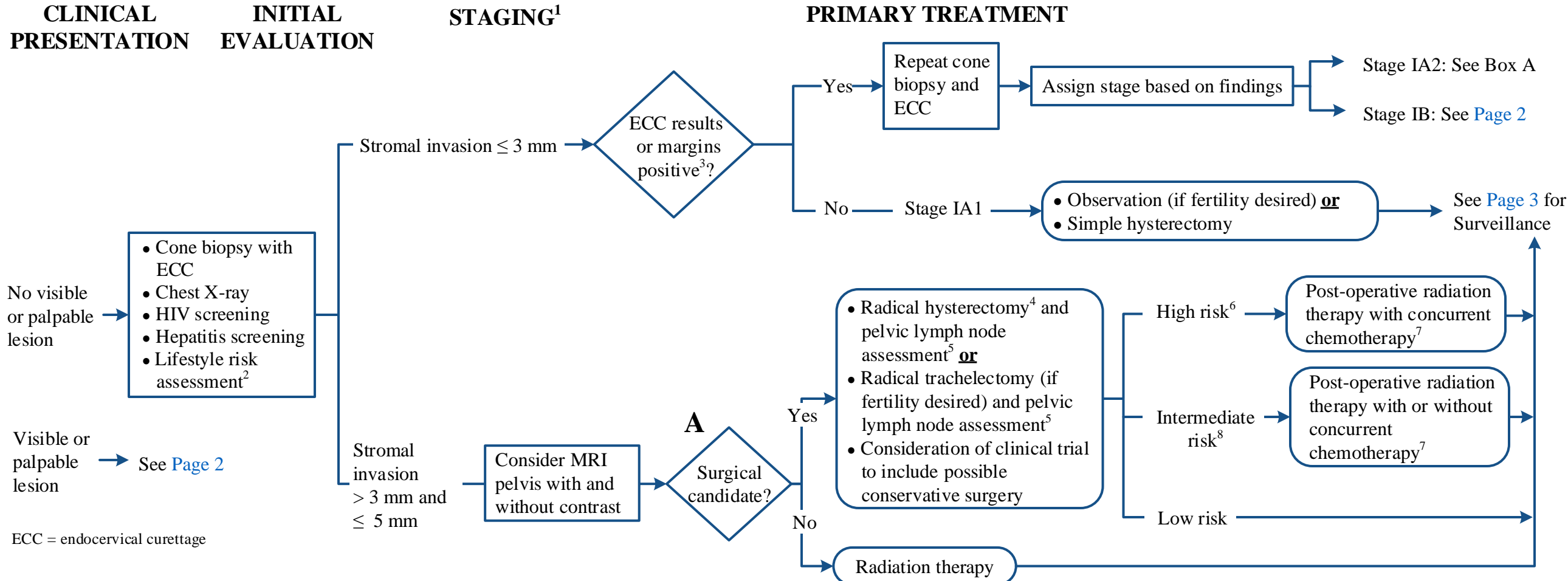


Invasive Cervical Cancer: Squamous Cell, Adenocarcinoma, Adenosquamous

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

Note: If available, clinical trials should be considered as preferred treatment options for eligible patients (www.mdanderson.org/gynoncctrials). Other co-morbidities are taken into consideration prior to treatment selection. All patients with invasive cervical cancer should be referred to a Gynecologic Oncologist.

