenosquamous carcinoma associated with parametrial invasion or pelvic lymph node metastasis (estimated 5-year survival rate of 85.5 ± 3.9%).
- High risk: Pure AC associated with parametrial invasion or pelvic lymph node metastasis with common iliac/paraaortic node metastasis (estimated 5-year survival rate 25.1 ± 9.7%).

All patients with lymph node micrometastasis (LNmM), regardless of its size, are considered LVSI positive. LVSI (RR=2.64, 95% CI 1.67 to 5.49) and lymph node micrometastasis (LNmM) <2 mm (RR=2.44, 95% CI 1.58 to 3.78) has double the risk of recurrence following surgical resection of early-stage cervical cancer.
• Histopathological reports of cervical cancer should include core histological data, which are:  
  1. Tumour type (based on WHO classification)
  2. Tumour grade (based on modified Broders grading)
  3. Tumour dimension (depth and maximal horizontal dimension)
  4. If tumour is multifocal in origin, to be indicated, staging is based on the largest focus
  5. Presence of LVSI
  6. Status of resection margins (presence of tumour, distance of tumour and location of the closest excision margin)*
  7. Lymph node status (number of nodes retrieved and involved), presence of micrometastases and extranodal spread*
  8. Involvement of other organs or tissue*
  9. Presence of involvement of endometrial cavity (endomyometrium)*
  10. Presence of involvement of paracervical, parametrial and vaginal tissue*

* included in post-surgical specimens

Refer to **Appendix 4** for proposed Reporting Proforma for Cervical Cancer in Excisional Cervical Biopsies/Hysterectomy Specimens.

There is preference for avoiding the term ‘microinvasive carcinoma’ and using the specific The International Federation of Gynecology and Obstetrics (FIGO) stage as a descriptor.  

Tumours should be staged according to the revised FIGO staging of 2009. The decision to use Tumour-Node-Metastases (TNM) as well as FIGO staging for cervical cancer is left to the discretion of the pathologist and the preference of their tumour board meetings.

**b. Frozen Section Assessment**

In most institutions, frozen section assessment is not used routinely for the evaluation of resection margins. However it may be performed on clinically suspicious lymph nodes to look for metastasis before proceeding with or abandoning a radical surgery.

Intraoperative frozen examination of sentinel node (SN) accurately predicts the status of pelvic lymph nodes and is effective for selecting intraoperatively the group of patients who will benefit from radical hysterectomy.  

- Sensitivity and negative predictive value (NPV) of frozen section pathological examination for the detection of macrometastatic disease are 100%.
- Sensitivity for the detection for macrometastatic and micrometastatic disease, excluding isolated tumour cells, and NPV are 88.9% and 98.8% respectively.
Refer to Chapter 8 on Treatment (Sentinel Nodes).

**Recommendation 1**

- In cervical cancer,
  - reporting of histopathological examination for surgical specimens of radical hysterectomy should be standardised and contained core histological data*.
  - frozen section assessment of suspicious pelvic or para-aortic lymph nodes may be performed intra-operatively.

*Refer to the yellow box above.
7. STAGING

a. Clinical Staging

Staging of cervical cancer plays an important role in determining further investigations and treatment as well as survival of patients. Hence, an adequate and appropriate staging is an integral part of management for these patients.

There are two commonly used staging systems for cervical cancer namely FIGO staging\(^{19}\) and TNM classification\(^{20}\). The latest revised FIGO staging of 2009 is currently the standard staging system used in Malaysia for all histological types (refer to Appendix 5).

FIGO staging is based on clinical examination. A thorough pelvic examination with/without anaesthesia is mandatory to provide information for the staging. When there is doubt as to which stage a particular cancer should be allocated, the lower stage is assigned.\(^{19}\)

The office pelvic examination has a weak but significant correlation with the actual extent of disease in determination of vaginal (\(r=0.255\), \(p<0.01\)) and parametrial invasion (\(r=0.174\), \(p<0.01\)). The overall accuracy is 70.4% for vaginal involvement and 74.5% for parametrial disease. It also has high accuracy in early FIGO stage cervical cancer (85.4% for stage IB1 and 77.4% for stage IB2) but low accuracy in FIGO stage II (35.5% for stage IIA and 20.5% for stage IIB).\(^{22}\)

The following examinations are permitted for the determination of FIGO staging, as indicated by presenting characteristics: palpation, inspection, colposcopy, endocervical curettage, hysteroscopy, cystoscopy, proctoscopy, intravenous urography, and X-ray examination of the lungs and skeleton. Blood tests should include full blood count, renal and liver function tests. Syphilis and human immunodeficiency virus serology need to be considered based on discussion with the patient about risk factors.\(^{21}\)

- **Initial assessment of microinvasive disease**
  - **Assessment of FIGO stage IA**
    Diagnosis of both Stage IA1 and IA2 should be based on microscopic examination of excised tissue, including cone biopsy with negative margins, trachelectomy or hysterectomy. If the margins of the cone biopsy are positive for cervical intraepithelial neoplasia III or invasive cancer, a second cone biopsy should be performed or the patient treated as FIGO stage IB1 disease.\(^{21}\)

  - **Assessment of FIGO stage IB and above**
    Biopsy of the visible lesions is mandatory to confirm the diagnosis of cervical cancer.
Chest X-ray and evaluation of hydronephrosis are mandatory in grossly invasive disease. Evaluation of hydronephrosis can be done using renal ultrasound, intravenous urography, computed tomography (CT) or magnetic resonance imaging (MRI). The bladder and rectum are evaluated by cystoscopy and sigmoidoscopy only if the patient is clinically symptomatic. The presence of bullous oedema alone on the bladder or rectal mucosa should not be assigned as FIGO stage IV. Suspected bladder or rectal involvement should be confirmed histologically.21, level III

CT and/or MRI with/without positron emission tomography (PET) may provide information on nodal status or systemic spread but are not mandatory.21, level III Refer to section on Radiological Staging for further details.

In our local context, as CT scan is widely available, the CPG DG suggests it is a preferred modality as part of the assessment of cervical cancer. In healthcare facilities where this modality is not readily available or if patients are not suitable for contrast studies, other modalities such as chest X-ray and ultrasound scan may be used.

The staging of cervical cancer is determined at the time of the primary diagnosis and cannot be altered, even at recurrence.

b. Radiological Staging

It is important to assess prognostic factors based on radiological imaging such as tumour size, parametrial and pelvic side invasion, adjacent organ invasion and lymph node metastases to complement clinical assessment. Utilisation of different imaging modalities depends on accessibility, patients' clinical stage, clinicians’ preference and cost, among others. Worldwide, CT and MRI are preferred over other modalities in cervical cancer staging. However, radiological imaging is not included in the revised FIGO staging.

In a meta-analysis of eight studies, MRI showed higher sensitivity compared to CT in locally advanced cervical cancer (LACC) in evaluating:23, level III

- parametrial invasion: 74% (95% CI 68 to 79) vs 55% (95% CI 44 to 66), p=0.0027
- bladder invasion: 75% (95% CI 66 to 83) vs 64% (95% CI 39 to 82)
- rectal invasion: 71% (95% CI 53 to 83) vs 45% (95% CI 20 to 73%)
- lymph node involvement: 60% (95% CI 52 to 68%) vs 43% (95% CI 31 to 57), p=0.047

However, heterogeneity is an issue in this study in terms of equipment and techniques used in the primary papers.
In a diagnostic study, MRI showed sensitivity of 100% and specificity of 85.7% to 90% in detecting vaginal infiltration and tumour extension to cervical stroma with an accuracy of 92.2%.\textsuperscript{24, level III}

Parametrial infiltration is an important parameter in determining management options of apparent early stage cervical cancer. In a diagnostic study, MRI appeared to perform better than examination under anaesthesia (EUA) although not statistically significant (NPV of 76.9% vs 65.3%, p=0.162). This evidence is limited by measurement bias.\textsuperscript{25, level III}

In cervical cancer FIGO stage IB\textsubscript{1}, preoperative MRI-measured tumour diameter is significantly associated with pathological prognostic factors namely parametrial involvement, lymph node metastasis, deep stromal invasion and LVSI. Tumour diameter ≤20 mm may serve as a strong predictor for absence of parametrial involvement (p=0.01).\textsuperscript{26, level II-3}

The use of transvaginal ultrasound (TVS) has recently been advocated in view of its accessibility and cost; however it is operator-dependent. In early stage cervical cancer (FIGO stage IA\textsubscript{2} to IIA):\textsuperscript{27, level II-3}

- TVS has better sensitivity and specificity than MRI in residual tumour detection and assessment of parametrial invasion. The results are not affected by the status of prior cone biopsies.
- TVS is comparable to MRI in tumour size and stromal invasion determination (κ of 0.81 and 0.77 respectively).
- TVS is excellent in classifying bulky tumours and detecting deep stromal invasion (κ of 0.82 and 0.81 respectively).

Diagnostic performance of PET or PET-CT for the assessment of para-aortic lymph nodes (PAN) metastases (prevalence of >15%) is acceptable when performed in those with FIGO stage III or IV.\textsuperscript{28, level II-2}

In normal-sized hypermetabolic lymph nodes, the diagnostic value of PET-CT requires further evaluation.\textsuperscript{29, level III} Fluorodeoxyglucose (FDG) PET/CT is useful for primary evaluation of locally advanced cervical cancer (LACC), monitoring treatment response and others.\textsuperscript{30, level III}

Pre-treatment PAN assessment surgically (laparoscopy or laparotomy) in FIGO stage II\textsubscript{B} - IVA cervical cancer planned for pelvic radiotherapy (RT) does not offer additional survival benefit compared with standard imaging techniques (CT scan or MRI).\textsuperscript{31, level I}

In grossly invasive disease, CT or MRI with/without PET may provide information on nodal status or systemic spread but such radiological modalities are not mandatory. Compared with CT and MRI, PET-CT is a more accurate imaging method for detecting nodal metastases that are >10 mm. Isolated and unexpected areas of PET enhancement should be confirmed histologically if possible, to confirm or exclude the presence of distant metastatic disease.\textsuperscript{21, level III}
The use of positron emission tomography computed tomography requires further evidence before it can be recommended in early stage cervical cancer.

In post-treatment LACC, there is a moderate correlation ($r=0.68$) between clinical and MRI assessments at three months which improved at six months ($r=0.86$).\textsuperscript{32, level II-3}

The role of abdominal or pelvic CT, MRI PET or TVS as part of routine follow-up has not been fully evaluated in prospective studies.\textsuperscript{33, level I}

**Recommendation 2**

- Clinical staging with/without anaesthesia should be performed before initiating cervical cancer treatment.
- In early stage cervical cancer, magnetic resonance imaging (MRI) may be used to complement examination under anesthesia for surgical decision-making.
- Computed tomography scan or MRI, when available, may be offered to assess nodal status and systemic spread in grossly invasive cervical cancer.
8. TREATMENT

• Patients’ involvement in decision-making is essential in the management of cervical cancer.

a. Primary Treatment

Surgery is the preferred modality of treatment for early stage cervical cancer, if it is not contraindicated. Similar survival outcomes have been reported in surgically treated early stage cervical cancer compared with RT.\(^{34,\text{ level I}}\) It also has the advantage of preserving coital and ovarian function in young patients.

i. Surgery

• Fertility-preserving surgery

Cervical cancer is the third most common cancer in women younger than 40 years. Up to 42% of all cervical cancers are diagnosed in women before the age of 45 years, and up to 40% of early cervical cancers are diagnosed in young women who are potentially interested in a fertility-preserving surgery.\(^{35,\text{ level III}}\) Therefore, simple and radical trachelectomy has been increasingly used.\(^{35 - 36,\text{ level III}}\)

Fertility-preserving surgery may be considered in young patients with early stage cervical cancer. The surgical options include cervical conisation, large loop excision of transformation zone (LLETZ), simple and radical trachelectomy via vaginal or abdominal approaches. These procedures may be combined with pelvic lymph nodes dissection (PLND).

Careful patient selection is important to ensure low complication rates and optimal obstetric and oncologic outcomes. Cases should be evaluated and managed by experienced gynae-oncologists. Careful evaluation of the initial diagnostic specimens from cervical conisation or trachelectomy by experienced pathologists is needed.\(^{35,\text{ level III}}\)

There is no evidence retrieved specifically for the treatment of FIGO stage IA1 cervical cancer. In Malaysia, such condition is treated by cervical conisation for those who want to preserve fertility or otherwise simple hysterectomy. Pelvic lymphadenectomy is not recommended for treatment in FIGO stage IA1 disease.\(^{17}\)

Cold knife conisation or LLETZ combined with PLND may be offered to women having FIGO stage IA2 and microscopic IB1 cervical cancer with no LVSI requesting fertility preservation.\(^{17}\) A less radical surgery,
such as cervical conisation or simple hysterectomy, combined with pelvic lymphadenectomy in this group of patients has 100% recurrence-free survival at median follow-up of 56 months and low post-operative morbidity.\(^{37}\) level II-2

In women with FIGO stage IB1 cervical cancer who desire to preserve fertility, radical trachelectomy in combination with PLND is recommended, provided that the tumour diameter is less than 2 cm and absence of LVSI.\(^{17}\) Techniques available include vaginal, abdominal, laparoscopic and robotic approaches.\(^{35,}\) level III Type II radical abdominal trachelectomy (RAT) has similar obstetrics and oncologic outcomes as type III RAT with better recovery of bladder function (p<0.01).\(^{36,}\) level III

In FIGO stage IA to IB1, radical vaginal trachelectomy (RVT) is associated with shorter hospital stay, less blood loss and significantly fewer blood transfusions, compared with radical hysterectomy (RH). The oncologic outcomes appear uncompromised. There is no statistical difference in 5-year overall survival (OS) and 5-year progression-free survival (PFS) between the two types of surgery.\(^{38,}\) level I The recurrence rate is low (4.2% at median follow-up of 48 months) and obstetrics outcomes are good with 59% term delivery rate after RVT. First and second trimester loss are 13% and 19% respectively.\(^{39,}\) level III

RAT has similar surgical and pathological outcomes [i.e. histologic type, residual disease in specimen, conversion to hysterectomy, median hospital stay and the use of post-operative adjuvant RT or concurrent chemoradiotherapy (CCRT)] with RVT. However, RAT allows a significantly wider parametrial resection.\(^{40,}\) level II-3

The following criteria can be used as a guide for choosing modality of surgery when fertility preservation is required:

1. Cervical conisation
   - FIGO stage IA1
   - Squamous cell carcinoma (SCC), AC or adenosquamous carcinoma histological type
   - Age 40 years old or younger.

2. Simple trachelectomy
   - Age 40 years old or younger.
   - FIGO stage IA2 or microscopic FIGO stage IB1
   - Absent of LVSI
   - SCC, AC or adenosquamous carcinoma histological type.
   - No deep stromal invasion, endocervical or lower uterine segment involvement, parametrial involvement and nodal metastasis on pelvic MRI
3. Radical trachelectomy
   - Age 40 years old or younger
   - Small volume FIGO stage IB1 up to 2 cm tumour size
   - SCC, AC or adenosquamous carcinoma histological type
   - No deep stromal invasion, endocervical or lower uterine segment involvement, parametrial involvement and nodal metastasis on pelvic MRI
   - Limited endocervical extension on colposcopic evaluation

Future pregnancy plan: \(^{35, \text{level III}}\)
   - It is advisable to wait for 6 to 12 months after radical trachelectomy before attempting pregnancy to allow healing and to exclude early cancer recurrence.
   - Pregnancy after radical trachelectomy is at higher risk of cervical stenosis, prematurity and obstetrics complications.
   - Delivery is via caesarean section.

Recommendation 3
   - Women with early stage cervical cancer desiring fertility preservation is preferably managed by gynae-oncologists and the following may be offered:
     - FIGO stage IA1: cervical conisation without pelvic lymph node dissection (PLND)
     - FIGO stage IA2: cold knife cervical conisation with PLND
     - Microscopic FIGO stage IB1: simple trachelectomy with PLND
     - FIGO stage IB1: radical trachelectomy with PLND

   - Non-fertility-preserving surgery
     Simple hysterectomy is the standard treatment for FIGO stage IA1 cervical cancer, while simple hysterectomy and PLND is the treatment of choice for FIGO stage IA2.

     RH and PLND is the preferred treatment for FIGO stage IB1 cervical cancer, if there are no contraindications to surgery. Simple hysterectomy and PLND may be an alternative for small volume (microscopic) FIGO stage IB1 cervical cancer with excellent prognosis. \(^{37, \text{level II-2}}\)

     Controversy arises over the best primary management options for bulky tumour >4 cm (FIGO stage IB2 and IIA2) which can be either surgery or
CCRT. There is no recent evidence addressing this issue but the CPG DG favours CCRT, as the risk of nodal involvement is high and thus requires post-operative chemoradiotherapy.

The outcome of early stage AC (FIGO stage IA to IIB) treated with either primary RT/CCRT or surgery are comparable in terms of 5-year survival (OR=0.67, 95% CI 0.20 to 2.26), disease-free survival (OR=0.43, 95% CI 0.13 to 1.43) and complications (OR=3.32, 95% CI 0.61 to 18.12). Although not statistically significant, the trend of survival rate favours surgery.34, level I

Intra-operative detection of nodal metastasis in patients undergoing RH for early stage cervical cancer raises a management dilemma i.e. whether to proceed or abandon the surgery. These patients would still require RT/CCRT. However, given the lack of well-designed randomised controlled trials (RCTs), no definite conclusion can be made regarding the superiority of one approach over another.41, level III; 42, level II-2

• Treatment for patients with intra-operative detection of nodal metastasis should be individualised.

The incidence of ovarian metastasis in patients with early stage cervical cancer is low (0.9% - 3.7%). The most significant factor associated with the metastasis is the AC histological type.43 - 44, level II-2; 45, level III Other factors are older age group (>45 years old), bulky tumour size (>4 cm), FIGO stage IB2 to IIA43, level II-2 and the presence of gross vascular erosion.45, level III The incidence of ovarian metastases in FIGO stages IB to IIB is higher in AC compared to SCC.44, level III

Ovarian preservation is safe during radical surgery in young patients with early stage SCC of cervix.43, level II-2; 44 - 46, level III The incidence of subsequent complication in the retained ovary is rare.46, level III However in AC, bilateral salpingo-oophorectomy should be performed.44, level II-2; 46, level III

There is no significant difference in survival rate between SCC and AC in patients with confirmed metastasis on the removed ovaries (p>0.05).44, level II-2
Recommendation 4

- In women with early stage cervical cancer who do not require fertility preservation,
  - simple/extrafascial hysterectomy should be performed for FIGO stage IA1 cervical cancer.
  - simple/extrafascial hysterectomy with pelvic lymphadenectomy may be performed for FIGO stage IA2.
  - radical hysterectomy with pelvic lymphadenectomy is the preferred treatment for FIGO stage IB1 cervical cancer.
  - concurrent chemoradiotherapy is the preferred treatment for bulky cervical cancer (FIGO stage IB2 and IIA2).
  - ovarian preservation during radical surgery may be offered in young patients with early stage squamous cell carcinoma of cervix. However in adenocarcinoma, bilateral salpingo-oophorectomy should be performed.

- **Laparoscopic and Robotic Surgery**

  Laparoscopic and robotic surgeries in oncology are getting more attention with the advancement in the field of minimally invasive surgery.

  In a Cochrane systematic review, there was no reliable evidence in the efficacy, safety and long term outcomes of laparoscopic-assisted vaginal radical hysterectomy in the treatment of early stage cervical cancer.47, level I

  Laparoscopic radical hysterectomy and robotic radical hysterectomy, compared with radical abdominal hysterectomy (RAH), are associated with lesser blood loss (p<0.05), lower post-operative infectious morbidity (p=0.005) and shorter hospital stay (p<0.05).48, level II-2 However, there is no evidence on long-term oncologic outcomes.48, level II-2

  There is insufficient evidence to support surgical assessment of para-aortic nodal status (laparoscopy or laparotomy) prior to pelvic RT.31, level I

  - Laparoscopic and robotic radical hysterectomy has short-term benefits but require further evidence on long term outcomes before any recommendation can be made.
  - Laparoscopic and robotic radical hysterectomy should be performed by a trained personnels in the presence of a gynae-oncologist.

- **Sentinel Nodes (SN)**

  Systematic lymphadenectomy followed by histological assessment is the standard technique currently used to detect nodal spread. In
histologically proven nodal metastases, CCRT is the primary treatment. According to the SN hypothesis, histologically tumour-negative SN predicts that the remaining lymph nodes will be tumour-free.

There is a higher probability in determining lymph node status in cervical cancer by SN biopsy compared with imaging methods such as CT scan, MRI and PET scan ($OR=18.49$, $95\%\ CI\ 3.59\ to\ 95.17$). In a meta-analysis of 21 studies, the pooled sensitivity of positive SN in detecting nodal metastasis was $89\%$ ($95\%\ CI\ 83\ to\ 94$) with no significant difference in detection techniques used ($p=0.17$).

There is no significant difference in the detection rate of SN using either $^{99m}$Tc or blue dye and also in the methods in identifying and retrieving SN (laparotomy versus laparoscopy). Combined $^{99m}$Tc and blue dye has a significantly higher SN detection rate compared to $^{99m}$Tc or blue dye alone ($97\%$, $88\%$ and $84%$ respectively).

### Recommendation 5
- Sentinel nodes detection may be considered to detect nodal metastasis in early stage cervical cancer where facilities are available.

### ii. Definitive Chemoradiotherapy/Radiotherapy

The role of definitive chemoradiotherapy in FIGO stage IB2 and above is well established. The treatment consists of external beam radiotherapy (EBRT) 45-50.4 Gray (Gy) in 25-28 fractions over five to six weeks concurrent with weekly cisplatin-based chemotherapy and brachytherapy. The recommended total tumour dose in 2 Gy per fraction radiobiologic equivalence to Point A is 80 to 90 Gy, depending on the initial stage of the disease.

Earlier RCTs have shown that CCRT is superior to RT alone for LACC. This treatment has been the standard of care for LACC since 1999.

Two meta-analyses showed that CCRT improved OS, PFS and disease-free survival compared to RT alone in FIGO stage IB to IVA cervical cancer. Most of these trials were using platinum-based chemotherapy. In a systematic review of limited quality, CCRT caused significant increase of acute haematological and gastrointestinal toxicities and no significant difference in late toxicities. In view of the consistent survival benefit from CCRT, the additional acute toxicities described may be justified.
Extended field RT, which involves treating the pelvis and the PAN with or without chemotherapy, may be considered for cervical cancer patients with PAN involvement at the expense of increased but manageable toxicities.\textsuperscript{53 - 54, level II-2} The decision for this treatment should be made at the discretion of the treating oncologist.

Intracavitary brachytherapy (ICBT) is an essential part of RT for cervical cancer, treating mainly the primary tumour. High doses of radiation can be delivered to the tumour while the surrounding normal tissues, such as rectum, are relatively spared. High dose rate (>12Gy/hour) ICBT is as efficacious and safe as low dose rate (<2Gy/hour) ICBT in LACC in terms of OS, disease specific survival, relapse free survival, local regional recurrence and distant metastasis. The additional advantages of high dose rate ICBT are convenient outpatient treatment and rigid immobilisation for better accuracy of source applicator positioning.\textsuperscript{55, level I}

The treatment time (from first fraction of RT to the last fraction of RT or brachytherapy) should not be more than 56 days as this would adversely affect the local control rate. However, this is not associated with distant failure or disease-specific mortality.\textsuperscript{56, level II-1}

**Recommendation 6**

- Concurrent chemoradiotherapy should be given as the primary treatment in FIGO stage IB\textsubscript{2} to IVA (locally advanced cervical cancer). The treatment time should not exceed eight weeks.
- Intracavitary high dose rate or low dose rate brachytherapy should be given in locally advanced cervical cancer.

**b. Adjuvant Treatment**

**i. Surgery**

The role of adjuvant post-radiation hysterectomy for patients with FIGO stage IB\textsubscript{2} cervical cancer has been a source of controversy since this combined approach was first advocated. It is suggested that these bulky tumours and the associated tumour hypoxia was better addressed by hysterectomy than by additional intra-cavitary radiation.

In a large RCT, adjuvant surgery with extrafascial hysterectomy after radiation in FIGO stage IB cervical cancer had no clinical benefit compared with no adjuvant surgery. Even though there was a trend towards reduction in progression of disease and death but it was non-significant (RR for progression=0.77, p=0.07; RR for death=0.89, p=0.26). This may be due to lower cumulative incidence of local relapse (14% vs 27%) but higher distant progression (20% vs 16%) in the adjuvant surgery group at five years. Further analysis showed a
significant 28% reduction in progression of disease in bigger tumours (4 to 6 cm) in the adjuvant surgery group. The rates of grade 3 and 4 adverse events were similar at 10% in both group.\textsuperscript{57, level I}

In cervical cancer patients with localised residual disease after primary radiation therapy, adjuvant hysterectomy is an effective salvage procedure even in patients with FIGO stage III disease and in those with non-SCC. The 5-year survival rate in the adjuvant surgery group is significantly higher than the group without adjuvant surgery (68.6% vs 14.5%). Apart from that:\textsuperscript{58, level II-2}

- there is no difference in survival between SCC and non-SCC (p=0.6862).
- there is a trend for better survival of smaller tumours compared with larger tumours, although non-significant (p=0.053).

Adjuvant hysterectomy after unsuccessful ICBT does not offer advantage in recurrence-free and survival nor increase late toxicity.\textsuperscript{59, level II-2}

- 50% of patients treated with pelvic EBRT alone have recurrent disease, whereas none among adjuvant hysterectomy patients (p=0.068).
- 43% of patients treated with pelvic EBRT alone have died of disease recurrence, whereas none among adjuvant hysterectomy patients (p=0.152).
- No patients develop late toxicity such as fistulae, wound dehiscence or bowel stenosis.

**Recommendation 7**

- Adjuvant surgery should not be routinely offered in cervical cancer.
- Hysterectomy after primary radiation therapy may be offered as a salvage procedure in cervical cancer with bulky primary tumour >4 cm or post-treatment localised residual tumour.

**ii. Chemotherapy**

Adjuvant chemotherapy is chemotherapy given after primary treatment. In a multi-centered open label RCT, the addition of gemcitabine to standard CCRT, followed by adjuvant chemotherapy with gemcitabine and cisplatin improved OS (HR=0.68, 95% CI 0.49 to 0.95) and PFS (HR=0.68, 95% CI 0.49 to 0.95). The addition of gemcitabine increased grade 3/4 acute haematological (neutropenia) and non-haematological toxicities (vomiting and diarrhoea). When further analysed, the gemcitabine-related toxicities occurred mostly during the preadjuvant phase. There was no difference in the incidence of late toxicities with or without gemcitabine.\textsuperscript{60, level I}
In view of the different regime used as primary treatment in the RCT, further studies are warranted before any recommendation can be made on adjuvant chemotherapy in cervical cancer.

iii. Chemoradiotherapy/Radiotherapy

- Pathological factors that increase the risk of recurrence for early cervical cancer following radical surgery:61 - 62, level I
  - positive lymph nodes
  - parametrial or vaginal margin involvement
  - LVSI
  - lower uterine segment involvement
  - deep stromal invasion
  - non-squamous histology
  - high grade tumour
  - tumours >4 cm in size

Adjuvant platinum-based chemoradiotherapy after radical surgery may be required for high risk factors mentioned above. The modified Delgado score is accepted to stratify the risk for adjuvant chemoradiotherapy (refer to Appendix 6).63

Two meta-analyses have shown that chemoradiotherapy is more efficacious than RT alone:
- Reduces the risk of death (HR=0.56, 95% CI 0.36 to 0.87) and disease progression (HR=0.47, 95% CI 0.30 to 0.74) in early stage cervical cancer (FIGO stage IA2 to IIA).62, level I
- Acute grade 4 toxicity occurred more frequently in the chemoradiotherapy group (RR=5.66, 95% CI 2.14 to 14.98). However, long term data is limited.62, level I
- Improves OS (RR=0.74, 95% CI 0.64 to 0.86) in locally advanced, bulky FIGO stage IB or post-operative high-risk cervical cancer.64 level I

Adjuvant RT alone reduces risk of local recurrence (HR=0.6, 95% CI 0.4 to 0.9) without improvement of OS in FIGO stage IB cervical cancer compared to no further treatment. Adverse events are not significantly increased.61, level I

**Recommendation 8**
- Adjuvant chemoradiotherapy should be considered in cervical cancer patients with high risk of recurrence* after radical surgery.
- Patients with cervical cancer who are medically unfit for chemoradiotherapy may be offered adjuvant radiotherapy alone.