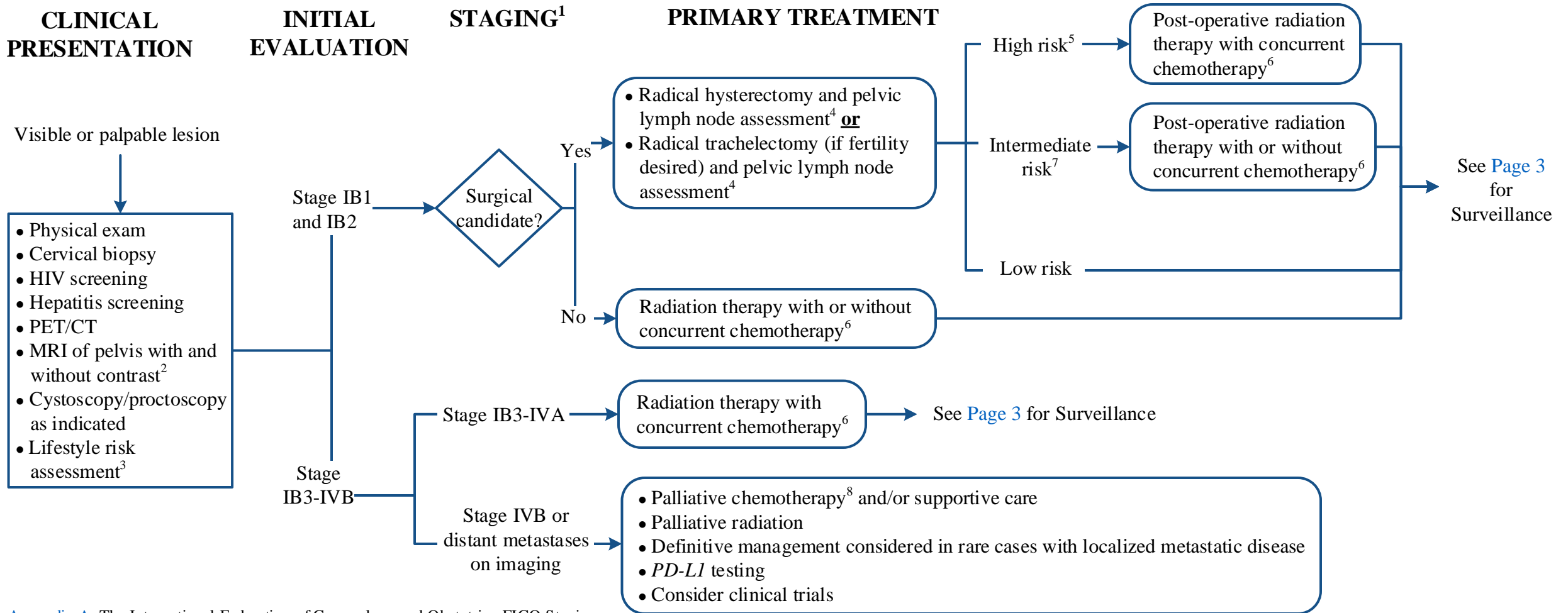


¹ See Appendix A: The International Federation of Gynecology and Obstetrics (FIGO) Staging
² See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
³ Positive margins includes dysplasia
⁴ All procedures should be done open; minimally invasive surgery is no longer acceptable for radical hysterectomy or trachelectomy
⁵ Lymphatic mapping with sentinel lymph node biopsy and/or lymph node dissection
⁶ High risk factors: positive nodes, positive margins, and/or parametrial involvement
⁷ Weekly cisplatin
⁸ Intermediate risk factors: stromal invasion, capillary lymphatic space involvement and/or large clinical tumor diameter. See Appendix B: Gynecological Oncology Group (GOG) Sedlis Criteria

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Note: If available, clinical trials should be considered as preferred treatment options for eligible patients (www.mdanderson.org/gynoncctrials). Other co-morbidities are taken into consideration prior to treatment selection. All patients with invasive cervical cancer should be referred to a Gynecologic Oncologist.



¹ See [Appendix A](#): The International Federation of Gynecology and Obstetrics FIGO Staging

² MRI should be completed on all patients receiving definitive radiation and all patients undergoing trachelectomy

³ See [Physical Activity](#), [Nutrition](#), and [Tobacco Cessation](#) algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

⁴ Lymphatic mapping with sentinel lymph node biopsy and/or lymph node dissection

⁵ High risk factors: positive nodes, positive margins, and/or parametrial involvement