*Refer to Appendix 6
iv. Neoadjuvant Chemotherapy (NAC)
CCRT is the standard treatment for early stage cervical cancer with bulky disease and locally advanced cervical cancer. NAC is used to downstage the tumour prior to surgery.

In a Cochrane systematic review, NAC followed by surgery, with or without RT, improved OS (OR=0.65, 95% CI 0.53 to 0.80) compared to RT alone in FIGO stage IB - IVA cervical cancer.52, level I

In another Cochrane systematic review, NAC followed by surgery had significantly better OS and PFS than surgery alone in early-stage or LACC.65, level I However, in a more recent systematic review with a well-defined study population (FIGO stage IB1 to IIA), there was no difference in OS and PFS between NAC followed by surgery and surgery alone.66, level I

NAC before surgery reduces the need of adjuvant RT by significantly decreasing tumour size and distant metastasis,66, level I as well as reducing nodal metastasis.65 - 66, level I In early stage or LACC, there is less parametrial infiltration with NAC (OR=0.52, 95% CI 0.30 to 0.91).65, level I

In one of the reviews, there was insufficient data for quantitative analysis on the adverse effects of NAC. Three studies stated that surgical morbidity was similar between the NAC and standard treatment groups while one suggested lower surgical morbidity in the NAC group which may be due to a lower frequency of urological events.65, level I In the other review, data showed that serious late toxicity to the bladder, gastrointestinal tract and vagina were similar in both study groups.52, level I

The addition of NAC may improve survival if given in shorter cycle length (<14 days) and higher dose intensity (≥25 mg/m2/week).52, level I; 65, level I

Patients who achieved response to NAC before surgery have a favourable prognosis, with significant improvement in PFS and OS up to five years.67, level II-2

• Neoadjuvant chemotherapy is not routinely recommended for patients in cervical cancer due to debatable evidence and the decision should be made at the discretion of treating gynae-oncologist/oncologist.
9. SPECIAL CIRCUMSTANCES

a. Pregnancy

Pregnancy does not worsen the prognosis of cervical cancer. Delaying treatment while awaiting foetal maturity in patients with early-stage disease diagnosed during first and second trimesters of pregnancy does not seem to have a major impact on patients’ survival.68, level III

- Factors to be considered in the management of cervical cancer in pregnancy:
  - stage of disease
  - tumour size
  - nodal status
  - histology subtype
  - gestational week
  - patient’s/couple’s desire for pregnancy preservation (if oncologically safe)

FIGO staging is the same for non-pregnant and pregnant states. MRI is the imaging procedure of choice for assessment of locoregional spread.69, level III If required, CT scan can be offered and preferably done after 15 weeks gestation. PET-CT is not recommended during pregnancy.68, level III

Histological assessment of lymph node is the gold standard for nodal status. Laparoscopic lymphadenectomy is feasible up to 20 weeks gestation. Lymphatic mapping and SN detection are technically feasible during pregnancy.68, level III

The following recommendations are modified from the French Recommendations on the Management of Invasive Cervical Cancer during Pregnancy.70, level III In the SCC and AC histological subtypes, treatment is based on gestational age and the stage/size of tumour:

i. For FIGO stage IB1
- If tumour is diagnosed when foetal maturity is considered attained,
  - deliver foetus, optimally by caesarean section followed by cervical cancer treatment thereafter.
  - consider radical hysterectomy during caesarean section for women who are multiparous or completed family.
- If tumour is diagnosed >18 - 22 weeks gestation but before foetal maturity and patient wishes to preserve pregnancy,
  - for tumour size <2 cm, close follow-up is required including clinical and radiological imaging.
  - for tumour size of 2 - 4 cm, management should be individualised. If tumour size is close to 4 cm, offer NAC and inform of the treatment risks.
o deliver foetus once maturity attained, followed by cervical cancer treatment as per standard of care.
• If tumour is diagnosed <18 - 22 weeks gestation (when pelvic laparoscopic lymphadenectomy is technically feasible and possible) and patient wishes to preserve pregnancy,
o consider laparoscopic pelvic lymphadenectomy for tumour size <2 cm. In the absence of nodal involvement, follow-up closely by clinical examination and imaging modality. If no disease progression, start cancer treatment as soon as foetal maturity is attained. In the presence of nodal involvement, consider termination of pregnancy (TOP) and start chemoradiation therapy thereafter.
o consider TOP for tumour size 2 - 4 cm as there is a higher risk of nodal involvement.

ii. For FIGO stage IB2 and above, CCRT is the standard treatment,
• If tumour is diagnosed when foetal maturity is considered attained,
o deliver foetus, optimally by caesarean section followed by cervical cancer treatment thereafter.
o nodal staging surgery (pelvic nodes with/without para-aortic nodes for tumor >4 cm or positive pelvic nodes) at the same sitting is recommended.
• If tumour diagnosed >22 weeks gestation but before foetal maturity is attained, and without extracervical spread, offer CCRT after caesarean section once foetal maturity attained, and do not delay treatment for >6 - 8 weeks. Dissect pelvic ± para-aortic lymph nodes for tumour >4 cm or positive pelvic nodes during caesarean section.
• For tumour diagnosed <20 - 22 weeks gestation, offer CCRT after uterus is evacuated (hysterotomy or other procedure) or with foetus in utero (if expulsion impossible and bulky cervical cancer).

iii. For non-SCC and non-AC, such as the more aggressive SCC, diagnosed during first or second trimester of pregnancy, treatment is individualised and pregnancy preservation is not advisable.

Recommendations on treatment of cervical cancer in pregnancy are based on expert opinion and discussion among the CPG DG members.
**Recommendation 9**

- Treatment of cervical cancer (squamous cell carcinoma and adenocarcinoma) in pregnancy should be based on gestational age and stage/size of tumour.
- If tumour is diagnosed when foetal maturity is attained, deliver foetus followed by cancer treatment.
- If tumour is diagnosed before foetal maturity, for FIGO stage IB1:
  - tumour <2 cm and patient wishes to preserve pregnancy, close follow-up till maturity attained and deliver, followed by cancer treatment.
  - tumour 2 - 4 cm, consider termination of pregnancy followed by cancer treatment.
- For FIGO stage IB2 and above:
  - if tumour diagnosed <20 - 22 weeks gestation, consider termination of pregnancy followed by concurrent chemoradiation therapy.
  - if tumour diagnosed >22 weeks gestation and absence of extracervical spread, offer concurrent chemoradiotherapy after caesarean section once foetal maturity is attained.
- Neoadjuvant chemotherapy may be offered to a patient with operable cervical cancer whose surgery is delayed more than six weeks to allow optimal foetal maturity.

As cervical cancer in pregnancy is uncommon, the use of chemotherapy during pregnancy is mostly described in case reports.

In a methodologically-limited systematic review of observational studies, platinum derivatives especially cisplatin, may be used safely during the second and third trimesters as its use in the first trimester increases the risk of abortion or congenital anomalies.\textsuperscript{71, level II-2}

Complete response (10%), partial response (63.4%) and stable disease (23.3%) were achieved after chemotherapy, whereas progression was observed in only 3.3% of cases. Chemotherapy was well tolerated with no serious adverse outcomes to both mothers and babies.\textsuperscript{71, level II-2}

**Recommendation 10**

- Platinum-based chemotherapy may be considered after the first trimester in pregnant women with cervical cancer.

### b. Tumour Arising from Cervical Stump

The incidence of cancer arising from the cervical stump in patients with prior subtotal hysterectomy is approximately 2%.\textsuperscript{72 - 73, level II-3}

Cancer of the cervical stump should be managed in the same way as cervical cancer arising in an intact uterus. This is supported by:
• Good OS (68% for 5-year survival rate) and low treatment morbidity (10%) when treated with either surgery followed by tailored adjuvant RT in operable disease, RT or CCRT.73, level II-3
• Prognosis is similar when managed with the same treatment regimen.72, level II-3

**Recommendation 11**
• Cancer of the cervical stump should be managed in the same way as cervical cancer arising in an intact uterus.

**c. Cervical Cancer Diagnosed after Hysterectomy for Benign Gynaecological Disorder**

Cervical cancer may be diagnosed incidentally after hysterectomy for benign gynaecological disease. Further management is based on clinical and pathological parameter. The choices are include no further treatment, further surgery with parametriectomy and lymphadenectomy and chemoradiation therapy.

Cervical cancer of FIGO stage IA1 diagnosed after simple hysterectomy can be followed up safely without further treatment regardless of LVSI status.74, level II-2

In FIGO stage IA2 – IIA cervical cancer,
• adjuvant treatment such as RT, CCRT or surgery [radical parametrectomy + paraaortic lymphadenectomy (RP + PLND)] significantly increases 10- year DFS compared to observation alone or chemotherapy; however, there is no significant difference in OS.74, level II-2
• surgery vs RT/CCRT have comparable DFS and OS with lower rate of late complications observed in surgery.74, level II-2
• post-operative radiotherapy gives high relapse-free and OS but has high overall treatment related complications.75, level II-2

Surgery (RP + PLND) alone is a safe option and achieves good OS rate in patients who fulfill these criteria,
• SCC, AC or adenosquamous cancer
• disease FIGO stage IA2 and IB1
• no evidence of deep invasion or tumour at margin and
• no clinical evidence of residual disease at vagina vault or parametrium

It avoids radiation therapy in 83% of patients and hence, preserves ovarian function and reduces sexual dysfunction.76, level II-2
Recommendation 12

- In cervical cancer diagnosed after hysterectomy for benign gynaecological disorder,
  - followed up safely without further treatment in FIGO stage IA1.
  - adjuvant treatment [radiotherapy, concurrent chemoradiotherapy or surgery (radical parametrectomy + pelvic lymphadenectomy] should be considered in FIGO stage IA2 - IIA.

**d. Neuroendocrine Cancers**

Most neuroendocrine cancers (NEC) of the cervix are small cell carcinomas, which account for up to 2% of cervical cancers.\(^{77, \text{ level III}; 78, \text{ level II-2}}\)

Median age of diagnosis is in the fifth decade. The usual presenting symptom is vaginal bleeding and a cervical mass can often be identified on examination. Some patients have abnormal pap smears.\(^{77, \text{ level III}}\)

In rare cases, patients may present with clinical or biochemical evidence of ectopic hormone production including corticotropin (Cushing’s syndrome), vasopressin (syndrome of inappropriate anti-diuretic hormone secretion), insulin (hypoglycemia), serotonin (carcinoid syndrome) and parathyroid hormone (hypercalcemia) or myasthenia gravis.\(^{77, \text{ level II}}\)

There is an increased risk for LVSI and high rate of extrapelvic recurrence in NEC which correlates with poor prognosis.\(^{77, \text{ level III}; 79, \text{ level II-2}}\) Most common sites of extrapelvic metastasis are bone, supraclavicular lymph nodes and lungs. Imaging evaluation generally includes CT scan of thorax, abdomen and pelvis or PET/CT scan. Head CT scan is not recommended on initial evaluation for small cell NEC of the cervix.\(^{77 - 80, \text{ level III}}\)

Surgery is primarily used either to achieve a diagnosis and for resection of early stage disease. RH, which is the standard surgery for FIGO stage IB to IIA cervical cancer of the ordinary type, has been adopted for the treatment of NEC. For early stage disease, patients with complete surgical resection should be considered for adjuvant chemotherapy. Recent data supports the use of platinum with or without etoposide in small cell and large cell NEC in improving survival.\(^{77, \text{ level III}; 79, \text{ level II-2}}\)

CCRT is offered in non-surgical candidates (such as locally advanced disease, unfit for surgery, early disease with evidence of lymphadenopathy or FDG-avid nodal metastasis) and it is typically given with concurrent etoposide/cisplatinum.\(^{81, \text{ level II-2}}\) For advanced stage disease, metastatic sites are treated with platinum-based combination chemotherapy. Extrapolating from small cell lung cancer, vincristine/doxorubicin/cyclophosphamide and topotecan are considered as alternative or second-line therapies.\(^{77, \text{ level III}}\)
In local practice, CCRT regime is similar to other histological types; however additional adjuvant chemotherapy (cisplatin/etoposide) is given for 4 - 6 cycles.

NAC or adjuvant radiation does not improve survival. Multimodality treatment appears to produce the best outcomes for this disease. Primary tumours <4 cm and no clinical evidence of lymph node metastasis have better prognosis.77, level III

The follow-up is similar to other histological types with particular emphasis on periodic full body imaging with either CT or PET/CT. Brain imaging should be considered if patient is symptomatic.77, level III

**Recommendation 13**
- Neuroendocrine cancer of cervix should be managed by gynaec-oncologists/oncologists.
10. FOLLOW-UP

The most appropriate follow-up strategy for clinically disease-free cervical cancer patients after receiving primary treatment varies from institution to institution.

There is modest low quality evidence to inform the most appropriate follow-up strategy. The majority of cervical cancer recurrences (62% to 89%) are detected within two years of primary treatment.82, level III A total of 58% of cervical cancer recurrences occur in the pelvis. Most of the patients (65%) are symptomatic at recurrence. Among them, 53% are found by exclusive pelvic examination.83, level III All asymptomatic pelvic recurrences are diagnosed by pelvic examination.84 - 85, level III A high percentage (85%) of the cancer can be diagnosed by pelvic examination and/or CT.83, level III

DFS for cervical cancer significantly correlates with site of relapse, type of relapse and symptoms at relapse. A better OS from relapse is observed in localised pelvic recurrence as compared to distant sites.83, level III

Follow-up is recommended for every three months in the first year, every four months in the second year, every six months in the third to fifth year and annually thereafter.83, level III

At a minimum, follow-up visits should include a complete physical examination with a patient history to detect symptomatic and asymptomatic recurrence.82, level III Cervical cytology or vault smears are not indicated to detect asymptomatic recurrence as it does not permit earlier detection of recurrence and does not increase survival.82, level III; 86, level III

Routine use of chest X-ray, abdominal and pelvic ultrasound, PET, CT, MRI, intravenous pyelography or blood analysis/tumour markers (CA 125 and SCCA) is not recommended as their role has yet to be evaluated in a definitive manner.82, level III MRI or CT should be considered initially to assess potential clinical recurrence in symptomatic patients. A whole body PET scan or PET-CT should be recommended on all patients in whom recurrent or persistent disease has been demonstrated on MRI or CT and in whom salvage therapy (either pelvic exenteration or RT) is being considered.

Patients should return to annual population-based general physical and pelvic examination after five years of recurrence-free follow-up.82, level III

Short-term hormone replacement therapy (HRT) does not appear to have an adverse effect on oncologic outcome in most gynecologic cancer survivors and improves quality of life (QOL). The treatment appears to be safe although not as effective as HRT in the treatment of
vasomotor symptoms, selective serotonin reuptake inhibitors (SSRIs) and alpha-2 adrenergic agonists are reasonable alternatives.87, level II-2

**Recommendation 14**

- After primary treatment, patients with cervical cancer may be followed up every three months in the first year, four months in the second year, six months in the third to fifth year and annually thereafter.
  - Physical examination including pelvic examination should be performed during follow-up.
11. RECURRENT DISEASE

a. Pelvic exenteration

In advanced and recurrent cervical cancer, the role of surgery is limited. In this situation, pelvic exenteration may be an option in selected group of patients.

Primary or secondary pelvic exenteration with curative or palliative intention is an effective option with high percentage of long-term survival in LACC FIGO stage IVA:

- Median survival between 29 – 30 months
- 5 - years OS ranging from 36.8% to 52%

Patients who have undergone pelvic exenteration of curative intent have higher OS compared with those of palliative intent (5-year and 10-year OS are 64% and 57% for curative intent vs 19% and 18% for palliative intent). There is no significant difference in 5-year OS when pelvic exenteration is performed in SCC or AC cervical cancer (p>0.05).

In a mixed population that includes cervical cancer, 61% 5-year OS is achieved when resection margin is negative.

For cervical cancer patients who have undergone pelvic exenteration, the following factors are significantly associated with lower OS:
- positive pelvic lymphnode
- positive resection margin
- shorter time between primary treatment and recurrence
- surgery of palliative intent
In pelvic exenteration:
• the overall complication rates range between 51.6% and 66%.\textsuperscript{91, level II-2; 92, level II-1; 94, level II-2}
• the early complication rates (≤30 days) range between 44.8% and 50%.\textsuperscript{89 - 90, level II-2; 94 level II-2}
• the late complication rates (>30 days) range between 48.5% and 74%.\textsuperscript{89 - 90, level II-2; 94, level II-2}
• the rate of major complication requiring surgical treatment is 20%.\textsuperscript{95, level II-2}
• the rates of infectious morbidity, intestinal obstruction and fistula are 86%, 33% and 23%.\textsuperscript{93, level II-2}
• the rate of operative mortality is 5.5%.\textsuperscript{91, level II-2}

- Contraindication for pelvic exenteration:
  o distant metastasis/extra pelvic spread
  o pelvic side wall involvement such as hydronephrosis/hydrourerter and lumbosacral plexopathy
  o poor performance status
- Common complications for pelvic exenteration are infectious morbidity, intestinal obstruction, fistula formation, anastomotic leak and prolonged hospital stay.

**Recommendation 15**
- In patients with cervical cancer, pelvic exenteration may be considered in locally advanced disease or in pelvic recurrence, after thorough counselling on its benefits and risks.

**b. Chemotherapy**
Chemotherapy with palliative intent may be an option in patients with recurrent or metastatic cervical cancer with Eastern Cooperative Oncology Group (ECOG) Performance Status grades 0 to 2 (refer to Appendix 7).

In recurrent or metastatic cervical cancer,
- there is no difference in response rates between platinum-containing regimens and non-platinum-containing regimens (RR=1.33, 95% CI 0.50 to 3.54).\textsuperscript{96, level I}
- combination cisplatin-based chemotherapy has better response (complete and partial response) and improve survival compared to single-agent cisplatin chemotherapy.\textsuperscript{96 - 97, level I}
- combination of paclitaxel and platinum chemotherapy has better response compared to non-paclitaxel-containing combination (RR=1.47, 95% CI 1.01 to 2.15).\textsuperscript{96, level I}
- response rate towards platinum-containing chemotherapy is better in out-of-radiotherapy-field (non-irradiated site) recurrence compared to in-radiotherapy-field (irradiated site) recurrence. (RR=0.62, 95% CI 0.46 to 0.83).\textsuperscript{96, level I}
• combination chemotherapy has more toxicities compared to single agent chemotherapy.96 - 97, level I

**Recommendation 16**

- Combination chemotherapy* may be offered to patients with recurrent or metastatic cervical cancer with good performance status.

* Refer to **Appendix 8** on Systemic Therapy of Cancer (revised edition MoH and MoE Malaysia) for suggested chemotherapy regime.

c. **Salvage Radiotherapy/Chemoradiotherapy**

The treatment for recurrent cervical cancer depends on the mode of primary treatment and the site and extent of recurrent disease. Salvage RT or CCRT may be a feasible treatment option for locally recurrent cervical cancer following surgery with high salvage rate (41 – 45 %) and acceptable late complication rate.98 - 99, level II-2

**Recommendation 17**

- In radiotherapy naïve cervical cancer patients with local recurrence, salvage radiotherapy to the pelvis may be offered.
12. TREATMENT COMPLICATIONS

Radiation proctitis and cystitis are known complications of radiation therapy. Acute radiation complication refers to radiation-induced injury during the time of treatment and for up to 90 days after completion of RT. This is a frequently occurring early adverse effect and the pathology is of an inflammatory process affecting the rectal or bladder mucosa, and is generally self-limiting.

Late radiation complications are complications occurring more than 90 days after completing radiotherapy treatment and are relatively rare. The underlying pathology is of submucosal injury with a combination of fibrosis, ischaemia, and subsequent ulceration, which can be localised, diffuse or full thickness penetrating the wall of the rectum. The clinical presentation may have an inflammatory component producing tenesmus, urgency, diarrhoea, constipation, anal sphincter dysfunction (affecting the control of the bowels), mucoid or bloody discharge per rectum or frank bleeding with ulceration which may perforate. These chronic and episodic symptoms will cause impaired QOL of the patients.

At present, there is no recommended standard treatment for both late radiation proctitis and cystitis in view of lack of evidence with regards to effectiveness and impact on QOL by the treatment approaches or methods. There is no recent evidence on the above issues and thus the CPG DG has decided to use the best available evidence beyond the scope of the search.

a. Radiation Proctitis
Late radiation proctitis is episodic and variable in nature. A Cochrane systematic review on non-surgical interventions for the management of late radiation proctitis had identified several treatment approaches with varying results.\textsuperscript{100, level I}

- Rectal sucralfate showed greater clinical improvement for proctitis than anti-inflammatories (OR=14, 95% CI 1.46 to 134.26), though no difference was seen for endoscopic improvement (OR=2.74, 95% CI 0.64 to 11.76). Other effective medications were combination of metronidazole and anti-inflammatory drugs, and rectal hydrocortisone.
- Short chain fatty acid enemas did not appear to be efficacious compared to placebo.
- Thermal coagulation therapy appeared to have clinical improvement in the management of haemorrhagic radiation proctitis refractory to other treatments.
- Hyperbaric oxygen therapy improved radiation proctitis compared to placebo (RR=2.7, 95% CI 1.2 to 6.0; NNT=3).
b. Radiation Cystitis
Late radiation cystitis is relatively uncommon treatment complication. The same Cochrane systematic review found no evidence from trials determining the effects of non-surgical treatments for late radiation cystitis. Therefore, there is no standard treatment in managing patients with radiation cystitis. ¹⁰⁰, level I

- There is insufficient good quality evidence to recommend treatment for late radiation proctitis and cystitis in cervical cancer. Therefore, the treatment should be individualised according to the attending doctor.

c. Lymphoedema
Refer to Chapter on Palliative Care (Lymphoedema).

d. Chronic Bladder Dysfunction
It is a common late complication of radical hysterectomy ranging from 0-44% and the most distressing one, requiring voiding by the clock with the help of abdominal muscles and in some cases, self-catheterisation.¹⁰¹

Radicality of the surgery is closely related to post-operative bladder dysfunction. Compared with the extent of lateral parametrial resection, the extent of vaginal resection has stronger association with bladder dysfunction.¹⁰²

Direct, nerve-sparing radical hysterectomy is a technique that spares the pelvic autonomic nerves without compromising radicality, providing another approach to improve quality of life and reduce bladder and bowel morbidity.¹⁰³, level III
13. PALLIATIVE CARE

There is an increasing trend of integration of modern cancer care with palliative medicine. Palliative care focuses on preventing and relieving suffering, optimising symptom control, preserving hope and improving QOL.\(^{104}\)

All healthcare providers should be trained to deliver basic palliative care. Specialist palliative care providers may be required for management of complex symptoms and end of life issues.\(^{105}\) Inpatient specialised palliative care units and community hospices nationwide are listed in Appendix 9.

This chapter aims to address some common issues experienced by patients with advanced disease which include:

- pain
- malignant/malodorous wounds
- thrombosis and haemorrhage
- fistulae
- lymphoedema
- malignant ureteric obstruction
- end of life care

- Appropriate symptom management in advanced cervical cancer can be complex and a clear understanding of prognosis is essential to guide assessment and subsequent management.

a. Pain

Principles of pain management are described in the Clinical Practice Guidelines for the Management of Cancer Pain by MoH.\(^{106}\)

Patients with advanced cervical cancer may experience complex neuropathic pain as a complication of RT or chemotherapy, or develop lumbar plexopathy from nerve infiltration.\(^{107,\ \text{level III}}\)

Management of selected pain syndromes may benefit from specialist consultations for intrathecal or epidural procedures in addition to conventional analgesic medications. A combination of opioids, local anaesthetics and clonidine can be used for temporary neural blockade while neurolytic agents such as alcohol are used for permanent blockade.\(^{17}\)

Malignant psoas syndrome refers to proximal lumbosacral plexopathy by painful fixed flexion of the ipsilateral hip, with radiological or pathological evidences of ipsilateral psoas major muscle malignant involvement. Treatment options include opioids, agents for neuropathic pain, muscle relaxants to counter psoas muscle spasm, agents to reduce peritumoural oedema and anti-tumoural agents if suitable.\(^{108,\ \text{level III}}\)
b. Malignant/Malodorous Wounds
Patients with malodorous malignant wounds often associate the condition with advance, progressing disease. This not only causes physical discomfort, but also significant psychological and social impact, and negatively affects the woman’s body image and sense of worth.\textsuperscript{107, level III}

Malodorous discharges are generally caused by tissue breakdown from ulcerating necrotic tissue, erosion into a hollow viscous such as the bowel or urinary tract, and/or an added infection of the fluid. Benign lesions such as pressure-related breakdown can also contribute to the malodour.\textsuperscript{107, level III}

Management involves treating infection, containing or removing fluid loss, reducing local irritation and improving QOL.\textsuperscript{(17)} There is limited published evidence guiding the management of wounds in cancer patients and no evidence regarding QOL improvement.\textsuperscript{109, level I}

Surgical methods to manage malodour may include removal or debridement of necrotic tissue, and nephrostomies or defunctioning colostomies for fistula-related urinary or faecal incontinence. Tumour burden may also be reduced by interventional radiology techniques to reduce tumour circulation, palliative RT or chemotherapy.\textsuperscript{107, level III}

Patients using topical metronidazole, mesalt dressing, activated carbon ointment and curcumin ointment can control the odour of malignant fungating wounds.\textsuperscript{110, level II-3} Other suggested methods include:\textsuperscript{17, level III; 107, level III}
- systemic metronidazole
- aromatherapy
- pads and tampons
- vaginal douches
- topical steroids
- barrier creams to avoid local skin irritation and excoriation
- treatment of bacterial and fungal infections
- oral tranexamic acid 1000 - 1500 mg two to three times daily for bleeding wounds
- octreotide and hyoscine butylbromide to reduce faecal loss from enterovaginal fistulae
- suprapubic catheterisation for vesicovaginal fistulae

c. Fistulae
The risk to develop vesicovaginal and/or rectovaginal fistulae is high (22 – 48\%) after curative RT with or without chemotherapy in patients with FIGO stage IVA cervical cancer.\textsuperscript{111, level III} Fistula formation occurs between six and 48 months after RT, with possible serious complications occurring even after five years.\textsuperscript{107, level III} The routine use
of EUA, cystoscopy and proctoscopy at the time of initial diagnosis helps in counseling women about the likelihood of this complication.\textsuperscript{112, level III}

Appropriate radiological investigations are often needed to establish the fistula site and its complexity. Surgical interventions may include:\textsuperscript{17, level III; 107, level III}

- fistula repair
- formation of ileal conduit
- stoma formation for enterovaginal fistulae
- colonic stenting in bowel obstruction
- percutaneous nephrostomies or internal ureteric stents for urological fistulae

Primary exenteration surgery for selected patients in FIGO stage IVA have been suggested to avoid morbidity associated with fistula formation.\textsuperscript{111, level III}

Patients with advance disease where non-surgical measures are more appropriate may benefit from:\textsuperscript{17}

- octreotide, hyoscine butylbromide or glycopyrronium to reduce discharge volume
- codeine phosphate or loperamide to reduce motility and increase stool consistency
- barrier creams to prevent local irritation and excoriation
- topical steroids
- tampons and pads
- low residue diet

d. Thrombosis and Haemorrhage

Venous thromboembolism (VTE) causes high mortality and morbidity in patients with cancer, and is the second most common cause of death after cancer progression.\textsuperscript{113, level III}

The risk of thromboembolic events is up to seven times higher in cancer patients, with the incidence being highest in the first few months of diagnosis. Others at high risk are those with metastatic disease at the time of diagnosis and after tumour recurrence.\textsuperscript{113, level III} Cancer patients receiving anticoagulant treatment for VTE also showed a two to threefold increased risk of developing recurrent VTE.\textsuperscript{114 - 115, level I}
The mechanisms of VTE in cancer patients can be summarised in the following table:

### Table 2. Mechanism of VTE in Cancer Patients

<table>
<thead>
<tr>
<th>Mechanism of VTE in Cancer Patients</th>
<th>Non-tumour associated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumour-associated</td>
<td></td>
</tr>
<tr>
<td>• Extrinsic vascular compression and invasion</td>
<td>• Central venous access devices</td>
</tr>
<tr>
<td>• Tissue factor production</td>
<td>• Anti-neoplastic mediated platelet activation</td>
</tr>
<tr>
<td>• Cancer pro-coagulant production</td>
<td>• Anti-neoplastic mediated endothelial cell damage</td>
</tr>
<tr>
<td>• Accentuated platelet activation</td>
<td>• Anti-angiogenesis therapy</td>
</tr>
<tr>
<td>• Inflammation-mediated increases in factor VIII, vWF and fibrinogen</td>
<td>• Anthracycline-induced congestive heart failure</td>
</tr>
<tr>
<td>• Impaired fibrinolysis due to high PAI-1</td>
<td>• Immobility</td>
</tr>
<tr>
<td>• Acquired deficiencies of natural anticoagulants</td>
<td></td>
</tr>
</tbody>
</table>

**Source:** Ministry of Health. Prevention and Treatment of Venous Thromboembolism. Putrajaya: MoH; 2013

- **Initial management of VTE**
  For the initial management of VTE in cancer patients, low molecular weight heparin (LMWH) is superior to unfractionated heparin (UFH), with reduced risk of mortality (RR=0.71, 95% CI 0.52 to 0.98) and no significant difference in recurrent VTE events. Among various LMWH regimes, once daily treatment is as safe and efficacious as twice daily treatment, and is more convenient for the patient.