⁶ Weekly cisplatin

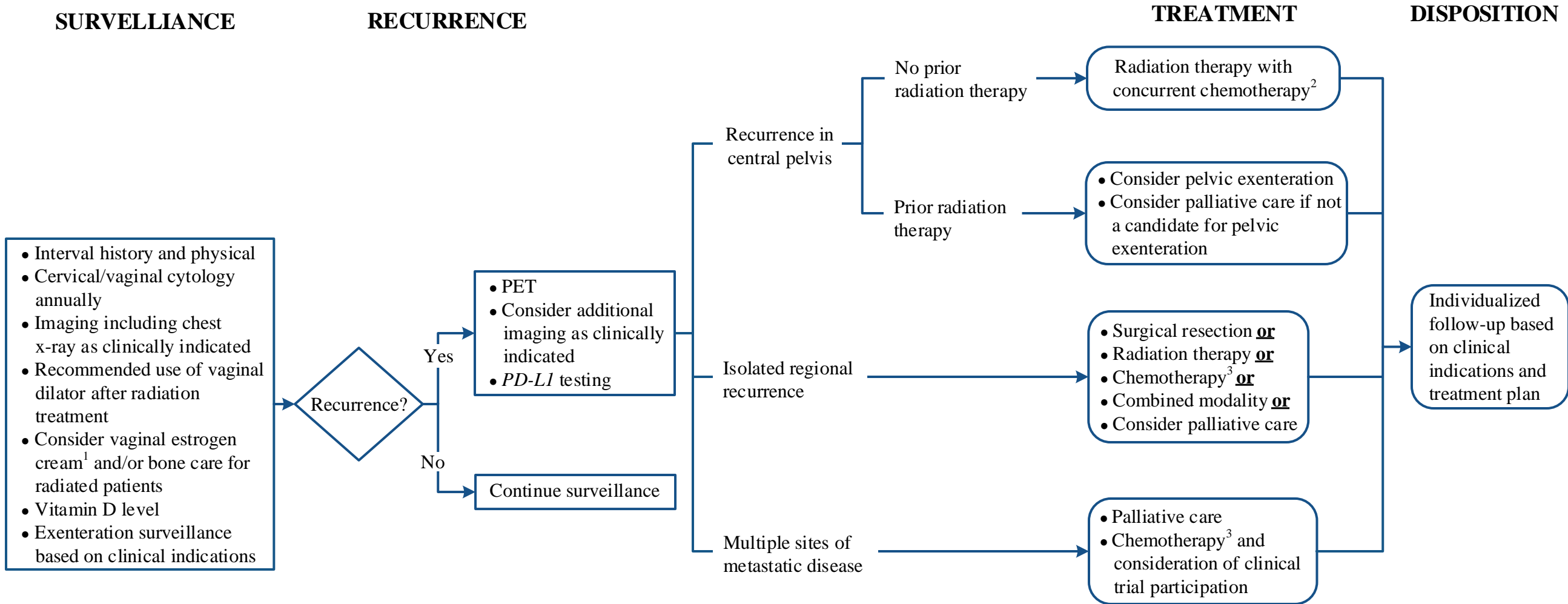
⁷ Intermediate risk factors: stromal invasion, capillary lymphatic space involvement and/or large clinical tumor diameter. See [Appendix B](#): Gynecology Oncology Group (GOG) Sedlis Criteria.

⁸ Taxol cisplatin and avastin

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Note: If available, clinical trials should be considered as preferred treatment options for eligible patients (www.mdanderson.org/gynoncctrials). Other co-morbidities are taken into consideration prior to treatment selection. All patients with invasive cervical cancer should be referred to a Gynecologic Oncologist.



¹ Long term use of vaginal estrogen requires progesterone

² Weekly cisplatin

³ See [Appendix C](#): Recurrent or Metastatic Chemotherapy Regimens

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APPENDIX A: The International Federation of Gynecology and Obstetrics (FIGO) Staging

Stage	Description
I	<p>Carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded)</p> <p>IA: Invasive carcinoma which can be diagnosed only by microscopy, with deepest invasion < 5 mm¹</p> <p>IA1: Measured stromal invasion < 3 mm in depth</p> <p>IA2: Measured stromal invasion ≥ 3 mm and < 5 mm in depth</p> <p>IB: Invasive carcinoma with measured deepest invasion ≥ 5 mm (greater than stage IA), lesion limited to the cervix uteri²</p> <p>IB1: Invasive carcinoma ≥ 5 mm depth of stromal invasion and < 2 cm in greatest dimension</p> <p>IB2: Invasive carcinoma ≥ 2 cm and < 4 cm in greatest dimension</p> <p>IB3: Invasive carcinoma ≥ 4 cm in greatest dimension</p>
II	<p>Carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina</p> <p>IIA: Involvement limited to the upper two-thirds of the vagina without parametrial invasion</p> <p>IIA1: Invasive carcinoma < 4 cm in greatest dimension</p> <p>IIA2: Invasive carcinoma ≥ 4 cm in greatest dimension</p> <p>IIB: With parametrial involvement but not up to the pelvic wall</p>
III	<p>The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or paraaortic lymph nodes³</p> <p>IIIA: Tumor involves lower third of the vagina, with no extension to the pelvic wall</p> <p>IIIB: Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause)</p> <p>IIIC: Involvement of pelvic and/or paraaortic lymph nodes, irrespective of tumor size and extent (with r and p notations)³</p> <p>IIIC1: Pelvic lymph node metastasis only</p> <p>IIIC2: Paraaortic lymph node metastasis</p>
IV	<p>IVA: Spread or growth to adjacent organs</p> <p>IVB: Spread to distant organs</p>

¹ Imaging and pathology can be used, when available, to supplement clinical findings with respect to tumor size and extent, in all cases

² The involvement of vascular/lymphatic spaces does not change the staging. The lateral extent of the lesion is no longer considered.