A Cochrane systematic review showed fondaparinux was as safe and efficacious as UFH, and dalteparin as safe and efficacious as tinzaparin in the initial management of VTE in cancer patients.

- **Long-term management of VTE**
  For the long-term treatment of VTE in cancer patients, LMWH reduces recurrent VTE events (HR=0.47, 95% CI 0.32 to 0.71) but not death when compared with vitamin K antagonists (VKA).

If VKA is the choice of long-term treatment, current Malaysian VTE guidelines recommend starting warfarin within 24 hours of diagnosis in combination with LMWH or fondaparinux. Treatment with LMWH is to be continued for five days or until International Normalised Ratio (INR) is above 2 for at least 24 hours, whichever is longer. Anticoagulation should be continued indefinitely or until cancer is resolved.

Currently, there is insufficient evidence on the usage of novel anticoagulants (such as dabigatran and rivaroxaban) in the management of VTE in cancer patients.
More than 50% of cancer patients have renal insufficiency, in turn affecting treatment choices and dosages. In severe renal insufficiency, UFH is used for the initial treatment, followed by VKA or long-term LMWH with anti-Xa monitoring. Tinzaparin may be a safe option for the treatment and prevention of VTE in cancer patients with renal failure. 113, level III

Patients with Deep Vein Thrombosis (DVT) who receive home treatment, compared with inpatient treatment, are less likely to have recurrence of VTE (RR=0.61, 95% CI 0.42 to 0.90), have a lower mortality (RR=0.61, 95% CI 0.42 to 0.90) and show a trend for fewer major bleeding complications but more minor bleeding complications. 118, level I

Vena caval filter (VCF) usage for the prevention of pulmonary embolism increases risk of long-term lower limb DVT (HR=1.52, 95% CI 1.02 to 2.27) with no significant improvement in mortality or reduction in the rate of pulmonary embolism or DVT. 119, level I Current Malaysian VTE guidelines list only two indications for the insertion of a VCF which are contraindication to anticoagulation and the presence of large free floating iliocaval thrombus.

- **Haemorrhage**

Patients with cervical cancer may suffer from bleeding problems due to advanced or metastatic disease. Chemotherapy causing thrombocytopenia and myelosuppression, vitamin K deficiency and adverse drug effects are factors contributing to clotting and bleeding problems. 107, level III

Palliative RT for cervical carcinoma results in complete cessation of vaginal bleeding in up to 45% of patients after the first radiation fraction. 120, level III Other methods suggested to treat minor haemorrhage include fibrinolytic inhibitors such as oral or intravenous tranexamic acid. 17

- **Lymphoedema**

In patients with cervical cancer, 12.2% of them have a clinical diagnosis of lower limb lymphoedema. They are 3.5 times more likely to develop lower limb lymphoedema if they receive pelvic RT and have 3.3 times higher risk if pelvic lymph nodes are surgically removed. 121, level III Lymph node metastases, infiltrative carcinoma and pressure from large tumours also contribute to secondary lymphoedema.

Patients report a poor QOL due to pain, changes in lower limb sensation, appearance, restriction in activities and distress. 17 Those at risk of lymphedema should be identified early, monitored and taught of self-care. Patients and carers should be offered information about lymphoedema, its prevention and management. 122, level III
General approaches to minimise the risk of developing lymphoedema are:\textsuperscript{122, level III}
- good care of skin and nails
- maintain optimal body weight
- eat a balanced diet
- avoid injury to area at risk
- avoid tight underwear, clothing, watches and jewellery
- avoid exposure to extreme temperatures
- use high factor sunscreen and insect repellent
- wear prophylactic compression garments, if prescribed
- perform exercise/movement and limb elevation
- wear comfortable, supportive shoes

Diagnosis criteria for lymphoedema have been identified as:\textsuperscript{17}
- increase in limb circumference
- changes in sensation: fullness, tightness, heaviness, throbbing and shooting pains
- reduce in limb flexibility
- palpable changes to the skin or subcutaneous tissue such as fibrosclerosis that may be pitting or non-pitting

Severity of disease is classified into stages as described by the International Society of Lymphology (refer to Appendix 10).

The evidence for treatment of lymphoedema is poor with no clear conclusions on the efficacy of benzo-pyrones,\textsuperscript{123, level I} and weak evidence supporting usage of multi-layer bandaging over hosiery.\textsuperscript{124, level I}

A consensus report outlines the approach to managing lymphoedema:\textsuperscript{122, level III}
- exercise and movement
- swelling reduction and maintenance by compression garments, multi-layer bandaging, exercise and lymphatic massage
- skin care
- pain management
- psychosocial management

Lymphoedema is best managed by specialist lymphoedema practitioners, usually physiotherapists, who are available at some healthcare settings.\textsuperscript{122, level III}

f. **Malignant Ureteric Obstruction**
Obstructive renal failure occurs due to locally advanced cervical cancer. Patients may be asymptomatic, but may complain of pelvic pain or uraemic symptoms due to renal failure.\textsuperscript{125, level II-2}
Treatment options are:  
- retrograde stenting  
- percutaneous nephrostomy (PN) with/without antegrade stenting  
- conservative management

Endoscopic placement of ureteral stents are often considered as the first-line option for relieving ureteral obstruction. If retrograde stenting is unsuccessful, alternative options would be PN and/or antegrade stenting.

PN can be of clinical benefit for patients with performance status 1 - 3 (refer to Appendix 7). High levels of morbidity (44%) have been reported with median OS of 8.9 weeks after the surgery. Half of the patients experience clinical benefit, as measured by recovery from uraemic symptoms, lumbar pain or generally poor renal function.

Malignant ureteric obstruction indicates poor prognosis. Palliative surgical interventions may be inappropriate if patients are terminally ill with irreversible renal failure. The high morbidity associated with palliative diversion may impair QOL. Treatment decisions should be based on clear discussions of options, prognosis, cost, complications and QOL, between patients and a multidisciplinary team.

g. Malignant Bowel Obstruction

The incidence of malignant bowel obstruction (MBO) in gynaecologic cancer appears to be commonest in ovarian cancer (54.5%), followed by cervical or endometrial cancer (27.3%). Patients often have high morbidity due to symptoms such as abdominal pain, colic, nausea and vomiting, as well as from treatment such as surgery, nasogastric tube insertion and intravenous therapy.

Management of MBO should be tailored to the underlying aetiology, stage of disease and goals of care. Treatment options may include surgical management with corrective or non-corrective laparotomies, venting tubes and stent insertions, or medical management such as symptomatic relief with opioids, anti-emetics, anti-spasmodics, anti-secretory drugs and steroids.

In patients with advanced gynaecologic cancers who present with MBO, treatment with dexamethasone (6 - 16 mg/day) may resolve bowel obstruction but will not improve survival. A therapeutic trial of four to five days is suggested. Octreotide may be considered in these patients, and will reduce overall nausea, vomiting and nasogastric drainage volume.

There are no clear recommendations for surgery in resolving symptoms of MBO in advanced gynaecologic cancer. Consider medical
management for patients with advanced stage cancer and a shorter time interval between cancer diagnosis and bowel obstructions.\textsuperscript{129}, level III

\textbf{h. End of Life Care}

The final phase of terminal illness can be the most challenging time for the patient, their carers and healthcare providers. Increased clinical vigilance on symptom control, psychosocial and spiritual distress is needed, along with sensitive communication and decision making.\textsuperscript{130, level III} Those closely affected by a death should be offered bereavement, emotional and spiritual support appropriate to their needs and preferences.\textsuperscript{131}

\begin{center}
\begin{tabular}{|l|}
\hline
\textbf{Recommendation 18} \\
\hline
• Patients with advanced cervical cancer should receive palliative care and be referred to a specialised palliative team if necessary. \\
• Low molecular weight heparin should be used for the initial and long-term treatment of venous thromboembolism in cervical cancer, where available. \\
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\end{tabular}
\end{center}
14. PSYCHOSEXUAL CARE AND SOCIAL SUPPORT

In cervical cancer patients, psychological distress is often unrecognised. Therefore, a simple and practical screening tool such as the Distress Thermometer may help to identify underlying issues and make necessary referrals. Refer to Appendix 11 for Distress Thermometer Screening Tool.

Following diagnosis of cervical cancer, women often experience distress in many domains of life such as:\textsuperscript{132, level III}
- emotional (feelings of sadness, down or depressed, anxiety and worry that treatment is beyond control)
- physical (lack of energy and unable to do things they used to do)
- psychological (fears about cancer returning and spreading)
- social (concerns about the worries of close ones)

Locoregional cervical cancer survivors report chronic fatigue after RT. They also experience lower pleasure and QOL, higher discomfort and higher levels of depression and anxiety, than those without chronic fatigue.\textsuperscript{133, level III}

Sexual dysfunction is a common problem after cervical cancer treatment. Many factors contribute to this including the loss of psychologic self-esteem, distorted physical appearance, or deterioration of organ function. Although most women resume sexual activity after radical hysterectomy, 41\% of them have decreased sexual satisfaction while 36\% have increased dyspareunia.\textsuperscript{134, level III} Physical intimacy and body image are highly vulnerable to disruption after cancer diagnosis and treatment.\textsuperscript{135, level I}

Patients should be advised that their physical and psychological functions are likely to deteriorate in the initial post-treatment period, but they should anticipate improvement thereafter.\textsuperscript{17}

**Recommendation 19**
- Psychosocial assessment should be performed in all cervical cancer patients.
- Psychoeducation regarding potential deterioration and treatment outcome-related to the cervical cancer should be offered after diagnosis.
- The sexual health of women diagnosed with cervical cancer should be assessed pre-treatment and monitored during the treatment.

Women with cervical cancer require help for various needs. These needs should be identified early so that resources and intervention can be put in place as promptly as possible.\textsuperscript{132, level III} Many women
report an increase need for emotional and physical closeness with their spouse.\textsuperscript{135, level I}

Some women show concern about their sexual health, which include:\textsuperscript{134, level III}
- potential harm from sexual activity on health
- appropriate time to resume sexual activity
- ways to relieve pelvic pain or increase sexual desire
- self-awareness of being feminine

Several psychological interventions for patients with cervical cancers have been evaluated. Couple-focused intervention has stronger effects compared to women-focused intervention. It improves most sexual aspects including adjustment, drive, satisfaction and intimacy. It also has strong effects for the male partners’ sexual drive and satisfaction.\textsuperscript{135, level I}

Other psychological interventions with some positive effects:
- Cognitive Behavioural Therapy on changing unhelpful thoughts or behaviour and coping skills.\textsuperscript{136, level I}
- counselling on emotional distress including anxiety and depression.\textsuperscript{136 level I}
- relaxation and guided imagery on emotional distress and body discomfort.\textsuperscript{137, level III}
- information-based intervention on disease, treatment options and coping strategies.\textsuperscript{136, level III}
- social support (including family, friend and special person) is associated with higher quality of life and lower rate of depression and anxiety.\textsuperscript{137, level III}

- In cervical cancer:
  - couple-focused intervention is preferred over women-focused intervention to improve sexual health.
  - Cognitive Behavioural Therapy can reduce psychosocial distress.
  - social support improves quality of life and reduces negative mood symptoms, including depression and anxiety.
15. IMPLEMENTING THE GUIDELINES

It is important to standardise the management of cervical cancer at all healthcare levels in Malaysia by using an evidence-based CPG. This aims to prevent long-term morbidity and mortality.

a. Facilitating and Limiting Factors
Existing facilitators for application of the recommendations in the CPG include:

- dissemination of CPG
  - availability and dissemination of CPG to healthcare providers (hardcopies and softcopies)
  - conferences and updates on management of cervical cancer
- implementation of CPG
  - public awareness via Cervical Cancer Awareness
  - accessibility to relevant multidisciplinary teams
  - active involvement of government and non-governmental organisations

Existing barriers for application of the recommendations of the CPG are:

- limited awareness in managing and referrals among primary care providers
- variation of practice and treatment at different levels of care
- limited facilities and human resources
- inadequate training at all levels of healthcare providers
- lack of networking between public and private health-care providers

b. Potential Resource Implications
To implement the CPG, there must be a strong commitment to:

- distribute the CPG widespread to healthcare providers
- strengthen training on cervical cancer management for healthcare providers
- establish a cervical cancer registry in Malaysia
- develop of multidisciplinary teams in secondary and tertiary care levels
To assist in the implementation of the CPG, the following is proposed as clinical audit indicator for quality management:

\[
\text{Percentage of patients with cervical cancer receiving definitive treatment within six weeks of histological diagnosis in a year} = \frac{\text{Number of patients with cervical cancer receiving definitive treatment within six weeks}}{\text{Number of patients with cervical cancer with histological diagnosis in the same period}} \times 100\%
\]

\[
\text{Percentage of patients with cervical cancer completing CCRT within eight weeks in a year} = \frac{\text{Number of patients with cervical cancer completing CCRT within eight weeks}}{\text{Number of patients with cervical cancer receiving CCRT in the same period}} \times 100\%
\]

Implementation strategies will be developed following the approval of the CPG by MoH. These include a Quick Reference and a Training Module.
References

2. WHO Classification of tumours of the female reproductive organs 20142014.


101. Covens A. Differences in morbidity of radical hysterectomy between gynecological oncologists.pdf.
106. Mx of Cancer pain malaysia.pdf.