³ Notation of r (imaging) and p (pathology) to indicate the findings that are used to allocate the cases to stage III: If imaging indicates pelvic node metastasis, r should be added to the stage allocation e.g., stage IIICr. If staging confirmed with pathological findings, p should be added to the stage allocation e.g., IIICp. The type of imaging modality or pathology technique should be documented. When in doubt, the lower staging should be assigned.

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APPENDIX B: Gynecology Oncology Group (GOG) Sedlis Criteria

LVSI	Stromal Invasion	Tumor Size
Positive	Deep third	Any
Positive	Middle third	≥ 2 cm
Positive	Superficial third	≥ 5 cm
Negative	Deep or middle third	≥ 4 cm

LVSI = lymphovascular space invasion

APPENDIX C: Recurrent or Metastatic Chemotherapy Regimens

First Line	Second Line
<ul style="list-style-type: none"> • Paclitaxel, cisplatin and bevacizumab • Paclitaxel and cisplatin • Paclitaxel and carboplatin • Topotecan and cisplatin • Cisplatin and gemcitabine • Cisplatin • Carboplatin • Paclitaxel • Paclitaxel (protein-bound) 	<ul style="list-style-type: none"> • Bevacizumab • Docetaxel • Fluorouracil • Gemcitabine • Ifosfamide • Irinotecan • Mitomycin • Topotecan • Pemetrexed • Vinorelbine • Pembrolizumab

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SUGGESTED READINGS

- Barakat, R. R. (2013). Principles and practice of gynecologic oncology: Edited by Richard R. Barakat. (6th ed.). Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins.
- Huang, B., Cai, J., Xu, X., Guo, S., & Wang, Z. (2016). High-Grade Tumor Budding Stratifies Early-Stage Cervical Cancer with Recurrence Risk. *PLOS One*, 11(11) doi:10.1371/journal.pone.0166311
- Jung, P. S., Kim, D. Y., Lee, S. W., Park, J. Y., Suh, D. S., Kim, J. H., ... Nam, J. H. (2015). Clinical role of adjuvant chemotherapy after radical hysterectomy for FIGO stage IB-IIA cervical cancer: Comparison with adjuvant RT/CCRT using inverse-probability-of-treatment weighting. *PLOS One*, 10(7) doi:10.1371/journal.pone.0132298
- Melamed, A., Margul, D. J., Chen, L., Keating, N. L., Del Carmen, M. G., Yang, J., ... Wright, J. D. (2018). Survival after minimally invasive radical hysterectomy for early-stage cervical cancer. *New England Journal of Medicine*, 379(20), 1905-1914. doi:10.1056/NEJMoa1804923
- National Comprehensive Cancer Network. *Cervical Cancer* (NCCN Guideline Version 5.2019). Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf
- Pecorelli, S. (2009). Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. *International Journal of Gynecology & Obstetrics*, 105(2), 103-104. doi:10.1016/j.ijgo.2009.02.012
- Ramirez, P. T., Frumovitz, M., Pareja, R., Lopez, A., Vieira, M., Ribeiro, R., ... Isla, D. (2018). Minimally invasive versus abdominal radical hysterectomy for cervical cancer. *New England Journal of Medicine*, 379(20), 1895-1904. doi:10.1056/NEJMoa1806395
- Salvo, G., Ramirez, P. T., Levenback, C. F., Munsell, M. F., Euscher, E. D., Soliman, P. T., & Frumovitz, M. (2017). Sensitivity and negative predictive value for sentinel lymph node biopsy in women with early-stage cervical cancer. *Gynecologic Oncology*, 145(1), 96-101. doi:10.1016/j.ygyno.2017.02.005
- Sedlis, A., Bundy, B. N., Rotman, M. Z., Lentz, S. S., Muderspach, L. I., & Zaino, R. J. (1999). A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: A Gynecologic Oncology Group Study. *Gynecologic Oncology*, 73(2), 177-183. doi:10.1006/gy.1999.5387
- Tewari, K. S., Sill, M. W., Long III, H. J., Penson, R. T., Huang, H., Ramondetta, L. M., ... Michael, H. E. (2014). Improved survival with bevacizumab in advanced cervical cancer. *New England Journal of Medicine*, 370(8), 734-743. doi:10.1056/NEJMoa1309748

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