EXAMPLE OF SEARCH STRATEGY

The following MeSH terms or free text terms were used either singly or in combination, search was limit to English, human and last 10 years:-

1. Uterine Cervical Neoplasms/
2. (uterine cervical adj1 (cancer$ or neoplasm$ or carcinoma or tumo?r$ or malignanc$)).tw.
3. (uterine cervix adj1 (cancer$ or neoplasm$ or carcinoma or tumo?r$ or malignanc$)).tw.
4. 1 or 2 or 3
5. Recurrence/
6. recurr*.tw.
7. recrudescen*.tw.
8. relaps*.tw.
9. 5 or 6 or 7 or 8
10. 4 and 9
11. Antineoplastic Agents/
12. ((drug* or agent*) adj1 anticancer).tw.
13. (chemotherapeutic anticancer adj1 (agent* or drug*)).tw.
14. (cancer chemotherapy adj1 (drug* or agent*)).tw.
15. chemotherapy drugs cancer.tw.
16. chemotherapy agent cancer.tw.
17. chemotherapy agents cancer.tw.
18. chemotherapy drug cancer.tw.
19. (antitumo?r adj1 (drug* or agent*)).tw.
20. antineoplastic*.tw.
21. (antineoplastic adj1 (agent* or drug*)).tw.
22. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23. 10 and 22
24. limit 23 to (english and humans and last 10 years)
Appendix 2

CLINICAL QUESTIONS

1. Epidemiology/Risk factors/Clinical presentation
   1.1 What is the epidemiology of cervical cancer?
   1.2 What are the risk factors of cervical cancer?
   1.3 What are clinical presentations of cervical cancer?

2. Referral
   2.1 When should the patients with cervical cancer be referred to gynae-oncology/oncology team?

3. Diagnosis and Staging
   3.1 What are the important histopathological parameters in the diagnosis of cervical cancer?
   3.2 What is the role of frozen section assessment in cervical cancer?
   3.3 Is clinical staging effective in the assessment of cervical cancer?
   3.4 What is the role of imaging in the assessment of cervical cancer?

4. Treatment
   4.1 Are the following modalities effective and safe in the primary treatment of cervical cancer?
      • Surgery
      • Definitive Chemoradiotherapy/Radiotherapy
   4.2 What are the effective and safe adjuvant therapies in cervical cancer?
      • Surgery
      • Chemotherapy
      • Chemoradiotherapy/Radiotherapy
      • Neoadjuvant Chemotherapy
   4.3 What are the effective and safe management of cervical cancer in the following special circumstances?
      • Pregnancy
      • Tumour arising from cervical stump
      • Cervical cancer diagnosed after hysterectomy for benign gynaecological disorder
      • Neuroendocrine cancers
   4.4 What are follow-up plans for patients with cervical cancer?
   4.5 What are the effective and safe modalities for diagnosis, assessment and treatment of recurrent cervical cancer?
      • Surgery
      • Chemotherapy
      • Salvage radiotherapy/Chemoradiotherapy
4.6 What are the effective and safe management of complications following treatment of cervical cancer?
4.7 What are the effective and safe palliative care following treatment of cervical cancer?
4.8 What are the effective psychosexual care and social support for patients and carers?
# Appendix 3

## WHO histological classification of tumours of the uterine cervix

### Epithelial tumours

**Squamous tumours and precursors**
- Squamous cell carcinoma, not otherwise specified 8070/3
- Keratinizing 8071/3
- Non-keratinizing 8072/3
- Basaloid 8083/3
- Verrucous 8051/3
- Warty 8051/3
- Papillary 8052/3
- Lymphoepithelioma-like 8082/3
- Squamotransitional 8120/3
- Early invasive (microinvasive) squamous cell carcinoma 8076/3

**Squamous intraepithelial neoplasia**
- Cervical intraepithelial neoplasia (CIN) 3 / 8077/2
- Squamous cell carcinoma in situ 8070/2

**Benign squamous cell lesions**
- Condyloma acuminatum
- Squamous papilloma 8052/0
- Fibroepithelial polyp

### Glandular tumours and precursors

- Adenocarcinoma 8140/3
  - Mucinous adenocarcinoma 8480/3
  - Endocervical 8482/3
  - Intestinal 8144/3
  - Signet-ring cell 8490/3
  - Minimal deviation 8480/3
  - Villoglandular 8262/3
  - Endometrioid adenocarcinoma 8380/3
  - Clear cell adenocarcinoma 8310/3
  - Serous adenocarcinoma 8441/3
  - Mesonephric adenocarcinoma 9110/3

- Early invasive adenocarcinoma 8140/3
- Adenocarcinoma in situ 8140/2

**Glandular dysplasia**
- Benign glandular lesions
  - Müllerian papilloma
  - Endocervical polyp

**Other epithelial tumours**
- Adenosquamous carcinoma 8560/3
- Glassy cell carcinoma variant 8015/3
- Adenoid cystic carcinoma 8200/3
- Adenoid basal carcinoma 8098/3
- Neuroendocrine tumours
  - Carcinoid 8240/3
  - Atypical carcinoid 8249/3
  - Small cell carcinoma 8041/3
  - Large cell neuroendocrine carcinoma 8013/3
- Undifferentiated carcinoma 8020/3
Mesenchymal tumours and tumour-like conditions

Leiomyosarcoma 8890/3
Endometrioid stromal sarcoma, low grade 8931/3
Undifferentiated endocervical sarcoma 8805/3
Sarcoma botryoides 8910/3
Alveolar soft part sarcoma 9581/3
Angiosarcoma 9120/3
Malignant peripheral nerve sheath tumour 9540/3
Leiomyoma 8890/0
Genital rhabdomyoma 8905/0
Postoperative spindle cell nodule

Mixed epithelial and mesenchymal tumours

Carcinosarcoma (malignant müllerian mixed tumour; metaplastic carcinoma) 8980/3
Adenosarcoma 8933/3
Wilms tumour 8960/3
Adenofibroma 9013/0
Adenomyoma 8932/0

Melanocytic tumours

Malignant melanoma 8720/3
Blue naevus 8780/0

Miscellaneous tumours

Tumours of germ cell type
Yolk sac tumour 9071/3
Dermoid cyst 9084/0
Mature cystic teratoma 9080/0

Lymphoid and haematopoetic tumours

Malignant lymphoma (specify type)
Leukaemia (specify type)

Secondary tumours

1. Morphology code of the International Classification of Diseases for Oncology (ICD-O) (921) and the Systematized Nomenclature of Medicine (http://snomed.org). Behaviour is coded /0 for benign tumours, /2 for in situ carcinomas and grade 3 intraepithelial neoplasia, /3 for malignant tumours, and /1 for borderline or uncertain behaviour.
2. Intraepithelial neoplasia does not have a generic code in ICD-O. ICD-O codes are only available for lesions categorized as squamous intraepithelial neoplasia grade 3 (e.g. cervical intraepithelial neoplasia 3) = 8077/2, squamous cell carcinoma in situ = 8070/2, glandular intraepithelial neoplasia grade 3 = 8148/2 and adenocarcinoma in situ = 8140/2.

### REPORTING PROFORMA FOR CERVICAL CANCER IN EXCISIONAL CERVICAL BIOPSIES / HYSTERECTOMY SPECIMENS

#### MACROSCOPIC

Specimen labelled as:

- Type of procedure/specimen:
  - LLETZ
  - CONE Biopsy
  - Trachelectomy
  - Radical Trachelectomy
  - Simple Hysterectomy
  - Radical Hysterectomy

Orientation markers:

Specimen gross/external appearance:

#### SPECIMEN MEASUREMENTS

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of specimen</td>
<td>mm</td>
</tr>
<tr>
<td>Length of canal</td>
<td>mm</td>
</tr>
<tr>
<td>Ectocervix diameter (3-9 o'clock)</td>
<td>mm</td>
</tr>
<tr>
<td>Ectocervix diameter (6-12 o'clock)</td>
<td>mm</td>
</tr>
</tbody>
</table>

#### UTERINE DIMENSION

<table>
<thead>
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<th>Units</th>
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<tbody>
<tr>
<td>Cervix-fundus</td>
<td>mm</td>
</tr>
<tr>
<td>Anterior-posterior</td>
<td>mm</td>
</tr>
<tr>
<td>Distance between cornu</td>
<td>mm</td>
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</table>

#### ADNEXA

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<tr>
<th>Measurement</th>
<th>Present</th>
<th>Absent</th>
<th>Normal</th>
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<tbody>
<tr>
<td>Right ovary dimension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right fallopian tube</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ovary dimension:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left fallopian tube:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Vaginal cuff dimension:

\[ \text{length} \times \text{width/circumferential} \times \text{thickness} \]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parametrium included</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paracervix included</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macroscopically visible tumour</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Number of visible tumour(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumour location (position)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Anterior</th>
<th>Posterior</th>
<th>Right</th>
<th>Left</th>
<th>Circumferential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross appearance of tumour</td>
<td>Exophytic</td>
<td>Endophytic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>-----------</td>
<td>------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumour size:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mm (vertical/length) x mm horizontal/width</td>
<td></td>
<td>mm depth/thickness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thickness of cervical wall at</td>
<td>mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>deepest invasion site</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macrotscopic involvement of vagina</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macrotoscopic involvement of parametrium</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macrotoscopic involvement of</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>paracervix</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymph nodes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MICROSCOPIC</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Tumour</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple tumours</td>
<td>Present</td>
<td>Absent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histological tumour type</td>
<td>Squamous carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adenocarcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adenosquamous carcinoma</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Neuroendocrine carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (Specify)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma subtype</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histological tumour grade</td>
<td>Well / Grade 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate / Grade 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Poor / Grade 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not assessable / Not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum depth of invasion</td>
<td>mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical wall thickness</td>
<td>mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum thickness of uninvolved cervical stroma</td>
<td>mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulceration</td>
<td>Present</td>
<td>Absent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Horizontal measurement</td>
<td>mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transverse measurement</td>
<td>mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Management of Cervical Cancer (Second Edition)**

### Tumour Size:

\[ \text{Tumour size: } \underline{\text{mm}} \text{ (vertical/length) } \underline{\text{mm}} \text{ (horizontal/width) } \underline{\text{mm}} \text{ (depth/thickness)} \]

### Thickness of Cervical Wall

- **At Deepest Invasion Site**

### Macroscopic Involvement

- **Vagina Cuff**
- **Parametrium**
- **Paracervix**

### Associated Conditions

- **AIS**
- **CIN**
- **SMILE**

### Margin Status

- **Invasive Tumour**
- **Endocervical Margin**
- **Ectocervical Margin**
- **Radial Margin**

### Non-Invasive Component

- **Margin Status of AIS**
- **Margin Status of CIN**
- **Margin Status of SMILE**

### Ancillary Test
Revised FIGO Cervical Cancer Staging 2009

Cancer of the cervix uteri

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>The carcinoma is strictly confined to the cervix (extension to the uterus corpus should be disregarded).</td>
</tr>
<tr>
<td>IA</td>
<td>Invasive cancer identified only microscopically (all gross lesion even with superficial invasion are Stage IB cancers).</td>
</tr>
<tr>
<td></td>
<td>Invasion is limited to measured stromal invasion with a maximum depth of 5 mm and no wider than 7 mm.</td>
</tr>
<tr>
<td></td>
<td>IA1: Measured invasion of stroma ≤ 3 mm in depth and ≤ 7 mm width</td>
</tr>
<tr>
<td></td>
<td>IA2: Measured invasion of stroma &gt; 3 mm and &lt; 5 mm in depth and ≤ 7 mm width</td>
</tr>
<tr>
<td>IB</td>
<td>Clinical lesions confined to the cervix, or preclinical lesions greater than stage IA</td>
</tr>
<tr>
<td></td>
<td>IB1: Clinical lesions no greater than 4 cm in size</td>
</tr>
<tr>
<td></td>
<td>IB2: Clinical lesions &gt; 4 cm in size</td>
</tr>
<tr>
<td>II</td>
<td>The carcinoma extends beyond the uterus, but has not extended onto the pelvic wall or to the lower third of vagina.</td>
</tr>
<tr>
<td>IIA</td>
<td>Involvement up to the upper 2/3. No obvious parametrial involvement</td>
</tr>
<tr>
<td></td>
<td>IIA1: Clinically visible lesion ≤ 4 cm</td>
</tr>
<tr>
<td></td>
<td>IIA2: Clinically visible lesion &gt; 4 cm</td>
</tr>
<tr>
<td>IIB</td>
<td>Obvious parametrial involvement but not onto the pelvic sidewall</td>
</tr>
<tr>
<td>III</td>
<td>The carcinoma has extended onto the pelvic sidewall. On rectal examination, there is no cancer-free space between the tumor and pelvic sidewall. The tumor involves the lower third of the vagina. All cases of hydronephrosis or non-functioning kidney should be included unless they are known to be due to other causes.</td>
</tr>
<tr>
<td>IIIA</td>
<td>Involvement of the lower vagina but no extension onto the pelvic sidewall</td>
</tr>
<tr>
<td>IIIB</td>
<td>Extension onto the pelvic sidewall, or hydronephrosis/non-functioning kidney</td>
</tr>
<tr>
<td>IV</td>
<td>The carcinoma has extended beyond the true pelvis or has clinically involved the mucosa of the bladder and/or the rectum.</td>
</tr>
<tr>
<td>IVA</td>
<td>Spread to adjacent pelvic organs</td>
</tr>
<tr>
<td>IVB</td>
<td>Spread to distant organs</td>
</tr>
</tbody>
</table>

---

Adapted from FIGO Committee on Gynecology Oncology (2)

The depth of invasion should not be more than 5mm taken from the base of epithelium, either surface or glandular, from which it originates. Vascular space invasion should not alter the staging.

## Modified Delgado’s Prognostic Risk Scoring System

### Relative risk of recurrence after radical hysterectomy for cervical cancer

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Depth of tumor penetration (mm)</strong></td>
<td></td>
</tr>
<tr>
<td><em>Superficial</em></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.0</td>
</tr>
<tr>
<td>4</td>
<td>3.0</td>
</tr>
<tr>
<td>5</td>
<td>7.2</td>
</tr>
<tr>
<td>6</td>
<td>14.0</td>
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<td>7</td>
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<td>8</td>
<td>26.0</td>
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<td>10</td>
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<tr>
<td><em>Middle</em></td>
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<td>5</td>
<td>20.0</td>
</tr>
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<td>6</td>
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<td>28.0</td>
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<tr>
<td>12</td>
<td>32.0</td>
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<td>14</td>
<td>36.0</td>
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<tr>
<td><em>Deep</em></td>
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</tr>
<tr>
<td>7</td>
<td>28.0</td>
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<td>8</td>
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<tr>
<td>18</td>
<td>49.0</td>
</tr>
<tr>
<td>19</td>
<td>54.0</td>
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<td><strong>Clinical tumor size (cm)</strong></td>
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<tr>
<td><em>Occult tumor</em></td>
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</tr>
<tr>
<td>1</td>
<td>1.6</td>
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<tr>
<td>2</td>
<td>1.9</td>
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<td>2.4</td>
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<td>2.9</td>
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<td>6</td>
<td>4.4</td>
</tr>
<tr>
<td>8</td>
<td>6.6</td>
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<tr>
<td><strong>Capillary/lymphatic space involvement</strong></td>
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</tr>
<tr>
<td><em>No</em></td>
<td>1.0</td>
</tr>
<tr>
<td><em>Yes</em></td>
<td>1.7</td>
</tr>
</tbody>
</table>

The GOG score is calculated by multiplying the relative-risk for depth x tumour size x capillary/lymphatic space involvement.

**Source:** Greater Metropolitan Clinical Task force. Gynaecological Cancer Guidelines 2009. Sydney: NSW Department of Health; 2009
## ECOG PERFORMANCE STATUS

<table>
<thead>
<tr>
<th>Grade</th>
<th>ECOG</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all pre-disease performance without restriction</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, such as light house work and office work</td>
</tr>
</tbody>
</table>
| 2     | • Ambulatory and capable of all self-care but unable to carry out any work activities  
        • Up and about more than 50% of waking hours |
| 3     | Capable of only limited self-care, confined to bed or chair more than 50% of waking hours |
| 4     | • Completely disabled  
        • Cannot carry on any self-care  
        • Totally confined to bed or chair |
| 5     | Dead |

## Systemic Therapy Cancer Protocol

### CERVICAL CANCER CHEMOTHERAPY

#### Concurrent chemo-radiotherapy

**Single agent cisplatin**

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Cycle length (days) = 21</th>
<th>Anti-emetic = 4</th>
<th>Dose (mg/m²)</th>
<th>Route</th>
<th>Infusion Time</th>
<th>Days</th>
</tr>
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<tbody>
<tr>
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<td>30 - 40</td>
<td>IV</td>
<td>1 hour</td>
<td>1</td>
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*N.B. In practice, 50 mg total dose per week of cisplatin could be used*

#### Palliative chemotherapy

**Single agent cisplatin**

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<thead>
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<th>Anti-emetic = 4</th>
<th>Dose (mg/m²)</th>
<th>Route</th>
<th>Infusion Time</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>50</td>
<td>IV</td>
<td>1 hour</td>
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**Cisplatin-5FU**

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<th>Anti-emetic = 4</th>
<th>Dose (mg/m²)</th>
<th>Route</th>
<th>Infusion Time</th>
<th>Days</th>
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<tr>
<td>Cisplatin</td>
<td>50 - 75</td>
<td>IV</td>
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<tr>
<td>Fluorouracil</td>
<td>750 - 1000</td>
<td>IV</td>
<td>24 hour</td>
<td>1 - 5</td>
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**Cisplatin-MTX**

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<th>Route</th>
<th>Infusion Time</th>
<th>Days</th>
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<tbody>
<tr>
<td>Cisplatin</td>
<td>50</td>
<td>IV</td>
<td>1 hour</td>
<td>1</td>
<td></td>
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<tr>
<td>Methotrexate</td>
<td>100</td>
<td>IV</td>
<td>Bolus</td>
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**Paclitaxel-cisplatin**

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<th>Days</th>
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<tr>
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*Carboplatin can be used if the patient is unable to tolerate cisplatin*

## Appendix 9

### Pain Management and Palliative Care Service Providers

#### PAIN CLINICS

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Tel No.</th>
<th>Tel No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Selayang, Selangor</td>
<td>603-61203233</td>
<td><a href="http://www.hselayang.moh.gov.my">http://www.hselayang.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Melaka, Melaka</td>
<td>606-2822344</td>
<td><a href="http://www.hmelaka.moh.gov.my">http://www.hmelaka.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Sultan Ismail, Johor</td>
<td>607-3565000</td>
<td><a href="http://wwwhsi.moh.gov.my">http://wwwhsi.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Raja Permaisuri Bainun, Perak</td>
<td>605-2533333</td>
<td><a href="http://www.hipoh.moh.gov.my">http://www.hipoh.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Raja Perempuan Zainab II, Kelantan</td>
<td>609-7452000</td>
<td><a href="http://www.hrpz2.moh.gov.my">http://www.hrpz2.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Tengku Ampuan Rahimah, Selangor</td>
<td>603-3375000</td>
<td><a href="http://www.htar.moh.gov.my">http://www.htar.moh.gov.my</a></td>
</tr>
<tr>
<td>Pusat Perubatan Univeristi Malaya, Kuala Lumpur</td>
<td>603-79494422</td>
<td><a href="http://www.ummc.edu.my">http://www.ummc.edu.my</a></td>
</tr>
<tr>
<td>Pusat Perubatan Universiti Kebangsaan Malaysia, Kuala Lumpur</td>
<td>603-91455555</td>
<td><a href="http://www.ppukm.ukm.my">http://www.ppukm.ukm.my</a></td>
</tr>
<tr>
<td>Hospital Universiti Sains Malaysia, Kelantan</td>
<td>609-7663000</td>
<td><a href="http://www.hselayang.moh.gov.my">http://www.hselayang.moh.gov.my</a></td>
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#### PALLIATIVE CARE UNITS

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<thead>
<tr>
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<th>URL</th>
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</thead>
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<tr>
<td>Hospital Selayang, Selangor</td>
<td>603-61203233</td>
<td><a href="http://www.hselayang.moh.gov.my">http://www.hselayang.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Bukit Mertajam, Kedah</td>
<td>604-5383333</td>
<td><a href="http://www.hospbm.moh.gov.my">http://www.hospbm.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Duchess of Kent, Sabah</td>
<td>6089-212111</td>
<td><a href="http://www.hdok.moh.gov.my">http://www.hdok.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Melaka, Melaka</td>
<td>606-2707653</td>
<td><a href="http://www.hmelaka.moh.gov.my">http://www.hmelaka.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Pulau Pinang, Pulau Pinang</td>
<td>604-2293333</td>
<td><a href="http://www.hpp.moh.gov.my">http://www.hpp.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Queen Elizabeth, Sabah</td>
<td>6088-206258</td>
<td><a href="http://www.qeh.moh.gov.my">http://www.qeh.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Raja Permaisuri Bainun, Perak</td>
<td>605-5222245</td>
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</tr>
<tr>
<td>Hospital Sultanah Aminah, Johor</td>
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<tr>
<td>Hospital Sultanah Bahiyah, Kedah</td>
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<tr>
<td>Hospital Sultanah Nur Zahirah, Terengganu</td>
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<td><a href="http://www.hsnzkt.moh.gov.my">http://www.hsnzkt.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Tawau, Sabah</td>
<td>6089-773533</td>
<td><a href="http://www.htwu.moh.gov.my">http://www.htwu.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Tengku Ampuan Afzan, Pahang</td>
<td>609-5133333</td>
<td><a href="http://www.htaa.moh.gov.my">http://www.htaa.moh.gov.my</a></td>
</tr>
<tr>
<td>Hospital Tuanku Ja’afar, Negeri Sembilan</td>
<td>606-7623333</td>
<td><a href="http://www.htjs.moh.gov.my">http://www.htjs.moh.gov.my</a></td>
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<tr>
<td>Hospital Umum Sarawak, Sarawak</td>
<td>6082-208069</td>
<td><a href="http://www.hus.moh.gov.my">http://www.hus.moh.gov.my</a></td>
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<td><a href="http://www.ummc.edu.my">http://www.ummc.edu.my</a></td>
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<td>603-91455555</td>
<td><a href="http://www.ppukm.ukm.my">http://www.ppukm.ukm.my</a></td>
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</table>

### Malaysian Hospice Directory

<table>
<thead>
<tr>
<th>Hospice Name</th>
<th>Address</th>
<th>Contact Person</th>
<th>Email/Website</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PERSATUAN HOSPICE ARK</strong></td>
<td>No. 2, 2A, 2B Jalan Sutera Merah 3, Taman Sutera, 81200, Johor Bahru, Johor</td>
<td>Ms Alice</td>
<td><a href="mailto:hospice_ark@hotmail.com">hospice_ark@hotmail.com</a></td>
</tr>
<tr>
<td><strong>PALLIATIVE CARE ASSOC. OF JOHOR BAHRU</strong></td>
<td>44, Jalan Tun Abdul Razak, Susur 1, 80000 Johor Bahru</td>
<td>Ms Nancy Yee</td>
<td><a href="mailto:nancyyee.pcajb@gmail.com">nancyyee.pcajb@gmail.com</a></td>
</tr>
<tr>
<td><strong>PERSATUAN HOSPIS KEDAH</strong></td>
<td>d/a Pej Kesihatan Kota Setar, Lebuhraya Darul Aman, Jalan Bakar Bata, 05100 Alor Setar, Kedah</td>
<td>Ms Alice</td>
<td>hospiskedah.blogspot.com</td>
</tr>
<tr>
<td><strong>PERSATUAN HOSPIS NEGERI KELANTAN</strong></td>
<td>Hospital Raja Perempuan Zainab II, 15586 Kota Bharu, Kelantan</td>
<td>Ms Nancy Yee</td>
<td><a href="mailto:drmisairi@klt.moh.gov.my">drmisairi@klt.moh.gov.my</a></td>
</tr>
<tr>
<td><strong>HOSPICE MALACCA</strong></td>
<td>621-F, Jalan Delima 12, Tmn Bkt Melaka, Bukit Beruang, 75450 Melaka</td>
<td>S/N Chong Fei Gin</td>
<td>hospismalacca.org</td>
</tr>
<tr>
<td><strong>PERTUBUHAN HOSPICE NEGERI SEMBILAN</strong></td>
<td>No. 41, Off Jalan Rasah, 70300 Seremban, Negeri Sembilan</td>
<td>Ms Kala</td>
<td><a href="mailto:hospicens2012@yahoo.com">hospicens2012@yahoo.com</a></td>
</tr>
<tr>
<td><strong>PERSATUAN HOSPIS PAHANG</strong></td>
<td>A4614 Lorong Alor Akar 19, 25250 Kuantan, Pahang</td>
<td>S/N Chong Fei Gin</td>
<td><a href="http://www.pahanghospice.org">www.pahanghospice.org</a></td>
</tr>
<tr>
<td><strong>PERSATUAN HOSPIS TERENGGANU</strong></td>
<td>Klinik Bedah Pakar, Kompleks Rawatan Harian, Hospital Sultanah Nur Zahirah, 20400 KT, Terengganu</td>
<td>Ms Chitra Alagan</td>
<td><a href="mailto:dmona31765@gmail.com">dmona31765@gmail.com</a></td>
</tr>
<tr>
<td><strong>NCSM PENANG</strong></td>
<td>Rumah Hospis Pulau Pinang, 250A, Jalan Air Itam, 10460 Penang</td>
<td>Ms Askin Abd Kadir</td>
<td><a href="mailto:penanghospicesociety@gmail.com">penanghospicesociety@gmail.com</a></td>
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<tr>
<td><strong>PENANG HOSPICE SOCIETY</strong></td>
<td>c/o Rumah Hospis Pulau Pinang, 250A, Jalan Air Itam, 10460 Penang</td>
<td>Ms Chitra Alagan</td>
<td><a href="http://www.penanghospice.org.my">www.penanghospice.org.my</a></td>
</tr>
<tr>
<td><strong>PURE LOTUS HOSPICE OF COMPASSION</strong></td>
<td>73, Jalan Utama, 10460 Penang</td>
<td>Ms Leong Lai Peng</td>
<td><a href="mailto:iveraliew@hotmail.com">iveraliew@hotmail.com</a></td>
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<tr>
<td><strong>CHARIS HOSPICE</strong></td>
<td>15, Cangkat Median, Jalan 12, 11700 Penang</td>
<td>Ms Leong Lai Peng</td>
<td><a href="http://www.charishospice.org.my">www.charishospice.org.my</a></td>
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<tr>
<td><strong>PERAK PALLIATIVE CARE SOCIETY</strong></td>
<td>54, Jalan Sultan Ahmad Shah, 31400 Ipoh, Perak</td>
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<td><a href="http://www.ppcps.org.my">www.ppcps.org.my</a></td>
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<tr>
<td><strong>TAIPEING PALLIATIVE SOCIETY</strong></td>
<td>48, Jalan Lim Sam Kip, 34000 Taiping, Perak</td>
<td>Ms Veronica Liew</td>
<td><a href="mailto:veraliew@hotmail.com">veraliew@hotmail.com</a></td>
</tr>
<tr>
<td>HOME CARE HOSPICE PROGRAMME, SABAH</td>
<td>PALLIATIVE CARE ASSOCIATION OF KOTA KINABALU, SABAH</td>
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<tr>
<td>c/o Sabah Cancer Society</td>
<td>PWD 7396 &amp; 7397 Taman Rose, Off Jin Penampang, 88300 Kota Kinabalu, Sabah</td>
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</tr>
<tr>
<td>No.15, Lorong Tupai 3, Teck Guan Villa, Jalan Penampang, 88300 Kota Kinabalu, Sabah</td>
<td>Tel: 088-231 505 Fax: 088-231 506</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tel: 088-222 315 Fax: 088-210 377</td>
<td>Contact Person: Ms Grace Chong</td>
<td></td>
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</tr>
<tr>
<td>E-mail: <a href="mailto:sabahcancersociety@yahoo.com">sabahcancersociety@yahoo.com</a></td>
<td>E-mail: <a href="mailto:pcakk@yahoo.com">pcakk@yahoo.com</a></td>
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<th>THE HOSPICE ASSOCIATION OF SANDAKAN</th>
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<tbody>
<tr>
<td>TB 14748 Mile 3.5, Jalan James Power, Off Jalan Kuhara, 91008 Tawau, Sabah</td>
<td>P.P.M No 324, Elopura</td>
</tr>
<tr>
<td>Tel: 089-711 515 Fax: 089-711 514</td>
<td>90000 Sandakan, Sabah</td>
</tr>
<tr>
<td>Contact Person: Mr Victor Raja</td>
<td>Tel: 089-632 219 Fax: 089-632 269</td>
</tr>
<tr>
<td>E-mail: <a href="mailto:hospistwu@gmail.com">hospistwu@gmail.com</a>, <a href="mailto:vicraja@gmail.com">vicraja@gmail.com</a></td>
<td>Contact Person: Ms Michelle Chong</td>
</tr>
<tr>
<td></td>
<td>E-mail: <a href="mailto:hcs98@hospicesdk.com">hcs98@hospicesdk.com</a></td>
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<th>PERSATUAN HOSPICE ST. FRANCIS XAVIER</th>
<th>KUCHING HOSPICE CANCER CARE</th>
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<tbody>
<tr>
<td>St. Francis Xavier’s Mission, Peti Surat 92, 89007 Keningau, Sabah</td>
<td>287, Lot2643 Central Park Commercial Centre, Jalan Rock, 93250 Kuching, Sarawak</td>
</tr>
<tr>
<td>Tel/Fax: 087-339 114</td>
<td>Tel: 082-337 689 Fax: 082-488 444</td>
</tr>
<tr>
<td>E-mail: <a href="mailto:liewlucy@hotmail.com">liewlucy@hotmail.com</a></td>
<td>E-mail: <a href="mailto:cancercare.kuching@gmail.com">cancercare.kuching@gmail.com</a></td>
</tr>
<tr>
<td>Contact Person: Shelly</td>
<td>Contact Person: Ms Molly</td>
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<th>SARAWAK HOSPICE SOCIETY</th>
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<tbody>
<tr>
<td>c/o Radiotherapy Unit, Sarawak General Hospital, 93586 Kuching, Sarawak</td>
<td>Daycare centre, Hospital Miri, Jalan Cahaya, 98000 Miri, Sarawak</td>
</tr>
<tr>
<td>Tel: 082-276 575 Fax: 082-414 443</td>
<td>Tel: 085-420033 Fax: 085-416514</td>
</tr>
<tr>
<td>E-mail: <a href="mailto:tangtiengswee@gmail.com">tangtiengswee@gmail.com</a></td>
<td>Contact Person: Dr. Frances Wilkinson</td>
</tr>
<tr>
<td><a href="http://www.sarawakhospicesociety.org">www.sarawakhospicesociety.org</a></td>
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<tr>
<th>HOSPICE KLANG</th>
<th>ASSUNTA PALLIATIVE CARE CENTRE</th>
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<tbody>
<tr>
<td>82 Jalan Sri Sarawak 4, Tmn Sri Andalas, 41200 Klang, Selangor</td>
<td>Assunta Hospital, No. 83 Jalan Templer 46990 Petaling Jaya, Selangor</td>
</tr>
<tr>
<td>Tel: 03-3324 2125 Fax: 03-3324 3125</td>
<td>Tel / Fax: 03-7954 3389</td>
</tr>
<tr>
<td>Contact Person: Ms Tan Guat Hong</td>
<td>Email: <a href="mailto:aspacc.assuntahospital@gmail.com">aspacc.assuntahospital@gmail.com</a></td>
</tr>
<tr>
<td>E-mail: <a href="mailto:hpstklang@gmail.com">hpstklang@gmail.com</a></td>
<td><a href="http://www.aspacc.org">www.aspacc.org</a></td>
</tr>
<tr>
<td><a href="http://www.hospiceklang.org">www.hospiceklang.org</a></td>
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<tr>
<th>KASHI HOSPICE CARE SOCIETY</th>
<th>HOSPI MALAYSIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>No 7, Jalan 14/29 aka Jalan Dato Abdul Aziz, 46100 Petaling Jaya, Selangor</td>
<td>2 Jalan 4/96, off Jalan Seku, Tmn Sri Bahtera, Jalan Cheras, 56100 Kuala Lumpur</td>
</tr>
<tr>
<td>Tel: 03-7960 7424</td>
<td>Tel : 03-9133 3936</td>
</tr>
<tr>
<td>E-mail: <a href="mailto:admin@kashi.foundation.org">admin@kashi.foundation.org</a></td>
<td>Fax: 03-9133 3941</td>
</tr>
<tr>
<td><a href="http://www.kashi.foundation.org">www.kashi.foundation.org</a></td>
<td>Email: <a href="mailto:info@hospismalaysia.org">info@hospismalaysia.org</a></td>
</tr>
<tr>
<td>Fax 03-7956 6442</td>
<td><a href="http://www.hospismalaysia.org">www.hospismalaysia.org</a></td>
</tr>
</tbody>
</table>

Source: Malaysian Hospice Council (available at http://www.malaysianhospicecouncil.org)
## International Society of Lymphology (ISL) Lymphoedema Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISL Stage 0</td>
<td>A subclinical state where swelling is not evident despite impaired lymph transport. This stage may exist for months or years before oedema becomes evident</td>
</tr>
<tr>
<td>ISL Stage I</td>
<td>This represents early onset of the condition where there is accumulation of tissue fluids that subsides with limb elevation. The oedema may be pitting at this stage</td>
</tr>
<tr>
<td>ISL Stage II</td>
<td>Limb elevation alone rarely reduces the swelling and pitting is manifest</td>
</tr>
<tr>
<td>ISL late Stage II</td>
<td>There may or may not be pitting as tissue fibrosis is more evident</td>
</tr>
<tr>
<td>ISL Stage III</td>
<td>The tissue is hard (fibrotic) and pitting is absent. Skin changes as such thickening, hyperpigmentation, increased skin folds, fat deposits and warty overgrowth develop</td>
</tr>
</tbody>
</table>

Appendix 11

Distress Thermometer Screening Tool

SCREENING TOOLS FOR MEASURING DISTRESS

Instructions: First please circle the number (0-10) that best describes how much distress you have been experiencing in the past week including today.

Second, please indicate if any of the following has been a problem for you in the past week including today. Be sure to check YES or NO for each.

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child care</td>
<td></td>
</tr>
<tr>
<td>Housing</td>
<td></td>
</tr>
<tr>
<td>Insurance/financial</td>
<td></td>
</tr>
<tr>
<td>Transportation</td>
<td></td>
</tr>
<tr>
<td>Work/school</td>
<td></td>
</tr>
<tr>
<td>Practical Problems</td>
<td></td>
</tr>
<tr>
<td>Child care</td>
<td></td>
</tr>
<tr>
<td>Housing</td>
<td></td>
</tr>
<tr>
<td>Insurance/financial</td>
<td></td>
</tr>
<tr>
<td>Transportation</td>
<td></td>
</tr>
<tr>
<td>Work/school</td>
<td></td>
</tr>
<tr>
<td>Family Problems</td>
<td></td>
</tr>
<tr>
<td>Dealing with children</td>
<td></td>
</tr>
<tr>
<td>Dealing with partner</td>
<td></td>
</tr>
<tr>
<td>Ability to have children</td>
<td></td>
</tr>
<tr>
<td>Physical Problems</td>
<td></td>
</tr>
<tr>
<td>Appearance</td>
<td></td>
</tr>
<tr>
<td>Bathing/dressing</td>
<td></td>
</tr>
<tr>
<td>Breathing</td>
<td></td>
</tr>
<tr>
<td>Changes in urination</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
</tr>
<tr>
<td>Eating</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
</tr>
<tr>
<td>Feeling Swollen</td>
<td></td>
</tr>
<tr>
<td>Fevers</td>
<td></td>
</tr>
<tr>
<td>Getting around</td>
<td></td>
</tr>
<tr>
<td>Indigestion</td>
<td></td>
</tr>
<tr>
<td>Memory/concentration</td>
<td></td>
</tr>
<tr>
<td>Mouth sores</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
</tr>
<tr>
<td>Nose dry/congested</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td></td>
</tr>
<tr>
<td>Sexual</td>
<td></td>
</tr>
<tr>
<td>Skin dry/itchy</td>
<td></td>
</tr>
<tr>
<td>Sleep</td>
<td></td>
</tr>
<tr>
<td>Tingling in hands/feet</td>
<td></td>
</tr>
</tbody>
</table>

Other Problems: ________________________________

## Medication List

<table>
<thead>
<tr>
<th>Chemotherapy Drug</th>
<th>Common side effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cisplatin</strong></td>
<td>• Peripheral neuropathy • Nausea, vomiting • Myelosuppression • Nephrotoxicity • Ototoxicity</td>
<td>• Adequate hydration and urinary output at least 24 hours after administration • Obtain baseline renal function, then monitor renal function (SCr, CrCl) at every cycle. Observe for cumulative renal toxicity. • Recommend to perform baseline audiography and prior to each subsequent dose • Observe for anaphylactic-like reactions during infusion • Monitor renal function (SCr, CrCl) • Observe for anaphylactic-like reactions during infusion</td>
</tr>
<tr>
<td><strong>Carboplatin</strong></td>
<td>• Electrolyte imbalance (hyponatremia, hypomagnesaemia, hypocalcaemia, hypokalaemia) • Nausea, vomiting • Myelosuppression</td>
<td>• Monitor renal function (SCr, CrCl) • Observe for anaphylactic-like reactions during infusion</td>
</tr>
<tr>
<td><strong>Paclitaxel</strong></td>
<td>• Alopecia • Nausea, vomiting • Myelosuppression • Peripheral neuropathy • Arthalgia/myalgia</td>
<td>• Monitor for hypersensitivity reaction during infusion</td>
</tr>
<tr>
<td><strong>Gemcitabine</strong></td>
<td>• Fever • Nausea, vomiting • Myelosuppression • Increased hepatic transaminases</td>
<td>• Monitor liver function</td>
</tr>
<tr>
<td><strong>Topotecan</strong></td>
<td>• Myelosuppression • Nausea, vomiting</td>
<td>• Monitor for interstitial lung disease</td>
</tr>
<tr>
<td><strong>5-Fluorouracil</strong></td>
<td>• Diarrhoea</td>
<td>• Monitor for hand-foot syndrome</td>
</tr>
<tr>
<td><strong>Mitomycin-C</strong></td>
<td>• Myelosuppression</td>
<td>• Observe for extravasation (vesicant) • Monitor for haemolytic-uremic syndrome</td>
</tr>
</tbody>
</table>

- To monitor FBC and serum electrolytes prior to every cycle of chemotherapy.

**Source:**
## LIST OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC</td>
<td>adenocarcinoma</td>
</tr>
<tr>
<td>AGC-H</td>
<td>Atypical glandular cells - hyperplasia</td>
</tr>
<tr>
<td>AGC-US</td>
<td>Atypical glandular cells of undetermined significance</td>
</tr>
<tr>
<td>ASCUS</td>
<td>Atypical Squamous Cells of Undetermined Significance</td>
</tr>
<tr>
<td>CCRT</td>
<td>concurrent chemoradiotherapy</td>
</tr>
<tr>
<td>CI</td>
<td>confidence interval</td>
</tr>
<tr>
<td>CIN</td>
<td>cervical intraepithelial neoplasia</td>
</tr>
<tr>
<td>cm</td>
<td>centimeter</td>
</tr>
<tr>
<td>CPG(s)</td>
<td>clinical practice guidelines</td>
</tr>
<tr>
<td>CT</td>
<td>computed tomography</td>
</tr>
<tr>
<td>DVT</td>
<td>deep vein thrombosis</td>
</tr>
<tr>
<td>DFS</td>
<td>disease free survival</td>
</tr>
<tr>
<td>DG</td>
<td>Development Group</td>
</tr>
<tr>
<td>ECOG</td>
<td>Eastern Cooperative Oncology Group</td>
</tr>
<tr>
<td>EUA</td>
<td>examination under anaesthesia</td>
</tr>
<tr>
<td>EBRT</td>
<td>external beam radiotherapy</td>
</tr>
<tr>
<td>FDG-PET</td>
<td>Fluorodeoxyglucose positron emission tomography</td>
</tr>
<tr>
<td>FIGO</td>
<td>The International Federation of Gynecology and Obstetrics</td>
</tr>
<tr>
<td>Gy</td>
<td>Gray</td>
</tr>
<tr>
<td>HPV</td>
<td>Human Papilloma Virus</td>
</tr>
<tr>
<td>HR</td>
<td>hazard risk</td>
</tr>
<tr>
<td>HRT</td>
<td>hormone replacement therapy</td>
</tr>
<tr>
<td>HSIL</td>
<td>high-grade squamous intraepithelial lesion</td>
</tr>
<tr>
<td>HTA</td>
<td>health technology assessment</td>
</tr>
<tr>
<td>INR</td>
<td>International Normalised Ratio</td>
</tr>
<tr>
<td>ICBT</td>
<td>intracavitary brachytherapy</td>
</tr>
<tr>
<td>LLETZ</td>
<td>large loop excision of transformation zone</td>
</tr>
<tr>
<td>LACC</td>
<td>locally advanced cervical cancer</td>
</tr>
<tr>
<td>LACC</td>
<td>locally advanced cervical cancer</td>
</tr>
<tr>
<td>LSIL</td>
<td>low grade squamous intraepithelial lesion</td>
</tr>
<tr>
<td>LMWH</td>
<td>low molecular weight heparin</td>
</tr>
<tr>
<td>LNmM</td>
<td>lymph node micrometastasis</td>
</tr>
<tr>
<td>LVSI</td>
<td>lymph vascular space involvement</td>
</tr>
<tr>
<td>MoH</td>
<td>Ministry of Health</td>
</tr>
<tr>
<td>MRI</td>
<td>magnetic resonance imaging</td>
</tr>
<tr>
<td>MBO</td>
<td>malignant bowel obstruction</td>
</tr>
<tr>
<td>NPV</td>
<td>negative predictive value</td>
</tr>
<tr>
<td>NAC</td>
<td>neoadjuvant chemotherapy</td>
</tr>
<tr>
<td>NEC</td>
<td>neuroendocrine cancers</td>
</tr>
<tr>
<td>OR</td>
<td>odds ratio</td>
</tr>
<tr>
<td>OS</td>
<td>overall survival</td>
</tr>
<tr>
<td>PAN</td>
<td>para-aortic lymph nodes</td>
</tr>
<tr>
<td>PN</td>
<td>percutaneous nephrostomy</td>
</tr>
<tr>
<td>PET</td>
<td>positron emission tomography</td>
</tr>
<tr>
<td>PET-CT</td>
<td>positron emission tomography-computed tomography</td>
</tr>
<tr>
<td>PLND</td>
<td>pelvic lymph nodes dissection</td>
</tr>
<tr>
<td>PPV</td>
<td>positive predictive value</td>
</tr>
<tr>
<td>PCB</td>
<td>postcoital bleeding</td>
</tr>
<tr>
<td>PFS</td>
<td>progression-free survival</td>
</tr>
</tbody>
</table>
ACKNOWLEDGEMENT

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- Technical Advisory Committee for CPG for their valuable input and feedback
- All those who have contributed directly or indirectly to the development of the CPG

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